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Dermatopathology 101: Part 1 – Inflammatory skin diseases

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Summary

Dermatopathology is an indispensable tool in the diagnostic workup of inflammatory and neoplastic lesions. For the dermatologist in everyday clinical practice, basic knowledge of dermatopathology is highly valuable, as it allows for proper classification and interpretation of histological findings, as well as their correlation with the clinical picture (especially in case of inflammatory skin diseases). Such basic understanding is also important with regard to selecting the appropriate biopsy technique, thus increasing the overall diagnostic quality. The present article describes the diagnostic approaches taken by dermatopathologists in the histological workup of inflammatory skin diseases. The basic principles of this workup are highlighted on the basis of key histological patterns. Published in an upcoming issue, the second part of this article will address the histological characteristics of the most common skin tumors.

Introduction

The present CME article is aimed at dermatology residents as well as board-certified specialists who wish to refresh their basic dermatopathology knowledge. Dermatopathology is an important component in the diagnostic workup of complex skin lesions. The quality of the communication between the dermatopathologist and the clinician correlates not only with the clinical knowledge of the former but also with the dermatopathology knowledge of the latter. Basic understanding of the methodology as well as the possibilities and limitations of dermatopathological studies can significantly increase their quality. The present article describes the methodological spectrum of histopathological examinations as well as potential pitfalls in the histological workup of inflammatory skin diseases. Using specific histological algorithms of common dermatoses, we will highlight important aspects of the diagnostic approach taken by dermatopathologists.

Methods used in routine histology

Biopsy

By employing the appropriate biopsy technique and method of shipping, as well as by providing adequate clinical information, the clinician can have considerable impact on the quality of the histological findings.

Qualitatively adequate histopathological processing first and foremost depends on the size of the biopsy, which must be sufficiently large (also in terms of depth) and, if at all possible, not be secondarily altered. Selecting the appropriate biopsy technique requires anatomical knowledge of the skin in order to be able to assess

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in advance which skin layer is affected by the pathological changes associated with the suspected diagnosis (Table 1). For example, the diagnosis of panniculitis can only be ascertained if the biopsy includes representative parts of the adipose tissue; a superficial and deep perivascular inflammatory pattern can only be diagnosed in its entirety if parts of the deep dermis are included.

For tissue fixation, the dermatosurgeon immediately places the biopsy in aqueous formaldehyde solution (4–10 %). The time required for fixation of the specimen in formalin depends on the kind of tissue and its size. For best results, at least 6–24 hours of tissue fixation is recommended [2].

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The histology request form provides the dermatopathologist with valuable information with respect to clinicopathological correlation. Particularly important information includes patient age, type and duration of lesions, biopsy site, as well as any previous treatments and associated illnesses. In individual cases, it may be useful to also attach photographs. Stating a suspected diagnosis can have substantial impact on the histopathological approach, for example, with respect to the selection of special stains. One such example is the suspected clinical diagnosis of urticaria pigmentosa. Although it is a histologically frequently "invisible" disorder, it may be unequivocally diagnosed using Giemsa or chloroacetate esterase staining. On the other hand, nonspecific details such as "unclear erythema" tend to be misleading to the dermatopathologist.

In turn, the histological report provides the clinician with a description of the morphological changes (possibly using special stains), a histological diagnosis, and suggestions on how to classify the diagnosis including possible differential diagnoses. The more advance information the dermatopathologist is provided on the histology request form, the more specific can histological tissue processing and the classification of histological findings on the part of the dermatopathologist be. This especially applies to skin diseases where the histological changes are less specific and associated with a wide range of differential diagnoses.

Processing at the histopathology laboratory

Technical processing of the biopsy tissue is carried out at the laboratory [3]. The first step involves the cutting to size of the specimen, a procedure that depends on

Table 1 Biopsy procedures in accordance with the suspected diagnosis (after Böer-Auer [1]).

Suspected diagnosis	Biopsy procedure
Inflammatory skin diseases	Representative, fully developed, untreated lesion; rapid fixation (buffered formalin 4–10 %), punch biopsy
Autoimmune bullous dermatoses	In addition, perilesional biopsy for direct immunofluorescence (normal saline, modified Michel's transport medium, or immediate immersion in liquid nitrogen)
Panniculitis	Deep biopsy (scalpel)
Vasculitis of larger vessels	Deep biopsy (scalpel)
Alopecia	Punch biopsy from the periphery of the alopecic area, including skin that still contains hair follicles; biopsy at an oblique angle in the direction of hair growth

the size of the biopsy, the suspected diagnosis, and the clinician's requests. Initial processing has a considerable impact on the further course of the histological examination. In case of inflammatory skin diseases, this generally involves punch biopsy material that is cut to size in simple vertical cross-sections. On the other hand, the diagnostic workup of hair follicle disorders requires both vertical and horizontal cross-sections. Subsequently, the tissue is further processed based on histological protocols that may vary from laboratory to laboratory. Usually, the tissue is dehydrated through a series of graded ethanol baths, followed by xylene clearing and paraffin infiltration in an automated embedding machine. Fixation and embedding may lead to a reduction in tissue volume of up to 30–50 % [4]. The dehydrated and paraffinized tissue is then cast in a paraffin block. In doing so, it is important to ensure the correct position of the specimen, with the epidermis serving as structure for alignment. In case of incorrect embedding, there is a risk of important parts of the specimen not being fully included when preparing tangential sections on the microtome. Said risk increases dramatically in the case of shave biopsies or small punch biopsies (2–3 mm). The slices thus prepared and mounted on slides are approximately 0.004 mm in thickness, and subsequently undergo staining.

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Stains

The various stains are characterized by their affinity to different pH values in the tissue or to different chemical structures [4]. A mixed stain using hematoxylin and eosin (H&E) has become established as standard staining method in the routine diagnostic workup. The Giemsa stain adequately stains mast cells, nuclei, and bacteria; the PAS stain exhibits an affinity to glycogen – for example, in the basement membrane – and to fungal elements. The Ziehl-Neelsen stain is used to detect acid-fast rods; the Warthin-Starry stain is used for spirochetes; and Congo red staining for amyloid deposits.

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In the context of inflammatory skin diseases, immunohistochemical processing may also be useful. For this purpose, the tissue to be examined is incubated with antibodies conjugated to an enzyme that catalyzes a color-producing reaction. This method allows for a large number of pathogen-related skin diseases to be reliably diagnosed [5] (Table 2). In the diagnosis of infectious skin diseases, further molecular biology workup may be useful, especially in cases where antibody-based tests are not available or pathogen typing is required. Such workup should be arranged or performed by the dermatopathologist [6, 7]. In addition, immunohistochemical studies and other molecular biology procedures such as clonality testing are useful – and frequently required – in differentiating inflammatory from neoplastic infiltrates [8] (Table 2).

Direct immunofluorescence studies

In direct immunofluorescence studies, morphological detection of tissue autoantibodies is carried out using secondary antibodies (anti-IgG, -IgM, -IgA, -C3) labeled with a fluorescence dye. This technique is of particular importance in the diagnosis of bullous dermatoses, connective tissue disorders, and vasculitides, and involves the incubation of cryostat sections from fresh tissue (without prior treatment with formalin) with fluorescence-labeled antibodies. Using a fluorescence microscope, autoantibody deposits in the epidermis, basement membrane, or vessels can thus be readily detected.

Direct immunofluorescence is of particular importance in the diagnosis of bullous dermatoses, connective tissue disorders, and vasculitides.

Table 2 Common histological/immunohistochemical stains in the diagnosis of inflammatory skin diseases.

Stain	Staining characteristics
Hematoxylin and eosin (H&E)	Standard stain in routine histology
Periodic acid-Schiff (PAS)	Fungi, glycogen, amyloid
Giemsa	Bacteria, parasites, mast cells
Prussian blue	Hemosiderin
Kossa	Solid calcium salts
Elastica/van Gieson	Elastic fibers, collagen fibers, muscle fibers
Ziehl-Neelsen	Acid-fast rods
Chloroacetate esterase	Mast cells, neutrophils, myelomonocytic cells
Congo red	Amyloid
Thioflavin	Amyloid
Alcian blue	Mucin
Gram	Bacteria
CD1a (clone MTB1)	Leishmania
Anti-treponemal antibodies	Treponema
Anti-herpes simplex virus antibodies	Herpes simplex virus
Anti-varicella zoster virus antibodies	Varicella zoster virus
Anti-dermatophyte antibodies	Dermatophytes, molds
Anti-leishmania antibodies	Leishmania

Frozen-section studies in the diagnosis of inflammatory skin diseases

Frozen sections are not useful in the workup of inflammatory skin diseases, as the lack of fixation limits the extent to which a specimen can be assessed. Given the fulminant clinical course and the therapeutic urgency associated therewith, the diagnosis of (or ruling out) Lyell's syndrome/toxic epidermal necrolysis (TEN), respectively its differentiation from other bullous dermatoses, is the only rational indication for frozen-section studies and, in this context, of key importance. Fresh tissue (without prior formalin fixation) is immediately flash-frozen in liquid nitrogen in order to obtain cryostat sections, which are then stained using routine staining procedures (primarily H&E and PAS). At the same time, another part of the specimen should be fixed in formalin, and routinely processed for subsequent confirmation of the diagnosis.

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Histological appraisal

Morphological procedure for examining histological specimens

In order to obtain an overview of the architecture and number of sections, all specimens are initially microscoped at low power. While every dermatopathologist

ultimately has his or her own strategy, a systematic approach has proven useful, for instance, beginning with an assessment of epidermal changes (stratum corneum, the epidermis as a whole, basement membrane zone), followed by dermal changes, the subcutaneous adipose tissue, as well as vessels and adnexal structures.

Various histopathological algorithms and clues are available that may prove particularly helpful in classifying the histological changes observed, thus allowing for a histological diagnosis and potential differential diagnoses to be established. The more specific the histological changes are, the more reliably can a diagnosis be made. The more nonspecific the histological changes are, the greater the need for additional information (on the histology request form). It is up to the clinician to correlate the histological with the clinical diagnosis, as only he has comprehensive insight into the clinical picture, the case history, and the disease course. In the event of discrepancies, it is always recommended to confer with the dermatopathologist to exchange additional information.

Only the clinician has comprehensive insight into the clinical picture, the case history, and the disease course. In the event of discrepancies with respect to the histological findings, it is always recommended to confer with the dermatopathologist to exchange additional information.

For the clinician, basic knowledge of histological terminology [9] (Table 3) as well as the most common inflammatory patterns and their differential diagnoses is highly valuable for the correct classification and interpretation of histological findings.

Special diagnostic workup of inflammatory skin disorders

Given that clinically unambiguous cases rarely require biopsy, the majority of specimens of inflammatory skin diseases do not exhibit a typical histological picture. Consequently, for a correct diagnosis of inflammatory lesions to be made, the dermatopathologist frequently requires clinicopathological correlation. On the one hand, there are dermatoses that usually cannot be differentiated on histological grounds, or only with great difficulty (Figure 1). On the other hand, depending on disease stage (acute, subacute, chronic, in the process of resolution), one and the same disorder is frequently characterized by varying histological features (life of lesions) (Figure 2). In addition, there is variation in the histological picture depending on location, prior treatment, associated disorders or comorbidities, patient age, as well as artifacts, which may be patient-induced (for example, scratching), or caused by an inadequate biopsy technique and subsequent tissue processing.

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In principle, the algorithmic method based on pattern analysis according to A. Ackermann has proven useful in the systematic approach to inflammatory skin diseases [10]. In the following paragraphs, these basic principles will be presented in simplified form (an up-to-date, complete, and detailed presentation can be found in the current edition of "Histologic diagnosis of inflammatory skin diseases" [10].

A distinction can be made between various distribution patterns of inflammatory infiltrates:

- Perivascular dermatitis
- Nodular and diffuse dermatitis
- Vasculitis and vasculopathy
- Periinfundibulitis/perifolliculitis and alopecia
- Fibrosing dermatitis
- Panniculitis
- Pustular dermatitis
- Vesicular dermatitis (intraepidermal and subepidermal vesicular dermatitis)

In addition to the aforementioned distribution patterns, other criteria – including the composition of the inflammatory infiltrate, epidermal changes, or deposits

Table 3 Important histological terms.

Epidermis	
Atrophy	Thinning
Hyperkeratosis	Thickening of the corneal layer
Orthokeratosis	Regular cornification
Parakeratosis	Impaired and incomplete cornification with nuclear material detectable in cells of the corneal layer
Dyskeratosis	Premature or impaired cornification of individual keratinocytes
Hypergranulosis	Thickening of the granular layer
Agranulosis	Absent granular layer
Acanthosis	Thickening of the epidermis (without stratum corneum)
Ballooning degeneration	Intracellular edema, large and pale keratinocytes
Spongiosis	Intercellular edema
Acantholysis	Loss of adhesion or impaired formation of (new) intercellular junctions between keratinocytes; associated with round keratinocytes.
Psoriasiform hyperplasia	Epidermal hyperplasia with elongation of rete ridges, frequently associated with parakeratosis
– regular	*Prototype:* psoriasis
– irregular	*Prototype:* chronic eczema
Interface dermatitis	Degeneration and necrosis of basal keratinocytes with vacuolization of the basement membrane zone; lymphocytes along the dermoepidermal junction
– vacuolar	*Prototype:* erythema multiforme; only sparse lymphocytes in the papillary layer
– lichenoid	*Prototype:* lichen planus; dense, band-like lymphocytic infiltrate
Pustule	Vesicle filled with neutrophils
Exocytosis	Migration of inflammatory cells from the dermis to the epidermis
Pigment incontinence	Pigment transfer into the upper dermis due to basal cell necrosis; pigment deposition in macrophages
Dermis	
Fibrosis	Cell-rich connective tissue proliferation
Sclerosis	Cell-poor connective tissue proliferation; thickening and/or hyalinization of collagen fibers
Actinic elastosis	UV-induced basophilic connective tissue degeneration

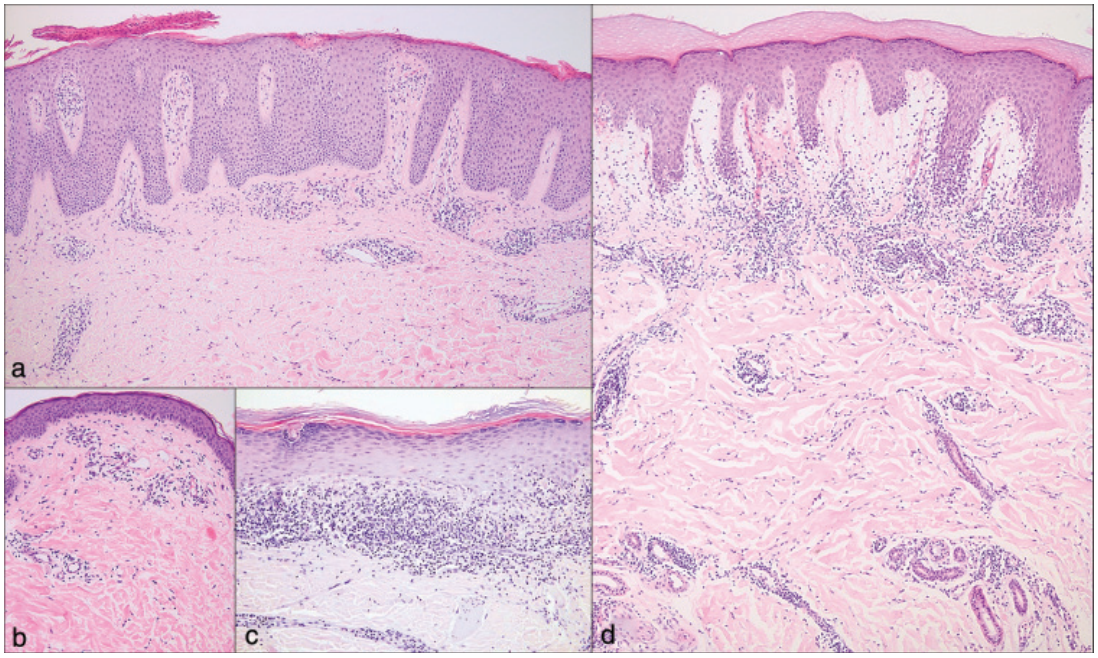

Figure 1 Diagnoses that cannot be differentiated on histological grounds, or only with great difficulty. Psoriasis with secondary changes or chronic eczema? Hyperparakeratosis with incorporation of neutrophils and serum. Acanthosis of the epidermis with widened and elongated but also somewhat plump rete ridges; rarefaction of the granular layer (hematoxylin-eosin stain [H&E], original magnification x 100) (a). Drug rash or viral rash? No significant epidermal changes but a superficial perivascular lymphocytic inflammatory infiltrate (H&E, x 100) (b). Lichen planus, lichenoid drug eruption, or graft-versus-host disease? Orthohyperkeratosis and hydropic changes of the basal cell layer with single cell necrosis; band-like lymphocytic inflammatory infiltrate; pigment incontinence (H&E, x 100) (c). Chilblain lupus or frostbites? Regular epidermis, pronounced dermal edema, and a dense perivascular and periadnexal lymphocytic inflammatory infiltrate without evidence of mucin deposits (H&E, x 100) (d).

– are used to arrive at a diagnosis or at least narrow it down to a specific group of differential diagnoses.

Perivascular dermatitis

Histopathologically, the majority of inflammatory skin diseases exhibit the basic pattern of perivascular dermatitis as described by Ackermann.

Histopathologically, the majority of inflammatory skin diseases exhibit the basic pattern of perivascular dermatitis as described by Ackermann. Consequently, there is a wide spectrum of differential diagnoses. Histologically, a distinction can be made between superficial perivascular (inflammatory infiltrate is located in the papillary or upper reticular dermis) and superficial and deep perivascular (inflammatory infiltrate is also located in deeper areas of the dermis). Based on changes in the epidermis and the quality of the inflammatory infiltrate, a wide range of disorders may be included in the differential diagnostic considerations. With respect to the epidermis, the finding of interface dermatitis (Table 3) constitutes a key criterion for the classification of perivascular inflammatory patterns. The term interface dermatitis designates a lymphocytic inflammatory response at the dermoepidermal junction with subsequent apoptosis of keratinocytes. This leads to vacuolization of the basement membrane zone, which, in its most severe form, may result in cleft formation. The most important differential diagnoses of perivascular dermatitis are presented in Table 4.

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However, pattern analysis does have its limits (Figure 1): merely on morphological grounds, a more accurate diagnosis of superficial perivascular dermatitis

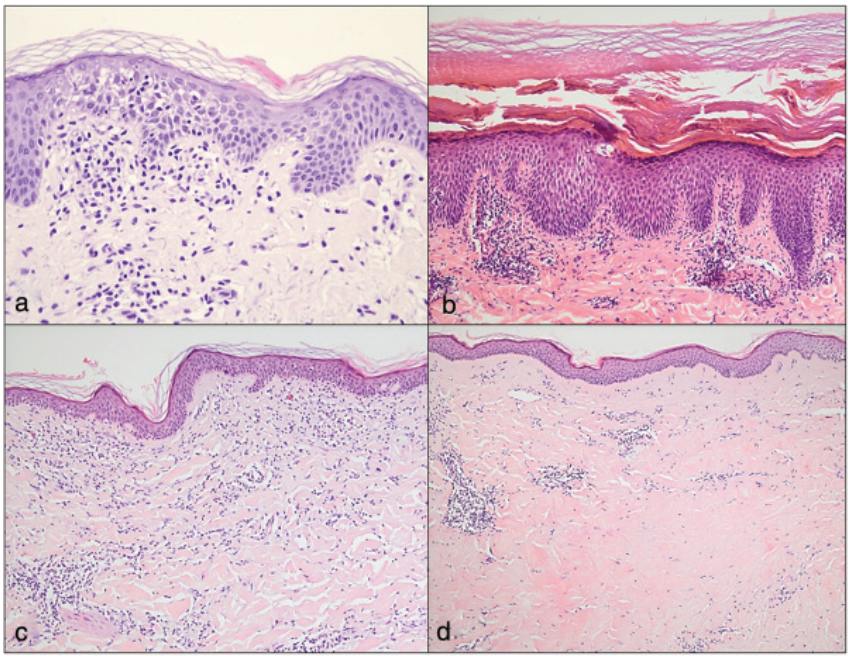

Figure 2 Life of lesions. Acute dermatitis: the typical pattern is that of superficial perivascular lymphocytic spongiotic dermatitis (hematoxylin-eosin stain [H&E], original magnification x 200) (a). Chronic eczema: in addition, there is irregular acanthosis of the epidermis with hypergranulosis and parakeratosis, which may correspond to 'psoriasiform dermatitis' (H&E, x 100). Early-stage morphea: regular epidermis, expansion of the reticular dermis with a moderate perivascular and interstitial inflammatory infiltrate (H&E, x 100) (b). Late-stage morphea: increased and thickened collagen bundles as well as lymphocytes and plasma cells (H&E, x 100) (c).

without epidermal involvement as drug rash or viral rash is not possible (Figure 1b). Similarly, it may be very difficult to precisely diagnose a psoriasiform dermatitis lesion as plaque psoriasis or chronic eczema, especially in case of pretreatment or secondary changes, which may blur the clear distinction (loss of typical psoriasiform hyperplasia) (Figure 1a). Figure 3 presents further examples of perivascular dermatitis marked by various epidermal changes.

Nodular and diffuse dermatitis

A nodular accumulation of histiocytes is referred to as granuloma.

Nodular and diffuse dermatitis is characterized by an inflammatory infiltrate that shows a circumscribed nodular distribution in case of the former, and a dense distribution across the entire dermis in case of the latter variant. Depending on the composition of the infiltrate, a number of potential histological differential diagnoses exist. A nodular accumulation of histiocytes is referred to as granuloma. Based on their structure, a distinction can be made – among others – between tuberculoid granulomas, typically rimmed by lymphocytes, sarcoidal granulomas, characterized by no or only scarce lymphocytic infiltrates (Figure 4a, b), palisading granulomas, marked by mucin and fibrin deposits at the center and surrounded by radially arranged histiocytes (Figure 4c, d), and suppurative granulomas, with central neutrophil accumulations (Figure 4e, f). A simplified list of the most common differential diagnoses of nodular dermatitis is presented in Table 5.

Table 4 Perivascular dermatitis (according to Ackermann).

Distribution of the infiltrate	Epidermal changes	Differential diagnosis
Superficial	Without epidermal involvement	Urticaria Dermatophytosis Drug rash or viral rash (Fig. 1)
	Spongiosis	Allergic contact dermatitis (Fig. 2) Nummular dermatitis Dyshidrotic eczema Photodermatitis Pityriasis rosea
	Psoriasiform	Psoriasis (Fig. 3) Seborrheic or chronic dermatitis (Fig 2) Dermatophytosis
	Interface dermatitis	
	– vacuolar	Erythema multiforme (Fig. 3) Drug rash Pityriasis lichenoides
	– lichenoid	Lichen planus (Fig. 3) Mycosis fungoides Drug eruption
Superficial and deep	Without epidermal involvement	Lupus tumidus Polymorphic light eruption
	Spongiosis	Arthropod reaction Photodermatitis
	Psoriasiform	Dermatophytosis Syphilis Mycosis fungoides
	Interface dermatitis	Lupus erythematosus (Fig. 3) Fixed drug eruption

Diffuse dermatitis rich in plasma cells should raise suspicion for a pathogen-induced skin disease (for example, borreliosis, syphilis, or leishmaniasis).

Depending on the composition of the inflammatory infiltrate, the term "diffuse dermatitis" encompasses a very heterogeneous group of differential diagnoses. An infiltrate rich in plasma cells should always raise suspicion for a pathogen-induced skin disease (for example, borreliosis, syphilis, or leishmaniasis); a large number of mast cells, on the other hand, is indicative of mastocytosis. In this context, additional immunohistochemical tests may prove useful (Table 2). If the inflammatory infiltrate contains a large number of foamy histiocytes, disorders such as xanthelasma, xanthoma, or xanthogranuloma have to be considered.

Vasculitis and vasculopathy

There are various schools of thought with regard to the nomenclature and classification of vasculitides and vasculopathies. However, the following rule applies in principle: an occlusive vascular disorder, vasculopathy is characterized by only secondary vascular inflammation, whereas vasculitis constitutes primary vessel inflammation.

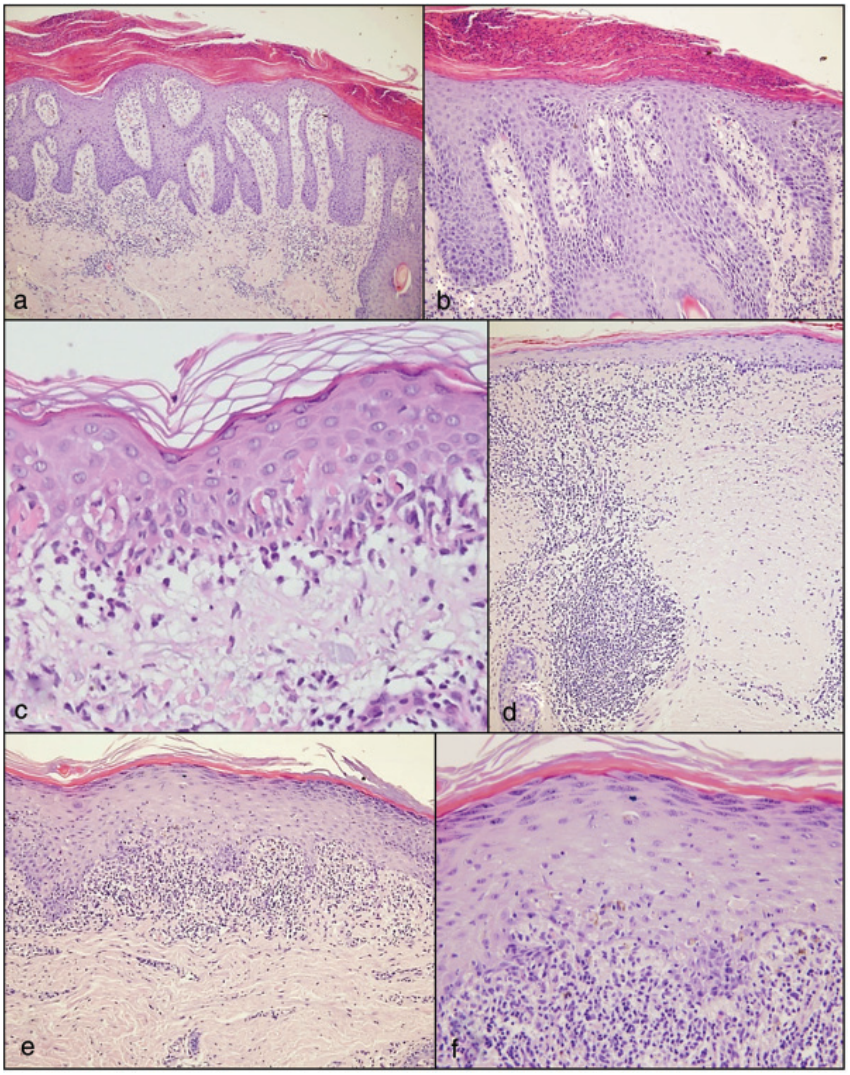

Figure 3 Common dermatoses with a perivascular inflammatory infiltrate yet different epidermal changes. Psoriasis (panoramic view): superficial perivascular psoriasiform dermatitis. Pronounced hyperparakeratosis and regular acanthosis with elongated rete ridges (hematoxylin-eosin stain [H&E], original magnification x 100) (a). Psoriasis (high power): hyperparakeratosis with pustular accumulation of neutrophils, loss of the granular layer, basal cell mitoses, and epidermal atrophy above the papillae (H&E, x 200) (b). Erythema multiforme: superficial perivascular and lichenoid interface dermatitis with vacuolar degeneration of keratinocytes (H&E, x 400) (c). Lupus erythematosus. Superficial and deep perivascular and periadnexal lymphocytic infiltrate; vacuolar degeneration of basal keratinocytes. Mucin deposits in the dermis (H&E, x 100) (d). Lichen planus (panoramic view): 'Sawtooth' acanthosis of the epidermis with hypergranulosis; superficial perivascular and lichenoid interface dermatitis (H&E, x 100) (e). Lichen planus (high power): orthohyperkeratosis, hypergranulosis; vacuolar degeneration and single cell necrosis of basal keratinocytes. Band-like lymphocytic inflammatory infiltrate (H&E, x 200) (f).

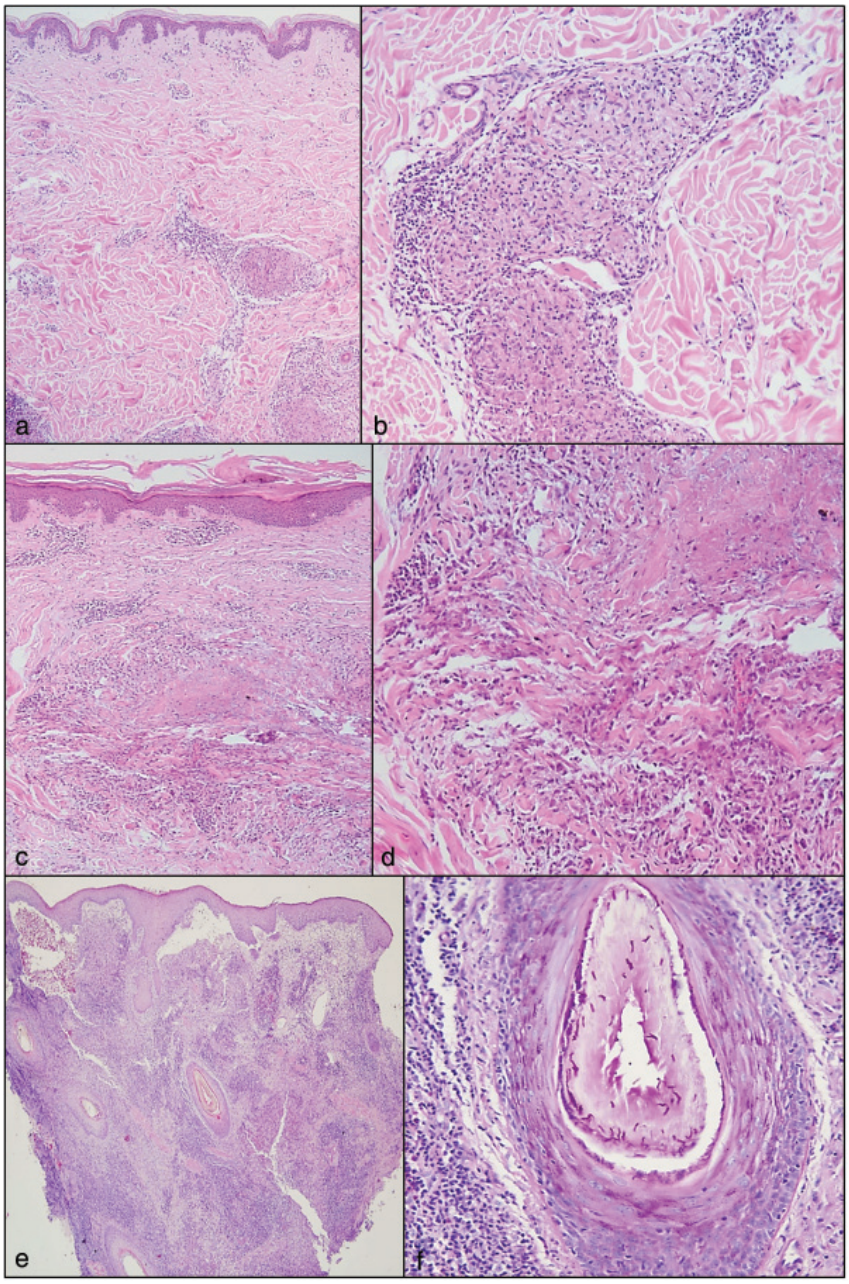

Figure 4 Nodular dermatitis. Sarcoidosis (panoramic view): regular epidermis; in the mid-dermis, nodular accumulation of epithelioid histiocytes (hematoxylin-eosin stain [H&E], original magnification x 40) (a). Sarcoidosis (high power): typical "naked" epithelioid cell granuloma with only very few lymphocytes (H&E, x 400) (b). Granuloma annulare (panoramic view): nodular interstitial accumulation of spindle-shaped histiocytes in the mid-dermis (H&E, x 100) (c). Granuloma annulare (high power): radially arranged interstitial spindle-shaped histiocytes with circumscribed mucin deposits at the center (H&E, x 400) (d). Deep mycosis (panoramic view): suppurative granuloma with perifollicular nodular accumulation of neutrophils, epithelioid histiocytes, as well as multinucleated giant cells (H&E, x 40) (e). Deep mycosis (high power, PAS): detection of PAS-positive fungal elements in the hair shaft of a destroyed follicle, which gave rise to suppurative granuloma (PAS stain, x 400) (f).

Table 5 Nodular Dermatitis (according to Ackermann).

Composition of the infiltrate	Differential diagnoses
Lymphocytes	Lymphoma Pseudolymphoma
Neutrophils	Sweet's syndrome Ruptured hair follicle cyst
Histiocytes (granulomas)	
– tuberculoid	Tuberculosis, leishmaniasis
– sarcoidal	Sarcoidosis (Fig. 4), orofacial granulomatosis
– palisading	Granuloma annulare (Fig. 4), necrobiosis lipoidica, gout
– suppurative	Atypical mycobacteriosis, deep mycosis (Fig. 4), foreign body granuloma

The most common cutaneous vasculitis, leukocytoclastic vasculitis predominantly affects small superficial dermal vessels.

Using a broad schematic classification, a distinction can be made between vasculitis of small vessels, found throughout the dermis, and vasculitis of larger vessels (subcutis). Depending on the age of the biopsied lesion (life of lesions), there are a number of histomorphological criteria of vasculitis [4]. Irrespective of the type of vasculitis and the characteristics of its infiltrate, inflammatory infiltrates of acute lesions are located inside the lumen and within the vessel wall, sometimes associated with destruction thereof as well as intramural or intraluminal fibrin deposits. Features of longstanding lesions, on the other hand, include – among others – vessel wall fibrosis and luminal occlusion [4]. The most common cutaneous vasculitis, leukocytoclastic vasculitis predominantly affects small superficial dermal vessels (Figure 5). It is characterized by a neutrophil-rich perivascular infiltrate with erythrocyte extravasation and neutrophil degradation (leukocytoclasia). Using direct immunofluorescence, intravascular and perivascular deposits of autoantibodies directed against C3, IgA, IgM, IgG, and fibrinogen can be detected in fresh lesions within the first 24–48 hours. While leukocytoclastic vasculitis can occur in the context of various disorders such as Henoch-Schönlein purpura and urticarial vasculitis, there are also post-infectious or paraneoplastic forms, as well as those occurring in association with connective tissue disorders and autoinflammatory syndromes. Here, too, the exact pathogenetic classification decisively hinges on clinicopathological correlation. In case of subcutaneous large-vessel involvement, differential diagnostic considerations will have to include polyarteritis nodosa, giant cell arteritis (Figure 5), or Wegener's disease.

Periinfundibulitis/perifolliculitis and alopecia

For deep trichophytia to be diagnosed, it is essential to biopsy a fresh lesion that includes hair shafts, as dermatophytes can only be detected in hair shafts but not in the affected tissue.

Periinfundibulitis and perifolliculitis are marked by a broad and heterogeneous clinical spectrum. In the case of perifolliculitis, inflammatory infiltrates are located in direct vicinity of the hair follicle; this applies, for example, to alopecic disorders, rosacea, lichen planopilaris, and CDLE. Folliculitis is characterized by a superficial or deep suppurative inflammatory response. Important differential diagnoses include dermatophytosis, furuncle, or secondary syphilis. For deep trichophytia to be diagnosed, it is essential to biopsy a fresh lesion that includes hair shafts, as dermatophytes can only be detected in hair shafts but not in the affected tissue. In case of clinical and histological suspicion of deep trichophytia, the dermatopathologist

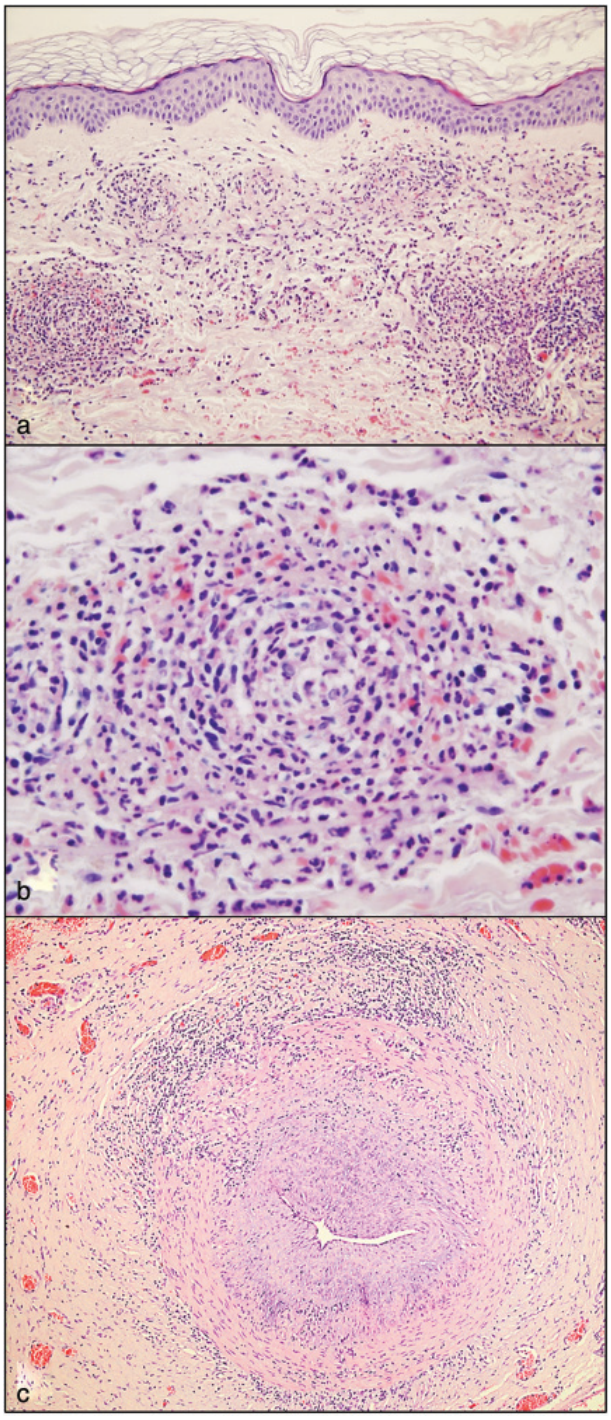

Figure 5 Vasculitis. Leukocytoclastic vasculitis (panoramic view): cuff-like perivascular accumulation of (predominantly) neutrophils in the upper and mid-dermis (hematoxylin-eosin stain [H&E], original magnification x 100) (a). Leukocytoclastic vasculitis (high power): thrombosed venule with endothelial swelling and fibrin deposits; marked leukocytoclasia of neutrophils with nuclear dust and erythrocyte extravasation (H&E, x 400) (b). Giant cell arteritis: significant narrowing of the vascular lumen resulting in near occlusion. Aggregates of histiocytes and giant cells are found within the thickened vessel wall (H&E, x 40) (c).

has to closely examine all available hair shafts (PAS staining), sometimes in numerous serial sections.

It is not uncommon for pseudopelade-like scalp conditions to be biopsied with the objective to determine which inflammatory skin disease actually caused the scarring (lichen planopilaris, lupus erythematosus, folliculitis decalvans, frontal fibrosing alopecia). Histologically, the dermatopathologist then frequently encounters dermal fibrosis with angiofibrotic strands that have replaced the follicles, often without specific inflammatory infiltrates to suggest one disorder or the other. In order to avoid this situation, it is recommended to biopsy a fresh lesion at the periphery of the alopecic area that still contains hair follicles; the biopsy should be taken at an oblique angle in the direction of hair growth. It is important to make a remark on the histology request form with regard to the suspected diagnosis so that transverse sections can also be prepared, if the dermatopathologist considers them diagnostically useful.

In order to be able to diagnose specific inflammatory changes, it is recommended to biopsy a fresh lesion at the periphery of the alopecic area that still contains hair follicles; the biopsy should be taken at an oblique angle in the direction of hair growth.

Fibrosing/sclerosing dermatitis

Frequently resulting from an inflammatory process, trauma, or neoplasm, the group of disorders referred to as fibrosing/sclerosing dermatitis is marked by a broad spectrum of differential diagnoses. Changes in connective tissue – collagen fibers, elastic fibers, and fibroblasts – are the hallmark of fibrosing/sclerosing dermatitis. While a proliferation of fibroblasts and collagen fibers in association with a loss of elastic fibers is referred to as fibrosis, a decreased number of fibroblasts accompanied by an increase in the number or density of collagen fibers is designated as sclerosis. A combination of these two patterns is called fibrosclerosis. Cutaneous fibrosis and sclerosis can, on the one hand, be a secondary manifestation in the context of chronic inflammatory responses such as prurigo nodularis or panniculitis but also occur as regression phenomenon in neoplasms. On the other hand, there are primary inflammatory conditions associated with fibrosis, sclerosis, or fibrosclerosis. The most prominent example of sclerosing dermatitis is morphea (Figure 2). Late-stage lichen sclerosus et atrophicus frequently shows fibrosclerosis of the connective tissue, with an increase – and in particular homogenization/hyalinization – of collagen fibers, as well as a reduction in the number of fibroblasts and elastic fibers.

Cutaneous fibrosis and sclerosis may be a secondary manifestation in the context of chronic inflammatory responses.

Panniculitis

The term panniculitis refers to an inflammation of the subcutaneous adipose tissue. Depending on the predominant distribution pattern of the inflammatory infiltrate, an initial distinction can be made between predominantly septal panniculitis (the inflammatory infiltrate is mostly located in the septa) and predominantly lobular panniculitis (the inflammatory infiltrate is mostly located within the lobules of the adipose tissue) (Figure 6). Given that longstanding lesions may show an overlap between septal and lobular panniculitis, said differentiation may become problematic. Fresh lesions are therefore best suited to accurately diagnose panniculitis. Other important histological characteristics used in classifying panniculitis include the presence of vasculitis as well as the quality of the inflammatory infiltrate. The prototype of septal panniculitis without vasculitis, erythema nodosum is the most common form of panniculitis, associated with a predominantly histiocytic inflammatory infiltrate interspersed with neutrophils and late-stage septal fibrosis. The differential diagnostic spectrum of lobular panniculitis is considerably broader and more diverse. Table 6 contains a list of important differential diagnoses of panniculitis.

Depending on the predominant distribution pattern of the inflammatory infiltrate, an initial distinction can be made between septal panniculitis (the inflammatory infiltrate is mostly located in the septa) and lobular panniculitis (the inflammatory infiltrate is mostly located within the lobules of the adipose tissue).

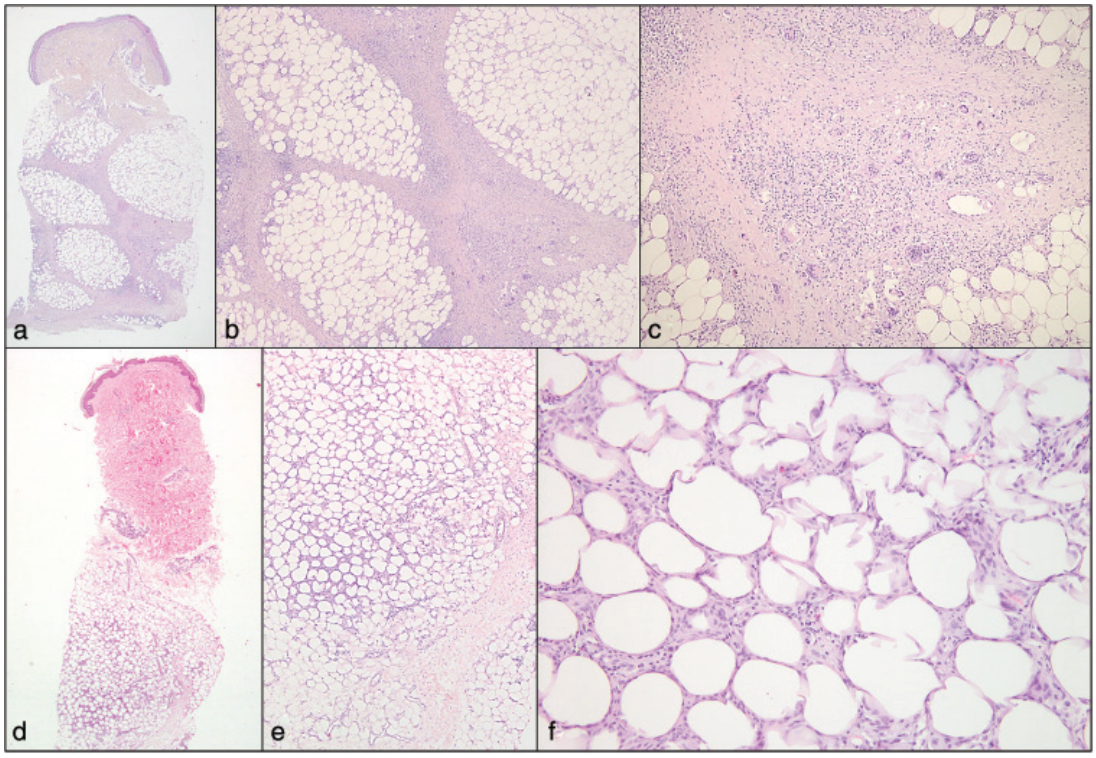

Figure 6 Panniculitis. Erythema nodosum (panoramic view): predominantly septal panniculitis (hematoxylin-eosin stain [H&E], original magnification x 20) (a). Erythema nodosum (high power): significantly widened septa of the adipose tissue, with inflammatory cells that also infiltrate the peripheral adipose tissue lobules (H&E, x 40) (b). Erythema nodosum (high power): the septa contain numerous histiocytes, neutrophils, and multinucleated giant cells (H&E, x 100) (c). Cold panniculitis (panoramic view): predominantly lobular panniculitis (H&E, x 20) (d). Cold panniculitis (high power): inflammatory infiltrate between the lobules, largely regular septa (H&E, x 40) (e). Cold panniculitis (high power): ruptured adipocytes (H&E, x 200) (f).

Pustular dermatitis

Common examples of intraepidermal pustular dermatitis include dermatophytosis, acute generalized exanthematous pustulosis (AGEP), impetigo, and pustular psoriasis.

A pustule is characterized by intraepidermal accumulation of neutrophils, most commonly intracorneally or subcorneally. The location of said accumulation as well as associated epidermal changes, such as spongiosis or acantholysis, determine the various differential diagnoses to be considered. For a more detailed presentation, see reference [10]. Common examples of intraepidermal pustular dermatitis include dermatophytosis, acute generalized exanthematous pustulosis (AGEP), impetigo, and pustular psoriasis.

Table 6 Panniculitis (according to Ackermann).

	Septal panniculitis	Lobular panniculitis
Without vasculitis	Erythema nodosum (Fig. 6) Necrobiosis lipoidica	Lupus panniculitis Pancreatic panniculitis Alpha-1 antitrypsin deficiency-associated panniculitis Cold panniculitis (Fig. 6)
With vasculitis	Polyarteritis nodosa Thrombophlebitis	Erythema nodosum leprosum Erythema induratum of Bazin

Vesicular dermatitis

Based on the level of cleft formation, vesicular skin diseases are generally classified as intraepidermal vesicular and subepidermal vesicular dermatoses. Showing a broad etiological spectrum, clinical manifestations include primary autoimmune and hereditary vesicular dermatoses, disorders associated with secondary blistering such as bacterial and viral infections, as well as drug eruptions or reactions to physical noxae. Common to all these different disorders is the loss of adhesion, either between keratinocytes or along the basement membrane zone.

Vesicular skin diseases are characterized by loss of adhesion, either between keratinocytes or along the basement membrane zone.

Intraepidermal vesicular dermatitis

Intraepidermal vesicles represent markedly pronounced epidermal changes caused by acantholysis, spongiosis, or keratinocyte ballooning. Based on these epidermal changes, intraepidermal vesicular skin diseases can be further differentiated. The most common differential diagnoses are presented in simplified form in Table 7. Essential elements in the accurate diagnosis of intraepidermal vesicular autoimmune dermatoses include the detection of autoantibodies as well as antigen characterization. Apart from the clinical picture and histological findings, genetic tests aimed at detecting the mutation responsible for the impaired intraepidermal adhesion are of key importance in the diagnostic workup of hereditary vesicular disorders. With respect to secondary intraepidermal blistering, further differentiation is based on the level of cleft formation, the pattern of the infiltrate, and other potential epidermal changes (such as single cell necrosis, dyskeratosis, virus-induced cytopathic changes with ballooning degeneration, eosinophilic nuclear inclusions, peripheral nuclear chromatin, and multinucleated keratinocytes, as well as the detection of bacteria or fungal elements). Table 7 contains a list of the most common intraepidermal bullous dermatoses.

Essential elements in the accurate diagnosis of intraepidermal vesicular autoimmune dermatoses include the detection of autoantibodies as well as antigen characterization.

Subepidermal vesicular dermatitis

The diagnostic differentiation of subepidermal vesicular skin diseases is very challenging, as the basement membrane zone presents as a fine and homogeneous structure under the light microscope. Only on electron microscopy is it possible

Table 7 Intraepidermal vesicular dermatitis (excerpts).

Epidermal changes	Differential diagnoses
Acantholysis	Pemphigus foliaceus Pemphigus vulgaris (Fig. 7) Grover's disease Darier's disease (Fig. 7) Hailey-Hailey disease Staphylococcal scalded skin syndrome
Spongiosis	Arthropod reaction Dermatophytosis Allergic contact dermatitis
Ballooning	Herpesvirus infection (Fig. 7) Pellagra

Detection of autoantibodies and antigen characterization are crucial in the diagnosis of subepidermal vesicular autoimmune dermatoses. The workup of hereditary subepidermal vesicular dermatoses is aimed at identifying mutations in associated structural proteins.

to subdivide the basement membrane zone into its two main components: lamina lucida and lamina densa. Detection of autoantibodies (Figure 8) and antigen characterization are crucial in the diagnosis of subepidermal vesicular autoimmune disorders. The workup of hereditary subepidermal vesicular dermatoses, on the other hand, is aimed at identifying mutations in associated structural proteins. Table 8 shows the most common differential diagnoses depending on the composition of the inflammatory infiltrate.

Differentiation of bullous dermatoses using immunofluorescence studies

Direct immunofluorescence studies allow for the detection of tissue-bound autoantibodies and complement factors (in vivo). By contrast, indirect immunofluorescence is used to detect circulating serum autoantibodies directed against intercellular or basement membrane antigens.

Direct and indirect immunofluorescence studies play a key role in the differentiation of vesicular dermatoses. In this context, attention should be paid to the correct biopsy technique (Table 1). Direct immunofluorescence studies allow for the detection of tissue-bound autoantibodies and complement factors (in vivo). By contrast, indirect immunofluorescence is used to detect circulating serum autoantibodies directed against intercellular or basement membrane antigens. Autoimmune bullous dermatoses with intraepidermal cleft formation are characterized by intercellular IgG (rarely also IgA and IgM) and C3 deposits in the epidermis (Figure 7). Typical findings in subepidermal vesicular dermatoses include linear C3, IgG, and IgA deposits along the basement membrane (such as bullous pemphigoid [Figure 8], epidermolysis bullosa acquisita, linear IgA dermatosis) or in the dermal papillae (Duhring's disease). The exact location of the autoantibodies can only be determined by direct immunofluorescence on salt-split skin. Here, incubation with saline (1 mol/L) induces a defined artificial split in the basement membrane, with the lamina lucida forming the blister roof and the lamina densa the blister base. Thus, bullous pemphigoid (IgG and C3 predominantly at the blister roof) can be differentiated from epidermolysis bullosa acquisita (IgG and C3 predominantly at the base of the blister).

Table 8 Subepidermal vesicular dermatitis (excerpts).

Composition of the infiltrate	Differential diagnoses
Hardly any infiltrate	Epidermolysis bullosa acquisita Hereditary epidermolyses Cell-poor bullous pemphigoid Porphyria cutanea tarda
Lymphocytes	Bullous lichen planus Erythema multiforme, TEN/Lyell's syndrome Bullous drug eruption
Neutrophils	Duhring's disease Linear IgA dermatosis Epidermolysis bullosa acquisita Anti-p200 pemphigoid Bullous lupus erythematosus
Eosinophils	Bullous pemphigoid (Fig. 8) Bullous arthropod reaction Pemphigoid gestationis

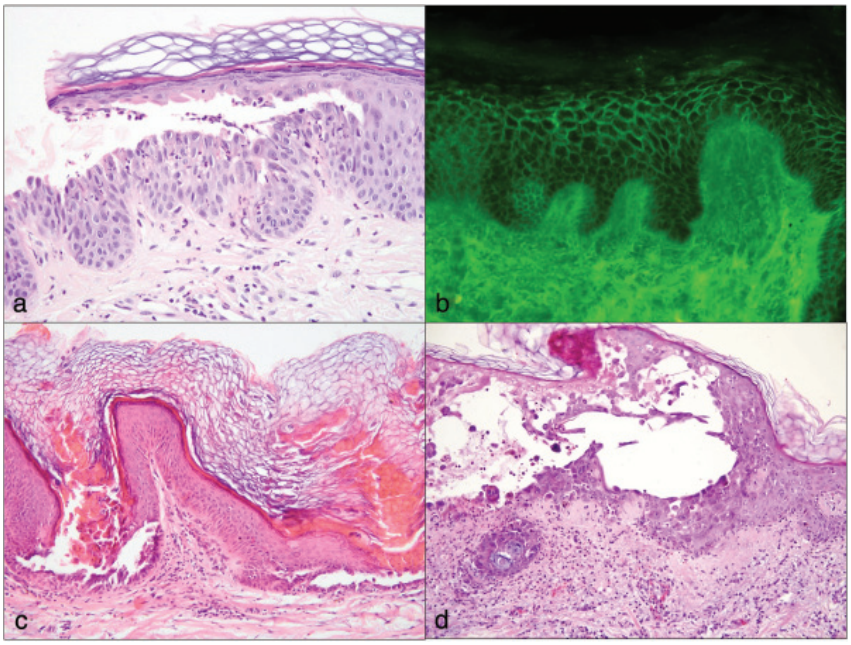

Figure 7 Intraepidermal vesicular dermatitis. Pemphigus vulgaris: intraepidermal blister formation with complete acantholysis (hematoxylin-eosin stain [H&E], original magnification x 200) (a). Direct immunofluorescence in pemphigus vulgaris, showing reticular intraepidermal IgG deposits between keratinocytes (anti-IgG, x 200) (b). Darier's disease: columnar parakeratosis and focal suprabasal acantholysis with dyskeratotic keratinocytes (H&E, x 100) (c). Herpesvirus infection: intraepidermal blister formation with acantholysis as well as ballooned, partly multinucleated keratinocytes with inclusion bodies (H&E, x 200) (d).

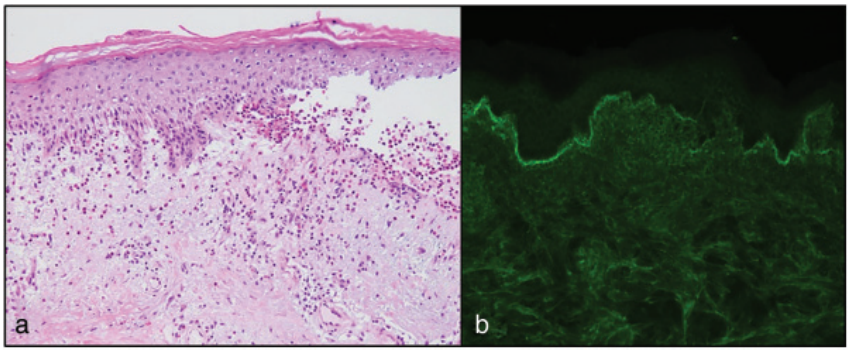

Figure 8 Subepidermal vesicular dermatitis. Bullous pemphigoid: subepidermal blistering with an eosinophil-rich inflammatory infiltrate and eosinophilic spongiosis (hematoxylin-eosin stain [H&E], original magnification x 100) (a). Direct immunofluorescence in bullous pemphigoid: linear IgG deposits along the basement membrane (anti-IgG, x 200) (b).

Differentiation of bullous dermatoses using frozen-section studies

Given the fulminant clinical course and the therapeutic urgency associated therewith, the differentiation of Lyell's syndrome/TEN from other bullous dermatoses is the only rational indication for frozen-section studies in the context of

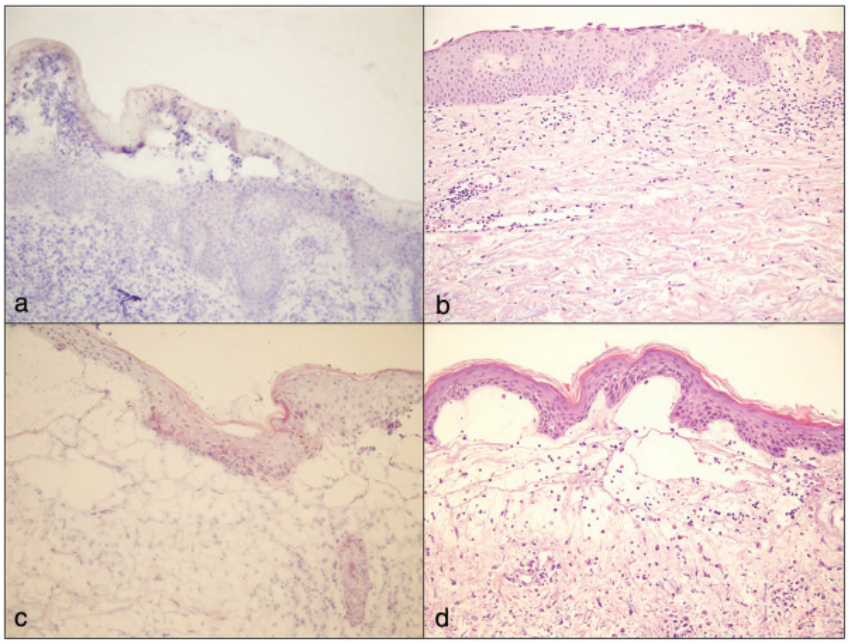

Figure 9 Two examples of clinical suspicion of Lyell's syndrome/TEN ruled out by frozen sections. For comparison, routine histology of the same patient is marked by far superior morphological quality, thus allowing for much better assessment. The frozen section shows a subcorneal blister with an intact epidermis underneath. In this case, Lyell's syndrome/TEN was ruled out (hematoxylin-eosin stain [H&E], original magnification x 40) (a). Routine histology with acantholysis of the upper stratum spinosum and the granular layer, as well as a neutrophil-rich inflammatory infiltrate. In combination with the clinical picture, these findings were consistent with staphylococcal scalded skin syndrome (H&E, x 40) (b). Frozen section showing a subepidermal blister with an intact epidermis on top (H&E, x 100). Here, too, Lyell's syndrome/TEN was ruled out (c). Routine histology confirms the findings obtained by frozen section. As there was no epidermal necrosis caused by massive apoptosis of keratinocytes, the eventual diagnosis was bullous drug eruption (H&E, x 100) (d).

inflammatory skin diseases (Figure 9). Histologically, Lyell's syndrome/TEN is marked by pronounced epidermal necrosis due to massive apoptosis of keratinocytes with subsequent subepidermal cleft formation. Due to the less-than-ideal morphology, frozen-section studies are only suitable with respect to the histological detection of blisters, their location (intraepidermal or subepidermal), and the detection of (or ruling out) confluent single cell necroses. Frozen sections also allow for conclusions to be drawn as to the characteristics of the infiltrate. Simultaneously, it is imperative that the diagnosis be confirmed on paraffin sections.

Table 9 presents the most important differential diagnoses in case of clinical suspicion of Lyell's syndrome/TEN, according to the level of cleft formation.

Summary

The histological diagnosis of inflammatory skin diseases is based on systematic pattern analysis. The more specific the pattern, the more clearly can the differential diagnoses be narrowed down. This task becomes increasingly difficult with nonspecific or overlapping patterns. In such cases, detailed clinical information may be of great help in addition to special stains. In order to be able to correctly classify histological

Table 9 Important differential diagnoses in case of clinical suspicion of Lyell's syndrome/TEN using frozen sections, according to the level of cleft formation.

Level of cleft formation	Differential diagnoses
Subcorneal (epidermis intact below the cleft; above the cleft, there is only the corneal layer)	Staphylococcal scalded skin syndrome Bullous impetigo Pemphigus foliaceus IgA pemphigus Friction blister
Intraepidermal with acantholysis	Pemphigus vulgaris HSV/VZV infections
Subepidermal (intact epidermis above the cleft; below the cleft, there is only dermis)	Epidermolysis bullosa acquisita Bullous pemphigoid Bullous lupus erythematosus Porphyria cutanea tarda Linear IgA dermatosis Pemphigoid gestationis Duhring's disease

findings in the clinical context and to choose the appropriate biopsy technique, a basic understanding of the most important histological patterns is indispensable for clinical dermatologists. The quality of the mutual communication correlates not only with the dermatopathologist's clinical knowledge but also with the clinician's dermatopathology knowledge. The clinician's primary means of communication is the histology request form; that of the dermatopathologist, the histology report. Such communication should result in a situation where the clinical dermatologist is able to turn the histological diagnosis into a clinical diagnosis, and also to discover any discrepancies that may have occurred due to deficiencies in the biopsy material or its processing, or due to missing information on the request form. Thus, the clinician can have considerable impact on the quality of the histological findings.

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Fragen zur Zertifizierung durch die DDG

1. Das jeweilige Biopsieverfahren muss entsprechend der Verdachtsdiagnose ausgewählt werden. Welche der folgenden Aussagen trifft **nicht zu?**

a) Bei der klinischen Verdachtsdiagnose einer Pannikulitis sollte eine tiefe Skalpellbiopsie durchgeführt werden um das Fettgewebe zu erfassen.
b) Bei der klinischen Verdachtsdiagnose einer Vaskulitis der größeren Gefäße sollte eine tiefe Skalpellbiopsie durchgeführt werden, da sich die großen Gefäße in der tiefen Dermis und im Korium befinden.
c) Bei der klinischen Verdachtsdiagnose einer Mykobakteriose sollte eine zusätzliche Biopsie für die mikrobiologische Diagnostik entnommen werden.
d) Bei der klinischen Verdachtsdiagnose einer blasenbildenden Autoimmundermatose sollte eine läsionale Biopsie für die direkte Immunfluoreszenz erfolgen.
e) Bei entzündlichen Hauterkrankungen sollte eine Biopsie aus einer repräsentativen, voll entwickelten, unbehandelten Läsion erfolgen.

2. Welche Aussage zur labortechnischen Aufarbeitung einer Gewebeprobe trifft zu?

a) Das entnommene Gewebe wird vom Operateur unmittelbar in Paraffin eingelegt und so fixiert.
b) Bevor das Gewebe abhängig von Größe und Verdachtsdiagnose zugeschnitten wird, erfolgt zuerst eine Dehydration des Gewebes.
c) Durch Fixierung und Paraffineinbettung kann es zu einem Volumenverlust von 30–50 % des Gewebes kommen.
d) Der auf den Objektträger gezogene Schnitt ist ca. 1 mm dick.
e) Die Standardfärbung in der Routinediagnostik entzündlicher Hautveränderungen ist die Gram-Färbung.

3. Welche der folgenden Aussagen zu dermatohistologischen/immunhistochemischen Färbungen in der Diagnostik entzündlicher Dermatosen trifft **nicht zu?**

a) Hämatoxylin und Eosin (HE) ist die Standardfärbung in der Routinehistologie.
b) Die Chloracetatesterase-Färbung kann sehr hilfreich bei der Fragestellung „Mastozytose?“ sein.
c) Mit der PAS-Färbung werden Pilze, Glykogen und Amyloid dargestellt.
d) Die Anti-Treponema-Ak-Färbung ist sinnvoll um eine Lues zu diagnostizieren.
e) Mit der Kongorot- und Thioflavin-Färbung lassen sich Bakterien nachweisen.

4. Die Kenntnis der histologischen Grundbegriffe ist die Voraussetzung zum Verständnis des histologischen Befundes. Welche der folgenden Aussagen trifft **nicht zu?**

a) Eine Akanthose bezeichnet eine Verdickung der Epidermis.
b) Bei den Interface-Dermatitiden unterscheidet man den vakuolären vom lichenoiden Typ.
c) Eine Spongiose bezeichnet ein interzelluläres Ödem.
d) Eine Akantholyse bezeichnet das vorzeitige oder fehlerhafte Verhornen einzelner Keratinozyten.
e) Bei der Sklerose kommt es zu einer zellarmen Bindegewebsvermehrung mit Verbreiterung und/oder Hyalinisierung kollagener Fasern.

5. Der Großteil der entzündlichen Dermatosen fällt in das Grundmuster der perivaskulären Dermatitis. Welche der folgenden Aussagen trifft **nicht zu?**

a) Bei den perivaskulären Dermatitiden unterscheidet man zunächst zwischen „oberflächig“ und „oberflächig und tief“, je nach Verteilung des Entzündungsinfiltrats in der Dermis.
b) Bei der allergischen Kontaktdermatitis, beim nummulären Ekzem und der photoallergischen Dermatitis zeigt sich histologisch eine oberflächlich perivaskuläre Dermatitis mit Spongiose.
c) Der Lupus erythematodes ist typischerweise gekennzeichnet durch eine Spongiose der Epidermis.
d) Der Lichen ruber ist der Prototyp der lichenoiden Interface-Dermatitis.
e) Bei einer psoriasiformen oberflächlich und tief perivaskulären plasmazellulären Dermatitis sollte unter anderem an eine Lues gedacht werden.

6. Bei der nodulären Dermatitis zeigt sich eine knotige Verteilung des Entzündungsinfiltrats in der Dermis. Welche der folgenden Aussagen trifft **nicht zu?**

a) Eine knotige Ansammlung von Lymphozyten bezeichnet man als Granulom.
b) Eine Differenzialdiagnose einer nodulären, neutrophilenreichen Dermatitis ist unter anderem das Sweet-Syndrom.
c) Palisadenartige Granulome sind typisch für ein Granuloma anulare.
d) Die Leishmaniose und die Tuberkulose können tuberkuloide Granulome bilden.
e) Eine tiefe Trichophytie geht mit einem suppurativem Granulom einher.

7. Welche der folgenden Aussagen zur Vaskulitis trifft **nicht zu?**

a) Die leukozytoklastische Vaskulitis ist die häufigste Vaskulitis der Haut und betrifft meist die kleinen, oberflächlich gelegenen Gefäße der Dermis.
b) Bei der leukozytoklastischen Vaskulitis zeigt sich ein perivaskuläres, neutrophilenreiches Infiltrat mit Erythrozytenextravasaten und Zerfall von Leukozyten (Leukozytoklasie).
c) Sind die großen Gefäße im Bereich der Subkutis betroffen, muss differenzialdiagnostisch u. a. an eine Polyarteriitis nodosa, eine Riesenzellarteriitis oder einen Morbus Wegener gedacht werden.
d) Die Purpura Schönlein-Henoch ist typischerweise eine lymphozytäre Vaskulitis.
e) In der direkten Immunfluoreszenzuntoklastischen können an einer frischen Läsion einer leukozytischen Vaskulitis intra- und perivaskuläre Ablagerungen von C3, IgM, IgG und Fibrinogen nachgewiesen werden.

8. Intraepidermal bullöse oder pustulöse Dermatitiden können histologisch durch die Art der epidermalen Veränderungen weiter differenziert werden. Welche der folgenden Aussagen trifft **nicht zu?**

a) Beim Pemphigus vulgaris stellt die Spongiose das Hauptpattern dar.
b) Bei einer Herpesvireninfektion kommt es zur Ballonierung der Keratinozyten.
c) Akantholyse kann u. a. ein differenzialdiagnostischer Hinweis für einen Morbus Grover, einen Morbus Darier und einen Morbus Hailey-Hailey sein.
d) Eine ausgeprägte allergische Kontaktdermatitis zeigt intraepidermale Vesikelbildung durch Spongiose.
e) Eine Dermatophytose kann mit intraepidermaler Vesikelbildung durch Spongiose einhergehen.

9. Subepidermale bullöse Dermatosen können anhand der Zusammensetzung des entzündlichen Infiltrats sowie der Autoantikörperablagerungen weiter differenziert werden. Welche Aussage trifft **nicht zu?**

a) Beim bullösen Pemphigoid zeigen sich in der direkten Immunfluoreszenzuntersuchung lineare C3- und IgG-Ablagerungen an der Basalmembran.
b) Bei der Dermatitis herpetiformis Duhring zeigen sich in der direkten Immunfluoreszenzuntersuchung IgA-Ablagerungen in den Papillarkörperspitzen.
c) Die Porphyria cutanea tarda ist gekennzeichnet durch ein dichtes neutrophilenreiches entzündliches Infiltrat.
d) Eosinophile Granulozyten sind typische Entzündungszellen für die Diagnose eines bullösen Pemphigoids.
e) Erst im Rahmen einer direkten Immunfluoreszenzuntersuchung an in sogenannter Salt-Split-Skin-Technik aufgearbeiteten Haut kann die genaue Lokalisation der Autoantikörper bestimmt und somit ein bullöses Pemphigoid (Autoantikörper vorwiegend am Blasendach) von einer Epidermolysis bullosa acquisita (Autoantikörper vorwiegend am Blasenboden) abgegrenzt werden.

10. Welche klinische Verdachtsdiagose ist die einzige Indikation für eine Schnellschnittdiagnostik bei entzündlichen Dermatosen?

a) bullöses Pemphigoid
b) Lyell-Syndrom/TEN
c) allergische Kontaktdermatitis
d) Psoriasis
e) Porphyria cutanea tarda

Liebe Leserinnen und Leser,

der Einsendeschluss an die DDA für diese Ausgabe ist der 28. February 2017.

Die richtige Lösung zum Thema „Ein mehrstufiger Algorithmus zur Diagnose seltener Genodermatosen“ in Heft 10 (October 2016) ist: 1d, 2b, 3d, 4e, 5a, 6e, 7c, 8c, 9d, 10b.

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