

Patch testing experience with 1000 patients

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ABSTRACT

Background: Patch testing is a definitive tool for diagnosing allergic contact dermatitis (ACD). It reveals the prevalence and trends of contact sensitization in the community, thereby paving the way for better standard series. There is paucity of large series of patch-tested patients from India. **Aim:** To report the 9-year patch-test data from a single general dermatology centre in North India. **Methods:** Consecutive patients presenting with signs/symptoms of suspected ACD were patch tested from May 1997 to April 2006. The Indian Standard Series was used. Parthenium was tested only in selected patients and cetrimide and chloroxylenol were added to the series. **Results:** In total, records of 1000 patients (566 male, 434 female) were analyzed, yielding 1155 positive reactions in 590 (59%) patients. Footwear dermatitis was the commonest suspected diagnosis, followed by ACD to medicaments, cosmetic dermatitis and plant dermatitis. Out of the allergens that were tested in all the patients, positivity to nickel was the commonest (12.9%), followed by potassium dichromate (11.1%) neomycin (7%), mercaptobenzthiazole (6.6%), nitrofurazone (6%), colophony (5.7%), fragrance mix (5.5%) and cobalt chloride (5.4%). However, parthenium was the commonest allergen based on the proportion of patients tested with it (14.5%). In men, potassium dichromate (30%) was the commonest sensitizer and in women, nickel (43%) was the commonest to show patch-test positivity. **Conclusion:** Our study revealed higher prevalence of footwear and medicament dermatitis in comparison to existing data. Allergy to antiseptics is significant in our patients. Further collaborative studies involving patients from other parts of India are required to have an overall view of ACD in India.

Key Words: Allergic contact dermatitis, Chromate, Dermatitis medicamentosa, Footwear dermatitis, Nickel, Parthenium, Patch testing

INTRODUCTION

As human life becomes increasingly complex, our skin is exposed to an ever-increasing spectrum of chemical and biological products. Inevitably, the incidence of allergic sensitization is showing a steady rise. A recent study of the general population from an area of Norway^[1] reported sensitization rates as high as 35.4% in women and 14.8% in men. There have been no large-scale population-based studies of contact sensitization in our country; however, with rapid industrialization, westernization of society and poor labeling laws, India is ready for a contact sensitization "explosion."

Allergic contact dermatitis (ACD) develops in only a small proportion of sensitized individuals and population estimates

vary from 1.7^[2] to 6%.^[3] However, the true incidence of ACD in a society is very difficult to estimate since its diagnosis depends on several factors such as the demographic profile of patients, local industrial development, index of suspicion of the physician, and availability of patch testing. Common sensitizers also vary with place, patient profile and over the passage of time. Since optimal treatment of patients with ACD is predicated on accurate advice about prevention, regular patch testing followed by estimation of relevance is imperative in all suspected cases. We present herein our experience with patch testing in dermatology clinic attendees at a single centre at Allahabad in North India over a 9-year period.

METHODS

A total of 1003 patients with suspected ACD were involved

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in this retrospective analysis of records. As a part of our standard protocol, demographic variables, clinical history, pattern of dermatitis and clinical diagnosis were recorded. The Indian Standard Series (ISS) was used for patch testing with the following modifications: Plant antigens were tested only in patients who were strongly suspected of having plant dermatitis based on history and clinical examination. Products brought by the patient himself were also used for testing whenever appropriate. Some initial patients were tested with a preliminary version of ISS that had fewer allergens. Cetrimide (0.5% aq.) and chloroxylonol (1% pet) were added to the patch-test battery based on the personal experience of the author (AKB) regarding local sensitivity patterns.

Patches were applied to the upper back using aluminium patch-test chambers mounted on a micropore tape. They were removed after 2 days and readings were taken on day 2 and day 4 for majority of the patients. Grading of the reactions was performed based on the ICDRG guidelines and only those reactions that persisted till day 3 or day 4 were considered to be positive. Relevance (present, past, probable or unknown) was established by a post-patch test interview of the patients. It was ascertained whether the dermatitis was chronologically and clinically congruent with the following: exposure (present relevance), past exposure (past relevance), exposure at any time probable (probable relevance), or indeterminate exposure (unknown relevance).

RESULTS

Over a period of 9 years from May 1997 to April 2006, 1003 patients were included in the study; three of them were excluded from the final analysis due to the positive reactions to the control test chamber. The age of the remaining 1000 patients ranged from 8 years to 87 years with a median of 35.9 years. There were 566 males and 434 females. A total of 590 (59%) patients (336 males, 254 females) showed positivity to one or more allergens. Of these, 13 reacted only to their own product(s). There were no statistically significant differences between the sensitization rates in males and that in females. Nickel was the commonest allergen in women, with 109 of the 254 (43%) women showing positive reactions of being sensitive to it. In men, potassium dichromate was the predominant allergen with 100 of 338 (30%) reacting to it.

Suspected footwear dermatitis was the commonest clinical pattern in 310 patients, followed by suspected medicament dermatitis in 101 patients, cosmetic dermatitis in 88 patients, plant (airborne) dermatitis in 86 patients, atopic dermatitis in

76 patients, hand dermatitis in 71 patients, infective eczema in 39 patients. Other unclassified patterns of dermatitis were observed in 229 patients.

Positive reactions were noted to all the allergens tested [Table 1]. The maximum numbers of positive reactions (49.6%) were recorded in the age range of 21 to 40 years. The most frequent sensitizers were parthenium (14.6%), nickel sulfate (12.9%), potassium dichromate (11.1%), neomycin (7.0%), mercaptobenzthiazole (6.6%) and nitrofurazone (6.0%). Out of the 1155 positive reactions, relevance to the present episode of dermatitis was established in 913 (79%) patients. Relevance data is mentioned in detail in Table 2. Out of the 71 parthenium-positive patients, 63 (88.7%) had the classical airborne pattern of dermatitis. Rest of the parthenium-positive patients had disseminated photosensitive dermatitis (2 patients), generalized dermatitis (2 patients), atopic dermatitis (2 patients) and hand dermatitis (2 patients).

Among the 310 patients with suspected footwear dermatitis, 190 (61.3%) showed positivity to one or more allergens. Details of positivity in these patients are presented in Table 3. A higher rate of patch-test positivity (68%) was observed in patients with dermatitis medicamentosa, who showed positivity to 12 different allergens [Table 4].

In metal allergic patients, 52 (41.4%) of patients showing positivity to nickel had relevance to the current dermatitis, whereas 59.6% had past relevance correlating with ear piercing. On the other hand, 93.6% of chromate sensitive reactions had obvious relevance to the present dermatitis. Out of the 111 chromate-sensitive patients, 66 (59.5%) had footwear dermatitis, 22 (19.8%) had construction-work related hand/foot dermatitis and the rest had other patterns of dermatitis. Cobalt positivity was associated in all cases with concurrent positivity to nickel (41.8%), potassium dichromate (71%) or both nickel and potassium dichromate (23.6%).

DISCUSSION

Almost 60% of all patch-tested patients in this study had one or more positive reactions. This figure is much higher than the positivity rate of 32.3% that was reported recently from Turkey in a very similar study^[4] conducted over a comparable period. However, prior studies from other parts of India^[5,6] have reported patch-test positivity rates comparable to those seen in our patients. Our tropical climate may be partly responsible for this phenomenon. A more prosaic reason is possibly the low overall rate of patch testing in our patients, owing to the inconvenience and loss of wages associated with

Table 1: Patch-test positivity in study subjects

Allergen	Total positives	Total No. of patients tested	Percentage
Potassium dichromate 0.5%	111	1000	11.1
Neomycin sulfate 20%	70	1000	7
Cobalt chloride 1%	54	1000	5.4
Benzocaine 5%	20	1000	2
Formaldehyde 1%	11	1000	1.1
4-phenylenediamine 1%	53	1000	5.3
Parabens 15%	24	1000	2.4
Nickel sulfate 5%	129	1000	12.9
Colophony 20%	57	1000	5.7
Gentamicin 20%	25	1000	2.5
Propylene glycol 2%	18	1000	1.8
Mercapto mix 2%	62	964	6.4
Epoxy resin 1%	8	1000	0.8
Fragrance mix 8%	55	1000	5.5
Mercaptobenzthiazole 2%	66	1000	6.6
Nitrofurazone 2%	60	1000	6
Polyethylene glycol (400) 100	10	1000	1
Chlorocresol 1%	12	1000	1.2
Lanolin alcohol 30%	2	1000	0.2
Balsam of Peru 25%	23	1000	2.3
Thiuram mix 1%	33	1000	3.3
Chinoform 3%	19	1000	1.9
Kathon CG 0.67%	6	926	0.65
Ethylenediamine hydrochloride 1%	3	926	0.3
Black rubber mix 0.6%	3	978	0.3
p-tert-butyl phenol 1%	7	978	0.7
Quaternium 15 1%	1	913	0.1
<i>Parthenium hysterophorus</i> 1%	71	487	14.6
<i>Xanthium strumarium</i> 1%	6	61	10
<i>Chrysanthemum</i> 1%	3	58	5.1
Cetrimide 0.5%	55	1000	5.5
Chloroxylenol 1%	12	1000	1.2

the three visits in 4 days that are required for this procedure. This would lead to artificially high rates of patch-test positivity, since only the more clinically suggestive patients would be submitted to patch testing. This also explains the relatively higher relevance rate (79%) observed in this study in comparison to the reports from western countries. Interestingly, recent reports from India have reported even higher relevance rates.^[6]

There was no statistically significant difference in the sensitization rates between males and females in this study group. In contrast, many prior studies have reported higher rates of patch-test positivity in females^[7,8] and some in males.^[9] Most of this disparity between the sexes can be accounted for by the high rates of nickel positivity in women due to ear piercing. This trend was also observed in our patients with almost 85% (109 out of 129) of nickel-positive patients being women. However, in this study, 100 out of the 111 (90%) chromate-sensitive patients were men and this nullified the effect of the sex disparity in nickel sensitivity.

Similar to this study, high rates of chromate positivity have also been reported by Sharma *et al.*^[7] from Chandigarh.

Western countries have reported a sharp decline in chromate positivity since the addition of ferrous sulfate to cement, which converts the easily absorbable hexavalent chromium to the less-sensitizing trivalent form.^[10] In France, the removal of chromium from a popular brand of household bleach resulted in a dramatic decline in chromate sensitivity in women.^[11] However, in our patients, the main source of chromium was from leather footwear. Wearing thick absorbent socks and using other nonchromate chemicals for tanning and curing leather can minimize this form of exposure.

In this study, the commonest clinical pattern was footwear dermatitis followed by medicament and airborne contact dermatitis. In contrast, most of the large studies from abroad report hand dermatitis as the commonest pattern.^[12-14] This difference may be due to variations in local culture, customs, occupational factors and climate. For instance, footwear dermatitis may be common in our patients due to poor quality of tanning of the leather, the practice of wearing shoes without socks and a hot and humid climate. Chemicals such as potassium dichromate (34.2%), mercaptobenzthiazole (30%) and mercapto mix (28%) were the leading allergens in patients with footwear dermatitis in our cohort. A significant number

Table 2: List of allergens with relevance

Allergen	Positives	Relevance			
		Present	Past	Probable	Unknown
Nickel sulfate	129	52	77	-	-
Potassium dichromate	111	104	-	4	3
<i>Parthenium hysterophorus</i>	71	71	-	-	-
Neomycin	70	66	3	-	1
Cobalt chloride	54	10	-	1	43
Mercapto mix	62	57	-	4	1
Mercaptobenzthiazole	66	62	-	4	-
Nitrofurazone	60	25	35	-	-
Patients' own material	58	58	-	-	-
Colophony	57	50	-	5	2
Fragrance mix	55	46	-	7	2
<i>p</i> -phenylenediamine	53	48	3	2	-
Thiuram mix	33	26	-	5	2
Gentamicin	25	25	-	-	-
Parabens	24	20	1	3	-
Balsam of Peru	23	21	-	1	1
Benzocaine	20	6	-	5	9
Chloroxylenol	20	19	1	-	-
Chinoform	19	19	-	-	-
Propylene glycol	18	17	1	-	-
Chlorocresol	12	12	-	-	-
Formaldehyde	11	5	0	1	5
Polyethylene glycol 400	10	10	-	-	-
Xanthium	6	5	-	-	1
Kathon CG	6	5	-	1	-
Chrysanthemum	3	3	-	-	-
Black rubber mix	3	2	-	-	1
Wool alcohol	2	2	-	-	-
Cetrimide	55	53	-	2	-
Epoxy resin	8	7	-	1	-
Quaternium 15	1	1	-	-	-
Ethylenediamine hydrochloride	3	-	-	1	2
<i>p</i> -tert-butyl phenol formaldehyde resin	7	6	-	-	1
Total	1155	913	121	47	74

Table 3: Sensitivity rates of 190 patch-test positive patients with suspected footwear dermatitis

Allergens	Number of positive reactions (%)
Potassium dichromate	65 (34.2)
Mercaptobenzthiazole	57 (30)
Mercapto mix	53 (28)
Nickel	42 (22)
Colophony	23 (12)
Nitrofurazone	19 (10)
Neomycin	19 (10)
<i>p</i> -phenylenediamine	11 (5.5)
Gentamicin	5 (2.6)

of these patients also reacted to topical antimicrobials. The emergence of topical medicaments, particularly antibiotics as important allergens in patients with foot dermatitis has also been documented recently by Holden and Gawkrödger^[15] from England and Rani *et al.*^[16] from Pakistan.

Prior Indian studies from North India have reported airborne (parthenium) dermatitis as the leading pattern,^[6,7] while some have found hands and/or feet^[5] dermatitis to be the most frequent sites affected. In our series, parthenium dermatitis

Table 4: Sensitivity rates of 68 patch-test positive patients with suspected dermatitis medicamentosa

Allergens	Number (%) of positive reactions
Cetrimide	19 (28)
Nitrofurazone	17 (25)
Neomycin	16 (23.5)
Chloroxylenol	8 (12)
Nickel	8 (12)
Potassium dichromate	8 (12)
Chinoform	6 (9)
Parabens	5 (7)
Propylene glycol	5 (7)
Gentamicin	4 (6)
Chlorocresol	4 (6)
Polyethylene glycol	2 (3)

is under-represented in numerical terms in spite of being the commonest pattern seen in the clinic. This is because less than half of the patients with parthenium dermatitis were tested with it. Even then, it was proportionately the commonest allergen in our series. Because many parthenium sensitive patients presented with a highly distinct pattern of dermatitis, testing was not performed due to the risk of very strongly positive reactions. Sometimes the dermatitis was

so unremitting that corticosteroids could not be sufficiently lowered to patch test them. Men predominated in the parthenium sensitive group with 61% of the parthenium-positive patients being males. This male predominance has been reported earlier by several workers.^[5-7] and reflects greater outdoor exposure in men. Similar to our findings, Sharma *et al.* recently reported the varied clinical patterns of parthenium dermatitis viz. classical airborne, chronic actinic dermatitis type and mixed type.^[17] They postulated that the differing patterns of parthenium dermatitis are a function of time; dermatitis always starts as the classical airborne pattern and gradually changes to an actinic or mixed pattern. While this is probably true in many cases, in our opinion, clinical pattern of parthenium dermatitis possibly depends on other factors such as occupation, clothing pattern, underlying atopy and route of (re)exposure. It has been argued by Mahajan *et al.*^[18] that a generalized pattern of dermatitis in these patients may be the result of systemic, possibly inhalational exposure resulting in a systemic contact dermatitis.

Other compositae plants such as xanthium and chrysanthemum were tested in relatively few patients ($\approx 5\%$) in our cohort based on the history of specific exposure.

In this study, medicament dermatitis was the second most common diagnosis, which has been a relatively a small subset in prior studies of general dermatology patients.^[5-7] Our patch-test yield was increased by the inclusion of cetrimide and chloroxylenol in the series, which accounted for an additional 67 positive reactions. Out of these, 27 patients had clearly relevant medicament exposure leading to the present dermatitis. We added cetrimide to our series based on our earlier study in which it was found to be a significant source of dermatitis medicamentosa.^[19] In most of the cases in this study, exposure was related to Savlon, which contains cetrimide and chlorhexidine gluconate. Cetrimide positivity was observed in 55 (5.5%) patients; this is much higher than the most reported series involving a recent multicentric study from France.^[20] However, a recent study of 50 patients with cosmetic dermatitis from Rohtak, India^[21] reported cetrimide positivity in 12.2% cases. These high rates of cetrimide allergy may reflect increasingly indiscriminate use of antiseptic agents in bath water and as a final rinse while washing clothes. However, cetrimide can produce irritant reactions at the concentration used by us (0.5%)^[22] and inclusion of some mild irritant reactions in our cases cannot be ruled out.

Chloroxylenol is the active ingredient of the popular antiseptic Dettol[®] and it also cross-reacts with the preservative chlorocresol.^[23] In our series, 12 (1.2%) patients each reacted

to chloroxylenol and chlorocresol with four patients reacting to both the allergens.

Among antimicrobials, neomycin and nitrofurazone were the leading allergens, with 7% and 6% positivity respectively, followed by gentamicin (2.5%). However, nitrofurazone use has declined over the years but its widespread use in the past^[19] in adhesive bandages and ointments still contributes to significant patch-test positivity. Reflecting this trend, nitrofurazone positivity in our patients was due to past topical exposure to the drug in almost 60% of positive patients. The rising use of topical gentamicin and neomycin was also reflected by high rates of positivity to these antimicrobials. In contrast to nitrofurazone, positive reactions to neomycin and gentamicin were relevant to the present exposure in more than 90% of cases.

Patients with hand eczema had a less than 50% positivity rate in our study with majority of them showing positivity to nickel. Nickel is a well-known cause of hand eczema and both topical and systemic exposure have been linked to it.^[24]

To conclude, patch testing at our centre over the past 9 years has revealed that the commonest allergens in our patient population are parthenium, nickel, potassium dichromate and neomycin. Significant positivity is still observed with nitrofurazone despite its decreasing use and the rise in gentamicin positivity. Antiseptics such as cetrimide and chloroxylenol are also important allergens in our patient population. These agents merit further testing in other areas of the country and if significant positivity rates are found, a case for their inclusion in the ISS can be made. In view of the differences in clinical patterns, positivity rates etc. reported from different parts of India, we owe it to our patients to clarify the epidemiology of this important problem. A multicentric study from all the major geographic areas of the country is required to initiate further studies in this matter.

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