

Transient Acantholytic Dermatositis (Grover's Disease): A Contemporary Review

Valentina Broshtilova¹, Sonya Marina^{2*}, Yoanna Velevska³, Irina Yungareva⁴ and
Yoanna Petkova¹

¹Department of Internal Medicine, Pharmacology and Clinical Pharmacology, Pediatrics, Epidemiology, Infectious and Skin Diseases, Faculty of Medicine, Sofia University "St. Kliment Ohridski", Sofia, Bulgaria.

²Research and Education Sector, Medical Institute of the Ministry of Interior, Sofia, Bulgaria.

³Department of Otorhinolaryngology, Ophthalmology and Dermatovenereology, Faculty of Medicine, Prof. Asen Zlatarov University, Burgas, Bulgaria.

⁴Department of Dermatology and Venereology, Medical Institute of the Ministry of Interior, Sofia, Bulgaria.

***Correspondence:**

Sonya Marina, Research and Education Sector, Medical Institute of the Ministry of Interior, Sofia, Bulgaria.

Received: 03 Sep 2026; **Accepted:** 04 Oct 2026; **Published:** 15 Oct 2026

Citation: Valentina Broshtilova, Sonya Marina, Yoanna Velevska, et al. Transient Acantholytic Dermatositis (Grover's Disease): A Contemporary Review. J Med - Clin Res & Rev. 2026; 10(10): 1-13.

ABSTRACT

Transient acantholytic dermatosis (TAD), also known as Grover disease, is an acquired acantholytic dermatosis characterized by intensely pruritic erythematous papules and papulovesicles, predominantly involving the trunk. It occurs most commonly in middle-aged and older men and may be underrecognized because of its considerable clinical and histopathological variability.

Aim: To provide a comprehensive overview of the current evidence regarding the epidemiology, etiopathogenesis, clinical manifestations, diagnosis, differential diagnosis, treatment, prevention, and prognosis of TAD.

Materials and Methods: A literature search was conducted in PubMed/MEDLINE, Scopus, and Web of Science for publications indexed between July 2000 and July 2026. Original research articles, systematic reviews, retrospective studies, and relevant clinical case reports were considered. Particular emphasis was placed on recent advances in the understanding of disease pathogenesis, diagnostic approaches, therapeutic strategies, and emerging treatment options. The identified literature was critically evaluated and synthesized to provide an updated overview of the current understanding and management of TAD.

Results: The etiopathogenesis of TAD remains incompletely understood and is considered multifactorial. Proposed contributing factors include heat and sweating, ultraviolet exposure, impaired epidermal barrier function, drug-related reactions, and abnormalities in keratinocyte differentiation and intercellular adhesion. Diagnosis is primarily clinical, with histopathological examination playing an important role in atypical or diagnostically challenging cases. Treatment is mainly symptomatic and includes avoidance of potential triggers, emollients, topical corticosteroids, phototherapy, and systemic retinoids. Dupilumab has recently emerged as a potential off-label therapeutic option for selected patients with chronic or treatment-refractory disease; however, the available evidence remains limited and is based predominantly on case reports and small case series.

Conclusions: TAD generally has a favorable prognosis, but chronic or recurrent disease and persistent pruritus may substantially impair quality of life. Accurate diagnosis, appropriate differentiation from clinically and histopathologically similar disorders, and individualized treatment are essential for optimal disease management. Further prospective, controlled, and multicenter studies are needed to elucidate the pathogenesis of TAD, identify prognostic factors, and establish evidence-based diagnostic and therapeutic strategies.

Keywords

Transient acantholytic dermatosis, Grover disease, Acantholysis, Pruritus, Dupilumab, Treatment, Review.

Abbreviations

EGFR inhibitors: Epidermal growth factor receptor inhibitors, BRAF inhibitors: B-Raf proto-oncogene inhibitors, MAPK: Mitogen-activated protein kinase, TCA: Trichloroacetic acid, NB-UVB: Narrowband ultraviolet B, PUVA: Psoralen plus ultraviolet A, JAK: Janus kinase, MEK inhibitors: Mitogen-activated protein kinase kinase inhibitors.

Introduction

Transient acantholytic dermatosis (TAD), also known as Grover disease, is an acquired, non-contagious acantholytic dermatosis first described by R. W. Grover in 1970 [1]. The disease predominantly affects men over 50 years of age, although cases have also been described in women and younger patients. Clinically, it is characterized by the sudden appearance of intensely pruritic erythematous papules, papulovesicles, or small keratotic papules. The eruption most commonly involves the chest and back, with a tendency to spread to the proximal extremities. Although initially defined as “transient”, TAD follows a chronic-relapsing course lasting months or even years in a significant proportion of patients [1-5].

The etiopathogenesis of TAD remains unclear. A multifactorial mechanism is presumed, involving impaired adhesion between keratinocytes, potentially triggered or facilitated by factors such as heat, profuse sweating, occlusion, prolonged bed rest, ultraviolet radiation, and xerosis. In recent years, a number of associations with systemic diseases have been described, including malignant neoplasms and chronic renal failure, as well as organ transplantation. An association with the use of various medications has also been reported, including immunotherapeutic agents, BRAF inhibitors, cytotoxic chemotherapy, and other targeted anticancer therapies [5-10].

Histopathologically, the disease is characterized by focal acantholysis, often combined with varying degrees of dyskeratosis. Different histological patterns resembling Darier disease, familial benign chronic pemphigus (Hailey–Hailey disease), pemphigus vulgaris, or spongiotic acantholysis may be identified within the same biopsy specimen. This morphological diversity necessitates careful clinicopathological correlation to establish an accurate diagnosis [4,11,12].

The diagnosis is based on the characteristic clinical presentation and histological demonstration of acantholysis. In atypical cases, direct immunofluorescence may be performed to exclude autoimmune bullous dermatoses. Treatment is primarily symptomatic and includes topical corticosteroids, emollients, and antihistamines, while systemic retinoids, phototherapy, or systemic corticosteroids are considered in severe or persistent forms. Due to the lack of randomized controlled trials, therapeutic recommendations are based primarily on case series, retrospective

studies, and systematic reviews [3,5,6,11].

Epidemiology

TAD is a relatively common acquired acantholytic dermatosis, although its true incidence remains unknown due to misdiagnosis and misclassification. The disease predominantly affects fair-skinned men over 50 years of age, with a male-to-female ratio ranging from 2:1 to 3:1. The mean age at diagnosis is approximately 61 years, with the highest incidence observed during the sixth and seventh decades of life [2,4].

The higher frequency among fair-skinned individuals is probably related to chronic ultraviolet exposure and the characteristic photoaged phenotype. TAD is less common in women, individuals with darker skin, and patients younger than 40 years, although cases have been described across all age groups, including children and young adults [2,4].

In addition to demographic characteristics, a number of external and internal factors are considered potential triggering or predisposing circumstances. The most frequently described include intense sweating, high ambient temperature, prolonged sun exposure and bed rest, febrile states, hospitalization, occlusion, xerosis, and mechanical friction. These factors are thought to impair the epidermal barrier and intercellular adhesion, thereby creating conditions conducive to the development of acantholysis [2,5,11].

Increasing evidence suggests a possible association between TAD and certain neoplastic and systemic diseases. The most frequently reported association is with hematological malignancies, including acute and chronic leukemias, lymphomas, and multiple myeloma. Associations with solid tumors, chronic renal failure, hemodialysis, and organ transplantation are also described. Although a causal relationship has not been convincingly demonstrated, an underlying systemic disease should be considered in patients with sudden onset or atypical disease manifestations [7].

During the COVID-19 pandemic, isolated cases of TAD or TAD-like acantholytic eruptions occurring during the febrile phase of SARS-CoV-2 infection were reported. It has been suggested that hyperthermia, increased sweating, and the inflammatory immune response could act as triggering factors [13].

Over the past decade, the number of reports of drug-induced TAD has increased. BRAF inhibitors, including vemurafenib and dabrafenib, as well as in combination therapy with MEK inhibitors are considered most suspicious. Cases have also been reported with cytotoxic chemotherapeutic agents, immune checkpoint inhibitors, epidermal growth factor receptor inhibitors (EGFR inhibitors), and other targeted anticancer therapies [8-10]. These observations highlight the importance of a detailed drug history in patients with newly developed or atypically presenting TAD.

Etiology

The etiology of transient acantholytic dermatosis (TAD) remains incompletely understood. Currently, TAD is considered a

multifactorial disorder in which individual susceptibility interacts with a range of exogenous and endogenous factors. The final common pathway is thought to involve disruption of intercellular adhesion between keratinocytes, resulting in focal acantholysis. However, none of the proposed pathogenic mechanisms fully accounts for the diverse clinical and histopathological features of the disease [5,6,11].

One of the leading hypotheses implicates the eccrine sweat glands and ducts in the pathogenesis of TAD. The frequent occurrence or exacerbation of the disease following prolonged exposure to heat and profuse sweating supports a potential role for eccrine dysfunction. Sweat retention and functional abnormalities of the eccrine ducts may contribute to localized epidermal injury and impair keratinocyte–keratinocyte adhesion, thereby facilitating the development of acantholysis [5,11].

Age-related alterations in epidermal barrier function and xerosis may also contribute to disease susceptibility. Reduced skin hydration, cumulative photodamage, and structural changes within the epidermis may adversely affect the integrity and function of desmosomes, thereby weakening keratinocyte adhesion. These mechanisms may, at least in part, explain the increased prevalence of TAD among older individuals with chronically photodamaged skin [5,11].

In drug-induced forms of TAD, the underlying mechanisms are likely to be heterogeneous and remain incompletely characterized. One proposed mechanism involves direct or indirect epidermal injury caused by the excretion of the drug or its active metabolites through the eccrine sweat glands. Subsequent impairment of desmosomal integrity may result in keratinocyte dissociation, leading to acantholysis and dyskeratosis. The preferential localization of lesions to areas characterized by increased sweating, together with clinical improvement following withdrawal of the suspected causative medication, provides indirect support for this hypothesis, although a causal relationship has not been definitively established [9,10].

Particular interest has focused on TAD associated with BRAF inhibitors, including vemurafenib and dabrafenib. These agents may induce paradoxical activation of the MAPK (mitogen-activated protein kinase) signaling pathway in BRAF wild-type keratinocytes. This aberrant pathway activation may alter keratinocyte proliferation and differentiation and subsequently impair intercellular adhesion, thereby contributing to the development of acantholysis. This mechanism represents one of the best-characterized molecular explanations for BRAF inhibitor-associated Grover disease [8,10].

The spectrum of drug-associated TAD continues to expand. In addition to BRAF and MEK inhibitors, TAD has been reported in association with immune checkpoint inhibitors, cytotoxic chemotherapeutic agents, monoclonal antibodies, and other targeted anticancer therapies [8-10]. Although the precise mechanisms underlying these associations remain unclear, different drug

classes may interfere with keratinocyte differentiation, epidermal homeostasis, or intercellular adhesion through distinct molecular pathways [9,10].

Regarding SARS-CoV-2 infection, current evidence does not support a direct causal relationship between COVID-19 and the pathogenesis of TAD. Importantly, the publication by I. Colmenero et al. describes COVID-19-associated pernio (chilblains), rather than Grover disease, and therefore should not be cited as direct evidence for a pathogenic mechanism underlying TAD [13,14].

In summary, TAD is best regarded as a heterogeneous, multifactorial disorder in which physical triggers, medications, systemic conditions, and individual susceptibility may interact to disrupt epidermal homeostasis and keratinocyte adhesion. These processes ultimately converge on a common histopathological pathway characterized by focal acantholysis, frequently accompanied by varying degrees of dyskeratosis [3,5,10].

Clinical Presentation

TAD clinical presentation is variable, but the disease most commonly presents with an abrupt onset of intensely pruritic papules on the trunk. Although TAD was initially described as a self-limiting disorder, a substantial proportion of patients develop a chronic-relapsing course characterized by recurrent exacerbations interspersed with periods of partial or complete remission [1-4,6].

The seasonal variation in TAD remains controversial. Some studies have reported a higher incidence during the winter months, potentially related to increased xerosis and impaired epidermal barrier function, whereas others have observed a greater frequency during the summer, when elevated temperatures and excessive sweating may act as precipitating factors. These apparently discrepant findings may reflect differences in geographic location, climate, patient characteristics, and individual susceptibility to environmental triggers [2,3,6].

The characteristic distribution of TAD involves the central chest, upper back, and interscapular region, with frequent extension to the proximal portions of the upper extremities. Less commonly, lesions may involve the abdomen, neck, shoulders, and thighs. Involvement of the face, palms, soles, or mucous membranes is distinctly uncommon and, when present, should prompt consideration of an alternative diagnosis [2-4,6].

The primary lesions are typically small (approximately 2–5 mm), erythematous papules, papulovesicles, or keratotic papules, often accompanied by fine scaling. Vesicles are usually short-lived and may rapidly rupture, resulting in superficial erosions and the formation of serous crusts. Persistent pruritus and scratching frequently produce excoriations and secondary crusting. The eruption may therefore become polymorphic, with papules, vesicles, erosions, excoriations, and crusts occurring simultaneously, potentially obscuring the characteristic morphology and complicating the clinical diagnosis [2-4,6].

Pruritus is the predominant clinical symptom and is typically moderate to severe. In some patients, it may be sufficiently intense to substantially impair sleep, daily functioning, and overall quality of life. Rarely, the eruption may be asymptomatic or associated only with mild burning or discomfort. Importantly, the intensity of pruritus does not necessarily correlate with the extent or severity of the cutaneous lesions [3,6].

The clinical course is highly variable. In the classic form, lesions may undergo spontaneous resolution within 2–4 weeks, even in the absence of specific treatment. However, in a proportion of patients, TAD follows a chronic-relapsing course, with persistent or recurrent lesions occurring over months or, in some cases, years. Exacerbations may be precipitated by heat, excessive sweating, physical exertion, febrile illnesses, or exposure to specific medications [2,3,6].

Several atypical clinical variants of TAD have been described, including vesiculobullous, linear, follicular, eczematous, seborrheic-like, and generalized forms. Such atypical presentations may further complicate the clinical diagnosis and increase the likelihood of diagnostic overlap with other inflammatory, follicular, or acantholytic dermatoses. More extensive and treatment-refractory disease has also been reported in immunosuppressed patients and in individuals with underlying malignant disease [7].

Complications of Transient Acantholytic Dermatitis

TAD is generally a benign disorder with a favorable prognosis; however, persistent pruritus, disruption of the epidermal barrier, and chronic inflammation may lead to secondary complications in some patients. The most frequently described complication is secondary eczematous change, which may substantially modify the clinical appearance of the disease and complicate its recognition [3,6]. A characteristic manifestation is a nummular (discoid) eczematous reaction, presenting as round or oval erythematous plaques with a dry, scaly surface or, in more exudative lesions, serous or hemorrhagic crusting. These lesions typically develop on the chest and back but may subsequently extend to the upper and lower extremities. Persistent scratching may result in excoriations, lichenification, and post-inflammatory pigmentary alterations [3,6].

Secondary eczematous changes are thought to result from persistent impairment of the epidermal barrier combined with mechanical trauma caused by repeated scratching. Barrier disruption may facilitate the penetration of external irritants and contribute to perpetuation of the inflammatory response. In some patients, the eczematous component may become more prominent than the primary acantholytic lesions, thereby obscuring the characteristic clinical features of TAD and further complicating diagnosis [3,6].

Secondary bacterial infection may occur when erosions and excoriations compromise the cutaneous barrier. The most commonly implicated pathogen is *Staphylococcus aureus*. Clinical features suggestive of secondary infection include increasing pustule formation, purulent crusting, tenderness. When bacterial

superinfection is clinically suspected or microbiologically confirmed, antibiotic therapy may be indicated. The choice of treatment should be guided by the clinical severity and, when appropriate, the results of microbiological testing [3,6].

Persistent, severe pruritus represents an important source of morbidity in patients with TAD and may have a substantial negative impact on quality of life. Sleep disturbance, impairment of daily activities, and psychological distress may be present in patients with chronic-relapsing disease. Consequently, effective control of pruritus should be considered a central component of disease management, alongside treatment of the cutaneous lesions and identification of factors that may precipitate exacerbations [3,6].

Overall, serious complications of TAD are uncommon. Nevertheless, chronic or recurrent disease, secondary eczematous changes, excoriations, and bacterial superinfection may increase disease burden, prolong the need for treatment, and further impair quality of life. Early recognition of these complications and timely therapeutic intervention are therefore important for achieving adequate symptom control and maintaining patients' quality of life [3,6].

Diagnosis

The diagnosis of TAD is based on a comprehensive assessment of the clinical presentation, localization and morphology of the skin lesions, medical history, and, when necessary, histopathological findings [3,4,11]. The diagnostic algorithm is presented in figure 1.

Dermoscopy is increasingly used as an additional non-invasive diagnostic method. Reported findings include central yellowish-brown keratotic structures, peripheral white scales, a pink background, and dotted or linear vessels. Although these findings are not pathognomonic, they may assist clinical evaluation and selection of an appropriate site for skin biopsy. Further studies are needed to validate and standardize dermoscopic criteria for TAD [3,6].

In cases with a typical clinical presentation, the diagnosis may be established on the basis of clinical findings. In atypical, generalized, persistent, or treatment-resistant cases, skin biopsy is recommended. Histopathological examination is essential for confirming the diagnosis and excluding other acantholytic and bullous dermatoses. The most characteristic finding is focal acantholysis, often accompanied by varying degrees of dyskeratosis. Acantholytic changes may be limited to small areas of the epidermis; therefore, it is important to obtain the biopsy from a representative, preferably fresh lesion. The dermis often shows a mild to moderate perivascular lymphocytic infiltrate, while spongiosis, hyperkeratosis, and parakeratosis may be present in the epidermis [4,11]. In some patients, spongiosis and inflammatory changes may dominate the histological picture and make it difficult to distinguish TAD from eczematous dermatoses. Therefore, histopathological findings should be interpreted in the context of the clinical presentation and lesion distribution [4,11]. Classically,

four major histopathological patterns of TAD are described, which may occur individually or in various combinations within the same biopsy [4,11]: Darier-like pattern – characterized by acantholysis and prominent dyskeratosis, including the presence of corps ronds and grains; Hailey–Hailey-like pattern – characterized by widespread acantholysis with the characteristic “dilapidated brick wall” appearance; Pemphigus-like pattern – characterized by prominent acantholysis, predominantly in the suprabasal layers of the epidermis, with minimal or absent dyskeratosis; and Spongiotic pattern – characterized by predominant spongiosis and inflammatory changes, with acantholysis potentially being only subtle. Not all biopsies demonstrate a classic acantholytic pattern and that more than one histological pattern may be present in the same patient, which represents the most challenging verification feature of the disease [4,11].

Direct immunofluorescence is usually negative and is primarily

useful in the differential diagnosis of autoimmune bullous dermatoses, particularly when pemphigus is suspected. It is not routinely required in cases with a typical clinical and histopathological presentation of TAD but may be useful in atypical cases or when there are findings suggestive of an autoimmune bullous disease [11,12,15].

Recent studies suggest possible involvement of immune-mediated mechanisms in the pathogenesis of TAD. Alterations in the expression of molecules involved in cell adhesion have been described, along with evidence of activation of certain inflammatory pathways, including Th2-mediated mechanisms. These observations may be relevant to the therapeutic effect of dupilumab in some patients. Nevertheless, immunohistochemical and other molecular investigations do not currently have an established routine diagnostic role and remain primarily research tools [16,17].

CLINICAL SUSPICION

- Pruritic erythematous papules and/or papulovesicles, predominantly involving the chest, back, and proximal extremities
- Acute or subacute onset
- Worsening with heat, sweating, and occlusion



HISTORY AND PHYSICAL EXAMINATION

- Evidence of triggering factors – heat, sweating, and occlusion
- Assessment of the extent and severity of skin lesions
 - Assessment of comorbidities
 - Detailed medication history



DERMOSCOPY (when available)

- Dotted and linear vascular structures
- White and/or yellowish structures and scales
- Non-specific findings supporting clinical assessment



ASSESSMENT OF THE NEED FOR SKIN BIOPSY

Typical clinical presentation



Clinically probable TAD



Differential diagnosis



Assessment of the need for additional investigations

Atypical clinical presentation / persistent or recurrent lesions / inadequate therapeutic response



SKIN BIOPSY

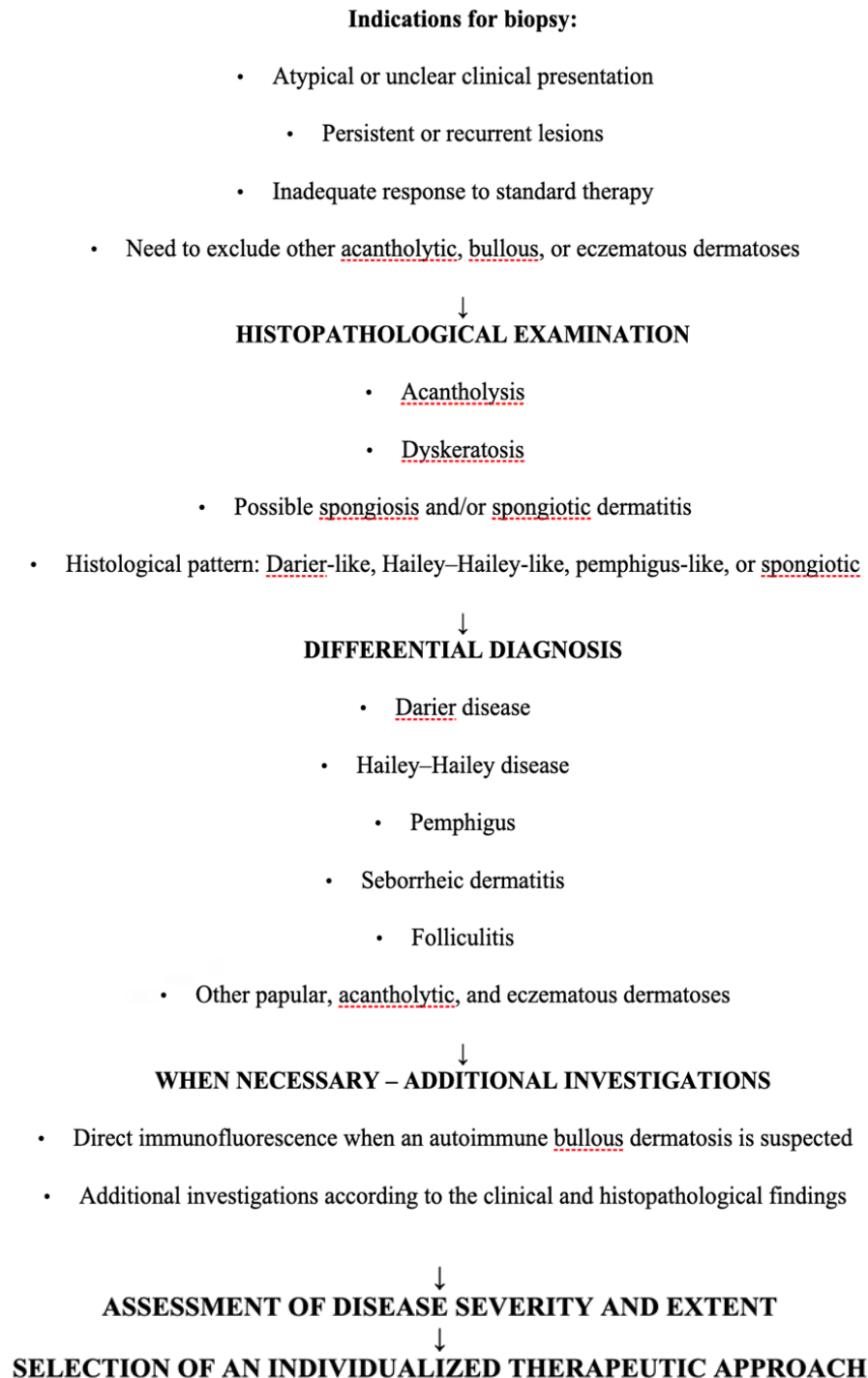


Figure 1: Diagnostic algorithm for transient acantholytic dermatosis.

Table 1: Differential diagnosis of transient acantholytic dermatosis.

Disease	Clinical features	Histological features	Distinguishing features from TAD	Literature
Darier disease	Onset most commonly during adolescence or young adulthood; keratotic papules in seborrheic areas; characteristic nail and mucosal changes; possible family history	Acantholysis and prominent dyskeratosis with corps ronds and grains	Inherited genodermatosis associated with ATP2A2 mutations; earlier onset and chronic course	[18,19]
Hailey–Hailey disease	Recurrent erosive plaques, predominantly in intertriginous areas; frequent family history	Widespread suprabasal acantholysis with characteristic “dilapidated brick wall” appearance	Inherited genodermatosis associated with ATP2C1 mutations; predilection for skin folds; earlier onset	[20]
Miliaria rubra	Small pruritic erythematous papules and papulovesicles following exposure to heat and intense sweating	Obstruction and dilation of eccrine sweat ducts; level of obstruction varies according to the clinical type	No acantholytic changes; usually rapidly resolves after removal of triggering factors	[21,22]
Malassezia folliculitis	Monomorphic follicular papules and pustules, most commonly involving the chest, back, and shoulders; often associated with pruritus	Folliculocentric inflammation with the presence of yeasts of the genus <i>Malassezia</i>	Follicular localization, monomorphic eruption, and absence of acantholysis	[23]
Gram-negative folliculitis	Follicular papules and pustules, often involving the face; may develop following prolonged antibiotic therapy	Neutrophilic folliculitis; microbiological identification of the causative organism	Pustular and follicular character of lesions and positive microbiological findings	[24]
Pemphigus vulgaris	Flaccid bullae and erosions, often with painful mucosal involvement	Suprabasal acantholysis	Positive direct immunofluorescence with intercellular IgG and/or C3 deposits; circulating antibodies against desmoglein 3	[12]
Pemphigus foliaceus	Superficial erosions, erythema, and crusts, predominantly involving seborrheic areas and the trunk; mucosal involvement is usually absent	Subcorneal or superficial acantholysis	Positive direct immunofluorescence and antibodies against desmoglein 1	[12]
Nummular eczema	Coin-shaped, pruritic erythematous plaques, often with exudation, scales, and crusts	Spongiotic dermatitis with varying degrees of exocytosis; primary acantholysis is absent	Typical nummular morphology and absence of acantholytic changes	[25]
Contact dermatitis	Erythematous, pruritic, and eczematous lesions located in areas of contact with an allergen or irritant	Marked spongiosis with varying degrees of inflammatory changes	Relationship to exposure to a specific contactant; absence of primary acantholysis	[26]

Differential Diagnosis

The differential diagnosis of TAD includes a broad spectrum of papular, vesicular, follicular, eczematous, and acantholytic dermatoses (Table 1). Due to its diverse clinical presentation and considerable histopathological variability, the disease may resemble both inflammatory and autoimmune bullous dermatoses. Diagnosis requires careful clinicopathological correlation and, in atypical or diagnostically unclear cases, histopathological examination and, when an autoimmune bullous dermatosis is suspected, direct immunofluorescence [3,4,6,11,12,15].

Differentiation of TAD from Darier disease and Hailey–Hailey disease is particularly important because these disorders may exhibit overlapping histopathological features, including varying degrees of acantholysis and dyskeratosis. Unlike TAD, however, Darier disease and Hailey–Hailey disease are inherited genodermatoses that typically present at a younger age and have characteristic clinical distributions and associated findings. A positive family history, persistent or recurrent disease beginning

early in life, typical anatomical distribution, and the presence of nail or mucosal abnormalities may support the diagnosis of an inherited genodermatosis rather than TAD [11,12,15].

Autoimmune bullous dermatoses, particularly pemphigus vulgaris and pemphigus foliaceus, should also be considered because acantholysis may be a prominent histopathological feature in both conditions. In patients with clinical or histopathological findings suggestive of pemphigus, direct immunofluorescence (DIF) is an important diagnostic investigation. In contrast to pemphigus, DIF is typically negative in TAD. When indicated, serological testing for circulating autoantibodies against desmoglein 1 and desmoglein 3 can provide additional diagnostic support and help distinguish pemphigus foliaceus from pemphigus vulgaris [12,15].

The differential diagnosis should also include follicular and sweat duct disorders. In patients presenting with monomorphic follicular papules and pustules, *Malassezia* folliculitis and Gram-negative folliculitis should be considered. A folliculocentric distribution, together with the presence of pustules and appropriate

microbiological or mycological findings, favors a follicular disorder rather than TAD. Similarly, miliaria rubra should be considered in patients with pruritic papules or papulovesicles that develop or worsen in association with heat and excessive sweating. The absence of acantholysis on histopathological examination and the characteristic clinical setting can help distinguish miliaria from TAD [3,6,11].

TAD diagnosis should be based on an integrated assessment of the clinical presentation, lesion distribution, disease course, relevant medical and medication history, and, when indicated, histopathological findings. Skin biopsy is particularly useful in atypical, persistent, recurrent, or treatment-resistant cases, whereas DIF and additional serological, microbiological, or mycological investigations are performed selectively according to the clinical and histopathological differential diagnosis. This clinicopathological approach is essential for distinguishing TAD from other acantholytic, autoimmune bullous, follicular, and eczematous dermatoses and for avoiding misdiagnosis based solely on the presence of acantholysis [3,4,11,12,15].

Treatment

At present, there is no specific etiological therapy for TAD. Treatment is primarily directed toward controlling pruritus and inflammation, reducing the frequency and severity of exacerbations, promoting clearance of cutaneous lesions, and improving patients' quality of life. The therapeutic approach should be individualized according to disease severity and extent, intensity of pruritus, disease duration, response to previous treatment, and the presence of comorbidities and concomitant medications [3,5,6]. The proposed therapeutic algorithm for TAD is presented in table 2.

General Measures

An important component of management is the avoidance of potential exacerbating factors, particularly excessive heat, profuse sweating, and prolonged occlusion. Patients are advised to maintain a cool environment, wear loose, breathable clothing, and avoid prolonged physical activity in hot and humid conditions when possible. These measures may help reduce pruritus and the occurrence of new lesions, although robust evidence supporting their preventive efficacy is limited [3,5,6].

Regular application of emollients and moisturizers is recommended to support restoration of the epidermal barrier and reduce xerosis, which may exacerbate pruritus. When appropriate, topical antipruritic preparations may also be used, with the choice guided by lesion location, disease severity, and individual tolerability [3,6].

Topical Therapy

Topical corticosteroids represent a mainstay of treatment for mild-to-moderate TAD. Preparations of medium to high potency may be applied as creams, lotions, or emulsions, particularly for lesions involving the trunk. Their therapeutic effect is primarily related to suppression of cutaneous inflammation and reduction of pruritus; however, they do not directly target the underlying acantholytic

process. Prolonged or repeated use, particularly of potent corticosteroids, should be accompanied by periodic reassessment because of the risk of local adverse effects [3,5,6].

In selected patients, topical corticosteroids may be combined with a vitamin D analogue, most commonly calcipotriol. Vitamin D analogues may influence keratinocyte differentiation and exert additional anti-inflammatory effects. However, evidence supporting their use in TAD remains limited and is derived mainly from small case series and clinical observations [3,6].

For persistent or treatment-resistant localized lesions, topical trichloroacetic acid (TCA) has been reported to produce favorable clinical responses. TCA induces a controlled chemical injury to the epidermis, followed by re-epithelialization. Given the limited evidence regarding its efficacy and the potential for local adverse effects, TCA is not considered routine therapy and should be reserved for carefully selected patients [27].

Physical Modalities

Cryotherapy with liquid nitrogen may be considered for individual or localized, persistent lesions that are resistant to conventional topical treatment. The procedure produces localized destruction of the affected epidermis, followed by subsequent re-epithelialization. However, evidence supporting its use is limited, and treatment may result in pain, blistering, scarring, or transient or persistent hypo- or hyperpigmentation. These pigmentary complications may be particularly relevant in patients with darker skin phototypes. Consequently, cryotherapy is not recommended as routine treatment and should be reserved for selected lesions and patients [28].

Systemic Therapy

Systemic retinoids are considered in patients with severe, extensive, generalized, or chronic-relapsing disease, particularly when adequate control cannot be achieved with topical therapy. Acitretin is the systemic retinoid most commonly used and may be administered at an individualized dose, commonly within the range of 10–30 mg daily, depending on disease severity, clinical response, and tolerability. Retinoids influence epidermal differentiation and keratinization and may produce substantial clinical improvement in some patients. Nevertheless, recurrence following discontinuation of treatment is common, and long-term therapy may be required in chronic-relapsing disease [3,5,6].

Isotretinoin may be considered as an alternative systemic retinoid in selected patients, particularly when acitretin is contraindicated or poorly tolerated. The choice of retinoid should take into account the patient's comorbidities, potential drug interactions, adverse-effect profile, and the requirements for laboratory and pregnancy monitoring [3,5,6].

During systemic retinoid therapy, periodic monitoring of liver function and serum lipid levels is recommended. In women of reproductive potential, strict pregnancy-prevention measures and the applicable pregnancy-testing requirements must be followed

in accordance with the safety requirements of the specific retinoid used.

Systemic corticosteroids are generally not recommended as routine or long-term treatment because of their unfavorable adverse-effect profile and the potential for rapid recurrence after treatment withdrawal. Nevertheless, a short course may occasionally be considered in selected patients with severe acute exacerbations when other therapeutic options are ineffective, contraindicated, or unsuitable [3,5,6].

Phototherapy

Phototherapy is considered in patients with extensive or refractory disease, particularly when topical treatment is insufficient. Narrowband ultraviolet B (NB-UVB) and psoralen plus ultraviolet A (PUVA) are the modalities most frequently reported. In selected patients, phototherapy may reduce pruritus and promote regression of cutaneous lesions [3,5,6].

The response to ultraviolet radiation is variable, and UV exposure may paradoxically precipitate or exacerbate TAD in some patients. Therefore, phototherapy should be considered on an individualized basis after careful assessment of the potential benefits and risks. Appropriate treatment selection, dosing, and monitoring are essential to minimize the risk of disease exacerbation and phototoxic or other treatment-related adverse effects [3,5,6].

Emerging Therapeutic Options

In recent years, several case reports, small case series, and retrospective observations have described the use of dupilumab in patients with chronic, recurrent, and treatment-refractory TAD. Some patients have demonstrated substantial reductions in pruritus and partial or complete regression of cutaneous lesions following treatment. However, the available evidence remains limited, and adequately powered, controlled clinical trials are lacking. Therefore, dupilumab should not currently be considered standard therapy for TAD. Nevertheless, it may represent a promising off-label treatment option for carefully selected patients with severe or refractory disease [16,17,29-31].

Individual case reports have also described the use of methotrexate and low-dose naltrexone in chronic or treatment-resistant TAD. Although clinical improvement was reported in some patients, the available evidence is insufficient to establish their efficacy or safety in TAD. Accordingly, neither treatment can currently be recommended as an established therapeutic option, and their use should be considered only in selected cases after careful assessment of the potential benefits and risks [29,30,32].

Given the potential involvement of inflammatory signaling pathways in the pathogenesis of acantholytic dermatoses, Janus kinase (JAK) inhibition has emerged as a potential area of therapeutic interest [33]. However, clinical evidence regarding the efficacy and safety of JAK inhibitors in TAD remains insufficient. At present, these agents should therefore be regarded as investigational rather than established or recommended therapy.

Well-designed prospective studies are needed to determine whether JAK inhibition has a clinically meaningful role in the management of TAD [33].

In cases of drug-induced TAD, identification of the suspected causative medication is a fundamental component of management. When clinically feasible, discontinuation of the suspected drug or substitution with an appropriate alternative should be considered. However, such decisions must be individualized and balanced against the therapeutic importance of the medication, particularly in patients receiving essential treatment for underlying malignancies or other serious systemic diseases [8-10].

In conclusion, the management of TAD remains predominantly symptomatic and should be individualized according to disease severity, extent, chronicity, and treatment response. For most patients, initial management consists of avoidance of potential exacerbating factors, regular use of emollients, and appropriate topical corticosteroid therapy. Phototherapy or systemic retinoids may be considered in patients with extensive, severe, persistent, or recurrent disease. In treatment-refractory cases, dupilumab may represent a promising off-label therapeutic option, although its efficacy and long-term safety in TAD require further investigation. Other emerging therapies, including methotrexate, low-dose naltrexone, and JAK inhibitors, currently lack sufficient evidence to support routine clinical use. The absence of standardized treatment algorithms and the limited quality of available evidence underscore the need for prospective, controlled clinical studies to establish evidence-based therapeutic strategies for TAD [16,17,29-33].

Follow-up and Long-Term Management

Because TAD may follow a chronic-relapsing course, the frequency and intensity of follow-up should be individualized according to disease severity, relapse frequency, treatment response, and the therapy being administered. More frequent clinical assessments are appropriate when systemic treatment is initiated, discontinued, or modified, whereas the interval between visits may be extended once the disease has reached a stable state.

During follow-up, clinical disease activity should be assessed, including the extent and distribution of cutaneous lesions, intensity of pruritus, frequency and duration of exacerbations, and the impact of the disease on quality of life. In patients receiving systemic therapy, appropriate laboratory investigations and monitoring for treatment-related adverse effects should also be performed according to the specific medication used [3,5,6].

The main principles of long-term management include regular clinical follow-up; maintenance of the epidermal barrier through consistent use of emollients; identification and avoidance of individually recognized exacerbating factors; early recognition and treatment of disease flares; and assessment for secondary complications, including eczematization, excoriations, and secondary bacterial infection. In patients receiving systemic treatment, the ongoing need for therapy, its efficacy and tolerability,

Table 2: Therapeutic algorithm for transient acantholytic dermatosis.

Therapeutic step	Therapeutic approach	Indications	Quality of evidence	Literature
General measures	Avoidance of heat, intense sweating, and occlusion; maintenance of a cool environment; wearing loose cotton clothing; regular use of emollients	All patients	C	[3,5,6]
First-line therapy	Medium- to high-potency topical corticosteroids for a limited period; emollients; topical antipruritic agents when necessary	Mild and moderate forms	C	[3,5,6]
Alternative topical therapy	Combination of topical corticosteroid and calcipotriol	Inadequate response to topical monotherapy	C	[3,6]
Local destructive methods	Cryotherapy or topical application of trichloroacetic acid (TCA)	Limited, persistent, or resistant lesions	C	[27,28]
Phototherapy	NB-UVB or PUVA with individualized frequency and dosing	More widespread lesions or inadequate response to topical therapy	C	[3,5,6]
Systemic therapy	Systemic retinoids – acitretin 10–30 mg/day; isotretinoin as an alternative; laboratory monitoring required	Generalized, chronic, recurrent, or severe TAD	C	[3,5,6]
Refractory forms	Dupilumab in selected patients; other off-label approaches, including methotrexate or low-dose naltrexone, in individual cases	Severe, chronic-relapsing, or treatment-resistant TAD	C	[16,17,29-32]
Drug-induced TAD	Discontinuation or replacement of the suspected causative medication when clinically feasible; follow-up	Drug-induced forms	C	[8-10]

Quality of evidence: C – limited clinical data, including expert opinion, individual clinical cases, or small case series.

Note: At present, there are insufficient clinical data supporting the use of JAK inhibitors in TAD. Therefore, they are not included in the algorithm as a recommended therapeutic approach and should be considered only as a potential future therapeutic option.

and the potential need for dose adjustment, continuation, or discontinuation should be periodically reassessed [3,5,6].

During periods of active disease or following a change in treatment, follow-up visits may be scheduled at approximately 4–8-week intervals, with subsequent adjustment according to clinical response and disease stability. However, the optimal follow-up interval should be determined on an individual basis, particularly in patients with severe disease, frequent relapses, significant comorbidities, or ongoing systemic therapy.

Patient education is an important component of long-term management, particularly in chronic-relapsing TAD. Patients should be informed about the typical clinical features of exacerbations and encouraged to recognize early signs of disease recurrence. They should also be advised to identify and minimize personal triggering factors, such as excessive heat, sweating, and occlusion, when these are relevant to their disease. This proactive approach may facilitate early intervention, reduce the severity and duration of exacerbations, and potentially decrease the need for more intensive treatment [3,6].

Prevention and Prophylaxis

Because the etiology of TAD remains incompletely understood, no specific evidence-based strategy for primary prevention is established. Nevertheless, avoidance of potential exacerbating factors and maintenance of an intact epidermal barrier are reasonable measures that may help reduce the frequency or severity of disease flares and relapses [3,5,6].

Patients are advised to minimize prolonged exposure to excessive heat, profuse sweating, and prolonged skin occlusion, particularly

when these factors have been identified as individual triggers. Maintaining a cool environment, wearing loose and breathable clothing, and avoiding prolonged physical exertion in hot and humid conditions may help reduce symptoms and the risk of exacerbations [3,5,6].

Regular application of emollients and moisturizers is recommended to maintain epidermal barrier function and reduce xerosis, which may contribute to pruritus. This measure may be particularly beneficial in patients with clinically significant dry skin and in older individuals [3,5,6].

In suspected drug-induced TAD, a thorough review of the drug history is essential. When a plausible temporal and clinical association with a particular medication is identified, discontinuation or substitution should be considered when clinically feasible. Resolution of the cutaneous manifestations may occur following withdrawal of the suspected causative agent. However, when the medication is essential for management of the underlying disease, particularly in patients with malignancies, any modification of therapy should be carefully individualized and undertaken in collaboration with the appropriate treating specialist [8-10].

Particular consideration is warranted in patients receiving BRAF inhibitors, including vemurafenib and dabrafenib. The combination of a BRAF inhibitor with a MEK inhibitor alters the spectrum and frequency of some cutaneous adverse events compared with BRAF inhibitor monotherapy. This may be related, at least in part, to simultaneous inhibition at different levels of the MAPK signaling pathway and consequent effects on paradoxical MAPK activation in BRAF wild-type keratinocytes. However, evidence

specifically demonstrating that BRAF/MEK combination therapy prevents TAD is limited. Therefore, such combination therapy should not be regarded as an established prophylactic strategy for TAD [8,34,35].

In patients with a chronic-relapsing course, periodic assessment of disease activity is appropriate. Follow-up should include evaluation of the frequency and severity of relapses, treatment response, the need for continued topical or systemic therapy, and the occurrence of treatment-related adverse effects. Patients receiving systemic retinoids should undergo appropriate laboratory monitoring, including assessment of liver function and lipid levels, while monitoring for other systemic therapies should be guided by the specific safety profile and monitoring requirements of the agent used [3,5,6].

Patient education is an essential component of long-term disease management. Patients should be informed about the chronic-relapsing nature of TAD, potential individual triggers, appropriate skin-care measures, and the early clinical manifestations of exacerbations. Although specific prophylactic therapy has not been established, a comprehensive approach combining avoidance of individual triggers, maintenance of epidermal barrier function, prompt treatment of exacerbations, and individualized follow-up may improve long-term disease control and quality of life [3,5,6].

Prognosis

The prognosis of TAD is generally favorable because the disease is benign and spontaneous regression of the skin lesions occurs in a significant proportion of patients. However, the clinical course is variable and may range from a single, short-lived episode to chronic-relapsing disease persisting for months or years [2-4,6].

In the classic form of TAD, skin lesions may spontaneously regress within several weeks, including without specific treatment. In some patients, however, the disease develops a chronic-relapsing course with alternating periods of exacerbation and remission, which may require prolonged symptomatic treatment and periodic follow-up [2,3,6].

Relapses are often associated with exposure to high temperatures, intense sweating, prolonged occlusion, febrile states, and, in some patients, certain medications or other individual triggering factors. Data regarding disease seasonality are conflicting. Some studies report more frequent exacerbations during the summer months, probably related to increased temperature and sweating, whereas others report a higher frequency during the winter, when xerosis is more pronounced. These differences probably reflect climatic, geographical, and individual characteristics of the populations studied [2,3,6].

In some patients, TAD follows a chronic-relapsing course, with symptoms persisting for months or years. In these cases, the main factor determining disease burden is intense pruritus. Persistent itch may significantly impair quality of life, sleep, and daily activities and may lead to secondary excoriations, lichenification,

and eczematization [2-4,6].

A less favorable clinical course may be observed in patients with extensive skin involvement, immunosuppression, concomitant malignant diseases, or drug-induced TAD, particularly when the suspected causative medication cannot be discontinued. These conditions may be associated with greater treatment resistance and a more prolonged course [7,10].

TAD is not associated with increased mortality and generally does not result in permanent structural damage to the skin. Post-inflammatory hyperpigmentation or hypopigmentation may temporarily persist following resolution of inflammatory lesions, particularly after intense inflammation and excoriation. Permanent scarring is atypical for the disease [3,6].

Overall, the prognosis of TAD is favorable, but the chronic-relapsing course in some patients may have a significant functional and psychosocial impact because of persistent pruritus. Early recognition of the disease, identification and avoidance of individual triggering factors, adequate symptom control, and individualized follow-up are essential for optimal long-term management and improvement of patients' quality of life [2,3,6].

Conclusion

TAD, also known as Grover disease, is a relatively common but probably underdiagnosed acquired acantholytic dermatosis. Despite its traditional characterization as a transient and self-limiting condition, a substantial proportion of patients develop a chronic-relapsing course, which may significantly impair quality of life [2-4,6].

The etiopathogenesis of TAD remains incompletely understood and is likely multifactorial. Impaired epidermal barrier function, physical and drug-related triggers, and abnormalities in keratinocyte differentiation and intercellular adhesion are thought to contribute to the development of acantholysis. The considerable clinical and histopathological variability of the disease emphasizes the importance of clinicopathological correlation. In atypical, diagnostically challenging, or treatment-resistant cases, histopathological examination and appropriate evaluation for alternative diagnoses are essential [4,5,8-12].

Treatment remains primarily symptomatic and should be individualized according to disease severity, extent, chronicity, and treatment response. Current therapeutic approaches include avoidance of potential triggering factors, regular use of emollients, topical corticosteroids, phototherapy, and systemic retinoids. For patients with refractory disease, several emerging therapeutic options are being investigated. Among these, dupilumab has shown encouraging results in individual reports and small case series; however, the available evidence remains limited, and its efficacy and safety have not been established sufficiently to support routine use or definitive treatment recommendations [16,17,31].

Given the limited quality and quantity of available evidence,

further well-designed prospective, controlled, and multicenter studies are needed to better define the pathogenesis of TAD, identify clinical and prognostic factors, and evaluate the efficacy and safety of emerging therapeutic strategies. Such studies may facilitate the development of more standardized diagnostic and treatment algorithms and ultimately improve long-term disease control and quality of life in patients with TAD.

References

- Grover RW. Transient acantholytic dermatosis. *Arch Dermatol.* 1970; 101: 426-434.
- Parsons JM. Transient acantholytic dermatosis Grover's disease a global perspective. *J Am Acad Dermatol.* 1996; 35: 653-666.
- Bellinato F, Maurelli M, Gisondi P, et al. Clinical features and treatments of transient acantholytic dermatosis Grover's disease a systematic review. *J Dtsch Dermatol Ges.* 2020; 18: 826-833.
- Davis MDP, Dinneen AM, Landa N, et al. Grover's disease clinicopathologic review of 72 cases. *Mayo Clin Proc.* 1999; 74: 229-234.
- Scheinfeld N. Grover's disease a review of the disease pathogenesis and treatment. *Dermatol Online J.* 2008; 14: 6.
- Aldana PC, Khachemoune A. Grover disease review of subtypes with a focus on management options. *Int J Dermatol.* 2020; 59: 543-550.
- Gantz M, Butler D, Goldberg M, et al. Atypical features and systemic associations in extensive cases of Grover disease a systematic review. *J Am Acad Dermatol.* 2017; 77: 952-957.
- Chu EY, Wanat KA, Miller CJ, et al. Diverse cutaneous side effects associated with BRAF inhibitor therapy a clinicopathologic study. *J Am Acad Dermatol.* 2012; 67: 1265-1272.
- Beer J, Rosenbach M. Grover disease associated with chemotherapy review of potential pathophysiology current treatments and future directions. *J Drugs Dermatol.* 2020; 19: 1056-1064.
- Awe O, Pavlidakey P, Kole L, et al. Drug-induced Grover's disease a case report and review of the literature. *Int J Dermatol.* 2022; 61: 591-594.
- Weaver J, Bergfeld WF. Grover disease transient acantholytic dermatosis. *Arch Pathol Lab Med.* 2009; 133: 1490-1494.
- Bolognia JL, Schaffer JV, Cerroni L. *Dermatology.* 4th ed. Philadelphia. Elsevier. 2018.
- Daneshgaran G, Dubin DP, Gould DJ. Cutaneous manifestations of COVID-19 an evidence-based review. *Am J Clin Dermatol.* 2020; 21: 627-639.
- Colmenero I, Santonja C, Alonso-Riaño M, et al. SARS-CoV-2 endothelial infection causes COVID-19 chilblains histopathological immunohistochemical and ultrastructural study of seven paediatric cases. *Br J Dermatol.* 2020; 183: 729-737.
- Schmidt E, Kasperkiewicz M, Joly P. Pemphigus. *Lancet.* 2019; 394: 882-894.
- Butler DC, Kollhoff A, Berger T. Treatment of Grover disease with dupilumab. *JAMA Dermatol.* 2021; 157: 353-356.
- Amara S, Hawkins K, Skaggs E, et al. Efficacy of dupilumab for treatment-resistant Grover disease a retrospective study. *Br J Dermatol.* 2025; 192: 941-943.
- Labbouz S, Hovnanian A, Xiong G, et al. Darier disease-A review highlighting new insights from the Darier Disease International Task Force. *J Eur Acad Dermatol Venereol.* 2026; 40: 1626-1647.
- Ettinger M, Kimeswenger S, Deli I, et al. Darier disease Current insights and challenges in pathogenesis and management. *J Eur Acad Dermatol Venereol.* 2025; 39: 942-951.
- Porro AM, Seque CA, Miyamoto D, et al. Hailey-Hailey disease clinical diagnostic and therapeutic update. *An Bras Dermatol.* 2024; 99: 651-661.
- Feng E, Janniger CK. Miliaria. *Cutis.* 1995; 55: 213-216.
- Palaniappan V, Sadhasivamohan A, Sankarapandian J, et al. Miliaria crystallina. *Clin Exp Dermatol.* 2023; 48: 462-467.
- Henning MAS, Hay R, Rodriguez-Cerdeira C, et al. Position statement Recommendations on the diagnosis and treatment of Malassezia folliculitis. *J Eur Acad Dermatol Venereol.* 2023; 37: 1268-1275.
- Neubert U, Jansen T, Plewig G. Bacteriologic and immunologic aspects of Gram-negative folliculitis a study of 46 patients. *Int J Dermatol.* 1999; 38: 270-274.
- Leung AKC, Lam JM, Leong KF, et al. Nummular eczema an updated review. *Recent Pat Inflamm Allergy Drug Discov.* 2020; 14: 146-155.
- Streit M, Braathen LR. Contact dermatitis clinics and pathology. *Acta Odontol Scand.* 2001; 59: 309-314.
- Kouba DJ, Dasgeb B, Deng AC, et al. Effective treatment of persistent Grover's disease with trichloroacetic acid peeling. *Dermatol Surg.* 2006; 32: 1083-1088.
- Galamgam J, Lee DJ. Treatment of transient acantholytic dermatosis with liquid nitrogen. *JAAD Case Rep.* 2020; 6: 341-343.
- McCarter M, Cleaver D, Lane J. Treatment of refractory Grover's disease with dupilumab a case study. *Cureus.* 2025; 17: e88695.
- Kaprive JF, Washburn S, Emerson CM, et al. Successful treatment of resistant Grover's disease with dupilumab. *Int J Womens Dermatol.* 2024; 10: e140.
- Magnano M, Michelucci A, Mancin A, et al. Recalcitrant Grover's disease treated with dupilumab two long-term cases and review of the literature. *J Dtsch Dermatol Ges.* 2025; 23: 1335-1337.
- Correa C, Cheng CE. Low-dose naltrexone for refractory Grover disease a case report. *JAAD Case Rep.* 2023; 34: 44-47.

-
33. Zhou MH, Stirrat TP, Edminister JR, et al. Acantholytic disorders Update on pathophysiology diagnosis and management. J Am Acad Dermatol. 2026; 95: 138-147.
34. Long GV, Stroyakovskiy D, Gogas H, et al. Combined BRAF and MEK inhibition versus BRAF inhibition alone in melanoma. N Engl J Med. 2014; 371: 1877-1888.
35. Robert C, Karaszewska B, Schachter J, et al. Improved overall survival in melanoma with combined dabrafenib and trametinib. N Engl J Med. 2015; 372: 30-39.