

Antigen recognition in Filipinos, Japanese, Chinese, and Caucasians

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INTRODUCTION

The role of genetics in antigenic sensitivity has been described among various Caucasian and non-Caucasian groups. Further, it has been reported that Chinese in Mainland China are relatively insensitive to grass pollen,¹ while their counterparts in America are twice as sensitive to grasses as Caucasians and 21 times more likely than those without this sensitivity to react to certain trees.² A similar finding has been observed in Japanese subjects.³ In addition, there are reports concerning the cross-reactivity among Japanese subjects allergic to Japanese cedars and to cypress pollen.⁴ Finally, it is known that Filipinos (who are neither Asian nor Caucasian) in America have a significantly higher serum IgE and significantly greater incidence of atopy than their American Caucasian counterparts.⁵ It was against this background that we elected to compare and contrast the grass and tree pollen reactivity of Filipinos to that of Chinese, Japanese, and Caucasian Americans.

MATERIALS AND METHODS

Forty-five Filipinos, 50 Japanese, 54 Chinese, and 540 Caucasians were prick skin tested to a group of grasses* as well as to three trees (ce-

dar, cypress, and juniper**). All patients were referred to the author for uncontrolled clinical problems of hay fever or asthma. The subjects paralleled distribution for sex, symptom severity, age, and physical findings among the four groups. Geographic distribution was generally equal among San Francisco Bay Area counties. In addition to the allergen prick test, a histamine phosphate and Coca saline control were applied to each patient. This data, patient selection, and testing methods have been described previously.³

RESULTS

The first question we asked was that if a group reacted to grasses, was there a greater risk of reacting to at least one of three trees? In all four group situations there was a significant difference in reactions to trees if the group reacted to grasses (Table 1). The odds ratio of reactivity was greatest in Japanese and least in Caucasians. Reactivity to grasses profoundly affected reactivity to at least one of three trees ($P < .0005$). All four groups exhibited grass reactivity first to amplify their sensitivity to one or more trees but the Caucasian reaction was modest compared with the Filipino, Chinese, and Japanese groups, which were two, four and six times greater, respectively. Within given groups the differences were even greater. The Japanese, for example, reacted to trees 31 times more frequently if they first reacted to grass.

In the second situation we asked

that if a group reacted to grass, was there a greater risk of reacting to any two of three trees? The answer here was affirmative—in all four cases, if a racial group reacted to grass pollens, there was a significantly greater risk that it would react to two or more trees ($P < .0005$) (Table 1). The odds ratio was similar but less than in the first situation, reflecting the diminished frequency of reactivity to a larger number of antigens. In general, there was an approximately 30% decrease in odds ratio for non-Caucasians while the Caucasian group did not diminish.

The third question elucidated whether or not there was a greater risk of reacting to all three trees if a group reacted to grasses. In three of four situations there was a significantly greater risk of reacting to all three trees if a group also reacted to grasses (Table 1). In this situation the odds ratio for Japanese remained the same as in the second situation ($P < .0001$). There was no difference with regard to the Chinese and it doubled in the case of the Filipinos. In Caucasians the odds ratio compared with the first and second situations remained essentially unchanged. The P value for Chinese in this test equaled .01, which under these conditions was assigned borderline significance. Because of the small group numbers, only values of .005 or smaller were given significance. For the other three racial groups the odds ratio was greatest for Filipinos and least for Caucasians.

To further evaluate the role of the initial grass reactions as a herald for reactions to trees, we contrasted the four groups to determine if there was a greater risk of tree reactivity

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* Bermuda-Cydon dactylon; Rye-(a) Italian rye-Lolium multiflorum, (b) Perennial rye-Lolium perenne; Timothy-Phleum pratense; Johnson-Sorshum halepense; June-Pao pratensis; Oats-(a) Wild oats-Avena barbata, (b) Wild oats-Avena fatua; Orchard-Dactylis glomerata; Redtop-Agrostis; Velvet-Holcus lanatus; Beardless wild rye-Elymus triticoides; Cultivated rye-Secale cereale.

** Western red cedar-Thuja placcata; Western juniper-Juniperus occidentalis; Arizona cypress-Cypripinus arizonica. (Hollister-Stier Laboratories, Box 3145, Spokane, Washington 99220-3153).

where there was no grass reactivity. In all four racial groups in six contrasting tests there was no significant difference in reactivity to one or more trees when the subjects did not first react to grasses (Table 2).

Seeking to analyze the racial differences in antigen recognition among the four groups we asked a different question in situation five. If a subject reacted to grasses, was there a racial difference in group reactions to at least one tree? In all

conditions the Caucasians were significantly less reactive than the other three groups ($P < .0005$). There was no difference between Chinese and Japanese, Chinese and Filipino, or Japanese and Filipinos. The odds ratios of the significantly different groups were greatest among Japanese and Chinese versus Caucasians and least among Filipinos versus Caucasians (Table 2).

When we contrasted the three grass-reactive non-Caucasian groups

we found no significant differences. When the Caucasian group was contrasted with the other ethnic groups, a significant difference was noted (Table 2). Japanese and Chinese were approximately 12 times and Filipinos four times more likely than Caucasians to react to tree pollen.

In the sixth situation, reactivity to trees was ignored and only reactivity to grass among the four groups was considered. Japanese subjects reacted 2.7 times more frequently to grasses than Caucasians. Chinese reacted 2.3 times more frequently than Caucasians and all three non-Caucasian groups combined reacted twice as often as Caucasians (Table 3).

The last study consisted of six tests involving non-Caucasian groups and six with Caucasians alone. We looked for a difference in reactivity to grasses, comparing those who reacted to trees as follows: (A) no trees to one tree; (B) no trees to two trees; (C) no trees to three trees; (D) one tree to two trees; (E) one tree to three trees, and (F) two trees to three trees.

Significant differences were noted for the non-Caucasian groups in contrasting "no trees" reactions and reactions to one, two, and three trees respectively ($P < .0005$) (Table 4). For the Caucasians, significant differences involved two and three trees. There were no significant differences for any of the groups in tests involving one or more trees.

The data was analyzed using the χ^2 analysis or Fisher's Exact test if necessary. Because of the number of tests performed, statistical significance was taken at .005. This was done to maintain an overall type I error rate of 0.05 or less (Bonferroni's Correction).

DISCUSSION

Data from similarly matched Chinese, Japanese, and Filipinos suggest that these racial groups recognize antigens of grasses and tree pollens as more non-self than do

Table 1. Situation: Within Each Group Does a Grass Reaction Effect a Reaction to at Least 1 of 3 Trees; at Least 2 Trees; and All 3 Trees

	No Grass	Grass	P Value	Odds Ratio
Japanese				
No trees	12	4	<.0005	31.0
=> 1 tree	3	31		
<= 1 tree	12	6	<.0005	19.3
=> 2 trees	3	29		
<= 2 trees	14	15	<.001	18.7
= 3 trees	1	20		
Chinese				
No trees	14	5	<.0005	21.7
=> 1 tree	4	31		
<= 1 tree	15	3	<.0005	17.5
=> 2 trees	3	28		
<= 2 trees	16	18	NS	NS
= 3 trees	2	18	NS	NS
Filipino				
No trees	18	7	<.0001	10.3
=> 1 tree	4	16		
<= 1 tree	19	9	<.0001	9.9
=> 2 trees	3	14		
<= 2 trees	21	12	.001	19.2
= 3 trees	1	11		
Caucasian				
No trees	256	161	<.0005	4.5
=> 1 tree	32	91		
<= 1 tree	269	177	<.0005	6.0
=> 2 trees	19	75		
<= 2 trees	276	208	<.0005	4.9
= 3 trees	12	44		

Key: => greater than and <= less than.

Table 2. Column A: For All Subjects Non-Reactive to Grass Is There a Greater Risk of a Reaction to at Least One Tree? Column B: For All Subjects Reactive to Grass Is There a Difference Between Racial Groups in Reacting to at Least One Tree?

	A	B	A	B	A	B
Japanese			Chinese			
No trees	12	4	14	5		
=> 1 tree	3	31	4	31	NS	NS
Japanese			Filipino			
No trees	12	4	18	7		
=> 1 tree	3	31	4	16	NS	NS
Japanese			Caucasian			
No trees	12	4	256	161		
=> 1 tree	3	31	32	91	NS	$P < .0005$ Odds ratio = 13.7
Chinese			Filipino			
No trees	14	5	18	7		
=> 1 tree	4	31	4	16	NS	NS
Chinese			Caucasian			
No trees	14	5	256	161		
=> 1 tree	4	31	32	91	NS	$P < .0005$ Odds ratio = 11.0
Filipino			Caucasian			
No trees	18	7	256	161		
=> 1 tree	4	16	32	91	NS	$P < .0005$ Odds ratio = 4.0

Table 3. Situation: Is There a Difference in Reactivity to Grass Among the Four Groups?

	Allergy to Grass		
	No Grass	Grass	
All 3 non-Caucasian groups	55	94	$P < .0005$ Odds ratio = 2.0
Caucasian	288	252	
Japanese	15	35	
Chinese	18	36	NS
Japanese	15	35	
Filipino	22	23	
Japanese	15	35	NS
Caucasian	288	252	
Chinese	18	36	
Filipino	22	23	$P < .005$ Odds ratio = 2.7
Chinese	18	36	
Caucasian	288	252	
Filipino	22	23	NS
Caucasian	288	252	

Table 4. Situation: Does Reactivity to Grass Influence the Risk of a Reaction to an Exact Number of Trees by the Caucasian Group and by the Three Combined Non-Caucasian Groups?

		Ja + Ch + F*	Ca*
0 trees to 1 tree:	P	<.005	NS
	Odds ratio	9.6	
0 trees to 2 trees:	P	<.0005	<.0005
	Odds ratio	12.1	7.0
0 trees to 3 trees:	P	<.0005	<.0005
	Odds ratio	33.7	5.8
1 trees to 2 trees:	P	NS	NS
	Odds ratio		
1 trees to 3 trees:	P	NS	NS
	Odds ratio		
2 trees to 3 trees:	P	NS	NS
	Odds ratio		

* Ja = Japanese, Ch = Chinese, F = Filipino, and Ca = Caucasian.

Caucasians. It is not known why grass pollen reactivity involves an amplified response to certain tree antigens. In previous studies we found no unusual frequency of reactions to other trees such as walnut and oak.³

The reasons are not clear for the immunologic differences between the Filipinos and the Japanese and Chinese groups, nor do we have an explanation for the immunologic similarities of the Japanese and Chinese. It is important to note that Filipinos are both Spanish and Asian. What is clear is a pattern that reflects the similarity between Chinese, Japanese, and Filipinos and their differences vis-a-vis Caucasians. Similarity is greatest between Chinese and Japanese; the Filipinos fall between the Asians and the Caucasians.

It is known that Asians have up to 10 times greater polymorphism to certain antigens than Caucasians.⁶ The ability of certain racial groups to recognize an antigen better than other races does not neces-

sarily imply that races with heightened recognition experience established symptoms from a specific antigen.⁷

It is not known if the subjects who are more reactive to the test antigens possess different HLA antigen groups than those who are less sensitive. There is, however, a known association of HLA and other diseases with a propensity to specific races.⁸⁻¹⁰ Salivary antigen secretions in man have been shown to occur in association with certain pathologic situations, including rheumatic diseases and immunoglobulin A concentrations.¹¹

In this study, when each group was evaluated according to grass reactivity in relation to at least one of the three trees, significant differences appeared for each racial group: the greater the number of trees the lower the risk (Tables 1-3). Why Caucasians failed to recognize tree antigens as frequently as the other three races regardless of whether the tree was cedar, cypress, or juniper remains unanswered. On

the other hand, if a group failed to react to grass, it was as though its ability for a "heightened" reactivity to trees was not "activated." This was exemplified in Table 2. No significant difference was found in all six combinations, demonstrating that for all subjects not allergic to grass, there was no difference in racial group reactivity to even one tree.

The fact that the three trees grow in China, Japan, and the Philippines may have affected the subjects' reactivity. Chinese subjects in this study descended from people who came to the United States three generations ago. Whether they came from the mountains or the plains there was no apparent difference in their reactivity to trees. In the fifth century, Li dow Yuan wrote a 40-volume botanical work in which he described cedar, cypress, and juniper trees growing over approximately half of the 10 million square miles of China.¹² But in 1979, cedar, cypress, and juniper were not listed in the top ten airborne pollens surveyed for the Beijing area of China.¹

Although cedar has flourished in Japan for at least a million years, the first report of respiratory allergy from its pollen was about 20 years ago.¹³

The role of both genetics and diet are known to be important in skin test reactivity.¹⁴ Genetics may be the pivotal factor in this study as we could identify no foodstuffs in the non-Caucasian diet that were not also in the Caucasian diet. If diet is of minor importance in this observation and the role of genetics uncertain, then what of the environment? In 1973 it was reported that ragweed-sensitive Caucasians were more sensitive to Timothy grass than those not sensitive to ragweed.¹⁵ Nine years later it was reported that allergy to grasses was not of prime importance in China and only sixth in order following other plants including weeds and trees.¹ The other role of environment may be that of a possible adjuvant effect

in IgE production.¹⁶ The allergist especially should be aware that the three non-Caucasian groups are more sensitive to cedar, cypress, and juniper. When hyposensitization is entertained, the clinical significance of these three trees should be carefully examined.

The theoretical significance of the observed differences may be noted in several areas: it would be interesting if certain HLA antigens paralleled the four groups' differences. If this were the case it would have importance for numerous clinical settings, including organ transplantation rejection. Other ramifications of these differences might be found in variation in antibiotic sensitivity, stinging insect reactivity, allergic and "idiopathic" drug reactions, and blood transfusions. Not only should HLA typing be studied in atopic subjects of these four groups but the success rate as well of organ transplantation in non-atopic subjects (eg, Caucasian to Chinese versus Chinese to Chinese).

One may ask if the greater pollen reaction susceptibility is related to a separate gene. Could this gene infer increased susceptibility to pollen and allergic reactions, yet diminish susceptibility to a more threatening disease that may exist in the Far East but not in the West? Another hypothetical explanation could be that the increased pollen response reflects a raised immunity to other more threatening diseases that do not exist today. An example of the first theoretical situation exists in malaria-exposed Africans who carry the sickle cell gene which confers protection from the parasite but allows other pathology evolving from the red blood cell.

SUMMARY

Allergic Chinese, Japanese, Filipinos, and Caucasian groups were compared and contrasted according to their skin test reactivity to pollens of grasses and trees. If a subject reacted to grasses, there was a significantly greater risk of reaction to trees ($P < .0005$). The risk was profoundly greater in the three non-Caucasian groups (Filipino, Chinese, and Japanese) compared with the Caucasian group ($P < .0005$). Reactivity to grass appeared to amplify the risk of reaction to trees. This effect was particularly striking in the non-Caucasian groups.

In groups that did not react to grasses, there was no difference between races in reactivity to trees.

The non-Caucasian races did not demonstrate significant differences in their reaction to grasses.

All three non-Caucasian groups appear to be more sensitive than the matched Caucasians to cedar, cypress, and juniper.

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