

Allergic contact dermatitis: Sex differences

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Using the repeated insult test, Jordan & King (1977) observed that contact sensitization was more readily induced in females than in males. We reviewed data obtained by maximization testing of 185 test substances of which 73 were allergenic. The overall male-female sensitization rates were respectively 9.9 and 9.2 %. Only with the weakest allergens (sensitizing one or two subjects of a 25-member panel) was there a possibility of female predominance in that there were twice as many panels having only female reactors as males exclusively. In these instances, the test agents were mainly fragrances. We have concluded that sex differences, in the prevalence of sensitization to particular substances, reflect past exposure and are not due to sex differences.

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Jordan & King (1977) recently reported a striking difference between males and females in the capacity to become contact sensitized. Using a modification of the Draize repeated insult test and 10 different allergens, he found that with three agents the sensitization rate was significantly greater in females; moreover, with five of the remaining seven compounds, there was a trend toward greater sensitizability of the female. The overall sensitization rate was 10.6 for females and 4.4 in males.

If true, this finding has great biological significance. Contact sensitization is a useful clinical marker of cell-mediated immunity. The implication is that there might be a sex difference in T-cell dependent functions, viz., susceptibility to viral and fungus infections, allergic drug reactions, auto-immune disorders and malignancy.

Previous work in which contact allergic

dermatitis was experimentally induced in animals and humans does not support the concept that females are more easily sensitized. In the guinea pig, males and females were equally sensitizable to contact allergens (Magnusson & Kligman 1970). No sex difference was observed in experimentally induced contact sensitization in humans (Walker et al. 1967).

In this paper we shall review our experience in the course of evaluating the allergenicity of numerous substances in humans.

Methods

In the past 2 years, our laboratories have evaluated 185 materials by the updated maximization procedure for identifying contact allergens (Kligman & Epstein 1975). The test substances embraced a wide spec-

Table 1. Summation of allergic reactions according to sex and race

	White	Male Black	White	Female Black
Contact allergy	153 (9.8 %)	40 (10.4 %)	195 (9.8 %)	50 (7.4 %)
Non-reactive	1,415	342	1,799	630
Total sensitive		193 (9.9 %)		245 (9.2 %)

trum ranging from fragrances, lipsticks, make-ups, moisturizing creams, deodorants, astringents, foundation liquids and creams, cleansing lotions, hair sprays, and shampoos. The materials were evaluated in panels of 25 healthy young adults, aged 18-30. There was no particular method of selection except that the subjects were recruited from a student population who volunteered for a fee. Of the 4,624 panelists, 1,950 were males, 2,674 were female. There were 3,562 whites and 1,062 blacks. Each panel was more or less sexually balanced, always containing at least 10 members of one or the other sex.

Results

Table 1 summarizes the results. A total of

438 allergic reactions developed in the 4,624 panelists, a reaction rate of 9.5 %. Overall, 9.9 % of males and 9.2 % of females became sensitized. No significant differences were found between blacks and whites, the percentages being 8.5 % and 9.7 %. Black females were slightly less often sensitized than black males.

The allergenic materials were then sorted out into classes according to the grading system of Kligman (1966a), grade V being very strong sensitizers and grade I very weak (two or fewer subjects being sensitized). With grade I sensitizers there was a slight suggestion of a sex difference. There were 28 allergens in this class, mainly perfumes and some eye make-ups. In 14 panels the sensitized subjects were exclusively females while in seven only males were

Table 2. Male vs. female sensitization in relation to strength of sensitizer

Grade of sensitizer *	Number of allergic materials	Male only	Female only	Male > Female	Female > Male	Female = Male
I	28	7	14	7	14	7
II	21	2	0	9	7	5
III	14	0	1	4	6	4
IV	5	0	0	3	2	0
V	5	0	0	2	2	1
	73	9	15	24	31	15

* According to Kligman (1976a) in panels of 25 subjects

I = 0-2 reactors

II = 3-7 reactors

III = 8-13 reactors

IV = 14-20 reactors

V = 21-25 reactors.

sensitized; in seven others, one male and one female became sensitized.

Discussion

We have data on 73 allergens, ranging from weak to strong, compared to Jordan's 10 allergens. No sex difference was observed. One might dispute this conclusion with grade I sensitizers in which twice as many panels (14) were exclusively females. It is of interest that these were chiefly perfumes. Of greater importance, however, is that "exclusive" generally signified that one female or one male became sensitized. Chance alone could account for such a tiny difference unless one had data on hundreds of grade I allergens, not 28 as in our series.

We hold that bonafide sex differences in prevalence rates to contact allergens reflect the intensity of past exposure. Nickel sensitivity occurs predominantly in females, as would be expected from the greater contact with jewelry. Likewise, allergy to perfumes is far more frequent in females. These disparities may soon change as males more and more adopt practices which were formerly the province of females. On the other hand, males predominate in chromium allergy because of occupational exposures such as in the cement industry.

We mention here one test substance, a perfume, in which there were eight allergic reactors, all females. We would interpret this to mean that these women had been previously exposed to the same or chemically related perfumes. The latter are, of course, complex mixtures.

Sub-clinical contact sensitization is certainly a reality. We refer to that state in which patch tests have not yet become positive but the subject has moved along the path toward clinical sensitization. The gradual acquisition of sensitization can be demonstrated with weak sensitizers, e.g. on

maximization testing (five 48-h exposures) a weak sensitizer may sensitize only a few subjects the first time. Repeating the procedure three to four more times causes a progressively greater number to reach a demonstrable level of clinical sensitization (Kligman 1966b, Kligman & Opdyke, unpublished).

This raises the question of how to select subjects for forming test panels. Should recruitment be random? Since females generally have had frequent contact with perfumes would it not be better to use "unbiased" all-male panels in perfume tests? Or perhaps, only females should be recruited to increase the sensitivity of the test? Is the latter ethical? These questions are too complex for treatment here. Our policy is to use fresh panels each time and to strike a rough sex balance.

Finally, if we are right in discounting an immunological difference between males and females, is it possible that females have more reactive, more irritable skin and thus can express inflammation more readily? Various opinions are held by dermatologists regarding whether females, the "tender sex," are more susceptible to irritants. Bjornberg (1975) put this to the test and could not demonstrate a sex difference. Our experience is concordant.

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