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Antigenic/allergenic characterization of American and German cockroach extracts

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Cockroach allergens have been implicated as clinically significant sensitizing agents in the induction/exacerbation of "urban asthma." In the present study, approximately 50% of atopic, predominantly inner-city residents had immediate wheal-and-flare cutaneous reactivity to a commercial American cockroach whole body extract. Crude whole body extracts were prepared in our laboratory from both American (Periplaneta americana) and German (Blattella germanica) cockroach species. Crossed immunoelectrophoresis of American cockroach whole body extract (AWBE) and German cockroach whole body extract (GWBE) detected a total of 50 and 56 precipitin peaks, respectively, when extracts were reacted with hyperimmunized rabbit antisera. Crossed radioimmuno-electrophoresis identified at least five electrophoretically distinct allergens each in AWBE and GWBE. Cockroach whole body extracts produced two major protein peaks when extracts were fractionated on Sephadex G-75. RAST-inhibition studies demonstrated allergens in both peak 1 and the immediate trailing fractions of the column. Direct RAST and end point prick skin testing confirmed the presence of significant/important allergens in column "fraction 2" of AWBE. Skin testing and RAST analysis suggested the occurrence of shared and species-specific allergens between AWBE and GWBE. Collectively, these studies confirm the important sensitizing potential of cockroach allergens, characterize their number and size distribution by crossed radioimmuno-electrophoresis and column chromatography, support the occurrence of significant allergens in column "fraction 2," and suggest the occurrence of both species-specific and shared interspecies allergens. (J ALLERGY CLIN IMMUNOL 1988;81:563-70.)

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Although clinically significant associations exist between allergic respiratory disease and cockroach sensitization, relatively little is known about the major sources of specific cockroach allergens that may induce symptoms. Unlike the isolation, characterization, and clinical use of other important allergens (eg, mite), work with cockroach allergens can only be considered preliminary. Richman et al.,¹ with RAST-test analyses of sera obtained from 13 cock-

Abbreviations used

AWBE:	American cockroach whole body extract
GWBE:	German cockroach whole body extract
CIE:	Crossed immunoelectrophoresis
CRIE:	Crossed radioimmuno-electrophoresis

roach sensitive subjects, proposed that whole bodies and cast skins contained the clinically relevant allergens of cockroach and that allergens of German and American cockroach demonstrate little cross-reactivity. In contrast, Twarog et al.² identified three "major" allergens in crude AWBEs and suggested "similarities" in German and American cockroach allergens based on physicochemical characteristics. The present studies were undertaken to extend these early observations by identifying and characterizing clinically significant allergens from AWBEs and GWBEs.

MATERIAL AND METHODS**Crude cockroach extracts**

American cockroach (*Periplaneta americana*) and German cockroach (*Blattella germanica*) whole bodies were obtained from the Carolina Biological Supply Co., Burlington, N.C., and were of both sexes. Crude whole body extracts were prepared by freezing live roaches and weighing and suspending the whole bodies in physiologic saline (pH 7.4), followed by mixing in a Waring (Waring Products Div., Dynamics Corp. of America, New Hartford, Conn.) blender for 5 minutes at room temperature (five 1-minute pulses). The mixture was stirred overnight at 4° C and was then centrifuged at 18,000 g for 30 minutes at 4° C. Supernatants were concentrated by Amicon ultrafiltration (YM2, Amicon Corp., Danvers, Mass.) (molecular weight cutoff, 1000 daltons) and filtered through a 0.45- μ m Millipore (Millipore Corp., Bedford, Mass.) filter. For allergen fractionation studies, whole body extracts were dialyzed (by dilution and concentration with Amicon filters, YM2) against appropriate elution buffers. Glycerol was added in equal volumes with saline to allergen preparations for use in skin testing. Extracts were stored at 4° C.

Cockroach-sensitive subjects and skin testing

One hundred subjects, attending an adult allergy clinic at Charity Hospital, New Orleans, La., were prick skin tested with commercial extracts of common inhalant allergens, including American cockroach (Greer Laboratories, Lenoir, N.C.). After informed consent, cockroach skin test-positive subjects (immediate wheal-and-flare reaction with a wheal 2 mm greater than wheal of saline control) were enrolled in our study. Cockroach whole body extracts (prepared as above) and purified fractions (see below) were sterile filtered (0.45- μ m Millipore filter) before use and tested for the presence of microorganisms by culturing on trypticase soy agar. Toxicity testing was performed by in-

traperitoneal inoculation of test material into mice before human testing. Guidelines for the care and the use of animals were followed according to the "Guide for the Care and Use of Laboratory Animals" prepared by the National Academy of Sciences. These extracts were used for end point titration, prick skin testing of subjects with positive and negative immediate skin test reactions to the commercial American cockroach extract. Prick skin testing was performed at concentrations of extract ranging from 1 μ g/ml to 1 mg/ml. Reactions were considered positive if skin testing produced a wheal 2 mm greater than wheal of saline control.

RAST testing and inhibition

Direct RAST was performed with the use of CNBr-activated paper disks for the detection of circulating IgE antibodies specific for crude and fractionated cockroach allergens.³ For the RAST, antigen was coupled to CNBr-activated paper disks at either 1 mg per five disks (Sephadex G-75 column fractions) or 1 mg per disk (crude, whole body extract) to maximize protein binding. For the test, 100 μ l of patient serum was incubated overnight with an allergen disk. After washing with physiologic saline, disks were incubated overnight with 100 μ l of ¹²⁵I-labeled anti-IgE antiserum (25,000 cpm) (Kallestad Laboratories, Austin, Texas), washed with saline to remove unreacted material, and counted in a Beckman (Beckman Instruments Inc., Irvine, Calif.) gamma counter to determine radioactivity in counts per minute bound to the disks. For evaluation of results, a RAST percent binding was obtained by dividing the counts per minute of test disks by counts per minute of ¹²⁵I-labeled anti-IgE added. The percent of nonspecific binding of each disk was determined by use of individual sera from five subjects with similar IgE levels to those tested, but with negative skin test reactivity to cockroach allergens. For RAST inhibition, inhibiting antigen (eg, column fractions) was incubated with pooled sera from cockroach skin test-positive and direct RAST positive individuals (10 subjects) in the presence of allergen (whole body extract)-coated disks overnight on a rotator at 24° C. Disks were washed, and radiolabeled anti-IgE was added, followed by overnight incubation, washing, and counting the disks on a gamma counter. Results were expressed as the percent inhibition of radiolabeled anti-IgE bound by the serum pool incubated with allergen-coated disks.

CIE

Hyperimmune antisera were raised in four adult female New Zealand white rabbits. For immunization, animals received initial injections in the footpads and at subcutaneous sites on the back with 10 mg/ml of cockroach extracts emulsified with an equal volume of complete Freund's adjuvant. Thereafter, the animals received weekly booster injections of 5 mg of the extract in incomplete Freund's adjuvant at multiple subcutaneous sites on the back. Blood was obtained after each weekly booster injection and tested by capillary tube precipitation to confirm the presence of antibodies. Multiple serum samples from rabbits were collected, pooled, aliquoted, and stored at -70° C. CIE was used to determine the number of antigenic components in cockroach

TABLE I. AWBE RAST studies

Subject		Serum IgE (IU/ml)	AWBE	RAST % binding			
				Fraction			
				1	2	3	4
1	F. B.	1100	40	14	12	9	3
2	J. L.	300	40	13	12	8	2
3	B. J.	520	28	30	14	16	4
4	D. Hf.	640	28	29	24	18	NT
5	D. Hm.	330	27	2	11	3	1
6	R. S.	330	27	14	19	5	2
7	V. K.	800	19	14	15	14	3
8	J. R.	56	14	14	18	7	6
9	G. G.	360	14	9	13	4	1
10	J. J.	300	13	2	4	2	1
11	S. H.	300	10	6	5	9	1
12	C. T.	200	8	5	4	2	1
13	S. G.	NT	3	4	4	32	2
14	J. C.	1500	3	3	12	3	2
15	S. M.	360	3	2	8	2	1
	A. N. P.*	300	2	2	3	3	2
No. +/No. tested			12/15	10/15	11/15	8/15	1/14

NT = not tested.

*Pool of five atopic, cockroach skin test-negative subjects.

crude whole body extracts and column fractions. Briefly, an appropriate dilution of antigen (depending on initial concentration) was introduced into wells cut into 1% agarose gel and electrophoresed toward the anode at 10 V/cm for 25 minutes. Strips containing the antigens were cut from the gel and transferred to a new 5 by 7 cm gel bond. A 1.5 cm-wide middle strip of 1% agarose was poured next to the antigen-containing strip. Finally, molten 1% agarose containing an optimal dilution of hyperimmune rabbit antiserum was poured on the remaining area of the plate. The plate was electrophoresed overnight at 2 to 3 V/cm, with adequate cooling, so that the antigen migrated into the hyperimmune serum (i.e., at 90 degrees to the original direction). Plates were washed, pressed, stained with 0.5% Coomassie brilliant blue dye in 10% acetic acid, cleared with 10% glacial acetic acid in ethanol/water, and examined on a light box for precipitin arcs. Precipitin peaks were numbered consecutively from the anode to the cathode.

CRIE

CRIE was used to determine which of the peaks identified by CIE had allergenic properties. For CRIE, 400 μ l of patient's sera, in 6.6 ml of phosphate buffer, was incubated overnight at room temperature with CIE plates that had been processed as above, but with a final wash in saline and no staining. After incubation, plates were washed with saline, flooded with ^{125} I-labeled anti-IgE antiserum containing 250,000 cpm, and incubated overnight. After washing to remove unreacted radiolabeled anti-IgE, autoradiography was performed.

Sephadex G-75 column chromatography

Crude whole body extracts prepared as above were fractionated on 2.5 by 100 cm Sephadex G-75 (Pharmacia Fine Chemicals, Piscataway, N.J.) columns. Elution was performed by gravity flow at 25 to 30 ml/hr and at 4°C. Four-milliliter fractions were collected with phosphate-buffered saline (0.15 mol/L, pH 7.4) as eluant. Absorption of protein was read at 280 and 230 nm. Columns were calibrated with markers of known molecular weight, including blue dextran (molecular weight >2,000,000 daltons), bovine serum albumin (molecular weight 70,000 daltons), and cytochrome C (molecular weight 12,384 daltons).

RESULTS

Cockroach-induced skin reactions and direct RAST to AWBE

Forty-eight percent (46/95) of atopic (wheal-and-flare skin test reactivity to at least two common inhalant allergens) skin tested subjects, representing predominantly inner-city residents, had immediate cutaneous reactivity to crude, commercial American cockroach extract. Fifteen skin test reactive subjects and 10 subjects nonreactive to commercial cockroach extract were recruited for end point titration, prick skin testing to crude AWBE prepared in our laboratory. Although all 15 subjects reactive to commercial cockroach extract also reacted to either 100 μ g/ml or 1 mg/ml (dry weight) of AWBE, many subjects (28%)

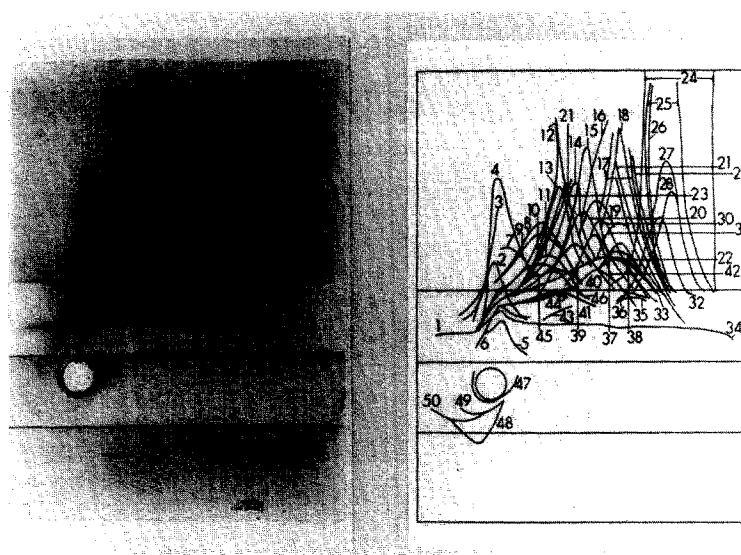


FIG. 1. CIE of AWBE. CIE precipitin pattern of AWBE reacted with pooled rabbit AWBE antiserum. The gel contained 15 μ l (150 μ g dry weight) of extract reacted with 250 μ l of antiserum (*top gel*) and 50 μ l of antiserum (*bottom gel*).

TABLE II. American cockroach crude and fractionated whole body skin test studies

Subject		Whole body	Fraction			
			1	2	3	4
1	R. S.	+	+	+	—	—
2	F. B.	+	+	+	+	—
3	J. J.	+	+	+	—	+
4	S. M.	+	—	+	+	—
5	J. C.	+	—	+	—	—
6	G. G.	+	+	+	—	—
7	N. M.	+	+	+	—	—
8	M. C.	+	—	+	+	+
9	S. G.	+	—	+	+	—
10	B. A.	+	—	+	+	—
No./+No. tested		10/10	5/10	10/10	5/10	2/10

had positive prick skin tests to 10 μ g/ml (dry weight) of crude extract. None of 10 atopic subjects with negative immediate skin test reactivity to commercial American cockroach extract were reactive to prick skin testing with 1 mg/ml (dry weight) of AWBE.

AWBE was coupled to CNBr-activated paper disks, and RAST percent binding was calculated for sera obtained from the 15 roach-positive subjects and a pool of five roach-negative control subjects (Table I).

CIE and CRIE of AWBE

CIE was used to define the number of antigens in the crude AWBE. A total of 50 precipitin peaks was

detected by rabbit antisera elicited to AWBE (Fig. 1). CRIE of AWBE was performed with sera from 10 subjects with positive skin test and direct RAST reactivity to whole body extract (subjects 1 to 10, Table I). Seven of the 10 sera were reactive by CRIE with AWBE. Five electrophoretically distinct allergens were identified in AWBE (Fig. 2). Two sera each produced patterns identical to patients 1, 2, and 3, whereas one serum produced the pattern depicted by patient 4.

Column chromatography of AWBE

AWBE was fractionated by Sephadex G-75 column chromatography. A representative elution profile of 35 mg (dry weight) of extract is provided in Fig. 3, *upper panel*. Protein determinations of AWBE performed by the biuret method differed by <7% from dry weight determinations, suggesting that nonproteinaceous material contributed relatively little to the crude extract. Column chromatography identified two major protein peaks, as defined by their absorbance at 280 nm. The first protein peak was excluded on both Sephadex G-75 and G-200 (data not presented), whereas the second major peak was dialyzable.

RAST inhibition of AWBE column chromatography fractions

A pool of the 10 highest RAST percent binding sera (equal aliquots) (Table I) was subsequently used in RAST-inhibition analysis of sequential five tube pools of Sephadex G-75 column fractions of AWBE (Fig. 3, *lower panel*). Significant RAST-inhibition

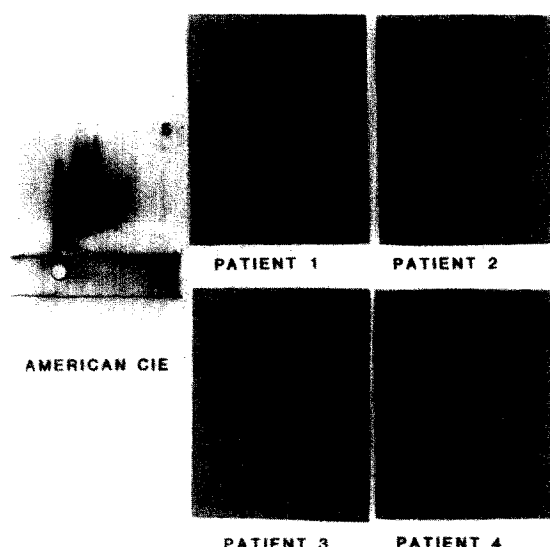


FIG. 2. CIE of AWBE and CRIE of individual, AWBE RAST-positive sera reacted with AWBE. For the American CIE, the gel contained 15 μ l (150 μ g dry weight) of AWBE reacted with 250 μ l of antiserum (top gel) and 50 μ l of antiserum (bottom gel). Patients 1 to 4 represent individual antiserum responses by CRIE selected to demonstrate the different allergens present in AWBE; 16 days autoradiography.

activity (>25%) was localized to the first major protein peak and the immediate trailing fractions. To define further the allergen components of AWBE, we separated the Sephadex G-75 column fractions into four pools on the basis of their protein profiles (absorbance at 280 nm) and RAST inhibition. Fraction 1 (tubes 38 to 50) contained the first major protein peak that produced significant RAST inhibition, whereas fraction 2 encompassed tubes 51 to 80 and corresponded to those tubes that produced >25% RAST inhibition. Fraction 3 contained tubes 81 to 100 and represented tubes that produced <25% RAST inhibition, whereas fraction 4 (tubes 101 to 135) contained the second, dialyzable, major protein peak that did not produce significant RAST inhibition.

Skin testing, direct RAST, and CIE analysis of AWBE column chromatography fractions

All four fractions, defined as above, were used in end point titration prick skin testing (1 μ g/ml to 1 mg/ml dry weight) of 10 subjects with immediate skin test reactivity to crude AWBE (Table II). In addition, each fraction was coupled to CNBr-activated paper disks, and RAST percent binding was calculated for the same 15 roach-positive subjects described in Table I. Significant skin test and direct RAST-binding activity were present in fractions 1, 2, and 3. Only

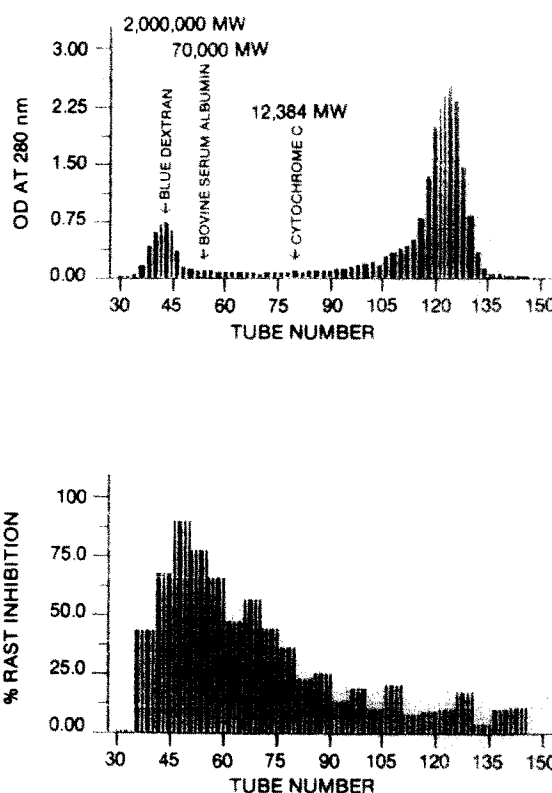


FIG. 3. Sephadex G-75 column chromatography profile (top) of AWBE. AWBE (35 mg) was applied to a 2.5 by 100 cm Sephadex G-75 column, and protein was eluted by gravity flow at 25 ml/hr and at 4° C. Four-milliliter fractions were collected with phosphate-buffered saline (0.15 mol/L, pH 7.4) as eluant. Absorption of protein is plotted at 280 nm. The column was calibrated with blue dextran (molecular weight >2,000,000 daltons), bovine serum albumin (molecular weight 70,000 daltons), and cytochrome C (molecular weight 12,384 daltons). RAST inhibition (bottom) by column fractions (sequential five tube pools) of a pool of American cockroach whole body, RAST-positive sera (10 subjects). Equal aliquots (volume) of sequential five tubes from Sephadex G-75 column chromatography were pooled and used to inhibit the RAST of pooled sera (equal aliquots) from subjects 1 to 10 (Table I) reacted with AWBE-coated disks. Results are expressed as the percent inhibition of radiolabeled anti-IgE bound by the serum pool incubated with AWBE-coated disks.

one of 14 and two of 10 subjects had RAST or skin test reactivity to fraction 4. CIE analysis of AWBE and fractions 1 to 4 is presented in Fig. 4.

Comparison between AWBE and GWBE by CIE, CRIE, skin testing, direct RAST, column chromatography, and RAST-inhibition studies

A total of at least 56 precipitin arcs were detected by rabbit antisera to GWBE (Fig. 5). CRIE of GWBE

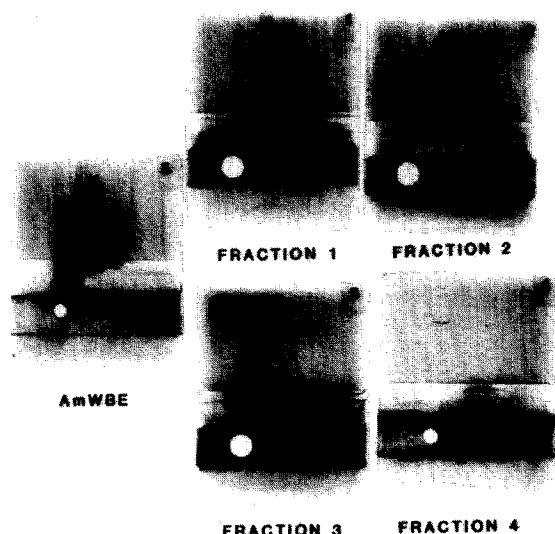


FIG. 4. CIE of AWBE and Sephadex G-75 column chromatography fractions 1 through 4. AWBE represents CIE of AWBE (15 μ l and 150 μ g dry weight) reacted with 250 μ l of pooled rabbit AWBE antiserum (*top gel*) and 50 μ l of antiserum (*bottom gel*). Fractions 1 through 4 represent separate fractions of AWBE protein chromatographed on Sephadex G-75 and further characterized by RAST-inhibition activity (see text for details). The gels for fractions 1 to 3 contained 50 μ l (150 μ g dry weight) of fraction 1, 2, or 3, respectively, reacted with 250 μ l of pooled rabbit AWBE antiserum (*top gel*) and 50 μ l of antiserum (*bottom gel*). The gel for fraction 4 contained 20 μ l (200 μ g dry weight) of fraction 4 reacted with 250 μ l of pooled rabbit AWBE antiserum (*top gel*) and 50 μ l of antiserum.

was performed with sera from 10 subjects with positive skin test and direct RAST reactivity to GWBE (Table III). Nine of the 10 sera were reactive by CRIE to GWBE. Six of the nine positive sera each identified two electrophoretically similar allergens in GWBE. At least five electrophoretically distinct allergens were identified in GWBE (Fig. 5). Column chromatography of GWBE on Sephadex G-75 produced two major protein peaks with similar molecular weight distribution to AWBE. Subsequent RAST-inhibition analysis of GWBE column chromatography fractions produced a profile not unlike that obtained with AWBE (data not presented). End point titration prick skin testing and direct RAST analysis with GWBE of 15 subjects with reactivity to AWBE are presented in Table III. All 15 subjects with prick skin test reactivity to AWBE demonstrated positive reactions to GWBE. Of interest, sera from three subjects (Nos. 11, 12, and 13) were positive by RAST to AWBE but unreactive with GWBE. Finally, as little as 0.9 μ g (dry weight) of GWBE produced 50% inhibition of a pool of AWBE, RAST-positive sera, when sera were re-

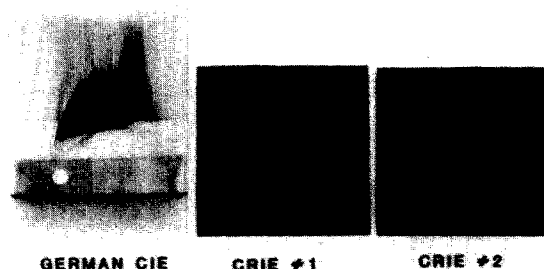


FIG. 5. CRIE of individual, GWBE, RAST-positive sera reacted with GWBE. For the German CIE, the gel contained 20 μ l (180 μ g dry weight) of GWBE reacted with 250 μ l of pooled rabbit GWBE antiserum (*top gel*) and 50 μ l of antiserum (*bottom gel*). CRIE Nos. 1 and 2 represent individual antiserum responses by CRIE selected to demonstrate the different allergens present in GWBE; 20 days autoradiography.

acted with AWBE-coated disks. Increasing amounts of GWBE produced up to 88% inhibition of the above RAST. By comparison, 0.5 μ g (dry weight) of AWBE produced 50% inhibition of this same pool of AWBE, RAST-positive sera when sera were reacted with AWBE-coated disks. Increasing amounts of AWBE produced up to 92% inhibition of this same RAST.

Skin test reactivity to commercial house dust and American cockroach extracts

The immediate prick skin test reactivity of the original 100 atopic subjects tested with commercial extracts of house dust and American cockroach (Greer Labs, Lenoir, N.C.) is presented in Table IV. Ninety-five of the 100 subjects were reactive to at least two common inhalant allergens. Many (36%) of these atopic individuals reacted to both house dust and cockroach extract; however, a significant population (13%) reacted to cockroach and not house dust extract.

DISCUSSION

It was the purpose of this study to identify and partially characterize clinically significant allergens from American cockroach whole bodies. Although this approach to cockroach allergen characterization is restrictive, Richman et al.,¹ using RAST analyses, established the clinical importance of American cockroach whole bodies as a source of significant allergens. Indeed, in the present study, we have elicited immediate skin test reactivity to American cockroach whole bodies in approximately 50% of subjects with a history of atopy. Most subjects were black male and female adults from the inner-city area of New Orleans who reported the presence of cockroach contamination of their households. Environmental surveys conducted by our laboratory have confirmed the presence of both American and German cockroach

TABLE III. American and German cockroach whole body skin test and RAST results

Subject	Serum IgE (IU/ml)	AWBE		GWBE*	
		ST	RAST	ST	RAST
1 J. L.	300	+	40	+	44
2 F. B.	1100	+	40	+	42
3 B. J.	520	+	28	+	19
4 V. K.	800	+	19	+	41
5 J. R.	56	+	14	+	9
6 S. H.	300	+	10	+	11
7 C. T.	200	+	8	+	12
8 D. V.	150	+	4	+	10
9 S. M.	360	+	3	+	3
10 G. G.	360	+	14	+	7
11 R. S.	330	+	27	+	3
12 D. H.	330	+	27	+	2
13 P. W.	330	+	10	+	1
14 J. C.	1500	+	3	+	1
15 S. G.	NT	+	3	+	2
16 A. N. P.†	300	—	2	—	1

ST = skin test.

*Immediate prick skin test reactivity and RAST percent binding.

†Pool of five atopic, cockroach skin test-negative subjects.

species in all households. Most (>50%) subjects had a clinical diagnosis of asthma, which may in part be exacerbated by cockroach exposure. Although it is only suggested by this study, other investigations have clearly supported the importance of cockroach sensitization in the induction/exacerbation of "urban asthma."^{4, 5}

In this study, with the use of prick skin testing and both direct RAST and RAST inhibition, clinically significant allergens from AWBE were identified and subsequently fractionated by column chromatography. Sephadex gel filtration separated the cockroach whole body extract into two major protein peaks. The first peak (fraction 1) was excluded on both Sephadex G-75 and G-200. Conceivably, as supported by recent results using the technique of sodium dodecyl sulfate-polyacrylamide gel electrophoresis, fraction 1 contains aggregated proteins. Although it may be premature to label AWBE fraction 2 as representing a "major" cockroach allergen(s), these studies are encouraging from the standpoint of purification of cockroach allergens and the identification/characterization of significant sensitizing components in cockroach whole body extract.

Admittedly, our present studies have focused on the characterization of AWBE allergens. Indeed, subjects chosen for study were originally defined by their skin test reactivity to a commercial AWBE. It is important

TABLE IV. Commercial house dust and AWBE skin test studies

Skin test reactivity*		
House dust	American cockroach	% Of subjects tested
+	+	36
+	—	37
—	+	14
—	—	24

*Immediate wheal-and-flare reaction with a wheal 2 mm greater than saline control wheal.

to note, however, that subsequent skin test analyses with AWBE and GWBE (prepared in our laboratory) in 100 atopic subjects have demonstrated reactivity to GWBE alone in only two subjects and reactivity to both AWBE and GWBE in 52 subjects. No subject reacted to only AWBE. Accordingly, analysis of GWBE supports the occurrence of a similar number of allergens (at least five) as AWBE, with both extracts possessing similar immunochemical/physicochemical properties (as determined by column chromatography, RAST inhibition, and CRIE analysis). Prick skin testing, direct RAST, and RAST-inhibition studies strongly support the occurrence of important, shared, interspecies cockroach allergens. Collectively, these observations are in agreement with the work of Twarog et al.² and are important from the standpoint of defining common or "major" cockroach allergens for purposes of epidemiologic studies, diagnostic testing, and immunotherapy.

As early as 1956, Feinberg et al.⁶ concluded, "Recent findings have indicated that dust from disintegrated insects may constitute a common type of antigen responsible for asthma and hay fever." This early speculation was subsequently supported by the observation that cockroach antigens could be detected in house dust obtained from homes with reported cockroach presence.⁷ Clearly, common household dust represents a logical, significant source for cockroach exposure. However, commercial preparations of house dust used for prick and/or intradermal skin testing are inadequate substitutes for intracutaneous testing with cockroach. Morris et al.,⁸ in a study of 45 inner-city children with perennial rhinitis and/or asthma, identified 13 children (29%) who were skin test negative to house dust and yet were skin test positive to a commercial cockroach extract. In our study, approximately 25% of subjects reactive to commercial American cockroach extract had a negative skin test to house dust.

In summary, the above results support the importance of American cockroach whole body allergens as significant sensitizing agents in the induction/exacerbation of allergic respiratory disease. Our findings also suggest the presence of "major" allergens in "fraction 2" of AWBE and support the presence of both species-specific and shared, interspecies allergens between AWBE and GWBE.

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Intranasal nedocromil sodium in the treatment of ragweed-allergic rhinitis

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*Nedocromil sodium (NS), a new pyranoquinoline dicarboxylic acid derivative, reported to be effective against both mucosal and connective tissue-type mast cells, was studied in ragweed-allergic rhinitis (RAR). Thirty-six patients with RAR were studied in an 8-week, double-blind, placebo-controlled trial. Stratification was based on prick skin test sensitivity and severity of signs and symptoms of previous RAR. NS (1% solution) in a dose of 0.13 ml of nasal spray was administered to each nostril, a minimum twice daily. Concomitant medications were limited to ingested terfenadine, ocular cromolyn, and inhaled medications. Symptoms and medications were noted daily. Active-treatment and placebo-treatment groups were comparable. There were less symptoms of runny nose and itchy eyes in the active-treatment group ($p < 0.05$) and also less antihistamine, $p < 0.004$. Patients in the active-treatment group were more likely to conclude that symptoms were improved by the nasal spray ($p < 0.01$). No side effects were reported. This study indicates that NS is effective and well tolerated in RAR. (*J ALLERGY CLIN IMMUNOL* 1988;81:570-4.)*

NS is a new pyranoquinoline dicarboxylic acid derivative that is reported to be effective against both mucosal and connective tissue-type mast cells.¹ In

Abbreviations used

NS: Nedocromil sodium
RAR: Ragweed-allergic rhinitis

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contrast, cromolyn sodium appears to be effective only against connective tissue-type mast cells.² NS has been demonstrated to be effective in treatment of asthma³ and inhibiting the airway responses to exer-