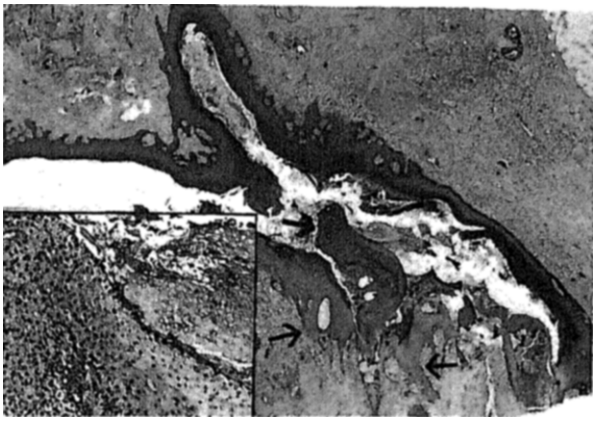

Fig. 2. Invagination of the epidermis *(arrows)* with extrusion of pilomatricoma cells and ghost cells (*bold arrow* and *inset*). (Hematoxylin-eosin stain; ×25; *inset*, ×150.)

ciated from the basaloid areas. A diagnosis of perforating pilomatricoma was made.

Discussion. Pilomatricomas are composed of basophilic, basaloid cells and ghost cells and, as such, are histologically distinctive. Ghost cells characterized by a central unstained area at the site of the disintegrated nucleus are claimed to be seen in no other tumor,[3] although focal ghost cells may be seen in any follicular adnexal tumor.[4] In the majority of cases, therefore, there is no histologic diagnostic difficulty.

Diagnostic difficulty may be experienced with perforating pilomatricoma. Tumor cells perforate the epidermis by the process of transepidermal elimination. This process was described by Mehregan[5] and comprises hyperplasia or invagination of the epidermis or follicular epithelium to surround and extrude material or tissue from the dermis. Knowledge of the existence and morphology of this variant of pilomatricoma is necessary since the basaloid and ghost cell components are frequently detached from one another. Either or both components may be overlooked, as occurred with the small initial incisional biopsy in this case, and the diagnosis will be missed. Additionally, if the perforating tissue is the basaloid component and the ghost cell component is subtle, the lesion may closely resemble basal cell carcinoma. This is especially true on frozen section examination.

Perforating pilomatricoma appears to be rare. Only three other individual case reports of perforating pilomatricoma are found in the literature.[6-8] Two occurred in children[6,7] while one appeared in a 52-year-old man.[8]

This case illustrates the existence of a rare clinical variant of pilomatricoma and stresses the necessity for adequate biopsy.

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Fenoprofen-induced toxic epidermal necrolysis

To the Editor: We report two cases of toxic epidermal necrolysis associated with the use of fenoprofen (Nalfon), a nonsteroidal anti-inflammatory agent. Erythema multiforme and toxic epidermal necrolysis have been reported in association with the use of other nonsteroidal anti-inflammatory drugs,[1,2] but to our knowledge there have been no reports of erythema multiforme or toxic epidermal necrolysis associated with fenoprofen.

Case reports

Case 1. A 69-year-old white woman suffered a hairline fracture of the right neck of the femur and was treated with fenoprofen, 600 mg three times daily. On the 16th day of fenoprofen therapy she developed fever, a sore throat and mouth, vesicular lip lesions, conjunctivitis, and a generalized erythematous, macular, pruritic eruption. Fenoprofen was discontinued and 2 days later she was admitted to the University of California, San Diego Medical Center. On admission she was confused and had a temperature of 39.5° C. An erosive stomatitis and cheilitis were present, as was a purulent conjunctivitis. There was a widespread, brightly erythematous,

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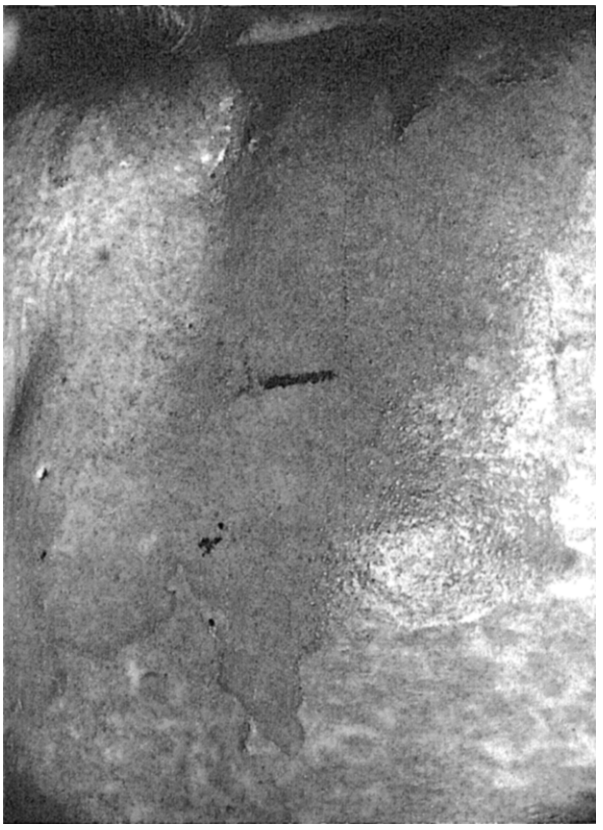

Fig. 1. Extensive epidermal sloughing of upper and mid portions of back with peripheral macular and target lesions.

edematous morbilliform eruption involving the face, neck, back, and proximal extremities. Extensive areas of epidermal sloughing were present on the center of her back, with intact flaccid bullae peripheral to the denuded areas (Fig. 1). Bullae and erosions were also present on the face, neck, chest, and lateral aspect of the thigh. Nikolsky's sign was positive.

The patient had no past history of severe drug reactions and had previously taken fenoprofen for 1 year. This therapy was discontinued approximately 1 year prior to admission. Other possible causes of toxic epidermal necrolysis were excluded by history and by appropriate laboratory studies.

Biopsy of an intact bulla was interpreted by the department dermatopathologist as being consistent with toxic epidermal necrolysis. It showed a subepidermal separation, necrosis of the basal cell layer, and a patchy lymphocytic infiltrate in the papillary dermis extending focally into the overlying necrotic epidermis. Full-thickness necrosis of the epidermis, acantholysis, and vasculitis were not evident. Biopsy for direct immunofluorescence taken from perilesional skin showed negative findings with the use of anti-IgG, anti-IgM, anti-IgA, and anti-C3 antibodies.

Case 2. A 74-year-old white man was prescribed fenoprofen, 600 mg four times daily, for osteoarthritis. On the

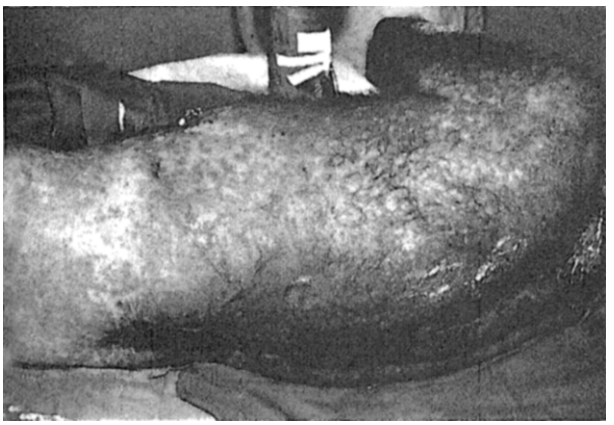

Fig. 2. Large areas of erythematous, denuded skin on upper and lower portions of back, some partially covered by detached epidermal sheets. Multiple erythematous macules with central pallor are visible on the buttocks, flanks, and upper part of the arm.

12th day of fenoprofen therapy he developed conjunctival crusting, crusting and bleeding of his lips, and pharyngitis. On the 14th day of fenoprofen therapy he developed an erythematous macular eruption of the trunk and back, conjunctival, labial, and oral erosions, and fever. He was initially admitted to a local community hospital, but because of progression of the macular eruption to cutaneous denudation, 2 days later he was transferred to the University of California, San Diego Medical Center.

On admission he was intermittently disoriented, with a temperature of 39.4° C. Prominent oral, labial, nasal, scrotal, and conjunctival erosions were present. Large flaccid bullae were present on his abdomen and large areas of denuded skin, partially covered by detached sheets of epidermis, were present on his back (Fig. 2). Nikolsky's sign was positive. Erythematous macules with central pallor were present on the palms, arms, anterior aspect of the abdomen, lower part of the back, and buttocks.

The patient had no previous history of drug allergies or drug reactions. He had previously taken fenoprofen without incident for approximately 4 months, 1 year prior to admission. A complete evaluation to exclude other causes of toxic epidermal necrolysis and Stevens-Johnson syndrome was negative.

Biopsy of an intact bulla was interpreted as being consistent with toxic epidermal necrolysis. It showed subepidermal separation, partial necrosis of the epidermis, and a moderately dense, patchy lymphocytic dermal infiltrate, interpreted as being consistent with toxic epidermal necrolysis. Biopsy for direct and indirect immunofluorescence, taken from perilesional skin, showed negative findings with the use of anti-IgG, IgM, IgA, and anti-C3 antibodies.

Comment. Toxic epidermal necrolysis is a relatively rare, fulminant, and potentially life-threatening gen-

eralized mucocutaneous disorder that most commonly occurs in association with the use of certain medications. Infections, leukemias, and lymphomas are also reported incitants.

The onset of our patients' skin eruptions on the 12th and 16th days of fenoprofen therapy and the absence of clinical or laboratory evidence of other known causes of erythema multiforme or toxic epidermal necrolysis suggest that fenoprofen was responsible for the cutaneous eruptions. There are few reports of adverse cutaneous reactions of any kind to fenoprofen in the literature.[1] Fenoprofen, ibuprofen, naproxen, and benoxaprofen are propionic acid derivatives. Toxic epidermal necrolysis, erythema multiforme, and erythema multiforme–like bullous eruptions have been reported with the use of ibuprofen, naproxen, and benoxaprofen, but not with fenoprofen. To our knowledge, these two patients are the first reports of toxic epidermal necrolysis or acute disseminated epidermal necrolysis type 2 secondary to fenoprofen.

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Management of eczema herpeticum

To the Editor: The letter by Muelleman et al entitled "Eczema Herpeticum Treated With Oral Acyclovir" (J AM ACAD DERMATOL 1986;15:716-7) raises some important points. It seems to us that a number of widely held assumptions about eczema herpeticum, several of which appear in this letter, may be incorrect. These include the view (1) that eczema herpeticum is uncommon, (2) that it is serious, with a high mortality, and (3) that antiviral therapy with acyclovir is always indicated.

We run a busy specialist pediatric dermatology service in two of London's major children's hospitals and see many hundreds of eczematous children each year. It has been our experience that eczema herpeticum occurs frequently in children with atopic eczema but that its occurrence is likely to go unrecognized both by parents and physicians. Our observations suggest that eczema herpeticum is usually mild and localized. The majority of these episodes resolve spontaneously without specific treatment and without threatening the child at all. It is unusual for the lesions to spread widely and for the child to be systemically unwell; more extensive eczema herpeticum usually occurs in the setting of severe atopic eczema, particularly in the more erythrodermic type of presentation.

The mortality rate for eczema herpeticum is undoubtedly low in relation to the total number of cases. Where the child is at risk, clearly it is right to use systemic acyclovir. A problem with acyclovir is that the child may die despite treatment if this is not started early during the course of the disease. We are aware of two children who died recently in London from fulminant eczema herpeticum; in both cases diagnosis was delayed and treatment with acyclovir, when it was eventually started, was completely without effect even though it was given intravenously and in adequate dosage. Some would argue that systemic acyclovir should be used in every case of eczema herpeticum, and this is widespread practice throughout the world. We are worried that the use of acyclovir could interfere with the normal development of immunity following primary infection with herpes simplex. It has been our impression that recurrences of eczema herpeticum are much more common in children treated with acyclovir; these occurrences often occur very rapidly after treatment is discontinued, as in the case described by Muelleman et al.

Our comments are based on observation and are therefore of limited value, but we feel that there should be clear criteria for deciding whether and how those with eczema herpeticum should be treated with acyclovir. In our view there are two important questions that should be asked before embarking on treatment: (1) is the number of lesions still increasing and (2) is the patient unwell? If the phase of extension of lesions is over, as it usually will be by about the fifth day, and if the patient is well, systemic treatment is probably unnecessary. It is unclear whether the resolution of eczema herpeticum in the patient described by Muelleman et al occurred any more rapidly than it would if the patient had not been treated. If the decision to treat is taken, then oral therapy is unjustified because this is associated with a longer delay in achieving adequate blood levels; high-dose intravenous therapy should be given with the use of a dose of 1.5 gm/m^2 per day.

In summary, we seek clearer thinking on the subject