Arthropods in dermatology

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Arthropods are important in medicine for a multitude of reasons. Their bites and stings may induce allergic reactions, ranging from annoying to life-threatening. Many arthropod products are also capable of inciting allergic responses in sensitized persons. In recent years, bites and stings have gained greater attention owing to increased concern about disease transmission. A common hypersensitivity response to arthropod bites, stings, and products is papular urticaria. This eruption occurs primarily in children, who eventually "outgrow" this disease, probably through desensitization after multiple arthropod exposures. Papular urticaria is most often caused by fleas or bedbugs, but virtually any arthropod is capable of inducing such a reaction. Two arthropod classes of medical importance are the Arachnida (spiders, scorpions, ticks, and mites) and the Insecta (lice, fleas, bedbugs, flies, bees, and ants). Animals in these two classes are probably responsible for more morbidity and mortality worldwide than are any other group of venomous creatures. In general, the diagnosis of arthropod bites and stings is dependent on maintenance of a high index of suspicion and familiarity with the arthropod fauna not only in one's region of practice, but also in the travel regions of one's patients. (J Am Acad Dermatol 2004;50:819-42.)

Learning objective: At the completion of this learning activity, participants should be familiar with the clinical manifestations caused by a variety of arthropods as well as the treatment and possible sequelae of arthropod attacks.

Since time immemorial, insects and related arthropods have been a source of nuisance, economic loss, and illness. Although arthropods are invaluable members of the animal kingdom, their bites and stings may cause severe allergic reactions and transmit disease.[1-4]

Papular urticaria is a term used to describe a chronic or recurrent eruption of pruritic papules, often grouped in irregular clusters, frequently seasonal in incidence, and affecting predominantly children between the ages of 2 and 7 years.[5,6] Adult cases are seen but are less common than childhood cases. Many causes were attributed to papular urticaria in the late 19th century and early to mid 20th century.[7] We now believe that a hypersensitivity to arthropod bites is the principal cause.[8]

The diagnosis of insect bite reactions may be difficult, partly because of mimicry of other clinical conditions and partly because of the lack of history of recent contact with an appropriate arthropod. One can sometimes recognize patterns of insect bites and stings, including the diffuse eruption of papular urticaria. Often, the correct diagnosis is suspected on clinical grounds; histologic examination is usually helpful.

PAPULAR URTICARIA

Papular urticaria was originally described in 1813 by Bateman.[9] The condition consists of small, 3- to 10-mm diameter, pruritic, urticarial papules, sometimes surmounted by a vesicle, that are present on exposed areas. More persistent than typical urticaria, the papules may last from weeks to months and, in some cases, years.[10,11] They form in clusters and are characteristically distributed on the extensor surfaces of the arms and legs[5,12-14]; however, location is dependent on the arthropod involved.[5,15] The genital, perianal, and axillary regions are usually uninvolved.[12] Excruciating pruritus frequently leads to excoriations, which may become secondarily impetiginized.[16,17] The lesions generally persist for 2 to 10 days and may result in temporary hyperpigmentation once they resolve.[5]

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Etiology

For decades, the cause of papular urticaria has been debated. Often, infants and adults who live in the same household as the patient have no signs of the illness. Many believed that if the disease were caused by some parasite, all members of a household would be affected. Frequently, if the papules were thought to be caused by a biting insect, no such parasite could be found. Suspected causes included digestive disturbances and food allergies, psychologic factors, nasopharyngeal infections, and parasites (including arthropods).[18-20]

The role of arthropods in papular urticaria gradually gained support because of several observations: the lesions usually appeared in the summer months; the disease was more common in lower socioeconomic groups; papular urticaria was seen with greater frequency among households with pets; and most important, the disease was cured simply by admission to a hospital.[12] The histologic appearance of papular urticaria was identical to that of the eruptions of persistent insect bite reactions, a finding that lent further credence to the idea that arthropods were the cause of papular urticaria.[16]

The primary lesion of papular urticaria is an erythematous wheal, which is followed by the formation of a firm, brownish-red papule.[21] Because papular urticaria is an allergic hypersensitivity reaction to arthropod bites, patients with the condition must be previously sensitized to parasitic antigens. Although cases have been described in infants as young as 2 weeks old, papular urticaria is not often seen in neonates.[5] Most infants are not sufficiently exposed to biting insects to develop a hypersensitivity response. Experiments have shown that with repeated exposure to antigen, hyposensitization takes place, and children "outgrow" the condition.[21] The adolescent response to an insect bite is the same as that of most adults: a transient wheal develops, but no persistent papule forms.

It is clear that papular urticaria can be produced by many different parasites.[22] The most commonly implicated are the cat flea *(Ctenocephalides felis),* the dog flea *(C canis),* the human flea *(Pulex irritans),* and the bedbug *(Cimex lectularius).*[12,19,23-29] Other arthropods capable of producing papular urticaria include mosquitoes and various species of mites.[30-38]

Histology

In papular urticaria, one sees a localized perivascular infiltrate with lymphocytes, histiocytes, eosinophils, and mast cells in the upper dermis, variable edema between collagen fibers, and a light scattering of eosinophils and mast cells away from vessels in the upper and mid dermis.[39] In the epidermis overlying the most marked and superficial perivascular infiltrate, there is spongiosis with exocytosis and vesicle formation. In older excoriated lesions, the histologic changes are usually modified by the effects of scratching, with the development of epidermal necrosis, crusting, and a dermal infiltrate with neutrophils and more abundant lymphocytes, making histologic diagnosis more difficult. Whenever possible, one should subject to biopsy only newly formed lesions that are not excoriated.[16,40] In a histopathologic study of 30 patients with papular urticaria, T lymphocytes (CD45RO, CD3) and macrophages (CD68) were present in all cases, while B lymphocytes (CD20) and dendritic antigen-presenting cells (S100) were entirely absent.[41] Immunofluorescence staining for the deposition of immunoglobulin (Ig) A, IgG, IgM, C3, and fibrin was negative in all cases.[41]

Differential diagnosis

Papular urticaria may be mistaken for varicella (chickenpox) in its early stages, scabies, prurigo simplex, "true" urticaria, and delusions of parasitosis.[42,43] Other lesions that should be considered include atopic dermatitis, papular drug reaction, id reaction, miliaria rubra, allergic contact dermatitis, and papulovesicular polymorphous light eruption.[5] A thorough history taking and the distribution of the rash will aid in the diagnosis.

Treatment

The ideal treatment for papular urticaria is identification and removal of its cause. In some instances, such a response may be difficult, if not impossible, and patients should undergo treatment for symptoms while the source of the rash is sought. We advocate mild topical steroids and systemic antihistamines for control of pruritus. Secondary infection warrants the use of oral antibiotics. Disinfection of all pets, along with fumigation of the home, may produce a dramatic cure.[26,44-46] Patients should apply insect repellent to the skin before they go outdoors.

OTHER REACTIONS TO ARTHROPOD BITES AND STINGS

All arthropods are invertebrates with chitinous exoskeletons, bilateral symmetry, true segmentation, and jointed true appendages that vary from few to many.[47] Two classes of importance are arachnids (Arachnida: spiders, scorpions, ticks, and mites) and insects (Insecta: lice, fleas, bedbugs, flies, bees, and ants). Centipedes and millipedes are members of the classes Chilopoda and Diplopoda, respectively. Arthropods produce parasitic disease, either by living

Table I. Arthropods and associated illnesses

Arthropod	Examples of associated illnesses
Insecta	
Lice	Typhus, trench fever, relapsing fever
Fleas*	Bubonic plague, typhus, tungiasis
Bedbugs*	Pruritic papules, possibility of HBV transmission
Flies, mosquitoes*	Cutaneous myiasis, malaria, yellow fever, dengue fever, viral encephalitis, onchocerciasis, leishmaniasis, sleeping sickness, West Nile fever
Bees, wasps, ants	Local reactions, anaphylaxis
Reduviid bugs	Chagas disease, papulobullous reactions, anaphylaxis
Arachnida	
Spiders	"Necrotic arachnidism," paralysis
Scorpions	Local tissue damage, neurotoxicity, cardiorespiratory collapse
Ticks	Granuloma formation, Lyme borreliosis, Rocky Mountain spotted fever, tick paralysis, Colorado tick fever, babesiosis, ehrlichiosis, Q fever, tularemia
Mites*	Hypersensitivity dermatitis, scrub typhus, scabies, possibility of role in rosacea
Others	
Centipedes, millipedes	Local tissue damage, "mahogany" stain

*Commonly cause papular urticaria.

permanently on the skin, as do scabies mites, or by transiently contacting the skin for feeding, as do lice. In both cases, irritant or allergic reactions occur in the human host. Pruritus often leads to secondary bacterial infection. Seemingly innocent insect bites may actually foretell more serious bacterial, rickettsial, viral, or parasitic disease (Table I).

ARACHNIDS (ARACHNIDA)

The three medically important orders of Arachnida are Araneae (spiders), Scorpiones (scorpions), and Acari (ticks and mites). Arachnids are distinguished from insects in that the adults have no wings or antennae and have four pairs of legs and two body segments.

Spiders

Spiders are important and useful members of the animal kingdom. While all spiders are harmful to their prey, few are dangerous to human beings, and even fewer are capable of causing significant morbidity or mortality.[48-52] Within the Unites States, the genera *Loxosceles* and *Latrodectus* include the primary species whose venoms produce significant toxic effects in humans.

Fig 1. *Loxosceles reclusa* (brown recluse spider). A characteristic "violin" or "fiddle" marking appears on the head and thorax. (Courtesy of Dr. Robert G. Breene, American Tarantula Society, South Padre Island, Texas.)

Spiders of the genus *Loxosceles* have earned the names "fiddleback spider" and "violin spider" because of a dark brown marking in the shape of a violin on the head and thorax (Fig 1). Bites of the brown recluse spider *(Loxosceles reclusa)* vary from mild, local reactions to severe ulcerative necrosis with eschar formation, known as necrotic arachnidism.[52-69] A transient erythema may be followed by vesiculation, with necrosis in 3 or 4 days and eschar formation between the fifth and seventh days.[70,71] The bite often appears as a central blister with mottling and a blanched halo with surrounding erythema.[72] The lesion may mimic erythema migrans of Lyme disease or pyoderma gangrenosum when ulcerated.[73,74] Microscopic examination of an early bite site reveals a neutrophilic perivasculitis with hemorrhage and edema; older ones show epidermal necrosis and ulceration with arterial wall necrosis and a prominent eosinophilic infiltrate.[67] Lesions from other arthropod species and a variety of medical conditions may mimic bites of the brown recluse spider. There are reports of both a chemical burn and a cutaneous anthrax infection being mistaken for bites of the brown recluse spider.[75,76] This potential for misdiagnosis has led to the development of a sensitive enzyme-linked immunosorbent assay for *Loxosceles* species venom that may eventually have useful clinical applications.[77]

The brown recluse is a nonaggressive spider and will seek out shelter in undisturbed places, such as attics, closets, and storage areas for bedding and

clothing. Although the natural habitat for these spiders is outdoors, heated homes have allowed them to exist in more northern climates. Humans may be bitten after donning clothing that has recently been taken out of storage.[1] While the brown recluse is most abundant in the Midwest, it has been identified from Maine to northern Florida and southern California, and from southern Texas north to Nebraska and east to eastern Tennessee.[54] General treatment measures include cleansing the bite site and applying cold compresses. Patients should also receive mild analgesics to control pain. A significant percentage of patients may need antibiotics after envenomation for the treatment of secondary infection. Warm compresses and strenuous exercise are to be avoided.[1] Although *Loxosceles* antivenins have been developed and are frequently used in South America, little evidence supports their effectiveness, particularly against local effects.[78] As with any arthropod attack, tetanus prophylaxis should also be considered following brown recluse envenomation.

The predominant cause of necrotic arachnidism in the Pacific Northwest of the United States is the hobo spider or "aggressive house" spider *(Tegenaria agrestis)*.[79] The local effects of envenomation by the hobo spider are similar to those caused by the brown recluse.[80] The bite reaction may range from mild to serious. The initial bite is often painless, and induration of the site usually develops within 30 minutes. An erythematous area up to 15 centimeters in diameter may develop around the site. Blisters often develop during the first 36 hours and may rupture, producing a serous exudate. In cases of severe reaction, an eschar may form at the wound site, with necrosis and sloughing of the underlying tissue. Although wounds usually heal within 45 days, bites in fatty tissue may take up to 3 years to resolve. The most common systemic effect of a hobo spider bite is a severe headache that develops within minutes to hours and can persist for up to 1 week.[81] Other symptoms may include nausea, fatigue, and memory impairment. Although quite rare, death can occur owing to severe systemic effects, including aplastic anemia.[81]

A member of the same family as the Australian funnel-web spider, the hobo spider is native to Europe but was introduced into the Seattle area during the 1920s or 1930s.[82] The hobo spider can now be found in an area ranging from the Alaskan panhandle to Utah.[82] Although *Loxosceles* species are not found in this geographic distribution, bites from hobo spiders are often mistaken for brown recluse bites.[83] These spiders, which build funnel-shaped webs in crawl spaces, basements, and wood piles, are brown with a gray herringbone pattern on the abdomen.[84,85] Most bites occur from July to September, when the more venomous male spiders are seeking mates.[85] The wearing of gloves and other protective clothing while handling firewood or working in crawl spaces may help prevent bites. Recommended treatment for hobo spider bites is the same as that for brown recluse bites, although no hobo spider antivenin is available.

Like the brown recluse, the maligned black widow is a shy creature that bites only when provoked. Bites of the southern black widow spider *(Latrodectus mactans),* which may be painful, are usually associated with mild dermatologic manifestations.[72] Local erythema, sweating, and piloerection may appear at the wound site within the first half hour, and urticaria and cyanosis may also occur at the bite site.[86] Black widow venom causes depletion of acetylcholine at motor nerve endings and release of catecholamine at adrenergic nerve endings.[87,88] Consequently, black widow bites may produce agonizing abdominal pain and muscle spasm, which may mimic an acute abdomen.[89] Other signs and symptoms include headache, paresthesias, nausea, vomiting, hypertension, and sometimes paralysis; fortunately, death is not common.[87,88,90] Black widow bite may be misdiagnosed, on the basis of the spectrum of symptoms, as drug withdrawal, appendicitis, meningitis, or tetanus, to name a few.[89]

Most of the 26 species of widow spiders are jet-black and often can be identified from their characteristic red "hourglass" marking on the undersides of their abdomens (Fig 2).[72] Members of the *Latrodectus* genus are trapping spiders, which spin webs and await their prey. Webs are in protected areas, such as the undersides of eaves and the angles of doors and windows. Because webs can be found around outdoor toilet seats, bites may occur on or near the genitalia.[1] Of the five species of widow spiders found in the United States, *Latrodectus mactans* is most common, ranging from the South to southern New England and west to California and Oregon.[1] Current treatments for black widow envenomation include intravenous calcium gluconate, analgesics, and *L mactans* antivenin for severe cases.[66,86]

Scorpions

Scorpions are terrestrial arachnids that are easily recognized and well known for their stinging propensities. A bulbous sac and pointed stinger at the end of their tail-like abdomens are characteristic. Scorpions also possess strong, lobsterlike pedipalps for grasping their prey. Within the United States, scorpions are of medical interest primarily in the arid areas of the Southwest.[91-94] The main concern about

Fig 2. A widow spider, *Latrodectus indistinctus.* (Courtesy of Dr. Ansie Dippenaar, Agricultural Research Council, Pretoria, South Africa.)

scorpion envenomation, although capable of producing significant local wounds, is the potential for serious, even lethal, cardiovascular complications.[47,95-102] The scorpion of primary concern in the United States is *Centruroides exilicauda* (formerly *Centruroides sculpturatus*), whose sting is potentially fatal. In general, scorpion stings produce an immediate, sharp, burning pain that may be followed by numbness extending beyond the sting site. Regional lymph node swelling may also occur. Less often, ecchymosis and lymphangitis develop.[103] *Centruroides exilicauda* is a small scorpion, ranging from 1.3 to 7.6 cm in length, depending on maturity.[103] It possesses a small spine, or tubercle, at the base of its stinger, a feature common to *Centruroides* species, which may help distinguish it from other species of scorpion.[91,98] *C exilicauda* possesses a powerful neurotoxin capable of producing muscle spasticity, excessive salivation, nystagmus, blurred vision, respiratory distress, and slurred speech in its human victims.[50,94,96-98,103-105] Untreated stings may be fatal in infants and young children; death is less common in adults.[91]

Scorpions are most common in arid regions, including the southwestern United States and northern Africa. Nocturnal creatures, they seek shelter under stones and bark during the day. Despite their fearsome appearance, scorpions are shy and sting humans only in defense.[92] Stings occur when putting on shoes or clothing that were in storage or when walking barefoot in scorpion-infested areas.[95] Because scorpions are commonly found underneath tabletops, attempts to move tables may also result in stings. Treatment for mild envenomation is largely symptomatic. Analgesics and local ice packs may suffice. However, any child stung by a scorpion, especially one identified as *C exilicauda,* should be admitted to a pediatric intensive care unit, where respiratory, cardiac, and neurologic status can be monitored closely.[103] After life-supporting measures are instituted, specific antivenin is the treatment of choice for severe envenomations.[95,100] Studies indicate that *C exilicauda* antivenin is relatively safe, with a low incidence of anaphylactic reaction after infusion.[106] Although self-limited serum sickness is common after antivenin infusion, it is easily managed with antihistamines and corticosteroids.[106]

Mites

Mites have long been recognized as a cause of dermatitis. Mites injure the skin with their feeding habits and are vectors of a number of important diseases. They are easily distinguished from other arachnids by the possession of a distinct gnathosoma (capitulum with the mouthparts) and the lack of a division between the abdomen and cephalothorax.[107] Mites of most interest to the clinician are the follicle, food, fowl, grain, harvest, murine, and scabies mites.[47,108] With the exception of *Demodex* and scabies mites, they do not burrow and usually drop off after feeding. All mites may produce pruritus or allergic reactions through salivary proteins deposited during feeding.[47] Generally, lesions caused by mites are pruritic, somewhat erythematous eruptions composed of papules that may or may not be associated with a wheal. Each papule, usually 1-10 millimeters in diameter, may have at its center a small punctum or vesicle.[109] Aside from eliminating the causative species, treatment of mite-induced dermatoses includes the use of topical antipruritics, such as those containing menthol, camphor, or pramoxine; oral antihistamines are helpful for nocturnal pruritus.

The *Demodex* mite, a type of follicle mite, can be found in normal hair follicles and sebaceous glands.[110] The mites are wormlike in appearance and approximately 0.4 mm long (Fig 3). After copulation, the mites move downward into the hair follicle or sebaceous gland orifice, where they feed on sebum. *Demodex* mites are most often found on the nose, cheeks, and forehead but may also occur

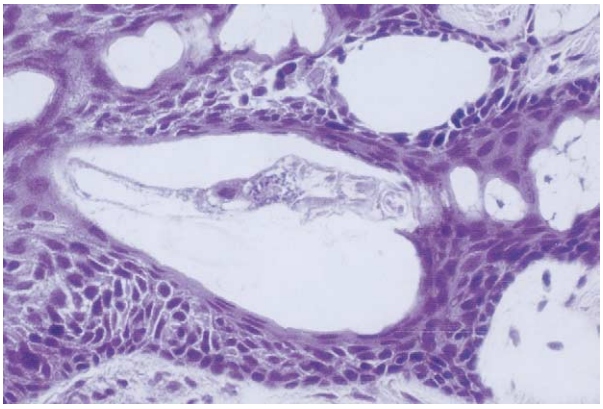

Fig 3. *Demodex* mite within a biopsy specimen obtained from the face. (Hematoxylin-eosin stain; original magnification ×400.)

on the neck and chest.[107] They have been implicated as an etiologic agent of rosacea, possibly through an immunologic response.[47,111,112] *Demodex* mites have also been associated with pityriasis folliculorum, a rough, sandpaper-like eruption of the face with flushing and follicular plugging.[107,110] However, no study has definitively linked *Demodex* mites with human disease.

Among several species of mites that infest food is the cheese mite *Glyciphagus.*[47] Other mites are commonly known to infest flour, sugar, dried meats and vegetables, grains, cereals, and feathers used as stuffing for pillows and mattresses. These parasites crawl onto the exposed skin of persons who handle food, migrating under the scales of the stratum corneum or through cracks in the epidermis. The resulting dermatitis is probably caused by a hypersensitivity to the mites and their products, as they do not feed on blood. Tiny, erythematous papulovesicles and pustules occur on exposed surfaces such as the hands, arms, and face, and pruritus may be intense.[107] An occupational history, along with skin scrapings that show the mite, allows correct identification of the species.

"House dust" mites are worldwide in distribution and include the species *Dermatophagoides pteronyssinus, D farinae, D avium, D americanum,* and *Euroglyphus maynei.* These mites are free-living on the skin of mammals and birds, and are often found in human dwellings, where they are hypothesized to feed on human skin scales and other forms of detritus. Carpets, mattresses, and upholstery are the major breeding sites within homes.[113] Allergens are in the exoskeletons and feces of living and dead mites; therefore, relief from mite eradication may not be immediate. The definitive role of house dust mites in atopic dermatitis and other eczemas is still in question.[107] When feasible, carpets should be replaced with wood or tile floors, and curtains with blinds. The prevalence of live mites fluctuates seasonally, with the highest levels occurring during humid summer months, which are more favorable for breeding and survival.[113] Reducing the relative humidity within the home may keep mite populations under control.

Office workers, homemakers, and bird fanciers may be affected by mites that infest birds, especially pigeons, that have nests near air conditioner intake ducts. *Dermanyssus gallinae* and *D avium* are most often implicated.[47] *Ornithonyssus sylviarum* is an uncommon fowl mite that may harbor and transmit western equine encephalitis virus.[47,111] *Pyemotes ventricosus* is a grain mite that infests both animals and human beings, occasionally producing epidemics after exposure to hay, grains, grasses, or straw.[114] The eruption may be generalized, with the forearms, trunk, and neck being extensively involved.[28] Affected patients may develop fever, diarrhea, anorexia, and malaise. However, the specific salivary component responsible for these constitutional symptoms is unknown. Clinically, the lesions vary from bright red macules to varicelliform papulovesicles.[115]

Perhaps the most common mite to attack humans in the United States is the chigger, sometimes called "harvest mites" or "red bugs." Chiggers are the larval form of mites in the Trombiculidae family, with the most common species being *Eutrombicula alfreddugèsi.*[38,107] Contact with the mite usually occurs during summer and fall, when outdoor activities are maximal. The gravid female mite lays eggs in the soil, and the red chigger larvae emerge and crawl in search of a suitable host. The larvae insert their feeding mouthparts into the epidermis, but rather than taking a blood meal, they suck up lymph and tissue dissolved by the mite's proteolytic saliva. Frequently, the only signs of exposure are intensely pruritic, 1- to 2-mm-diameter papules on the ankles, legs, or belt line, since the bright red mites typically fall off after feeding.[47,114,116] The bite is not felt, and pruritus begins 3-24 hours later. The number of new eruptions may increase for 2 days, and although the chigger is not present, the papules may persist for up to three weeks.[107] In some parts of the world, species of *Trombicula* carry the bacterium *Rickettsia tsutsugamushi,* the causative agent of scrub typhus.[38,47]

Persons working in areas commonly inhabited by rats and mice (groceries, granaries, restaurants, storehouses) may be affected by murine mites.[117,118] Like the reactions caused by most mites, those produced by murine mites are pruritic, urticarial papules that may be confused with flea bites or scabies.

Allodermanyssus sanguineus, the house mouse mite, is a vector of rickettsialpox.[47] *Ornithonyssus bacoti,* although called the tropical rat mite, can be found on several species of rat in both temperate and tropical regions. The initial outbreak of this mite as a pest to man was coincident with a large increase in the number of rats in the early 1920s.[117] When the usual host is not in abundance, the mites seek out other prey, such as human beings. They tend to accumulate near areas of warmth, such as crevices near heaters, radiators, stoves, and the backs of television sets.[107] The bites, which are painful and very pruritic, appear as grouped, 4-mm-diameter papules. The face, hands, ankles, and parts of the body where clothing fits tightly are the areas most frequently involved.[115,117] Treatment is centered on eradication of the rodent reservoir.

Dogs, cats, and rabbits frequently harbor the nonburrowing mite *Cheyletiella*.[118-121] In general, *C yasguri* is the species found on dogs, while *C blakei* and *C parasitvorax* are associated with cats and rabbits, respectively.[118-123] All three of these mite species have been associated with human dermatoses.[117] Even heavily infested pets will remain symptomfree, hence the term *walking dandruff.* Although the pet is asymptomatic, the person holding the pet experiences marked pruritus when the mites feed on her or his skin; however, unlike scabietic mites, which burrow into the skin, these mites, like most, bite and fall off, rapidly returning to their animal host. The mites are highly contagious, especially among young host animals. Human eruptions vary from a mild, pruritic, papular rash to a severe response with blister formation. Papules and vesicles may quickly evolve into pustules, which become necrotic.[117] The eruption is usually symmetric and occurs in areas with the greatest contact with the pet: the inner arms, chest, and abdomen. Since the mite is almost never found on the patient, the diagnosis is made by means of microscopic examination of scrapings from the animal's fur. Human beings should undergo treatment for their symptoms. With the cure of pets, the rash should subside within a few weeks. Dogs and cats must undergo thorough treatment, usually with the help of a veterinarian.[124-126]

Scabies has been a scourge among humans for thousands of years. Descriptions of this highly pruritic affliction can be found in ancient writings from the Greeks, Egyptians, Romans, and medieval Europeans. Historically, epidemics of scabies occurred during times of war, famine, and overcrowding. Scabies was also endemic in areas of poor sanitation, such as mental institutions and other long-term-care facilities. In recent times, scabies has resurged, especially among those persons infected with HIV. Because of its highly contagious nature, scabies continues to be a considerable source of morbidity. The condition is caused by the mite *Sarcoptes scabiei,* var. *hominis,* the adult being barely visible to the naked eye (Fig 4). [127-133] The organism is an obligate parasite, requiring an appropriate host for survival. The mites subsist on a diet of dissolved human tissue but do not feed on blood.

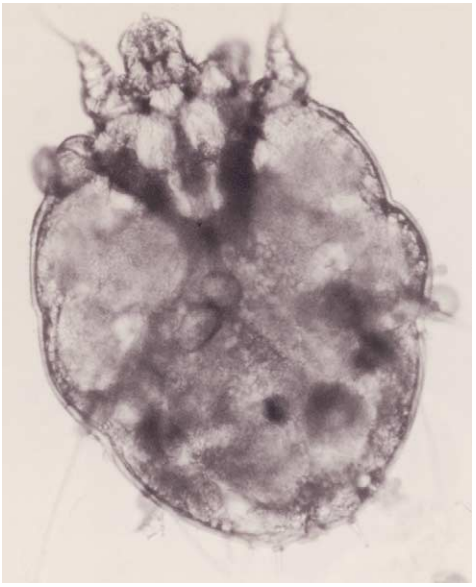

Fig 4. Adult gravid female *Sarcoptes scabiei* mite. (Original magnification ×100.)

Human scabies is transmitted mainly by direct personal or sexual contact and, less often, by contact with infested bedding or clothing.[134-143] While the mites cannot fly or jump, they can crawl as fast as 2.5 cm/min on warm skin.[138] After mating on the surface of the skin, the gravid female mite dissolves the stratum corneum with proteolytic secretions; then, using her jaws and cutting claws on the forelegs, burrows headfirst into the skin.[129] Eggs are laid, at the rate of 2 to 3 per day, as she travels forward; up to 40 ova may be produced by a single mite. Young mites develop quickly, leaving the burrows to enter hair follicles and skin folds in which to hide and feed. Mature adults are formed in 10 to 14 days,[138] and mating then takes place on the skin surface to begin a new cycle of burrowing and egg laying. The average infected adult human has 10 to 15 live adult female mites on his or her body at any given time.[138]

The disease is characterized by severe pruritus that is often worse at night. The characteristic primary lesion is the burrow. It is formed by the female mite and appears as a white or gray threadlike, linear, wavy papule with a small vesicle at one end and is most often found in the interdigital spaces of

the hand, on the flexor surfaces of the wrists and elbows, on the areola in women, and on the penis, scrotum, umbilicus, and belt line.[134-137] Secondary papules, pustules, vesicles, and excoriations are usually evident. These secondary lesions are more numerous and prominent than burrows, especially when the infestation has been present for some time.[127] The rash does not correlate well with the distribution of the adult mites; it is possible that the secondary lesions are the result of an immune response to the immature mites within the hair follicles. The intensely pruritic eruption begins 10 to 30 days after the onset of infestation.[134,138,144]

While scabietic lesions are uncommon above the neck in children and adults, infants may have involvement of the face. Neonates and infants may present with extensive, crusted, erythematous papules and pustules. Burrows, common in adult patients, can also be seen. Infected infants may display irritability and poor feeding.[129] Scabies in an infant usually means that a close adult contact is the source of the infection.

Norwegian or *crusted scabies* is used to describe heavy infestations, with severe cutaneous crusting and hundreds to thousands of adult mites on a patient's body.[127,138,144-146] The term *Norwegian scabies* was first used in 1848 to describe severe scabietic infestations in patients with leprosy.[144] Patients with this form of scabies are usually immunocompromised owing to some underlying genetic or medical defect.[127] In contrast to conventional scabies, erythematous papules and burrows may be limited or absent, and pruritus is variable. The crusted lesions, teeming with adult mites, may be seen in the head and neck and, in homosexual men, on the buttocks and perianal regions.[129] Norwegian scabies is most common in homeless AIDS patients, who have little or no access to care; in neonates, who are relatively immunocompromised; and in debilitated, neglected, nursing home residents. Highly contagious hospitalized or institutionalized patients with Norwegian scabies may be the source of epidemics among medical personnel.[127]

Scabies should be suspected in any patient with pruritus. Proof of the infestation may be achieved by visualizing the mite, its ova, or its excreta (scybala) (Fig 5). One method of scabies diagnosis is skin scraping. An oil-covered scalpel blade should be scraped across burrows; the oil helps scraped material adhere to the blade. Scrapings can then be placed on a slide with a coverslip for microscopic examination. The best sites for examination are new, nonexcoriated burrows in the interdigital areas of the hand.[129] Because few mites may be present, repeated scrapings are often necessary. Another method of detecting scabies is videodermatoscopy. Videodermatoscopy has been demonstrated to be an effective and sensitive diagnostic tool, allowing for noninvasive, in vivo visualization of the skin at magnifications of up to 600 times to detect signs of infestation (mites, eggs, and feces).[147-149] Videodermatoscopy can be utilized for primary diagnosis, posttherapy follow-up, and screening of family members.[147-149] It is particularly useful in cases of nonspecific clinical findings. Because the technique is painless, it has a high compliance rate, especially in children, who may refuse skin scraping.[147-149]

Fig 5. Ova of *Sarcoptes scabiei* mite. (Original magnification ×400.)

Treatment of scabies involves the control of symptoms and secondary infections, and eradication of the mites themselves. Pramoxine-containing lotions can be used to control pruritus, and somniferous doses of oral antihistamines may be needed. One should employ oral antibiotics for secondary bacterial infection. Destruction of the mites can be accomplished with a number of different agents.[128] Topical antiscabietic agents that have been used include sulfur compounds, benzyl benzoate, crotamiton, lindane, malathion, permethrin, and ivermectin. Lindane was the primary treatment for several decades and was effective and reliable.[150] Rare cases of seizure, coma, and even death resulted in some patients, particularly infants, because of the neurotoxic properties of lindane.[150] Permethrin, a synthetic pyrethrin-like compound, is now preferred over lindane as an antiscabietic agent.[151] Permethrin has little transcutaneous absorption and has proven effective, even in cases of lindane-resistant scabies.[151] A bedtime application of 5% permethrin should be used over all skin surfaces, especially the fingernails, waist, and genitalia.[129] The cream should be washed off in the morning. All family members, regardless of symptoms, should undergo treatment at the same time as the patient. We instruct the patient and symptomatic household members to repeat the application 1 week later. In addition, all clothes and bedding must be washed in hot water.

In our experience, treatment failures have arisen from poor patient understanding. Another treatment for scabies is topical precipitated sulfur. Although not commonly used in the United States, 5% to 10% topical precipitated sulfur in petrolatum has also proven to be a safe and effective antiscabietic agent.[152] It is used in many parts of the world where other agents are either unavailable or prohibitively expensive, and its favorable safety profile makes it particularly useful in children.[152] One barrier to the compliance of treatment with sulfur is its foul odor.[152]

Treatment of crusted or Norwegian scabies is often difficult. Hyperkeratosis often prevents adequate penetration of topical scabicides. In addition, immunosuppression hinders the host's ability to eliminate the mites. Treatment failures are frequent in cases of crusted scabies, even with the use of adjunctive keratolytics to improve penetration of topical antiscabietics. Repeated daily applications and the sequential use of several agents are often necessary to eliminate the mites. Relapses can occur from untreated areas, such as the scalp and subungal regions. Studies have shown that ivermectin, an anthelmintic and drug of choice for onchocerciasis (African river blindness), may be effective as a single oral dose (150-200 μg/kg) in the treatment of scabies, including cases of crusted scabies in the setting of HIV infection.[146,153-155] Oral ivermectin is easily and rapidly administered and effectively treats all cutaneous surfaces. Although it is generally well tolerated, there have been rare reports of deaths following administration of oral ivermectin for scabies, particularly in elderly patients.[145]

Although mites are species-specific, mites from one species of mammal may occasionally transfer to another species. Not uncommon is infection of humans working with domesticated animals. This transference has led to terms like *pig handler's itch* (pig scabies) and *cavalryman's itch* (equine scabies) to describe the subsequent irritation.[156] Families may acquire canine scabies when a puppy is brought into the home. The distribution of lesions on humans infected with dog scabies is distinctively different from that of the human variety. A child that hugs an infested family pet will make greatest contact with his trunk and arms; for this reason, most eruptions of canine scabies are seen in this very distribution. Characteristically, it spares the hands.[157] Canine scabies manifests itself within 24 to 96 hours and is generally self-limiting in humans, since the mites cannot complete their life cycle and therefore do not survive for more than a few days on the foreign host.[156,158] For those patients unwilling to wait for canine scabies to resolve on its own, 5% permethrin applied topically is the treatment of choice.[158] The assistance of a veterinarian is recommended for treating the pet.

Ticks

Of the approximately 800 known species of ticks, nearly 100 species are capable of transmitting bacterial, viral, and protozoal agents to humans. Worldwide, ticks are important vectors of systemic disease. In the United States, they are probably responsible for the transmission of more vector-borne diseases than any other agent.[159] Ticks ingest blood from a diversity of vertebrate hosts: reptiles, birds, and mammals, including humans.[109,159-165]

Humans often become infested by their association with domestic animals, such as cats and dogs, or by their contact with tall grass or brush that harbors the unfed ticks, waiting to attach to a passing host. Ticks are attracted to the smell of sweat, the color white, and body heat.[160] A tick that has attached itself to a host will not bite immediately but may spend up to 24 hours on a host in search of a protected site to feed, such as a skinfold or the hairline.[162] Using specialized mouthparts, ticks will engorge themselves with the host's blood. When full, they drop off. This period of feeding may last from 2 hours to 7 days (Fig 6). [160]

Tick bites are not painful, as an anesthetic and anticoagulant substance is introduced.[162] Ticks are sometimes seen or, more often, felt by a person while scratching or bathing.[109] Tick bites may induce foreign body and hypersensitivity reactions.[47] Rarely, delayed hypersensitivity reactions occur, with fever, pruritus, and urticaria.[160] A red papule, which may or may not be pruritic, is usually seen at the bite site.[163] This papule can progress to local swelling and erythema.[109] A cellular reaction can lead to induration and nodularity after a few days. Granulomatous foreign body reactions occur when mouthparts are retained in the patient's skin after vigorous attempts at removal of the tick.[162] Chronic tick bite granulomas present diagnostic problems and may persist for years.[164-166]

Bites occur most often in the spring and summer, coinciding with the life cycle of the tick. Many different species are responsible for local tick bite reactions and transmission of disease. In the United States, *Ixodes scapularis* (deer tick), *Dermacentor andersoni* (American wood tick), and *D variabilis* (American dog tick) are most common.[49] Among diseases transmitted by ticks are Lyme disease, ehrlichiosis, and babesiosis *(Ixodes scapularis)*[167-169]; Rocky Mountain spotted fever *(Dermacentor variabilis* and *D. andersoni)*[169,170]; and Colorado tick fever, Q fever, and tularemia *(D. andersoni)*.[47,109,169]

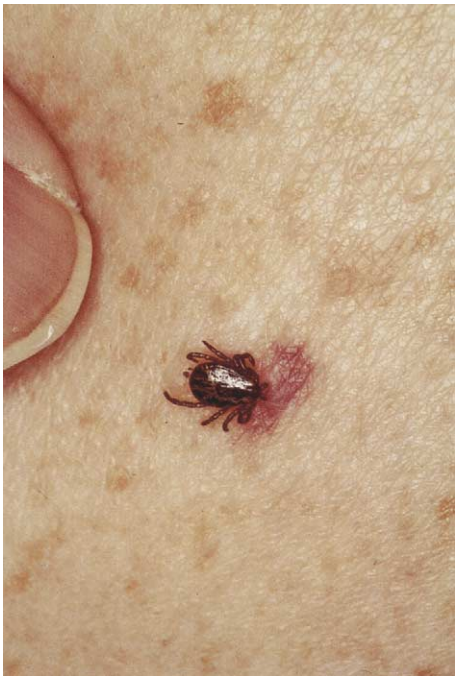

Fig 6. *Dermacentor* tick feeding on skin.

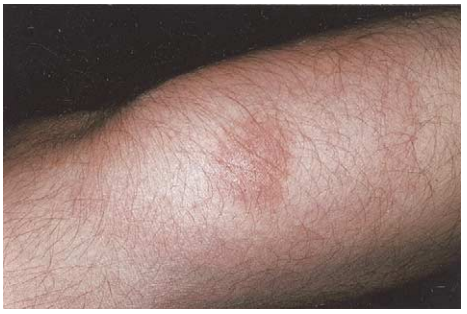

Fig 7. Erythema migrans, Lyme borreliosis. (Courtesy of Mark Lebwohl, MD.)

Lyme borreliosis, or Lyme disease, was first described during an epidemic of arthritis in 1975, in the areas surrounding Old Lyme, Connecticut.[171] Not until 1982 was the causative agent, the spirochete *Borrelia burgdorferi,* identified.[159,172-180] Several species have been identified within the *B burgdorferi sensu lato* complex that are capable of causing Lyme disease. *B burgdorferi sensu stricto* is found in the United States and Europe.[169,171] *B garinii* and *B afzelii* are found in Europe and Japan.[169,171] *B japonica* has been suggested as a possible cause of Lyme disease in Japan.[181] Lyme disease is widely distributed throughout the northern hemisphere and has emerged as the leading vector-borne disease in the United States.[182-184] From 1992 to 2000, the reported incidence of Lyme disease doubled.[182] In 2000, 17,730 cases were reported to the Centers for Disease Control.[182] The northeastern, mid-Atlantic, and north central regions of the United States have the highest reported incidence.[185]

B burgdorferi is spread mainly by Ixodidae ticks.[184] Within the continental United States, most cases of Lyme borreliosis are caused by bites of the ticks *Ixodes scapularis* and *Dermacentor variabilis* on the East Coast, and by *I pacificus* on the West Coast.[169] *I dammini* was thought to be closely related to *I scapularis,* but they are now considered the same species, *I scapularis.*[186] In Europe and Asia, the ticks *I ricinus* and *I persulcatus* are the most common vectors.[169] Most cases of Lyme disease occur from May through August, corresponding to peak nymphal-stage activity. The percentage of nymphal deer ticks carrying *Borrelia burgdorferi* may range from 15% to 85% in highly endemic areas.[187] The natural reservoirs for the spirochete in the wild include deer, sheep, bison, small rodents, and lizards.[188] Studies have shown that the longer a *B burgdorferi*-infected tick remains attached to its host, the greater the rate of transmission of the spirochete.[189] Therefore prompt removal of any feeding tick is wise.

The hallmark cutaneous manifestation of Lyme disease is erythema migrans (Fig 7).[169,190-193] It is the most common early manifestation of Lyme borreliosis.[193] Classically, the rash is that of an erythematous, annular patch that expands centrifugally from the site of the tick bite, leaving a central clearing.[167] The rash of erythema migrans may extend over large areas of skin when fully developed, but smaller and atypical rashes occur frequently.[159] Commonly, the involved area is warmer than the surrounding normal-appearing skin.[193] With the possible exception of mild pruritus, the patch often goes unnoticed by the patient.[193]

Borrelia burgdorferi spreads locally in the skin, eliciting interleukin-1 production by skin macrophages.[194] In addition to systemic flulike symptoms, hematologic spread of the spirochetes may trigger multiple annular erythematous patches, urticaria, and lichenoid exanthemas. The presence of multiple lesions of erythema migrans always indicates disseminated disease. The histopathologic appearance of a biopsy specimen taken from the center of an erythema migrans patch, with the exception of the presence of spirochetes, is no different from reactions caused by other arthropod bites, such as fleas and mosquitoes, in which one sees a perivascular infiltrate of lymphocytes, eosinophils, and histiocytes.[191,195,196]

Erythema migrans may be present in only 50% of Lyme disease patients and, when present, may develop anytime from 4 days to 3 weeks after infec-

tion.[167,169] In addition, not all cases of erythema migrans will be in the classical bull's-eye pattern. Variants include diffuse, speckled, homogeneous, and vesicular patches.[197] Erythema migrans can also be hemorrhagic or nonmigratory.[169] Erythema migrans may spontaneously regress within weeks or months but may also persist and spread. Patches remaining for 4 weeks or longer are referred to as erythema chronicum migrans. Other conditions, such as granuloma annulare, fixed drug eruptions, cellulitis, contact dermatitis, and dermatophytoses, may be confused with atypical erythema migrans.[192] Therefore neither the presence nor the absence of this sign can be relied on for the diagnosis and institution of treatment.

Another cutaneous manifestation of Lyme borreliosis is borrelial lymphocytoma (lymphadenosis benigna cutis, lymphocytoma cutis).[193,198-200] This illness usually presents as a solitary, 1- to 5-cm-diameter, bluish-red papule, plaque, or nodule. A lymphoreticular proliferation is seen within the dermis or subcutis; the epidermis is generally unaffected.[195] Lymphocytomas belong to the group of pseudolymphomas, which are benign lymphoreticular disorders that may simulate true lymphomas both clinically and histologically. Pseudolymphomas arise in response to antigenic stimulation, as can be seen in tattooing, vaccination, acupuncture, and *Borrelia burgdorferi* infection.[198] Most cases have been reported in central, eastern, and northern Europe and in immigrants from these regions.[198] In most patients with borrelial lymphocytoma, the borrelial lymphocytoma is the first and only cutaneous sign of Lyme disease.[199] The reaction may develop at the site of the tick bite or some distance away. The incubation period may be weeks to many months. Sites of predilection are the earlobe, areola, nose, and scrotum, probably reflecting the spirochete's preference for lower body temperature.[193,198] Recent studies indicate the condition may be more common in children.[193] When *B burgdorferi* is suspected as the cause, a trial of penicillin or doxycycline may be worthwhile.

A late cutaneous manifestation of Lyme borreliosis is acrodermatitis chronica atrophicans.[201-204] This lesion is characterized by an initial inflammatory phase appearing as a bluish-red edematous erythema that, if left untreated, may lead to atrophy of all skin layers and usually occurs on the dorsal portion of the hand, elbow, foot, or knee.[205] Acrodermatitis chronica atrophicans is seen in middle-aged and elderly European patients and in immigrants from Europe.[202] *Borrelia burgdorferi* has also been implicated in anetoderma and sclerotic skin lesions, including morphea-like plaques and lichen sclerosis et atrophicus.[206,207]

There may be differences in the manifestations of Lyme disease based on geographic region. In Japan, for instance, patients may follow a relatively milder course, with erythema chronicum migrans being the only manifestation of the disease in most patients.[181] As mentioned previously, acrodermatitis chronica atrophicans, a late cutaneous manifestation of the disease, is seen almost exclusively in European patients.[202] It is possible that these variations may be due, at least in part, to regional differences in *Borrelia* species. Clearly, clinicians must keep the regional variations of Lyme disease and the travel history of patients in mind when diagnosing and treating the disease.

The diagnosis of Lyme borreliosis is critical, since early treatment can definitively eradicate the spirochete. Successful treatment of late infections is more difficult and, in some cases, futile. The results of enzyme-linked immunosorbent assays that detect antiborrelia antibody are commonly falsely negative, as reactive immunoglobulins may be bound up in immune complexes.[169] In addition, up to 6 weeks may pass before detectable quantities of antibody to the spirochete develop in a patient.[208-213] Until better laboratory tests are widely available, the diagnosis of Lyme disease should be based on compatible clinical findings in a patient with a reasonable risk for exposure to ticks in a Lyme-endemic area.[159,169] Early Lyme disease responds readily to a variety of oral antibiotics (eg, amoxicillin, doxycycline, erythromycin), usually taken for 2 to 3 weeks.[169,214-217] Lyme disease with neurologic involvement warrants treatment with an antibiotic, such as ceftriaxone, that penetrates the blood-brain barrier.[159,169,218-223]

Prevention of bites is the most important measure in controlling both local and systemic tick-related diseases. Permethrin, when applied directly to clothing, may be the most effective tick repellent, given its long duration of action and actual ability to kill ticks.[170] DEET can be applied to exposed skin surfaces.[169] Vaccines have been developed for Lyme disease with the use of recombinant *B burgdorferi* lipidated outer surface protein as the antigen.[187] LYMErix (GlaxoSmithKline, Philadelphia, Pa) was licensed by the Food and Drug Administration in 1998 for use in patients aged 15 to 70 years old.[224] However, the vaccine was removed from commercial use in the United States in 2002 owing to insufficient demand.[225]

CHILOPODA AND DIPLOPODA

Centipedes are distinguished from millipedes in that the former have one pair of legs per body

segment and the latter have two pairs per body segment.[226] Centipedes are nocturnal carnivores that may produce painful bites. The *Scolopendra* species, found throughout the western United States, may attack when its habitat is disturbed.[227] In addition to severe pain and erythema, localized sweating, edema, secondary infection, and ulceration may be seen.[47,228] Treatment consists of analgesia, including opiates if necessary, and antihistamines.[229,230]

Millipedes are generally harmless vegetarians that do not bite. However, when disturbed or threatened, they may emit a toxic substance from repugnatorial glands on either side of each segment.[47] This fluid may produce burning and blistering, but severe reactions are seen mainly in tropical species. The oily, viscous material causes a brownish discoloration of the skin that may persist for months.[231,232] In one case, mahogany discoloration of a child's toes was misdiagnosed as gangrene.[231] Other cases have been mistaken for thermal injuries.[233] Some millipedes are capable of spraying noxious secretions.[234] This occurrence can result in various eye lesions, including periorbital discoloration, periorbital edema, conjunctivitis, or keratitis.[235]

INSECTS (INSECTA)

Insects that bite are the Anoplura (lice), Diptera (flies, mosquitoes), Hemiptera (bedbugs, kissing bugs), and Siphonaptera (fleas). Insects that sting are members of the order Hymenoptera (ants, bees, wasps).

Lice and psocoptera

Blood-sucking lice have long been successful obligate parasites of humans.[47,236-241] Pediculosis can be divided into three conditions: pediculosis capitis (head lice), caused by *Pediculus humanus* var. *capitis;* pediculosis corporis (body lice), caused by *P humanus* var. *corporis;* and phthiriasis pubis (pubic lice), caused by *Phthirus pubis*.[162,242] Lice range from 1.5 to 4.5 mm in length, depending on the species, and the female may lay up to 300 eggs, or nits, in her 30-day life cycle. Lice pierce the skin every few hours to receive a blood meal but can live away from the host for about 2 days.[162]

No age or economic stratum is immune to *Pediculus humanus capitis,* although crowded conditions are associated with a higher prevalence. *P humanus capitis* is the most prevalent parasitic infection of children in the United States.[243] African Americans are almost never affected, owing to the physical structure of their hair.[162] In general, the only complaint is pruritus. The nits can easily be seen at the base of the hairs; careful inspection may reveal the adult louse.[28] Head lice can be transmitted by direct contact or via fomites such as combs, hats, and bedding.[47,244,245] Treatment is simple: a 1% permethrin cream rinse. The cream is lathered through the hair, left on for 10 minutes, and thoroughly rinsed out. A fine-tooth comb should be used to remove adherent nits. Permethrin-resistant *P humanus capitis* lice have been identified in the United States.[246] In cases of these lice, 0.5% malathion lotion has proven effective.[246] Head lice can transfer to pillowcases, which pose a reinfection risk and should be cleaned as part of management.[244]

Unlike *P humanus capitis,* the body louse, *P humanus corporis,* has become less common in the general population.[47] It hides in the seams of clothing and is not usually on the skin except when it is taking a blood meal. Nits of the body louse adhere to fibers in the seams of clothing. Pruritus may be the only symptom of *P humanus corporis* infestation in some patients. However, small red papules can be found under the arms and on the upper parts of the shoulders, the flank, and the neck in some cases. Chronic scratching may result in characteristic hemorrhagic puncta and linear excoriations found most often on the neck and upper portion of the shoulders. Maculae ceruleae, which appear as bluish brown hemosiderin-laden macules, can also be found with body louse infestation.[247] Maculae ceruleae represent intradermal hemorrhage at sites where the lice have fed.[247] The body louse serves as a vector for diseases such as epidemic typhus *(Rickettsia prowazekii),* trench fever *(Bartonella quintana),* and relapsing fever *(Borrelia recurrentis).*[47,162,247] This role becomes especially troublesome during periods of war or natural disaster when sanitation is poor. Homeless people and refugees are also threatened by these diseases, as their living conditions, which may include overcrowding and poor sanitation, promote infestation by body lice. *Bartonella quintana* has reemerged as an important pathogen among homeless populations in cities in the United States and Europe.[248] This pathogen, which is spread by *P humanus corporis,* is capable of causing trench fever, endocarditis, and in immunocompromised hosts, chronic bacteremia, bacillary angiomatosis, and chronic lymphadenopathy.[248] Treatment of body lice should be directed at eradication of lice from clothing and the home. Lice can be eliminated from clothing by laundering in hot water or drying at a high temperature.[247]

The crab or pubic louse, *Phthirus pubis,* is usually transmitted by sexual contact but may be transferred by clothing or infested hairs (Fig 8). [162] Pubic lice are not limited to the pubic region and may be found on other short hairs of the body, such as body hair, eyebrows, and hair at the scalp line.[47] When they are

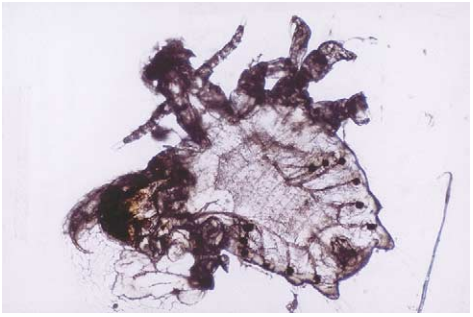

Fig 8. The crab or pubic louse, *Phthirus pubis*.

found on the eyelashes, the condition is termed *pediculosis ciliaris*.[249] Thirty days may elapse before pruritus begins. As with body louse infestation, pubic louse infestation can also cause maculae ceruleae.[247] Treatment is the same as that for pediculosis capitis, with the exception that pediculosis of the eyelashes should be treated with an occlusive ophthalmic ointment applied to the eyelid margins for 10 days.[249] Sexual contacts should be informed and undergo treatment as well.

Psocoptera are licelike insects that are ubiquitous in the environment. These insects feed on decaying matter, tree bark, stored grain, and even mildewed books, which has garnered them the name "book lice."[250] Human infestation by psocoptera can occur and is usually associated with an infestation of a pet habitat or a library.[250] Diagnosis may be achieved by means of microscopic examination of the louse. Treatment is directed at eliminating the environmental source of the psocoptera.[250]

Flies and mosquitoes

The order Diptera consists of the two-winged, or true, flies, and collectively, its members are responsible for the transmission of more diseases worldwide than any other arthropod order.[47,251] Malaria is transmitted by the *Anopheles* mosquito, while yellow and dengue fever are spread by the *Aedes* mosquito. *Culex* species transmit filarial diseases, as well as encephalitis viruses.[252] In the continental United States, female *Aedes* mosquitoes are responsible for most bites. Males are harmless, since they do not possess piercing mouthparts.

Pruritic wheals and papular lesions form in response to irritating salivary secretions that are injected to anticoagulate the blood. Depending on the sensitivity of the victim, mosquito bites may have an urticarial, vesicular, eczematoid, or granulomatous appearance.[47,253-257] Scents and bright colors, which are attractants for mosquitoes, are best avoided on warm summer nights.[258] The most effective repellent for all biting flies, including mosquitoes, is diethyltoluamide. In general, a product containing 10% to 30% diethyltoluamide is adequate protection for most outdoor activities.[170] For camping and other prolonged activities in wooded areas, long-acting diethyltoluamide formulations or traditional preparations that contain 40% to 50% diethyltoluamide are recommended.[170] Diethyltoluamide concentrations of less than 7% should be used on children.[186] Studies have shown the ability of the antihistamines cetirizine and ebastine, administered prophylactically as a single 10-mg dose, to decrease wheal formation and subsequent pruritus from mosquito bites.[254,258]

Mosquitoes are responsible for the recent outbreaks of West Nile virus in the United States. The first time West Nile virus was detected in the western hemisphere was during an outbreak of meningoencephalitis in the New York City area during 1999 that resulted in 7 deaths.[259] By 2002, West Nile virus had caused the largest arboviral meningoencephalitis outbreak ever recorded in North America.[260] West Nile virus is widely distributed in Africa, Asia, Europe, and Australia.[261,262] *Culex* mosquitoes serve as the principal maintenance and amplifying vectors of West Nile virus, which is maintained in a bird-mosquito-bird cycle, while *Aedes* and *Ochlerotatus* mosquitoes may also be bridging vectors, capable of spreading the virus to humans.[260-263] Because of similarities in hosts between West Nile virus and St. Louis encephalitis, and the wide distribution of St. Louis encephalitis in the western hemisphere, it is likely that West Nile virus will spread widely throughout North and South America.[260,261]

West Nile fever develops in approximately 20% of infected humans.[264] Other than the flulike illness seen with West Nile fever, an erythematous macular, papular, or morbilliform eruption affects the neck, trunk, and extremities of 20% of patients.[259,265] Fortunately, severe neurologic manifestations of West Nile fever, including meningitis and encephalitis, are rare. Advanced age is the most important risk factor for a fatal outcome with the disease.[260] Therapy for West Nile fever is generally supportive.

Other biting flies include midges, horse flies, deer flies, and black flies.[47,266,267] Black flies of the family Simulidae are vectors for onchocerciasis (African river blindness) and tularemia.[268] Cutaneous myiasis may be caused by the deposition of fly larvae into open wounds.[269-273] Other important flies worldwide are the sand fly *(Phlebotomus),* which is a vector for leishmanial parasites, and the tsetse fly *(Glossina),* which is a vector for trypanosomes that cause sleeping sickness.[50,252,274-277]

Diptera bites should be cleansed thoroughly with soap and water to avoid secondary infection. A short

course of topical steroids and systemic antihistamines may be used to control pruritus. Rare allergic reactions should be treated aggressively.

Bees, wasps, and ants

The order Hymenoptera includes bees, wasps, and ants.[47,278] Many have evolved poison glands, used by some for defense and by others for overcoming prey.[248] Hymenoptera stings are an important problem because of their high incidence and ability to produce fatal anaphylactic reactions.[279-297] Stings produce immediate burning and pain, followed by an intense, local, erythematous wheal. This "normal" reaction to hymenopteran stings usually subsides within several hours. However, more extensive local reactions can occur, such as swelling at the sting site greater than 6 inches in diameter and induration lasting as long as 7 days.[296,298] These large local reactions may be due to venom-specific IgE antibodies formed in sensitized persons. A cell-mediated immune response has also been implicated in these reactions.[296] Cool compresses, shake lotions (such as those containing calamine), mild analgesics, and oral antihistamines can be used to control pain and edema. Systemic steroids, such as prednisone, may be effective in cases of extensive, disabling local edema.[298]

Generalized systemic reactions to hymenopteran stings occur in 0.4% to 3% of patients. Anaphylaxis occurs in male victims about twice as often as in female victims, but this finding probably represents a difference in exposure rate rather than a true sex predilection.[281,298] Anaphylactic reactions to insect stings are not different from anaphylaxis due to other causes, and include generalized urticaria, angioedema, and bronchospasm.[47,285,287,288] Treatment for anaphylaxis includes subcutaneous epinephrine hydrochloride (0.5 mL of 1:1000 dilution) administered as soon as possible.[298] Oral or parenteral diphenhydramine may be added to control urticaria and pruritus. Oxygen may be necessary for laryngeal edema that leads to respiratory compromise. Acute anaphylaxis subsides within 20 minutes in most cases; when symptoms persist, systemic steroids should be given. Other than prior reaction, no clinical criteria exist to accurately predict those at risk for anaphylaxis from stings.[280,283] Intradermal skin puncture tests can be performed with very dilute quantities of venom.[296] Positive skin reactions will identify those patients with circulating, venom-specific IgE. People known to be at risk for hymenopteran anaphylaxis may undergo venom immunotherapy, which has been shown to be an effective prophylactic technique.[282] These individuals should always carry a preloaded epinephrine-filled syringe for emergency self-administration.

In any case of bee sting, one should carefully remove the stinger, if it is present. One should avoid using his or her fingers or tweezers, as they may squeeze additional venom into the victim. Ideally, the blade of a butter knife, or even a credit card, should be used to remove the stinger. The honeybee leaves a barbed ovipositor and paired venom sacs impaled in the victim. Attached musculature will continue to pump venom if the sac is not removed.[299] A honeybee dies after stinging, since it eviscerates itself by depositing its venom sac. Bumblebees and wasps do not have barbed stingers and therefore may sting repeatedly.[47]

Imported fire ants *(Solenopsis invicta),* originally from Brazil, are well established in the southeastern United States.[300-317] They were first noted in the port city of Mobile, Alabama, in the 1930s, having apparently been stowaways on a shipment of nursery stock and sod.[307] The ants now occupy more than 310 million acres in 12 states.[318] Because they attack in groups, they are particularly vicious. Should their anthill be disturbed, they will swarm and sting any passerby with the venomous apparatus at the base of their abdomens.[319] The stings begin as an intense inflammatory, wheal-and-flare reaction, which becomes a sterile pustule.[47,320] The epidermis covering the pustule sloughs off over a period of 48 to 72 hours.[321] Localized necrosis and scarring may result.[319] Sensitized persons may develop striking bullous reactions (Fig 9). The pustules tend to form in the shape of a ring, since the ants bite the flesh and then pivot and sting in a circular pattern.[47] Because of their tendency to swarm, and the fact that each ant may sting multiple times, up to 3,000 stings on one person are not uncommon.[319] There are also reports of attacks that occur indoors against residents of health care facilities.[322] Studies have shown, on the basis of allergic-specific IgE, that imported fire ants may be the arthropod posing the greatest risk for anaphylaxis to adults who live in endemic areas.[323] Conventional and rush immunotherapy performed with imported fire ant whole-body extract have proved effective and safe for the treatment of imported fire ant hypersensitivity.[324]

Bedbugs

Most hemiptera (or true bugs) feed on plants. Only the Cimicidae family, which includes bedbugs *(Cimex lectularius),* and the Reduviidae family, which includes kissing bugs (*Triatoma* species), commonly feed on humans.[47]

The common bedbug *(Cimex lectularius),* like its cousins, the Anoplura, or lice, has for centuries been

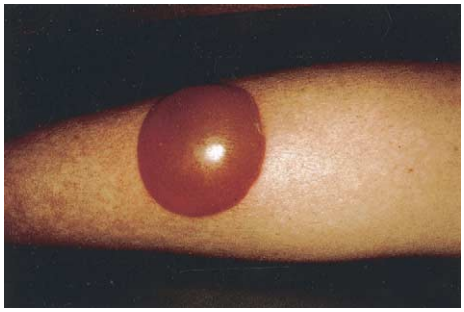

Fig 9. Bullous reaction to fire ant bite on arm. (Courtesy of Mark Lebwohl, MD.)

the source of much grief for mankind. Although economic progress and improved sanitation in developed countries have led to a steady decline in recent years, bedbugs continue to be a problem in tropical and subtropical regions of developing countries. The bedbug characteristically is very flat dorsoventrally and has an oval, broad body. The insect is 3 to 6 mm in length and wingless and, although incapable of flight or jumping, can run rapidly with its six legs when ambient temperatures are sufficiently warm.[325-327]

The bedbug is a nocturnal feeder, coming out of hiding when its victim has retired to bed. When not feeding, it stays hidden in the cracks and crevices of headboards and furniture, behind loose wallpaper, in picture frames, or any dark place that can accommodate its flattened body.[327] Bedbugs are spread chiefly in clothing and baggage of travelers and visitors, secondhand beds, and laundry.[28,325] The bites are painless, and these bloodsuckers are not usually noticed unless large numbers are present.[47] Unlike head and pubic lice, the bedbug does not remain on the body after feeding. After the 4 to 12 minutes necessary to complete a meal, the bedbug will return to its place of hiding.[327] Bites are usually multiple and may be arranged in an irregular, linear fashion. Bites that occur in a row of three are sometimes referred to as "breakfast, lunch, and dinner."[328] Reactions to the bites consist of wheals and papules,[29] with a small hemorrhagic punctum at the center.[327] Blood that oozes from the wounds may be seen as flecks on the bedsheets.[50] As already mentioned, sensitized persons may develop papular urticaria in response to bedbug bites (Fig 10). Bullous reactions are not uncommon.[327] Minimal symptomatic treatment and good hygiene to prevent pruritus and secondary infection are sufficient in most cases.[329] In the presence of a secondary infection, topical antiseptic lotion or antibiotic cream should be applied.[330]

Along with the roles of other blood-sucking arthropods in the transmission of infectious disease, that of the bedbug has gained increasing interest in recent years. Laboratory studies have shown that the bedbug is a good incubator for *Leishmania donovani, Leishmania tropica,* and *Rickettsia burnetii,* the causative agent of epidemic typhus. There is currently no convincing evidence that *Cimex* species act as vectors in the natural state; however, studies that show transmission of the hepatitis B virus from infected bedbugs to laboratory rabbits and guinea pigs raise the possibility of such transmission to human beings in endemic areas.[325,326,331,332]

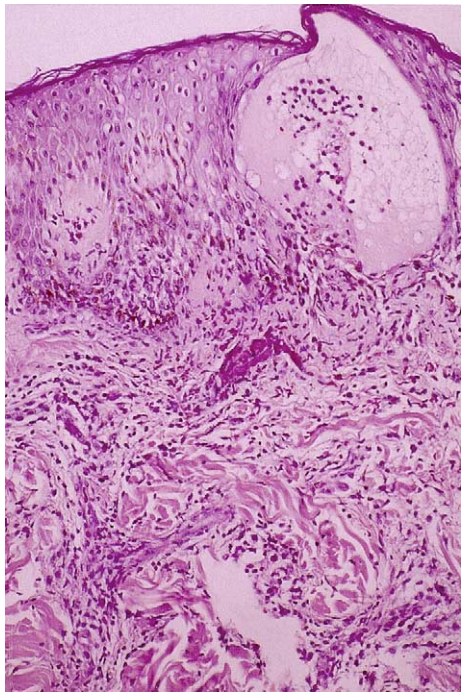

Fig 10. Center of arthropod bite shows subepidermal vesiculation, eosinophils between collagen bundles and perivascular eosinophils, and edema of the papillary dermis. Retained mouthparts are present. (Hematoxylin-eosin stain; original magnification ×100. Courtesy of W. Clark Lambert, MD, PhD.)

Reduviid bugs

The kissing or assassin bugs (*Triatoma* species) belong to the family Reduviidae of the order Hemiptera, or "true bugs."[248] Reduviidae are distinguished by a triangular shape on their backs, just behind the head, formed by the meeting of the membranous wings.[248] All are bloodsuckers and possess piercing mouthparts, complete with four pairs of stylets, to penetrate the skin of their victims.[332] Most of the 4,000 species of Reduviidae are found in the Americas, with a few species in Africa, Asia, and Europe.[47] Reduviidae are medically important because they spread *Trypanosoma cruzi,* the

causative agent of Chagas disease, which affects 15 to 20 million people in South and Central America. Kissing bugs earned their name for their predilection to bite on or near the lips.[333-339] Using their specialized probosci, kissing bugs take a blood meal, then characteristically turn around and defecate immediately after feeding. The trypanosomes are inoculated when the victim subsequently scratches the infected feces into the wound.[47] Within South and Central America, *T cruzi* is the leading cause of heart disease, accounting for one-quarter of all deaths in the 25- to 44-year age group.[333] *T cruzi* can also involve the esophagus, colon, and nervous system.[340]

Kissing bugs are found in the southwest United States, especially from Texas to California.[337] These large (3-cm diameter) winged insects are brown to black, with small stripes of red or orange in some species.[334] The bites of these nocturnal insects occur almost exclusively in rural areas, where the reduviid can find refuge in animal burrows and in the cracked walls of poorly constructed buildings.[333] Kissing bugs usually prey on rodents, but during periodic flights, they move toward the lights of desert homes.[319] The painless bite occurs only while the host is sleeping, since the blood meal takes ten or more minutes to complete.[334] Bites have been associated with papular, urticarial, and bullous reactions[319,334,335]; hemorrhagic wounds that resemble bites of the brown recluse spider have also been reported.[307,339] A small proportion of those bitten may develop generalized, acute allergic reactions. In these instances, the victim awakens with the sudden onset of anaphylactic signs and symptoms.[336-339]

Fleas

Fleas are exclusive bloodsuckers belonging to the insect order Siphonaptera.[25] They are small (about 3 mm long), wingless, and capable of jumping to a height of 7 inches.[47] Certain species, most notably the rat fleas *(Xenopsylla cheopis* and *X braziliensis),* transmit bubonic plague and typhus.[47,341-343] Other species are also capable of transmitting disease. A tropical species called *Tunga penetrans* (sand flea) is the etiologic agent of tungiasis, an infestation caused by penetration of the adult flea into the skin of human feet, usually in the web spaces, leading to pain, pruritus, bacterial infection, and sometimes, autoamputation of toes.[15,344] During the feeding process, a flea's specialized mouthparts pierce the host's skin to siphon blood, while saliva is secreted to prevent coagulation. Flea saliva is highly antigenic, capable of producing a pruritic, papular rash.[26,345] As mentioned previously, fleas are one of the most common causes of papular urticaria. Fleas must be eradicated from the environment to effectively eliminate the problem of bites. Topical corticosteroids and antipruritics, along with oral antihistamines, should be used to decrease the intense pruritus and to lessen the chance of secondary infection due to scratching.

OTHER ARTHROPODS

Moths and butterflies

The Lepidoptera order is medically important because of the irritant and allergenic properties of the hairs (setae) of caterpillars, moths, and butterflies.[47,346-350] In the spring of 1981, the northeastern part of the United States had a massive infestation of the gypsy moth caterpillar, *Lymantria dispar*. Thousands of patients with an unusual pruritic dermatitis presented with stinging, pruritic, erythematous papules often arranged in linear streaks.[349] Dyspnea and respiratory difficulties were also reported.[349] The cutaneous reactions were distributed on both covered and uncovered areas, especially on the upper and lower extremities. Almost all cases resolved within a few days to 2 weeks.[347,349]

An estimated 50 to 150 species within the Lepidoptera order are thought to produce lepidopterism, which describes the aggregate of medical effects caused by caterpillars, moths, and butterflies.[346] Theories regarding the pathophysiology of lepidopterism include mechanical irritation by pointed setae, cell-mediated hypersensitivity to the setae, and toxin injection through hollow setae.[346,348] No single hypothesis adequately explains the variety of reactions observed; in all likelihood, lepidopterism is caused by a combination of the aforementioned mechanisms. Warm spring weather is associated with an increase in the incidence of this dermatitis, as outdoor activities lead to contact with the free, wind-blown setae. House pets may possibly contribute to the incidence of lepidopterism by transporting the allergenic setae on their fur into the home or workplace.[346]

Treatment of the acute disease is largely symptomatic. Systemic antihistamines and topical preparations that contain menthol and camphor can be used to control pruritus. Moderate- to high-potency topical steroids may help alleviate itching in some cases, and systemic steroids should be reserved for severe reactions.[346,348] Setae can be removed from the skin by "stripping" with adhesive tape.[348]

Whereas pruritus is characteristic of caterpillar dermatitis, the hallmark of the sting of the asp or puss caterpillar *(Megalopyge opercularis)* is intense pain out of proportion to the size of the lesion produced.[47,319,351-353] A characteristic train-track pattern of purpura often appears at the site of the sting.[352] This caterpillar possesses hairs that pene-

trate the skin and inject venom, not unlike a hypodermic syringe.[319] The range of the puss caterpillar is from Maryland down the eastern seaboard to Florida and across the states bordering the Gulf of Mexico. Texas is considered to harbor the largest population of this caterpillar.[346,350] Intractable pain caused by the sting of the puss caterpillar may require oral or parenteral narcotic analgesics.[346,351-353]

Beetles

Since there are more than 250,000 species of beetles, Coleoptera is the largest order in the animal kingdom.[47] Blister beetle dermatosis is a distinctive, seasonal vesiculobullous skin disorder produced by more than 200 species of beetles distributed worldwide.[354-361] The Spanish fly, *Lytta vesicatoria,* is the most famous of the blister beetles and is found in southern Europe.[47,354] Several other blister beetle species are found in the central and southeastern areas of the United States.[8] Although these beetles neither bite nor sting, tense vesicles or bullae are produced when cantharidin, a chemical product of the beetles, is rubbed onto the skin after the insects are crushed.[47,362-364] Cantharidin is sometimes used in the treatment of common warts and molluscum contagiosum. Affected areas should be washed with soap and water, and bandaged until the blisters resolve.[8]

Several species of carpet beetles are found in the United States, the most common being the black carpet beetle, *Attagenus megatoma,*[45] and the common carpet beetle, *Anthrenus scrophulariae.*[365] Allergic papulovesicular dermatitis arises in response to the larvae of the beetles but not to the beetle itself.[47] Larvae of these species feed on wool, hide, and other organic materials.[45,223,322]

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Answers to CME examination

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Questions 1-30, Steen CJ, Carbonaro PA, Schwartz RA. J Am Acad Dermatol 2004;50:819-42.

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