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Increase in sensitization to oil of turpentine: recent data from a Multicenter Study on 45,005 patients from the German-Austrian Information Network of Departments of Dermatology (IVDK)

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Contact allergy to oil of turpentine was reported to have become rare. However, the evaluation of standardized data of 45,005 patients tested 1992–1997 in 30 Dermatological Centers associated with the German-Austrian Information Network of Departments of Dermatology (IVDK) showed an increase in positive patch test reactions to turpentine from 0.5% during the years 1992–1995, up to 1.7% in 1996 and 3.1% in 1997. In particular, 17,347 patients tested in 1996–1997 were evaluated in detail by comparing 431 individuals with positive patch test reactions with the rest of the group found negative to turpentine. Using the so-called MOAHLFA index, the following characteristics were shown. Turpentine allergy (a) was found to be significantly less frequent in **m**en and in patients with **o**ccupational dermatitis, (b) showed no difference in its association with **a**topic dermatitis, (c) patients with turpentine allergy had significantly less symptoms of the **h**ands, more symptoms of the **l**egs or in the **f**ace and (d) were significantly more often **a**ged over 60 years. Also, patients sensitized to turpentine had increased rates of additional sensitizations. The definite reason for the increase in turpentine sensitization in the population tested here is not clear. Therefore, a detailed exposure analysis is necessary; the new increase in turpentine allergies may be due to popular topical remedies or household chemicals.

Key words: turpentine; terpene; MOAHLFA index; tea tree oil; patch test; contact dermatitis; allergy; surveillance system; sentinel health event © Munksgaard, 2000.

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Oil of turpentine, often simply called turpentine, is an ingredient in many liniments, cold remedies, and veterinary medications. Other commonly used products traditionally containing turpentine include varnishes, sealing wax, paint thinners, dry cleaning materials, shoe and floor polishes, printers' ink, and various adhesives, including adhesive tape. The skin of citrus fruits contains oleoresins related to turpentine (1).

Turpentine is obtained from pine trees and represents the volatile oily fraction derived from the distillation of turpentine, while the non-volatile residue is known as colophony. Oil of turpentine is a mixture of terpenes; pinenes, limonene, △-3-carene and other components (Table 1). The concentration of each fraction varies with the botanical species and the geographical source, for example, in turpentine originating from Indonesia, Sweden, Finland or Russia the proportion of △-3-carene is higher than in turpentine originating from Portugal or Spain (1–3).

Turpentine is both an irritant and a sensitizer. Old, oxidized turpentine is more irritating and sensitizing than is the freshly made product. When turpentine is allowed to stand, especially with exposure to light, oxidation results in the formation of formic acid and aldehydes, which may be irritating to the skin. Oxidation products of turpentine may cause allergic sensitization and cross-react with the oils in orange peels and other essential oils (1, 4). The major contact allergen of turpentine was identified as △-3-carene hydroperoxide, an oxidation product of △-3-carene, especially in oils originating from Finland and Sweden (1, 5). How-

Table 1. Compostion of different turpentines used for patch testing

Components	Turpentine 10% pet. GDR	Turpentine 10% pet. Hermal[a)]
alpha-pinene	50%	72%
carenes	17%	<0.1%
beta-pinene	6%	15%
camphene	–	1%
dipentene (limonene)	0.5%	5%
caryophyllene	?	2%
myrcene	?	1%
longifolene	?	1%
unidentified components	26.5%	3%
peroxide degree	<5	30

[a)] Information provided by the producer.

ever, patients specifically reacting to other allergens, i.e., to oxidation products of limonene, α- and β-pinene, have been described (6–10).

We report here a significant increase in sensitization to oil of turpentine found during the years 1996–1997 in patients registered by the German-Austrian Information Network of Departments of Dermatology (IVDK).

Patients, Materials and Methods

In the years 1992–1997, data on patch test reactions to turpentine were collected from 30 dermatological centers in Germany and in Austria that are members of the IVDK* (11). Patch tests were performed in 45,005 patients, using the standard series of the German Contact Dermatitis Research Group (DKG), which includes turpentine 10% in petrolatum (pet.) (Hermal, Reinbek, Germany). According to the producer, the turpentine preparations delivered during the whole time of investigation period originated from Portugal. Moreover, from 1992–1995, parallel patch tests were performed in 1813 patients in 5 dermatological centers (Berlin UMC Charité, Dresden, Erlangen, Göttingen, Halle), using another turpentine oil 10% pet., a product marketed in the former GDR (Table 1). 16 patients (3.7%) out of those testing positive to turpentine during the years 1996–1997 (n=431) were tested in a non-standardized manner with their own tea tree oil preparations at different concentrations (0.1–100%) and in different vehicles (aqua dest., olive oil). Patches were removed after 1 day in 11 centers and after 2 days in 19 centers and reading was carried out according to the guidelines of the German Contact Dermatitis Research Group (DKG) (12). For the data analysis, reactions were grouped as follows:

–	no reaction;
?	faint erythema or follicular reaction, not clear if of allergic or irritant origin;
+	allergic reaction with erythema, infiltration, few papulovesicles;
++	allergic reaction with strong erythema, infiltration, papulovesicles;
+++	allergic reaction with strong erythema, infiltration, aggregated papulovesicles with confluation, bullous reaction or spreading of reaction to the surrounding skin;
irr	irritant reaction of different character.

Only readings at day (D) 3 were considered. Sensitization rates to allergens of the standard series were calculated for the total study population. Standardization of data was done following the recommendation of PAFS (population adjusted frequency of sensitization) (13), standardization of age on the basis of two age groups (</⩾ 40 years), standardization of sex on the standard distribution of 35% men and 65% women. Statistical analysis was performed using the SAS system (SAS Institue, Cary, NC) on a mainframe computer of the Department of Medical Informatics of the University of Göttingen.

In all patients tested throughout the years 1992–1997, indications for patch testing and the following demographic items were considered in detail: sex (**m**ale/female), suspected **o**ccupational dermatitis, **a**topic dermatitis, **h**and dermatitis, **l**eg dermatitis, **f**ace dermatitis, **a**ge (i. e. MOAHLFA index) (11). In patients with sensitization to turpentine diagnosed in the years 1996–1997, we additionally assessed the final diagnosis and coexisting factors triggering the clinical symptoms. Moreover, we evaluated the association between sensitization to turpentine and concomitant sensitizations to other contact allergens. Statistical evaluation of items in the disjunct groups of patients was done by using the χ^2-test. A p-value of <0.05 was considered significant.

* The following Departments contributed data to the present study: Aachen (Dickel), Augsburg (Ludwig, Hirschsteiner), Berlin UMC Benjamin Franklin (Tebbe, Treudler), Berlin UMC Charité (Zuberbier), Berlin UMC Rudolf-Virchow (Grabbe, Zuberbier), Dortmund (Frosch, Pilz), Dresden (Richter), Duisburg (Schaller), Erlangen (Peters), Essen (Ockenfels, Hillen), Göttingen (Fuchs, Schnuch), Graz (Aberer, Kränke), Halle (Graber, Lübbe), Hamburg (Kiehn, Vieluf), Heidelberg (Schulze-Dirks, Hartmann), Homburg/Saar (Koch), Halle (Gaber), Jena (Gebhardt), Kiel (Brasch), Lübeck (Kreusch, Grabbe), Mainz (Becker), Marburg (Effendy), München LMU (Rüeff, Przybilla), München Schwabing (Agathos, Breit), München TU (Rakoski, Szliska), Nürnberg (Müller), Osnabrück (Uter), Rostock (Abrokat, Heise), Tübingen (Lischka), Ulm (Gall), Wuppertal (Mainusch).

Table 2. Data on 45,005 patients tested with the DKG* standard series during the years 1992–1997

	No. patients tested	No. patients with positive patch tests to turpentine	% of positive reactions, non standardized for sex and age	% of positive reactions, standardized for sex and age
1992	5922	34	0.6	0.6
1993	6714	35	0.5	0.5
1994	6735	20	0.3	0.3
1995	8287	40	0.5	0.5
1996	8868	157	1.8	1.7
1997	8479	274	3.2	3.1

* DKG – German Contact Dermatitis Research Group.

Results

Between 1992–1997, 45,005 patients were patch tested with the DKG standard series, including turpentine 10% pet. Hermal (Table 2). We found no significant changes concerning the criteria of the MOAHLFA index throughout the years with 34–36% of **m**en, 14–17% **o**ccupational dermatitis, 17–20% **a**topic dermatitis, 27–32% **h**and dermatitis, 7–9% **l**eg dermatitis, 13–16% **f**ace dermatitis and 53–58% **a**ged ⩾40 years.

The indications for patch testing were (a) suspicion of allergic contact dermatitis in 38–40%, (b) exclusion of allergic contact dermatitis in 35%, (c) medical report in 10–12%, (d) others or no data in 15%. No significant changes were documented throughout the years 1992–1997.

From 1992–1995, positive reactions to turpentine 10% pet. Hermal were seen in 0.3–0.6% of these patients, while in 1996, we noticed an increase up to 1.8% (age- and sex-standardized 1.7%), and, in 1997, up to 3.2% (3.1%) (Fig. 1). Most test reactions observed were of minor strength. In 1996 and 1997, 17347 patients were patch tested. 431 had positive (+,++ or +++) and 16640 negative reactions to turpentine. 276 patients showed doubtful (?) or irritant (irr) reactions. For analysis of demographic items, the latter group was excluded, so that differences between patch-test positive and negative patients became more distinct (Table 3). Patients with turpentine sensitization were significantly more women ($p<0.001$), were significantly older (>60 years; $p<0.001$), had significantly less often clinical symptoms on the hands ($p<0.001$) and more often on the legs ($p>0.001$) and on the face ($p=0.025$). In turpentine-positive patients, the allergen causing the patient's skin symptoms was mainly suspected in drugs for external use (28.3% compared to 17.9% of patients being negative to turpentine; $p<0.001$) or in cosmetics (18.8% versus 16.9%; n.s.). There were no significant differences between turpentine-positive and turpentine-negative patients concerning the frequency of atopic dermatitis, hayfever and bronchial asthma. The final diagnosis confirmed an allergic contact dermatitis in 54.3% of the turpentine-positive versus 25.3% of the turpentine-negative patients ($p<0.001$). In 7% of turpentine-positive versus 3.9% ($p=0.001$) of turpentine-negative patients, we registered venous insufficiency as a coexisting factor triggering the clinical symptoms.

The analysis of the patients' occupations gave no hint of any relevant occupational exposure, most of them being pensioners, housewives, students, office clerks or unemployed (59.4% of the turpentine-positives, 40.2% of the turpentine-negatives).

In the years 1992–1997, the ratio of positive reactions (allergens) per patient ranged from 1.3 to 1.5. In the patients not reacting to turpentine in 1996/1997, this ratio was the same, i. e., 1.3 allergens per patient. Turpentine-positive patients, however, showed on average positive reactions to 5.1 allergens per patient. The most striking differences compared to turpentine-negative patients were seen for fragrance mix (45.6% versus 9.4%), balsam of Peru (Myroxylon Pereirae) (28.9% versus 6.8%), colophony (colophonium) (23.1% versus 3.1%), wool wax alcohols (lanolin alcohol) (11.7% versus 3.4%), para-tertiary-butyl-phenol-formaldehyde resin (PTPB-FR; 7.3% versus 0.9%), formaldehyde (7.2% versus 1.6%) and the preserv-

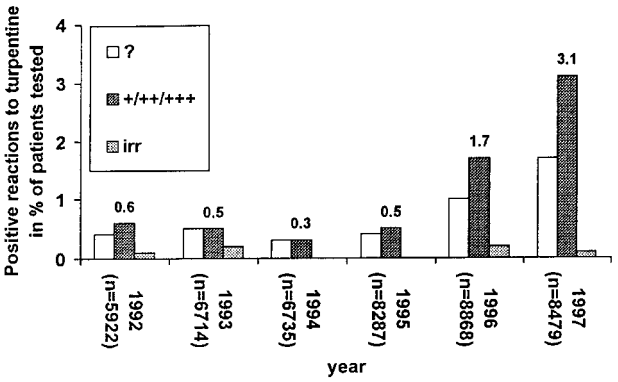

Fig. 1. Increasing sensitization to turpentine in the German and Austrian patients registered by the IVDK; the numbers of patients tested each year (ranging from 5922–8868) are shown.

Table 3. Analysis of the MOAHLFA index in patients with sensitization to turpentine (1996–1997)

Parameters	Turpentine patch test positive	Turpentine patch test negative	Significance
Number	431	16,640	
Male	26.5%	36%	
Female	73.5%	64%	$p<0.001$
Occupational dermatitis	9.5%	14.9%	$p=0.002$
Atopic dermatitis	15.5%	18.6%	n.s.; $p=0.11$
Hand dermatitis	17.6%	28.5%	$p<0.001$
Leg dermatitis	16.2%	8.3%	$p<0.001$
Face dermatitis	19.0%	15.1%	$p=0.025$
Age ⩾40 years	69.6%	56.8%	$p<0.001$
⩾60 years	35.0%	22.1%	$p<0.001$

Table 4. Parallel patch testing with 2 different preparations of turpentine performed in 1813 out of 27,658 of all patients patch tested during the years 1992–1995

		Turpentine used in the former GDR: positive (+/++/+++)	Turpentine used in the former GDR: not positive (−,?,irr)	
turpentine delivered by Hermal	positive (+/++/+++)	0	2	2
	not positive (−,?,irr)	55	1756	1811
		55	1758	1813

atives methylchloroisothiazolinone/methylisothiazolinone (MCI/MI; 9.5% versus 2.3%) and methyldibromoglutaronitrile/phenoxyethanol (DBGN/PE; 7.3% versus 2.2%). Comparison of parallel patch testing with 2 different preparations of turpentine in 1813 patients (29.8% male, 70.2% female) showed that the turpentine 10% pet. GDR gave more positive reactions than the turpentine 10% pet. Hermal (3.1% versus 0.2%). None of the patients who had reacted to either of the turpentines showed a positive reaction to the other preparation (Table 4).

16 (3.7%) out of 431 turpentine-positive patients from the years 1996–1997 were tested with the patients' own tea tree oil preparations. 10 of these patients showed positive patch test reactions at concentrations ranging from 0.1% to 100%, indepent of the vehicle used.

Discussion

In Europe, turpentine was a frequent cause of occupational allergic contact dermatitis until the mid-70s in painters, mechanics, shoe repairers and home decorators (2, 5, 9, 14). During the subsequent decades, however, allergy to turpentine became rather rare, mainly due to increasing use of oils containing only small amounts of △-3-carene. Another reason was the introduction of less allergenic substitutes, especially limonene/dipentene, citrus oils and citrus terpenes as natural solvents that had a pleasant smell (2, 4, 15). A transient reemergence of occupational turpentine allergy was recently described in employees in the pottery industry after a change from Portuguese to Indonesian turpentine with higher amounts of △-3-carene (6). Data of the IVDK between 1992 and 1995 had shown a low prevalence of turpentine allergy in Germany and in Austria, in only about 0.5% of patients tested. Data from other countries were also comparably low (2, 6, 16–19), so that the International Contact Dermatitis Research Group and commercial suppliers removed this allergen from their standard series for patch testing (1, 2).

Surprisingly, the present IVDK data now indicate a dramatic increase in sensitization to turpentine, during the last two years, and preliminary data of the year 1998 confirm this trend by showing a sensitization rate of 4.8% (age- and sex-standardized). This increase was due neither to a change in testing procedure, nor to a change in indications for testing, nor to changes in the population as characterized by the MOAHLFA index. Positive reactions to turpentine were found to be more frequent in females and in patients older than 60 years. These individuals more often had symptoms on the legs or the face, less often on the hands. The higher rate of concomitant allergies goes well with the frequent use of ointments and creams in patients with leg problems, such as dermatitis due to venous insufficiency or leg ulcers. The high rates of positive reactions to fragrances, balsam of Peru and colophony may be explained by group or cross allergies. The overall ratio of positive reactions per patient, however, did not increase during recent years. Therefore, the increase in reactions to turpentine does not represent the result of more selective testing.

The cause of the increased rate of turpentine sensitization shown here for the years 1996–1997 in a large group of individuals tested in Germany and in Austria is not clear. According to our analysis, the increase was due neither to a change in testing procedure, nor to a change of indications for testing, nor to changes in the population as characterized by the MOAHLFA index. Moreover, the producer of the testing substances confirmed that during the whole study period there was no change in the origin (from Portugal) or the composition of the turpentine delivered; it consists of a purified oil of turpentine (according to the German drug codex/DAC from 1986) with a standardized peroxide degree of 30, containing 72–85% of alpha-pinene, 13–22% of beta-pinene and less than 0.5% of △-3-carene. Nevertheless, as oil of turpen-

tine is a heterogeneous mixture of potential allergens, there may be some differences in the sensitizing potency of different supplies, with varying amounts of its allergenic components.

In the present study, the influence of different patch test preparations was shown by comparing the findings with turpentine 10% pet. delivered by Hermal (peroxide degree 30) to those with turpentine 10% pet. used in the former GDR (peroxide degree <5). Patients reacted more often to turpentine 10% pet. used in the former GDR, without any cross-reactions between the two substances. This does not support the hypothesis that higher degrees of turpentine peroxidation go along with a higher sensitization rate. The most striking difference between the 2 turpentine preparations is their content of Δ-3-carene. The increased number of reactions to turpentine 10% pet. used in the former GDR may especially reflect sensitization to this particular allergen. In addition to oxidation products of Δ-3-carene, however, oxidation products of limonene as well as α-terpineol and β-pinene were also found to be important contact allergens by other groups (7, 10, 20). The lack of cross-reactivity between the 2 turpentine preparations used might, however, be due to the high level of unidentified components, possibly representing unknown allergens, in the GDR turpentine.

Another possible reason for the frequent sensitizations to turpentine in our study group is the appearance of cross-reactions due to increasing use of other related sensitizing substances. Many other compounds have been shown to cross-react with turpentine, including ragweed, chrysanthems, peppermint and bergamot oil (20, 21). A major German producer of household products and cosmetics confirmed that, in the comparison with the years 1990–1995, in 1996/1997 there was an increasing use of oil of turpentine (+28%) and of citrus oils/citrus pentenes (+20%). Even though these data are not representative for the whole of industry, they may indicate an increasing exposure to terpenes in private life during recent years.

Moreover, over the last few years, popular literature and medical reports in the media have encouraged the use of tea tree oil for self-treatment of various skin diseases, including acne, candidiasis, furunculosis, dermatitis, gingivitis, hemorrhoids, herpes, insect stings, psoriasis, scabies, sunburn, varicosities, viral exanthema and warts. Tea tree oil is also supposed to relieve symptoms in arthritis, asthma, cough, muscle aches and other diseases so heterogeneous in their clinical picture that its therapeutic effect would seem to be questionable. Tea tree oil preparations are available in form of body lotions, deodorants, lipsticks, massage lotions, ointments, soaps, shampoos, toothpastes, shower gels, etc. Tea tree oil is a mixture of many terpenes. According to international guidelines, it should consist of at least 30% terpinene and not more than 15% cineol. Allergenic components of tea tree oil seem to be limonene, α-terpinene and aromadendrene (23, 24), and these substances may cross-react with turpentine (4). As there does not exist a defined and standardized substance for testing for suspected allergy to tea tree oil, its prevalence is difficult to estimate.

The outstanding increase in sensitization rates to turpentine in our study group within a short period of time must be regarded as a sentinel health event detected by the multicenter-based surveillance system on contact allergies (25). Further exposure analysis appears, therefore, to be neccessary. Meanwhile, we believe that turpentine should be maintained in the patch test standard series. The compound used for testing should be standardized not only for its grade of peroxidation but also for its content of allergenic components.

References

1. Fisher A A (ed). *Contact dermatitis*, 4th edition. Philadelphia: Lea and Febiger. 1994: 629–630.
2. Cronin E. Oil of turpentine – a disappearing allergen. *Contact Dermatitis* 1979: *5:* 308–311.
3. Pirilä V, Kilpiö O, Olkkonen A, Pirilä L, Siltanen E. On the chemical nature of the eczematogens in oil of turpentine. *Dermatologica* 1969: *139:* 183–194.
4. Beckmann B, Ippen H. Teebaum-Öl. *Dermatosen* 1998: *46:* 120–124.
5. Hellerström S, Thyresson N, Blom S G, Widmark G. On the nature of the eczematogenic component of oxidized 3-carene. *J Invest Derm* 1955: *24:* 217–224.
6. Lear J T, Heagerty M, Tan B B, Smith A G, English J S C. Transient re-emergence of oil of turpentine allergy in the pottery industry. *Contact Dermatitis* 1996: *35:* 169–172.
7. Cachao P, Menezes Brandão F, Carmo M, Frazao S, Silva M. Allergy to oil of turpentine in Portugal. *Contact Dermatitis* 1986: *14:* 205–208.
8. Rudzki E et al. Contact allergy to oil of turpentine: a 10-year retrospective view. *Contact Dermatitis* 1991: *24:* 317–318.
9. Hindson T C. Contact allergy to alpha-pinene in boot polish. *Contact Dermatitis Newsletter* 1969: *6:* 115–117.
10. Karlberg A T, Magnusson K, Nilsson U. Air oxidation of d-limonene – the citrus solvent – creates potent allergens. *Contact Dermatitis* 1992: *26:* 332–340.
11. Schnuch A et al. National rates and regional differences in sensitization to allergens of the standard series. Population-adjusted frequencies of sensitization (PAFS in 40.000 patients from a multicenter study) (IVDK). *Contact Dermatitis* 1997: *37:* 200–209.
12. Schnuch A, Martin V. Der Epikutantest. In: Korting HC, Sterry W (eds): *Diagnostische Verfahren in der Dermatologie*. Blackwell, Berlin 1997: 99–116.
13. Schnuch A. PAFS. Population adjusted frequency of sensitization. Influence of sex and age. *Contact Dermatitis* 1996: *34:* 377–382.
14. Klaschka F. Allergy to turpentine: Examination of systemic trigger action. *Contact Dermatitis* 1975: *1:* 319–320.
15. Vente C, Fuchs T. Contact dermatitis due to oil of turpen-

tine in a porcelain painter. *Contact Dermatitis* 1997: *37:* 187.
16. Brun R. Evolution of contact dermatitis factors in a population. Epidemiology 1975–1981. *Dermatologica* 1982; *165:* 24–29.
17. Gollhausen R, Enders F, Przybilla B, Burg G et al. Trends in allergic contact sensitzation. *Contact Dermatitis* 1988: *18:* 147–154.
18. Kiec-Swierczynska M. Occupational allergic contact dermatitis in Lodz: 1990–1994. *Occup Med* 1996: *46:* 205–208.
19. Oleffe J. Epidemiologic, social and economical aspects of occupational dermatoses in Belgium. *Archives Belges de Dermatologie* 1973: *29:* 93–104.
20. Romaguera C, Camarasa J M, Grimalt F, Alomar A. Turpentine: an attempt to explain sensitization to this allergen in Spain. *Contact Dermatitis* 1983: *9:* 384–386.
21. Zacher K D, Ippen H. Contact dermatitis caused by bergamot oil. *Derm Beruf Umwelt* 1984: *32:* 95–97.
22. Dooms-Goossens A, Degreef H, Holvoet C, Maertens M. Turpentine-induced hypersensitivity to peppermint oil. *Contact Dermatitis* 1977: *3:* 304.
23. Knight T E, Hausen B M. Melaleuca oil (tea tree oil) dermatitis. *J Am Acad Dermatol* 1994: *30:* 423–427.
24. Ippen H. Limonene – depentene, citrus oils and citrus terpenes. *Dermatosen* 1998: *46:* 1: 18–25.
25. Uter W, Schnuch A, Geier J, Frosch PJ. Epidemiology of contact dermatitis: the information network of the departments of dermatology (IVDK) in Germany – a surveillance system on contact allergies. *Eur J Dermatol* 1998: *8:* 36–40.

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