Dermatitis herpetiformis is associated with diarrhea linked to gluten-sensitive enteropathy and produces tremendous pruritus in areas of papulovesicular rashing on extensor surfaces of the extremities. Histopathologic examination reveals neutrophilic microabcesses in dermal papillae and direct immunofluorescence within perilesional skin reveals granular IgA within these same dermal papillae.

Epidermolysis bullosa commonly presents in infants and in its most serious dystrophic forms is horribly scar-ring. Variants can display a wide variety of histopathologic features including dermal-epidermal blisters with modest underlying inflammation.

Drugs (Rx) can be associated with blistering photodermatitis. Tetracyclines, sulfonamides, hydrochlorothiazide, furosemide, diltiazem, psoralens, and fluoroquinolones are common causes of photodermatitis. Topical agents, such as psoralen from celery and lime, can cause phytophotodermatitis with blistering. Medium heat and liquid nitrogen are physical causes of dermal-epidermal blisters; a history will usually provide confirmation of these cases.

Linear IgA bullous dermatosis can be idiopathic or drug-induced and has a unique linear IgA staining pattern at the dermal-epidermal junction on direct immunofluorescence of perilesional skin. Clinically, lesions are mildly pruritic and can be arranged in a herpetiform or circinate pattern. Histology can look very similar to bullous pemphigoid and dermatitis herpetiformis but may reveal neutrophils aligned along the basement membrane.

Lichen planus has a rare bullous form where the Max-Joseph spaces above the dense band of lymphocytic inflammation in the upper dermis become coalescent and produces dermal-epidermal blisters. The typical purple, polygonal, planar papules of lichen planus are usually readily identifiable. Lichen sclerosis et atrophicus with its white porcelain plaques on genital areas or elsewhere can also produce dermal-epidermal blistering. A band of eosinophilic edema in the papillary dermis confirms this diagnosis. 🍊
Differential Diagnosis of Subepidermal Blistering Disorders: A Memorable Guide

From physical trauma to drugs to systemic disease, easily recall the causes of subepidermal blisters.

By Major Jeffrey J. Bidinger, MD and Robert T. Brodell, MD

Blistering is etiologically associated with a wide range of disorders from banal suction blisters to autoimmune diseases, such as bullous pemphigoid, which carry significant morbidity. Constructing a thorough differential diagnosis in any patient with blistering guides evaluation. An accurate diagnosis ensures proper treatment.

Bullous diseases are classified by the level of the blister within the skin. More superficial blisters within the epidermis generally do not lead to scarring. Clinical examination in these cases reveals the base of the blister is similar in color to normal skin. Subepidermal blisters often produce scarring. The base of the blister is clinically white or red since the basal layer and stratum malpighii, which contain pigment, are denuded. Visible evidence of a subepidermal blistering process should provoke a thorough history and physical examination in order to render a specific diagnosis.

The nature of the blisters and their duration, distribution, and arrangement must be obtained with emphasis on presence of pruritus, pain, or burning. Histopathologic examination and direct immunofluorescence are sometimes important methods to confirm a specific diagnosis. The mnemonic, SUBEPIDERMAL recalls the causes of subepidermal blistering.

A history of local exposure to negative pressures confirms suction blisters.

Lupus erythematosus is associated with 11 criteria developed by the American Rheumatological Association. Cutaneous signs include photosensitivity, butterfly rash, discoid lesions, mucous membrane ulcerations, and alopecia. In addition to dermal-epidermal blistering, histopathology demonstrates reduplication of the basal lamina, follicular plugging, a sparse lichenoid inflammatory infiltrate, and a lupus band on direct immunofluorescence.

Bullous pemphigoid shows widespread tense bullae that may be on an erythematosus or skin-colored base. Fixed urticarial lesions are also often present. Pruritus is severe. Histopathologic examination reveals an interstitial inflammatory infiltrate with numerous eosinophils beneath the dermal-epidermal blister and eosinophilic spongiosis. IgG and complement are present at the dermal-epidermal junction of perilesional skin on direct immunofluorescence.

Erythema multiforme is characterized by tender target lesions that can involve the palms and soles. A history of oral or genital herpes simplex or exposure to sulfUR drugs is commonly associated with recurrent erythema multiforme. Histopathologic examination reveals dyskeratosis, epidermal necrosis, and underlying sparse lichenoid inflammation.

Porphyria cutanea tarda is often associated with liver disease caused by hepatitis C or alcohol abuse. Blisters are typically localized to the backs of the hands or other sun-exposed surfaces and show little inflammation. Direct immunofluorescence will reveal IgG at the dermal-epidermal junction. Urinary porphyrin studies confirm this diagnosis. Pseudoporphyria associated with renal disease can show similar findings but negative urinary porphyrin studies. Hypertrichosis on the cheeks is also common.

Cicatricial pemphigoid is associated with blistering and scarring of mucous membranes. Ocular symptoms are prominent and include pain, burning, itching, and foreign body sensation. Histopathologic and direct immunofluorescence are indistinguishable from bullous pemphigoid.

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