Some Aspects Of Insect Allergy

Joseph H. Shaffer
SOME ASPECTS OF INSECT ALLERGY

JOSEPH H. SHAFFER, M.D.

Within the past few years, numerous articles dealing with various phases of allergy to insects have appeared in scientific journals and lay press. In a dramatic fashion, they call our attention to the way in which insects cause allergic reactions which may at times pose a real threat to life.

An article appeared in the June, 1959, issue of The Journal of Lifetime Living entitled, "Is there a Killer in your Back Yard?" and was also abstracted in the Reader's Digest that same month. The author related in graphic detail his experience when stung by a swarm of angry wasps. This article listed six recent fatalities, in various sections of the United States, following insect stings in which sudden death occurred before medical aid could be summoned. These articles were called to our attention by telephone calls and letters. Inquires were mostly from persons who had experienced generalized symptoms following stings by insects; they were alarmed by these stories and were anxious to have treatment and, if possible, protection from serious reactions should they be stung again. Having been exposed to the body proteins contained in the insect venom at the time of a sting, such persons could well have become sensitized and are therefore candidates for anaphylactic response to subsequent stings.

Since insects have always been with us and are likely to continue as co-inhabitants on this earth, and since the health and life of certain sensitized individuals are constantly endangered by their presence, I thought it proper to review briefly the role that insects play in the production of allergic symptoms, along with some suggestions as to treatment. This problem is deemed of sufficient importance that the American Academy of Allergy has a committee to review and encourage research in this field.

EXPOSURE BY INHALATION

Allergic disorders of the respiratory tract have been associated with sensitivity to butterflies, caddis flies, moths, May flies, bees and other flying insects. Inhalation of scales, hairs, wing and body fragments, and other body emanations, given off in flight, are found in atmospheric dust when these insects are prevalent at certain seasons of the year. Persons may become sensitized to such substances and may experience conjunctivitis, rhinitis, bronchitis and bronchial asthma. Patients who suffer from pollen sensitivity may have identical symptoms. It is, therefore, necessary at times to consider insects in addition to pollens as etiological factors in the production of seasonal symptomatology.

Some thirty years ago, Figley found certain patients living along the shores of Lake Erie near Toledo and Port Clinton, Ohio, who had symptoms from June to early August that were caused by May flies. Patients were subjected to conjunctival, inhalation and intradermal tests and were found sensitive to extracts of the pellicle given off during the moultng season. Pellicles were thin and friable, easily fragmented

*Division of Allergy.
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by the wind, and could be carried long distances. Thus available for inhalation, they could and did produce allergic sensitization. Figley, in his studies, found extracts of dried whole caddis flies just as effective as pellicle extracts for testing and for desensitization. He reported complete relief from symptoms in his patients following desensitization. Others have reported similar results in the treatment of caddis fly sensitivity.

EXPOSURE FROM BITES

Percutaneous instillation of salivary secretions during bites from chiggers, ants, mosquitoes, gnats, fleas, house-flies and other flies and biting insects produces local discomfort. Such bites may, however, cause marked erythema, swelling, pruritis, ecchymosis and angioneurotic edema, the latter of which may not appear for 24 to 48 hours.

One of my patients (M. LeF.), a white female attorney, age 63, with a negative history for other forms of allergy, experienced malaise, chills and fever, generalized urticaria, extreme weakness and collapse following the bite from a fly. The specimen brought to us was identified by an entomologist as “deer-fly”, a Diptera of the Family of Tabanids. Patients sensitive to this group of biting insects may be tested and treated with insect whole body extracts.

EXPOSURE FROM STINGS

The most important insects in the production of serious and potentially fatal anaphylactic reactions are the Arthropods of the Hymenoptera group. This group includes the honey-bee, bumble-bee, wasp, yellow and black hornet, and the yellow jacket. (Fig. 1.) A sting may cause intense localized redness, swelling and pain which may persist for several hours. Individuals may experience local reactions of diminishing intensity with subsequent stings due to natural immunization. Such repeated exposures to the body proteins present in the venom sac contents may, in other individuals, produce sensitization, or an altered reactivity on the part of body tissues. It is difficult to predict which symptoms may be produced by subsequent stings when such an allergic state exists.

SYMPTOMS

Symptoms may consist of one or more of the following: localized pain, swelling, generalized erythema, a feeling of intense heat throughout the body, headache, swollen and tender joints, generalized pruritis, urticaria, weakness, abdominal cramps, dyspnea, constriction of the chest, asthma, vascular collapse and possible death from anaphylaxis within a very few minutes. Such patients have on occasion been found dead — and erroneously recorded as death due to heart attack or sunstroke because the sting site had gone unnoticed.

Barnard reported three deaths from insect stings. One patient died in congestive failure and anaphylactic shock following stings from a wasp. Post-mortem examination on a second patient who died following stings from a yellow jacket showed visceral congestion and petechial hemorrhages with acute gastroenteritis and myocarditis. A third patient was stung by a bee and died of suffocation due to edema of the larynx.
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STINGING INSECTS

Figure 1

Serious and potentially fatal anaphylactic reactions may be caused by stings from the Arthropods of the Hymenoptera group of insects. Drawings from What's New, No. 211, 1959, courtesy of Abbott Laboratories.

Insects of the Hymenoptera group, except the bee, retain their stinger and are in a position to sting repeatedly, thus causing multiple traumatic areas, each time injecting some portion of the venom sac contents. The honey-bee, however, leaves its barbed stinger at the site of the sting. Should the bee be brushed off, the venom sac separates from the body of the bee. Although separated from the body, the smooth muscles of the venom sac continue to contract for two to three minutes and each contraction forces some of the contents of the venom sac through the stinger shaft until the sac is emptied.

NATURE OF THE VENOM

The complex chemical substances found in the venom cause marked local irritative reaction, while the protein fractions of the venom may produce allergic response. Benson and Semenov subjected bee venom to chemical analysis and were able to detect the presence of an indol derivative (probably tryptophan), choline, glycerol, phosphoric acid, palmitic and other fatty acids, and a non-nitrogenous substance thought to be saponin. Formic acid and histamine were not found. Saponin, or saponin-like substance, was thought to release histamine from the skin through
the interaction of dermolyisin. They concluded that sensitization following a sting by a bee was caused by proteins inherent in both the body and the secretions found in the venom sac. Microscopic studies of the stinging technique and stinger of the bee failed to show pollen contamination of the stinger as a possible factor in the production of the allergic reaction.

Perlman states that little is known of the nature and number of excitants in insect allergens that produce immediate whealing response and antibodies that may readily be passively transferred. The integument of the Arthropods is generally presumed to contain the allergenic substances. Chemical analysis of insect cuticle contains protein, carbohydrate and sulfur-containing compounds. Perlman prepares allergenic extracts from live or quick-frozen whole insects, defats the broken-up insects with ethylether, then extracts with isotonic buffered aqueous solution. After lyophilizing, the material is stored in dry powdered form in a dessicator. From this powdered antigen a glycerinated buffered extract is prepared for testing and treatment.

Foubert and Stier prepared separate extracts from the pulped bodies of honey-bees, wasps, black hornets, yellow hornets and yellow jackets and compared antigens found in the five extracts. By employing the gel diffusion technique of Ouchterlony they found that each of the insects contained from four to six antigenic protein fractions, two of which seemed identical and present in each of the five insects. The remaining two to four fractions were specific for each species, but were shared in common by wasps and honey-bees, but not by hornets and yellow jackets. Since a person may have been sensitized to only one of the antigens, and with subsequent stings may become sensitive to other antigens present, it is desirable to use an antigen mixture that will protect against all insects in this group. Although there is some difference of opinion among allergists as to whether venom sac contents alone, or extracts from the whole body of the insect should be used for diagnostic tests and treatment, it is generally accepted that insect whole body extracts are more potent antigenically and are the treatment material of choice.

TESTING AND DESENSITIZATION

It has been suspected that a refractory period of ten to fourteen days persists (as in experimental anaphylaxis) following an insect sting, during which time skin tests may be negative. Tests should therefore be delayed for several weeks after the stinging of the patient, and should be applied with extreme caution. It has been our experience, as it has with others, that patients sensitized to insect allergens may give a positive reaction to an intradermal test dose as small as 0.025 cc. of a 1:100,000,000 dilution of the extract. Should the initial test with this weak dilution fail to give a positive reaction, successively stronger test dilutions should be applied until a positive reaction is obtained. The test dose that produces a positive reaction could be considered as a relatively safe dose for starting desensitization. We use commercially prepared single insect extracts for testing, and a multiple whole insect extract mixture (containing honey-bee, wasp, hornet and yellow jacket) for desensitization.

*Hollister-Stier Laboratories.
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Table 1
DESENSITIZATION WITH POLYVALENT INSECT ANTIGEN
Dosage Schedule*

<table>
<thead>
<tr>
<th>Dilutions</th>
<th>1-1,000,000</th>
<th>1-100,000</th>
<th>1-10,000</th>
<th>1-1,000</th>
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<tr>
<td>0.05 cc</td>
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<td>0.40</td>
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*Given at intervals of 4 to 7 days until maximum tolerance dose is reached — then maintain at 3 to 4 week intervals.

Desensitizing treatments are given at intervals of seven days and in accordance with a graduated dosage schedule as recommended by the manufacturer.* (Table 1.) Dosages are regulated so as to avoid marked local reactions at the site of the injection which is given subcutaneously. We try to avoid causing a systemic reaction from over-dosage or by accidental injection into the blood stream. Should a reaction occur immediately or during the twenty minute observation period after treatment, a tourniquet is applied above the injection site and epinephrine hydrochloride 1-1000 dilution is administered in divided doses (0.20 to 0.30 cc.) and repeated as necessary until the reaction has subsided. We have been able to reach a dose of 0.40 cc. of 1-100 dilution. The patient is maintained on that level every two weeks for two to three months, then every three weeks for a few months, then continued on maintenance therapy every four weeks on a year round basis.

Mueller reviewed 120 cases of allergy to stinging insects and found only three instances where capture and proper identification of the insect that delivered the sting had been possible. Educational programs along this line met with little success. He points out that knowledge of the nesting habits of these insects could be helpful. Small honey-comb type or mud nests of the wasp are found in protected areas around buildings, yellow jackets' nest under logs or rocks and in the ground, and the papier-maché foot-ball sized hornets' nest in bushes and trees. Bees are usually encountered around fields of clover. Unless the stinging insect can be positively identified, Mueller recommends broad protection by treating with multiple insect whole body extracts.

PROTECTIVE EFFECT OF DESENSITIZATION

Mueller desensitized 76 patients who had experienced systemic reactions to stings. Thirty were re-stung and only one suffered systemic symptoms while on maintenance
therapy, or after having completed three years of desensitization treatment. (Table 2.)

Table 2

<table>
<thead>
<tr>
<th></th>
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<tr>
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<td>Patients Reported</td>
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<tr>
<td>Mueller</td>
<td>76</td>
<td>1*</td>
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<tr>
<td>Jones and Laws</td>
<td>20</td>
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</tr>
<tr>
<td>Swinny</td>
<td>41</td>
<td>0</td>
</tr>
<tr>
<td>Thomas</td>
<td>18</td>
<td>0</td>
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</tbody>
</table>

*Re-stung after treatment and experienced anxiety and itching.
**Local reactions—minimal to moderate.

Jones and Laws reported their experiences with 20 patients who had experienced generalized allergic reactions to the venom of stinging insects. Six of these patients were re-stung while undergoing or after completion of desensitization therapy; they experienced moderate local reactions only at the sting site.

Swinny states that desensitization can be effective and is often life-saving. He reported 41 patients who had anaphylactic types of reactions to insect stings; and 19 of this group were subsequently stung but had local reactions only.

Thomas reports 12 of 18 patients who were hyposensitized and subsequently stung or bitten and none of whom suffered systemic or constitutional reactions, but had local reactions only. He recommends that all patients who have had severe local reactions as well as systemic reactions be considered for hyposensitization as they are potential candidates for severe systemic reactions, some of which may be fatal.

One of the four patients (Case 1) reported in this paper was re-stung while receiving maintenance doses of 0.20 cc. of a 1-100 dilution of polyvalent insect antigen every four weeks. He experienced a minimal local reaction only at the site of the sting.

**EMERGENCY TREATMENT**

If we are to effectively combat serious reactions caused by insects, it is imperative that we have a well thought out treatment plan to put into effect with the least possible delay. Our patients are furnished with an emergency kit and are instructed to keep it readily available. (Fig. 2.) It contains tourniquets (sufficiently long to encompass the thigh) to apply proximal to stings on the extremities, and tweezers for removing bee stingers, isoproterenol, 10 mg. tablets, for sublingual absorption, and epinephrine hydrochloride (Medihaler Epi) for rapid aerosol inhalation. The patient and members of the family are instructed in the administration of these preparations. Antihistamine ointments applied locally along with oral preparations have controlled itching and urticaria. Cold packs to the sting area have proved soothing and helpful in reducing local discomfort.
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**EMERGENCY TREATMENT FOR INSECT ALLERGY**

1. Remove bee stinger with tweezers at once.
2. Dissolve white tablet (Isuprel) under the tongue.
3. Use inhaler (epinephrine) for difficult breathing.
4. Apply tourniquet on arm or leg above sting site.
5. Cleanse sting area with antiseptic towelette.
6. Apply cold pack to sting area.
7. Read instruction sheet carefully.
8. Call your doctor at once!

First aid measures, as just mentioned, may prove sufficiently effective to counteract the effect of the insect venom. There are occasions, however, when the services of a physician are necessary to “take over” in the treatment of the violent generalized anaphylactic reactions which may prove fatal. Such a situation may require epinephrine hydrochloride in divided doses, intravenous fluids containing levarterenol bitartrate (Levophed), cardiac stimulants, and possibly epinephrine administration intracardially.
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Ethynorepinephrine hydrochloride (Bronkephrine) given hypodermically may be substituted for epinephrine, thus avoiding the pressor effect which may be undesirable in treating patients with hypertension or cardiac disease. Should swelling of the neck and throat, or edema of the larynx occur, it may be necessary to perform tracheotomy or to insert an airway for administration of oxygen.

CASE REPORTS

(Case 1.) R.P., a white male age 49, while working as a tree-trimmer for a local power company, was stung several times in quick succession by yellow jackets. Shortly thereafter he developed a severe and generalized rash. He was taken to the company doctor who administered adrenalin injections and antihistaminics. Twenty-four hours later the rash had cleared, and the doctor warned him to rush to the hospital for immediate treatment should he be stung again.

The patient's wife, in a letter to us, referred to the article in the Reader's Digest which stated that immunization injections could be given. Since her husband was repeatedly exposed to stinging insects in his work, they were greatly worried and were anxious that he receive immunization therapy. The patient was tested on September 9, 1959, and showed a 2 plus reaction to 0.025 cc. intradermal test dose of a 1-1,000,000 dilution of yellow jacket extract. He was started on treatment with dosages of this dilution, using a multiple whole insect extract. While on a maintenance dose of 0.20 cc. of a 1-100 dilution, given at intervals of four weeks, he stepped on a bee. He experienced minimal localized swelling only at the sting site.

(Case 2.) K.D., a white male student, age 18, was brought to the clinic by his father October 21, 1960. This boy had been stung several times by insects over the previous two years but had experienced no great difficulty until the summer of 1959. While on an automobile trip he was stung by a bumble-bee. Local swelling had persisted for several hours, but alarming symptoms developed within a twenty-four hour period which caused them to stop in a nearby village for medical assistance. The patient had high fever, chills, extreme weakness and became semi-delirious. Although the original sting site showed nothing, the left eye was completely closed by swelling. Symptoms cleared within 48 hours with treatment by the physician.

The patient was tested October 21, 1960, and was found sensitive to wasp, 1 plus, and negative to bee, hornet and yellow jacket by intradermal tests with 1-10,000 dilutions. A 2 plus positive reaction was obtained to 0.05 cc. intradermal test with a 1-100,000 dilution of mixed whole insect antigen. He was placed on treatment with this dilution as a starting dose and is now receiving his injections under the direction of his local physician. The patient was furnished a kit containing tourniquets, ephedrine sulfate Gr. 3/8 capsules, Isuprel (10 mg.) sublingual tablets. He was instructed in the use of the tourniquet, medications, and application of ice packs.

(Case 3.) A.B., age 46, a staff surgeon of our hospital, was seen in our clinic August 9, 1960. While working in his yard on August 7th, he was stung on the right knee by a "sweat bee." Although there was very little localized swelling, ten minutes later he developed generalized giant urticaria, the lips became swollen, and
there was difficulty in swallowing. He realized he was having a reaction and sought assistance from an internist who lived nearby. After treatment with divided doses of epinephrine hydrochloride, Depo-Medrol and oral cortisone, symptoms cleared.

The patient stated that bee stings over the years had caused no difficulty, but that bites from horseflies caused large welts on the skin. Six months before, he had a dermatitis on the wrists from printer's ink. The personal and family histories were otherwise negative for allergy.

On August 9th (48 hours after the allergic episode), scratch tests to wasp, hornet, bee and yellow jacket were negative to 1-100,000 dilution. Retesting was done on August 30, 1960, using mixed whole insect antigens of the above insects with the following results:

1-1,000,000 dilution — negative; 1-100,000 dilution — weak, one plus. 1-10,000 dilution, 4 plus with marked pseudopodial reaction. This patient was started on desensitization with a dose of 0.025 cc. of a 1-100,000 dilution of mixed whole insect antigen containing wasp, hornet, bee and yellow jacket.

(Case 4.) C.B., a white male, age 57, came to our clinic December 15, 1960, at which time the following history was elicited. While cutting grass at his cabin in Northern Michigan in September, 1960, he was stung on the abdomen by an insect which “appeared to have come out of a nest in the ground.” There was immediate redness, swelling and pain at the sting site but in five minutes he was aware of tachycardia and vertigo which caused him to lie down. He became confused and semi-comatose but roused in an estimated twenty minutes and again started for his cabin. His wife was alarmed at his pallor and profuse sweating. He crawled into bed and covered himself and as he became warm he broke out with a generalized urticaria with associated swelling of the lips and tongue and there was difficulty in swallowing.

The patient was rushed to a clinic in a nearby town where he was given injections of epinephrine and Benadryl with effective relief. The physician furnished the patient with Isuprel linguets, syringe, needle and injectable Benadryl with instructions as to their use, should he be stung again.

Although the patient had been stung repeatedly in childhood this was the first time he had experienced generalized symptoms. There was a negative history for other forms of allergy. His mother however developed hives after eating certain foods.

Intradermal tests with insect whole body extracts were done on December 15 and 16 with the following results: mixed antigen (wasp, bee, hornet, yellow jacket) 1-1,000,000 dilution — negative; 1-100,000 dilution — negative; hornet — 1-100,000 dilution — negative; yellow jacket 1-100,000 dilution — 2 plus; honey-bee 1-10,000 dilution — 1 plus; wasp 1-10,000 dilution — 1 plus; hornet 1-10,000 dilution — 1 plus.

This patient was instructed in the use of an emergency kit with which he was furnished and was started on desensitization with mixed insect whole body extracts in a 1-100,000 dilution.
SUMMARY

1. Symptoms caused by various kinds of insects are reviewed. Inhalation of body proteins and emanations of butterflies, caddis flies, moths, May flies, and bees and other flying insects may cause allergic symptoms of the respiratory tract. Protection may, in most instances, be furnished by desensitization with whole insect body extracts.

2. Bites from insects such as chiggers, ants, mosquitoes, gnats, fleas, houseflies and other flies may cause local trauma only, or local and systemic allergic symptoms. Desensitization with whole insect body extracts may again be helpful in prevention of such allergic symptoms.

3. The most violent allergic reactions are caused by stings from insects of the Hymenoptera group (honey-bees, bumble bees, wasps, yellow and black hornets and yellow jackets). Persons who have been stung and have experienced mild to moderate local reactions only, may not need desensitization. Those persons who have experienced severe local and/or generalized allergic reactions from previous stings should, however, receive desensitization therapy with polyvalent, or mixed whole insect body extracts.

4. Although desensitization is effective in approximately 95% of the patients treated, it is well to furnish all patients who are allergic to insects with an emergency kit along with specific instructions as to its use. This kit should be readily available to the patient whether at home, on vacation trips, or in pursuit of daily activities.

5. Sudden death from anaphylaxis is a real threat to human life when persons, once sensitized to the protein substances of stinging insects, are re-stung. Effective emergency treatment and desensitization therapy can, in most instances, nullify this threat to life.

REFERENCES

5. Perlman, F.: Personal communication to the author.