

ALLERGIC AND TOXIC REACTIONS TO NON-STINGING ARTHROPODS¹

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INTRODUCTION

Insects, other arthropods, and their products are capable of eliciting in humans adverse reactions that range from mild seasonal annoyance to anaphylactic shock and death. Dermal irritation resulting from contact with arthropods or infested products is well documented and often occupational in nature with entomologists, food handlers, and others. Respiratory allergies due to arthropod parts and products can have etiologies and symptoms similar to those of hay fever and can affect large populations in the infested area. The ill effects of Lepidoptera larvae were described in early Greek medical writings (1), and the poisoners of ancient Rome were suspected of including caterpillar extracts in their armamentarium (see 125). The skin patch test as we know it today was developed in 1870 by the naturalist Jean Henri Fabre during experiments in which he sensitized himself to extracts from the pine processionary caterpillar, *Thaumetopoea pinivora* (46). Deaths due to stinging Hymenoptera have been reported for centuries. One of the earliest documented cases occurred in 2641 BC when King Menes of Egypt died from a wasp or hornet sting, according to the hieroglyphics found in his tomb (33).

The range of reactions to arthropods and their products depends on several factors, which include the type and source of the material; the route, intensity, and duration of exposure; and the individual's immune response capabilities

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and history of prior exposure in cases of allergic reactions (135). Arthropods and their products present a broad spectrum of materials capable of stimulating the immune system. In addition to the classical proteinaceous antigens, components of defensive or salivary secretions, as well as complex venoms, elicit a range of immune responses. In some instances it may be difficult to determine when clinical symptoms can be attributed to reaginic hypersensitivity and IgE antibodies and when the reactions are due to the nonallergenic components of venoms and arthropod secretory products.

Harwood & James (50) listed the following ways in which arthropods and their products are introduced into or onto the body: (a) direct contact or inhalation of airborne material such as urticating hairs, wing scales, exuviae, feces, silk, and other body products or secretions; (b) bite, the introduction of digestive or salivary secretions through piercing mouthparts; (c) sting, the active injection of venom by specialized structures; and (d) active projection, the release or forceful ejection of defensive secretions.

In this review, emphasis will be placed on public health problems associated with exposure to insects as well as the occupational hazards encountered by entomologists and other individuals whose work brings them in contact with arthropods and their products. In a 1980 Entomological Society of America (ESA) survey, 28% of the 115 entomologists reporting allergies had to stop work or be transferred because of symptoms attributed to arthropod allergens (137). Allergic reactions to insect stings will not be addressed, as that topic warrants a separate review.

DIRECT CONTACT AND AIRBORNE MATERIALS

Among the general population, reactions to contact and airborne materials are often seasonal, with the frequency of exposure increasing as insect populations burgeon and as susceptible individuals renew outdoor activities. Notable examples of seasonal variation in public health or occupational exposure include reactions to the Ephemeroptera (mayflies) (52), Trichoptera (caddisflies) (52, 115), Diptera (flies) (23), and larval and adult Lepidoptera (primarily moths) (1, 32, 125) and may involve hundreds, or at times thousands, of individuals (68, 116, 126).

Reactions can result from direct contact with the offending insect or indirectly through contact with airborne materials. Three pathogenic mechanisms have been described in response to this exposure: (a) hypersensitivity reactions (allergies) from antigens of insect origin; (b) intracutaneous injection of toxic substance(s) through hollow setae; and (c) direct irritant effects of spines, setae, and other materials (1). Sequential occurrence of two or more of these mechanisms against larval Lepidoptera has been described among patients displaying a biphasic reaction to skin tests (46).

Responses to airborne materials or to direct contact with arthropods or their products have been well documented. Allergic reactions are addressed in review articles and books (29, 38, 41, 43, 93, 114, 119), and Bellas (10) referenced 400 articles in which insects were implicated as the source of inhalation allergens. The urticating setae of caterpillars have also been discussed by several authors (17, 26, 50, 85, 125).

Lepidoptera

"Lepidopterism" is the general medical term used to describe the ill effects that larval and adult butterflies and moths can have on humans. Included are problems associated with inhalation, ingestion, dermal contact, and tissue penetration by products or structures from any life cycle stage. The term "erucism" is occasionally used to describe the ill effects of the larval or caterpillar stage (Latin *eruca* = caterpillar) (95, 125). Erucism can be further divided to describe the "phanerotoxic" caterpillars, capable of introducing venoms into the skin through the offensive use of poisonous setae, and the "cryptotoxic" caterpillars, in which volatile or repellent emanations are released onto the integument or projected through an emission tube (95). The latter will be discussed in the section on active projection.

Urticating hairs or "netting" setae (macrotrichia) of caterpillars can be a source of contact dermatitis in an occupational environment and in some instances can be a significant public health problem (32, 126). These setae and spines, functionally divided into two groups, depending on the presence or absence of a poison gland at the setal base, are found in a variety of forms. The poison-containing type range from an individual seta or spine, groups of setae elevated on spines or tubercles (thought to increase effectiveness), to patches or large areas completely covered by these structures. Tips of the poisonous setae or spines may be solid, capped by a terminal detachable tip, or the hollow venom-filled shaft may be plugged with pigmented material. Venom discharge occurs when the terminal section is broken or ruptured as when brushed against or piercing the skin (125). Last instar *Thaumetopoea processionea* (78) and *Euproctis similis* (126) are estimated to carry over 600,000 and 2,000,000 urticating setae per caterpillar, respectively. Picarelli & Valle (96) describe the setae and spines present on the caterpillars of the principal families of urticating Lepidoptera.

The nonpoisonous setae and spines can also be strong irritants. They may fragment easily and those provided with barbs can be difficult to extract from skin and mucus membranes. If these enter the eye, fragments may embed in the eyelid and scratch the conjunctiva or cornea, or even penetrate into the interior resulting in loss of vision (46, 78, 125). This can occur through direct transfer of setae from the hands to the eye or from the use of towels or clothing that has come in contact with the caterpillars (46).

Direct contact with venom-containing setae can result in immediate, highly painful reactions or more delayed dermatological manifestations including erythema, edema, and urticaria, depending on the species encountered. More severe symptoms include headache, fever, nausea, vomiting, numbness, blistering, shock, and convulsions (41, 64). A chronic symptom involving long-term disability of the fingers exists among Brazilian rubber workers who contact larval urticating setae (see 50). Natives of Sarawak, Malaysia, reported that when bristles of an unidentified caterpillar were not removed they caused a severe necrosis with extensive sloughing of tissue and the possible loss of fingers or toes (125). Caterpillars of a Venezuelan saturniid, *Lonomia achelous*, are capable of injecting a powerful anticoagulant, and handling or even brushing against the bristles can result in serious hemorrhage (75). Secondary bacterial and viral infections of areas affected by larval setae have also been recorded (41). Caterpillars, cocoons, or adult moths that have contaminated bedding or clothing can cause irritation even after prolonged periods of drying (116, 125).

Lepidoptera larvae from the following families are known to contain at least some urticating species: Arctiidae, Anthelidae, Bombycidae, Eucleidae, Eup-terotidae, Lasiocampidae, Lithosiidae, Lymantriidae, Megalopygidae, Mor-phoidae, Noctuidae, Nolidae, Notodontidae, Nymphalidae, Saturniidae, and Sphingidae (46, 50, 125). Picarelli & Valle (96) and Pesce & Delgado (95) have documented geographic distributions of the urticating Lepidoptera.

The chemistry and pharmacology of the caterpillar venoms is poorly known because of difficulties in obtaining pure material in the required quantities, and reports are conflicting in some instances. Pesce & Delgado (95) stated that contact with setal poisons of neotropical caterpillars resulted in few cases of allergic sensitization because the toxins do not contain protein or other substances capable of acting as haptens. However, the active fractions of many caterpillar venoms are described as primarily proteinaceous in nature, with esterases and proteinases as the major components. The presence of these materials appears to be correlated with the intense itching and with the usually long-lasting human reactions to caterpillar venoms. Histamine, 5-hydroxytryptamine, and unidentified materials that stimulate histamine releases are also present (50, 113). Little quantitative data is available on these venom constituents; however, first and fifth instar gypsy moth larvae, *Lymantria dispar*, have whole body and setal histamine contents of 17 and 80 ng/organism, respectively (116). Fluid within the spines of a Brazilian saturniid (*Dirphia* sp.) contained 0.02–0.04% histamine, by guinea pig ileum assay, which corresponds to 86–172 ng/spine (78). Picarelli & Valle reported the absence of histamine, acetylcholine, and 5-hydroxytryptamine in extracts of setae from *Megalopyge* sp. caterpillars (96).

In the continental United States, larvae, and sometimes other stages, of the following have been reported as serious occupational and public health problems: the gypsy moth, *Lymantria dispar* (1, 32), the saddleback caterpillar, *Sibine stimulea*, the lo moth, *Automeris io*, and the browntail moth larva, *Euproctis chrysorrhoea*, in the East and Northeast (1, 50); the puss caterpillar and flannel moth, *Megalopyge* spp., in the southeastern and south-central states (79); and the Douglas fir tussock moth, *Orgyia pseudotsugata*, in the North-west (94, 99).

The gypsy moth was responsible for thousands of cases of pruritic dermatitis in the spring of 1981 with major outbreaks reported in Connecticut, Massachusetts, Pennsylvania, and Rhode Island (1). Despite heavy infestations in certain areas since its accidental introduction in 1869, no community outbreaks had been reported prior to this time. Favorable environmental conditions resulted in population increases of the gypsy moth in 1981, and over 4.8 million hectares (12 million acres) of forest were defoliated (32). Over 50,000 larvae may feed on an individual tree and behavior of the caterpillar increases airborne dispersal, via a silk thread, when wind velocities exceed 1.9 km/hr (see 9). Reports and distribution maps showed the highest incidence of dermatitis in areas with severe caterpillar infestation, and students in two schools in infested areas exhibited attack rates of 42% and 25% (1). General symptoms included pruritic rash and occasional urticaria, which were attributed to contact with free, windblown setae or to direct contact with the caterpillar. The reactions appear to be a delayed hypersensitivity response, as symptoms did not usually occur until 8–12 hr after outdoor activity (116), and reactions to laboratory patch tests, using caterpillar setae, required 24–48 hr contact (9). Contaminated clothing may hold the setae in skin contact, and localization of the rash supported this supposition. Almost all cases resolved within a few days to two weeks (116).

In a study of occupational allergy, 10 of 17 individuals (59%) involved with gypsy moth research reported dermatologic and/or pulmonary reactions associated with exposure to the caterpillars. Fifteen individuals (88%) exhibited positive scratch test reactions to gypsy moth extracts. Dermatologic reactions occurred 0.5 to 12 hr after exposure and were directly related to caterpillar contact. A hereditary predisposition for allergies may increase the likelihood that a worker will develop hypersensitivity (32). The gypsy moth was implicated in 29% of the occupational allergies reported in the ESA survey (137).

Favorable environmental conditions were also attributed to the increase in Douglas fir tussock moths, *Orgyia pseudotsugata*, which defoliated approximately 360,000 hectares (890,000 acres) of forests in Oregon, Washington, and Idaho in the summers of 1972 and 1973. Symptoms including itching, rhinitis, conjunctivitis, chest pain, and asthma were reported by timber and

forestry workers and were attributed to exposure to "the secretion, hairs, or other substances in the larvae or cocoons of the moth." As with the gypsy moth, a prior history of allergy appeared to predispose individuals to reactions to the tussock moth (99).

Periodic increases in populations of the puss moth, *Megalopyge opercularis*, have resulted in outbreaks of caterpillar dermatitis. In 1960 more cases were reported in South Carolina than during the preceding 25 years combined (29). Infestations in Texas have caused thousands of cases of dermatitis in children, and public schools have been closed until the infested areas could be sprayed (35). McGovern et al (79) described the results of a survey reporting 2130 cases of reaction, attributed to the puss caterpillar, occurring in Texas. Major signs and/or symptoms included severe local pain (98%), local swelling (92%), lymphadenopathy (32%), headache (29%), shock-like symptoms (5%), and convulsions (0.2%). No deaths were reported, but hospitalization of eight patients was required. Keegan (63) cites a second study in which similar findings were reported involving 54 cases of reaction to the puss caterpillar.

A public health problem of epidemic proportion was reported in 1972 when clinics near the city of Shanghai, People's Republic of China, became overcrowded with patients suffering from dermatitis, "almost unbearable itching," but no pain. Symptoms were attributed to windblown hairs of the mulberry tussock moth, *Euproctis similis*, and an estimated 500,000 individuals were affected (126). Another major outbreak was cited by Southcott (125) in which an estimated 250,000 persons were affected by the Oriental tussock moth, *Euproctis flava*, on Honshu Island, Japan in 1956. Areas throughout the Far East are routinely affected by this moth (64, 112, 125), and authorities believe that the reactions are often due to the larval setae, which are picked up and carried by the adult as it emerges from the cocoon. When the urticating hairs originate on the caterpillar and the adult is only a carrier, this phenomenon is referred to as "pseudolepidopterism" or "consigned" erucism (95). Urticating hairs have also been reported in larval webs and feces, and these are potential sources of contamination (78).

An outbreak of dermatitis in China caused by the yellow rice borer, *Schoenobius incertellus*, was also attributed to transfer of hairs between stages. Peasants who gathered yellow rice borer egg clusters from rice seedlings reported 712 cases of dermatitis, with an incidence rate of 80%. Results of patch tests using insect body parts and egg clusters showed that only scale hairs from the egg clusters and the tail yielded positive reactions (68). Anal tufts can be present in both sexes, but these are generally better developed in the female because the tuft setae are often used as protection for the eggs (78).

The highly irritating barbed setae of adult female *Hylesia* spp., referred to as "flechettes," are responsible for serious outbreaks of urticating rashes

and upper respiratory tract complications in South America, most notably in Brazil and Peru where cases may number in the thousands. Symptoms are usually seasonal in nature and many occur when the moths are attracted to lights in inhabited areas (50, 95, 103). Hill and associates report an incident where 31 (69%) of 45 crew members of a tanker ship were effected after exposure to *Hylesia* in Venezuela (54). Symptoms resulted from exposure to the moths and contact with contaminated bedding (54). This condition is referred to as "Caripito itch" by seamen familiar with the symptoms, since it seems to follow visits to the port of Caripito, Venezuela (41).

Rotberg (103) cites a similar incident in which anal tuft setae of *Hylesia* contaminated the houses of a small mining village in northern Brazil. Of the 1777 inhabitants, 707 (40%) were affected seriously enough to interfere with their ability to work. Lepidopterism in Brazil is primarily attributed to contact with the larvae of five families of nocturnal moths and one diurnal butterfly family, the Morphidae (103).

An incident in which no living lepidopteran could be implicated occurred when 600 of 3000 encamped Israeli soldiers developed severe dermal irritation and rash. Cocoons and dead larvae of *Thaumetopoea wilkinsoni* mixed with debris on the forest floor were contacted by the soldiers who slept on the ground. The typical allergic reactions were observed when this material was placed on the arms of volunteers (141). Allergies to *Thaumetopoea pinivora* are a seasonal problem in parts of the Middle East (124).

Lepidoptera were the predominant sources of allergies in the ESA survey, with 67% of the respondents attributing their symptoms to moths or butterflies. Most individuals believed that the suspected origin of their allergies was airborne or direct contact (76% and 63% respectively) with the scales of adults. Several Lepidoptera-rearing laboratories indicated that allergic reactions were major problems, and two institutions noted that 53% and 75% of their personnel developed symptoms to moth scales, even with the use of protective equipment. Symptoms included rhinitis, bronchial asthma, dermatitis, and eye irritation (137). Similar results were reported by T. E. Bellas (personal communication) in a survey of Australian entomologists, in which 14% of the 43 respondents reported allergies to Lepidoptera.

In addition to the above, cases of occupational allergies to Lepidoptera have been cited by Bellas (10) and others (29, 123, 125), primarily in individuals involved with rearing or with light trap sampling and analysis. Inasawa and co-workers (58) reported on bronchial asthma as a result of silkworm culturing in Japan. Maschwitz & Kloft caution that repeated contact with poisonous setae may result in severe reactions, including anaphylactic shock, especially in individuals with occupational exposure, such as preparators in entomological museums (78).

Diptera

Mass emergence of Chironomidae (non-biting midges) in some areas has been associated with a high incidence of allergic symptoms, especially bronchial asthma and rhinitis (61). Epidemics of allergic reactions, primarily to *Cladotanytarsus lewisi*, have resulted in serious problems along the Nile in northern Sudan since the late 1920s when dams for irrigation and flood control were built (71, 72). The number of individuals who are hypersensitive is uncertain, but it is estimated to be in the "several thousands" (23, 61). Midge populations at times reach levels that hinder or prevent work and recreation (71). The level of hypersensitivity was so severe that hospital camps were erected away from the breeding areas during the season of peak midge emergence, and consideration was given to moving an entire town (71). The presence of working dams on the Nile has created ideal environments where larval populations can reach 100,000 per square meter (42) and light trap catches of over 400,000 midges per night have been recorded (23). Immunological studies indicate that this hypersensitivity has the features of an immediate-type allergy commonly associated with pollens and other airborne allergens (22).

Midges may be accompanied by the emergence of mayflies (Ephemeroptera), caddisflies (Trichoptera), and plume midges (Diptera: Chaoboridae) in some areas. Water pollution, which increases some species and decreases others, contributes to outbreaks in urban areas. Population levels are increased by lights that attract these insects, and even minute species may accumulate in heaps measured by the kilogram. Palliative measures include the use of strong decoy lights to attract midges away from populated areas, which are lit with weak, reddish lights (42, 71).

The Chironomidae are one of the few insect families known to possess low-molecular weight hemoglobins, the primary structures of which have been completely elucidated for some species. Baur and co-workers (7) have shown that hemoglobins of chironomids are potent allergens in man, and they have localized the antigenic determinants within certain polypeptide sequences on hemoglobins of *Chironomus thummi thummi*. Testing was conducted on 99 individuals who had occupational contact with larvae of chironomids; 43 of this group had previously developed respiratory, conjunctival, or cutaneous hypersensitivity reactions from exposure to airborne constituents of these insects. Strong evidence for IgE-mediated sensitization to hemoglobin from both larvae and adults was reported with immunologic cross-reactivities among different species (7), which indicates that hypersensitivity may potentially be treated by desensitization (61). Baur et al suggest that the increase in asthmatic diseases reported in the Sudan (23, 71) and other areas (42, 91) during the chironomid season is predominantly caused by sensitization to hemoglobin molecules of this insect family (7).

Some investigators feel that the problem of allergy to the Chironomidae may

be more widespread than indicated by the literature. Grodhaus (48) and others (see 10, 42) document the nuisance problems associated with these insects; however, it is unknown whether the paucity of reported allergy cases is due to nonrecognition or if there are truly no cases (P. S. Cranston, personal communication). Not all Chironomidae larvae possess hemoglobins, and the correlation of species with and without these allergens with reports of hypersensitivity may elucidate this problem (T. E. Bellas, personal communication).

In addition to nuisance and hypersensitivity problems, swarms of midges can be dangerous and even fatal to people who are trapped in their path and may suffocate before being able to escape (91).

Inhalation and contact allergies to the screwworm, *Cochliomyia hominivorax*, have been reported in connection with a sterile male eradication program. Seventy percent of the persons involved in aerial dissemination of irradiated flies experienced allergic manifestations such as symptoms of eye irritation, nasal congestion, coughing, wheezing, and shortness of breath. Pilots of the planes used for release of the flies were also victims of asthmatic attacks. Symptoms appeared two weeks to six months after entering the program, persisted two to seven days after exposure was discontinued, and reappeared within a few minutes to three days after return to work (27).

In the ESA survey five of the nine reported allergies to Diptera were attributed to the Culicidae (mosquitoes), and most of the symptoms were attributed to adult scales (137). Of the surveyed Australian entomologists, 21% of the reported allergies were attributed to the Diptera, with inhalation reactions to blow flies (Calliphoridae) rapidly becoming a major problem (T. E. Bellas, personal communication). Bellas (10) and Ebeling (29) cite several references to occupational allergies in individuals rearing or working with dipterans.

Orthoptera

Dermal and airborne allergies to Orthoptera do not assume the public health importance of the Lepidoptera and Diptera. However, the orthopterans are a significant occupational hazard because of the potency of the allergenic material from this order and the severity of symptoms that are associated with it. Twelve percent of the ESA survey respondents (137) and 33% of those from Australia (T. E. Bellas, personal communication) implicated orthopterans as the allergen source. Bellas (10) cites 22 references to occupational allergies to locusts, grasshoppers, crickets, and cockroaches. There are three reports from research laboratories in which all of the individuals with occupational exposure to *Locusta migratoria* (43, 137) or *Periplaneta americana* (142) developed manifest symptoms within several years of beginning work. Symptoms included dermatitis, urticaria, rhinitis, bronchitis, and asthma. The three cases of anaphylactic shock reported in the ESA survey were attributed to exposure to the following orthopterans: *Melanoplus differentialis*, *Blattella germanica*,

and *Leucophaea maderae* (137). A case of anaphylaxis to *Periplaneta americana* was reported in the Australian survey (T. E. Bellas, personal communication).

Hypersensitivity to cockroach antigens appears to be worldwide, and positive reactions have been documented by skin tests on populations in various urban communities (12, 59). Over 3,500 species of cockroaches have been identified, but less than one percent are considered pests of man (105). In the United States, 7 or 8 of the approximately 55 known species of cockroaches are considered to be domesticated (11).

Sensitivity to the German cockroach, *Blattella germanica*, has been correlated with the intensity and duration of exposure (12, 14). Ethnic groups exposed to environments heavily infested with cockroaches demonstrated a greater frequency (59%) of skin test sensitivity than those in areas with lower infestation rates (5%) (21). In a similar study, crude extracts of American and German cockroaches elicited positive skin tests in 50% of patients with a positive, and in 4% with a negative, environmental history for exposure to cockroaches (57). Eight of nine individuals rearing *B. germanica*, *Periplaneta fuliginosa*, and *P. americana*, common domestic cockroaches in Japan, were positive for prick tests using crude extracts (60), and individuals rearing *P. americana* and *Leucophaea maderae* experienced dermal and respiratory problems (11, 142). Hulett & Dockhorn (57) suggest that the cockroach antigen may be as important as the mite in the etiology of house dust allergy in some populations. In the tropics, microscopic examination of slides for pollen and mold revealed the presence of numerous cockroach cuticular fragments (73).

The antigenic nature of the saliva, feces, and body tissues of *B. germanica* is well established (13, 14), and these materials can sensitize through contact, inhalation, ingestion, or bites (13, 105). Three major antigens have been isolated and purified from both the American and German cockroaches (132). Two of the larger heat-stable antigens, with molecular weights of 25,500 and 63–65,000 daltons, were capable of eliciting positive skin tests in approximately 70% of cockroach-sensitive individuals, the former antigen at concentrations as low as 3 µg/ml. The third, less well-characterized antigen elicited positive skin tests in 30% of the individuals sensitive to the crude extract (132).

The migratory locust, *Locusta migratoria*, the Australian plague locust, *Chortoicetes terminifera*, and other acridids were responsible for 13 of the 14 orthopteran allergies listed by the Australian entomologists surveyed (T. E. Bellas, personal communication). The locust allergen has been described as "aggressive," and Bellas (10) stated that this group should be of the most concern with respect to arthropod inhalation allergies. Very high sensitivities to locust extracts were reported by Fuchs & Gronemeyer (see 10), with positive skin responses observed at dilutions of 10^{-9} . Levels of IgE and IgG antibody correlated with the intensity of exposure among 43 individuals rearing these

insects (30). Workers who had a hereditary predisposition to allergies and who handled locusts developed occupational asthma more often and more quickly than similarly exposed "normal" workers (18). Reports of work-related symptoms are uncommon in individuals exposed to locusts in the field. There appears to be some antigenic similarity between locust and cockroach sensitivity (37).

Coleoptera

Among the Coleoptera, the dermestids and other beetles infesting stored products have caused the most significant allergy and irritation problems. Over 20 dermestid species that damage insect collections have been recorded (29), and a single *Trogoderma inclusum* larva can release over 3,000 urticating hastisetæ (90) that are capable of penetrating the skin (90, 122). Severe allergic reactions, asthma, and eye irritation have been reported by laboratory personnel working with dermestids (29, 65, 84, 90, 118), and dock workers unloading cargo heavily infested with dermestid larvae reported breathing difficulties associated with inhalation of the hastisetæ (122). *Trogoderma angustum* is a common household pest in parts of Germany (106), and intradermal endpoint titrations with larval skin extracts gave positive reactions in 34% of the patients with a hereditary predisposition for allergies, versus 2% of the controls (107). Unlike the hollow urticating setae of some Lepidoptera larvae, which may contain venom, irritation from dermestid hastisetæ appears to be solely mechanical.

The grain weevil, *Sitophilus granarius*, and the Mexican bean weevil, *Zabrotes subfasciatus*, are among the stored products insects implicated as sources of inhalant allergens. Occupational allergies to other Coleoptera have been recorded (10, 137), primarily among individuals rearing these beetles.

Acari

Most instances of mite-induced occupational dermatitis are observed in individuals whose work brings them in contact with infested materials (47). The majority of mites infesting stored and processed foods belong to the families Acaridae (= Tyroglyphidae), Carpoglyphidae, Glyciphagidae, and Pyroglyphidae (67, 117, 128). A specific type of product will usually harbor a given species. Baker's itch, cotton seed itch, bulb mite itch, vanilla itch, copra itch, cheese itch, grocer's itch, grain itch, barley itch and straw or hay itch are the common terms applied to mite-induced skin inflammations in the respective industries (29, 67, 117, 128). The Pyemotidae are primarily insect associates and are frequently encountered as predators in laboratory insect cultures, particularly those found in stored grains. However, certain pyemotids will readily attack humans when their preferred hosts are unavailable (6). Some mites in this family are known to produce a toxin, and severe skin lesions,

asthma, nausea, and other symptoms have been reported (67). Mite infestations stimulate a broad range of immune responses including immediate and delayed hypersensitivity and precipitating antibody (135).

A number of outbreaks of occupational dermatitis have been associated with the grain itch mite, *Pyemotes ventricosus*; a recent outbreak was traced to infested "Black Beard Wheat" (*Triticum* sp.), which was imported and sold for decorative purposes. Of the 92 stores in the import chain, employees of 82 stores (89%) reported bites or skin lesions. *Pyemotes ventricosus* dermatitis is characterized by violent itching and a rash resembling chicken pox; some individuals exhibit fever, malaise, and loss of appetite (6).

The two-spotted spider mite, *Tetranychus urticae*, was the source of four of the nine allergies attributed to the Acari in the ESA survey. A report from one laboratory stated that every individual who reared this mite had developed a contact allergy (137).

Infestations of humans by parasitic mites of animals have been described (2, 29, 51, 67, 117), and the etiology of the human scabies mite, *Sarcoptes scabiei*, has also been reviewed (29, 51, 117). Wikel (135) addressed the immunologic responses to the scabies and chigger mites. In instances of chronic infection, immune responses may play a protective role by reducing the mite burden; however, evidence also exists that the host immune defenses are impaired (135). Many contact allergies are invariably due to mite bites, secretions, and burrowing (51, 135). Dermal reactions can be greater to dead mites and their products than to living Acari (53, 128), and evidence for bites is often not present (128).

House dust allergy, in which several species of mites and insects may be the sources of the inhalation and contact allergens (59, 117, 134), is estimated to affect four percent of the US population (134) and is a significant public health problem. This topic has been discussed extensively (see 5, 29, 134).

Other Arthropods

Many less frequently documented respiratory and dermal occupational allergies to arthropods have been reported. In addition to the orders discussed, Bellas (10) cited allergies to the Trichoptera, Ephemeroptera, Hymenoptera, Thysanura, Psocoptera, Siphonaptera, Isoptera, Dermaptera, and Neuroptera.

Aerial studies of insect fauna revealed that Aphidae was the dominant family at all altitudes (see 93). Gaillard (see 10) also noted the tremendous airborne aphid populations and found minute particles of aphid exuviae in his study of allergy patients. He observed that 75 (62%) of 121 individuals whose symptoms were unexplained by known inhalant allergens gave positive reactions to aphid extracts.

Respiratory allergies to *Apis mellifera* body components in beekeepers and their families have been well studied (66, 102, 140). Insect and spider silks

have been identified as potent allergens (58, 111, 137). Several subfamilies of Theraphosidae (tarantula) spiders possess urticating hairs on their abdomen that can produce severe dermal irritation on contact (100). Respiratory problems in the cotton-ginning industry have been attributed to lygaeid bugs (45), and workers processing crabs in Alaska and prawns in Britain have developed asthma-like symptoms (44, 87). Brine shrimps (*Artemia*) and "water fleas" (*Daphnia*) are ingredients of fish food that can cause allergy type problems (T. E. Bellas, personal communication).

BITES

Biting arthropods are capable of penetrating the skin and introducing secretions through specialized piercing or chewing mouth parts. Bites may be in response to feeding activity or may be defensive in nature. Most bites of humans by arthropods are attributed to the following groups: Acari (mites and ticks), Anoplura (sucking lice), Araneida (spiders), Chilopoda (centipedes), Diptera (mosquitoes and other biting flies), Hemiptera (true bugs), and Siphonaptera (fleas).

The normal response to insect bites has been studied in detail with humans and other animals (34). Reactions in man have been found to be highly variable in time, manifestation, and severity; symptoms are attributed to both antigenic and toxic substances (50, 55). Feingold et al (34) classified the chronological progression of "normal" skin reactions from continued exposure to bites as follows: (a) no observable reactions, (b) delayed reactions, (c) immediate followed by delayed reactions, (d) immediate reactions only, and (e) no reactivity. Case studies and laboratory data verified that this sequence of reactivity to bites is due to hypersensitivity to salivary secretions rather than to toxic venoms. Allergic reactions to the bites of some disease vectors are thought to be in response to the introduced pathogen (see 34, 50). The immunologic aspects of the host response to blood-feeding arthropods were recently reviewed (135), with emphasis primarily on the long-term, host-arthropod contacts of the Anoplura, Acari, and the sheep ked, *Melophagus ovinus*.

Schmidt (113) defined an insect oral secretion as a venom if there was evidence that it possessed a toxic activity responsible for rapid paralysis, death, or intense pain. Insect taxa were separated according to the strength of the venom produced, based on chemical and biological data. Hematophagous and phytophagous insects were excluded from Schmidt's review because of the lack of evidence of venoms in these insects. Irritation from the bites of hematophagous and phytophagous insects is attributed to mechanical puncture and a reaction to foreign proteins in the salivary secretions (113). The paucity of

information on the pharmacological and biochemical activity of oral venoms severely restricts discussion of this topic.

There are numerous reports in the literature on successful hyposensitization to biting insects using whole body extracts, but definite failures have also been reported (40, 55). Frazier (39) states that the most notable feature of these reports is the conflict of claims.

Heteroptera and Homoptera

Insects in fifteen families of Heteroptera and four families of Homoptera are known to bite or annoy humans (108, 110). Bites and allergic reactions from the hematophagous Triatominae (kissing or conenose bugs) and the Cimicidae (bed bugs) are significant public health problems in some areas (29, 108, 109). Results of a survey conducted in the southwestern US showed mild to severe reactions in 44% of the 142 respondents; it was estimated that 5–15% of the population in that area may react to bites of *Triatoma protracta* (139). Other species that produce hypersensitivity in residents of the southwestern US include *T. rubida*, *T. recurva*, and *Paratriatoma hirsuta* (109).

Feeding of the hematophagous Triatominae and Cimicidae usually occurs at night and, in general, little or no pain is associated with the bite (108, 109). Symptoms commonly reported by sensitized individuals after feeding by the bugs is completed include itching at the site of the bite, generalized itching, generalized hives, fainting, nausea and vomiting, swelling of the eyelids, tongue, and "throat," and difficulty in swallowing, speaking, and breathing (29, 40, 89, 133). Anaphylactic reactions as well as several deaths have been attributed to *Triatoma* bites (55, 108, 127).

Sensitivity can be species dependent and develops more slowly from bites of "domestic" *Triatoma*. Hypersensitivity is also affected by the age and size of the insect, as well as the amount of feeding that occurred at a given time (86, 109, 133). Immediate and delayed allergic reactions to bites can occur with the use of xenodiagnosis for detection of Chagas' disease and can become a significant problem in individuals who are tested repeatedly (22, 74, 133). The use of first instar bugs decreases the incidence of skin reactions (22).

Many of the 281 reports on bites from the Triatominae and Cimicidae, cited by Ryckman & Bentley (108, 110), are case studies or anecdotal in nature; however, the progressive symptoms of allergic reactions as defined by Feingold et al (34) are regularly evident in these references (108, 110). Marshall & Street (77) and Pinna et al (98) demonstrated evidence for IgE-mediated immediate and delayed hypersensitivity to salivary secretions of *Triatoma* spp. using radioallergosorbent and Prausnitz-Kistner tests. Using gel electrophoresis, Moretti & Chieffi (86) demonstrated a complex of proteins in the saliva of *Rhodnius prolixus* and *Triatoma brasiliensis* that may be involved in hypersensitivity reactions. The in vitro production of antigen, using *T. protracta*

ta salivary gland cell culture of Marshall (76), is a significant contribution to hyposensitivity therapy. The utilization of this technique could further elucidate the biochemical and pharmacological properties of other salivary secretions and venoms.

Ebeling (29) gives a detailed account of the Cimicidae with emphasis on the bed bug, *Cimex lectularius*. Allergic reactions (29, 108, 110), including anaphylaxis (55), to this insect have been reported, but details of the anaphylactic response were not given.

Bites from the predaceous Hemiptera can be intensely painful, especially those from the larger Reduviidae, Notonectidae, and Belostomatidae. The oral venoms of these hemipterans are usually described as powerful proteolytic enzymes that can result in localized destruction of tissue, necrosis, and ulceration; few venoms, however, have been studied in detail (29, 108, 113).

The homopterans assume less importance as etiological agents of trauma in respect to both the numbers of case reports in the literature and the severity of host reactions (108, 110).

Diptera

Results from two biting insect surveys attribute 63% and 39% of the reactions to the Culicidae (39, 40) and indicate that the most commonly occurring insect bites are from mosquitoes (55). As with the hemipterans, both immediate and delayed hypersensitivity reactions have been recorded in response to mosquito bites in man and experimental animals (4, 82).

Severing the salivary ducts of *Aedes stimulans* prevented characteristic allergic reactions in sensitized individuals. These bites were reported to be more painful than normal, which indicates the presence of an anesthetic in the saliva (56). The skin-reactive substance present in salivary secretions of *Aedes aegypti* was isolated using gel filtration chromatography and is reported to be a high molecular weight protein (88). Earlier reports in the literature indicated the presence of multicomponent antigenic materials in *A. aegypti* extracts (see 34). These sensitizing materials have been detected in larvae and pupae, as well as in adult males (80), with cross reactivity among some genera (36). However, the nature of the salivary secretions is known to differ among species (19, 20), and hyposensitization to one genus does not necessarily involve desensitization to others (20, 34, 80).

Christophers (19) noted that, in the case of *A. aegypti* bites, approximately six seconds of continued contact after puncture was required before a wheal developed in susceptible individuals. After this initial period the size of the wheal was generally proportional to the feeding time. Approximately 10^{-3} μ g of extractable material was required to produce reactions similar to those resulting from a mosquito bite (81).

Passive transfer of immediate and delayed hypersensitivities to *A. aegypti*, via sera and spleen cells, respectively, has been reported in guinea pigs and demonstrates the involvement of antibodies in reactions to mosquito bites (3).

Reactions to bites of the Simuliidae (black flies) (25, 92, 97), Ceratopogonidae (biting midges) (124), Psychodidae (sand flies) (129), Tabanidae (horse and deer flies) (29, 136), Muscidae (stable and horn flies) (49), Glossinidae (tsetse) (29), Therevidae (stiletto flies) (55), Asilidae (robber flies) (8), and Rhagionidae (snipe flies) (131) have also been reported.

Crosskey (25) stated that the Simuliidae include some of the most intolerable and voracious pests that bite man. He noted that the persistence of these pests has hindered economic development in some areas. Their bite can be painful and may result in continued bleeding after the bite, toxemia, and allergic reactions. In the eighteenth and nineteenth centuries, deaths attributed to black fly bites were reported from the lower Mississippi valley in the US and along the Danube in Central Europe (25). A recent seroepidemiological study presented evidence that a hemorrhagic syndrome was associated with the bites of *Simulium*, and several deaths were reported among immigrants living in forested areas along the Transamazon Highway in Brazil (97). An epidemiological study of 200 Japanese students revealed that 85 (43%) required treatment for black fly bites. Both immediate and delayed reactions were reported, with the "scar" from the bite usually remaining 4–5 days (92). Crosskey (25) lists the geographic locations of the most troublesome man-biting simuliids.

Bites from Ceratopogonidae have been reported as a public health problem in Brazil. In Salvador an increase in biting midges was correlated with the cessation of a control campaign against mosquitoes and decreasing sanitation standards (124).

Tabanid bites can be quite painful, resulting in a deep wound with considerable blood flow (29). Systemic reactions to bites of the deer fly, *Chrysops vittatus*, have been reported, with one patient suffering anaphylaxis. This hypersensitivity appeared to be mediated by reaginic antibody and was modified by systemic immunotherapy using aqueous deer fly extract (136).

Allergic reactions also can result from the bites of blood-feeding Muscidae and Glossinidae. Salivary gland removal from the tsetse prevented the bite reaction in a hypersensitized individual even though the fly fed to engorgement (29).

Other Insects

Reactions to Siphonaptera bites are discussed by Croce (24), Ebeling (29), and Smit (120). Harwood & James (50) cite numerous reports of annoyance from the bites of Thysanoptera (thrips). Any arthropod with piercing or biting mouthparts is capable of inflicting a wound, and an allergic reaction could result if the individual has been sensitized through prior exposure.

ACTIVE PROJECTION

Insects are noted for the diversity of the defensive chemicals they produce and their unique delivery systems. Defensive secretions may consist of the following reactive, irritating, or toxic materials: carboxylic acids, alcohols, aldehydes, alkaloids, ketones, esters, lactones, phenols, 1,4-quinones, hydrocarbons, steroids, and other miscellaneous compounds (16, 31, 104). Many of these defensive exudates have constituents that significantly increase their effectiveness by facilitating spreading or penetration. Delivery systems range from localized exudation and reflexive bleeding to remarkably accurate defensive sprays (31).

Some Lepidoptera larvae possess defensive glands that secrete or actively project odorous, repellent, or toxic substances. Larval Papilionidae have an eversible gland on the prothorax, the osmeterium, which emits a repellent odor when annoyed. The variable oakleaf caterpillar, *Heterocampa manteo*, releases a mist smelling like formic acid, which resulted in skin blistering after handling (62). The larvae of *Cossus ligniperda* (Cossidae) release an odorous, alkaline fluid from glands associated with the mandibles, and the vapor produces a burning sensation on human skin. Several Notodontidae larvae are capable of emitting jets of irritating fluid for distances of 2–3 cm (see 95).

Certain species of cockroaches produce secretions that are stored in specialized glands and that may be irritating to man. *Eurycotis floridana* ejects an aldehyde, 2-hexenal, which is irritating to sensitive areas of the skin of some individuals. Individuals cleaning the rearing cages of *Eurycotis decipiens*, a Trinidad cockroach, suffered vertigo, nausea, eye irritation, and loss of appetite. These cockroaches are capable of ejecting a secretion for a distance of up to one meter (105).

The hemipteran *Platymerus rhadamanthus* can accurately eject a salivary secretion that produces intense pain and edema when on mucous membranes (16).

The medical significance of the vesicating Coleoptera, including the Meloidae (blister beetles), Oedemeridae (false blister beetles), Staphylinidae (rove beetles), and Tenebrionidae (darkling beetles), has been discussed by Theodorides (130) and James & Harwood (50). A recent outbreak of rove beetle dermatitis was reported in which skin and eyelid blistering incapacitated the staff and some workers of a dam feasibility project and brought the work to a halt (83).

Commonly reared tenebrionid beetles are the richest source of 1,4-quinones in the animal kingdom (16), and these materials have been reported to be mutagenic (138) and carcinogenic (69). Several other species of stored-products arthropods can be detected by their odor; however, the composition of their exudates is unknown.

CONCLUDING REMARKS

Reactions to toxic and allergic products of non-stinging insects is more widespread than generally recognized. In an occupational environment these hazards may be reduced by limiting exposure to the causative agents. Interior design, sanitation, use of protective equipment, and education of personnel all play a role in the insectary or laboratory. Special emphasis should be placed on air filtration and circulation (137). Individuals should be informed of the potential problems inherent in working with arthropods, and those with a hereditary predisposition to allergies (atopy) should be especially mindful of limiting their exposure in the working environment. Continued research will be required to isolate and identify the exact causative antigens in most instances (101). A respiratory function survey performed on five insectary technicians, exposed to mosquitoes and organic debris from mouth pipetting of the insects, revealed no gross abnormality (28).

In an outdoor or home environment, judicious use of lighting and screening can greatly reduce exposure. Numerous reports in the literature stress the exacerbation of allergic reactions resulting from insects being attracted to and concentrated by lights in populated areas.

Individuals unable to eliminate exposure may consider hyposensitization therapy. Allergenic extracts are commercially available for many non-stinging insects, and efforts should be made to identify the responsible allergen(s), as preferable to whole body extracts, for use in hyposensitization. Hyposensitization to a variety of arthropods, primarily by injection with whole body extracts, resulted in significant desensitization in 82% of a test population. Some individuals, however, experienced more severe reactions (40). The application of sensitive analytical and biochemical techniques will greatly elucidate the pharmacological and biochemical properties of insect secretions and venoms.

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