

ORIGINAL RESEARCH

The first Australian Baseline Series: Recommendations for patch testing in suspected contact dermatitis

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ABSTRACT

Background and Objectives: Patch testing is a standard diagnostic tool used in the identification of causative allergens in allergic contact dermatitis. Ongoing surveillance of rates of allergen positivity is vitally important to detect trends and allow comparisons between countries. The objective of this study was to propose the first evidence-based Australian baseline series, based on retrospective review of our patch test data. We aimed to identify the most important and most relevant allergens in our population.

Methods: We conducted a 10-year (2001–2010) retrospective review of data from the contact dermatitis clinic and the occupational dermatitis clinic from our institution.

Results: We patch tested 5281 patients in all. The top 20 allergens with the highest number of relevant positive patch test reactions were: fragrance mix 1: nickel, potassium dichromate, *Myroxylon pereirae*, formaldehyde, p-phenylenediamine (PPD), thiuram mix, colophony (rosin), dermatophagoides mix, ammonium persulfate, quaternium-15, cobalt chloride, methylchloroisothiazolinone or methylisothiazolinone, diazolidinylurea, epoxy resin, 1,3-dimethylol-5,5-dimethyl hydantoin, Compositae mix, toluenesulfonamide formaldehyde resin, basic red 46 and imidazolidinyl urea.

Conclusion: We have elucidated the most frequent and relevant contact allergens in our patient population and used this information to construct the first Australian baseline series.

Key words: allergy, basic red 46, bufexamac, chloroacetamide, dermatitis, hand eczema, irritation, occupational, preservative, rubber chemical, tea tree oil, wool alcohol.

INTRODUCTION

Allergic contact dermatitis (ACD) affects about 7% of the general population.^{1,2} Patch testing is a standardised, evidence-based diagnostic tool in the identification of contact allergens.³ Dermatologists traditionally use a standard series of allergens, more recently termed the baseline series,⁴ representing the core series of allergens used to evaluate every patient undergoing patch testing. In specialised clinics this is supplemented by other series or individual allergens, based on the patient's occupation and history of exposures. The baseline series should ideally contain the most common contact allergens in the population being patch tested. It has been suggested that an allergen should be included in the standard series when > 0.5–1% of routinely tested patients react positively.⁵

Abbreviations:

2MBT	2-mercaptobenzothiazole
ACD	allergic contact dermatitis
CDC	contact dermatitis clinics
DMDM	1,3-dimethylol-5,5-dimethyl
MCI	methylchloroisothiazolinone
MIT	methylisothiazolinone
NSAID	non-steroidal anti-inflammatory drug
ODC	occupational dermatology clinic
PPD	p-phenylenediamine
TTO	tea tree oil

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There are, however, other important factors to consider, such as the relevance of these positive reactions and certain allergens, where missing a positive patch test reaction to a certain allergen would be detrimental to treatment; such as those used in medicament creams. It is, therefore, understandable that the baseline series will vary across centres, reflecting regional differences in allergen exposures and the threshold chosen for testing. The European standard series, North American Contact Dermatitis Group series and Mayo Clinic standard series are some examples. Significant differences between the frequency of sensitisation to common allergens in Europe and the USA have been highlighted.⁶

Ongoing surveillance of patch test reaction rates is the key to detecting trends in rates of allergenicity and they are imperative for identifying emerging allergens. Once such allergens are identified they can be added to the baseline series and rates of sensitisation in the general patch test population monitored. The ranking of allergens will not only allow dermatologists to recommend relevant up-to-date allergens for patch testing but may also allow them to identify issues of consumer and occupational safety. Thus, the baseline series needs to be dynamic and regularly reviewed.

The frequency of positive tests at any patch testing institution depends on a number of factors. These include the knowledge and skill of the physician, referral patterns, the healthcare system, which impacts on patch testing rates and access to patch testing, and finally, societal and environmental factors.⁷

The Skin and Cancer Foundation, Victoria is a tertiary referral centre for dermatological conditions in Melbourne, Australia. Patients are referred to the Occupational Dermatology Clinic (ODC) and contact dermatitis clinics (CDC) predominantly from dermatologists but also from allergists, occupational physicians, oral medicine physicians and general practitioners from the state of Victoria, which has a population of 5.4 million. These clinics provide most of the patch test services in the state.

The aim of this study was to retrospectively review our patch test data over a 10-year period in order to identify the most important and relevant allergens to include in the first Australian baseline series.

PATIENTS AND METHODS

We reviewed our data on patients patch tested at the Skin and Cancer Foundation over a 10-year period (1 January 2001–31 December 2010). The information was recorded on a standard computer program that we had developed to record clinic data (Contact Allergy Management Systems).

Patients were generally patch tested with an extended European standard series⁸ and additional allergens or series as deemed appropriate based on the dermatologist's assessment. The patients' own contactants were also tested at appropriate dilutions. Patch testing was performed according to the International Contact Dermatitis Research Group recommendations. Testing was performed using Finn chambers (Epitest, Tuusula, Finland; now Smart Practice, Phoenix, AZ, USA) on Scanpor tape (Norgesplaster

Aksjeselskap, Vennesla, Norway). The patches were applied to the upper back for 48 h. Readings were performed on both days 2 and 4. The allergens were purchased from both Chemotechnique Diagnostics (Vellinge, Sweden) and Hermal (Reinbek, Germany).

Test reactions were interpreted by the dermatologists on days 2 and 4 and a positive patch test reaction was defined by a reading of 1 + or greater. An allergen was defined as being relevant when the patch test was positive and the allergen was deemed to be the cause of the patient's presenting ACD, based on their history of exposure together with an appropriate clinical time course. In the determination of relevance we have not included data for allergens assessed as being of old relevance (such as; there was a history of ACD from previous exposure to the allergen) or of unknown relevance (such as; the allergen's relevance could not be determined despite directed history taking).

The primary outcome measure was the number of relevant positive reactions.

Other outcome measures included: (i) the number of positive reactions; (ii) the proportion of positive reactions for each allergen that were assessed to be relevant; (iii) the rate of relevant positive reactions for an allergen based on the total number tested to that allergen; (iv) the rate of positive reactions for an allergen based on the total number tested to that allergen; and (v) the rate of relevant positive patch test reactions for an allergen in the whole patch test population. The latter was calculated by dividing the total number of relevant positive reactions to an allergen by the patch test population ($N = 5281$). This assumed that patch testing for an allergen was available for the whole 10-year dataset and that patients not patch tested to the allergen would not have tested positive. Many rates of relevant positive reactions in the whole patch test population will therefore be considerably underestimated, yet this provided us with the most accurate comparison of allergens in order to propose a baseline series for testing the whole patch test population.

The rate of positive patch test reactions for an allergen in the whole patch test population was calculated similarly. Any allergen that was not commercially available or was a patient's own product was excluded.

RESULTS

The total number of patients seen was 5521, of whom 5281 underwent patch testing. In total, 2113 (40%) were from the ODC and 3168 (60%) were from the CDC. The average age of the patients was 41.0 years. The male occupational dermatitis, atopic dermatitis, hand dermatitis, leg dermatitis, face dermatitis and age index⁹ was used to describe our study population (Table 1). The male : female ratio for the ODC was 1:1.2 (970:1131), while the male : female ratio for the CDC was 1:2.5 (895:2272). In all, 78% (4111/5281) of patients patch tested had a positive reaction to at least one allergen. The most frequently affected site of dermatitis was the hands (36%), followed by the face (25%), arms (13%) and eyelids (12%). Hand dermatitis was more commonly seen in the ODC (54%) than the CDC (24%), whereas facial dermatitis was more commonly seen in the CDC (30.7%)

Table 1 Male occupational dermatitis, atopic dermatitis, hand dermatitis, leg dermatitis, face dermatitis and age index

Index	Patients (n)	Percentage of study population
Male	1865	35
Occupational dermatitis	1561	26
Atopic dermatitis	1576	30
Hand dermatitis	1894	36
Leg dermatitis	444	8
Face dermatitis	1507	25
Age above 40	2634	50

than the ODC (16%). ACD (32%) was the most common primary diagnosis made after the completion of patch testing, followed by endogenous eczema (24%) and irritant contact dermatitis (14%). In all, 21% of the total number of cases was assessed to be significantly work related and 5% was deemed to be partially work related, usually reflecting the aggravation of an underlying dermatosis.

Number of relevant positive patch test reactions

Our top 20 allergens with the highest number of relevant positive patch test reactions were: fragrance mix 1, nickel, potassium dichromate, *Myroxylon pereirae*, formaldehyde, p-phenylenediamine (PPD), thiuram mix, colophonium, dermatophagoides mix, ammonium persulfate, quaternium-15, cobalt chloride, methylchloroisothiazolinone (MCI)/methylisothiazolinone (MIT), diazolidinylurea, epoxy resin, DMDM hydantoin, Compositae mix, toluenesulfonamide formaldehyde resin, basic red 46 and imidazolidinyl urea (Table 2).

On the basis of the frequency and relevance of the allergic reactions, the Australian baseline series of 60 allergens is proposed (Table 2). The allergens are listed in order of the number of relevant positive reactions. Most of these 60 allergens had estimated positive patch test rates of more than 0.5% based on this study: the reason for the inclusion in our proposed baseline series of those that did not is discussed below. Those with rates of more than 0.5% but were not included are also discussed.

DISCUSSION

ACD is a common problem and studies have confirmed that the use of patch testing to make the diagnosis of ACD is associated with an improved quality of life.¹⁰ Early and accurate diagnosis of the causal allergen in ACD prevents progression to a chronic disease state that may be refractory to treatment.^{11,12} For a developed country with a predominantly urban population, the optimum rate of patch testing has been suggested to be 1 per 700 or 1416 per million per year.^{13,14} We know from a previous study that patch testing rates in our state are quite low at 1 : 6250 or 160 per million per year,¹⁵ despite probably being the highest in Australia. Of patients patch tested at our institution, 78% had a positive reaction to at least one allergen.

We have attempted to elucidate important and current allergens in our local population so as to provide Australian dermatologists with an appropriate and informed guide to patch testing. Apart from a few exceptions, the allergens with high positive patch test rates included the most commonly reported contact allergens from around the world such as nickel, fragrance, rubber accelerators, PPD, potassium dichromate, colophonium, preservatives and medications. However, there were some significant and interesting regional differences.

Notable inclusions to the Australian baseline series

Basic red 46 Basic red 46 is a cationic dye highly suitable for use on acrylics. It is also used to colour flame-resistant fabrics and paper. Basic red 46 is bluish-red in colour but it may be used as a shading component in a large range of colours, especially black and blue. The prevalence of contact allergy to this dye has been reported to be 0.2–3%.¹⁶ A previous study from our centre reported 17 patients with foot dermatitis caused by basic red 46 dye in particular types of acrylic blend socks.¹⁷ Textile dyes have been reported to cause up to 10% of cases of ACD of the feet.¹⁸ In this study, the estimated prevalence of positive patch test reactions in the total patch test population to basic red 46 was 1%, and most of the reactions (75%) were relevant. Hence, we believe that this is an important allergen in the setting of foot dermatitis in Australia, although the number of reactions occurring is now declining.

Bufexamac Bufexamac (4-butoxy-N-hydroxybenzene acetamide) is a non-steroidal anti-inflammatory drug (NSAID) belonging to the class of arylalkanoic acid derivatives. In Australia it is found in several over-the-counter topical medications marketed as remedies for burns, cuts, insect bites, sunburn, eczema and rectal itch. The prevalence of contact allergy appears to be rising. A study by Frosch and colleagues¹⁹ in 1987 reported a contact sensitisation rate of 0.25%, but more recent studies have reported higher sensitisation rates of 1–5%.^{20–22} It is now banned in Germany. Bufexamac was the leading contact allergen in a series of NSAID in a study of 371 patients.²³ In our study, 19/899 (2%) patients patch tested positively to bufexamac, of which 42% were relevant.

Chloroacetamide Chloroacetamide is a preservative used mainly in skin care products such as creams, lotions, shampoos, shower gels and bath foams. Contact allergy to chloroacetamide was described as early as 1971.²⁴ It has been deemed unsafe for use in cosmetics in the USA following a cosmetic ingredient review report that chloroacetamide is a human sensitizer at concentrations of 0.5 and 1%.²⁵ However, it remains in use in Australia and a common source of this preservative has been Redwin (Sydney, NSW, Australia) Sorbolene lotion, a popular Australian brand. Of 4576 patients tested to chloroacetamide in this study, there were 139 positive reactions (3%) with a

Table 2 The Australian baseline series (percentages rounded up to nearest whole number)

Ranking	Allergen name	Concentration (pet)	Tested	Relevant	Positive	Relevant/ positive (%)	Relevant/ tested (%)	Positive/ tested (%)	Relevant/ total (5281) (%)	Positive/ total (5281) (%)	ABS
1	Fragrance mix	8.0	5228	229	605	38	4	12	4	12	1
2	Nickel sulfate	5.0	5175	205	895	23	4	17	4	17	2
5	Potassium dichromate	0.5	5180	142	515	28	5	10	5	10	5
	Potassium dichromate [†]	0.25	761	74	101	73	10	15	1	2	
4	Myroxylon pereirae	25.0	5198	140	461	50	3	9	3	9	4
5	Formaldehyde (aq)	1.0	5144	119	279	43	2	5	2	5	5
6	4-phenylenediamine base	1.0	5153	117	256	50	2	5	2	5	6
7	Thiuram mix	1.0	5149	116	207	56	2	4	2	4	7
8	Colophonium	20.0	5148	111	388	29	2	8	2	7	8
9	Dermatophagoides mix (D. pteronyssinus/D. pharinae) [†]	40.0	519	91	198	46	29	62	2	4	
	Dermatophagoides mix [†]	30.0	206	67	125	55	33	60	1	2	
	Dermatophagoides mix [†]	20.0	114	22	55	42	19	47	0	1	
10	Ammonium persulfate [†]	2.5	1526	85	295	28	6	22	2	6	
11	Quaternium-15	1.0	5159	85	176	47	2	3	2	3	9
12	Cobalt chloride	1.0	5169	81	564	14	2	11	2	11	10
15	Methylchloroisothiazolinone/ methylisothiazolinone (Kathon CG) (aq)	0.01	5145	75	176	42	1	5	1	5	11
14	Diazolidinylurea	2.0	5159	60	140	43	1	3	1	3	12
15	Epoxy resin	1.0	5164	55	154	40	1	3	1	3	13
16	DMDM hydantoin (aq).	2.0	4296	52	115	46	1	3	1	2	14
17	Compositae mix	6.0	5088	50	171	29	1	3	1	3	15
18	Toluenesulfonamide formaldehyde resin	10.0	5130	49	89	55	1	2	1	2	16
19	Basic red 46	1.0	1845	48	64	75	3	4	1	1	17
20	Imidazolidinyl urea	2.0	5134	47	102	46	1	2	1	2	18
21	Lanolin (wool alcohols)	30.0	5157	46	219	21	1	4	1	4	19
22	Coconut diethanolamide	0.5	5088	43	139	31	1	3	1	3	20
23	Tea tree oil [†]	10.0	5087	43	129	33	1	3	1	2	
	Tea tree oil	5.0	794	12	28	43	2	4	0	1	21
24	2,5-diaminotoluene sulfate [†]	1.0	610	42	60	70	7	10	1	1	
25	Amerchol L 101	50.0	4794	40	219	18	1	5	1	4	22
26	Nutmeg [†]	25.0	525	39	202	19	7	39	1	4	
27	Cocamidopropyl betaine (aq)	1.0	4297	35	292	12	1	7	1	6	23
28	Hydroabietyl alcohol [†]	10.0	2801	34	139	25	1	5	1	3	
29	Hydroxyisohexyl 5-cyclohexene carboxaldehyde (Lyrall)	5.0	4804	33	99	33	1	2	1	2	24
30	2-nitro-4-phenylenediamine [†]	1.0	612	32	96	33	5	16	1	2	
31	Euxyl K400 [†]	0.5	5135	31	142	22	1	3	1	3	
	Methyl dibromoglutaronitrile	0.5	4644	16	75	21	0	2	0	1	25
32	Sesquiterpene lactone mix	0.1	5128	31	102	30	1	2	1	2	26
33	2-hydroxyethyl methacrylate	2.0	504	31	48	65	6	10	1	1	27
34	Chloroacetamide	0.2	4576	27	159	19	1	3	1	3	28
35	Mercury [†]	0.5	594	27	98	28	5	17	1	2	
36	Amalgam [†]	5.0	267	26	40	65	10	15	1	1	
37	Lemongrass oil [†]	2.0	837	25	45	56	3	5	1	1	
38	Dodecyl gallate [†]	0.25	3000	24	220	11	1	7	1	4	
39	Ethylene glycol dimethacrylate [†]	2.0	463	24	40	60	5	9	1	1	
40	4-Aminophenol [†]	1.0	572	23	42	55	4	7	0	1	
41	4-tert-butylphenol formaldehyde resin (PTBP)	1.0	5139	22	90	24	0	2	0	2	29
42	2-hydroxy-4-methoxybenzophenone (benzophenone 3)	10.0	3573	22	60	37	1	2	0	1	30
43	Mercury ammonium chloride [†]	1.0	549	22	50	44	4	9	0	1	
44	2-mercaptobenzothiazole	2.0	5147	21	79	27	0	2	0	2	31
45	Spearmint [†]	5.0	1583	21	68	31	2	5	0	1	
46	Mercuric chloride [†]	0.1	550	21	56	38	4	10	0	1	
47	2-hydroxypropyl methacrylate [†]	2.0	273	21	35	64	8	12	0	1	
48	Propolis [†]	10.0	4705	20	145	14	0	3	0	3	
49	Mercapto mix	2.0	5138	20	66	30	0	1	0	1	32
50	Lavender absolute [†]	2.0	1128	20	45	44	2	4	0	1	
51	2-hydroxy-4- methoxybenzophenone- 5-sulfonic acid (benzophenone 4)	10.0	1924	19	84	23	2	4	0	2	33
52	Ylang-ylang oil [†]	2.0	1020	19	64	30	2	6	0	1	
53	Propylene glycol (aq)	10.0	5072	19	62	31	0	1	0	1	34
54	Cetylstearyl alcohol	20.0	5095	17	68	25	0	1	0	1	35
55	Disperse blue 106 [†]	1.0	1174	17	66	26	1	5.6	0	1	
	Disperse blue 106 & 124 mix	1+1	3917	14	112	13	0	3	0	2	36
	Disperse blue 124 [†]	1.0	1186	14	65	22	1	5	0	1	
56	4-chloro-3-cresol	1.0	5094	16	55	30	0	1	0	1	37
57	Dipentene (limonene)	1.0	3093	16	48	33	1	2	0	1	38
58	Disperse orange 3 [†]	1.0	1280	16	42	38	1	3	0	1	

Table 2 *Continued*

Ranking	Allergen name	Concentration (pet)	Tested	Relevant	Positive	Relevant/ positive (%)	Relevant/ tested (%)	Positive/ tested (%)	Relevant/ total (5281) (%)	Positive/ total (5281) (%)	ABS
59	Parthenolide [†]	0.1	1114	16	40	40	1	4	0	1	
60	Dimethylaminopropylamine (aq)	1.0	584	16	37	43	3	6	0	1	
61	Fragrance mix II	14.0	855	16	37	43	2	4	0	1	39
62	Mixed dialkyl thiourea	1.0	4550	15	39	39	0	1	0	1	40
63	3-aminophenol [†]	1.0	571	15	26	58	3	5	0	1	
64	Triethylene glycol dimethacrylate [†]	2.0	454	15	26	58	3	6	0	1	
65	2-hydroxyethyl acrylate [†]	0.1	164	15	23	65	9	14	0	0	
66	Gold sodium thiosulfate [†]	0.5	352	14	69	20	4	20	0	1	
	Gold sodium thiosulfate [†]	2.0	528	9	114	8	2	22	0	2	
67	Black rubber mix	0.6	5132	14	53	26	0	1	0	1	41
68	Sandalwood oil [†]	2.0	986	14	51	28	1	5	0	1	
69	Disperse orange 1 [†]	1.0	797	13	39	33	2	5	0	1	
70	Neroli oil (orange flavour) [†]	2.0	477	13	20	65	3	4	0	0	
71	Octyl gallate [†]	0.25	2541	12	168	7	1	67	0	3	
72	Advantan Fatty Ointment [†] (mg)	1	4553	12	52	23	0	1	0	1	
	Methylprednisolone [†]	1.0	3966	9	52	17	0	1	0	1	
	Methylprednisolone (Advantan cream)	0.1	477	9	21	43	2	4	0	0	42
73	Tixocortol-21-pivalate	1.0	5128	12	51	24	0	1	0	1	43
74	Carba mix	5 × 1.0	939	12	46	26	1	5	0	1	44
75	Paraben mix	12.0	5138	12	45	27	0	1	0	1	45
76	Cananga oil [†]	2.0	823	12	39	31	2	5	0	1	
77	Glyceryl monothioglycolate [†]	1.0	270	12	22	55	4	8	0	0	
78	Methyl methacrylate [†]	2.0	494	12	20	60	2	4	0	0	
79	Potassium dicyanoaurate [†] (aq)	0.1	557	11	121	9	2	28	0	2	
80	Budesonide	0.1	5132	11	97	11	0	2	0	2	46
81	Lichen acid mix (atranorin, usnic acid, evernic acid) [†]	0.3	685	11	43	26	2	6	0	1	
82	Carvone (R & L) [†]	5.0	178	11	19	58	6	11	0	0	
83	Neomycin sulfate	20.0	5118	10	127	8	0	3	0	2	47
84	Benzocaine	5.0	5124	10	80	13	0	2	0	2	48
85	Disperse red 17 [†]	1.0	806	10	77	13	1	10	0	2	
86	Laurel oil [†]	2.0	681	10	31	32	2	5	0	1	
87	Triethyleneglycol diacrylate [†]	0.1	144	10	12	83	7	8	0	0	
88	Palladium chloride [†]	2.0	679	9	87	10	1	13	0	2	
89	Benzalkonium chloride	0.1	4063	9	80	11	0	2	0	2	49
	Outliers										
	Lidocaine	5.0	1208	9	19	47	1	2	0	0	50
	2-bromo-2-nitropropane-1,3-diol (bronopol)	0.25	4354	8	49	16	0	1	0	1	51
	4-chloro-3-xyleneol (PCMX)	0.5‡	1598	8	27	30	1	2	0	1	52
	Bufexamac	5.0	899	8	19	42	1	2	0	0	53
	Benzyl alcohol	5.0	4749	7	49	14	0	1	0	1	54
	Betamethasone-17-valerate	1.0	1322	6	16	38	1	1	0	0	55
	2-ethylhexyl-4-methoxycinnamate (Parsol MCX, Escalol 557)	10.0	2379	6	41	15	0	2	0	1	56
	Triamcinolone acetonide	1.0	1280	5	14	36	0	1	0	0	57
	Betamethasone -17, 21 dipropionate (Diprosone ointment)	0.5	2635	4	18	22	0	1	0	0	58
	Iodopropynyl butylcarbamate	0.2	4258	3	28	11	0	1	0	1	59
	Methylisothiazolinone (aq)	0.05aq	—	—	—	—	—	—	—	—	60

Allergens are listed in order of number of relevant positive reactions. They are grouped in the same number if they differ only in the patch test concentration. [†]not included in ABS. [‡]Concentration now 1.0 pet, as per Chemotechnique Diagnostics (Vellinge, Sweden). Advantan Fatty Ointment, CSL, Melbourne, Victoria, Australia, Diprosone Merck Sharp and Dohme, Sydney, NSW, Australia, Escalol Ashland, Lovington, KT, USA, Euxyl K400, Schulke and Mayr, Norderstedt, Germany, Kathon CG, Dow Chemical Company, Newark, DE, USA, Parsol MCX DSM Nutritional Products, Kaiseraugst, Switzerland. ABS, Australian baseline series; DMDM, 1,3-dimethylol-5,5-dimethyl.

relevance of 19%. The low relevance of 19% is likely to relate to the fact that patients had previously been sensitised to this allergen through the use of this Sorbolene lotion, but that it is not the cause of their presenting dermatitis. Nevertheless, we still believe this is an important and worthwhile allergen to include in the Australian baseline series, because of its high sensitisation rate.

Tea tree oil Tea tree oil (TTO), otherwise known as melaleuca oil, is an essential oil derived from the Australian native tea tree. It has antimicrobial and anti-inflammatory

properties and is increasingly used in commercial skin care products as a 'natural' remedy for conditions such as acne, wounds and eczema, especially in Australia.²⁶ While studies from American, Danish and Italian groups have reported allergenicity rates of TTO to be between 0.1–0.5%,^{27–29} Australian studies have reported higher rates. A study performed at our institution of 2320 patch tested individuals over a 4-year period found 2% to be patch test positive to TTO and 41% of these reactions were relevant.²⁶ Another earlier Australian study identified even higher prevalence rates of 3–5%.³⁰ Therefore, we strongly believe that TTO is

a sufficiently common allergen in our patch test population to be included in the Australian baseline series. We currently test at 5% pet as per Chemotechnique Diagnostics (Vellinge, Sweden).

In our proposed series, we have included two allergens: hydroxyisohexyl 3-cyclohexene carboxaldehyde (Lyrall [Sigma-Aldrich, St Louis, MI, USA]) and 2-mercaptobenzothiazole (2-MBT), which are also found in the mixes that we have included, fragrance mix 2 and mercapto mix, respectively.

Fragrance mix 2 and hydroxyisohexyl 3-cyclohexene carboxaldehyde (Lyrall) It has been reported that fragrance mix 1 (consisting of geraniol, cinnamaldehyde, hydroxycitronellal, cinnamyl alcohol, isoeugenol, eugenol, oak moss, α -amylcinnamaldehyde) misses as much as up to 33% of fragrance allergy.⁵¹ Fragrance mix 2 (consisting of Lyrall, citral, farnesol, coumarin, citronellol and α -hexyl cinnamal) has been demonstrated to be a useful additional marker of fragrance allergy, with contact allergy rates of up to 5%.^{32,55} Among the constituents of fragrance mix 2, Lyrall is the most common sensitiser, with sensitisation rates of 1–3% when tested in 5% pet at various European centres.^{54–59} Consequently, both fragrance mix 2 and Lyrall have been added to the European baseline patch test series.⁴ Lyrall alone is tested at 5% pet, yet it is at 2.5% pet in fragrance mix 2. We do not have complete data on fragrance mix 2 during our study period, as we had started testing to it only in 2008. The estimated prevalence for the total patch test population in Table 2 is thus likely to be markedly underestimated. A total of 37 of 855 (4%) patients tested positive to fragrance mix 2, with 43% of these reactions being relevant. A total of 99 out of 4804 (2%) patients tested positive to Lyrall, with 33% being relevant. We have included both fragrance mix 2 and Lyrall in our proposed baseline series, consistent with the European baseline series, although with further data, ongoing testing to Lyrall in a baseline series may not be needed as it is a constituent of fragrance mix 2.

Mercapto mix and 2-MBT Mercapto chemicals are used in the production of both natural and synthetic rubber. 2-MBT is tested at 2.0 pet alone and at 0.5 pet in the mercapto mix. In this study there were 21 relevant reactions (0.4%) and 79 positive (2%) of the 5147 patients tested to 2-MBT. There were 20 relevant (0.4%), and 66 positive (1%) of the 5138 patients tested to mercapto mix. We have included both 2-MBT and mercapto mix in our proposed baseline series, in accordance with recommendations from the European Environmental Contact Dermatitis Research Group. Their multicentre retrospective review found that if only 2-MBT was in the standard series, 22% of patients allergic to mercapto compounds would have been missed, and if only the mercapto mix was included 20% would have been missed.⁴⁰

Iodopropynyl butylcarbamate Iodopropynyl butylcarbamate is a preservative in the industrial and consumer

sector. Studies have quoted a patch test positive prevalence rate of 0.2–0.8% when tested at 0.1 or 0.2% pet and there are concerns that its use in personal care products is increasing.⁴¹ In our study period there were only three relevant reactions; however, there was a positive prevalence rate of 0.7% in those tested, and an estimated positive prevalence of 0.5% in the total patch test population. In light of its occurrence in a commonly used hospital skin cleanser⁴² we believe that this is currently an important allergen to monitor in a baseline series.

Lanolin (wool alcohol) and Amerchol L 101 Lanolin is a product derived from the sebaceous glands of sheep. It is used in topical medicaments and cosmetics. It is made up of sterols, fatty acids and fatty alcohols. Amerchol L101 (Amerchol, Edison, NJ, USA) is hydrogenated wool alcohol. Our estimated positive patch test rates to Amerchol L 101 and lanolin were both 4% in the total patch test population. However, there was discordance between reactions to Amerchol L101 and lanolin. If only Amerchol or only lanolin was tested, of the patients with positive reactions to Amerchol and/or lanolin, 40% would have been missed in both scenarios. Of the patients with relevant reactions to Amerchol and/or lanolin, 39% would have been missed if only Amerchol was tested, and 29% would have been missed if only lanolin was tested. This discrepancy in reactions to lanolin and Amerchol L 101 has also been highlighted in two other European studies.^{45,44} Hence, we recommend that both Amerchol L101 and lanolin be included in our proposed baseline series.

Medicaments We used a lower threshold for inclusion in our proposed baseline series of ingredients of common topical treatments that are known to have a potential for sensitisation. These include the topical corticosteroids; triamcinolone acetonide, betamethasone-17-valerate, budesonide, methylprednisolone and tixocortol-21-pivalate, local anaesthetics; benzocaine and lidocaine, a topical antibiotic; neomycin sulfate, topical NSAID; bufexamac and non-active preservatives; benzyl alcohol and benzalkonium chloride. These are all included in Australian topical preparations and thus a considerable number of patients are exposed to these uncommon allergens. It is very important to identify whether prescribed treatments are exacerbating a patient's condition.

MIT MIT is an emerging preservative contact allergen and has been tested only in isolation since the completion of the data set. It was initially used in combination with MCI, which was found to be a potent sensitising contact allergen.^{45,46} Studies indicated that MCI was more likely to cause allergic contact dermatitis than MIT.⁴⁷ Thus, in 2005, MIT alone was approved for use in cosmetics and household products. However, it has recently been suggested that MIT alone is also a strong sensitiser.⁴⁸ Three studies have documented the prevalence of positive patch test rates to MIT as 1–2%.^{45,46,49} There is worldwide concern that this is

markedly increasing.⁵⁰ Given this prevalence rate and its use as a preservative in a multitude of Australian products, it has been added to our proposed baseline series. The concentration for patch testing to MIT has also been recently recommended to increase from 200 to 500 ppm⁵¹ and it is possible that this concentration may be increased further.

Notable exclusions to the Australian baseline series

There are a number of allergens with estimated positive prevalence rates of above 0.5% that have not been included in our proposed standard series, as we believe that there is little value in patch testing them routinely in our population. These are discussed below.

Acrylates and methacrylates Dental acrylic monomers are well known to be common sensitizers, and this is confirmed in this study. We have decided to only include the most common sensitizer, 2-hydroxyethyl methacrylate, in our proposed baseline series, as there is considerable cross-reactivity among acrylic monomers⁵² and we believe there would be minimal clinical benefit in testing all of these in a baseline series.

Dental and cheilitis series At our institution, we work closely with an oral mucosal specialist, who is a strong advocate of patch testing. We thus have a referral bias towards patients with oral mucosal conditions and have recorded prevalence rates to some allergens in the dental and cheilitis series which would meet criteria for inclusion in a baseline series.⁵³ These allergens, which we have decided not to include in our baseline series but are included in our dental and/or cheilitis series, are nutmeg, mercury, amalgam, lemongrass oil, mercury ammonium chloride, spearmint, gold sodium thiosulfate, mercuric chloride, carvone and palladium chloride.

Dermatophagoides mix Dermatophagoides mix is now not routinely tested in our patients. We previously tested patients with suspected atopic eczema if there was a suspicion of dust mite being an aggravating factor for their eczema. Although our positive patch test rate and relevant positive patch test rate for dermatophagoides mix were high in those who were tested, we believe that this is likely to be of little significance or practical value. We wonder if many of our reactions were in fact irritant. Davis and colleagues found a high rate of reactivity to both 20% dermatophagoides mix and 0.1% mix in atopic and nonatopic populations. The reactions were thought to be either irritant or allergic, and if allergic, they were not often found to be of relevance.⁵⁴

Dodecyl gallate and octyl gallate Dodecyl gallate and octyl gallate are antioxidants added to cosmetics and foods to

prevent oxidation of unsaturated fatty acids. The prevalence of positive reactions to dodecyl gallate was 7% in those tested. The prevalence of positive reactions to octyl gallate was 7% in those tested. However, there was often no relevance found in these reactions (89 and 93% unknown relevance, respectively), which has been the subject of our recent review.⁵⁵

Essential oils An Israeli study quoted 13 of 16 patients with occupational contact dermatitis after using essential oils also had a positive reaction to fragrance mix 1.⁵⁶ They suggested that fragrance mix 1 in a baseline series is a good screening agent for essential oil allergy. In consideration of this, we have included neither ylang-ylang oil, lemongrass oil, lavender absolute, sandalwood oil, neroli oil, cananga oil, laurel oil, carvone nor propolis in our proposed baseline series.

Gold sodium thiosulfate Positive patch test reactions to gold are not uncommon, with widely variable rates of contact allergy between 1–23%.^{57–61} We found a rate of positive patch test reactions to gold sodium thiosulfate 2.0 pet of 22%, and to 0.5 pet of 20% in those tested. However, relevance could not be found in most (92 and 80%, respectively) of these cases. This is consistent with trends reported around the world.⁵⁸ Hence, we believe that patch testing to gold should be performed only when clinically indicated.

Hair dyes We have proposed to include PPD in our proposed baseline series due to its frequent use in hair dyes and high rates of sensitization. We have not included other hair dye ingredients; ammonium persulfate, 2,5-diaminotoluene sulfate, 2-nitro-4-phenylenediamine, 4-aminophenol or 3-aminophenol, which are included in the hairdressing series, and may be overrepresented in our data set, given the occupational bias of our population.

Ammonium persulfate is added as a booster to hydrogen peroxide for hair bleaching. It also has industrial uses. Ammonium persulfate is known to cause both irritant and allergic reactions.⁶² In this study, ammonium persulfate was one of the most common allergens, with a relevant positive rate of 6% in those tested, and an estimated positive prevalence rate of 6% in the whole patch test population. Relevant reactions were seen almost exclusively in hairdressers. We postulate that ammonium persulfate may be overrepresented in our study, as almost half of our study population were patients from the ODC, which is attended by many hairdressers. We also suspect that many of the reactions in non-hairdressers may have been irritant. Ammonium persulfate often causes irritant patch test reactions even when tested at the recommended concentration of 3% pet.^{7,63}

Hydroabietyl alcohol (Abitol [Eastman Chemical Company, Kingsport, TN, USA]) Hydroabietyl alcohol, derived from rosin acids that have been hydrogenated, was a common

allergen in this study. There were 34 relevant positive reactions (1%) and 139 positive reactions (5%) in 2801 patients patch tested to hydroabietyl alcohol, with an estimated positive prevalence rate of 3% in the total patch test population. However, given its cross-reactivity with colophonium,³ we have not included this in our proposed baseline series.

Size of the series

Baseline series vary in size around the world. The TRUE Test from Smart Practice (Sydney, Australia) includes 24–36 allergens, the European standard series consists of 29 allergens, the International Contact Dermatitis Research Group standard series is 32, the North American Contact Dermatitis Group standard series is 70 and the Mayo Clinic standard series is 63. With that in mind, and considering that many Australian dermatologists do not have access to individual allergens, we have chosen a series of 60 to fit onto six panels of 10 allergens, as we believe that it is preferable to have a comprehensive series, as the North Americans have also concluded. Nevertheless, it is recognised that having more allergens is more costly. The last three allergens have been included to round the numbers up to 60, and the authors were interested to monitor the incidence of ACD to these allergens: 2-bromo-2-nitropropane-1,3-diol, 4-chloro-3-xyleneol and the sunscreen, 2-ethylhexyl-4-methoxycinnamate (Parsol MCX [DSM Nutritional Products, Kaiseraugst, Switzerland], Escalol 557 [Ashland, Lovington, KY, USA]). However, in the future these allergens may be substituted with others. Practitioners could leave out these allergens if they prefer.

Limitations

The results of this study need to be interpreted in context, as the data emanate from a tertiary referral institution with a bias to occupational skin problems. Pooling data from other centres, especially inter-state, would allow for more accurate detection of allergens nationally. However, we here propose the first Australian baseline series despite these acknowledged limitations.

CONCLUSION

In the review of our patch test data 2001–2010, we found the 20 most relevant allergens to be fragrance mix 1, nickel, potassium dichromate, *Myroxylon pereirae*, formaldehyde, PPD, thiuram mix, colophonium, dermatophagoides mix, ammonium persulfate, quaternium-15, cobalt chloride, MCI/MIT, diazolidinylurea, epoxy resin, DMDM hydantoin, Compositae mix, toluenesulfonamide formaldehyde resin, basic red 46 and imidazolidinyl urea. Excluding dermatophagoides mix and ammonium persulfate, we have used this information to construct a series of 60 allergens that we believe provides an appropriate basis for patch testing in our population.

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