

# What's Eating You? Blister Beetles Revisited

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## PRACTICE POINTS

- Exposure to cantharidin presents initially with burning and tingling before progressing to bullae formation, sometimes in a linear fashion. Rupture of bullae and crust formation can occur.
- Washing of the exposed skin with soap and water may prevent development of blistering dermatitis.
- Clinical use of cantharidin is favorable in treating pediatric patients with common warts and molluscum contagiosum due to tolerability and painlessness of application.

Blister beetles are a group of insects that include the Meloidae, Oedemeridae, and Staphylinidae families. The most well-known family, Meloidae, has more than 200 species known for causing a blistering dermatitis in humans by emitting the substance cantharidin, which has been pharmacologically used as a vesicant and can cause deleterious effects if ingested. Most recently, blister beetles have been studied for their anticancer properties.

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## Classification

Blister beetles are both a scourge and the source of medical cantharidin (Figure 1). The term *blister beetle* refers to 3 families of the order Coleoptera: Meloidae, Oedemeridae, and Staphylinidae (Figure 2).

Meloidae is the most well-known family of blister beetles, with more than 200 species worldwide identified as a cause of blistering dermatitis.<sup>1</sup> The most notorious is *Lytta vesicatoria*, also known as the Spanish fly. Although some blister beetles are inconspicuous in appearance, most are brightly colored and easily spotted, making them attractive to small children.<sup>2</sup> They may be attracted to fluorescent lighting and commonly enter through open windows.<sup>3</sup> Blister beetles do not bite or sting; rather, they release

cantharidin via hemolymph, an oily yellow substance that is copiously expressed from the leg joints when disturbed by rubbing or pressing.<sup>1,3-5</sup> Blistering also is associated with exposure to the contents of crushed beetles, which is the source of pharmacologic cantharidin.<sup>2,4,6</sup>

Oedemeridae are the smallest and least known beetles within the Coleoptera family. They often are called false blister beetles, which is a misnomer. Oedemeridae beetles also produce cantharidin, similar to Meloidae beetles; however, because Oedemeridae beetles are smaller, the vesiculobullous eruptions also are less pronounced.<sup>1</sup>

A third well-known family of blister beetles is the Staphylinidae family. Rove beetles (genus *Paederus*) differ from the Meloidae and Oedemeridae families in that they produce the vesicant pederin rather than cantharidin. Pederin causes a more violent eruption called dermatitis linearis, which often is associated with intense urticaria prior to blistering.<sup>1</sup> Rove beetles are found in moist environments and tend to favor tropical and subtropical climates. They may emerge in large numbers after heavy rainfall.



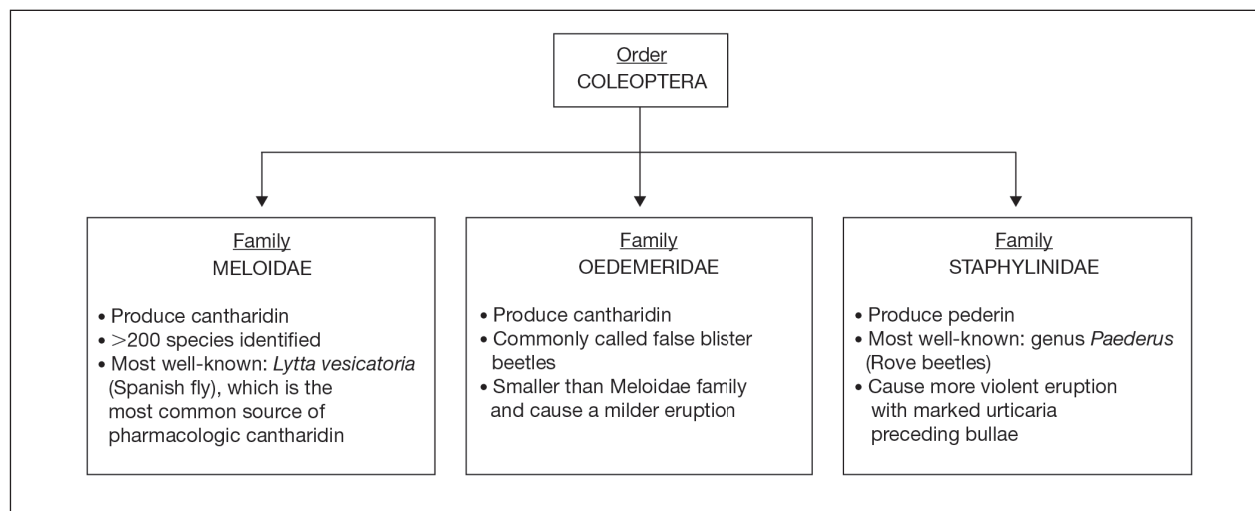
FIGURE 1. Blister beetles.

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Figure 1 is in the public domain.

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**FIGURE 2.** A simplified taxonomy of blister beetles.

### Clinical Presentation

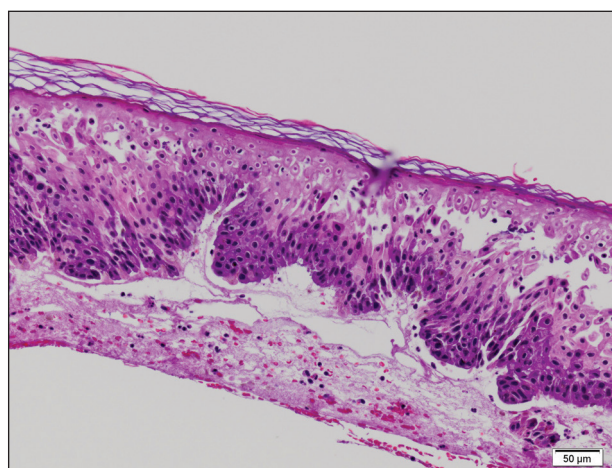
Blistering dermatitis—caused by exposure to cantharidin (families Meloidae and Oedemeridae) or pederin (genus *Paederus*)—begins as burning and tingling within minutes of exposure. Bullae later develop, often in a linear fashion, with subsequent bursting and crust formation.<sup>1,3</sup> Secondary infection can occur.<sup>5</sup> Exposure occurring on the elbows, knees, or mirroring skin folds results in lesions on opposing surfaces that come into contact, otherwise known as kissing lesions.<sup>1,3</sup> Acantholysis of supra-basal keratinocytes can be seen on histologic sections of blisters (Figure 3)<sup>1,7</sup> due to cantharidin activation of the serine/threonine protein phosphatases that cause detachment of tonofilaments from desmosomes.<sup>1,8</sup> Washing of exposed sites with soap or alcohol can potentially prevent development of blistering dermatitis; however, lesions usually heal without complication when treated with topical antibiotics.<sup>3</sup>

If blister beetles are ingested, they can cause poisoning characterized by abdominal pain and hematuria.<sup>1,3,9,10</sup> In fact, blister beetle ingestion by animals consuming baled hay is an important agricultural and economical implication. Several cases of fatal farm animal ingestion resulting in gastrointestinal erosion have been reported.<sup>4,6</sup>

### Medicinal Properties

Medicinal use of cantharidin has been recorded as early as the 19th century and is believed to have been part of ancient medicinal practices in China, Spain, South Africa, and pre-Columbian America for its vesicant, abortifacient, and supposed aphrodisiac properties.<sup>2,4,8</sup>

Toxicity from internal ingestion has been well documented.<sup>1,3,9,10</sup> The *Mylabris* and *Epicauta* genera of the family Meloidae, most commonly the Spanish fly, are used for modern extraction of cantharidin. Up to 5% of the dry weight of a blister beetle can be constituted by cantharidin.<sup>4</sup>



**FIGURE 3.** Typical histopathologic features of a dermatologic reaction to cantharidin (H&E, original magnification  $\times 200$ ). An intraepidermal vesicle demonstrating both acantholysis (as in pemphigus vulgaris) and superficial necrosis (as in a toxic response to topical agents). These features are typical for a reaction to cantharone, the active ingredient in blister beetle fluid.

Although its use has diminished due to limited availability, cantharidin is still used for treatment of common warts, periungual warts, and molluscum contagiosum. It is a favorable choice for treating pediatric patients because of the tolerability and painlessness of application. Due to its acantholytic properties, warts generally slough with the cantharidin-induced blister.<sup>11</sup>

In recent years, cantharidin has been studied for its anticancer properties. It has been shown to weaken cancer cell antioxidant properties by interfering with glutathione-related enzymes, thus inducing oxidative damage. Additionally, cantharidin is associated with decreased mitochondrial cytochrome C and increased cytosolic cytochrome C, an important signal for apoptosis.<sup>12</sup>

Furthermore, cantharidin recently was shown to increase expression of proapoptotic proteins and decrease expression of antiapoptotic proteins causing cell death in nasopharyngeal carcinoma, making it a potential anticancer treatment.<sup>13</sup>

## Conclusion

Blister beetles, long known for their production of vesicant agents, are both a cause of as well as a potential treatment of dermatologic disease. The blistering associated with exposure to a disturbed beetle generally is mild and heals without scarring if vital areas such as the eyelids are not affected.

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