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Research Letter

Dear Editor,

Sensitisation to antiseptics in Waikato, New Zealand, prior to the coronavirus disease 2019 pandemic

In the current pandemic era, there is increased exposure to antiseptic allergens, as a result of both surface and hand sanitisation[1] and their use as preservatives in medications and cosmetics. We wished to establish the prior rate of sensitisation to allergens of the antiseptic series (see Table 3), especially benzalkonium chloride, the prototypical quaternary ammonium disinfectant, to allow comparison in future years.

METHODS

We retrospectively reviewed records between 1 January 2009 and 31 December 2019 at the Waikato Hospital Department of Dermatology to identify patients who had been patch tested to the baseline series (the European and a local baseline series) and the antiseptic series (see Table 3) and/or benzalkonium chloride.

Patch test readings were performed on day two and day four. Readings were graded as per international guidelines [2]: – denoting a negative reaction, +/– a doubtful reaction and positive reactions were defined as a + (palpable erythema), ++ (oedematous or vesicular) or +++ (bullous or ulcerative).

The clinician performing the day four read categorised positive reactions as of historical, unknown, possible or

Table 1 Baseline characteristics of patients patch tested to the antiseptic series and benzalkonium chloride (n = 233)

	Number	Percentage of total (%)
Gender		
Male	63	27
Female	170	73
Ethnicity		
New Zealand European	146	63
Māori	28	12
Pacific Island	2	1
Asian	19	8
Other/not defined	38	16
Occupation		
Health care	15	6
Industrial, for example automotive, engineering, machinist, tradesperson	27	12
Professional, for example clerical, teacher	27	12
Cleaner	6	3
Unemployed or retired	20	9
Homemaker	10	4
Student	19	8
Other (including occupation unknown)	109	46
Occupational cause of dermatitis	32	14
Age > 40 years	117	50
Background of (atopic) dermatitis	76	33
Site/s		
Hands	99	43
Face	75	32
Leg	17	7
Multiple (≥ 2) sites	92	40

The mean age was 40 years; range 6–78 years and standard deviation 17 years.

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Conflict of interest: We declare we have no conflict of interest in this research.

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Table 2 Reactions to the antiseptic series in patients patch tested to the antiseptic series and benzalkonium chloride at Waikato Hospital from 1 January 2009 to 31 December 2019 (n = 233)

Antiseptic series allergen[†]	Positive	Current relevance	Relevant/positive %
Thimerosal 1%	6	0	0
2-n-Octyl-4-isothiazolin-3-one 0.1%	4	0	0
Diazolidinyl urea (Germall II) 2%	3	1	33
Povidone-iodine solution 50%	3	1	33
Imidazolidinyl urea 2%	2	0	0
Mercury ammonium chloride 1%	2	0	0
Chloroxylenol 0.5%	1	1	100
Hexachlorophene 1%	1	1	100
Ethylenediamine dihydrochloride 1%	1	0	0
Dichlorophene 1%	1	1	100
Benzalkonium chloride 0.1%	0	0	–
Glutaral	0	0	–
Chlorhexidine digluconate	0	0	–
Chlorhexidine diacetate	0	0	–

[†]The following allergens in the antiseptic series had no positive results over the study period: p-chloro-m-cresol, 2-bromo-2-nitropropane-1,3-diol (bronopol), phenyl mercuric acetate, sorbic acid, 2,6-ditert-butyl-4-cresol (BHT), 2-tert-butyl-4-methoxyphenol (BHA), chloroacetamide, 2-phenylphenol, triclosan and sodium-2-pyridinethiol-1-oxide.

current relevance to the patient (where the allergen was causally linked to the presenting dermatosis).

Patient demographics, clinical data and patch testing results were extracted from the clinical record. It was anonymised and entered in a tailored REDCap database[3] hosted at the University of Auckland. Data analysis was performed with Microsoft Excel.

Ethics approval was obtained from the Northern B Health and Disability Ethics Committee.

RESULTS

Over this period, 483 patients underwent patch testing, of which 233 had been tested to the antiseptic series and/or benzalkonium chloride. Their baseline characteristics are summarised in Table 1.

The median duration of symptoms prior to patch testing was 365 days (standard deviation 2207 days). Positive reactions were seen in 142 patients (60.9%) to one or more allergens overall. The most frequent of these are summarised in the Figures S1–S3.

At day four, 24 patients (10.3%) had a positive patch test result to one or more allergens in the antiseptic series (Table 2). Of the three patients with weak/irritant reactions to benzalkonium at day two, all became negative at day four. Five patients had allergic contact dermatitis to allergens in the antiseptic series; three reacted to antiseptic allergens and two to formalin releasing preservatives (Table 3).

DISCUSSION

We have found no cases of contact sensitisation to benzalkonium chloride in our patch testing population and a low rate of relevant contact allergy to allergens in the antiseptic series (5/233, 2.1%). None were health-care workers, a key risk group for contact dermatitis to antiseptic allergens, especially benzalkonium[4]; however, two of the five had sensitisation in health-care settings around wounds.

In addition to the use of benzalkonium chloride and other quaternary ammonium disinfectants in COVID decontamination settings[5], rising presentations of hyperkeratotic flexural erythema have been seen. This was attributed to benzalkonium chloride, used as a rinse aid in laundry and in antibacterial bath preparations. Patch

Table 3 Clinical characteristics of patients with clinically relevant reactions to the antiseptic series

Occupation	Gender/Ethnicity	Age (years)	Site of dermatosis	Relevant reaction/s	Source of allergen
Not recorded	F/Māori	37	Leg	Povidone-iodine	Skin antiseptic from wound dressings
Glazier	M/Māori	25	Hands	Chloroxylenol	Preservative in substances used at work
Retired	F/New Zealand European	74	Flanks, buttocks, thighs	Hexachlorophene	Skin antiseptic from joint surgery
Clerical - public relations	F/New Zealand European	31	Truncal, right popliteal fossa	Diazolidinyl urea (Germall II)	Personal care products
Professional - lawyer	F/New Zealand European	32	Hands	Formaldehyde, Quaternium 15, Dichlorophene	Cosmetics

F, female; M, male.

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testing of patients in published case series has not been reported.[6]

Publications on contact dermatitis in the current pandemic era document symptoms of irritant dermatitis in health-care workers[7] and case reports of contact allergy to face mask components.[8] Whether there is any relationship between the use of environmental antiseptics and allergic contact dermatitis remains to be seen. To pre-empt this, the American Contact Dermatitis Society's guidelines on hand dermatitis in the COVID era highlight potential allergens (e.g. benzalkonium chloride impregnated dressings) to avoid and recommend hand washing before and after use of antiseptics with antiviral activity.[9]

Our population had a high rate of patch test positivity (60.9%), with under-representation of Māori (12.0%) compared to the national (15.7%) and background Waikato Health Board population (22.8%).[10] This reflects the local public health system where limited access to dermatological (and by extension, patch testing) services results in more severe presentations; future research may identify whether these limitations have a particular ethnic bias.

Our study is limited by inter-observer variation: several dermatologists determined patch test results in the department over the study period. We used retrospective data from a single tertiary referral centre; this may not be representative of the rest of New Zealand. Some relevant records may be missing as there is no centralised database to store patch records.

In summary, we show an important low baseline rate of sensitisation to antiseptics which can be used as a comparator in years to come, especially as regular surface sanitisation becomes standard during the global pandemic.

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ETHICS APPROVAL

Ethics approval was obtained from the Northern B Health and Disability Ethics Committee, New Zealand.

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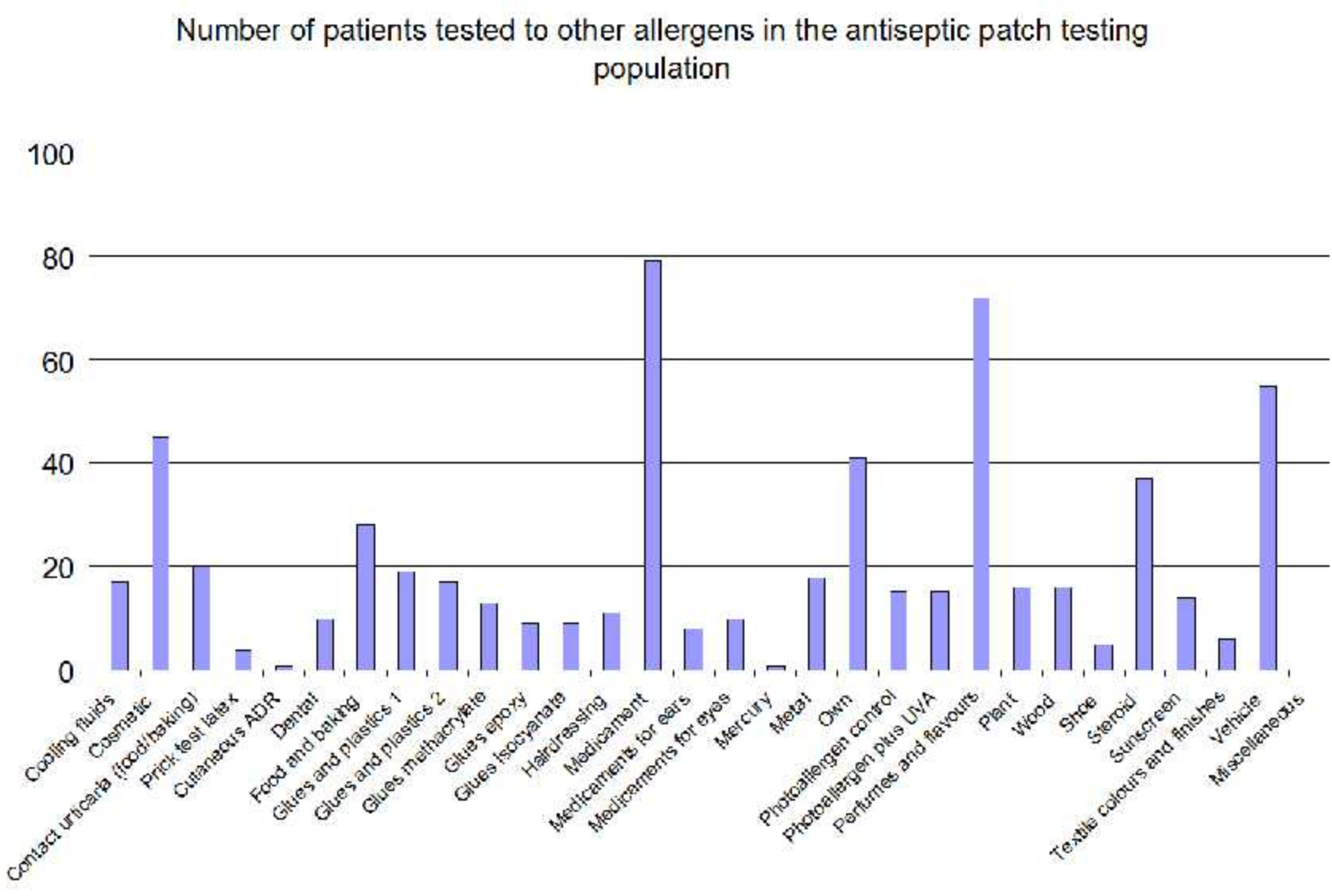
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Supporting Information

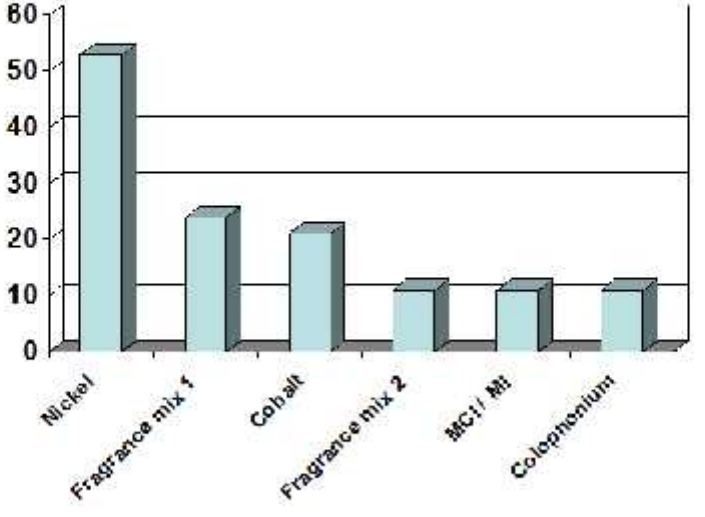
Additional Supporting Information may be found online in Supporting Information:

Figure S1. Graph showing the other 30 allergen series available in the department that the patients in the study were tested to and the frequencies of testing thereof.
Figure S2. Most frequent positive reactions were to nickel (53 patients), fragrance mix I (24), cobalt (21), with fragrance mix II, methylchloroisothiazolinone/methylisothiazolinone (MCI/MI) and colophonium affecting 11 patients each.
Figure S3. The most frequent reactions of current relevance were to thiuram mix (12 patients), fragrance mix 1 (11), nickel (10), p-phenylenediamine (8), with MCI/MI, MI and cobalt affecting seven patients each.

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Number of patients tested to other allergens in the antiseptic patch testing population
100
80
60
40
20
0
Cooling fluids
Cosmetic
Contact urticaria (food/baking)
Prick test latex
Cutaneous ADR
Dental
Food and baking
Glues and plastics 1
Glues and plastics 2
Glues methacrylate
Glues epoxy
Glues isocyanate
Hairdressing
Medicament
Medicaments for ears
Medicaments for eyes
Mercury
Metal
Own
Photoallergen control
Photoallergen plus UVA
Perfumes and flavours
Plant
Wood
Shoe
Steroid
Sunscreen
Textile colours and finishes
Vehicle
Miscellaneous

Most Frequent Positive Patch Test Reactions at 96 hours Overall



Most Frequent Positive Patch Test Reactions at 96 hours of Current Relevance

