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ARTHROPODS IN RESPIRATORY TRACT ALLERGY

Their Relationship to Allergens in House Dust

By

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SYNOPSIS - ABSTRACT

The role of insects and other arthropods as inhalant allergens gained our attention when the incident of positive skin test reaction was found to approach that for pollens, feathers, and even house dust. In the course of routine testing of a large number of patients with respiratory tract allergy (hay fever and asthma), over 40 per cent showed significant skin test reactions. Likewise, the reaginic antibodies were distinct for each of these allergens. These positive reactions showed no correlation with the reactions to conventional allergenic extracts.

Correlation of positive skin tests to arthropods with the production of clinical disorders remains unclear. Specific etiological diagnosis is made by inference while the specific hyposensitization must rely of such inference. Benefit from treatment of otherwise refractory cases adds weight to the importance of arthropods as inhalant allergens.

Insects and other arthropods are not often considered in the search for inhalant allergens as causes of asthma or allergic rhinitis. Although caddis flies (1) and May flies (2) have proved important in the Great Lakes and Mississippi River areas, the remaining vast number of species have usually been presented as isolated case reports (3). This phylum which represents almost 80 per cent of all animal life, must in sheer numbers contaminate the earth. To this can be added the shed structures during their metamorphosis, the debris from dying generations, and the secretory substances, particularly silk and webs which almost all of them produce.

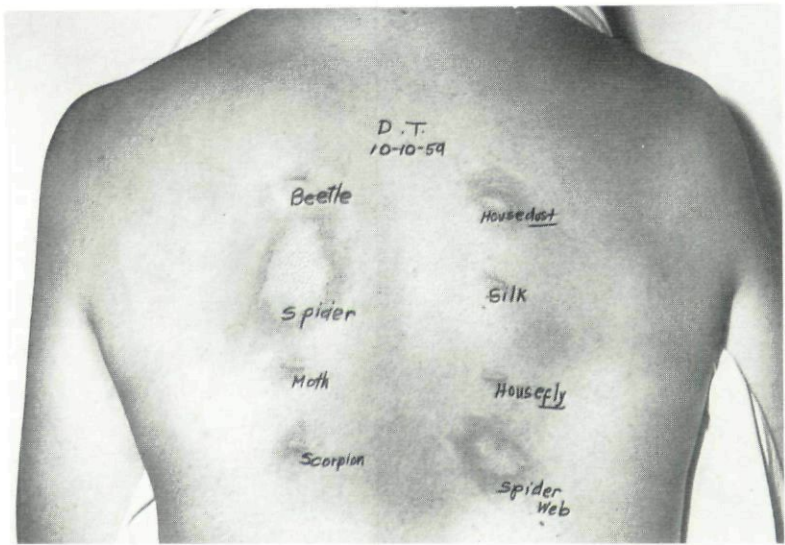


Fig. 1.

Positive scratch test reactions to spider and web with minimal reaction to house dust and none to silk or common insects.

The probability that most arthropods are capable of acting as inhalant allergens is strengthened when postulates are applied to them in a manner used for the allergenic implication of pollinating plants (4).

1. Arthropods contain excitants of allergic symptoms as evidenced by frequent strong, immediate wheal reactions on skin testing with aqueous extracts (Fig. 1). This is further demonstrated by the presence of reaginic antibodies in passive transfer (Fig. 2).

2. Arthropods are widely and abundantly distributed (5).

3. Arthropods appear in sufficiently large numbers to result in air contamination (6).

4. Arthropods at some stages of development, or their secretory substances, or debris, are sufficiently buoyant to be carried a considerable distance to reach the respiratory tract mucosa of the allergic person (7).

In spite of fulfilling these basic postulates, they are rarely

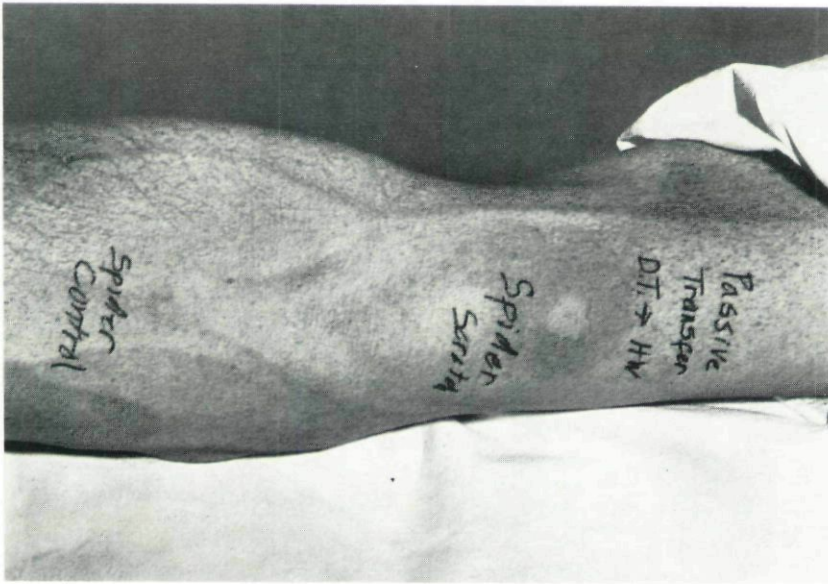


Fig. 2.

Passive transfer of serum from D.T. with site challenged by scratch method after 48 hours resulted in strong immediate wheal reaction.

considered in the search for inhalant allergens, chiefly because they are not readily detected in the inhaled air. Detection of airborne pollens in both numbers and varieties is a simple matter; on the other hand, present physical or chemical methods cannot readily identify fine particulate matter of arthropod origin. When such identification can be clearly made, then correlation of the contents of air samples to skin tests and clinical symptoms will become meaningful.

And so with limitation in our studies, it was necessary to implicate arthropods by inference. Their presumed presence as debris in the inhaled dust, the strong positive reactions on patients suffering from asthma and hay fever, and the favorable results from hyposensitization injections of appropriate extracts lend strength to these inferences.

Previously reported findings on 252 unselected patients (3) provided the following observations:

1. About 50 per cent of patients with allergic respiratory tract symptoms gave significant skin test reactions to one or more extracts of arthropods.

2. There was no significant variation in such sensitivity as to sex, race, occupation or geographic location.

3. Most frequently such reactions occurred among children and young adults. This was also true for pollens, house dust and other common inhalants.

4. There was no strong correlation of reactions to silk with reactions to arthropods, including silk moth itself.

5. There was no correlation of reactions to house dust, epidermals or to pollens with those to arthropods.

Current patient evaluation will include discussion of the possible presence of arthropod material in house dust extracts.

TABLE 1
*Protein Nitrogen Contents of Several Freshly Prepared Arthropod
and other Inhalant Extracts.*

Allergen	Protein Nitrogen in mg/ml
Aphid	0.65
Beetle	0.82
Cockroach	1.10
Housefly	0.43
Moth	0.50
Spider	1.20
Silk*	1.28
House dust*	0.95
Cow hair*	2.50
Grass pollens (mixed)	2.66

* Concentrated by precipitating with cold acetone.

MATERIALS AND METHODS

Arthropods were in many cases laboratory grown and freed of their culture media by mechanical removal as well as through starvation for several days. They were then processed from the live or quick frozen stage (3) by maceration, defatting with ethyl ether, then lyophilizing and grinding to a fine powder.

This dry powder was extracted with 50 per cent glycerosaline, buffered to 7.9 in the proportion of 1:10 dilution by weight-volume. These extracts proved to retain allergenicity for periods of months to years.

Biochemical analyses of extracts from various arthropods showed varying nitrogen contents. For example, one sample of moth with a total nitrogen of 2.07 mg per ml contained 0.535 mg protein nitrogen, while a cockroach extract containing 2.22 mg total nitrogen contained 0.964 mg of protein nitrogen (see also Table 1).

House dust and epidermals were concentrated by precipitating out with cold acetone the allergenic material (8). Protein nitrogen contents of these allergens are also included in Table 1. Although no attempt was made to adjust all extracts on the basis of protein nitrogen contents, the variation in such chemical analyses was not sufficiently significant to enter into the wide difference in skin reactions among the patients tested.

CLINICAL METHODS

The list of arthropods used for testing were reduced to workable numbers with presumption that within the classification of this Phylum the level of Order provided several of the readily available Families which could supply a representative allergen (9). In Tables 2 and 3 are shown a proposed list for routine testing as well as a number of arthropods less commonly encountered or important only in certain areas.

Skin testing was performed both by the scratch and the intradermal methods. Scratch testing was done first for safety since some patients would have very large immediate wheals. Had the intradermal method been applied first, unquestionably a systemic reaction would have resulted. In several patients mild systemic reactions were inadvertently produced by intradermal testing in spite of this precaution.

The intradermal tests were made on the flexor surface of the arm and forearm. A ten-fold dilution was used when the scratch test was negative or equivocal and the injection of 0.02 ml produced minimal non-specific reaction. Selected patients who gave strong positive scratch test reactions were further tested intradermally with highly diluted extracts to quantitate the level of dilution at which hyposensitization treatment with arthropod extracts should be started.

TABLE 2
Proposed List of Insects for Routine Testing.

Order*	Common Names of Insects†
<i>Class Hexapoda</i>	
1. Coleoptera	beetles, weevils
2. Lepidoptera	moths, butterflies
3. Hymenoptera	honeybees, hornets, yellow jackets
4. Diptera	flies, mosquitoes
5. Orthoptera	grasshoppers, locusts, cockroaches
6. Hemiptera	box-elder bugs, squash bugs
7. Homoptera	aphids, leafhoppers, cicadas, scales
8. Minor orders	mixture of common representative
<i>Class Arachnida</i>	
9. Aranea	spiders
10. Acarina	mites
<i>Class Crustacea</i>	
11. Isopoda	sowbugs
12. Branchiopoda	daphnia, fair shrimp

* The first four orders will encompass 80 per cent of the common species found in North America.

† Families and species not indicated. A mixture of those most abundant and most readily available may be used. (Courtesy, Journal of Allergy).

Patients for specific hyposensitization were selected with the following indications:

1. Clear evidence of symptoms following exposure to dust laden with arthropod material. Few patients in our area gave such clear-cut indications except those working with entomological materials.

2. Large skin test reactions to arthropod extracts and moderate to minimal reaction to dust, epidermals or pollens. There was a small number of patients in this group.

3. Lack of benefit from a program of environmental control and treatment with common allergens including dusts and pollens. This group included the largest number of candidates.

TABLE 3
Regional and Less Common Insects for Specific Problems

Order*	Common Names of Insects†
<i>Class Hexapoda</i>	
1. Order Ephemeroptera	May flies
2. Order Trichoptera	caddis flies
3. Order Neuroptera	lacewings
4. Order Thysanura	silverfish
<i>Class Myriapoda</i>	
5. Order Chilopoda	centipedes
6. Order Diplopoda	millipedes
<i>Class Crustacea</i>	
7. Order Copepoda	plankton (brine) shrimp

(Courtesy, Journal of Allergy).

CLINICAL AND IMMUNOLOGICAL OBSERVATIONS

In the smaller series of 169 unselected patients who were recently tested routinely because of a history of respiratory tract allergy, a number of interesting observations closely paralleled the findings of the larger series published previously. They may be summarized as follows:

1. Reactions to one or more of the arthropod extracts occurred in 69 case or 41 per cent.

2. Reactions to more than one arthropod was the rule. Occasionally reactions occurred to almost all of those tested; frequently many of the orders within a class reacts (especially hexapoda or true insects); usually within a single order most of the families represented did react.

3. Silk would in some give strong reactions while arthropods, including moth, failed to give any reaction (Fig. 3). The reverse, with positive reactions to arthropods and none to silk, also occurred (Fig. 1).

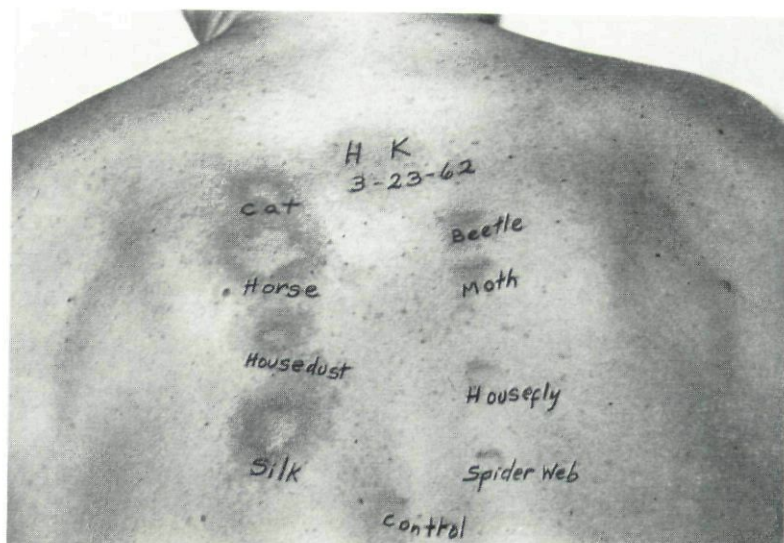


Fig. 3.

Strong scratch test reaction to epidermals, house dust, and silk but negative reaction to arthropods including insects and spider web.

4. Reactions to one or more epidermals occurred in 83 cases or 49 per cent.

5. Reaction to house dust extracts occurred in 100 patients or 59 per cent.

When 22 patients were tested with extracts of house dust obtained from various areas of the United States and Japan (Figs. 4 and 5), comparable strong skin test reactions were obtained. Only the house dust material prepared from the Florida sample gave equivocal reactions. It was noted that the crude dust contained material chiefly from carpeting. It was later learned that the vacuuming was done in the physician's newly furnished office and there was evidently very little "aged" material in this "house dust" (see Discussion).

The other house dust extracts prepared in the various laboratories were strongly allergenic but no biochemical adjustment was attempted to provide any uniformity of nitrogen contents. It is interesting to note that in spite of the diverse

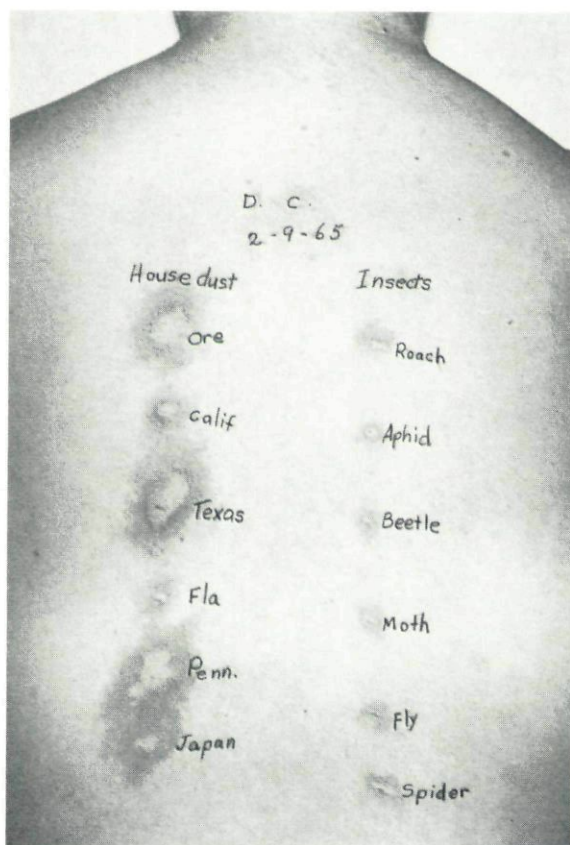


Fig. 4.

Strong scratch test reaction to house dust from various sources (except Florida, see Clinical Observations); negative reactions to all arthropods tested.

sources of these house dusts and differing methods of preparing them, the skin test reactions suggested some common allergens in all. It was also noted that none varied in their lack of relationship to the allergens in epidermals, pollens and arthropods.

6. Attempt at correlation of reactions to arthropod extract with those of house dust revealed the following:

a. Of 69 patients with positive reaction to arthropods, ne-

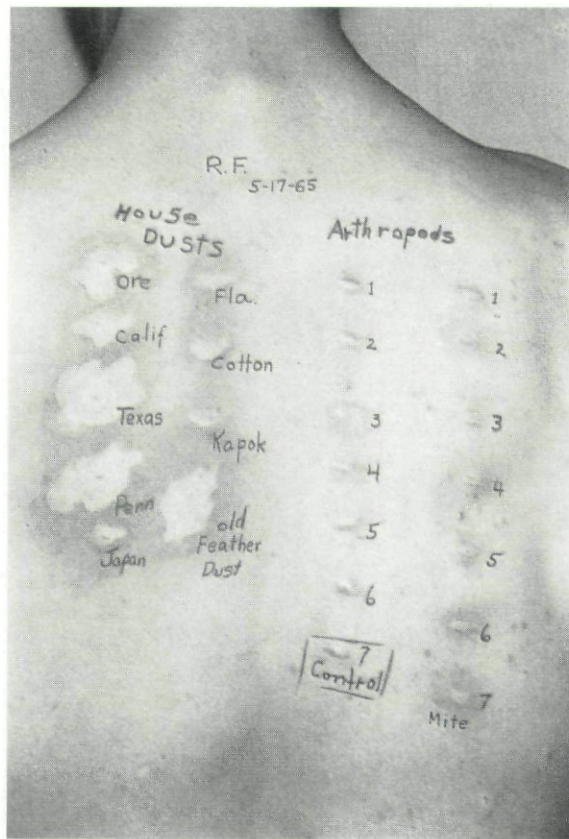


Fig. 5.

Strong scratch test reaction to various house dusts and to "old feather dust". Minimal reaction to unaged cotton linters and kapok and Florida dust. No reactions to the group of arthropods as listed in Table 2.

gative or equivocal reaction to house dust occurred in 12 (Fig. 6).

b. Of 100 patients with positive reactions to house dust, negative reactions to arthropods occurred in 41 (Figs. 4 and 5).

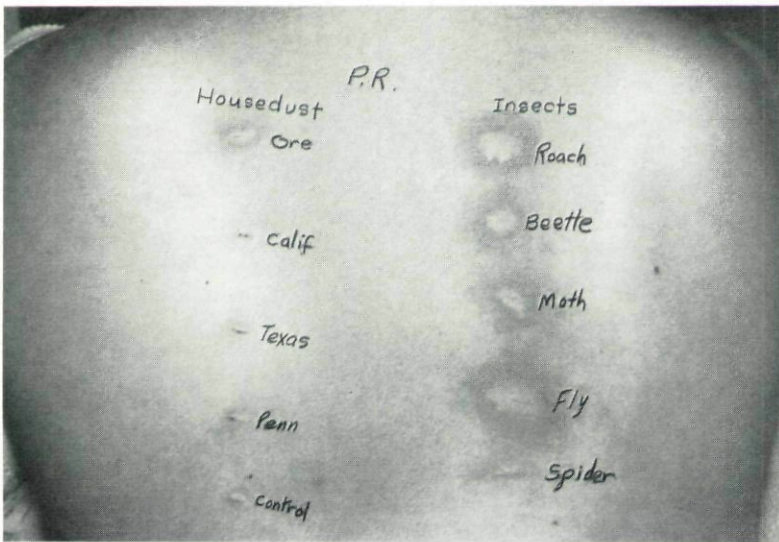


Fig. 6.

Strong scratch test reaction to arthropods; negative reaction to house dust except for slight reaction with that from Oregon.

DISCUSSION

It is evident that the extract of arthropods contain allergenic material and that a significant number of patients with respiratory symptoms of allergy possess reaginic antibodies for them. The allergens are probably multiple and varied, and it is unlikely that a common allergen or that even a small group of them will be found to represent this phylum. The excellent and painstaking work done with caddis fly (10) suggests a method for identifying this intrinsic allergen but only the method can be applied to the study of other arthropods. Testing with silk has often been proposed for the detection of insect allergy, but it was found that even the adult silk moth itself did not consistently react on patients who were sensitive to silk.

It appears, therefore, that testing with arthropods must be done individually in a manner similar to that for testing with various epidermals and pollens. To reduce the burden of

numerous skin tests the arbitrary grouping into orders proved reasonable (Tables 2 and 3). The significance of positive reactions remains unclear in spite of the ubiquitous nature of particulate matter of arthropod origin. It would be desirable to have some method of quantitating the presence of this material in the inhaled air rather than to rely on positive skin test reactions and subsequent benefit from the hyposensitization with the extract.

The question has frequently arisen of considering arthropod material as an integral part of house dust. Early in the study of house dust *Cooke* (11) expressed the view that this substance contains a specific allergen not necessarily identified with the sum of any individual animal or vegetable allergens in the house. Although this view has been frequently challenged, it has withstood the test of time. Recently immunological studies by *Voorhorst* (12) and *Phillip & Northey* (13) confirmed the clinical observation that house dust allergen probably has characteristics of a single substance.

Demonstrations by *Cohen, Nelson & Reinharz* (14) gave strong evidence that in house dust there were allergens closely related to those found in "aged" cotton linters, kapok, and feathers (Fig. 5). This would then raise the question of whether particulate matter of arthropod origin in "aging" would become identified with house dust. Such a question deserves serious consideration. Arthropods share our household in large numbers and in successive generations. In the winter additional hordes join us to share the warmth and shelter; and all year they are continually being attracted by light and by food (15). The resultant debris accumulates, blends, and ages with other particulate matter in the household.

In our studies, although most extracts were prepared from the live or freshly killed organisms, several of them, specifically moth and cockroach, might qualify as "aged or old" material. These and several other arthropods which were grown in large quantities were frozen, lyophilized, and finely powdered. After that they were stored in the desiccator for months and, in case of moths, for several years before being

recently prepared into aqueous extract for skin testing. Yet these are included among the group of testing material which gave strong skin reactions where house dusts failed to react or which showed no reactions in subjects who gave strong whealing with house dust extract. Therefore, at present we must presume that arthropods and house dust do not share skin reactive allergens in common except as gross contaminants. Routine testing would best be done separately with the various arthropod extracts as well as with house dust, epidermals, and pollens.

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