

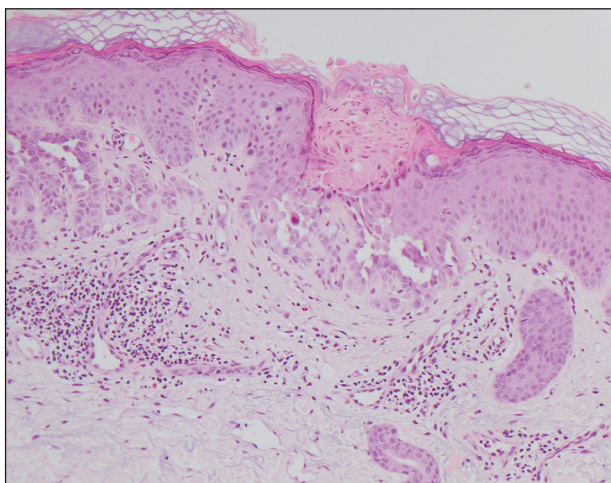
Pruritic Eruption on the Chest

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H&E, original magnification $\times 200$.

A 55-year-old man presented with small, erythematous, nonfollicular, pruritic papules on the mid chest.

THE BEST DIAGNOSIS IS:

- Darier disease
- Grover disease
- Hailey-Hailey disease
- pemphigus foliaceus
- pemphigus vulgaris

PLEASE TURN TO **PAGE 94** FOR THE DIAGNOSIS

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THE DIAGNOSIS: Grover Disease

Grover disease (also known as transient acantholytic dermatosis) was first described by Ralph W. Grover in 1970 as an idiopathic, acquired, monomorphic, papulovesicular eruption. Although originally characterized by solely transient acantholytic dermatosis, over time the term *Grover disease* has been expanded to include persistent acantholytic dermatoses. Grover disease chiefly affects white adults older than 40 years and is more prevalent in males than females. Cases generally are self-limited but correlate with age, as older adults are more likely to have prolonged eruptions.¹

Grover disease typically erupts with discrete, erythematous, edematous, acneiform, red-brown or flesh-colored papules, papulovesicles, or keratotic papules that primarily are seen on the trunk and anterior portion of the chest. As the rash spreads, it can erupt on the neck and thighs. The etiology of Grover disease is unknown, but many factors have been associated with the condition in a limited number of patients, including exposure to UV radiation, excessive heat or sweating, use of sulfadoxine-pyrimethamine and recombinant human IL-4, and infection with *Malassezia furfur* and *Demodex folliculorum*.¹ Grover disease also has been associated with other conditions such as asteatotic eczema, allergic contact dermatitis, and atopic dermatitis.²

Histologically, Grover disease (Figure 1) is an acantholytic process that can exhibit dyskeratosis (corps ronds and grains). Foci often are small and multiple foci are seen on shave biopsy. There also may be spongiotic

changes when associated with an eczematous element. A perivascular lymphohistiocytic infiltrate with eosinophils usually is seen.³ Basket weave keratin may be seen; however, as the lesions cause pruritus, erosions and ulcerations often are present.⁴

Grover disease has multiple histologic variants that may resemble Darier disease, Hailey-Hailey disease, pemphigus foliaceus, pemphigus vulgaris, and spongiotic dermatitis and can present in combination.⁵

The variant of Grover disease that has a Darier-like pattern is difficult to distinguish from Darier disease, an autosomal-dominant-inherited disorder classified by small papules that emerge in seborrheic areas during childhood and adolescence. Histologically, Darier disease (Figure 2) shows broad areas of dyskeratosis and acantholysis that lead to suprabasal cleavage. Follicular extension may be present. In addition, there often is prominent vertical parakeratosis in Darier disease.⁶ Histologic features that favor Darier disease over the Darier-like variant of Grover disease include a broad focus of acanthotic dyskeratosis with follicular extension; the presence of a hyperkeratotic stratum corneum; and a lack of spongiosis and eosinophils, which are notably absent in Darier disease but may be present in Grover disease.⁴

Another variant of Grover disease has a Hailey-Hailey-like pattern, which is characterized by Hailey-Hailey disease's dilapidated brick wall appearance or the diffuse suprabasal acantholysis of all epidermal layers without notable dyskeratosis.⁴ Hailey-Hailey

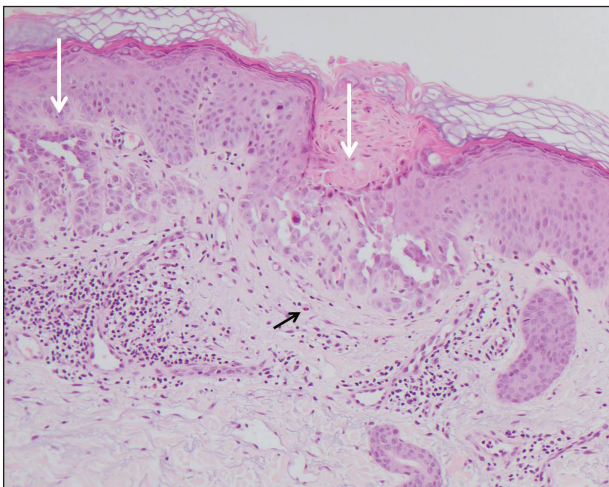


FIGURE 1. Grover disease. In the Darier-like pattern, there are multiple small foci (white arrows) of acantholysis and dyskeratosis. An inflammatory cell infiltrate, often with eosinophils, is seen in the dermis (black arrow)(H&E, original magnification $\times 200$).

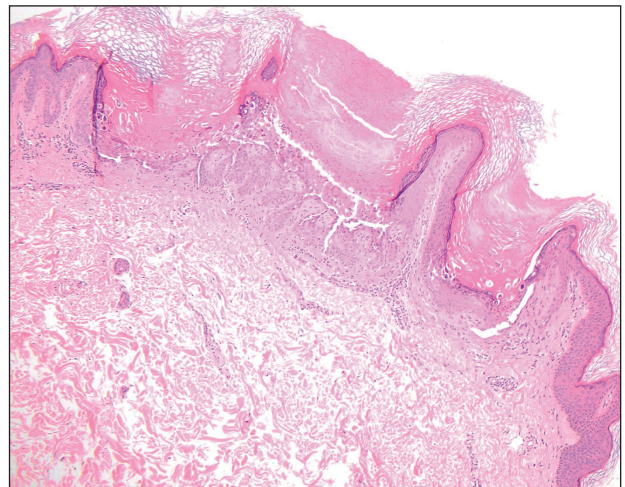


FIGURE 2. Darier disease. There is a broad suprabasal cleft with overlying acantholysis and dyskeratosis (corps ronds and grains). A thick keratotic plug with parakeratosis overlies the acantholytic dyskeratosis (H&E, original magnification $\times 100$).

disease, also known as familial benign pemphigus, is an autosomal-dominant disorder that presents with erythematous vesicular plaques in flexural areas. The plaques progress to flaccid bullae with rupture and crusting and spread peripherally.⁷ Pathology shows suprabasilar clefts and numerous acantholytic cells (Figure 3). Dyskeratotic keratinocytes are rare with infrequent corps ronds and rare grains. The epidermis also is less hyperplastic in Grover disease than in Hailey-Hailey disease.¹

Grover disease also may present histologically with a pemphiguslike pattern, mimicking pemphigus foliaceus and pemphigus vulgaris; however, direct immunofluorescence studies are negative in Grover disease.

Pemphigus foliaceus is an autoimmune disorder caused by autoantibodies to desmoglein 1, which are present on the surfaces of keratinocytes, and is

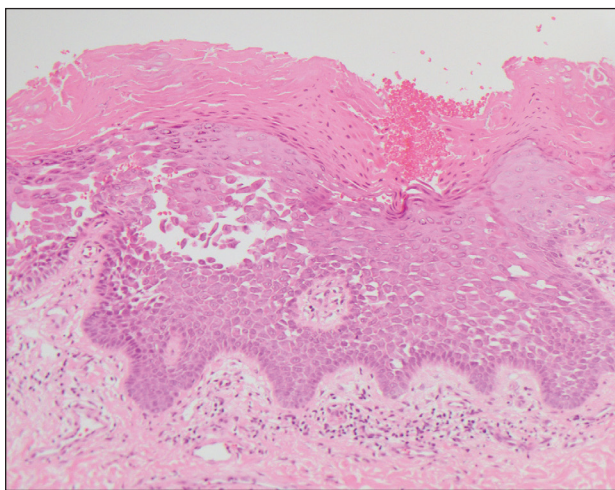


FIGURE 3. Hailey-Hailey disease. Acantholysis is seen at all levels of the epidermis giving the impression of a dilapidated brick wall (H&E, original magnification $\times 200$).

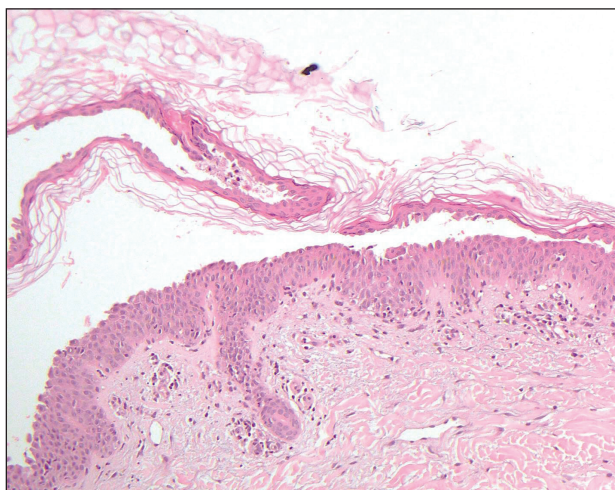


FIGURE 4. Pemphigus foliaceus. An intraepidermal blister is seen with acantholysis of keratinocytes (H&E, original magnification $\times 200$).

characterized by scaly crusts and blisters.⁸ Histologically, pemphigus foliaceus (Figure 4) shows a superficial epidermal blistering process. The acantholysis may be subtle and is commonly localized to the stratum granulosum, extending into the stratum corneum. Complete loss of the stratum corneum can be seen, resulting in only scattered acantholytic cells. Spongiosis also may be seen. The dermis shows a perivascular infiltrate that often contains eosinophils. Pemphigus foliaceus is confirmed by direct immunofluorescence.⁹

Pemphigus vulgaris is an autoimmune blistering disorder that is characterized by IgG autoantibodies to desmoglein 3, a component of desmosomes that are involved in keratinocyte-to-keratinocyte adhesion. Clinically, patients present with flaccid fragile blisters on the skin and mucous membranes that rupture easily, leading to painful erosions.¹⁰ Intraepidermal blisters are seen histologically (Figure 5) with the loss of cohesion (acantholysis) seen classically in the lower portions of the epidermis where desmoglein 3 is most prominent. When only the basal layer remains, the histology has been likened to a tombstone row.¹¹ Extension of the blister along the adnexa is common. The underlying dermis shows a perivascular infiltrate with eosinophils. Early lesions may show only eosinophilic spongiosis. Direct immunofluorescence studies show IgG and C3 in an intercellular pattern that resembles a fish net or chicken wire.^{4,11}

The spongioticlike pattern of Grover disease is marked by epidermal edema with separation of the keratinocytes and the revelation of their intracellular bridges,⁴ which manifests as vesiculation in the stratum corneum or upper layers of the epidermis.¹²

Grover disease is self-limited and may spontaneously resolve; however, the disease may be responsive to topical

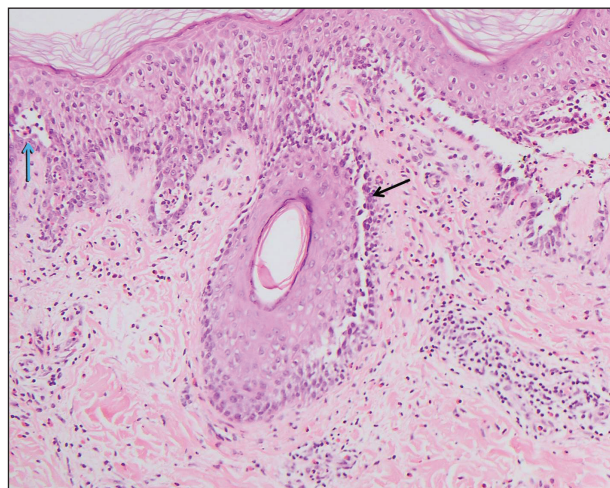


FIGURE 5. Pemphigus vulgaris. An intraepidermal blister is present immediately above the basal layer leaving a tombstone row of basilar keratinocytes. The separation is seen tracking down a hair follicle (black arrow). Eosinophils are seen in a spongiotic focus (blue arrow) (H&E, original magnification $\times 200$).

and systemic steroids. Additionally, avoidance of aggravating factors such as sunlight, heat, and sweating can improve symptoms.²

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