What's Eating You? Caterpillars

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PRACTICE **POINTS**

- Lepidopterism describes adverse reactions caused by the stings, hypersensitivity reactions, and lonomism (a hemorrhagic diathesis) of caterpillars, moths, and butterflies.
- Caterpillars can induce an adverse reaction by injecting venom stored in their bristles, inducing a foreign-body reaction to embedded bristles, or a combination of these mechanisms.
- A thorough history, skin scrapings, relevant examination of affected body parts (such as slit-lamp examination, in the case of eyes), and laboratory testing should be conducted to narrow the wide differential diagnosis associated with lepidopterism.

Caterpillar envenomation is a worldwide problem, with manifestations ranging from dermatitis to iridocyclitis and a fatal hemorrhagic diathesis. This article focuses on the diagnosis and management of dermatoses related to caterpillars.

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Causes of Lepidopterism

Caterpillars are wormlike organisms that serve as the larval stage of moths and butterflies, which belong to the order Lepidoptera. There are almost 165,000 discovered species, with 13,000 found in the United States.[1,2] Roughly 150 species are known to have the potential to cause an adverse reaction in humans, with 50 of these in the United States.[1] *Lepidopterism* describes systemic and cutaneous reactions to moths, butterflies, and caterpillars; *erucism* describes strictly cutaneous reactions.[1]

Although the rate of lepidopterism is thought to be underreported because it often is self-limited and of a mild nature, a review found caterpillars to be the cause of roughly 2.2% of reported bites and stings annually.[2] Cases increase in number with seasonal increases in caterpillars, which vary by region and species. For example, the *Megalopyge opercularis* (southern flannel moth) caterpillar was noted to have 2 peaks in a Texas-based study: 12% of reported stings occurred in July; 59% from October through November.[3] In general, the likelihood of exposure increases during warmer months, and exposure is more common in people who work outdoors in a rural area or in a suburban area where there are many caterpillar-infested trees.[4]

Most cases of lepidopterism are caused by caterpillars, not by adult butterflies and moths, because the former have many tubular, or porous, hairlike structures called *setae* that are embedded in the integument. Setae were once thought to be connected to poison-secreting glandular cells, but current belief is that venomous caterpillars lack specialized gland cells and instead produce venom through secretory epithelial cells located above the integument.[1] Venom accumulates in the hemolymph and is stored in the setae or other types of bristles, such as scoli (wartlike bumps that bear setae) or spines.[5] With a large amount of chitin, bristles have a tendency to fracture and release venom upon contact.[1] It is thought that some species of caterpillars formulate venom by ingesting toxins or toxin precursors from plants; for example, the tiger moth (family Arctiidae) is known to produce venom containing biogenic amines, pyrrolizidine, alkaloids, and cardiac glycosides obtained through food sources.[5]

Even if a caterpillar does not produce venom, its setae might embed into skin or mucous membranes and cause an adverse irritant reaction.[1] Setae also might dislodge and be transported in the air to embed in objects—some remaining stable in the environment for longer than a year.[2] In contrast to setae, spines are permanently fixed

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into the integument; for that reason, only direct contact with the caterpillar can result in an adverse reaction. Although it is mostly caterpillars that contain setae and spines, certain species of moths also might contain these structures or might acquire them as they emerge from the cocoon, which often contains incorporated setae.[2]

Reactions in Humans

Lepidopterism encompasses 3 principal reactions in humans: sting reaction, hypersensitivity reaction, and lonomism (a hemorrhagic diathesis produced by *Lonomia* caterpillars). The type and severity of the reaction depends on (1) the species of caterpillar or moth and (2) the individual patient.[2] There are approximately 12 families of caterpillars, mainly of the moth variety, that can cause an adverse reaction in humans.[1] Tables 1 and 2 list examples of species that cause each type of reaction.[6]

Chemicals and toxins contained in the poison of setae and spines vary by species of caterpillar. Numerous kinds have been isolated from different venoms,[1,2] including several peptides, histamine, histamine-releasing substances, acetylcholine, phospholipase A, hyaluronidase, formic acid, proteins with trypsinlike activity, serine proteases such as kallikrein, and other enzymes with vasodegenerative and fibrinolytic properties

Stings: An Immediate Adverse Reaction—Depending on the venom, a sting might result in mild to severe burning pain, accompanied by welts, vesicles, and red papules or plaques.[2] Figure 1 demonstrates a particularly mild sting from a caterpillar of the family Automeris, examples of which are seen in Figures 2 and 3 and eFigure 1. Components of the venom determine the mechanism of the sting and the pain that accompanies it. For example, a recent study demonstrated that the venom of the *Latoia consocia* caterpillar induces pain through the ion-channel receptor known as transient receptor potential vanilloid 1, which integrates and sends painful stimuli from the peripheral nervous system to the central nervous system.[7] It is thought that a variety of ion channels are targets of the venom of caterpillars.

One of the most characteristic sting patterns is that of the caterpillar of family Megalopygidae (flannel moth) (eFigures 2 and 3). The stings of these caterpillars create a unique tram-track pattern of hemorrhagic macules or papules (Figure 4).[4] A study found that 90% of reported *M opercularis* envenomations consist primarily of cutaneous symptoms, with 84% of those symptoms being irritation or pain; 45% a puncture or wound; 29% erythema; and 15% edema.[3] Systemic findings can include headache, fever, adenopathy, nausea, vomiting, abdominal pain, and chest pain.[4] Symptoms normally are self-limited, though they can last minutes or hours.

Hypersensitivity Reaction—Studies demonstrate that the symptoms of this reaction are a mixture of type I hypersensitivity, type IV hypersensitivity, and a foreign-body response.[2] The specific hypersensitivity reaction depends on the venom and the exposed individual—most commonly including a combination of pruritic papules,

TABLE 1. Caterpillar Species Causing a Sting Reaction[6]

Species	Common Name	Location
Acharia stimulea	Saddleback caterpillar (eFigures 4 and 5)	Eastern North America, Mexico
Automeris io	Io moth (eFigure 1)	Southern Canada, Eastern United States to the Rocky Mountains, south to Costa Rica
Darna pallivitta	Stinging nettle caterpillar	Hawaii, Southeast Asia
Doratifera vulnerans, D oxleyi, D quadriguttata species	Cup moth	Australia
Hemileuca maia	Buck moth	Eastern United States
Hylesia species	*Palometa peluda* caterpillar	Mexico, Central America, South America
Hypolimnas misippus	Danaid eggfly	Southeast Asia, Africa, tropical Americas, Australia
Latoia (Parasa) lepida (Cramer)	Slug caterpillar	Japan
Megalopyge crispata	Flannel moth caterpillar	Southeastern United States, south to Central America
Megalopyge opercularis	Puss caterpillar (eFigure 2)	Southeastern United States, south to Central America
Nymphalis antiopa	Mourning cloak	North America, Eurasia
Thosea penthima	Billygoat plum stinging caterpillar	Australia
Uraba lugens	Gum leaf skeletonizer	Australia, New Zealand

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TABLE 2. Caterpillar Species Causing a Hypersensitivity Reaction[6]

Species	Common Name	Location
Acyphas leucomelas	None	Australia
Anaphe venata	None	Nigeria
Anthela nicothoe	None	Australia
Chelepteryx collesi	White-stemmed gum moth	Australia
Euproctis bipunctapex	None	Singapore
Euproctis chrysorrhea	Browntail moth	Europe, United States
Euproctis edwardsi	Mistletoe browntail moth	Australia
Euproctis flava	Asian mulberry tussock moth	Korea, Japan, China
Euproctis lutea (formerly *Porthesia lutea*)	Freshwater mangrove itchy caterpillar	Australia
Euproctis pseudoconspersa	Japanese tea tussock moth	Japan
Eutane terminalis	None	Australia
Hylesia continua	None	Mexico to Panama
Hylesia frigida	None	Mexico to Panama
Hylesia metabus	*Palometa peluda* moth	Argentina
Hylesia nigricans	None	Argentina
Leptocneria reducta	None	Australia
Lophocampa caryae	Hickory tussock moth	United States
Lymantria dispar	Gypsy moth	Europe, Eastern United States
Manuela replana	None	Australia
Ochrogaster lunifer	Australian bag-shelter moth	Australia
Orgyia anartoides	None	Australia
Orgyia leucostigma	White-marked tussock moth	Eastern United States, Canada
Orgyia pseudotsugata	Douglas-fir tussock moth	Pacific United States
Panacela lewinae	None	Australia
Spilosoma glatignyi	None	Australia

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urticarial wheals, flares, and dermatitis.[2] A reaction that is a result of direct contact with the caterpillar or moth will appear on exposed areas; however, because setae embed in linens and clothing, they might cause a reaction anywhere on the body. Although usually self-limited, a hypersensitivity reaction might develop within minutes and can last for days or weeks.

Stings and hypersensitivity reactions to caterpillars and moths tend to lead to a nonspecific histologic presentation characterized by epidermal edema and a superficial perivascular lymphocytic infiltrate, often with eosinophils.[6] After approximately 1 week, a foreign-body response to setae can lead to tuberculoid granulomas accompanied by neutrophils in the dermis and occasionally in subcutaneous tissues (Figures 5 and 6).[8] If setae have not yet been removed, they also might be visible in skin scrapings.

Additional complications can accompany the hypersensitivity reaction to setae or spines. Type I hypersensitivity reactions can lead to severe reactions on second contact due to previously sensitized IgE antibodies. Although the first reaction appears mild, second contact might result in angioedema, wheezing, dyspnea, or anaphylaxis, or a combination of these findings.[9] In addition, some patients who come in contact with *Dendrolimus* caterpillars might develop a condition known as dendrolimiasis, characterized by dermatitis in addition to arthritis or chondritis.[6] The arthritis is normally monoarticular and can result in complete destruction of the joint. Pararamose, a condition with a similar presentation, is caused by the Brazilian moth *Premolis semirufa.*[6]

Contact of setae or spines with mucous membranes or inhalation of setae also might result in edema, dysphagia, dyspnea, drooling, rhinitis, or conjunctivitis, or

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FIGURE 1. Sting from a caterpillar of the genus *Automeris*, characterized by mild papular urticaria and hyperhidrosis of the site, resolving in a few hours. Reproduced with permission of Eric W. Hossler, MD (Danville, Pennsylvania).

FIGURE 3. *Automeris io* (io moth) caterpillar, phenotypically unique from its co-genus member, *Automeris cecrops.* Reproduced with permission of Ronald P. Rapini, MD (Houston, Texas).

FIGURE 2. *Automeris cecrops* caterpillar of southern Arizona, where they are common. Reproduced with permission of Eric W. Hossler, MD (Danville, Pennsylvania).

FIGURE 4. Tram-track pattern of the sting of family Megalopygidae caterpillars. Reproduced with permission of Dirk Elston, MD (Charleston, South Carolina). This image is in the public domain.

a combination of these findings.[6] In addition, setae can embed in the eye and cause an inflammatory reaction—ophthalmia nodosa—most commonly caused by caterpillars of the pine processionary moth (*Thaumetopoea pityocampa*) and characterized by immediate chemosis, which can progress to liquefactive necrosis and hypopyon, later developing into a granulomatous foreign-body response.[2,10] The process is thought to be the result of a combination of the thaumetopoein toxin in the setae and an IgE-mediated response to other proteins.[10]

Due to their harpoon shape and forward-only motion, setae might migrate deeper, potentially even to the optic nerve.[11] Because migration might take years and the barbed shape of setae does not always allow removal, some patients require lifetime monitoring with slit-lamp examination. Chronic problems, such as cataracts and persistent posterior uveitis, have been reported.[10,11]

Lonomism—One of the most serious (though rarest) reactions to caterpillars is lonomism, a condition caused by the caterpillars of *Lonomia achelous* and *Lonomia obliqua* moths. These caterpillars have a unique combination of toxins filling their branched spines, which ultimately leads to the same outcome: a hemorrhagic diathesis.

The toxin of *L achelous* comprises several proteases that degrade fibrin, fibrinogen, and factor XIII while activating prothrombin. In contrast, *L obliqua* poison causes a hemorrhagic diathesis by promoting a consumptive coagulopathy through enzymes that activate factor X and prothrombin.

With initial contact with either of these *Lonomia* caterpillars, the patient experiences severe pain accompanied by systemic symptoms, including headache, nausea, and vomiting. Shortly afterward, symptoms of a hemorrhagic diathesis manifest, including bleeding gums, hematuria, bleeding from prior wounds, and epistaxis.[5] Serious complications of the hemorrhagic diathesis, such as hemorrhage of major organs, leads to death in 4% of patients.[5] A

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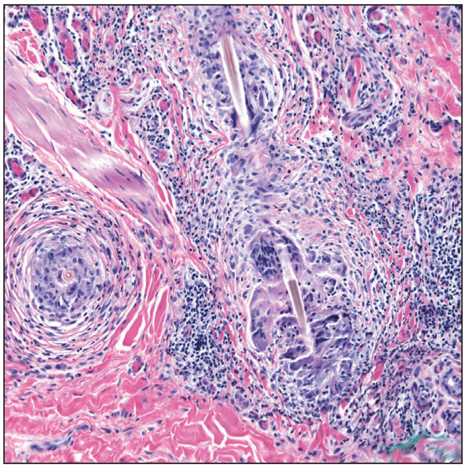

FIGURE 5. Foreign-body response to embedded caterpillar seta, characterized by granuloma formation (H&E, original magnification ×400). Reproduced with permission of Shawn E. Cowper, MD (New Haven, Connecticut).

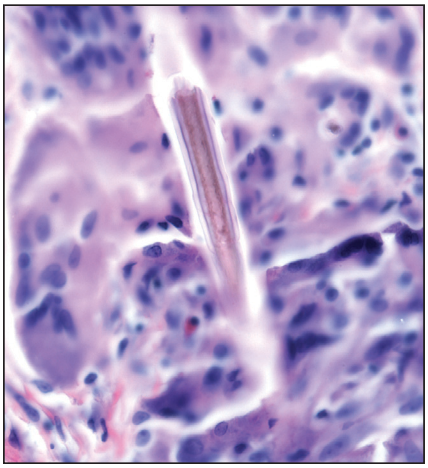

FIGURE 6. Caterpillar seta embedded in skin and surrounded by granuloma (H&E, original magnification ×600). Reproduced with permission of Shawn E. Cowper, MD (New Haven, Connecticut).

reported case of a patient whose *Lonomia* caterpillar sting went unrecognized until a week after the accident ended with progression to stage V chronic renal disease.[12]

Recent research has focused on the specific mechanism of injury caused by *Lonomia* species. A study found that the venom of *L obliqua* causes cytoskeleton rearrangement and migration in vascular smooth muscle cells (VSMCs) by inducing formation of reactive oxygen species through activation of nicotinamide adenine dinucleotide phosphate oxidase.[13] Thus, the venom directly contributes to the proinflammatory phenotype of endothelial cells seen following envenomation. The same study also demonstrated that elevated reactive oxygen species trigger extracellular signal-regulated kinase pathway activation in VSMCs, leading to cell proliferation, re-stenosis, and ischemia.[13] This finding was confirmed by another study,[14] which demonstrated an increase in Rac1, a signaling protein involved in the extracellular signal-regulated kinase pathway, in VSMCs upon exposure to *L obliqua* venom. These studies propose potential new targets for treatment to prevent vascular damage.

Reactions to Adult Organisms—Although it is more common for the caterpillar form of these organisms to cause an adverse reaction, the adult moth also might be capable of causing a similar reaction by retaining setae from the cocoon or by their own spines. The most notable example of this is female moths of the genus *Hylesia*, which possess spines attached to glands on the abdomen. The poison in these spines—a mixture of proteases and chitinase—causes a dermatitis known as Caripito itch—the name derived from a river port in Venezuela where this moth caused a memorable epidemic of moth-induced dermatitis.[7,15] Caripito itch is known for intense pruritus that most commonly lasts days or weeks, possibly longer than 1 year.

Diagnostic Difficulties

The challenge of diagnosing a caterpillar- or moth-induced reaction in humans arises from (1) the lack of clinical history (the caterpillar might not be seen at all by the patient or the examiner) and (2) the similarity of these reactions to those with more common triggers.

When setae remain embedded in the skin or mucous membranes, skin scrapings allow accelerated diagnosis. On a skin scraping prepared with 20% potassium hydroxide, setae appear as tapered and barbed hairlike structures, which allows them to be distinguished from other similar-appearing but differently shaped structures, such as glass fibers.

When setae do not remain embedded in the skin or when the cause of the reaction is due to spines, the physician is left with a nonspecific histologic picture and a large differential diagnosis to be narrowed down based on the history and occasionally the pattern of the skin lesion.

A challenge in sting diagnosis is differentiating a caterpillar or moth sting from that of another organism. In certain cases, such as those of the family Megalopygidae, specific patterns of stings might assist in making the diagnosis. Hypersensitivity reactions are associated with a wider differential diagnosis, including irritant or allergic dermatitis from other causes, scabies, eczema, lichen planus, lichen simplex chronicus, seborrheic dermatitis, and tinea corporis, to name a few.[6] Skin scrapings can be examined for other features, such as burrows in the case of scabies, to further narrow the differential.

Stings and hypersensitivity reactions lacking a proper history and associated with more severe systemic symptoms have caused misdiagnosis or led to a workup for the wrong condition; for example, the picture of abdominal pain, nausea, vomiting, tachycardia, leukocytosis, hypokalemia, and metabolic acidosis can simulate appendicitis.[16] Upon discovery of a puss caterpillar sting in

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a patient, her symptoms resolved after treatment with ondansetron, morphine, and intravenous fluids.[16]

In lonomism, the diagnosis must be established by laboratory measurement of the fibrinogen level, clotting factors, prothrombin time, and activated partial thromboplastin time.[4] The differential diagnosis associated with lonomism includes disseminated intravascular coagulation (DIC), snakebite, and a hereditary bleeding disorder.[4] The combination of laboratory tests and an extensive medical history allows a diagnosis. Absence of a personal or family history of bleeding excludes a diagnosis of hereditary bleeding disorder, whereas the absence of known causes of DIC or thrombocytopenia allows DIC to be excluded from the differential.

Treatment Options and Prevention

Treatment—The first step is to remove any embedded setae from the skin or mucous membranes. The stepwise recommendation is to remove any constricted clothing, detach setae with adhesive tape, wash with soap and water, and dry without touching the skin.[1] Any remaining setae can be removed with additional tape or forceps; setae tend to be fragile and are difficult to remove in their entirety.

Other than removal of the setae, skin reactions are treated symptomatically. Ice packs and isopropyl alcohol have been utilized to cool burning or stinging areas. Pain, pruritus, and inflammation have been alleviated with antihistamines and topical corticosteroids.[1] When pain is severe, oral codeine or local injection of anesthetic can be used. For severe and persistent skin lesions, a course of an oral glucocorticoid can be administered. Intramuscular triamcinolone acetonide has been shown to treat pain, dermatitis, and subcutaneous nodules otherwise refractory to treatment.[8]

Antivenin specific for *L obliqua* exists to treat lonomism and is therefore effective only when lonomism is caused by that species. Lonomism caused by *L achelous* is treated with cryoprecipitate, purified fibrinogen, and antifibrinolytic drugs, such as aprotinin.[6] Whole blood and fresh-frozen plasma have been noted to make hemorrhage worse when utilized to treat lonomism. Because the mechanism of action of the venom of *Lonomia* species is based, in part, on inducing a proinflammatory profile in endothelial cells, studies have demonstrated that inhibition of kallikrein might prevent vascular injury and thus prevent serious adverse effects, such as renal failure.[17]

Prevention—People should wear proper protective clothing when outdoors in potentially infested areas. Measures should be taken to ensure that linens and clothing are not left outside in areas where setae might be carried on the wind. Infestation control is necessary if the population of caterpillars reaches a high enough level.

Conclusion

Several species of caterpillars and moths cause adverse reactions in humans: stings, hypersensitivity reactions, and lonomism. Although most reactions are self-limited, some might have more serious effects, including organ failure and death. Mechanisms of injury vary by species of caterpillar, moth, and butterfly; current research is focused on further defining venom components and signaling pathways to isolate potential targets to aid in the diagnosis and treatment of lepidopterism.

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APPENDIX

eFIGURE1. Adult *Automeris io* (io moth), so-called because of markings resembling the letters "I" and "O" on the hindwing. Reproduced with permission of Ronald P. Rapini, MD (Houston, Texas).

eFIGURE 2. *Megalopyge opercularis* (southern flannel moth) caterpillar, a member of a family of caterpillars (Megalopygidae) known for causing a sting with a characteristic pattern. Reproduced with permission of Dirk Elston, MD (Charleston, South Carolina). This image is in the public domain.

eFIGURE 3. Caterpillar belonging to the Megalopygidae family, which is known for causing a sting with a characteristic pattern. Reproduced with permission of Ronald P. Rapini, MD (Houston, Texas).

eFIGURE 4. *Acharia stimulea* (saddleback caterpillar), known for causing a sting reaction. Reproduced with permission of Dirk Elston, MD (Charleston, South Carolina). This image is in the public domain.

eFIGURE 5. *Acharia stimulea* (saddleback caterpillar), known for causing a sting reaction. Reproduced with permission of Ronald P. Rapini, MD (Houston, Texas).

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