

RESEARCH PAPER

Allergy to tea tree oil: Retrospective review of 41 cases with positive patch tests over 4.5 years

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SUMMARY

Tea tree oil use is increasing, with considerable interest in it being a 'natural' antimicrobial. It is found in many commercially available skin and hair care products in Australia. We retrospectively reviewed our patch test data at the Skin and Cancer Foundation Victoria over a 4.5-year period and identified 41 cases of positive reactions to oxidized tea tree oil of 2320 people patch-tested, giving a prevalence of 1.8%. The tea tree oil reaction was deemed relevant to the presenting dermatitis in 17 of 41 (41%) patients. Of those with positive reactions, 27 of 41 (66%) recalled prior use of tea tree oil and eight of 41 (20%) specified prior application of neat (100%) tea tree oil. Tea tree oil allergic contact dermatitis is under-reported in the literature but is sufficiently common in Australia to warrant inclusion of tea tree oil, at a concentration of 10% in petrolatum, in standard patch-test series. Given tea tree oil from freshly opened tea tree oil products elicits no or weak reactions, oxidized tea tree oil should be used for patch testing.

Key words: allergen, antimicrobial, colophonium, concentrated, contact allergy, *Melaleuca alternifolia*, neat, patch test, sensitizer, standard series.

INTRODUCTION

Tea tree oil is the essential oil from the Australian native *Melaleuca alternifolia* or tea tree, indigenous to northern New South Wales and southern Queensland.¹ The oil is extracted by steam distillation from commercially grown trees, with 100 tea tree growers in Australia producing over 500 tonnes of tea tree oil per annum (2004/2005).² Demand for tea tree oil increased by 25% in 2003/2004 and 13% in

2004/2005.² The use of tea tree oil is becoming widespread in Europe and North America; however, only a small amount is produced outside of Australia.³ It is currently marketed as a 'natural' topical antimicrobial and anti-inflammatory in preparations at concentrations between 0.5% and 100%. As use has increased, there have correspondingly been more reports of tea tree oil skin reactions including ACD; however, until recently there had been fewer than 50 cases of ACD to tea tree oil reported in the literature.⁴

We present 41 cases of patients with positive patch tests to tea tree oil identified at our institution over a 4.5-year period, in order to raise awareness of tea tree oil ACD, particularly in Australia.

METHODS

All patients with positive patch tests to tea tree oil at either 5% or 10% concentration between January 2000 and June 2004 were identified from the contact dermatitis and occupational dermatitis databases at the Skin and Cancer Foundation, Melbourne, Australia.

Tea tree oil 10% is included in our extended European standard series and the 5% commercial allergen, provided by Chemotechnique Diagnostics® (Malmö, Sweden), was also used for patch testing in some patients. The 10% patch test was prepared by a pharmacist by diluting neat tea tree oil (purchased from a pharmacy) that had first been allowed to oxidize by standing the open bottle on a window ledge for several days, with white soft paraffin. This was kept in a sealed jar in the fridge and loaded into syringes for patch testing as required. Patients were patch-tested using allergens obtained from Chemotechnique Diagnostics® (Malmö, Sweden) and Trolab® Hermal (Reinbek, Germany) and their own products appropriately diluted. Patches were applied to the upper back using Finn Chambers® on Scanpore® (Epitest OY, Tuusula, Finland) and left on for 48 hours. Reactions were recorded 30 min after patch removal at

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Abbreviations:

ACD	allergic contact dermatitis
MP	<i>Myroxylon pereirae</i>

Table 1 Type of tea tree oil use and corresponding site of the presenting dermatitis in 17 patients with relevant positive patch test results to tea tree oil

Patient (age/sex)	Exposure to tea tree oil	Site of presenting dermatitis
73/F	Neat oil between toes	Feet only
55/F	Soap	Feet only
26/F, 32/F, 20/M	Applied to tinea pedis or 'foot rash' (three cases)	Feet only (two cases), feet, then spread to legs, arms, trunk (one case)
51/F	To clean shoes, socks and bathe feet	Initially feet, then spread to trunk
71/M	Neat oil to face as antiseptic to cuts and abrasions, hand cream	Face only
24/F	Face cream	Face only
72/M	Wood turner who worked with tea tree wood and applied oil topically	Face, neck
43/F	Deodorant and hand lotion	Face, hands, feet
38/M	Neat oil and lotion, site of application not recorded	Arms, face, abdomen
50/F	Neat oil as antiseptic applied to neck	Neck only
53/F	Applied as insect repellent and to insect bites	Neck, chest
44/F	Neat oil, site of application not stated	Neck and periorbital face
46/M	20% oil to hands	Hands only
19/F	Used as hand wash	Hands only
48/M	Used oil but type of use not recorded	Axillae only

F, female; M, male.

48 hours and at 96 or 120 hours according to the International Contact Dermatitis Research Guidelines. They were measured as irritant (irr), equivocal (+/-), weak positive (+), strong positive (++) or extreme positive (+++). Only the patients with positive reactions (+ or greater) were used for analysis.

RESULTS

In total we identified 42 positive reactions to tea tree oil; however, case notes were unavailable for one patient who was excluded from analysis, giving a prevalence of tea tree oil allergy of 41 of 2320 patients attending for patch testing (1.8%). On the same test population we recorded zero irritant reactions and eight (0.3%) equivocal (+/-) reactions to tea tree oil. Positive reactions were more common in women (24 patients) than men (17 patients), with a mean age of 49 years (range 12–87 years). Positive reactions were classified as relevant, not relevant or uncertain relevance as determined by the case notes, other patch-test results and, where possible, follow-up interviews with the patients. Of the 41 positive reactions 17 (41%) were relevant, as defined by a history of use of tea tree oil-containing products which explained the presenting dermatitis.

Follow-up telephone interviews were attempted with all 41 patients who had positive reactions and were conducted between 3 months and 5 years after their patch testing. Eight could be contacted for follow-up interview, all of whom had applied a tea tree oil preparation prior to their initial rash but not since patch testing. Seven of these patients had achieved complete resolution of their dermatitis and one, who also had multiple other positive patch tests results, continued to have a fluctuating rash but of lesser severity than prior to patch testing.

Of the 41 patients who tested positive to tea tree oil, 19 had reactions classed as not relevant (46%). This was because either their tea tree oil exposure could not reasonably explain their presenting dermatitis (10 patients), or

they denied prior contact with tea tree oil and had no greater than a (+) reaction (nine patients). Another five patients were classified as uncertain relevance because either they denied previous tea tree oil contact but had strong (++) reactions, or they had used tea tree oil previously but could not associate its use with flares of their dermatitis. Of the 41 positive cases, eight reported the use of neat tea tree oil. All of the 17 cases with relevant positive reactions recalled applying a tea tree oil preparation to conditions such as cuts or abrasions, tinea pedis or insect bites. At least four of the 17 had used neat tea tree oil. The sites of the presenting dermatitis most commonly involved the feet (seven of 17) and face (six of 17) and generally corresponded to the site of application of the tea tree oil-containing product (Table 1).

Twenty-five of 41 positive cases were tested to the 5% Chemotechnique Diagnostics® commercial allergen in addition to the 10% allergen. Three of these patients who were classified as relevant positives reacted to the 10% allergen but not to the 5% allergen and four patients classified as non-relevant positives tested negative to the 5% allergen but positive to the 10% allergen (Table 2). No patients reported sensitization as a result of patch testing (patients were asked to report any new skin reactions following testing).

The tea tree oil samples used for testing in our clinic are intentionally oxidized by exposure to light, moisture, heat and air to allow for the formation of degradation products such as peroxides, which increase in oxidized tea tree oil.⁵ Chemotechnique Diagnostics® also intentionally oxidize their test sample (pers. comm., B. Niklasson, Chemotechnique Diagnostics®, May 2006). In order to quantify the level of oxidation, samples of both our own 10% dilution and the 5% Chemotechnique Diagnostics® sample were sent to the laboratories of TP Health Ltd for measurement of peroxide values. The peroxide values were measured using the modified BP assay method and were elevated in both samples, measuring 78 in the 5% Chemotechnique

Table 2 Patch test results of patients tested to both 5% and 10% tea tree oil

Patient (age/sex)	Reaction to 10% tea tree oil		Reaction to 5% tea tree oil		96 hours or 120 hours
	48 hours	96 hours or 120 hours	48 hours	Relevance	
24/F	++	+++	++	++	R
38/M	++	+++	++	+++	R
50/F	++	+++	++	+++	R
73/F	++	+++	+	++	R
26/F	++	++	++	++	R
71/M	++	++	++	+++	R
46/M	++	++	++	++	R
44/F	+	++	-	-	R
55/F	+	++	+	++	R
20/M	++	+	+	+	R
51/F	+	++	-	++	R
48/M	+	+	-	-	R
53/F	+	+	-	-	R
54/M	++	++	+	+	UR
76/F	+	++	-	-	UR
87/M	+	+	+/-	+	UR
68/M	+	+	+	+/-	NR
67/M	++	+/-	-	-	NR
12/M	+/-	+	-	-	NR
30/F	-	+	+	++	NR
45/F	-	+	-	-	NR
70/F	+/-	+	-	-	NR
51/M	+	+/-	-	-	NR
24/F	+	+/-	-	-	NR
29/F	-	-	-	+	NR

F, female; M, male; NR, not relevant; R, relevant; UR, uncertain relevance.

Diagnostics® sample and 22 in our 10% sample (pers. comm., C. Dean, Founder/Executive Director, TP Health Ltd, 28 July 2006).

The positive reactions in the 24 patients whose reaction was not relevant or of uncertain relevance may have been a result of prior unrecognized or forgotten tea tree oil exposure or a cross-reaction to other allergens. Twelve patients recalled prior exposure to tea tree oil whereas the other half denied any exposure. Thirty-nine of 41 patients (95%) tested positive to at least one other allergen, with 20 (49%) testing positive to four or more additional allergens. We identified colophonium, fragrance mix and balsam of Peru, now known as MP resin, as the most common concomitant allergens (Table 3).

DISCUSSION

We report 17 people with ACD to tea tree oil of 41 patients who had positive reactions to tea tree oil from a total of 2320 people patch-tested. The prevalence rate of positive reactions to tea tree oil in this study (1.8%) is higher than has been reported in studies overseas: an Italian group identified one (0.1%) positive reaction from 725 clinic attendees patch-tested to 5% tea tree oil;⁶ a Danish patch-test clinic found one of 217 (0.5%) patch-tested to 10% tea tree oil and zero of 160 tested to a 5% tea tree oil lotion;³ a North American group identified five of 1603 (0.3%) clinic attendees with positive reactions.⁴ A previous Australian study

Table 3 Concomitant positive patch test reactions in 41 patients with positive reactions to tea tree oil

Allergen	No. patients (%)
Colophonium	15/41 (37)
Fragrance mix	14/41 (34)
<i>Myroxylon pereirae</i> resin	13/41 (32)
Formalin	7/41 (17)
Quarternium 15	6/41 (15)
Compositae mix	6/41 (15)
Lanolin	4/41 (10)
Nickel	4/41 (10)
Arnica montana	3/41 (7)
Euxyl 500	3/41 (7)
Other	29/41 (71)

Reactions (+) or greater.

identified higher prevalence rates than in our population, with 2.9–4.8% of 219 participants recording positive reactions to 10% tea tree oil. This number rose to 4.6–7.7% when only participants with prior exposure to tea tree oil were analysed.⁷

Several patients in our series had applied tea tree oil directly to broken or eczematous skin, which theoretically would be expected to increase the likelihood of sensitization and has been previously reported in the literature in patients with tea tree oil ACD.^{1,8,9} Indeed the first two cases of tea tree oil ACD reported in the literature in 1991 were

from patients applying tea tree oil to pre-existing rashes.¹⁰ When applied to tinea pedis at concentrations of 25% and 50%, dermatitis developed in one of 54 (1.9%) of the 25% concentration group and three of 51 (5.9%) in the 50% concentration group.¹¹ Several reports of tea tree oil ACD also describe application of neat oil⁹ and a study of tea tree oil irritancy with the daily application of 25% tea tree oil under occlusion for 5 days a week over 21 days elicited a severe allergic response in three of 28 participants (11%).¹² These results would suggest that the use of tea tree oil in concentrated forms, particularly on damaged skin, should be discouraged. However, concentrations of tea tree oil greater than 10% are readily obtainable and eight patients in our study reported application of neat tea tree oil.

Increasing reports of tea tree oil ACD in the literature have been partly attributed to an overall increase in tea tree oil use but also to the more widespread availability of neat tea tree oil.^{1,10,13} However, a major manufacturer of tea tree oil in Australia was unaware of any cases of ACD to tea tree oil in workers either harvesting the plant or in the production of oil over a 25-year period (pers. comm., C. Dean, Founder/Executive Director, TP Health Ltd, 13 December 2005).

Allergic contact dermatitis to tea tree oil may be associated with concomitant reactions to colophonium,^{14–18} MP resin,^{16,19} fragrance mix^{5,17,20} and other essential oils.^{17,18,21} We identified colophonium, MP resin, fragrance mix as well as several other allergens that were positive at higher rates than would be expected in a patch-test population.²²

At least 13 components of tea tree oil have been identified as potential sensitizers, the commonest and most important of which are terpinolene, ascardiol, α -terpinene, 1,2,4-trihydroxy methane and α -phellandrene.²³ Factors affecting the composition of tea tree oil include the distillation process of commercial tea tree oil and oxidation.⁵ Sensitizers increase with oxidation of the oil upon exposure to light, moisture, heat and air, such that oxidized tea tree oil has a sensitizing capacity three times stronger than fresh oil. If a tea tree oil bottle is opened daily, the degradation products increase after only a few days and continue to increase as the oil ages.²³ Because typical usage patterns of commercial tea tree oil products would result in intermittent exposure of the oil to light, moisture, heat and air over a prolonged period, patients' own products may actually be more allergenic than patch-test preparations. The components of tea tree oil are regulated by Australian and international standards²⁴ with considerable interest from industry to reduce the formation of sensitizers through the use of antioxidants in tea tree oil products (pers. comm., C. Dean, Founder/Executive Director, TP Health Ltd, 3 May 2006).

This study demonstrates that allergy to tea tree oil preparations is relatively common in our patch-test population and is often relevant to the presenting dermatitis. Excluding nickel and fragrance mix, individual allergens present in the standard patch test series have been found to be positive in approximately 0.5–5% of a patch-test population.²² Given our findings of tea tree oil allergy in 1.8% of such a population, tea tree oil allergy is sufficiently common to be added to all standard patch-test series in Australia. We recommend testing with 10% tea tree oil as it would seem to

increase the sensitivity of the patch test compared with testing at 5% concentration at the cost of a small number of false-positive results. However, currently Chemotechnique Diagnostics[®] supplies tea tree oil at a concentration of 5%. The antimicrobial effect of tea tree oil against common bacteria, fungi and herpes simplex virus generally occurs at concentrations of 10% or less in *in vitro* studies²⁴ although to our knowledge no clinical studies have demonstrated superiority of tea tree oil over existing pharmacological treatments. We strongly discourage the application of more concentrated solutions of tea tree oil, particularly on eczematous or broken skin, and suggest that manufacturers supply appropriate warnings on their products.

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