

Human papillomavirus types 6 and 11 account for 90% of condyloma acuminata, while types 16 and 18 are responsible for 70% of cervical cancer. Cutaneous warts are considered benign and self-limiting because they often spontaneously regress within 1 to 2 years. They are, however, cosmetically disfiguring and can impact one's quality of life as well as personal relationships. Types 1, 2, and 3 HPV are commonly implicated in verruca vulgaris and plantar warts.

The exact mechanism of action of the vaccine in verruca vulgaris is unknown, though hypotheses include cross-protection and a systemic response. Common capsid epitopes and significant homology of L1 between various HPV types result in cross-protection of the vaccine against other types of HPV not targeted by the vaccine. Also, there is evidence that some verruca vulgaris are caused by the types targeted by the vaccine. Though verruca vulgaris is predominantly caused by HPV types 1 through 4, HPV typing of verruca vulgaris has found types 11, 16, and 18 in some cases.

The quadrivalent HPV vaccine has been used in 4 patients with chronic verruca vulgaris and has resulted in resolution of all warts in 100% of cases. There is no doubt that a larger study is required. Prospective randomized controlled trials with typing of the warts will provide a definitive answer as to the therapeutic efficacy of the vaccine in verruca vulgaris.

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Effects of Bed Bug Saliva on Human Skin

Bed bug infestations are increasing in scope, frequency, and geographic distribution worldwide, and bed bug bites should be included in the differential diagnosis in cases of unexplained or cryptic insect bites and anaphylactoid reactions.¹⁻⁴ Some patients apparently develop sensitivity to bed bug bites, while others do not.^{5,6} The nature, type, and location of allergens in bed bugs causing dermatologic reactions in humans have not been elucidated. Presumably, bed bug allergens are located in the saliva. With appropriate institutional review board approval, we tested that hypothesis, feeding bed bugs, both with and without in-

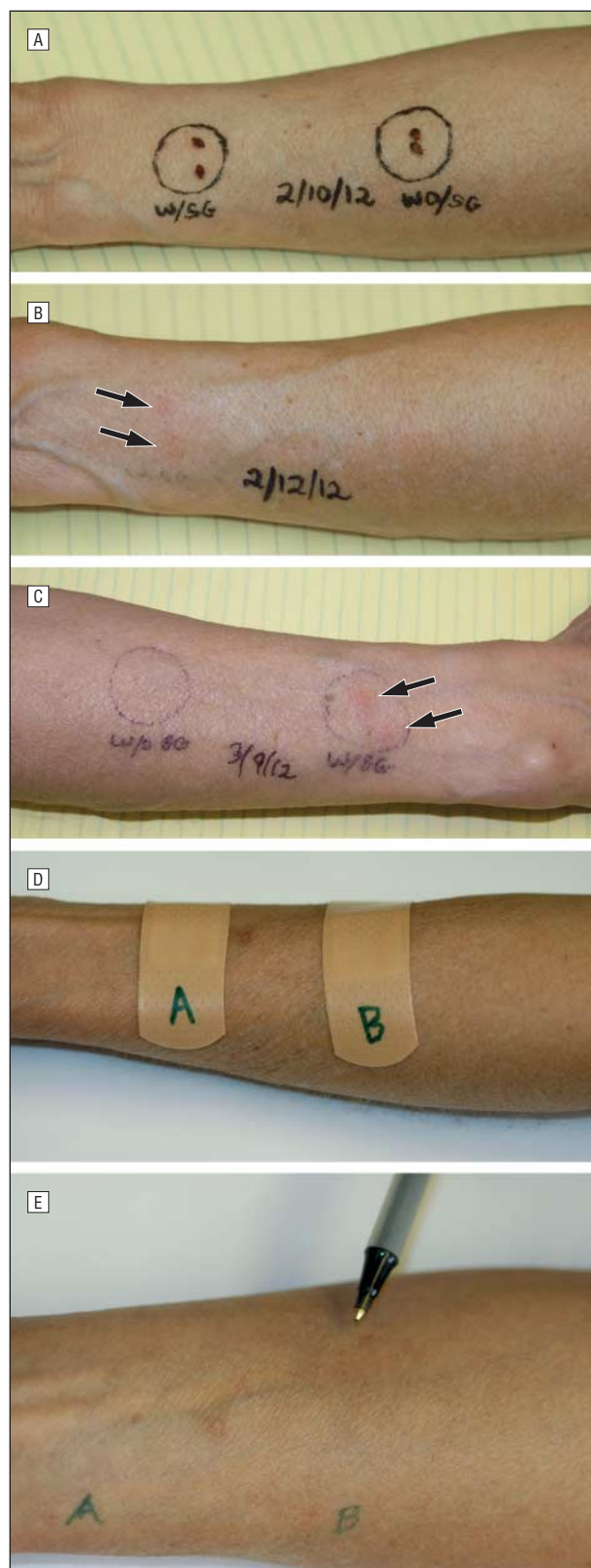


Figure. Clinical images of study volunteer's arms used for testing of bed bug bites. A, Left arm, bed bugs with and without salivary glands feeding. B, Left arm, 2 days post bite; arrows point to erythema at bite site of bed bugs with salivary glands intact. C, Right arm, 4 days post bite, arrows point to bite reaction to bed bugs with salivary glands intact. D, Direct application of bandages treated with phosphate-buffered saline (PBS) (bandage A) and bed bug saliva (bandage B). E, Arm with topically applied PBS and bed bug saliva after bandage removal; pen points to raised pruritic lesion from saliva 72 hours post application.

tact salivary glands, on a volunteer known to react to the bites.

Report of a Case. With the aid of a microscope and microdissecting tools, salivary glands were dissected out of 10 live adult bed bugs; 4 survived the process. Two of the most lively specimens were then placed on the arm of an adult female volunteer, with 2 intact bed bugs placed a few centimeters away as a control (**Figure, A**).

About a month later, this process was repeated (3 of 10 bed bugs survived dissection), and 2 bed bugs with salivary glands and 2 without were again placed on the volunteer's arm. In both cases, bed bugs with salivary glands produced itchy erythematous lesions within 2 to 5 days, while those without salivary glands attempted to feed, even piercing the skin, but failed to produce lesions (**Figure, B and C**). The volunteer reported that she could clearly feel the bed bugs without salivary glands "biting" her.

Finally, 2 months later, to determine if allergens are contained in bed bug saliva, we soaked one bandage with salivary extract derived from 50 adult bed bugs and another bandage with phosphate-buffered saline, as a control, and applied both to the volunteer's arm (**Figure, D**). In this case, the procedure was double-blinded—neither the researcher nor the volunteer knew which bandage contained which solution. At 36 hours post exposure, the volunteer reported intense itching at the site of bandage B (the one later revealed to contain bed bug salivary extract). By 72 hours, there was a raised, visible patch of discoloration with slight erythema at the B site (**Figure, E**).

Comment. This study demonstrates that allergens causing itching and skin lesions are most likely contained in the saliva of bed bugs. Interestingly, bed bugs without salivary glands attempted to feed but were unable to do so, indicating that saliva is necessary for the feeding process. Further, bed bug saliva was potent enough to cause pruritus and lesion development in a human volunteer by topical application alone, without breaking the skin.

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Livedo Reticularis and Skin Necrosis Due to Hyaluronic Acid Embolism

Report of a Case. A 63-year-old man with osteoarthritis received injections of hyaluronic acid (HA) into both knee joints from his rheumatologist. A month later he felt a sharp pain behind his right knee. Physical examination revealed livedo reticularis with 2 necrotic areas (**Figure 1**). All findings were normal for culture of skin biopsy specimen, Doppler ultrasonography (both legs), echocardiography, and blood analysis (blood cell count, biochemical assay, prothrombin time, fibrinogen level, activated partial thromboplastin time, activated coagulation time, antithrombin level, proteins C and S levels, plasminogen level, activated protein C resistance, presence of autoantibodies, lupus anticoagulant level, serum cryoglobulin levels, complement levels, and viral serologic measures). Skin biopsy specimens revealed dilated blood vessels in the reticular dermis and hypodermis, with intra-arterial foreign bodies composed of a basophilic amorphous material that tested negative under period acid-Schiff stain and positive under Alcian blue stain at a pH of 2.5 (**Figure 2**). Low-molecular-weight heparin was administered to prevent further embolic events. One month later, the lesions started to fade and were completely gone 6 months after the injection. At 1-year follow-up, the patient was free of lesions.

Comment. Injections of HA are used as dermal fillers for aesthetic purposes and as an intra-articular injections to treat osteoarthritis. The most frequently reported complications are associated with cosmetic use and include pain, bruising and swelling, migration, nodules, granuloma formation, and infections at the injection site. Vascular complications are less frequent than the rare hypersensitivity reactions and usually involve neovascularization with telangiectasia. Skin necrosis is a rare but severe complication (**Table** and eReferences; <http://www.jamaderm.com>) caused by interruption of the vascular supply by compression or obstruction of the vessels by the HA material or direct injury to the vessels.¹ While livedo reticularis is not often described as an adverse effect of cosmetic fillers, there is 1 report of livedo reticularis occurring after silicone injections on the buttocks.²

In the present case, HA occluded the deep vessels. The histopathologic features of this case are the same as those reported by Requena et al³ in their study of adverse reactions to injectable soft tissue fillers. In the previous reports of vascular complications, lesions and pain appeared within the first 24 hours (**Table**), but in our patient they appeared a month after the injection. Perhaps hyaluronic acid inside the joint escaped because of the rupture of a vessel due to microtrauma or endothelial activation.