

A likely explanation for the discrepancy between prior studies and that by Fabré et al is that the latter obtained the biopsy specimens of normal sun-exposed skin from the neck. This is in contradiction to the sun-exposed sites that usually undergo a biopsy in systemic lupus erythematosus, which are the extensor surface of the forearm or the deltoid area of the arm.^{2,5} It has been demonstrated that regional differences are present in the deposition of immunoglobulin in the skin of patients or animals with lupus erythematosus.^{6,7} Consequently, the high incidence of positive immunofluorescence in the study by Fabré et al was due to the site of skin selected for biopsy. If so, the implication of their study is not that direct immunofluorescence is of limited value in the evaluation of systemic lupus erythematosus but, rather, that when biopsy specimens are obtained for this purpose they should be taken from the recommended sites—the extensor surface of the forearm or the deltoid portion of the upper arm.^{6,7}

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In Reply.—We appreciate Bystry's comments and agree that a more appropriate site selection for immunofluorescence biopsy in patients in whom systemic lupus erythematosus is being considered is a less exposed area. Our study, however, was meant to address the rate of "false" positivity on an exposed surface such as the head or neck. We chose the lateral aspect of the neck to minimize the visibility of the scar from our punch biopsy. It is possible that the rate of false positivity would be even higher from facial skin. The most important issue that we addressed was the use of the immunofluorescence study to diagnose cutaneous lupus erythematosus.

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T-cell Subsets in Drug-Induced Toxic Epidermal Necrolysis

To the Editor.—We have read with great interest the immunohistochemical study by Miyauchi et al¹ demonstrating a predominance of CD8⁺ T lymphocytes in the epidermis of lesional skin in patients with toxic epidermal necrolysis. Using immunohistological techniques, we have analyzed the

lesional T-cell infiltrate in skin biopsy specimens from four individuals undergoing bullous drug reactions. Consistent with the data reported by Miyauchi et al, we have found that there is a predominance of CD8⁺ T cells in the epidermis in these reactions.

Additionally, six epidermal and dermal T-cell lines were derived from two patients with ampicillin-induced bullous exanthemas and from a patient allergic to penicillin who had a positive patch test reaction to penicilloyl and cephalothin. These cultured lesional T cells, which were expanded in vitro with interleukin-2, were found to be CD3⁺ (98% to 100%), CD4⁺ (0% to 14%), CD8⁺ (76% to 100%), and HLA-DR⁺ (78% to 100%) and were also found to express the α/β -chain configuration of the T-cell receptor. None of the T-cell lines exhibited suppressor activity when tested for inhibition of concanavalin A mitogenesis and pokeweed mitogen-induced Ig production. Cytotoxic activity against B-lymphoblastoid B cells was present in all T-cell lines when a bifunctional anti-CD3-anti-CD19 antibody was employed to cross-link the two cell types. Furthermore, the T-cell lines from positive patch test reactions to penicilloyl and cephalothin were found to proliferate in the presence of x-irradiated autologous, but not allogeneic, peripheral blood mononuclear cells. Antigen-specific proliferation was only seen in a dermal CD8⁺ T-cell line from an ampicillin-induced skin lesion. We have also observed preferential activation of CD8⁺ T-cells from blood samples taken from donors allergic to penicillin on in vitro stimulation with penicillin.²

In conclusion, our data support the findings of Miyauchi et al¹ that there is indeed a predominance of lesional epidermal CD8⁺ T cells in bullous drug reactions. In addition, isolated lesional epidermal and dermal T lymphocytes were found to mediate cytotoxicity but lacked suppressor activity. We agree with the hypothesis of Miyauchi et al that CD8⁺ cytotoxic T cells may contribute to the pathogenesis of blister formation by causing degeneration and necrosis of keratinocytes, since lymphocytic infiltrates are frequently seen in association with degenerated keratinocytes in these skin disorders. It is furthermore possible that in these reactions drugs are presented in such a way as to primarily activate CD8⁺ T lymphocytes.

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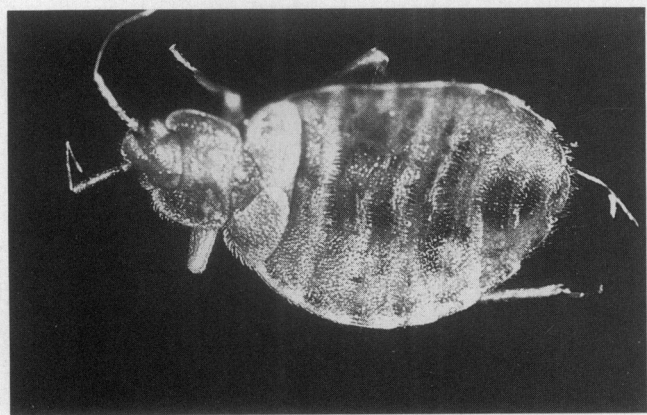
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Vignettes

Delayed Reaction to Bed Bug Bites

To the Editor.—The diagnosis of insect bite reactions is often difficult for the dermatologist, partly because of mimicry of other clinical conditions and because of the lack of history of recent contact with an appropriate arthropod. A history of contact is helpful, but a skin reaction is usually expected within 48 hours in genuine cases.

The timing and severity of reactions to repeated insect



The common bed bug, *Cimex laetularius*.

bites depends on previous exposure. Mellanby¹ showed that initial bites of *Aedes* mosquitoes produced little reaction, but, after repeated bites, a delayed reaction with an inflammatory weal occurs at about 24 hours. With further exposure, an immediate weal occurs that lasts for 2 hours and then disappears, to be replaced by the typical delayed reaction. With continuing exposure, subjects produce immediate reactions but no delayed response. Subjects who have had thousands of bites may eventually show no reaction at all.

This pattern of reaction has been recognized to occur with other biting insects, but, in some reports, it is obvious that bite reactions can be markedly delayed, as reported by Theodor.²

We describe two women in whom the time of exposure to bites (almost certainly bed bugs) was well defined but in whom skin reactions did not develop until 60 hours and 9 days later.

Report of Cases.—Two female, nonatopic patients arrived at a hotel in Paris, France, at 3 AM and slept in a shared bed for the rest of the night. The following night, they went to bed in the same room. Later, one woman awoke and noticed up to 50 flat, wingless beetle-like insects in the bed that, when crushed, had obviously been feeding on blood. Neither patient noticed any skin lesions or itching at this time. Although no insects were kept for identification, we assume that these were bed bugs (Figure). The next morning they complained, were given a different room, and no further bugs were seen.

Approximately 60 hours after disturbing the bugs, intensely itchy, papular lesions developed in one woman. On examination 4 days later, a florid, hemorrhagic, bullous rash with considerable edema was noted that affected the face, upper chest, and forearms with a few scattered lesions on the trunk and legs. Some lesions were in a linear distribution and showed evidence of central puncta. The patient was treated with reducing doses of prednisolone, with resolution over a period of 2 weeks.

Her companion, who had no rash at the time of initial examination, had a papular rash 9 days after exposure. A number of red, papular, nonitchy lesions on the face, neck, forearms, and thighs were noted, some of which had central puncta. No treatment was needed and the rash subsided.

Comment.—Experimental bed bug bites in one volunteer produced small red spots visible at 12 hours and small weals between 24 and 48 hours, which itched slightly at around 60 hours after the bugs had fed.³ On further exposure, a more marked reaction occurred with distinct weals and intense itching following a similar time course and subsiding by 72 hours. A reduction in reaction time from 7 days to 3 hours with repeated exposure has been reported.⁴

In patients who suffer from reactions to insect bites, it is often impossible to know when exposure and subsequent skin reaction occurred, but the two patients described here were

probably bitten on their first night in the hotel and were certainly bitten on the second night. This means that the first patient who reacted severely to the bites did not have the skin lesions develop until 60 (and probably 84) hours later, and her companion, who had a much milder reaction, had no skin lesions until 9 (and probably 10) days later. In the second case, the delay of 9 to 10 days before a reaction suggests that primary exposure was followed by the development of antibodies that reacted with antigen at the sites of the bites. Late-onset reactions are well described following insect stings⁵ but may be more common than is generally realized following insect bites.

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***Pseudomonas mesophilica* Cutaneous Infection in an Immunocompetent Patient**

To the Editor.—*Pseudomonas mesophilica* is a saprophyte organism that can be found on leaf surfaces and in the soil. It appears to infect immunocompromised hosts predominantly.^{1,2} Only once was human cutaneous infection by means of this organism reported with certainty. We report a case of *P. mesophilica* cutaneous infection in an immunocompetent patient.

Report of a Case.—A 28-year-old white woman visited in Ecuador from September 15 to December 15, 1989. During this period, she spent a lot of time in the countryside, where she often bathed in a river and suffered numerous skin excoriations. Around January 15, 1990, a small, subcutaneous nodule developed on the back of the first phalanx of the left index finger. During the ensuing 4 weeks, this nodule grew longer and ulcerated.

She was initially treated by her general physician with minocycline (100 mg twice a day) for 15 days, with no result.

She presented to the dermatology service 3 months later with a torpid, ulcerated lesion (diameter, 14 mm) whose floor was covered by a foul-smelling, grayish, purulent slough. This ulcer was surrounded by an inflammatory reaction (diameter, 20 mm) on the back of the first phalanx of the left index finger (Fig 1). The lesion was accompanied by three small, mobile, well-circumscribed, indolent, subcutaneous nodules of 5 mm in diameter, with a linear and sporotrichoid disposition, on the wrist and forearm. No satellite adenopathy was noted. The patient was healthy, and a review of systems was unremarkable.

Serologic studies for human immunodeficiency virus types 1 and 2, syphilis, histoplasmosis, blastomycosis, and coccidioidomycosis showed negative findings. Results from the usual laboratory analyses were normal.

Histopathologic examinations of biopsy specimens on the ulcerated border of the lesion and wrist nodule revealed an epithelioid, sometimes tuberculoid nodule aspect with the presence of a necrotic zone. The histopathologic picture first evoked a diagnosis of mycobacteriosis, especially *Sporotrichosis*, or an atypical mycobacterium.

Because of the clinical hypothesis of atypical mycobacteriosis or *Sporotrichosis* and the histopathologic results, the patient was