

California M E D I C I N E

OFFICIAL JOURNAL OF THE CALIFORNIA MEDICAL ASSOCIATION

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Volume 96

JANUARY 1962

Number 1

Insects as Allergen Injectants

Severe Reactions to Bites and Stings of Arthropods

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MANY ARTHROPODS are known to attack man for food or in defense or to carry on the life cycle. To a few persons the bites, stings or actual invasion of the skin by arthropods will cause excessive reactions which may take the form of large lasting local effect or systemic symptoms. Arthropods capable of producing such effects include chiefly those within the class *Hexapoda*. There are a few additional offenders in the class *Arachnida*¹ (Table 1).

Local reactions may vary from immediate urticaria to delayed lesions of tuberculin type to necrosis of granulomatous or even of Arthus type.⁵ Systemic symptoms may be mild and transient or severe and even fatal.²⁵ These violent systemic reactions resemble more the anaphylactic shock of laboratory animals than the common allergic disorders of man (Table 2).

The development of severe reactions to bites and stings has been found by us to be statistically no more frequent in patients with general allergic disorders than in the general population, nor is there any apparent hereditary component. The acquired nature of allergic reactions of this type is frequently demonstrated in entomologists bitten accidentally or intentionally to supply blood meals. This has been demonstrated with mosquitoes, biting flies, fleas, lice, kissing bugs and scorpions. Naturally induced anaphylactic state and acquired immunity are illustrated in the following two case histories:

Presented before the Section on Allergy at the 90th Annual Session of the California Medical Association, Los Angeles, April 30 to May 3, 1961.

• Arthropods capable of penetrating human skin often cause severe local and systemic reactions. Local reactions suggest delayed hypersensitivity while systemic symptoms resemble more the anaphylactic shock in animals.

The nature of the antigen remains obscure but predominant evidence suggests its presence throughout the entire organism.

Positive history of hypersensitivity to insect injectants was obtained in approximately 20 per cent of persons in the course of routine interviews of 1,078 patients.

Repeated bites and stings at long or irregular intervals often induce a state of hypersensitivity, while repeated regular injections of extracts of these insects at shorter intervals may greatly reduce the hypersensitivity.

The clinical evidence of allergic sensitivity to insect bites and stings cannot be readily confirmed by skin testing or by other immunological procedures. The history and the character of the lesions as well as certain entomological knowledge of the habits of the insects offer a better basis for specific diagnosis.

Treatment with extracts of the whole offending insect generally provides good results but the protection afforded by such treatment varies in degree and duration.

CASE 1. A 5-year-old child was stung on the foot in early June 1960, the sting resulting in no local or systemic symptoms. A second sting, in early July of the same year on the scalp, produced large local swelling which persisted for several days. The third sting, in early August 1961 on the finger, was followed within five minutes by swelling about the lips

and urticaria involving the entire trunk. The patient was rushed to the hospital where an injection of epinephrine gave prompt relief.

This strongly suggests naturally induced hypersensitivity by repeated stings at monthly intervals.

CASE 2. A 41-year-old man who was stung on the back of the neck developed within several minutes generalized itching, faintness and loss of sphincter control. Edema of the throat and tongue made breathing difficult. He was rushed to the hospital where epinephrine injection slowly reduced the tongue and throat edema, obviating the need for tracheotomy, which had been considered. Four days later the patient's brother-in-law, returning from

the woodshed after exterminating a yellow jacket nest, brought on his clothing one survivor which immediately flew to the patient, stinging him. The family rushed the victim to the hospital, but during the 15-minute auto trip he noted no physical ill effects. After waiting outside the hospital emergency station for an hour, he returned home without medication and without symptoms.

This case strongly suggests a "refractory stage" which can be experimentally produced in animal anaphylaxis.

The incidence of allergic reaction to insect injectants is not known. The history of such experience is rarely solicited even in detailed allergic survey. In our clinic during the past calendar year 1,078 new patients interviewed were specifically questioned concerning any severe allergic reactions to insect bites or stings. Rigid requirements for a positive history were established. The following question was asked:

"Do insect bites or stings—mosquito, flea or bee—(pause)—poison you more than they do other people?"

Almost invariably the positive answer came during the pause, before the question was completed. Further questioning evoked a description of the local lesion or systemic symptoms sufficient for a clinical diagnosis. Only a very few such cases were excluded because of equivocal details. Of the 1,078 patients interviewed, 220, or about 20 per cent, gave adequate histories of reactions to such insects. Their records were further reviewed and summarized in Table 3.

Diagnosis of these allergic reactions to bites and stings can often be made clinically. Systemic effect follows in a matter of minutes after the encounter.

TABLE 1.—Arthropods Whose Bites or Stings Are Known to Cause Allergic Reactions (Exclusive of Primary Venom Effect)

Classification	Common Names	Common Type Reactions	
		Local	Systemic
Class <i>Hexapoda</i> :			
Order <i>Hymenoptera</i>	Bees	x	x
	Hornets, wasps..	x	x
	Yellow jackets ..	x	x
	Ants	x	x
Order <i>Diptera</i>	Mosquitoes.....	x	—
	Deer, horse flies	x	x
	Stable flies	x	x
	Black flies.....	x	x
	“No-see-ums”	x	—
Order <i>Siphonaptera</i>	Fleas	x	—
Order <i>Hemiptera</i>	Bed bugs	x	x
	Assassin bugs ..	x	x
Order <i>Anoplura</i>	Sucking lice	x	x
	Crab lice	x	x
Class <i>Arachnida</i> :			
Order <i>Araneida</i>	Spiders	x	?
Order <i>Scorpionida</i>	Scorpions	x	x
Order <i>Acarina</i>	Mites, ticks	x	—

TABLE 2.—Comparison of Common Allergic Disorders, Anaphylaxis and Insect Allergy

Points of Comparisons of Common Allergic Disorders, Anaphylaxis and Insect Allergy	Phenomena Noted in Connection With		
	Common Allergic Disorders	Animal Anaphylaxis	Allergic Sensitivity to Insects
Heredity and development of allergic state	Strong hereditary evidence, not readily induced.	Readily induced.	Can be induced by repeated irregular exposure to bites and stings.
Nature of antigen	May be protein or protein conjugate.	Anaphylactogen is usually protein—minute amounts may cause anaphylactic death.	Not clear, but minute amount may cause anaphylactic type death.
Nature of antibodies	Reagin (skin sensitizing).	Anaphylactic antibody (precipitin, etc.). No skin sensitizing antibodies demonstrated.	No skin sensitizing or other antibodies readily demonstrated.
Clinical picture	Shock organ varies with individual.	Specific for species of experimental animal.	Systemic symptoms usually characteristic, varying chiefly in degree.
Results of repeated injection of antigen	Refractory period not regularly produced. "Desensitization" is partial.	Refractory period can be readily produced. Complete "desensitization" is possible.	Refractory period occurs after natural sting or bite. Apparent "complete desensitization" occurs.

TABLE 3.—Analysis of 1,078 Routine New Patients Interviewed As to History of Allergic Sensitivity to Insect Bites.

	Total	Per Cent
Positive history of reactions to bites or stings....	220	20
Types of reaction reported:		
Pronounced local swelling.....	176	80
Systemic symptoms only.....	22	10
Both local and systemic symptoms.....	22	10
Number of insects causing reaction:		
Single	163	74
Two or more.....	57	26
Relative frequency of insect offenders:		
Mosquitoes	119	54
Bees, wasps, etc.....	113	51
Fleas	23	10
Others	12	5
Results of skin testing with insect material:		
Positive scratch reactions with offending insect	10	
*Positive scratch reactions with nonbiting insects	28	
Positive intradermal reactions with offending insect:		
Immediate wheal (2+ or more).....	75	
24-hour erythema (3+ or more).....	89	

*A larger number of tests on each patient, using various nonbiting insects would account for the larger number of positive reactions. Among these patients many had hay fever or asthma and reacted to common inhalant allergens.

Sometimes the family or species of the arthropod cannot be determined but often the victim may readily report whether it is of the order *Diptera* (mosquitoes and biting flies) or of the order *Hymenoptera* (bees, yellow jackets, etc.). Diagnosis of local reaction may be obscured by the surrounding wheal, by excoriation or by secondary infection.¹² However, certain points may help toward a more specific diagnosis:

Flying insects often affect exposed areas whereas those that crawl or hop will affect portions of the body accessible to them. The flea affects the lower extremities while the fly, mosquito and bee often attack the face and upper extremities. The spider may bite about the head of persons walking through unfinished basements, or around the exposed buttocks in open privies. Biting flies, mosquitoes and bees produce single lesions (Figure 1) while the fleas bite several times (Figure 2) to get full blood meals.

Specific diagnosis of allergic sensitivity to injectants cannot be reliably made by the conventional skin tests with the allergenic extracts now available. Strong positive immediate whealing and large delayed reaction occur frequently without a positive history. Nonbiting insects elicit equally strong skin reactions, as noted in Table 3 (Figure 3). Yet, skin testing is routinely done by us in such patients, first by scratch method with the most concentrated material and then by intradermal method, using an appropriate dilution. The immediate whealing, and more importantly the delayed reaction, are used as



Figure 1.—Mosquito bite (ankle) producing bullous lesion.



Figure 2.—Flea bites producing characteristic group of urticarial lesions.

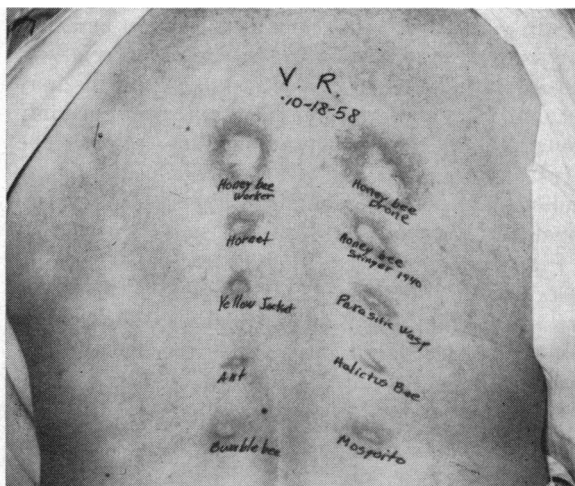


Figure 3.—Positive reactions (scratch tests) with *Hymenoptera*. Strongest reaction to honey bees, both worker and nonstinging drone. Similarly strong reaction to extract of isolated stinger sacs prepared 18 years previously.

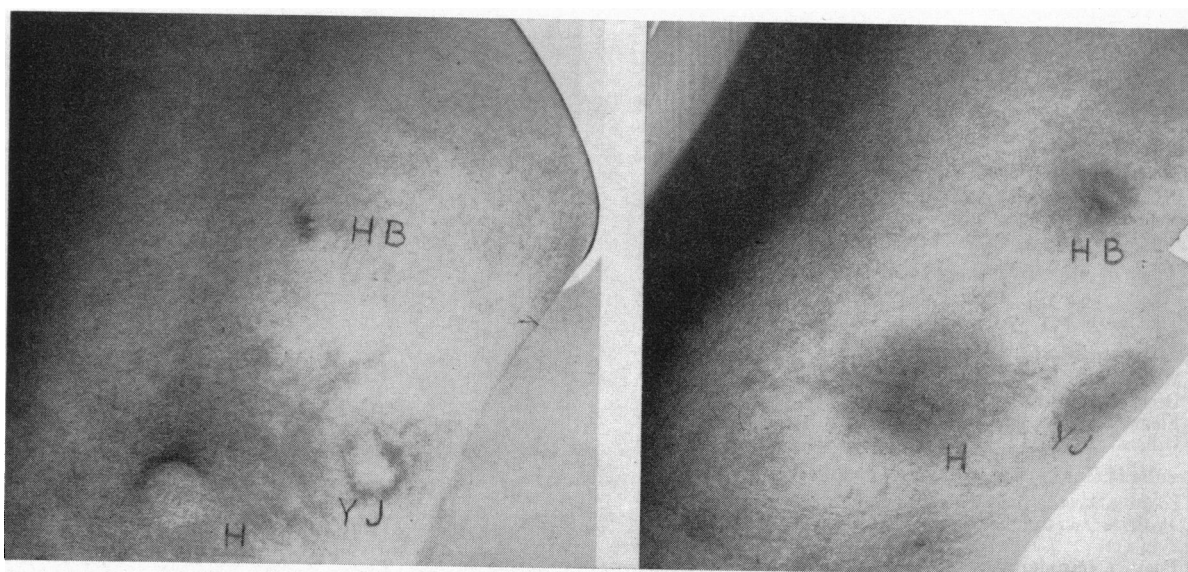


Figure 4.—Left: Reactions to skin tests (intradermal method) showing immediate reactions to honey bee (H.B.), yellow jacket (Y.J.), and hornet (H.), using 1:1,000 dilution after negative scratch test. Patient gave history of violent systemic reactions to stings. Right: Reactions after 24 hours.

guides in preparation of the material for specific immunization (Figures 4 and 5). Clinical results of treatment, however, appear to be as good in some patients with minimal skin reactions as they are in those showing large wheals or delayed erythema.

The nature of the allergen in these biting and stinging insects remains obscure. There is still some controversy as to whether it is in the venom sac¹⁷ and salivary glands or is common to the entire organism. Our studies have agreed with those of Benson and Semenov⁴ and Prince and Secrest³² that the allergen for treatment is present in the whole insect. This of course makes the preparation of allergenic extracts much easier than if we had to dissect out the salivary glands or the venom sacs. Head and mouth parts or stinging apparatus used in penetrating the skin may remain in the victim, especially if the insect is killed or violently removed. This may account for some systemic effect and does certainly contribute to chronic granulomatous lesions. The feces of lice, mites and ticks, which feed for long undisturbed periods, contain allergenic substances capable of causing local skin reactions.

Preparation of insect allergen extracts has been described in previous publications.^{28,29} They are processed from the live or quick-frozen stage so that deterioration and autolytic changes or bacterial invasion from the insect's gut will not occur. The defatted, desiccated, powdered material can then be kept indefinitely. Our aqueous extracts of a 1:10 by weight volume prepared in buffered 50 per cent glycerine have remained allergenically active for months and even years.

Treatment by subcutaneous injection of graduated doses of these extracts, using the offending in-

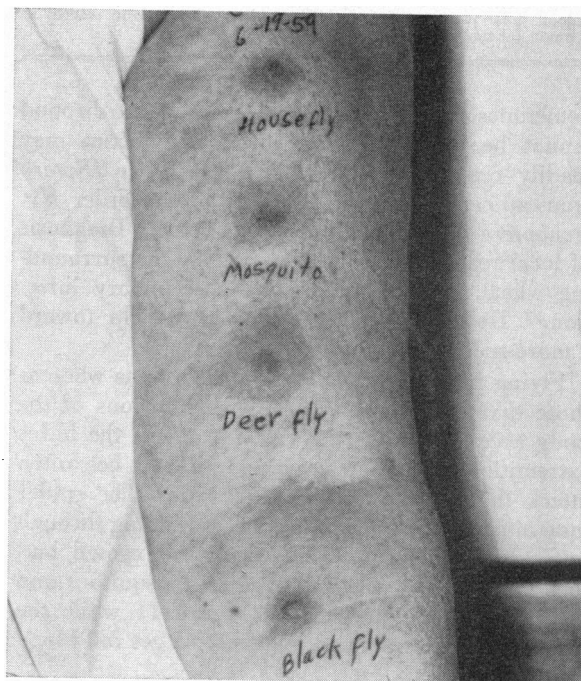


Figure 5.—Skin tests (intradermal method) showing 24-hour reactions to various families of biting *Diptera*. Reactions varied only in degree. The patient, who had severe disabling reactions to mosquito bites, was successfully treated with mixed mosquito antigen.

sects or closely related species or even family, has been our routine procedure. Intradermal route for treatment has been reported effective after even a few injections.^{3,18,24} If this method proves consistently reliable, it may also shorten the period of treatment and would conserve material. The "repository method" of single yearly doses is now

being used.³¹ It is still unproved either as to immediate or as to lasting effect. There remains the question of producing delayed hypersensitivity which may warrant caution in using an adjuvant known to augment the production in experimental animals of certain antibodies which in patients may mean new clinical problems.

Results of treatment are generally reported as gratifying by many investigators using different antigens and diverse routines of treatment. This suggests that the allergen is universal throughout the insect and duration of treatment is often carried out longer than necessary. Our experience with treatment for allergic reaction to various biting and stinging insects has been almost invariably good. It has often been observed that, after a series of injections of bee and flea antigen, the "immunized patient" (and even the experimental animal) is no longer attacked by that insect. This observation, however, is not true of patients who are immunized to severe reaction to mosquito bites. Immunity is lasting after treatment with allergens of some insects ("bees" and biting flies) but of shorter duration with others (flea).

Symptomatic treatment for local allergic reaction to bites and stings is directed for the most part toward temporary relief. Rest, elevation of extremity and the application of cold compresses will reduce the degree of swelling. Analgesics, antipruritics and antiseptics give comfort and control secondary infection. The antihistamines are usually of little help. Steroids have been used by us only for cases in which there has been excessive swelling and especially when it is essential to hasten relief from prolonged edema and inflammation.

For the systemic reaction the use of the most rapidly acting, parenterally administered drug may be life-saving. Minutes count, and epinephrine aqueous 1:1000 given deep subcutaneously is still our drug of choice. The exact dose is governed by circumstances—0.3 to 0.5 cc. for adults and 0.1 to 0.25 cc. for children 5 to 12 years of age. Mortality from bites and stings has, I am sure, been greatly reduced by an immediate injection of epinephrine. Antihistamines orally and isoproterenol sublingually do not always fulfill their theoretical purpose; but, if taken immediately after the sting, they will permit the patient to reach the physician for more heroic measures. The steroids as emergency measures, even intramuscularly or intravenously, are not the first drugs of choice. The victim may die within five to ten minutes, before adequate pharmacological action of these drugs can take place.

A brief discussion of each class and order of the various arthropods will exemplify these general remarks.

ORDER HYMENOPTERA

Family *Apidae* (honey bees)

Family *Bombidae* (bumble bees)

Family *Halictidae* (sweat bees)

Family *Vespidae* (wasps, hornets, yellow jackets)

Family *Formicidae* (ants)

The order *Hymenoptera* (Table 1) which includes bees, wasps, hornets, yellow jackets and ants comprises a number of families whose stings often result in severe local or systemic reactions. The clinical picture, the program of treatment and the gratifying benefit from such specific immunization are commonplace clinical experiences to allergists and to physicians in general. Medical literature is replete with well-documented observations.

A review of records of 41 patients in our series who returned satisfactory replies to a comprehensive questionnaire provided the following general observations:

1. Rarely did the patient have both severe local and systemic reactions from the stings.
2. Diagnosis was made from the clinical history or evident local reactions.
3. Skin testing alone showed no quantitative relationship between clinical experience of the patient and local skin reactions. However, positive skin test reactions, particularly of the delayed type, were used as an arbitrary guide in making up the antigen and outlining the program of treatment.
4. An extract of the whole insect was used and in most cases a mixture of several families of *Hymenoptera* was employed.¹¹
5. The number of injections administered to each patient varied from several (these patients discontinued of their own volition) to a large number extending over three years (at a maintenance dose of once a month when full dosage had been reached).
6. The longest record in this series was 23 years after treatment without adverse experience from stings.
7. Twelve, or almost 30 per cent, of the patients reported having been stung from one to four times after treatment. Only two patients indicated reactions that were more than moderate. One reported generalized hives. The other reported fever and "nervous upset." The patient herself suggested that symptoms may have been chiefly a manifestation of "apiphobia."

Results in this small series show gratifying benefit similar to that reported by other investigators,^{4,18,23} but here too the good results fail to provide strong positive answers to these basic questions:

1. The type of antigen to be used
2. Schedule and length of treatment to follow
3. Objective test that will give some assurance of effectiveness of treatment
4. Duration of effective immunity.

ORDER DIPTERA

Family *Culicidae* (mosquitoes)
Family *Tabanidae* (horse flies, deer flies)
Family *Muscidae* (stable flies)
Family *Simuliidae* (black flies or buffalo gnats)
Family *Heleidae* ("punkies," "no-see-ums," "sand flies")

The order *Diptera* (mosquitoes and biting flies, Table 1) embraces many members having mouth parts capable of penetrating skin and comprises one of the largest group of insects that produce abnormal local and severe systemic reactions.

Mosquitoes are the most frequent offenders, producing severe local effects; but rarely do they cause systemic symptoms. Abnormal delayed reaction occurring within four to 24 hours may vary from pronounced edema and erythema to large papular or vesicular or even bullous lesions. Cellulitis and lymphangitis or necrosis of Arthus type are not uncommon⁵

The nature of the antigen remains obscure. Testing with the nonbiting male mosquito produces equally strong reactions and treatment is often equally effective.^{21,24,34} Whether it is necessary to use antigen from the specific species or genus^{13,34} is still controversial, but from a practical standpoint this need not cause great concern since the important genus common to a local area in our temperate zone can be readily obtained in large numbers. However, a mixture of common genera has been used in treating our patients.

More and more patients violently sensitive to mosquito bites came to notice as specific questioning sought them out. More than 30 among those giving positive histories were tested with the mosquito antigen. Replies to our questionnaire were less satisfactory for analysis than with *Hymenoptera*. In only a small proportion of cases was it possible to get personal interviews a number of years after treatment with the mosquito antigen. Many of those whom we treated and later interviewed reported satisfactory continued relief so that camping or fishing trips became pleasurable. In one case a return trip to Central America was uneventful after a previous disastrous experience with mosquito bites. All of these patients but one reported experiencing mosquito bites with minimal local reaction. The exception, who obtained no benefit from the treatment, continued to have large, lasting, indurated lesions.

Biting flies including the family *Tabanidae* (horse flies and deer flies) and the family *Muscidae* (stable flies) inflict painful local lesions. In hypersensitive persons these bites may be followed by severe and prolonged swelling and not infrequently by systemic reaction similar to that resulting from the sting of the *Hymenoptera*.^{10,19} The great hazard occurs when these are encountered on fishing and hunting trips and prompt medical aid is not avail-

able. Three patients having such systemic reactions received treatment with our deer fly extract (*Chrysops discalis*). Thus far only one has since been bitten after treatment; he reported no untoward effect.

Black flies, sometimes called "buffalo gnats," also have vicious bites and are capable of producing severe swelling, often about the face and eyes. There are occasional reports of systemic reaction from such bites. These flies are commonly encountered throughout the northern United States and southern Canada. One patient who each year had disabling reactions to the bites of these insects was treated with extracts provided by us and administered under the close supervision of Dr. Lowell Henderson of Rochester, Minnesota. Following treatment the patient wrote:¹⁵

"I have been in the north country for the past five years with black flies and mosquitoes by the millions. I am glad to report your material saved me a lot of discomfort and suffering. I did not get any bad reactions from the black flies nor did the mosquitoes seem to annoy me as much as usual."

This report indicates not only relief from the allergic reaction by the injection of extracts of the specific family of black flies but suggests that the bites of other families (mosquitoes) were similarly reduced in their effects. Therefore, conversely, since black flies are difficult to collect in adequate numbers when specific extract is needed, possibly the use of a mixture of more readily available *Diptera* may be justified.

Biting midges (family *Heleidae*), predominantly in the southern United States, acquire different names in different areas. The commonest are "punkies," "no-see-ums" and "sand flies" (*culicoides*). They have vicious bites and are tiny enough to pass through ordinary screening.

The bites sometimes result in large local reactions with inflammation and vesiculation. Arean and Fox² described histological changes and give a discussion of the nature of the toxic agent and mechanism of production of the lesion. Immunization, using a specific genus or even family, is made impractical by the difficulty of collecting an adequate supply for preparation of an extract. Although there are no reports of treatment for this acute reaction it would be of interest to offer immunization injections to hypersensitive patients using a closely related family within the order *Diptera* on the basis of cross-antigenicity.³⁰

ORDER SIPHONAPTERA (FLEAS)

Family *Pulicidae*
Cat flea (*Ctenocephalides felis*)
Dog flea (*Ctenocephalides canis*)
Human flea (*Pulex irritans*)

Within this order of biting insects the family *Pulicidae* contains the chief offenders, and of these, cat fleas and dog fleas are the most frequently identified. Fleas inhabiting other mammals, such as rabbits, rarely attack man. Specific sensitivity at the level of genus or species was reported by Boycott,⁶ who demonstrated this on his wife, using human flea, rat flea and rabbit flea. Other observers⁷ have noted similar phenomena and have recommended that a mixture of the most likely genera of fleas be used in testing and treatment.

Abnormal reaction to flea bites takes varying forms, including papules, urticaria, induration and necrosis of Arthus type. Secondary infection and pustulation are common and produce typical discoloration seen on the lower extremities (Figure 6). Grouping of lesions is characteristic of flea bites and is an important finding in the specific diagnosis (See Figure 2).

Fleas are widespread throughout North America. The State of California, and especially the San Francisco Bay area, have a special reputation for infestation with these household pests. Many newcomers are plagued during the early weeks or months of residence but after a time they may become so adapted (probably through acquired immunity) as to be no longer troubled. A few, however, have to change residence or seek specific treatment in order to remain in these areas.⁷

Treatment with extract of common fleas has given gratifying relief but not so consistent or so lasting as the results with *Diptera* and *Hymenoptera* allergens. Small doses were recommended by Hatoff,¹⁴ who obtained benefit in 78 per cent of 129 children thus treated. Cheney and coworkers⁷ believed prolonged therapy led to a breakdown of immunity and warned against a continuous and uninterrupted program of treatment.

The following observations were made by the author in dealing with a series of patients having severe reactions to flea bites:

1. Diagnosis was based largely on the characteristic grouping of lesions, chiefly on the lower extremities. On the rare occasions that an insect was caught, it was identified as a cat flea.

2. Lesions often showed induration and secondary infections later, resulting in discoloration and disfiguration.

3. Positive skin test reactions occurred but the immediate wheal and delayed erythema were milder than with other insect antigens and of minimal value in confirming the diagnosis or providing a guide in treatment.

4. Concurrent treatment with staphylococcus vaccine reduced the frequency of occurrence of pyoderm and thus the severity and duration of the eruption.



Figure 6.—Flea bites—delayed reaction with induration, pustulation and discoloration.

5. Results of treatment for hypersensitivity to flea bites were not so consistently gratifying or as lasting as for hypersensitivity to other insects.

MISCELLANEOUS ORDERS

Order *Anoplura* (sucking lice)

Family *Haematopinidae*

Head and body louse (*Pediculus humanus*)

Crab louse (*Phthirus pubis*)

Order *Hemiptera* (true bugs)

Family *Cimicidae* (bed bugs)

Family *Reduviidae* (assassin bugs)

Kissing bug (*Reduvius personatus*)

Wheel bug (*Arilus cristatus*)

Various orders, including lice and true bugs, are sporadically reported to cause allergic reactions. The smaller number of documented reports is due in part to the relative infrequency of encounter with them on the North American continent. Development of severe reaction after successive bites in the laboratory indicates that these insects capable of penetrating human skin should be added to the list of arthropods which can produce allergic reactions.

Lice which were prevalent among the immigrants from eastern Europe in the earlier part of this century often produced urticarial reactions and delayed

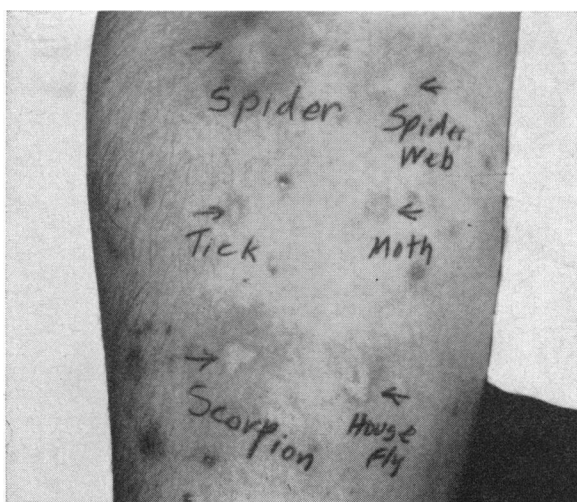


Figure 7.—Positive reactions (scratch tests) to various arachnids in a patient with atypical dermatitis suggestive of multiple bites and secondary eczematization.

inflammatory lesions. Moore²² reported acquired sensitivity, with symptoms, first in a technician and later in himself, after they had permitted a large number of lice to feed on them on successive days. Peacock²⁷ produced "marked anaphylactic phenomenon" after intravenous injection of filtrate of excreta of lice, and also a flare-up at the sites of previous bites which then remained swollen for five days. Safdi and Farrington³⁵ reported obscure fever relieved after local treatment for pubic phthiriasis.

Bed bugs likewise appear only sporadically in homes and hostleries. When attacking humans in full numbers they often cause generalized urticaria. In addition to primary lesions produced by the bites, large lasting local and severe systemic reactions also occur. Parsons²⁶ reported anaphylaxis after such bites. The reaction was first ascribed to coronary occlusion, but he was able to reproduce the symptoms with a single bite and then to relieve the symptoms with an injection of epinephrine.

Biting bugs of the family *Reduviidae*, including kissing bugs (*Triatoma*) and assassin bugs (*Arilus*), inflict vicious wounds and may leave portions of their biting apparatus in the lesions. Severe local reactions are frequently observed. Systemic reactions in addition to local effect, observed by Shields and Walsh³⁷ in a patient bitten in three successive years, again suggested acquired hypersensitivity. This is confirmed by reports that persons bitten while working with the kissing bug also soon became acutely sensitive.

Systemic reaction to *Triatoma*, reported by Wood,⁴⁵ Talley⁴¹ and Wolfe,⁴⁴ with manifestation of generalized eruption and respiratory distress was relieved by isoproterenol sublingually or epinephrine injection. Similar reactions from the bite of

the wheel bug (*Arilus cristatus*) were discussed by Smith and coworkers.¹⁶ This confirms again the axiom that all insect bites are capable of producing severe allergic reactions.

Although in the present study we observed no clinical manifestations from the biting bugs of the family *Reduviidae*, testing with this family and related families indicated a high incidence of positive immediate wheal formation. This was noted especially with a nonbiting³⁸ member, the box elder bug, which is a frequent invader in homes and may be more important as an inhalant allergen and cause sensitization to its biting relatives.

CLASS ARACHNIDA

- Order *Araneida* (spiders, tarantulas)
- Order *Scorpionida* (scorpions)
- Order *Acarina* (mites, ticks)

The class *Arachnida* includes several orders which attack man, a few of which (spiders and scorpions) produce envenomation as the cause for pronounced local and systemic symptoms. Some bury themselves in the skin during their adult life for purposes of feeding (ticks), while others invade the skin during their larval stages of development (mites).

Poisonous spiders (black widow and brown recluse) and the scorpions produce primary reactions through the toxic action of the venom.⁴³ Most spiders rarely if ever attack man, preferring insects as a source of food. Periodically patients report spider bites, usually about the head and face and usually acquired in unfinished attics or basements. It is difficult to confirm in such cases that a spider bite occurred or that a pronounced swelling is caused by spider bite.

Scorpions studies by Doro, Ornelas and Johnson⁹ showed they had in their venom a proteinaceous substance, which, however, was incapable of sensitizing guinea pigs. On the other hand, Stenhke,³⁹ in whose laboratories their work was done, reported cases of severe anaphylactic reactions from the sting of scorpions (*Centruroides*) in persons who "milked" venom from them. These employees may have been previously sensitized by inhalation of vapor sometimes created in the course of electrical stimulation of the scorpions.

Ticks belonging to the order *Acarina* and family *Ixodidae* are distributed across the breadth of this continent. Persistent local nodules are probably due to the residual portion of feeding apparatus at the site. These are readily relieved by simple excision. The infrequent development of severe local reactions to tick bites may be best explained by the local tissue response in the area of previous feedings. This may in time become a generalized immune reaction and is reflected in the lack of vigor

of the tick feeding on an immunized animal, the reaction having the effect of decreasing access to the blood.⁴²

Although in our studies we have seen no cases of severe allergic reaction to tick bites, we have observed large induced reactions. The earlier vaccines used for active immunization against Rocky Mountain spotted fever were extracts of ticks infected with the rickettsial organism. After yearly injections, some patients had decided swelling of an entire extremity. This suggested induced hypersensitization of the delayed type. Occasionally systemic symptoms of malaise and fever occurred, but only one case of acute anaphylaxis after injection of such a crude vaccine was brought to our attention. We have no record of any experience these hypersensitive persons may have had following subsequent tick bites.

Mites exceed true insects in total numbers. Although their primary medical importance is in the transmission of disease, in addition they do cause dermatological disorders by attacking or actually invading the skin. This is a familiar occurrence with "chiggers." In sensitive persons varying reactions, including a papular type of urticaria and atypical eczema, have been reported, especially from avian mites.^{8,20,33,36,40}

In our routine studies the arachnid antigen (spider, scorpion, etc.) has caused reaction more frequently and to a greater degree than have antigens of other arthropods. In several cases this occurred where obscure eczematous disorders were present (Figure 7). The frequency of positive skin reactions and the presence of specific skin sensitizing antibodies which we have readily demonstrated would go well with the ubiquitous nature of arachnids, especially of the minute members (mites). They may indeed be important both to the allergists and to the dermatologists.

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