

Cockroach hypersensitivity: Preliminary study of allergic cockroach asthma in Taiwan

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One hundred eighty-two atopic patients were skin tested with cockroach antigen. Of these 182 patients, 54.9% gave positive immediate skin reaction by intracutaneous test. Among those atopic patients tested, 57.5% of patients with asthma and 50.7% of patients with allergic rhinitis were sensitive to cockroach extracts. The specific IgE antibody was determined by fluoroallergosorbent test. Of 79 cockroach-positive atopic patients, 39.2% were found to contain IgE antibodies against cockroach. No specific IgE was detected in cockroach-negative atopic and nonatopic subjects. Bronchial provocation test with cockroach antigen was performed on 15 subjects. Immediate asthmatic response was detected in six of nine cockroach-positive subjects with asthma. Two cockroach-negative subjects with asthma and four nonatopic subjects demonstrated no significant decrease in FEV₁. The results indicate that cockroach induces antigen-specific IgE-mediated bronchial asthma, and cockroach is one of the major causes of allergic asthma. (J ALLERGY CLIN IMMUNOL 1988;82:736-40.)

Cockroach has been identified and recognized as a major cause of perennial rhinitis and asthma.¹⁻⁵ Early studies by Bernton and Brown⁶⁻⁸ and Bernton et al.⁹ clearly demonstrated that CRa has the capacity of inducing skin-sensitizing antibodies. More recently, the allergenicity of cockroach extract was demonstrated by end point skin test titrations and RAST among sensitive subjects.^{1, 2} High incidences of positive skin test to CRa in atopic population (20% to 53%) and in the population with asthma (49% to 61%) have been reported.^{1, 7, 10} The causative association of skin sensitivity to CRa with allergic bronchial asthma has been proved by BPT.^{1, 2, 9}

The study of cockroach hypersensitivity has not been reported in Taiwan. The warm and humid semitropical weather, the high population density, and unsatisfactory sanitary conditions may contribute to the

Abbreviations used

CRa: Cockroach antigen
BPT: Bronchial provocation test
FAST: Fluoroallergosorbent test

prevalence of cockroaches in the household that has been an important problem for the public health in Taiwan, as well as in other countries. In the present study, we investigated the population of cockroach asthma in Taichung, which is a main city of central Taiwan with 800,000 population. The prevalence of cockroach hypersensitivity was found to have a very similar rate of skin sensitivity compared to investigations in the United States. BPT demonstrated that inhalation of CRa induces the immediate asthmatic response in subjects with asthma with positive skin reaction to CRa.

MATERIAL AND METHODS

Patients

During a 6-month period (August 1986 to January 1987), 182 patients were selected from the allergy clinic at the Veterans General Hospital-Taichung, Taichung, Taiwan. All patients with symptomatic allergic rhinitis or asthma underwent skin tests with CRa in addition to 48 other common inhalant allergens. Fifty-five normal subjects were included as control subjects. The mean age of the patients was 37 years, with a range of 16 to 68 years.

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Supported in part by a National Science Council of the Republic of China Grant No. NSC76-0412-B075-05 awarded to C. H. Wu, PhD.

Received for publication Nov. 4, 1987.

Accepted for publication April 2, 1988.

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TABLE I. The frequency distribution of skin test reaction in the population sample

Population	No. of subjects	Allergy skin test					% Positive
		-	1+	2+	3+	4+	
Atopic subjects	182	82	28	42	28	2	54.9
Asthma	113	48	22	24	17	2	57.5
Allergic rhinitis	69	34	6	18	11	0	50.7
Normal subjects	55	46	6	1	0	0	12.7

Allergy skin test

Allergen extract (0.02 ml), with a 27-gauge disposable needle and a 1.0 ml syringe, was injected into the superficial layers of the skin for the intracutaneous technique. All intracutaneous test solutions were 1:5000 (wt/vol), except CRa. Five hundred protein nitrogen units per milliliter of cockroach (*Periplaneta americana*) extract (Holister-Stier, Spokane, Wash.) were used for the intracutaneous test. Physiologic-buffered saline and histamine phosphate solution (0.1 mg/ml) were used as negative and positive control, respectively. Results were read 15 minutes after the administration by measuring the diameter of wheals. The interpretation was recorded according to the following criteria: (-) wheal <6 mm in diameter, (1+) wheal 6 to 8 mm, (2+) wheal 8 to 10 mm, (3+) wheal 10 to 13 mm, and (4+) wheal >13 mm with pseudopods.

FAST

Cockroach IgE FAST (Allergentics, Mountain View, Calif.) was measured by a sandwich enzyme immunoassay as described by Tsay and Halpern.¹¹ The generated fluorescence was determined by fluorometer (Titertek Fluoroskan II, Flow Laboratories, McLean, Va.) with excitation at 365 nm and emission at 450 nm. A class-scoring system based on a fivefold increase in allergen-specific IgE was assigned according to the following criteria: class 0, <0.02 IU/ml of specific IgE; class I, 0.02 to 0.1 IU/ml; class II, 0.1 to 0.5 IU/ml; class III, 0.5 to 2.5 IU/ml; class IV, 2.5 to 12.5 IU/ml; class V, 12.5 to 62.5 IU/ml; and class VI, >62.5 IU/ml.

BPT

The procedure for the BPT and possible adverse reactions were explained to the subjects before the test. Subjects were free of acute asthma attack for at least 1 week before testing. All bronchodilators and antihistamines were withheld at least 8 to 12 hours before the test. BPT was carried out according to the modified protocol described by Chai et al.¹² and Kang.³ A volumetric spirometer (MultiSPIRO-PC, Medical Equipment Designs, Inc., Laguna Hills, Calif.) attached to a computerized processor (Biotrine Corp., Woburn, Mass.) was used to measure the reduction in FEV₁ and forced vital capacity. If the subject's FEV₁ was <70% of its predicted value or the buffered saline used as control

TABLE II. Percent correlation FAST versus CRa positive and negative population

Population	No. of subjects	FAST class score					% Positive
		0	I	II	III	IV	
CRa-positive atopic subjects	79	48	8	12	6	5	39.2
Asthma	49	27	6	7	4	5	44.9
Allergic rhinitis	30	21	2	5	2	0	30
CRa-negative atopic subjects	20	20	0	0	0	0	0
Nonatopic subjects	10	10	0	0	0	0	0

TABLE III. FAST class score in CRa-sensitive atopic subjects

Skin test	FAST class score				
	0	I	II	III	IV
1+	16	1	1	0	0
2+	22	5	3	1	2
3+	8	2	8	4	2
4+	2	0	0	1	1
Total patients	48	8	12	6	5

produced nonspecific bronchospasm (reduction of FEV₁ >15%), the subject was excluded from the study. Patients inhaled five breaths of CRa extract (1:100, wt/vol; Holister-Stier) each time, corresponding to a solution containing 30 PNU of CRa. Pulmonary functions were measured at 5, 10, and 15 minutes after a challenge, and at 5 minutes after isoproterenol inhalation. After BPT, patients were observed for 24 hours in the hospital. BPT was considered positive when FEV₁ was reduced 20% or more from the baseline value. BPT was considered negative when 300 PNU of CRa extracts was accumulated, and the reduction of FEV₁ was <20%.

RESULTS

Prevalence of immediate hypersensitivity to cockroach

During a period of 6 months (August 1986 to January 1987), 182 atopic patients, 113 with asthma and 69 with allergic rhinitis, were skin tested with cockroach extracts. Of 182 patients, 54.9% (100/182) gave positive immediate skin reaction. Among these 100 CRa-positive atopic subjects, 57.5% (65/113) of subjects with asthma and 50.7% (35/69) of subjects with allergic rhinitis were sensitive to CRa by skin test. They were also allergic to other common inhal-

TABLE IV. Characteristics of subjects studied for BPT with CRa

Subjects	Age	Sex	Duration of bronchial asthma (yr)	Result of skin reaction to CRa	Result of CRa FAST class score
1. T. C.	19	M	11	4+	IV
2. F. H.	18	M	5	3+	IV
3. C. H.	33	M	13	3+	IV
4. S. T.	38	M	12	3+	III
5. C. Y.	40	M	15	2+	IV
6. S. C.	32	M	3	3+	III
7. C. L.	21	F	18	3+	II
8. T. L.	24	M	18	3+	III
9. C. T.	28	F	4	3+	II
10. Y. L.	21	F	11	—	O
11. L. L.	59	M	18	—	O
12. C. W.	46	M	0	—	O
13. D. L.	40	M	0	—	O
14. C. J.	40	M	0	—	O
15. C. S.	26	M	0	—	O

ants besides CRa. In the normal population, positive reaction was found in 12.7% (7/55) of subjects. The results of prevalence and sensitivity of skin test reaction are presented in Table I.

FAST

To determine the specificity and sensitivity of intracutaneous skin test, sera of 79 CRa-positive patients were performed for specific IgE by FAST. Of 79 patients, 39.2% (31/79) were found to have IgE antibodies against CRa in their sera (Table II). Specific IgE was detected in 44.9% (22/49) of subjects with asthma and 30% (9/30) of subjects with allergic rhinitis. The results of FAST in skin test-positive atopic subjects are presented in Table III. Sera of 30 subjects, 20 CRa-negative atopic subjects, and 10 nonatopic subjects were also included in the study. No specific CRa IgE antibodies were detected in these subject's sera.

BPT

The clinical data on 15 subjects studied are summarized in Table IV. The first nine subjects with asthma who gave positive skin reaction to CRa were also allergic to house dust and at least four other common inhalants. Two subjects with asthma, nos. 10 and 11, were CRa negative by skin test. However, they were allergic to other allergens, such as house dust, mixed weed, and grass and tree pollens in subject 10, and house dust, *Candida*, dog hair, and duck feather in subject 11. The four remaining subjects, nos. 12, 13, 14, and 15, were nonatopic subjects, and skin test to CRa in these subjects was negative.

The results of CRa challenging studies are presented in Table V. In six of nine CRa-positive subjects with asthma, inhalation of CRa caused a significant and immediate decrease in pulmonary function ($>20\%$ fall in FEV₁) and induced various asthmatic symptoms, such as coughing, itchy throat, wheezing, and tightness in the chest. The bronchial response of the immediate changes in FEV₁ after the CRa challenge and its antigen specificity in allergic patients with asthma and control patients are illustrated in Fig. 1. At the termination of BPT, two breaths of isoproterenol were administered, and the restoration of pulmonary function was noted in these patients (Table V). Saline inhalation failed to produce bronchoconstriction in the population studied. Cockroach-negative subjects with asthma and nonatopic subjects demonstrated no significant immediate decrease in FEV₁, and no signs of asthmatic reactions were detected after the CRa challenge.

DISCUSSION

High incidences of skin sensitivity to cockroach extracts have been reported.^{1, 7, 10} Our finding (54.9% in atopic subjects and 57.5% in subjects with asthma) indicates that the prevalence of cockroach hypersensitivity in Taiwan is concordant with those reported by Bernton and Brown⁷ (44% in atopic subjects and 49% in subjects with asthma), Marchand¹⁰ (46% in atopic subjects and 52% in subjects with asthma), and Kang and Sulit¹ (53% in atopic subjects and 61% in subjects with asthma) in the United States. Positive skin reaction to cockroach was found in 12.7% (7/55) of the nonatopic subjects. The finding in this study is

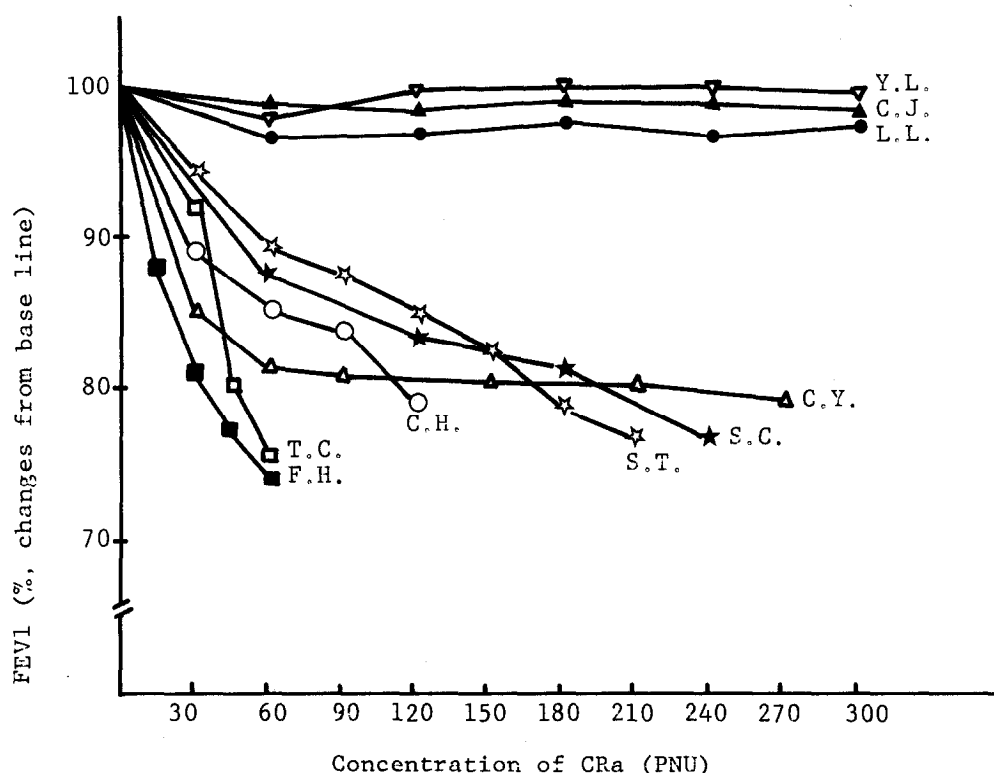


FIG. 1. Changes in FEV₁ after BPT with CRA. Patients with asthma, T. C., F. H., C. H., S. T., C. Y., and S. C. were allergic to CRA. CRA-negative subjects with asthma (Y. L. and L. L.) and a nonatopic subject (C. J.) demonstrated no change in FEV₁ after the antigen challenge.

TABLE V. Bronchial response of CRA-positive and CRA-negative subjects after BPT with antigen

Subjects	Total CRA (PNU) inhaled	FEV ₁ (%) before CRA challenge	FEV ₁ after CRA challenge	% Reduction in FEV ₁	FEV ₁ (%) after isoproterenol inhalation
1. T. C.	60	100.8	76.2	24.4	104.9
2. F. H.	60	97.1	74.3	23.5	100.8
3. C. H.	120	84.3	66.1	21.6	88.2
4. S. T.	210	73.7	56.5	23.3	82.0
5. C. Y.	270	74.7	59.1	20.8	78.1
6. S. C.	240	83.5	64.1	23.2	89.4
7. C. L.	300	85.9	85.5	0.46	90.2
8. T. L.	300	103.4	101.7	1.64	107.0
9. C. T.	300	76.2	71.2	6.56	80.2
10. Y. L.	300	88.4	86.8	1.81	90.2
11. L. L.	300	92.3	90.1	2.38	93.5
12. C. W.	300	94.6	92.0	2.74	ND
13. D. L.	300	90.2	87.3	3.21	ND
14. C. J.	300	91.6	90.2	1.52	ND
15. C. S.	300	87.3	83.7	4.1	ND

ND = not done.

higher than the result (7.5%) reported by Bernton and Brown,⁷ but 27% of nonatopic subjects has been reported sensitive to CRA in children by Kang and Sulit.¹

Early studies by several authors¹³⁻¹⁷ demonstrated good correlation between RAST and skin test results. An overall 69% correlation was reported by Hamburger¹⁸ in 408 RAST and skin tests performed

on 31 patients. In another study, the correlation between RAST and intradermal testing for eight allergens in atopic subjects was 68.8%, as reported by Caprio et al.¹⁹

The correlations of FAST, RAST, and skin prick tests have been reported by Seltzer et al.²⁰ From results of eight patients tested with 60 allergens, a total of 253 tests performed, FAST was concordant with 85.7% of the skin test results. They concluded that FAST appears to be a valid nonradioactive, time-efficient method for detection of specific IgE to common inhalant and environmental allergens. In this study, 39.2% (31/79) was found to contain specific IgE antibodies by FAST in CRa-positive atopic subjects. A 50% (14/28) false negative result of RAST in CRa-reactive atopic subjects was reported by Kang et al.² The sensitivity of FAST and RAST was poor for cockroach. However, no false positive results were obtained by their study or ours (Table II). The high incidence or false positive reactions on intradermal testing,²¹ the high threshold criteria of FAST, and the different allergen preparation (Holister-Stier versus Allergentics) may contribute to the poor correlation of skin test and FAST, in which FAST is negative and skin reactions are positive.

In 1972, cockroach-induced immediate asthmatic reaction in CRa skin-sensitive subjects with asthma was first demonstrated by Bernton et al.⁹ After the inhalation of 36 to 2480 PNU of the CRa extracts, six of their 10 patients with asthma demonstrated at least 15% reduction in FEV₁ from the baseline value. Subsequently, Kang et al.² and Kang³ confirmed the antigen-specific induction of bronchospasm in CRa-positive subjects with asthma. They documented the dual asthmatic responses (acute reaction in >90%, and late reaction in 68%) in skin-reactive subjects with asthma after the challenge of 400 to 800 PNU of CRa extracts. In this study, six of nine CRa-positive patients with asthma tested for BPT demonstrated immediate asthmatic reaction after CRa challenge with 60 to 270 PNU of antigen extracts (Table V). No late asthmatic reaction was noted for 24 hours on those patients after the termination of BPT.

In summary, the prevalence of cockroach sensitivity in Taiwan is consistent with the prevalence reported by other investigators in the United States. The finding in this study once again confirmed that the inhalation of CRa induces the immediate asthmatic response in subjects with asthma who have the positive skin reaction to the antigen. The CRa-induced asthmatic response is specific, since no bronchospasm was detected from CRa-negative subjects with asthma and nonatopic subjects.

We thank Dr. Kwang-Juei Lo, Superintendent of the hospital, for his encouragement and support during this study, the nursing staff of our allergy clinic for their help in performance of skin tests, Ms. Meei-Chyn Chen for manuscript preparation, and Huei-Jeng Lin for her skillful technical assistance.

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