

Common contact sensitizers in Chandigarh, India

A study of 200 patients with the European standard series

V. K. SHARMA AND A. CHAKRABARTI

Department of Dermatology, Venereology & Leprology, Postgraduate Institute of Medical
Education and Research, Chandigarh-160012, India

200 patients (122 male, 78 female) with suspected allergic contact dermatitis were patch tested with the European standard series (ESS) and the results compared with other Asian centres. 131 (65.5%) patients showed 1 or more patch test positives to the ESS. Patch tests were positive to all allergens except primin. Potassium dichromate was the most common allergen (20.5%) followed by nickel sulfate (16.5%), SQL mix (14%), PPD (11.5%), cobalt (8%), fragrance mix (7.5%), formaldehyde (6.5%), colophony (5.5%), neomycin sulfate and mercapto mix (5% each). In women, nickel sulfate was the commonest allergen (30.8%) followed by SQL mix (16.7%) and potassium dichromate (15.4%). In men, potassium dichromate was the commonest sensitizer (23.8%) followed by SQL mix and PPD (12.3% each). Our results are at variance with other centres in Asia. SQL mix was able to detect less than $1/2$ (42.2%) of patients allergic to ethanolic dilutions of ether extracts of parthenium. We conclude that the European standard series, with exclusion of primin, is suitable for detection of allergic contact dermatitis in India. However, SQL mix is not a adequate screen for parthenium sensitivity and patch testing with extracts of the plant should be continued, wherever indicated.

Key words: allergic contact dermatitis; standard series; patch testing; chromate; nickel; sesquiterpene lactone mix; para-phenylenediamine; cobalt; fragrance mix; formaldehyde; colophony; neomycin; mercapto mix; parthenium; compositae; plants. © Munksgaard, 1998.

Accepted for publication 29 September 1997

Allergic contact dermatitis (ACD) in India is not an uncommon disorder and accounts for 10–15% of dermatological patients. Patch testing is frequently carried out with locally-prepared allergens by using indigenous patch test units (1). There was no standard patch test series available in India till recently, but efforts are on to market a standard series approved by the Contact and Occupational Contact Dermatoses Forum of India (CODFI). We used the standard European patch test series to elicit the common causes of allergic contact dermatitis in Chandigarh, India, and compared them with other Asian centres.

Patients and Methods

200 patients with suspected ACD were recruited for the study. Clinical details, exacerbating factors, type of dermatitis and suspected allergens were recorded. The European standard series (ESS) was obtained from Chemotechnique Ltd., Sweden. Patch testing was carried out on the upper back

using aluminium patch test chambers mounted on Micropore by standard methods. Patch test readings were taken after 2 and 3 days and only reactions still positive at 3 days were considered positive. In addition, patch testing with ethanolic dilutions of ether extract of *Parthenium hysterophorus* leaves 1:200 and 1:100 was carried out wherever indicated.

The plant extracts were prepared by the method recommended by Hollister-Stier, USA, with slight modifications (2, 3). In brief, about 50 mature plants were collected and their flowers and leaves were separated and cut into small pieces. They were wrapped in brown paper and kept in an incubator at 37°C. The dried plant material was powdered with a tissue homogenizer and immersed in the solvent diethyl ether in conical sealed flasks covered with black craft paper. Approximately 500 ml of diethyl ether (Bengal Chemicals) was used for 50 g of plant power. It was kept for 24 h in a cool shaded place with frequent shaking. The extract thus obtained was filtered through What-

mann No. 1 filter paper. The ether was evaporated by keeping the beaker containing extract in a shaking water bath at 37°, till only 5 ml of the resinous extract remained (the stock solution). Appropriate dilutions (1:100 and 1:200) were prepared in ethanol every 3 months and stored in screw-capped amber-coloured bottles at 4°C. Diethyl ether was chosen for extraction as it is easily available and cheap. The dilutions were prepared in ethanol as per practice in the clinic. Parthenium extract was tested in 20 male agriculture workers without dermatitis to rule out false-positive reaction (3).

Results

The 200 patients included 122 males and 78 females, with age ranging from 9–85 years (mean – 39.8 years). Airborne contact dermatitis (ABCD), affecting the face, neck and flexures of the arms and legs, was the most common pattern seen, in 78 patients, followed by localized allergic contact dermatitis (ACD) affecting parts other than the hands and feet in 49 patients, hand dermatitis in 48 patients, foot dermatitis in 22 patients, and hand and foot dermatitis together in 13 patients. 10 patients had a combination of 2 clinical patterns.

131 (65.5%) patients showed 1 or more positive patch tests, of whom 76 were males and 55 were

Table 1. Patch test results according to sex

Chemical (concentration % and vehicle)	No. positive patch tests		
	total no. (%) (n=200)	men no. (%) (n=122)	women no (%) (n=78)
potassium dichromate (0.5, pet.)	41 (20.5)	29 (23.8)	12 (15.4)
4-PPD (1, pet.)	23 (11.5)	15 (12.3)	8 (10.3)
thiuram mix (1, pet.)	9 (4.5)	6 (4.9)	3 (3.8)
neomycin sulfate (20, pet.)	10 (5)	7 (5.7)	3 (3.8)
cobalt chloride (1, pet.)	16 (8)	13 (10.7)	3 (3.8)
benzocaine (5, pet.)	5 (2.5)	4 (3.3)	1 (1.3)
nickel sulfate (5, pet.)	33 (16.5)	9 (7.4)	24 (30.8)
quinoline mix (6, pet.)	5 (2.5)	4 (3.3)	1 (1.3)
colophony (20, pet.)	11 (5.5)	10 (8.2)	1 (1.3)
parabens (15, pet.)	4 (2)	4 (3.3)	0 (0.0)
black rubber mix (0.6, pet.)	3 (1.5)	3 (2.5)	0 (0.0)
wool wax alcohols (30, pet.)	8 (4)	7 (5.7)	1 (1.3)
mercapto mix (2, pet.)	10 (5)	7 (5.7)	3 (3.8)
epoxy resin (1, pet.)	3 (1.5)	3 (2.5)	0 (0.0)
balsam of Peru (25, pet.)	3 (1.5)	1 (0.8)	2 (2.6)
4 tert butyl formaldehyde resin (1, pet.)	2 (1)	0 (0.0)	2 (2.6)
MBT (2, pet.)	8 (4)	6 (4.9)	2 (2.6)
formaldehyde (1, aq.)	13 (6.5)	9 (7.4)	4 (5.1)
fragrance mix (8, pet.)	15 (7.5)	11 (9)	4 (5.1)
SQL mix (0.1, pet.)	28 (14)	15 (12.3)	13 (16.7)
quarternium 15 (0.1, pet.)	5 (2.5)	1 (0.8)	4 (5.1)
primin (0.01, pet.)	0 (0.0)	0 (0.0)	0 (0.0)
Kathon CG (0.67, aq.)	2 (1)	2 (1.6)	0 (0.0)

Table 2. Frequency of sensitization according to age group

Age group (years)	Men		Women	
	no. tested	no. (%) positive	no. tested	no. (%) positive
up to 20	6	3 (50.0)	9	5 (55.6)
21–40	35	18 (51.4)	42	28 (66.7)
41–60	64	46 (71.9)	26	21 (80.7)
above 60	17	9 (52.9)	1	1 (100.0)

Table 3. Patch test results to parthenium extract according to sex

No. patients	Male (n=88)	Female (n=41)	Total (n=129)
positive to parthenium extract	43 (48.9%)	21 (51.2%)	64 (49.6%)

females. The distribution of sensitization to the allergens according to sex is shown in Table 1.

Positive reactions were noted to all allergens in the ESS except primin (Table 1). The most common allergen was potassium dichromate (20.5%), followed by nickel sulfate in 16.5% and SQL mix (sesquiterpene lactone mix) in 14%. These were followed in order of frequency by PPD (11.5%), cobalt (8%), fragrance mix (7.5%), formaldehyde (6.5%), colophony (5.55), neomycin sulfate and mercapto mix (5% each). Reaction to other allergens occurred in 4.5% or less.

The majority of positive reactions to chromate were + (27 patients) followed by ++ (13 patients) and +++ (1 patient).

Nickel sulfate (30.8%) was the commonest allergen in women, followed by SQL mix (16.7%) and potassium dichromate (15.4%). In men, potassium dichromate (23.8%) was the commonest sensitizer, followed by SQL mix and PPD (12.3% each), and cobalt chloride (10.7%).

In men, allergic reactions were most frequent (72%) in the 41–60 years age group, followed almost equally by those above 60 years (52.0%), between 21–40 years (51.4%) and those below 20 years (50%). Amongst women, contact sensitivity was most frequent in the 41–60 years group (80.7%), followed by those between 21–40 years (66.7%) and below 20 years (55.6%) (Table 2). There was only 1 woman above the age of 60 years who was sensitized to cobalt chloride.

In men, potassium dichromate was the commonest allergen in all age groups except the elderly, in whom SQL mix was the commonest allergen. In the 21–40 years group, the next most common allergen was cobalt chloride, while it was PPD in the 41–60 years group. Contact sensitivity to nickel was the commonest allergen in women of all age

groups. SQL mix was the next most common allergen in women aged 21–60 years.

123 patients (88 male and 41 female) and 20 male controls were tested with ethanolic dilutions of ether extracts of parthenium and 43 males (49%) and 21 females (51.5%) were positive to parthenium (Table 3), only 1 out of 20 controls being positive to parthenium. Only 27 (42.2%) patients (14 males, 13 females) were positive to both parthenium and SQL mix. In only 1 instance was contact sensitivity to SQL mix detected in the absence of parthenium sensitivity.

Discussion

131 patients (65.5%) out of 200 patch tested with suspected ACD showed 1 or more positive reactions. This figure is comparable with the findings of El-Rab et al. (4) but higher than in the Zhang et al. (5) and Hammershoy studies (6).

The commonest clinical pattern in our study was contact dermatitis of the airborne type, in contrast to hand dermatitis in other studies (7–9). Parthenium grows in abundance in this city and its surrounding areas and is the commonest sensitizer (10).

The increased occurrence of contact sensitivity in women, as in our study, is well-known (6). Most studies indicate a decrease in the incidence of ACD with age (11), but in our study, positive reactions occurred more commonly in the middle-aged and elderly. This may be due to the inclusion of less patients above 65 years of age, and parthenium dermatitis being common in the elderly.

The pattern of contact sensitivity in our patients differs from that of other Asian centres where ESS or similar series has been used for patch testing (Table 4). In most of these centres namely Saudi Arabia (4), Beijing (5), Shanghai (12), Taipei (13) and Singapore (14), nickel sulfate has been the commonest allergen, whereas it was the 2nd most common allergen in Hong Kong (15), Manipal (16) and our study. Potassium dichromate was the most frequent sensitizer in our study, while it rank-

ed 2nd in all the other centres except Hong Kong and Singapore. Of the Asian centres, the incidence of chromate sensitivity is extremely low in Hong Kong (1.6%) and Singapore (2.7%) (Table 4). While the reason for the low incidence in Hong Kong is not known, in Singapore it is attributed to the decline in the construction industry. The cement in Singapore contains no ferrous sulfate (14). On the other hand, the high incidence of 35% in Saudi Arabia has been attributed to expansion in the construction industry. Fragrance mix was the commonest allergen in Hong Kong (15) and the 2nd most common allergen in Taipei (13) and Singapore (14), but ranked 6th in our study. The other common allergen in our study was PPD, the incidence of which is low in the other Asian centres except Beijing (5) and Saudi Arabia (4). SQL mix, which was the 3rd most common allergen in our study, has not been tested in any of the other Asian centres.

The incidence of chromate sensitivity in our study is rather high and especially in women (15.4%), the reported figures for women ranging between 1–7% (4, 17). Possible sources were leather footwear and artificial jewellery in 5 each, and in the remaining 2 housewives, other sources of chromate, such as detergent, bleaches, fabrics, safety matches, could have been responsible. In men, the source of chromate was occupational in 18 (62.1%) patients, including cement in 15, machine oil in 2 and welding in 1 patient. The non-occupational sources were leather footwear (6) and spectacles (3). In the remaining 2 patients, the source of chromate could not be determined. In all but 4 patients, positive to chromate, the reaction was relevant and a clear source of exposure to chromate was recorded. False-positive reactions were excluded by ignoring D 2 positives that became negative by D 3. We believe that there is a genuinely high incidence of chromate sensitivity, due to exposure in cement, leather, cheap jewellery, etc. However, since patch testing was not carried out with a lower concentration of potassium dichromate, a few irritant reactions cannot be totally excluded.

Table 4. Common allergens (%) in different Asian countries

	Allergen	Chandigarh	Hong Kong (15)	Saudi Arabia (4)	Beijing (5)	Shanghai (12)	Taipei (13)	Singapore (14)
1.	nickel sulfate	16.5	16.4	37.5	21.7	16.0	13.0	17.0
	potassium							
2.	dichromate	20.5	1.6	35.0	17.4	11.0	–	2.7
3.	fragrance mix	7.5	19.5	15.0	8.7	9.0	10.7	13.3
4.	cobalt chloride	8.0	11.3	32.0	17.4	6.0	10.7	4.5
5.	PPD	11.5	0.4	9.0	15.2	1.0	–	4.5
6.	SQL mix	14.0	NT	NT	NT	NT	NT	NT

NT: not tested.

Nickel, the ubiquitous allergen, ranked 2nd in our study, but when analyzed according to sex, the incidence in females (30.5%) is higher than in other centres in Asia. This can be attributed to the universal practice of ear piercing by Indian women and exposure to jewellery.

Cobalt chloride was a frequent sensitizer in Beijing (5), Taipei (13) and Saudi Arabia (4), but only 8% of our patients were allergic to this metal. Allergy to cobalt accompanies chromate sensitivity in men, as occurred in 34.5% of our cases, and nickel sensitivity in women, co-sensitivity to cobalt in nickel-sensitive subjects occurring in about 29% (18). Only 3 women reacted to cobalt, of whom 1 had co-sensitivity to chromate and none to nickel, which is surprising, considering the high incidence of nickel sensitivity in women in our study.

Allergy to PPD occurred in 23 (11.5%) patients, the use of hair dye accounting for 10 (43.5%), and footwear for 2 (8.7%), while in the remaining 11 patients, the source was not clear and exposure to rubber footwear could have been responsible.

Reactions to other allergens occurred in less than 8% of patients. The sex discrepancy in the reaction to colophony, with men being sensitized significantly more than females, is puzzling as many opportunities exist for a person to become exposed to rosin, and the NACDG has a list of over 300 products that contain rosin (19).

None of the patients reacted to primin, which is not a cause of plant dermatitis in India. Sensitivity to SQL mix was detected in 14% which is strikingly higher than the reported 1.5% (20), 1.8% (21) and 3.5% (22), in other studies. To the best of our knowledge, we are reporting sensitivity to SQL mix in parthenium dermatitis for the 1st time. The high figures reflect the high incidence of sensitivity to parthenium in this region and false-positivity was ruled out by testing 20 controls, of which only 1 was positive (3). Though sensitivity to SQL mix was high, even then, detection of contact sensitivity to parthenium with this mix was not complete. SQL mix was able to detect only 42.2% of those cases that were positive to ethanolic dilutions of ether extracts of the plant. The fact that the SQL mix is not an adequate screen for Compositae allergy is known with other Compositae plants (23). This is because the main structural group of the SQL of the Compositae plant in question may differ from the 3 lactones in the SQL mix, as is the case with parthenin, the principal allergen in *Parthenium hysterophorus*.

Parthenium dermatitis is reported to have a male predominance, especially in agricultural workers (3, 24), but the results of our study are to the contrary. Both men and women were equally affected, with a tendency for female predominance

that did not attain statistical significance. Female predominance was noted both with respect to SQL mix and ethanolic dilutions of ether extracts of parthenium. Contact sensitivity develops on direct exposure to the plant, and men and women irrespective of their occupation are equally exposed to this plant, as it grows widely in every vacant nook and corner in this region. This reflects the changing clinical pattern of parthenium dermatitis.

In conclusion, the European standard series, with the exclusion of primin, is suitable for the detection of ACD in India. Potassium dichromate (20.5%), nickel sulfate (16.5%), SQL mix (14%) and PPD (11.5%) are the 4 most common sensitizers in Chandigarh, India, which is at variance with other Asian centres. As SQL mix is not an adequate screen for parthenium sensitivity, patch testing with extracts of the plant is a must where it is the suspected allergen. Parthenium extracts can be made in water, acetone, ethanol or ether. Ether extracts approximately 3× the amount of parthenolide compared to an aqueous extract (25). Acetone and ethanol were considered marginally better than ether in extraction of parthenolide in another study (26). Aqueous extracts are widely used in India (27) but we have standardized extraction with ether and it has been used successfully for more than 5 years.

References

1. Pasricha J S. *Contact dermatitis in India*. New Delhi: The Offsetters, 1988: 12.
2. Sharma S C. A study of factors involved in photosensitivity dermatitis and use of phototherapy in the treatment of photosensitivity. MMS, Thesis, University of Dundee, UK, 1983: 101–105.
3. Mahajan V K, Sharma V K, Kaur I, Chakrabarti A. Contact dermatitis in agriculture workers: role of common crops, fodder and weeds. *Contact Dermatitis* 1996; 35: 373–374.
4. El-Rab MOG, Al-Sheikh O A. Is the European standard series suitable for patch testing in Riyadh, Saudi Arabia? *Contact Dermatitis* 1995; 33: 310–314.
5. Xiao-Min-Zhang, Niklasson B, Shi-Yin Li. Patch testing in cases of eczema and dermatitis in Beijing, China. *Contact Dermatitis* 1991; 25: 224–229.
6. Hammershoy O. Standard patch test results in 3225 consecutive Danish patients from 1973 to 1977. *Contact Dermatitis* 1980; 6: 263–268.
7. Agrup G. Hand eczema and other hand dermatoses in South Sweden. *Acta Dermatol-venereologica* 1969; 49 (suppl 61): 73, 74, 84.
8. Goh C L. An epidemiological comparison between occupational and non-occupational hand eczema. *Br J Dermatol* 1989; 120: 77–82.
9. Holness D L, Nethercott J R, Adams R M et al. Concomitant positive patch test results with standard screening tray in North America, 1985–1989. *Contact Dermatitis* 1995; 32: 289–292.
10. Sharma V K, Kaur S. Contact dermatitis to plants in

- Chandigarh. *Indian J Dermatol Venereol Leprol* 1987; 53: 26–30.
11. Weksler M E. The senescence of the immune system. *Hospital Practice* 1981; 16: 75–84.
 12. Xue M W, Yin F L, Xia F C, and P Z, Mei L Y. Patch testing with European standard series in Shanghai. *Contact Dermatitis* 1994; 30: 173–174.
 13. Sun C C. Epidemiology of contact dermatitis in Taiwan. *Proceedings 1st Pacific Symposium on Environmental and occupational dermatology*, Singapore 22–24 June, 1991, p. 74.
 14. Lim J T E, Goh C L, Ng S K, Wong W K. Changing trends in the epidemiology of contact dermatitis in Singapore. *Contact Dermatitis* 1992; 26: 321–326.
 15. Lee T Y, Lam T H. Patch testing of 490 patients in Hong Kong. *Contact Dermatitis* 1996; 35: 23–26.
 16. Sheno S D, Srinivas C R, Balachandran C. Results of patch testing with a standard series of allergens at Manipal. *Indian J Dermatol, Venereol Leprol* 1994; 60: 133–135.
 17. Cronin E, Metals. In *Contact dermatitis*. Edinburgh, Pa: Churchill Livingstone. 1980: 279–390.
 18. Menne T, Borgan O, Green A. Nickel allergy and hand dermatitis in a stratified sample of the Danish female population: an epidemiological study including a statistic appendix. *Acta Dermato venereologica* 1982; 62: 35–41.
 19. Mitchell J C, Fisher A A. Dermatitis due to plants and spices. *Contact Dermatitis*, 3rd edition. Philadelphia, Pa: Lea and Flebiger, 1986: ch 24, 418–453.
 20. Ducombs G, Benezra C, Talaga P et al. Patch testing with the “sesquiterpene lactone mix” a marker for contact allergy to compositae and other sesquiterpene-lactone plants. *Contact Dermatitis* 1990; 22: 249–252.
 21. Ross J S, Du Peloux Menage H, Hawk J L M, White I R. Sesquiterpene lactone contact sensitivity. Clinical patterns of compositae dermatitis and relationship to chronic actinic dermatitis. *Contact Dermatitis* 1993; 29: 84–87.
 22. Paulsen E, Andersen K E, Hausen B M. Compositae dermatitis in a Danish dermatology department in one year. *Contact Dermatitis* 1993; 29: 6–10.
 23. Green C, Ferguson J. Sesquiterpene lactone mix is not an adequate screen for compositae allergy. *Contact Dermatitis* 1994; 31: 151–153.
 24. Lonkar A, Jog M K. Epidemic contact dermatitis from *Parthenium hysterophorus*. *Contact Dermatitis Newsletter* 1972; 11: 291.
 25. Hausen B M. A simple method of isolating parthenolide from *Tanacetum* and other plants. *Contact Dermatitis* 1991; 24: 153–155.
 26. Tiwari V D, Sohi A S, Chopra T R. Allergic contact dermatitis to *Perthenium hysterophorus*. *Indian J Dermatol Venereol Leprol* 1979; 45: 392–400.
 27. Pasricha J S. Contact dermatitis caused by plants. In: Pasricha J S, Sethi N C, (eds): *Contact dermatitis in India*. Bombay, Lyka Lab Publications, 1981: 24–26.

Address:

V. K. Sharma
 Department of Dermatology, Venereology & Leoprology
 Postgraduate Institute of Medical Education
 and Research
 Chandigarh-160012
 India