Caterpillars and moths

Part I. Dermatologic manifestations of encounters with Lepidoptera

Eric W. Hossler, MD
Danville, Pennsylvania

Caterpillars are the larval forms of moths and butterflies and belong to the order Lepidoptera. Caterpillars, and occasionally moths, have evolved defense mechanisms, including irritating hairs, spines, venoms, and toxins that may cause human disease. The pathologic mechanisms underlying reactions to Lepidoptera are poorly understood. Lepidoptera are uncommonly recognized causes of localized stings, eczematous or papular dermatitis, and urticaria. Part I of this two-part series on caterpillars and moths reviews Lepidopteran life cycles, terminology, and the epidemiology of caterpillar and moth envenomation. It also reviews the known pathomechanisms of disease caused by Lepidopteran exposures and how they relate to diagnosis and management. Part II discusses the specific clinical patterns caused by Lepidopteran exposures, with particular emphasis on groups of caterpillars and moths that cause a similar pattern of disease. It also discusses current therapeutic options regarding each pattern of disease. (J Am Acad Dermatol 2010;62:1-10.)

Learning objectives: After completing this learning activity, participants should be able to appropriately use current terminology of adverse reactions to caterpillars and moths, understand the epidemiology of these reactions, and use our current understanding of the pathologic mechanisms of these reaction patterns to guide treatment.

Key words: dermatitis; insect bites and stings; Lepidoptera; moths; urticaria.

Caterpillars are the worm-like larval forms of Lepidoptera, the order of insects consisting of moths and butterflies. With an estimated 125,000 to 150,000 described species,[1] the Lepidoptera are one of the most prolific and diverse insect groups. In the United States alone there are approximately 13,000 known species, with 5000 found east of the Mississippi River.[2] Caterpillars and sometimes moths are an uncommon cause of disease in humans. Because these insects fall victim to many larger predators, they have developed irritating hairs, sharp spines, and various toxins to aid in their defense. Secondarily, these defenses occasionally can have impact on unwary humans. Myriad adverse reactions may result; these reactions have been historically lumped into broad categories that have little clinical value and often are used interchangeably. Although the pathogenesis of adverse reactions to Lepidoptera is poorly understood, a number of different mechanisms appear to be at work. Understanding these pathways may help guide appropriate therapy.

LIFE CYCLE AND TERMINOLOGY

Key points

- **Lepidoptera undergo four life stages: egg, caterpillar, pupa or chrysalis, and adult**
- **There has been confusion and overlap as to the terminology applied to adverse reactions to Lepidoptera**
- **Classifying reactions to Lepidoptera based on symptoms may be more useful than applying terms such as erucism and lepidopterism**

All Lepidoptera are holometabolous (ie, there are four distinct life stages). Moths and butterflies represent the reproductive phase of Lepidoptera. After mating, they lay eggs from which caterpillars hatch. Caterpillars are the growing phase of Lepidoptera and feed primarily on plants. As

From the Department of Dermatology, Geisinger Medical Center, Danville.
Funding sources: None.
Conflicts of interest: The authors, editors, and peer reviewers have no relevant financial relationships.
Reprint requests: Eric W. Hossler, MD, Department of Dermatology, Geisinger Medical Center, 115 Woodbine Ln, Danville, PA 17822. E-mail: ewhossler@geisinger.edu.
0190-9622/$36.00

doi:10.1016/j.jaad.2009.08.060

caterpillars grow, they periodically outgrow their skin, which must be molted. The time between molts is called an instar. At the end of the growing phase, caterpillars enter a dormant phase called a pupa or chrysalis. Inside the pupa or chrysalis, the moth or butterfly develops and eventually hatches, completing the life cycle.[1,2]

There is significant confusion as to the terminology referring to adverse events from contact with Lepidoptera. Erucism has been defined as either any reaction from caterpillars[3,4] or any reaction limited to the skin from caterpillars or moths.[5] Lepidopterism can mean any reaction to caterpillars or moths,[4,6,7] refer only to reactions from contact with scales or hairs from adult moths or butterflies,[5] or refer only to cases with systemic signs and symptoms, with or without cutaneous findings, resulting from contact with any lepidopteran source.[8,9] The word "erucism" derives from the Latin *eruca*, meaning caterpillar,[10] while "lepidopterism" stems from the Greek words *lepis*, meaning scale or flake, and *pteron*, meaning wing.[11] Strictly speaking, erucism should refer to any reaction from caterpillars and lepidopterism to reactions from moths or butterflies. Because reactions to both larval and adult Lepidoptera can cause a variety of either cutaneous and/or systemic symptoms, classifying reactions into erucism or lepidopterism is only of academic interest. I find it easier to avoid use of either term, and instead classify reactions based on predominant symptoms (eg, urticaria induced by contact with processionary caterpillars [genus *Thaumetopoea*]). In this manner, the clinician can continue to use familiar descriptive terms, such as urticarial or eczematous, and this approach will help both with diagnosis and treatment.

CAPSULE SUMMARY

- The order Lepidoptera comprises moths, butterflies, and their worm-like larvae, caterpillars.
- Caterpillars, and less commonly moths, may bear irritating hairs or spines that cause localized stings, eczematous eruptions, urticarial reactions, mucous membrane irritation, or, rarely, life-threatening hemorrhage.
- The pathophysiologic mechanisms of these reactions are poorly understood but may involve irritant reactions, hypersensitivity reactions, and toxic envenomation.

EPIDEMIOLOGY

Key points

- **Documentation of caterpillar and moth reactions is scarce in the medical literature, and likely underrepresents the true number of cases**
- **Epidemics of erucism and lepidopterism are facilitated by natural abundance, introduction of species into unnatural habitats, and, in some species, wind dispersion of larvae or setae**
- **Artificial illumination combined with natural abundance may congregate offensive species of moths, such as *Hylesia* and *Euproctis***
- **A large proportion of caterpillar reactions are reported in children**

Despite the diversity and nearly worldwide distribution of Lepidoptera, there are few species with clear documentation of adverse reactions in humans. Reasons for this are manifold and may include general medical disinterest, predominantly mild and self-limited reactions from Lepidoptera, difficulty in the accurate identification of offending species, and the occurrence of cases in tropical areas where medical reporting is either more difficult or less prioritized.[12] The number of adverse lepidopteran exposures is difficult to quantify. No studies have been performed in a controlled setting. However, of 94,552 bites and stings annually reported by phone to poison control centers in the United States, only 2094 (2.2%) were reportedly related to caterpillar exposure.[13] Considering that most reactions are mild and self-limited, these numbers likely underestimate the true number of adverse reactions.

Human—Lepidoptera interactions are infrequent. Therefore, adverse events in humans typically occur in only one or a few exposed individuals. However, several species of Lepidoptera are prone to seasonal abundance, leading to increased exposure frequency and "epidemics" of cutaneous or systemic symptoms. This is well known in the northeast United States, where gypsy moth caterpillars (*Lymantria dispar*) defoliate large tracts of forest each summer. Epidemics of dermatitis from this caterpillar have been reported in Massachusetts, Connecticut, and Pennsylvania.[14-16] Outbreaks of the Douglas-fir tussock moth caterpillar (*Orgyia pseudotsugata*) in the Pacific Northwest have caused several epidemics of papular urticaria amongst loggers,[17,18] and more recently in a Boy Scout camp in New Mexico.[19] In Venezuela, *Hylesia* moths may be so prevalent that schools and shops are closed early, and farmers and fisherman are unable to work because of a fear of rash and incapacitating itch.[20] The following species are also known to periodically outbreak: puss caterpillars (*Megalopyge opercularis*),[21-23] buck moth caterpillars (*Hemileuca maia*),[24] range caterpillars (*H oliviae*),[25] several *Euproctis* species,[26-29] and several species of processionary caterpillars (*Thaumetopoea*).[30-32] Temporary reduction in natural parasites was blamed for the abundance of *Hylesia alinda* moths, which caused an epidemic of dermatitis in Cozumel, Mexico, in 1989.[33] Introduced species, such as the gypsy moth, gum leaf skeletonizer moth (*Uraba lugens*), and stinging nettle moth (*Darna pallivita*) may benefit from a lack of natural predators, facilitating overabundance.

An additional problem is that some offending species have the ability to disseminate themselves widely. Newly hatched gypsy moth caterpillars, which may be more allergenic than mature larvae, are capable of wind dispersal by means of a silken thread, a behavior called "ballooning."[15,34,35] First instar larvae of the closely related Douglas-fir tussock moth are also capable of airborne dissemination in this manner.[17,36]

Caterpillar setae of some species are easily detached from larvae and can be widely dispersed by winds, causing dermatitis or ophthalmia nodosa.[37] This phenomenon has been documented with the oak processionary caterpillar (*T processionea*),[30,32,38] pine processionary caterpillars (*T pityocampa*),[39] mistletoe browntail moth (*Euproctis edwardsi*),[40] *E flava*,[28] and *Hylesia*.[41] Garments hung on clotheslines may collect airborne setae and cause dermatitis when the clothes are worn.[28,42] Outbreaks may be massive: larval abundance, dry weather, and strong winds contributed to a 1972 outbreak in Shanghai, China, in which an estimated 500,000 cases of dermatitis were caused by airborne setae from the caterpillar of the Asian mulberry tussock moth (*E flava*).[28]

Although caterpillars cause the vast majority of adverse events from lepidopteran exposures, adult moths may also cause adverse reactions. When attracted to artificial lighting, the irritating setae from these moths may cause irritant or allergic reactions. The most well recognized moth reaction is Caripito itch, which is caused by setae from female moths of the genus *Hylesia*. Dinehart et al[41] reported that 34 of 35 crewman on an oil tanker were continuously affected with a pruritic eruption stemming from the setae of dead moths and moth parts aboard their ship that had been docked overnight in Caripito, Venezuela, 3 weeks earlier. Similarly, 54 of 55 crewman aboard an oil tanker docked at the port of Caripito were affected in the report by Zaias et al.[43] Another offensive moth species is *Euproctis bipunctapex*. In 1990, 141 inhabitants of a public housing estate in Singapore suffered from a papular urticarial eruption caused by these moths; they had been attracted to the high-rise's lighting.[44]

Caterpillar and moth exposures are reported more frequently in children. Of the cases of caterpillar exposure reported to US Poison Centers, between 51.6% and 57% occurred in persons 18 years of age or younger.[45,46] Other series report that between 24% and 30% of exposures occur in children who are less than 6 years old.[13,47] In addition to these reports, a number of papers have independently reported a disproportionate number of children affected because of contact with the following species: the gum leaf skeletonizer (*U lugens*),[48] buck moth (*H maia*),[24] white-stemmed gum moth (*Chelepteryx collesi*),[49] *Euproctis similis*,[50] *Lasiocampa quercus*,[50] *Hylesia metabus*,[51] *H alinda*,[33] and *Lonomia obliqua*.[52] An outbreak of dermatitis and respiratory distress in a German kindergarten was blamed on an infestation of oak processionary caterpillars (*T processionea*) in nearby oak trees.[30] The reasons for this pediatric predominance are unclear, but may be related to frequent outdoor activity and increased curiosity. Derraik[48] postulated that the bright coloration of some caterpillars, such as the gum leaf skeletonizer (*U lugens*), may be attractive to children, resulting in increased direct contact.[48] An alternative hypothesis is that caterpillar and moth exposures are not actually more common in children, but that a greater proportion of exposures are reported, perhaps due to parental concern.

PATHOGENESIS

Key points

- **Some caterpillars bear setae and/or spines that may be directly irritating or possess venoms or toxins**
- **Although most moths are harmless, female *Hylesia* moths bear hollow spines**
- **Histamine has been extracted from several species and may play a role in human reactions**
- **Browntail moth (*Euproctis chrysorrhea*) caterpillar extracts have shown a wide variety of enzymatic properties**
- **Patch testing to caterpillar setae has shown an immediate hypersensitivity reaction, delayed-type hypersensitivity, or both**
- **Processionary caterpillars (genus *Thaumetopoea*) cause primarily a type I hypersensitivity reaction**

Fig 1. Close view of setae from a gypsy moth caterpillar (*Lymantria dispar*).

- ***Lonomia* caterpillars produce protein toxins that cause consumptive coagulopathy and fibrinolysis**
- **Ophthalmia nodosa may involve an immediate toxic response, followed by a foreign body granulomatous reaction**
- **Dendrolimiasis and pararamose both involve granulomatous inflammation involving joints**

Almost all exposures to toxic Lepidoptera or their products are caused by either (1) direct contact with allergenic or irritating Lepidoptera parts, such as hairs or scales, or (2) stinging spines that may contain venoms. Most reactions are from accidental exposure; however, occupational exposure may occur in persons who rear or work with Lepidoptera,[7,53] and cases of dermatitis from commercial silkworm (*Bombyx mori*) cocoons and textiles made from silk have been reported. These occupational exposures have been documented as eczematous dermatitis[54] and contact urticaria.[55] The allergen in raw silk is unknown.[56] Even more uncommon are moths that intentionally bite humans and feed on blood or tears.[3,57]

Spines and setae

Caterpillars have developed an immense array of cutaneous appendages designed to repel would-be attackers or predators. One type of appendage is the hair-like seta, arising singly or in large bunches from

Fig 2. Close view of spines from the saddleback caterpillar (*Acharia stimulea*).

the integument of the caterpillar (Fig 1). Spines are more robust multicellular processes that are contiguous with the integument (Fig 2).[1,3,58,59] Spines are relatively fixed, and cause adverse reactions only when the insect comes in direct contact with human skin. In contrast, caterpillar setae may be detachable and easily rubbed off, even becoming airborne in some instances, and can be incorporated into the structure of the cocoon, ostensibly for pupal protection.[3,59] Female moths of the genus *Hylesia* transfer setae from their abdomen onto their egg mass, which may provide protection from ants or larger predators.[60] Contact with setae from *Hylesia* cocoons, egg masses, or other fomites may cause adverse reaction even without direct contact with the caterpillar. Setae from the oak processionary caterpillar (*T processionea*) are environmentally stable for at least 1 year, causing symptoms long after caterpillars would normally be found.[32]

Spines and setae come in myriad forms; Mullen[3] described and illustrated seven types of setae and four types of spines of medical importance. Both setae and spines may cause mechanical irritation or contain substances that possess histamine or other irritating substances, trigger the release of histamine, or have other enzymatic actions.[3,61,62] Some spines and setae do not cause mechanical irritation and symptoms appear attributable only to venoms or toxins. One author found that setae of various caterpillars (species not identified) had no direct irritating properties when inserted into the skin after they were rinsed with water or alcohols, arguing that only the chemicals carried by the setae are able to instigate adverse reactions.[63]

Although adult moths are usually harmless, moths of the genus *Hylesia* are well known for the pruritic rash that follows exposure. Female *Hylesia* moths bear hollow-tipped spines attached to gland-like cells on the abdomen (Fig 3). Moths of the African genus *Anaphe* bear similar spines[64] and have been reported to cause dermatitis similar to *Hylesia*.[3,60,65]

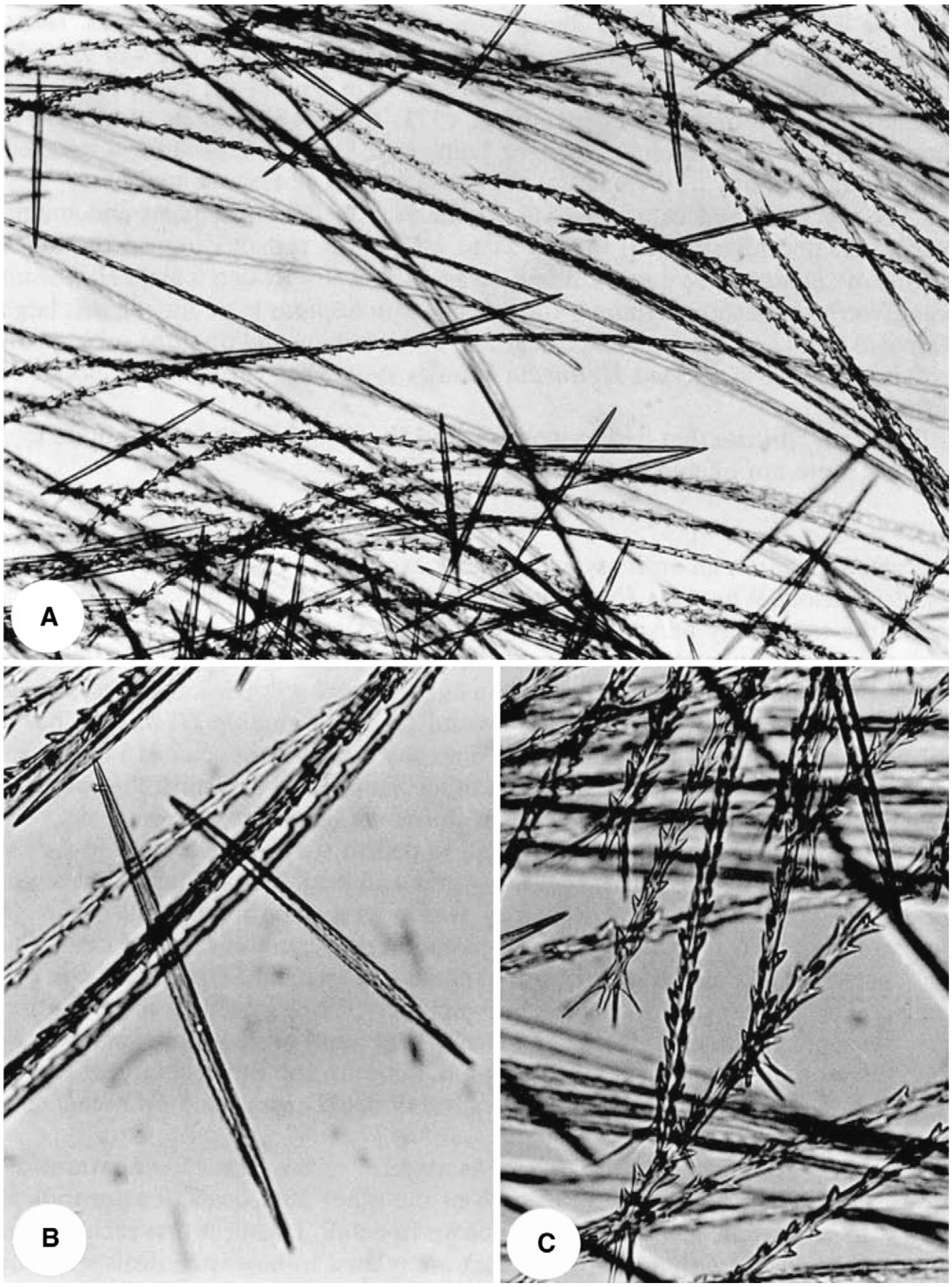

Fig 3. Spines from abdomen of female *Hylesia lineata*. **A**, Abdominal hairs (scales) from a female *H lineata*. A mix of these hairs forms the felt around the egg mass. **B**, Short urticating hairs (scales). Note barbs on lower ends. **C**, Modified felt-forming ends and barbs of long abdominal hairs (scales). (Reprinted with permission from Janzen DH. Natural history of *Hylesia lineata* in Santa Rosa National Park, Costa Rica. J Kansas Entomol Soc 1984;57:490-514.)

Euproctis bipunctapex[44] and *E flava*[28,29,66] moths may also cause dermatitis. Unlike *Hylesia*, *Euproctis* moths do not bear their own setae; instead, the caterpillar incorporates its setae into the cocoon when it pupates, and the moth picks up setae from the cocoon as it emerges.[7,44,50] Rarely, tibial spurs on larger moths can be strong enough to penetrate human skin and cause localized stings, dermatitis, or urticaria.[64,67] Finally, adult moths of the genus *Calyptra* have a stiff, barbed proboscis that can be used to penetrate intact mammalian skin in order to feed on blood.[3,57,68]

Chemical toxins and irritants

Considering the sheer number of species of Lepidoptera, it is not surprising that the chemical makeup of toxins and irritants is so diverse. Histamine may play a role in the symptoms of many species, and it has been isolated in setae from caterpillars of the genus *Dirphia*,[69] setae of the gypsy moth (*L dispar*),[70] whole caterpillars of the browntail moth (*Euproctis chrysorrhea*) and the Japanese tea tussock moth (*E pseudoconspersa*),[71-73] and the venom of the gum leaf skeletonizer (*U lugens*).[59] A histamine-like substance was found in the hairs of *Spilosoma lutea*.[74] One group found histamine in hairs from *Hylesia* moths[75] and found that intradermal injections of *Hylesia* moth extract cause wheals that were abated by the administration of diphenhydramine but not indomethacin.[75] However, others have failed to demonstrate histamine in setae from at least one *Hylesia* species (*H metabus*).[76,77]

Other chemicals isolated from Lepidoptera include acetylcholine, found in caterpillar setae, moths, and eggs of the great tiger moth (*Arctia caja*).[74,78] Formic acid, typically found in ants, has been found in the secretions of several Notodontid caterpillars. One Notodontid species, the variable oakleaf caterpillar (*Lochmaeus manteo*), has caused skin blistering after brief contact.[79] In a rat model, extracts from *Dirphia* caterpillar setae were able to cause pleuritis that was reduced by pretreatment with dexamethasone, rofecoxib, pyrilamine, and sodium diclofenac. The authors concluded that extracts caused tissue damage by inducing histamine, proinflammatory products of cyclooxygenase, and nitric oxide.[76]

More complex enzymatic compounds may play a role in the dermatitis caused by several species. Proteins with trypsin-like activity and vasodegenerative and fibrinolytic effects have been identified in *Hylesia* moths.[20,80] *Megalopyge urens* venom has direct hemolytic and proteolytic activity but lacked both histamine and acetylcholine.[81] *Euproctis* caterpillars have been shown to harbor a host of enzymes that serve as potential irritants. Aqueous solutions made from larval hairs of browntail moth caterpillars (*E chrysorrhea*) have trypsin- and chymotrypsin-like properties and fibrinolytic, proteolytic, hemolytic, and anticomplement activity.[61,72] These extracts were able to consume complement, initiate histamine release, and generate plasmin from plasminogen.[82] Serine proteases, including kallikrein, have been found in the spicule venoms of the browntail moth and the closely related *E subflava*.[83] Phospholipase A and esterase are also present in both of these species and have been theorized to be responsible for the cutaneous reactions.[72,82,84] Numerous studies have shown the ability of browntail moth setal extracts to cause spherocytosis.[82,85,86] The relevance of this last finding is unknown.

Two species of *Lonomia* caterpillars, *L obliqua* and *L achelous*, contain toxins that cause potentially fatal coagulation defects. Despite the clinical similarity of the hemorrhagic diathesis caused by envenomation, the toxin mechanisms for these two species appear to differ greatly. Caterpillars of *L achelous* contain several novel toxins ("Lonomins") that activate several hematologic pathways, including direct fibrinolysis, prothrombin activation, degradation of factor XIII, and factor Xa—like activity.[52,87,88] Conversely, caterpillars of *L obliqua* contain two procoagulant toxins: Losac (*Lonomia obliqua* Stuart-factor activator; an activator of factor X) and Lopap (*Lonomia obliqua* prothrombin activator protease; an activator of prothrombin).[52,89,90] In contrast to the direct fibrinolysis caused by Lonomins from *L achelous*, envenomation by *L obliqua* results in consumptive coagulopathy with secondary fibrinolysis.[88,89] Lopap may be the major toxin; infusion of Lopap into mice causes a similar hemorrhagic diathesis, and an antivenin directed against Lopap is effective in reversing the coagulation defects.[90] Despite the differences in venoms and venom actions, both caterpillars cause a similar clinical picture of hemorrhagic diathesis, fibrinolysis, and "unclottable" blood, resulting in potentially fatal cutaneous, mucosal, visceral, and intracranial bleeding, with or without renal failure. Recently, caterpillar venom from *Cerodirphia speciosa*, a related species of the same subfamily (Hemileucinae), was found to have two proteins similar to *Lonomia* venom.[91] Hemorrhage has not been reported after stings from this species.

Hypersensitivity reactions

In addition to mechanical irritation, venoms, and toxins, Lepidoptera are capable of causing hypersensitivity reactions in susceptible individuals. Some species cause immediate hypersensitivity reactions, others cause delayed-type hypersensitivity, and some appear capable of causing both. The following paragraphs summarize what is currently published in the literature. Understanding and prompt recognition of these reactions may help direct therapy.

There is evidence of a type 1 hypersensitivity to several species. Intradermal injections causing immediate wheal-and-flare reactions have been demonstrated with *Hylesia* moth and egg extracts and browntail moth (*E chrysorrhea*) and Japanese tea tussock moth (*E pseudoconspersa*) setal extracts. Preheating of the browntail moth extract reduced or eliminated these responses.[86] Scratch testing with gypsy moth caterpillars, cast caterpillar skins, and egg mass hairs caused wheal-and-flare reactions in 15 or 17 US Department of Agriculture Forest Service personnel who had been working with gypsy moths.[92] Prick testing with Douglas-fir tussock moth (*O pseudotsugata*) larvae, cocoons, shed larval hairs, adults, and egg masses showed a wheal and flare reaction in all participants who had previously reported reactions to caterpillar exposure.[93]

Prick testing with extracts from processionary caterpillars (genus *Thaumetopoea*), which are known to cause urticarial reactions, cause significantly higher rates of positive testing in individuals with previous exposure to caterpillars when compared to those without contact.[62,94-96] In addition, immunoglobulin E (to hair extracts) has been found in the sera of forest workers exposed to pine processionary caterpillars (*T pityocampa*)[39] and in almost all patients who report urticaria, angioedema, or bronchial asthma after exposure to this caterpillar.[96,97] It appears that last-instar larvae of pine processionary caterpillars are the most allergenic and that allergenicity increases with each molt.[98] Finally, a protein named "Thaumetopoein" has been isolated from *T pityocampa* that acts directly on mast cells, causing immunoglobulin E—independent degranulation.[99]

Patch testing with caterpillar or moth setae has shown the presence of an immediate hypersensitivity, delayed-type hypersensitivity, or both. Hellier and Warin[50] patch tested the forearms of healthy volunteers with pieces of three species of caterpillars: *Eriogaster lunestris*, *Spilosoma lubricipeda*, and *Euproctis similis*. All those tested to *Euproctis* had marked pruritus and erythema within 48 hours, and six of 10 subjects tested with *Eriogaster* or *Spilosoma* reacted within 48 hours, the rest having a more mild response after the patches were removed at 48 hours.[50] *Euproctis* caterpillars may cause both immediate and delayed-type hypersensitivity reactions. Patch testing with setae from browntail moth caterpillars (*E chrysorrhea*) revealed erythema and edema within 5 hours, often progressing to vesiculation at 72 hours.[86] Patch testing with setal extracts from the Japanese tea tussock moth (*E pseudoconspersa*) showed both immediate and delayed-type reactions.[73] Patch testing with gypsy moth (*L dispar*) caterpillar hairs caused delayed papulovesicular reactions in eight of eight patients with a history of dermatitis caused by gypsy moths, while only one of 11 healthy controls reacted.[100] Patch tests using Douglas-fir tussock moth (*O pseudotsugata*) larvae, cocoons, shed larval hairs, adults, and egg masses showed primary irritant reaction with erythema occurring within 45 minutes of application and vesiculation at 24 hours.[93] Closed patch testing using female *Hylesia* moths or egg masses caused erythema beyond the patch test site within 15 minutes and vesiculation within hours.[77] Taken together, this information lends credence to the theory that more than one mechanism of hypersensitivity may be at work, and that the cutaneous response may vary between individuals as well as species of Lepidoptera.

Other reactions

The mechanisms of ophthalmia nodosa are poorly understood. Both barbed and unbarbed hairs[101] cause immediate unilateral chemosis, which can progress to liquefactive necrosis and hypopyon acutely, and later can develop into a granulomatous reaction. Caterpillar hairs are frequently demonstrated within these granulomas,[102-104] suggesting a foreign body response. In many cases, however, the setae are never removed and the foreign hairs appear to be tolerated.[102,103,105]

Dendrolimiasis and pararamose (caused by exposure to *Dendrolimus* and *Premolis semirufa* caterpillars, respectively) are similar reactions that are both characterized by prominent arthritis in association with pruritic dermatitis. The mechanisms of these reactions are poorly understood, but both processes involve granuloma formation, often with bristle fragments embedded in periosteum, synovial membrane, or articular cartilage.[106-108] Dias and de Azevedo[108] found that setae from *P semirufa* were able to penetrate down to mouse perichondria, periosteum, tendon sheaths, and synovial bursae, causing granulomatous inflammation.[108] Huang[109] suggested that dendrolimiasis may be caused by allergic reaction, toxin envenomation, or secondary infection. Additional research is needed in this area.

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