Skin Disorders with Pruritus

Enas A. S. Attia, Azza E. Mostafa, and Mona M. Atef

Contents

Abstract

Pruritus or itch is a poorly localized, non-adapting, unpleasant sensation that elicits a desire to scratch or rub the skin. In any case presented with pruritus, initial careful examination of the skin should be done to search for visible signs of skin disease, secondary scratch lesions, and/or ichthyotic skin changes. In this chapter, pruritic skin conditions are highlighted.

Keywords

Pruritus · Itch · Scratch · Excoriation · Lichenification · Eczema · Contact dermatitis · Atopic dermatitis · Discoid eczema · Acute eczema · Subacute eczema · Urticarial · Mast cell · Wheal · Angioedema · Acute urticaria · Chronic urticaria · Anaphylaxis · Mastocytosis · Mastocytoma · Diffuse erythrodermic mastocytosis · Telangiectasia macularis eruptiva perstans · Urticaria pigmentosa · Darier sign · Papulosquamous disorder · Lichen planus · Wickham's striae · Civatte bodies · Psoriasis · Immunobullous disorder · Dermatitis herpetiformis · Celiac disease · Bullous pemphigoid · Autoimmune blistering disease · Pemphigoid gestationis · Herpes gestationis · Chronic bullous dermatosis of childhood · String of pearls sign · Fungal infection · Mycosis · Dermatophytosis · Dermatomycosis · Parasitic skin disease · Pediculosis · Scabies · Cutaneous T-cell lymphoma · Mycosis fungoides · Sézary syndrome · Epidermotropism · Primary cutaneous amyloidosis · Macular amyloidosis · Lichen amyloidosis · Congo red

E. A. S. Attia (✉) · A. E. Mostafa · M. M. Atef
Department of Dermatology, Venereology and Andrology, Faculty of Medicine, Ain Shams University, Cairo, Egypt
e-mail: annosah1974@yahoo.com; azzadermpath@gmail.com; monaatef77@hotmail.com

B. Smoller, N. Bagherani (eds.), *Atlas of Dermatology, Dermatopathology and Venereology*,
https://doi.org/10.1007/978-3-319-45134-3_28-2

1 Introduction

Pruritus or itch is a poorly localized, non-adapting, unpleasant sensation that elicits a desire to scratch or rub the skin. It is a central societal issue because of its high frequency and the substantial social disability with reduced quality of life of affected individuals (Bautista et al. 2014).

Pruritus is classified as pruritoceptive (due to cutaneous causes, such as scabies), neuropathic (due to lesions of afferent pathways of the nervous system, such as peripheral neuritis), neurogenic (due to centrally acting mediators, such as opioid peptides), and psychogenic (Twycross et al. 2003). It is also classified as pruritus in non-inflamed skin and pruritus in disease states.

In any case presented with pruritus, initial careful examination of the skin should be done to search for visible signs of skin disease, secondary scratch lesions (linear or round excoriation and ulceration, lichenification, hyper- or hypopigmentation, and atrophic scars), and/or ichthyotic skin changes. In this chapter, mainly pruritic skin conditions (pruritoceptive disorders) are explained.

2 Pruritic Inflammatory Skin Condition

2.1 Eczema

- **Definition**: Eczema is an inflammatory skin reaction characterized histologically by spongiosis. It is classified as (a) exogenous one, such as contact dermatitis (Fig. 1), and (b) endogenous one, such as atopic dermatitis (Figs. 2 and 3) and discoid eczema (Fig. 4) (Agarwal et al. 2014).
- **Clinical feature**: Acute eczema shows blistering and swelling (Fig. 4), while chronic eczema is characterized by dark lichenified skin (Fig. 3). Subacute eczema is a class with clinical presentations between those of acute and chronic one (Phelps et al. 2003) (Figs. 1 and 2). Prurigo nodularis can occur as a result of chronic pruritus (Fig. 5) (Olek-Hrab et al. 2016). On dermoscopy, it

Fig. 1 Contact dermatitis of the eyelids and face (subacute). (Taken by Prof. Enas Attia, Dermatology, Venereology and Andrology Department, Faculty of Medicine, Ain Shams University, Cairo, Egypt)

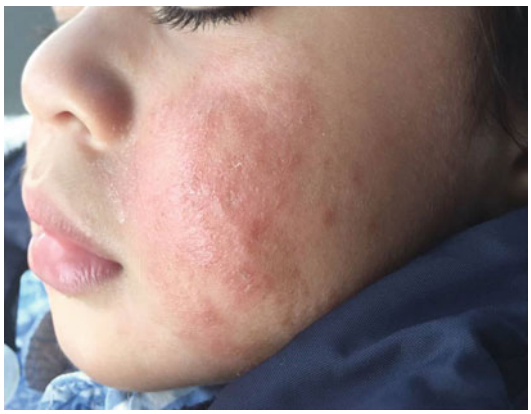

Fig. 2 Infantile atopic eczema on the face (subacute). (Taken by Prof. Enas Attia, Dermatology, Venereology and Andrology Department, Faculty of Medicine, Ain Shams University, Cairo, Egypt)

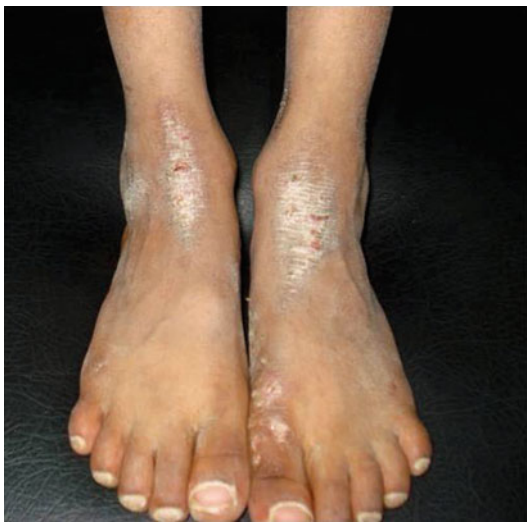

Fig. 3 Childhood atopic eczema on the feet (chronic lichenified). (Taken by Prof. Enas Attia, Dermatology, Venereology and Andrology Department, Faculty of Medicine, Ain Shams University, Cairo, Egypt)

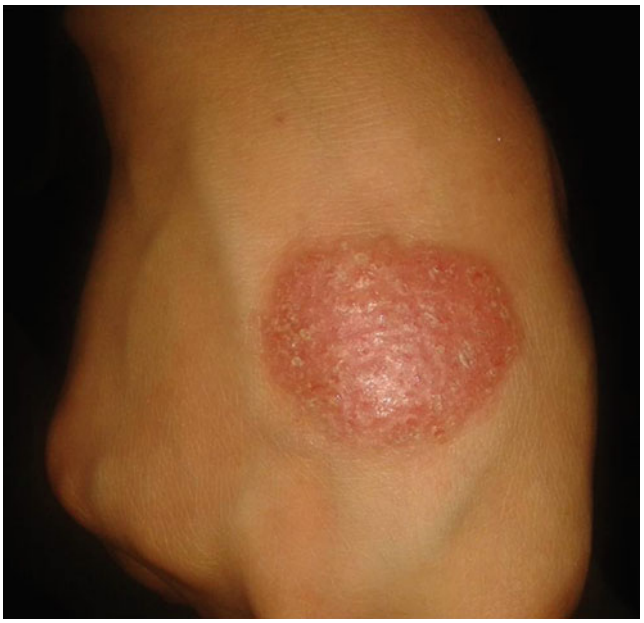

Fig. 4 Discoid eczema on the dorsum of the right hand (acute). (Taken by Prof. Enas Attia, Dermatology, Venereology and Andrology Department, Faculty of Medicine, Ain Shams University, Cairo, Egypt)

includes dotted vessels with yellow sero-crusts in acute eczema versus scaling in chronic lesions (Errichetti and Stinco 2016; Navarini et al. 2011) (Fig. 6).

- **Pathological manifestation**: Spongiosis resulting in formation of intraepidermal vesicles and exocytosis occurs in acute eczema (Fig. 7). In subacute eczema, spongiosis and exocytosis are mild to moderate (Fig. 8). In chronic eczema, spongiosis is often unrecognized (Phelps et al. 2003). Prurigo nodularis shows epidermal fibrosis and hypertrophy (Olek-Hrab et al. 2016).
- **Prognosis and treatment**: Eczema is often long term. Conventionally, it is treated with topical corticosteroids, oral antihistamines, and emollients (Agarwal et al. 2014).
- **Differential diagnosis**: Psoriasis, tinea corporis, hyper-IgE syndrome, dermatitis herpetiformis, and zinc deficiency (Siegfried and Hebert 2015).

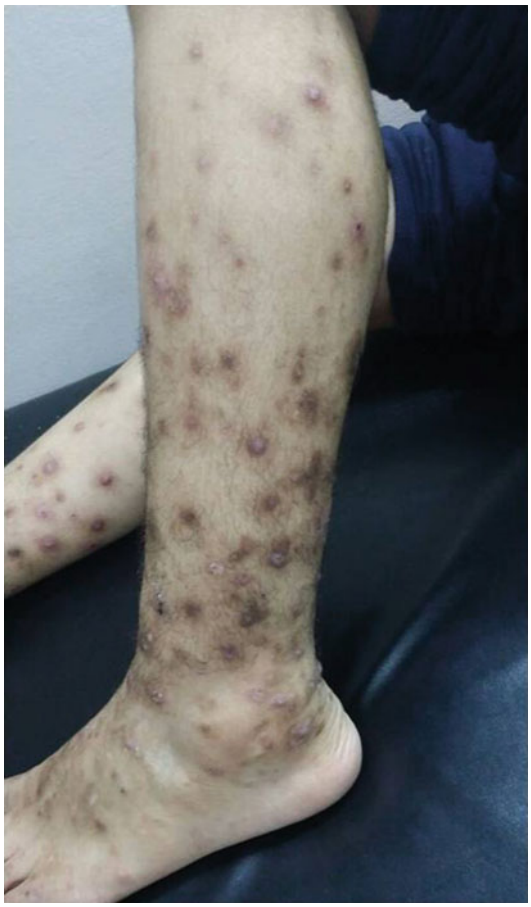

Fig. 5 Prurigo nodularis on the legs. (Taken by Dr. Azza Mostafa, Dermatology, Venereology and Andrology Department, Faculty of Medicine, Ain Shams University, Cairo, Egypt)

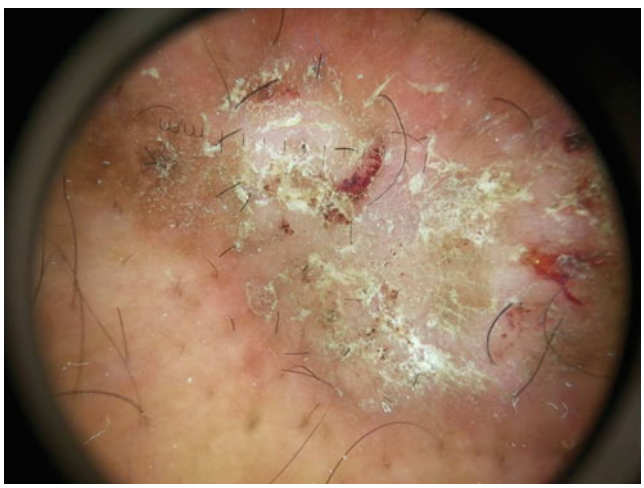

Fig. 6 Dermoscopy of chronic eczema showing yellow sero-crusts over a dull red background with focal brownish dots/globules. (Taken by Dr. Azza Mostafa, Dermatology, Venereology and Andrology Department, Faculty of Medicine, Ain Shams University, Cairo, Egypt)

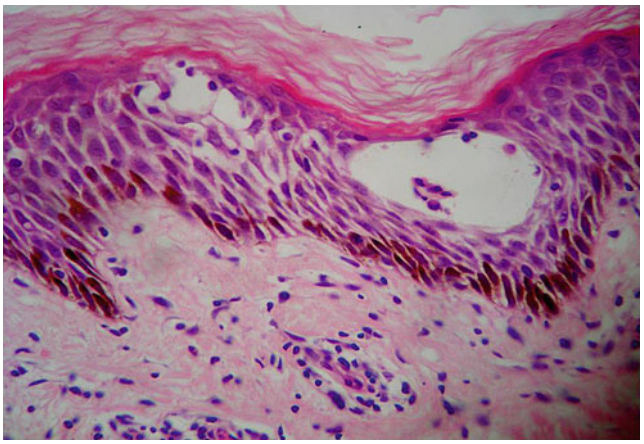

Fig. 7 Acute vesicular eczema; histopathological examination revealing spongiosis with vesicles containing inflammatory cells (Hematoxylin and Eosin stain x400). (Taken by Dr. Azza Mostafa, Dermatology, Venereology and Andrology Department, Faculty of Medicine, Ain Shams University, Cairo, Egypt)

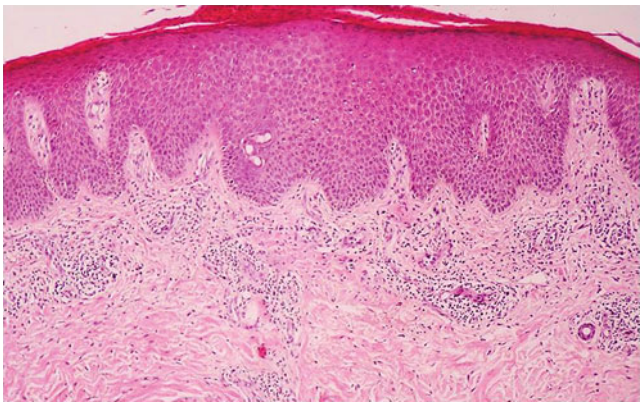

Fig. 8 Subacute eczema; histopathological examination revealing parakeratosis, acanthosis with mild spongiosis, and perivascular lymphocytic inflammatory infiltrate in the papillary dermis (Hematoxylin and Eosin stain x100). (Taken by Dr. Azza Mostafa, Dermatology, Venereology and Andrology Department, Faculty of Medicine, Ain Shams University, Cairo, Egypt)

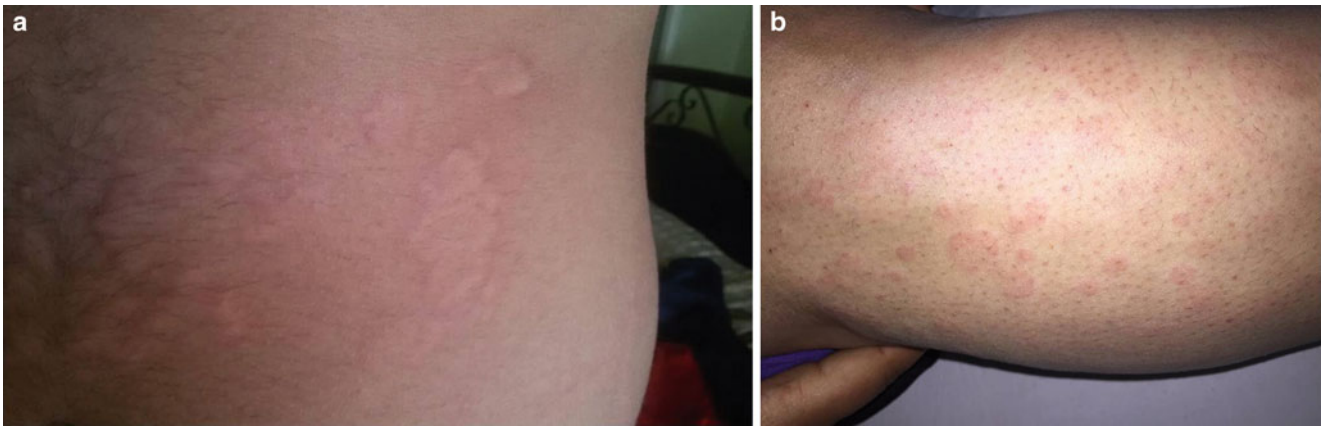

Fig. 9 (**a**, **b**) Urticarial wheals on the trunk. (Taken by Prof. Enas Attia, Dermatology, Venereology and Andrology Department, Faculty of Medicine, Ain Shams University, Cairo, Egypt)

2.2 Urticaria, Angioedema, and Mastocytosis

2.2.1 Urticaria

- **Definition**: Urticaria is a mast cell-driven disease presenting with wheals and/or angioedema (Zuberbier et al. 2014). Release of histamine and vasoactive substances from mast cells and basophils leads to extravasation of plasma into the dermis and intense pruritus (Hide et al. 1993).
- **Clinical feature**: Typical lesions are pruritic edematous pink or red wheals (Fig. 9). Acute urticaria may be associated with life-threatening angioedema and/or anaphylactic reaction (Simons et al. 2013). Individual acute urticaria lesions usually fade within 24 h (Amar and Dreskin 2008). Chronic urticaria has recurrent episodes lasting longer than 6 weeks (Kaplan 2002). In dermographism, itching, erythema, and wheals occur in areas stroked with a blunt object (Wong et al. 1984) (Fig. 10).

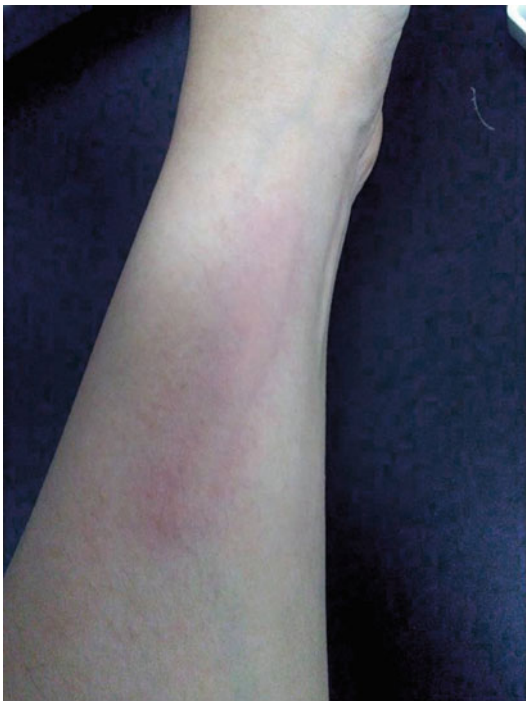

Fig. 10 Appearance of urticarial wheals on the left forearm after stroking with blunt object (dermographism). (Taken by Prof. Enas Attia, Dermatology, Venereology and Andrology Department, Faculty of Medicine, Ain Shams University, Cairo, Egypt)

- **Pathological manifestation**: Classical pathological findings include dermal edema and sparse perivascular infiltrate of neutrophils, eosinophils, macrophages, and lymphocytes (Fig. 11). Mast cells are relatively sparse, better demonstrated with special stains. Extravasated erythrocytes are present in 50% of the cases, but vasculitis is not observed (Barzilai et al. 2017).
- **Prognosis and treatment**: In acute urticaria, if anaphylaxis is present, immediate intervention shall be considered (Simons et al. 2013). The improvement and remission rates of chronic urticaria are relatively low (Hiragun et al. 2013). Therapy includes non-sedating H1 antihistamines (Krause et al. 2013); combination of H1 antagonist with H2 antagonist; corticosteroids; leukotriene receptor antagonists; sympathomimetics; immunomodulatory and anti-inflammatory therapies, such as cyclosporine, colchicines, and dapsone (Schaefer 2017); and omalizumab (an anti-IgE antibody) (Zuberbier et al. 2014).
- **Differential diagnosis**: Maculopapular drug eruption, insect bite, erythema multiforme, pityriasis rosea, and urticarial vasculitis (Frigas and Park 2009; Venzor et al. 2002).

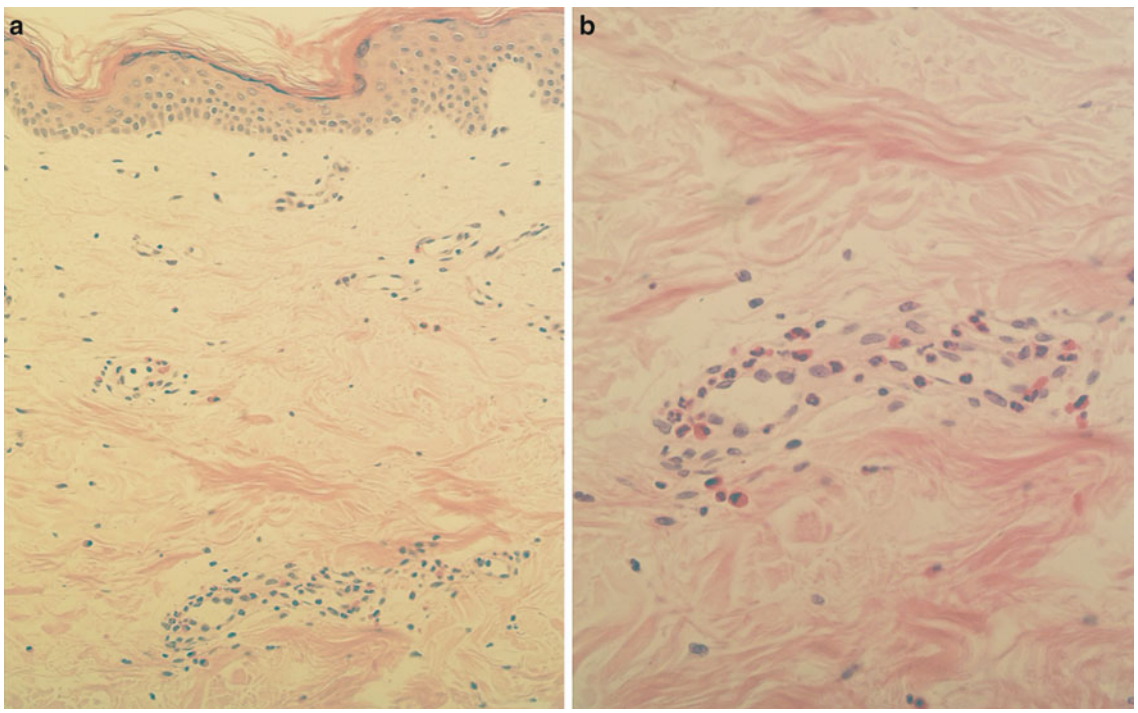

Fig. 11 Urticaria; (**a**, **b**) histopathological examination revealing dermal edema and sparse perivascular infiltrate of neutrophils, eosinophils, macrophages, and lymphocytes (Hematoxylin and Eosin stain). (Courtesy of Dr. Mohamed Ben-Gashir, Department of Laboratory Medicine and Pathology, Hamad Medical Corporation, Doha, Qatar)

2.2.2 Angioedema

- **Definition**: Angioedema is localized edema of the subcutaneous and submucosal tissues, with or without associated urticaria, due to a temporary increase in vascular permeability caused by the release of vasoactive mediators (Aberer 2014). Histamine and bradykinin are the most important vasoactive mediators in its pathogenesis (Oschatz et al. 2011).
- **Clinical feature**: Acute episodes often involve the lips, eyes, face, and genitalia (Fig. 12); however, it may affect other parts of the body, including respiratory and gastrointestinal mucosa.
- **Pathological manifestation**: Swelling of deep dermis, subcutaneous, or submucosal tissue due to vascular leakage is seen, following exposure to an allergen or caused by a defect in the immune system in cases with hereditary angioedema (Aberer 2014).

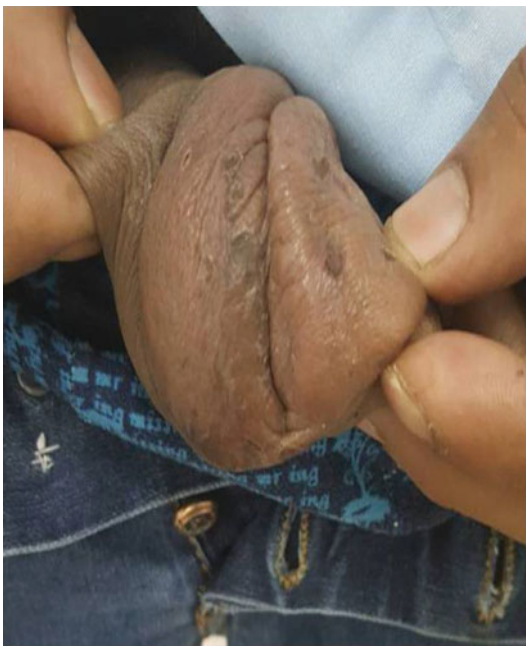

Fig. 12 Angioedema of the genital site. (Taken by Dr. Mona Atef, Dermatology, Venereology and Andrology Department, Faculty of Medicine, Ain Shams University, Cairo, Egypt)

- **Prognosis and treatment**: Laryngeal swelling can be life-threatening (Maurer et al. 2013). Therapy includes non-sedating H1 antihistamines (Krause et al. 2013), combination of H1 antagonist with H2 antagonist, corticosteroids, leukotriene receptor antagonists, sympathomimetics (Schaefer 2017), and omalizumab (Zuberbier et al. 2014). Epinephrine along with supportive care shall be used when laryngeal angioedema is suspected. Icatibant, a bradykinin receptor antagonist, leads to a fast resolution of angioedema (Zanichelli et al. 2012).
- **Differential diagnosis**: Hereditary angioedema, acquired angioedema, and insect bite (Mansi et al. 2015).

2.2.3 Mastocytosis

- **Definition**: Mastocytosis is a disorder characterized by mast cell proliferation within the skin (Valent 2006). Increased soluble mast cell growth factors in lesions stimulate mast cell proliferation, melanocyte proliferation, and melanin pigment production (Horny et al. 2007).
- **Clinical feature**: Mastocytoses confined to the skin are divided into solitary mastocytoma (Fig. 13), diffuse erythrodermic mastocytosis, telangiectasia macularis

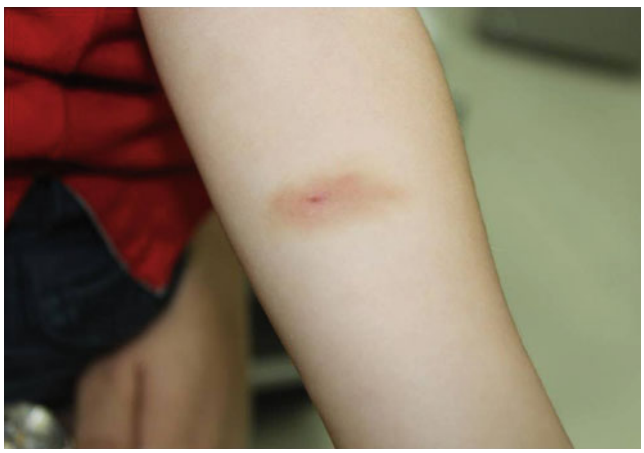

Fig. 13 Mastocytoma; itchy brown plaque on the left forearm, confirmed histopathologically. (Taken by Prof. Enas Attia, Dermatology, Venereology and Andrology Department, Faculty of Medicine, Ain Shams University, Cairo, Egypt)

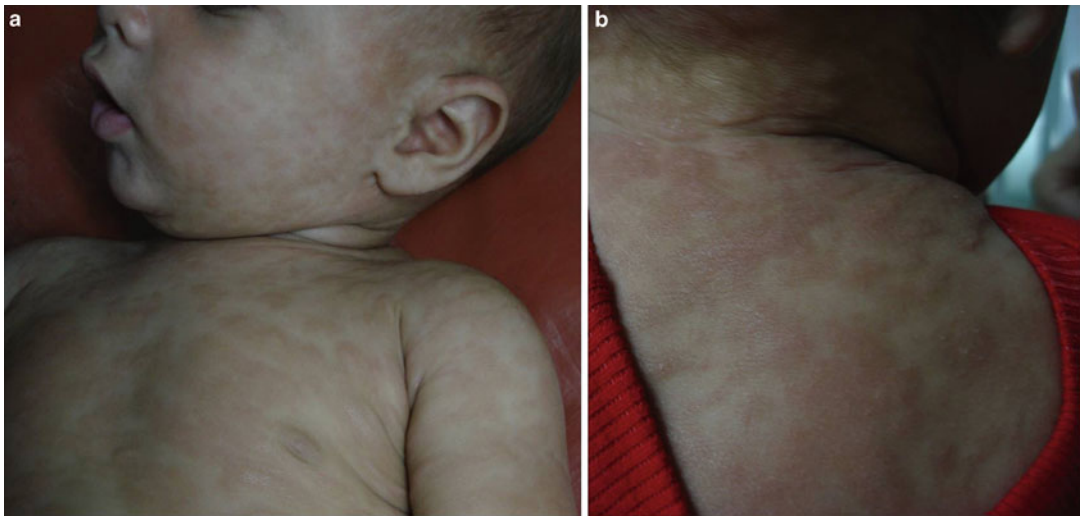

Fig. 14 Urticaria pigmentosa; (**a**, **b**) numerous confluent oval and rounded red-brown macules, papules, or plaques disseminated all over the body of an infant. (Taken by Prof. Enas Attia, Dermatology, Venereology and Andrology Department, Faculty of Medicine, Ain Shams University, Cairo, Egypt)

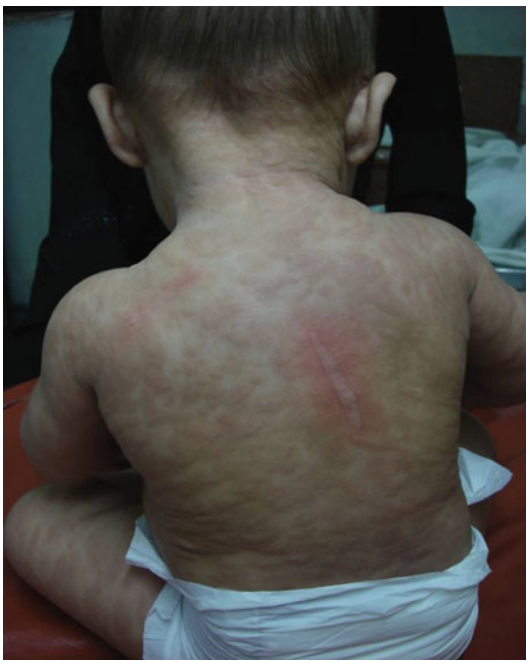

Fig. 15 Urticated lesions upon stroking (Darier sign). (Taken by Prof. Enas Attia, Dermatology, Venereology and Andrology Department, Faculty of Medicine, Ain Shams University, Cairo, Egypt)

eruptiva perstans, and urticaria pigmentosa (the most common) (Fig. 14). It is characterized by multiple oval or round red-brown macules, papules, or plaques (Valent 2006). When lesions of mastocytosis are stroked, it typically urticates, known as Darier sign (Fig. 15), due to mast cell degranulation (Bussmann et al. 2007). Some patients, especially those with extensive cutaneous disease, experience episodes of acute systemic symptoms including flushing, wheezing, rhinorrhea, gastrointestinal symptoms, and syncope (Valent 2006).

- **Pathological manifestation**: Histopathological examination reveals dermal mast cell infiltrates (Fig. 16). Mast cell granules are demonstrated using Giemsa or toluidine blue stain (Fig. 17).
- **Prognosis and treatment**: Therapy is prescribed for symptom relief because the prognosis of most patients is excellent. Therapy includes H1 and H2 antihistamines and disodium cromoglycate (Heide et al. 2008).
- **Differential diagnosis**: Café au lait spots, congenital melanocytic nevi, lentigines, cutaneous amyloidosis, and post-inflammatory hyperpigmentation (Habashy and Elston 2017).

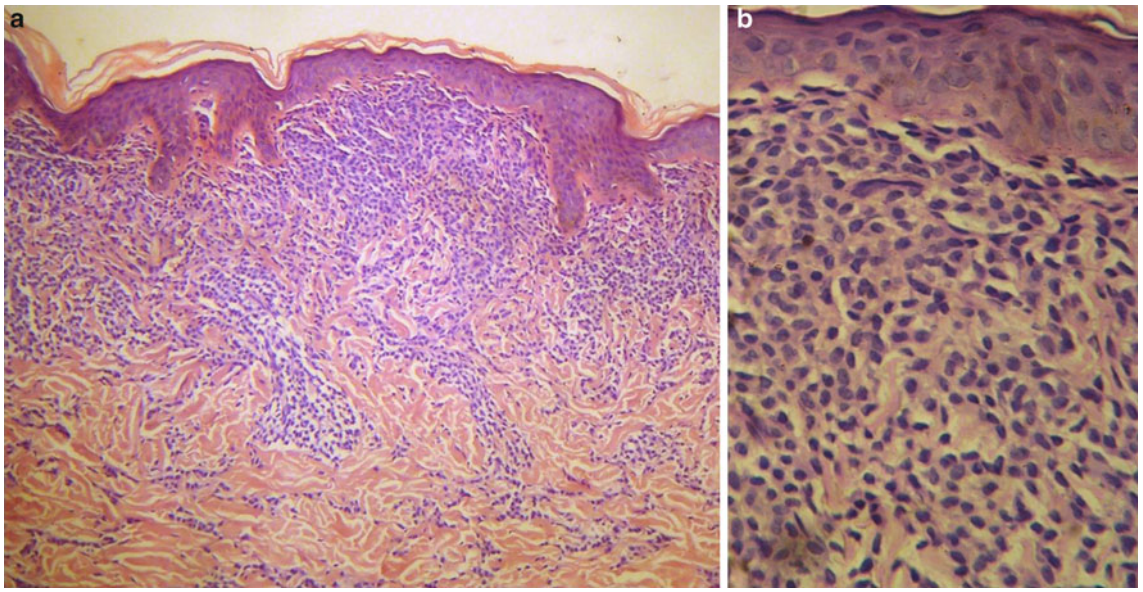

Fig. 16 Mastocytosis; (**a**, **b**) histopathological examination revealing dermal mast cell infiltrates, especially in the papillary dermis around blood vessels (hematoxylin and eosin stain). (Taken by Prof. Enas Attia, Dermatology, Venereology and Andrology Department, Faculty of Medicine, Ain Shams University, Cairo, Egypt)

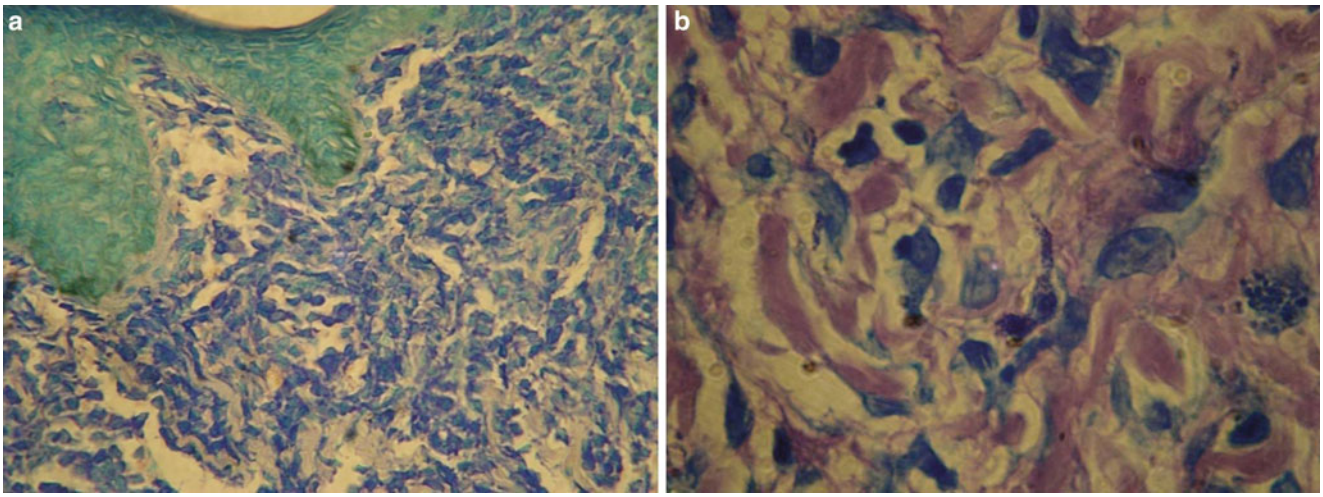

Fig. 17 Mastocytosis; (**a**, **b**) demonstration of mast cell granules using toluidine blue stain. (Taken by Prof. Enas Attia, Dermatology, Venereology and Andrology Department, Faculty of Medicine, Ain Shams University, Cairo, Egypt)

2.3 Papulosquamous Disorder

2.3.1 Lichen Planus

- **Definition**: Lichen planus is an inflammatory skin condition characterized by pruritic, violaceous flat-topped papules (Weston and Payette 2015).
- **Clinical feature**: Classic lesions commonly present with the four P's including purple, pruritic, polygonal, and papules/plaques (Fig. 18). The surface of the papules often has whitish streaks known as Wickham's striae. Many variants exist, including mucosal (Fig. 19), eruptive (Fig. 20), hypertrophic (Fig. 21), and bullous (Fig. 22), in

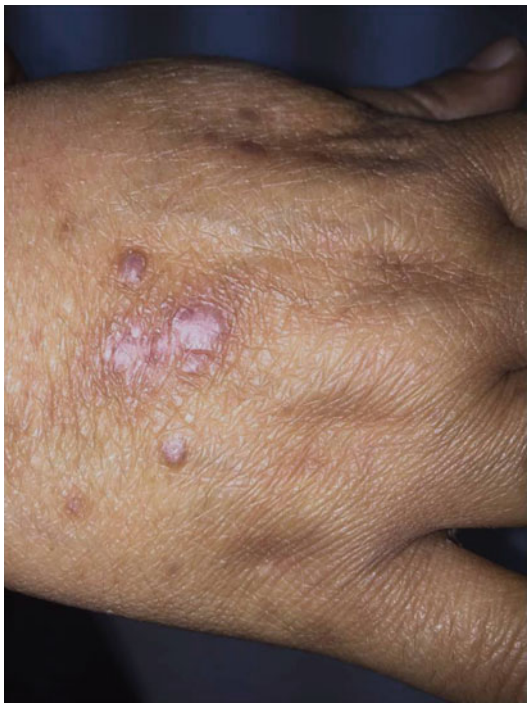

Fig. 18 Purple, flat-topped polygonal papules of lichen planus on the dorsum of the right hand. (Taken by Dr. Mona Atef, Dermatology, Venereology and Andrology Department, Faculty of Medicine, Ain Shams University, Cairo, Egypt)

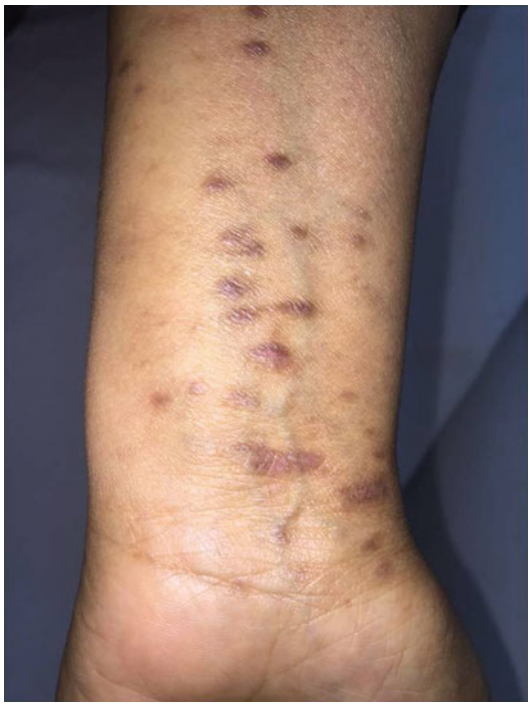

Fig. 20 Eruptive lichen planus on flexor aspect of the forearm and wrist. (Taken by Dr. Mona Atef, Dermatology, Venereology and Andrology Department, Faculty of Medicine, Ain Shams University, Cairo, Egypt)

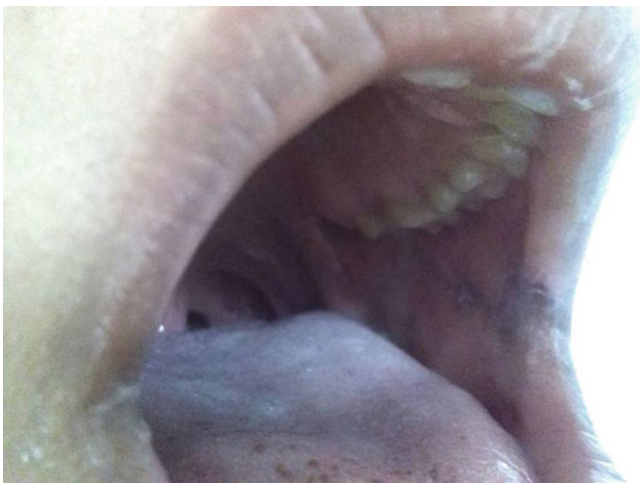

Fig. 19 Mucosal oral lichen planus with reticulate pigmented buccal lesions. (Taken by Prof. Enas Attia, Dermatology, Venereology and Andrology Department, Faculty of Medicine, Ain Shams University, Cairo, Egypt)

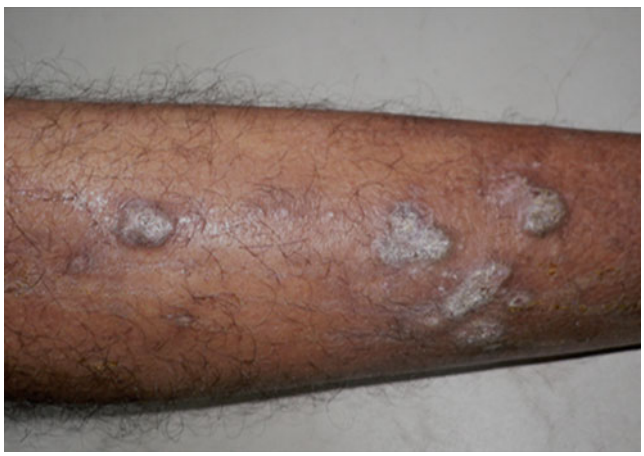

Fig. 21 Hypertrophic lichen planus on the right leg. (Taken by Prof. Enas Attia, Dermatology, Venereology and Andrology Department, Faculty of Medicine, Ain Shams University, Cairo, Egypt)

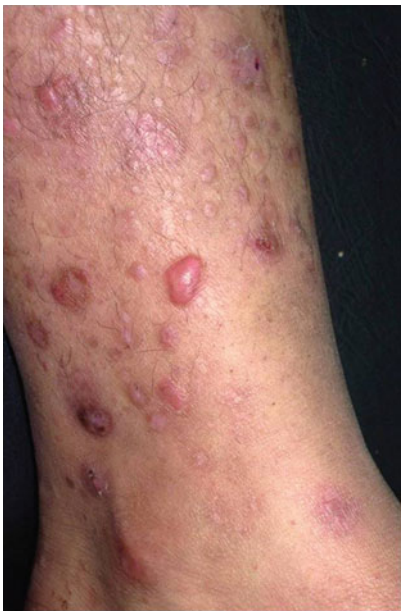

Fig. 22 Bullous lichen planus on the left leg. (Taken by Prof. Enas Attia, Dermatology, Venereology and Andrology Department, Faculty of Medicine, Ain Shams University, Cairo, Egypt)

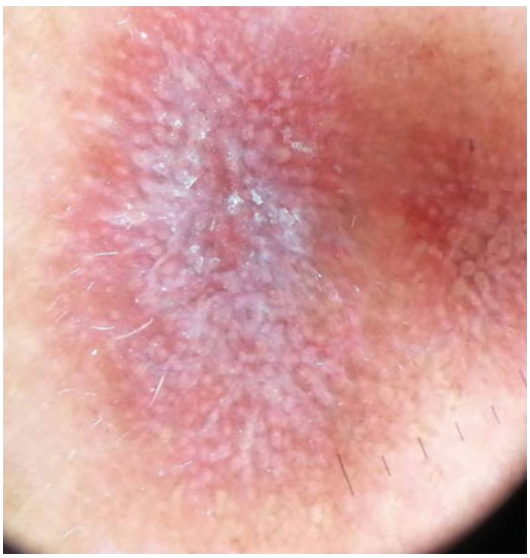

Fig. 23 Dermoscopy of lichen planus showing a network of pathognomonic, white, Wickham's striae with multiple follicular pluggings (original magnification X10). (Taken by Dr. Azza Mostafa, Dermatology, Venereology and Andrology Department, Faculty of Medicine, Ain Shams University, Cairo, Egypt)

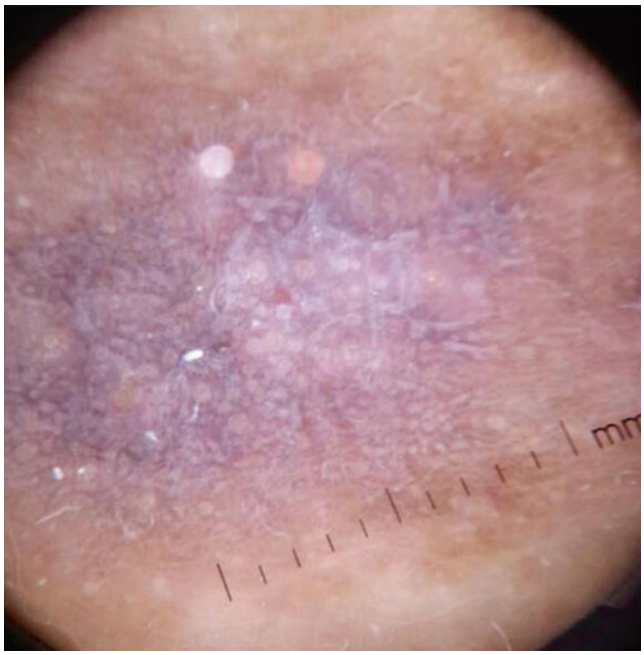

Fig. 24 Dermoscopy of lichen planopilaris on the scalp showing cicatricial white patch, annular blue-gray pigmentation, multiple follicular pluggings, and reduced follicular openings (original magnification X10). (Taken by Dr. Azza Mostafa, Dermatology, Venereology and Andrology Department, Faculty of Medicine, Ain Shams University, Cairo, Egypt)

addition to classic, actinic, pigmentosus, atrophic, annular, linear, follicular, palmoplantar, and nail lichen planus (Gorouhi et al. 2014). The dermoscopic hallmark is represented by Wickham's striae (Lallas et al. 2012) (Figs. 23 and 24).

- **Pathological manifestation**: Histopathological view shows circumscribed, wedge-shaped hypergranulosis in the epidermis, marked hyperkeratosis, and irregular saw toothlike acanthosis of rete ridges, with basal vacuolar degeneration, apoptotic keratinocytes (Civatte bodies), pigment incontinence, and band-like lymphocytic infiltrate that can obscure the dermal-epidermal junction (Weston and Payette 2015) (Fig. 25).
- **Prognosis and treatment**: Lichen planus may resolve spontaneously within 1–2 years, although recurrences are common. However, mucosal lichen planus may be more persistent and resistant to treatment (Usatine and Tinitigan 2011). Treatments include corticosteroids,

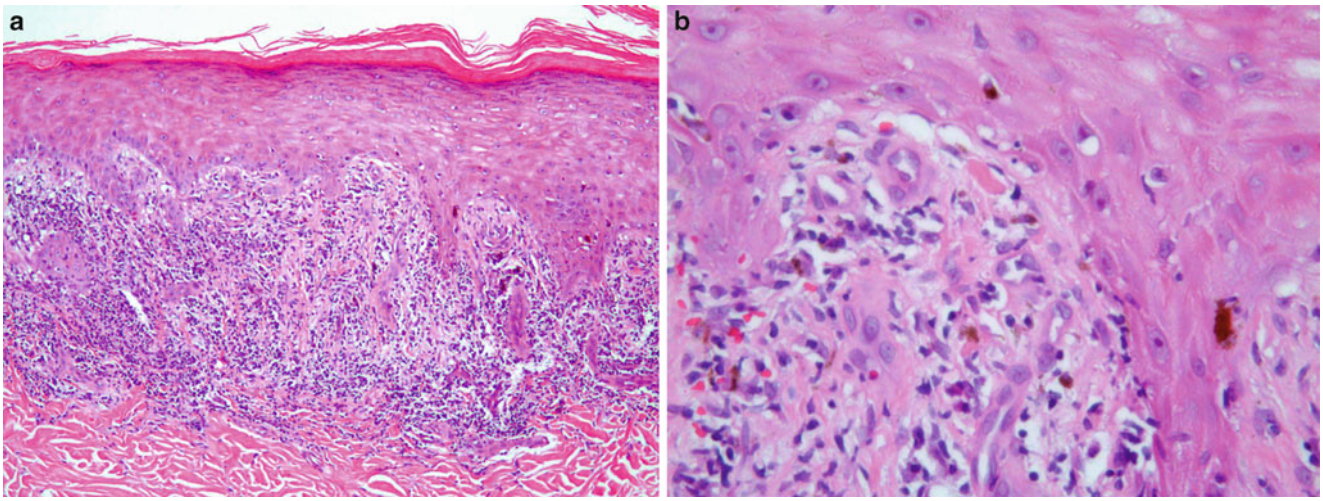

Fig. 25 Histopathological features of lichen planus; (**a**) wedge-shaped hypergranulosis in the epidermis, hyperkeratosis, irregular saw toothlike acanthosis of rete ridges, and characteristic dense, band-like lymphocytic infiltrate in the upper dermis obscuring the dermal-epidermal junction (hematoxylin and eosin stain x100), and (**b**) dermal-epidermal junction showing signs of vacuolar degeneration with apoptotic keratinocytes (Civatte body) (black arrow), and characteristic dense, lymphocytic infiltrate and pigment incontinence in the upper dermis (hematoxylin and eosin stain x400). (Taken by Dr. Azza Mostafa, Dermatology, Venereology and Andrology Department, Faculty of Medicine, Ain Shams University, Cairo, Egypt)

tacrolimus, retinoids, and phototherapy (Weston and Payette 2015).

- **Differential diagnosis**: Lichenoid eruption, psoriasis, lichen nitidus, lichen simplex chronicus, and pityriasis rosea (Gorouhi et al. 2014).

2.3.2 Psoriasis

- **Definition**: Psoriasis is a common chronic inflammatory skin disease, not considered typically itchy. However, several studies have documented itch in about 70–80% of individuals with psoriasis (Sampogna et al. 2004).
- **Clinical feature**: There is a spectrum of different clinical types. Plaque psoriasis is the most common type, characterized by well-demarcated erythematous plaques with silvery white scales (Campalani and Barker 2005) (Fig. 26). On dermoscopy, it includes regularly distributed red dots and globules on intense red background and diffuse white scales (Goncharova et al. 2015) (Fig. 27).
- **Pathological manifestation**: Three principal features are seen including regular epidermal hyperplasia, dilated dermal blood vessels, and dermal leukocytic inflammatory infiltrate (Griffiths and Barker 2007) (Fig. 28). Compared to non-pruritic, pruritic psoriasis demonstrates increased nerve fibers and selected neuropeptide receptors on nerve fibers and basal keratinocytes (Nakamura et al. 2003).

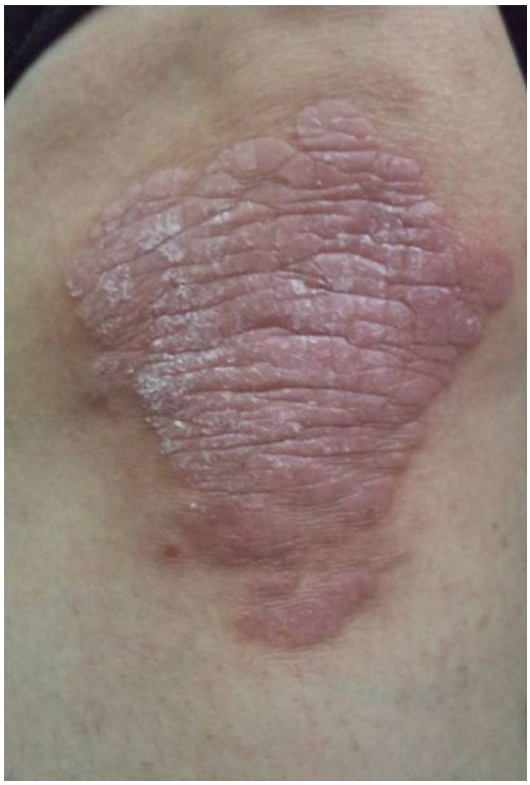

Fig. 26 Plaque psoriasis on the knee. (Taken by Dr. Mona Atef, Dermatology, Venereology and Andrology Department, Faculty of Medicine, Ain Shams University, Cairo, Egypt)

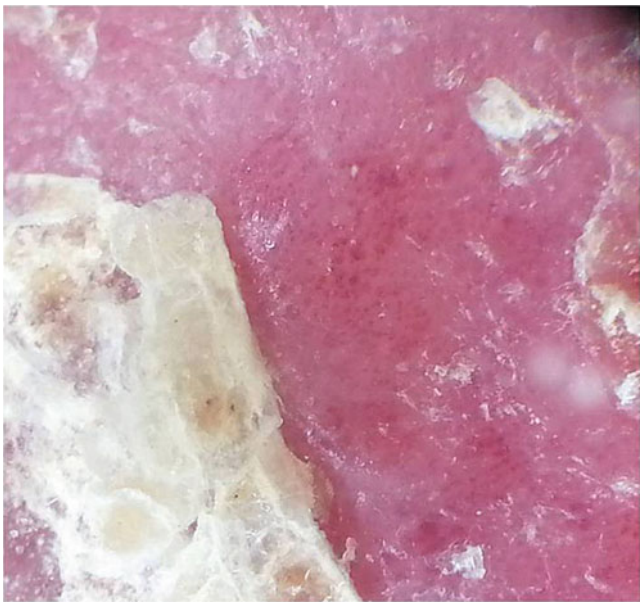

Fig. 27 Dermoscopy of psoriasis showing regularly arranged dotted vessels and white scales (original magnification x10). (Taken by Dr. Azza Mostafa, Dermatology, Venereology and Andrology Department, Faculty of Medicine, Ain Shams University, Cairo, Egypt)

- **Prognosis and treatment**: It may have a variable course presenting as chronic, stable plaques or acute rapidly progressing. Topical therapies including corticosteroids, vitamin D analogs, retinoids, and calcineurin inhibitors; systemic therapies including methotrexate, cyclosporine, acitretin, and biological therapy; and phototherapy are used as treatment (Menter 2016).
- **Differential diagnosis**: Eczema, fungal infection, mycosis fungoides, and parapsoriasis (Lisi 2007).

2.4 Immunobullous Disorder

2.4.1 Dermatitis Herpetiformis

- **Definition**: Dermatitis herpetiformis is an inflammatory cutaneous disease, with a chronic relapsing pruritic polymorphic lesions. It is considered the specific cutaneous manifestation of celiac disease (Caproni et al. 2009).
- **Clinical feature**: Symmetrical grouped polymorphic lesions consisting of erythema, urticarial plaques, and papules involving the extensor surfaces are seen in this

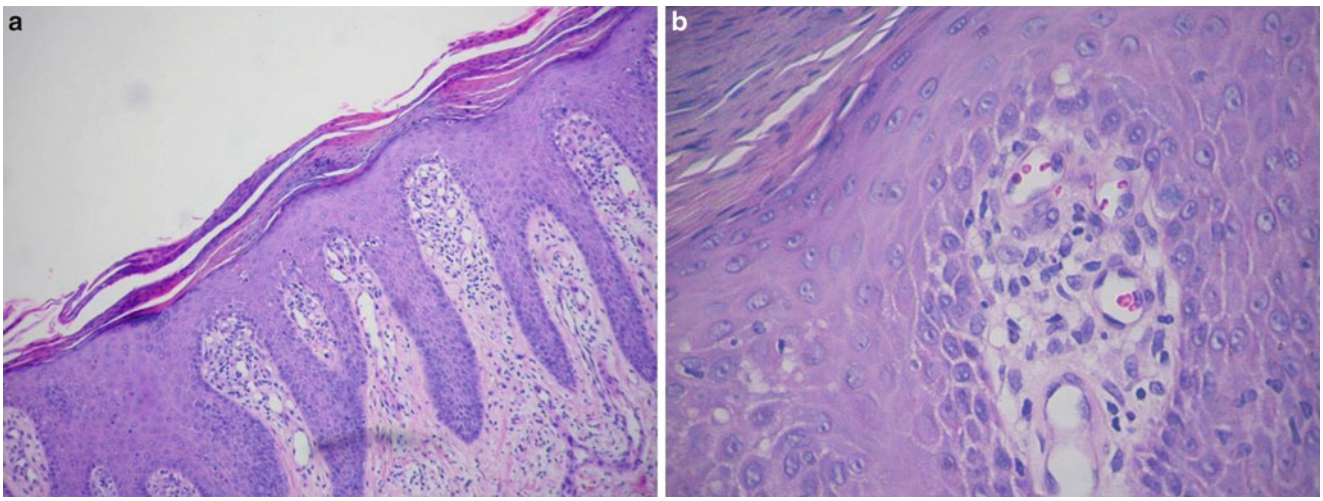

Fig. 28 (**a**, **b**) Histopathological features of psoriasis with regular elongation of rete ridges, absent granular cell layer, parakeratosis, and dilated prominent blood vessels in the dermis with surrounding inflammatory infiltrate (hematoxylin and eosin stain). (Taken by Prof. Enas Attia, Dermatology, Venereology and Andrology Department, Faculty of Medicine, Ain Shams University, Cairo, Egypt)

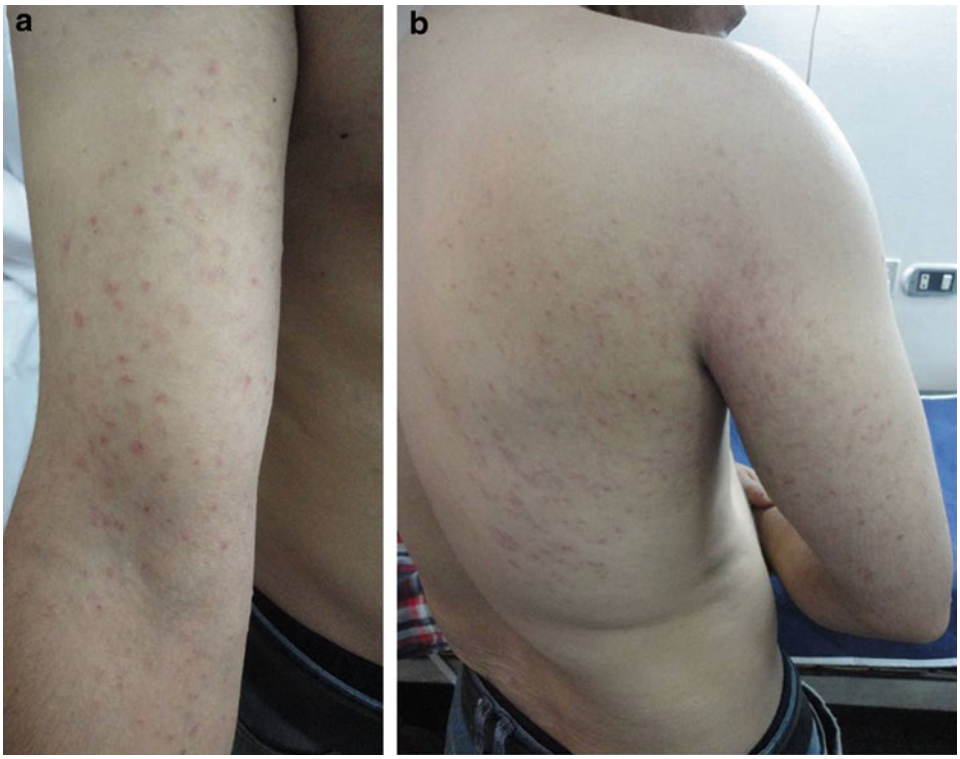

Fig. 29 (**a**, **b**) Grouped polymorphic lesions consisting of erythema, urticarial plaques, and excoriated papules of dermatitis herpetiformis. (Taken by Dr. Azza Mostafa, Dermatology, Venereology and Andrology Department, Faculty of Medicine, Ain Shams University, Cairo, Egypt)

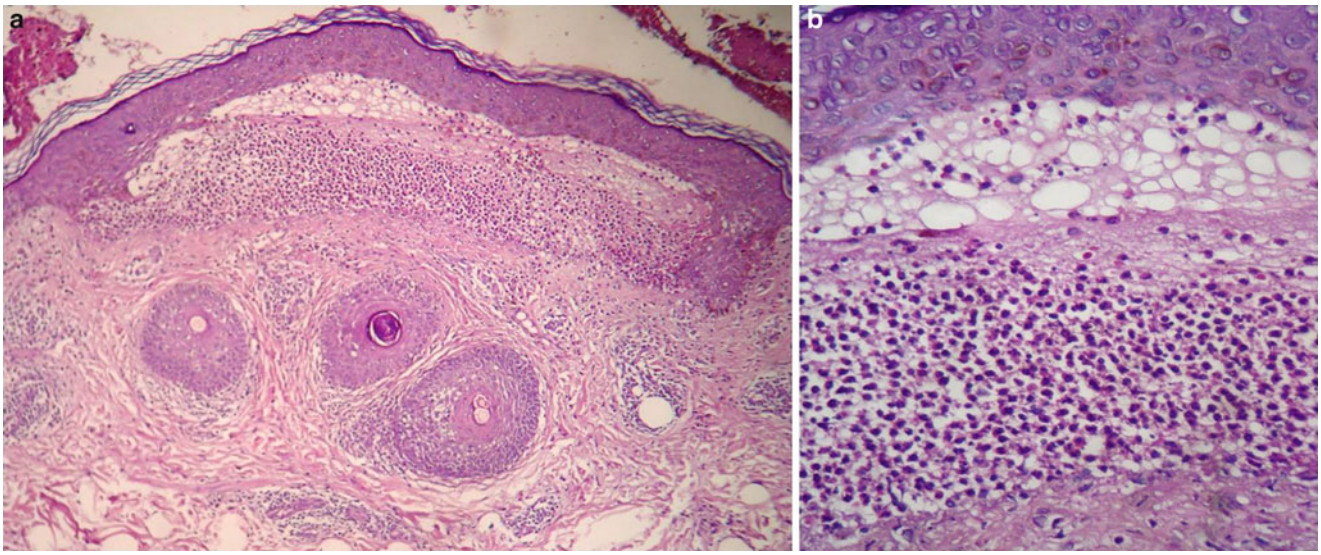

Fig. 30 Histopathology of dermatitis herpetiformis; (**a**) neutrophil-rich subepidermal bulla (hematoxylin and eosin stain x100), and (**b**) subepidermal bulla rich in fibrin network and neutrophils (hematoxylin and eosin stain x400). (Taken by Dr. Azza Mostafa, Dermatology, Venereology and Andrology Department, Faculty of Medicine, Ain Shams University, Cairo, Egypt)

disorder (Fig. 29). Herpetiform vesicles may occur later, often immediately excoriated, and are usually not seen in patients (Fry 2002).

- **Pathological manifestation**: The typical histopathological findings in the lesional skin consist of subepidermal vesicles and blisters associated with accumulation of neutrophils at the papillary tips (Nicolas et al. 2003) (Fig. 30). Direct immunofluorescence of perilesional skin shows granular IgA deposits in the dermal papillae which represent the gold standard for the diagnosis (Caproni et al. 2009).
- **Prognosis and treatment**: A lifelong gluten-free diet is the first-choice treatment of the disease. In the inflammatory phases of the disease, dapsone, sulfones, or corticosteroids can be prescribed (Antiga and Caproni 2015).
- **Differential diagnosis**: Eczema, other autoimmune blistering diseases (especially IgA linear disease and bullous pemphigoid), nodular prurigo, and urticaria (Caproni et al. 2009).

2.4.2 Bullous Pemphigoid

- **Definition**: Bullous pemphigoid is the most common subtype of autoimmune blistering disease, usually presented in elderly (Zhao and Murrell 2015).
- **Clinical feature**: It typically manifests with large tense bullae, proceeded by urticarial plaques and intense pruritus (Zhao and Murrell 2015) (Fig. 31). Atrophic scars, mucosal involvement, and lesions on the neck and head are often absent in this disorder (Joly et al. 2004).
- **Pathological manifestation**: Subepidermal blisters due to autoantibodies directed against the 180 kD antigen (BP180) and the 230 kD antigen (BP230), two components of adhesion complexes promoting dermo-epidermal cohesion, are seen in this disorder (Di Zenzo et al. 2012). In the setting of typical clinical features, tense bullae with dermal-epidermal separation on histology (Fig. 32), and positive direct immunofluorescence for IgG or C3 (Fig. 33), the diagnosis can be made.

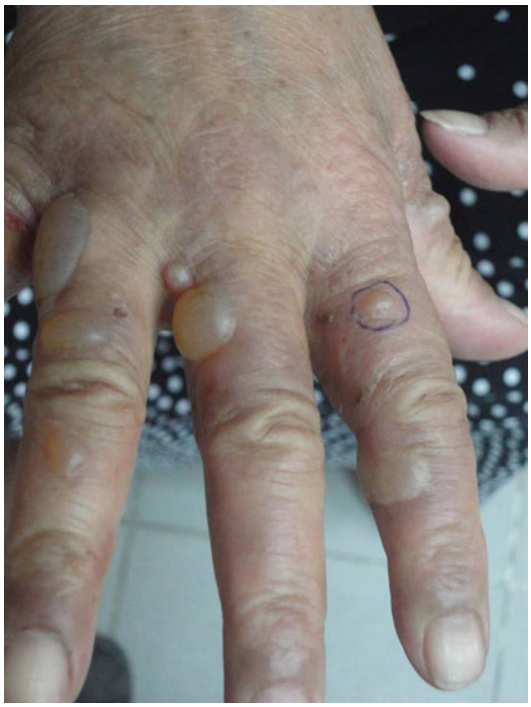

Fig. 31 Tense bullae of bullous pemphigoid. (Taken by Dr. Mona Atef, Dermatology, Venereology and Andrology Department, Faculty of Medicine, Ain Shams University, Cairo, Egypt)

- **Prognosis and treatment**: Patients with older age, circulating antibodies, dementia, and stroke are at greater risk of mortality (Liu et al. 2017). Treatments include corticosteroids and corticosteroid-sparing agents (azathioprine, cyclophosphamide, methotrexate, cyclosporine A, combination of tetracycline/minocycline and nicotinamide and mycophenolate mofetil) (Zhao and Murrell 2015).
- **Differential diagnosis**: Epidermolysis bullosa acquisita, cicatricial pemphigoid, and bullous eruption of systemic lupus erythematosus (Mihályi et al. 2012).

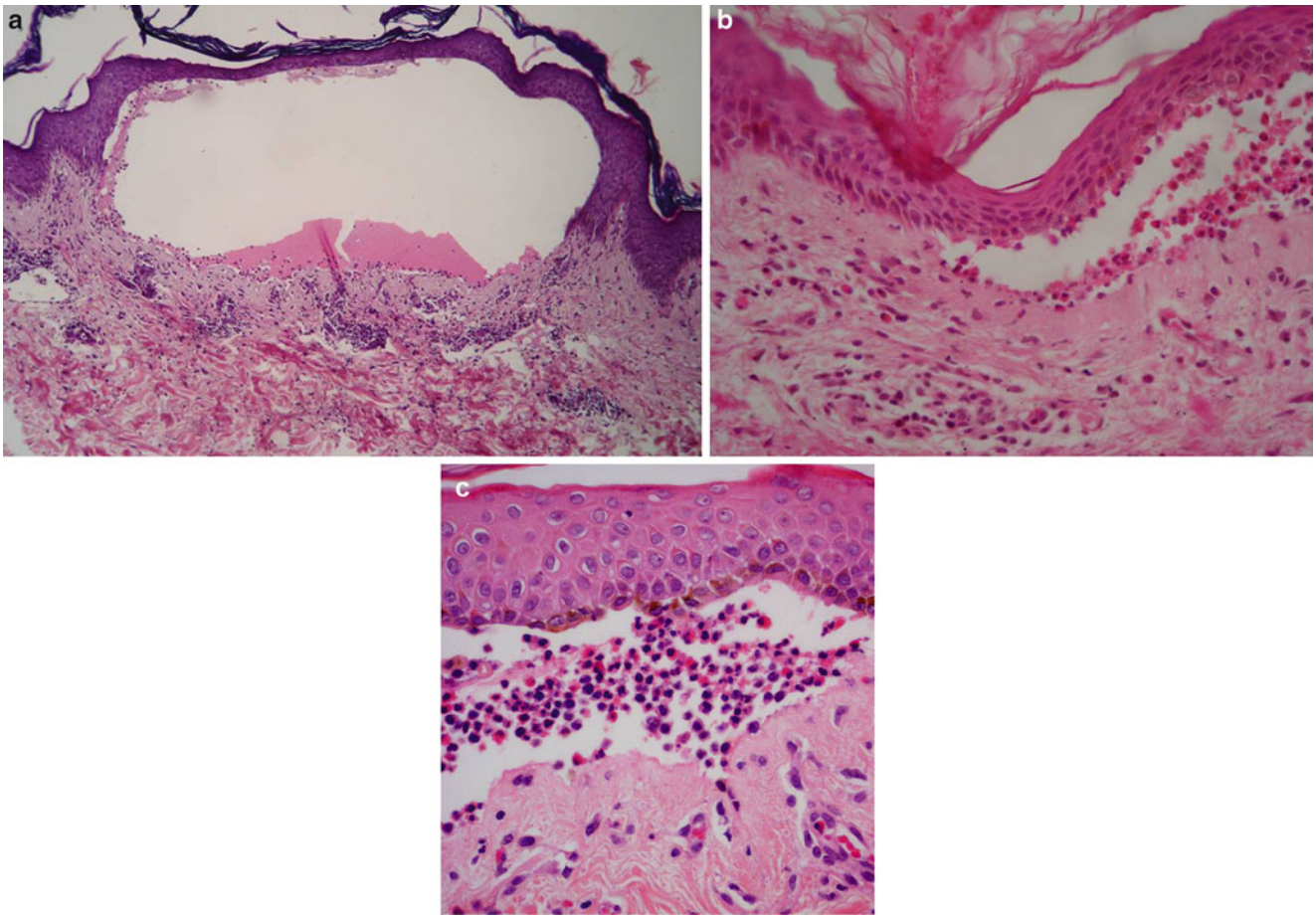

Fig. 32 Histopathology of bullous pemphigoid; (**a**) subepidermal bulla containing fibrin and inflammatory cells (hematoxylin and eosin stain x40), (**b**, **c**) eosinophil-rich subepidermal bulla and upper dermal perivascular eosinophil-rich mixed inflammatory infiltrate (hematoxylin and eosin stain x400). (Taken by Dr. Azza Mostafa, Dermatology, Venereology and Andrology Department, Faculty of Medicine, Ain Shams University, Cairo, Egypt)

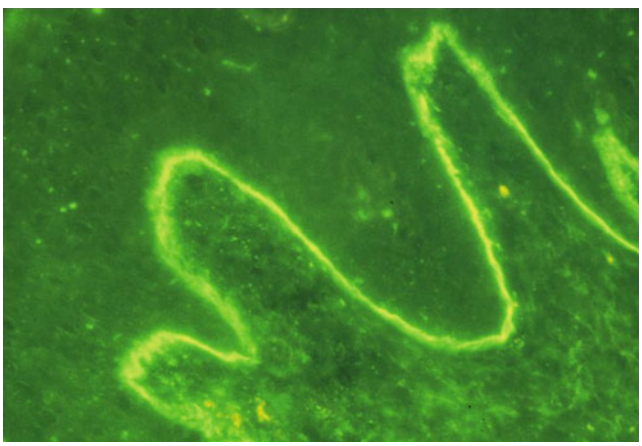

Fig. 33 Bullous pemphigoid; immunofluorescence staining with anti-IgG Antibodies showing linear deposition at dermal-epidermal junction. (Taken by Dr. Azza Mostafa, Dermatology, Venereology and Andrology Department, Faculty of Medicine, Ain Shams University, Cairo, Egypt)

2.4.3 Pemphigoid Gestationis

- **Definition**: Pemphigoid gestationis is a rare autoimmune skin disorder occurring during pregnancy. It was previously called herpes gestationis, which is a misnomer (Nanda et al. 2004).
- **Clinical feature**: It commonly occurs during the second or third trimester, characterized by intense abdominal itching usually beginning around the navel, with varied red papules, urticarial plaques, or annular target lesions, followed by blistering (Huilaja et al. 2014) (Fig. 34).
- **Pathological manifestation**: Autoantibodies against placental BP180 damage the skin basement membrane (Di Zenzo et al. 2007). There is blistering at the dermal-

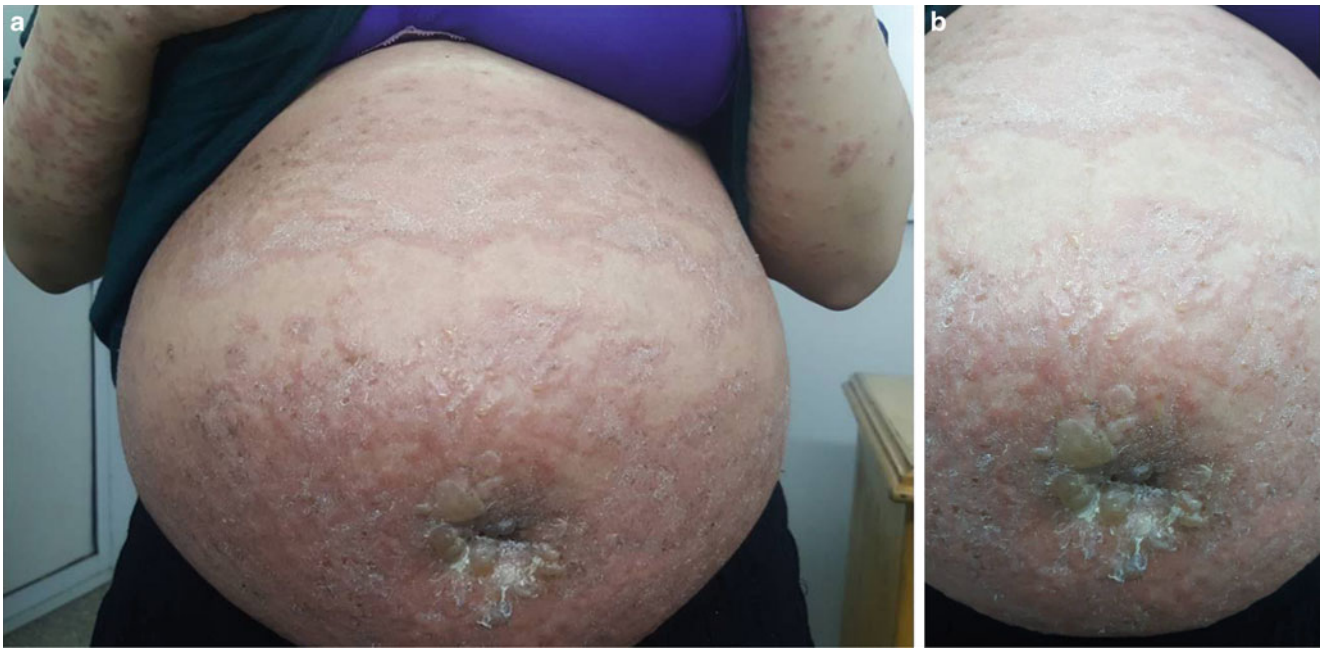

Fig. 34 Pemphigoid gestationis; itchy blistering condition affecting the abdomen, mainly periumbilical, of a pregnant woman in the third trimester. (Taken by Dr. Mona Atef, Dermatology, Venereology and Andrology Department, Faculty of Medicine, Ain Shams University, Cairo, Egypt)

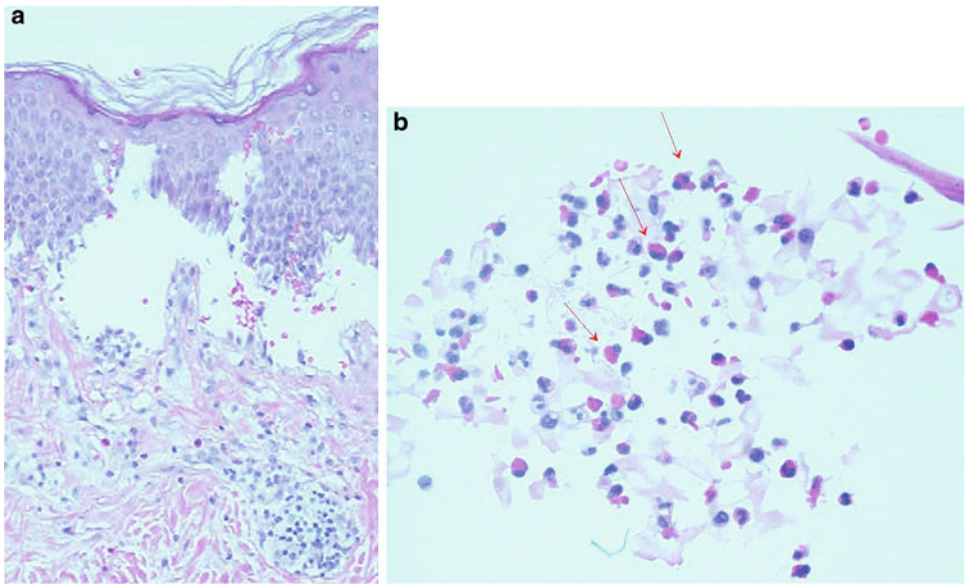

Fig. 35 Pemphigoid gestationis; (**a**, **b**) blistering at the dermal-epidermal junction and infiltrate of lymphocytes with scattered eosinophils (red arrows) (H&E stain). (Courtesy of Dr. Delaram Mohamed Mahmoud, Alborge Laboratories, Doha, Qatar)

epidermal junction and sparse, superficial mid-dermal perivascular infiltrate of lymphocytes with scattered eosinophils (Fig. 35). The diagnosis is confirmed by direct immunofluorescence showing linear deposition of C3 with or without IgG along the basement membrane. Serum BP180 antibody level assesses disease activity (Kneisel and Hertl 2011).

- **Prognosis and treatment**: It resolves spontaneously shortly after delivery. However, relapses in subsequent pregnancies are common. As it is linked to prematurity and fetal growth restriction, prenatal monitoring is

recommended. Mothers should also be informed about the risk of reactivation in subsequent pregnancies and taking hormonal contraception (Jenkins et al. 1999). Mild symptoms are treated with topical corticosteroids, while oral corticosteroids are used for severe diseases (Kneisel and Hertl 2011).

- **Differential diagnosis**: Prurigo of pregnancy, polymorphic eruption of pregnancy, and intrahepatic cholestasis of pregnancy (Huilaja et al. 2014).

2.4.4 Chronic Bullous Dermatosis of Childhood

- **Definition**: Chronic bullous dermatosis of childhood is the most common acquired chronic bullous dermatosis in the first 10 years of life (Wojnavrouska et al. 1988).
- **Clinical feature**: The disease commonly involves the perioral skin, trunk (Fig. 36), inner thighs, genitalia, and perineum (Wojnavrouska et al. 1988). The mucous membranes may also be affected (Marsden et al. 1980). Bullae are the major clinical finding, and their appearance is characteristic with annular blisters or "collarettes" of bullae around resolving crusted lesions, known as "string of pearls" sign (Chorzelski and Jablouska 1979) (Fig. 36). Pruritus can be mild to severe (Fahad and Ammar 2011).
- **Pathological manifestation**: It shows subepidermal bullae, with collections of neutrophils along the basement membrane and occasionally in the dermal papillary tips. On direct immunofluorescence, deposition of IgA in a linear pattern is noted along the basement membrane (Lear and Smith 1998).
- **Prognosis and treatment**: It resolves within 2 years of onset in most cases. It responds rapidly to dapsone or sulfa-pyridine. Some patients may require low-dose prednisone initially to suppress blister formation (Bickle et al. 2002).
- **Differential diagnosis**: Dermatitis herpetiformis, childhood form of epidermolysis bullosa acquisita, and bullous pemphigoid (Fahad and Ammar 2011).

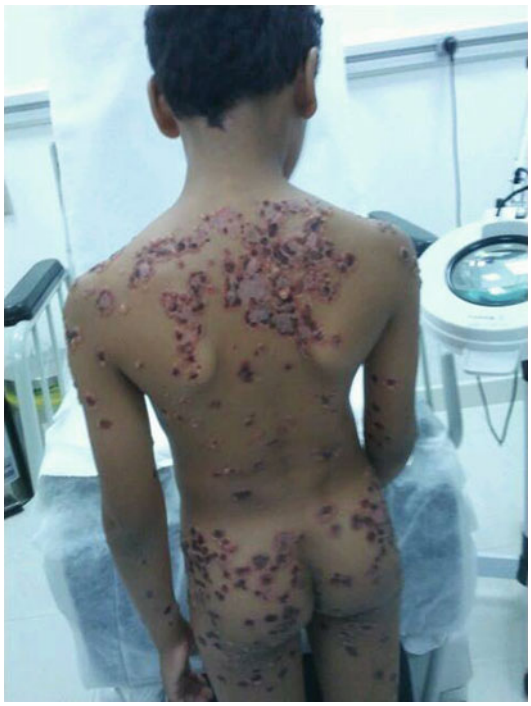

Fig. 36 Chronic bullous disease of childhood; itchy blistering condition with the characteristic "string of pearls" arrangement of lesions in a child. (Taken by Prof. Enas Attia, Dermatology, Venereology and Andrology Department, Faculty of Medicine, Ain Shams University, Cairo, Egypt)

3 Infectious Skin Disease

3.1 Fungal Infection (Mycosis)

- **Definition**: Fungal infections or mycoses cause a wide range of diseases in humans (Aly 1994).
- **Clinical feature**: Cutaneous mycoses, characterized by pruritic rash, are classified as dermatophytosis and dermatomycosis. Dermatophytoses (tinea circinata or ringworm) are caused by dermatophytes. Dermatomycoses are due to other fungi, commonly candida (Foster et al. 2004). Tinea corporis is dermatophytosis of glabrous skin (Aly

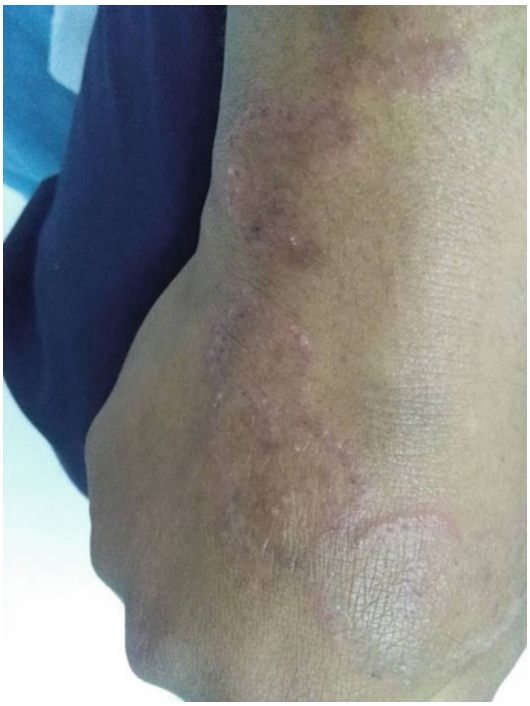

Fig. 37 Itchy circinate lesions of tinea corporis on dorsum of the right hand. (Taken by Prof. Enas Attia, Dermatology, Venereology and Andrology Department, Faculty of Medicine, Ain Shams University, Cairo, Egypt)

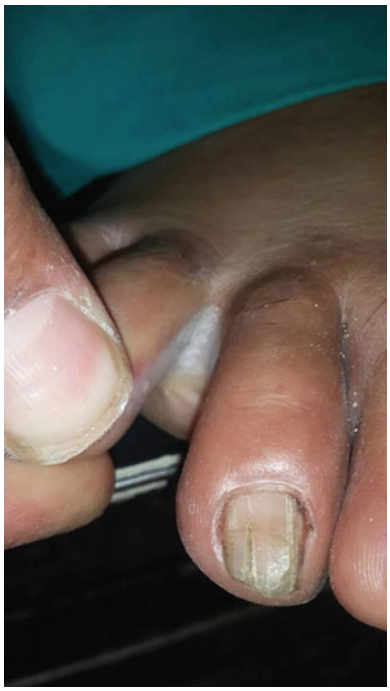

Fig. 39 Tinea pedis presented as itchy macerated toe webs. (Taken by Prof. Enas Attia, Dermatology, Venereology and Andrology Department, Faculty of Medicine, Ain Shams University, Cairo, Egypt)

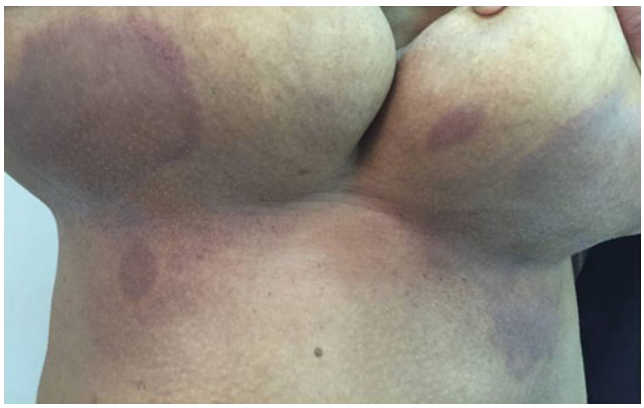

Fig. 38 Submammary tinea circinata (corporis) in a diabetic female. (Taken by Dr. Mona Atef, Dermatology, Venereology and Andrology Department, Faculty of Medicine, Ain Shams University, Cairo, Egypt)

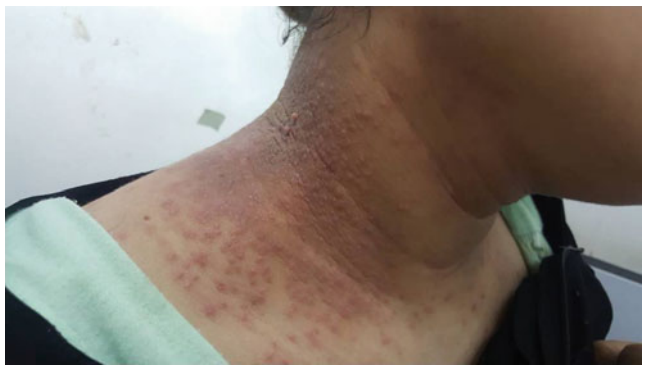

Fig. 40 Satellite lesions of cutaneous candidiasis in a diabetic female. (Taken by Dr. Mona Atef, Dermatology, Venereology and Andrology Department, Faculty of Medicine, Ain Shams University, Cairo, Egypt)

1994) (Figs. 37 and 38). Toe web spaces are a major reservoir for fungi (Fig. 39). Intertriginous candidiasis consists of moist erythematous rash with satellite lesions (Pires et al. 2014) (Fig. 40).

- **Pathological manifestation**: The demonstration of fungi in direct microscopy or culture of scrapings or smears should be considered significant, if clinically relevant (Fig. 41). Skin biopsies with hematoxylin and eosin staining occasionally demonstrate hyphae in the stratum corneum (Fig. 42), but special fungal stains such as periodic acid-Schiff may be required (Clayion 1992).

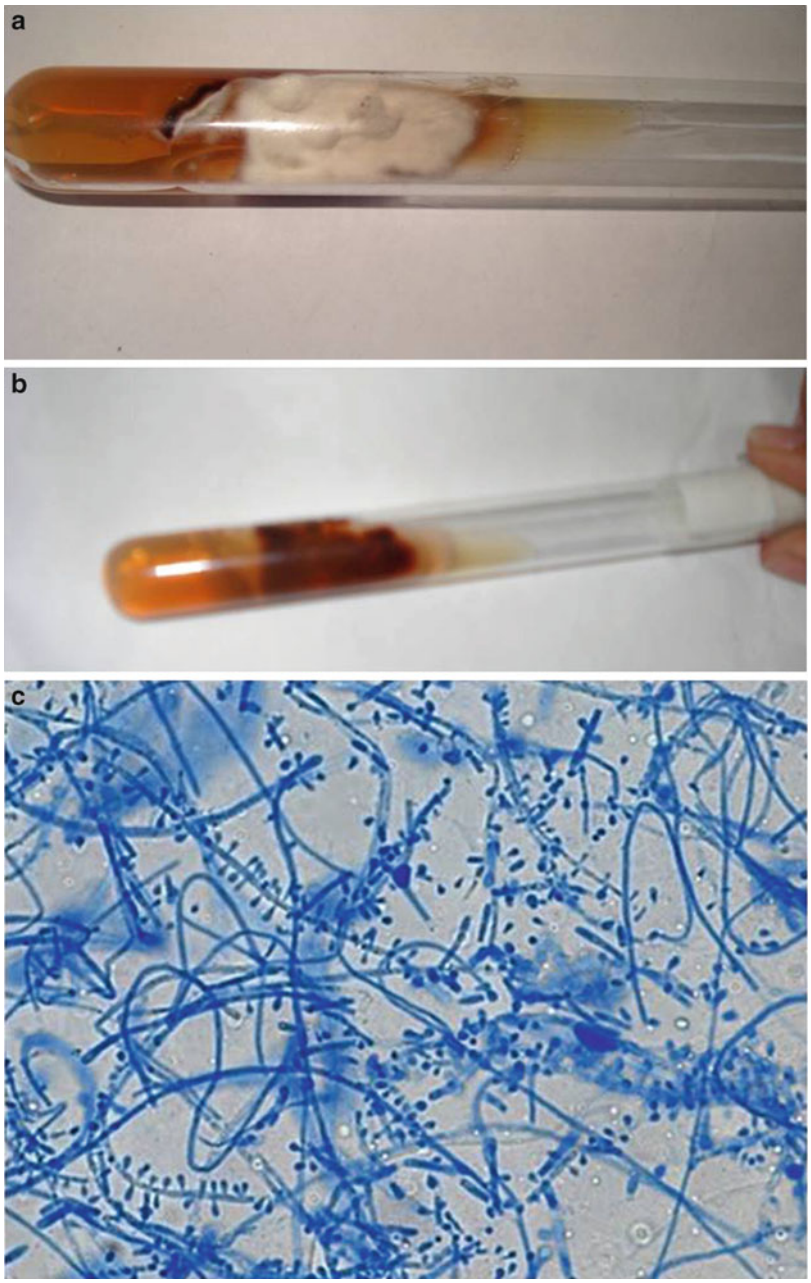

Fig. 41 Trichophyton rubrum; (**a**) front, and (**b**) back views of colonies on Sabouraud dextrose agar, and (**c**) direct examination of colony stained by lactophenol cotton blue (culture and staining done at Prof. Mohamed Taha Laboratory). (Taken by Dr. Azza Mostafa, Dermatology, Venereology and Andrology Department, Faculty of Medicine, Ain Shams University, Cairo, Egypt)

- **Prognosis and treatment**: Despite good prognosis, chronic and recurrent infections are common, which may partly be related to the prevalence of fungal spores, but possibly owing to incomplete eradication of the fungi by lack of compliance with conventional multi-dose treatments (Li et al. 2014). In uncomplicated few cutaneous lesions, topical antifungal agents are adequate (Weinstein and Berman 2002). In chronic or widespread infections, systemic antifungal therapies are required (Tsunemi 2016).
- **Differential diagnosis**: Intertrigo, annular psoriasis, eczemas, annular erythema, erythrasma, granuloma annulare, parapsoriasis, pityriasis rosea, and subacute cutaneous lupus erythematosus.

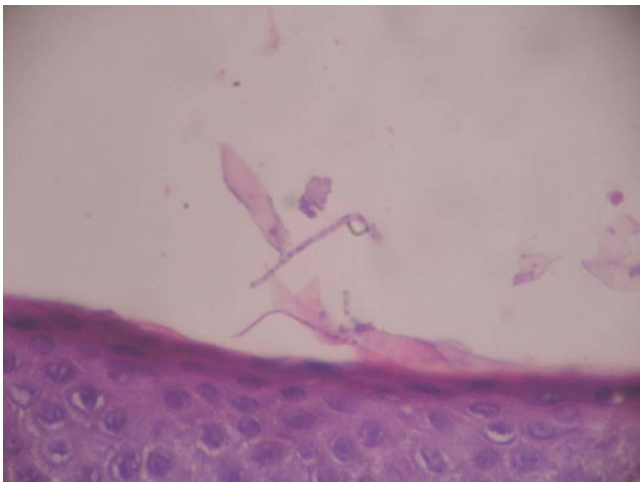

Fig. 42 Skin fungal infection; hematoxylin and eosin section showing fungal hyphae in stratum corneum (x400). (Taken by Dr. Azza Mostafa, Dermatology, Venereology and Andrology Department, Faculty of Medicine, Ain Shams University, Cairo, Egypt)

3.2 Parasitic Skin Disease

3.2.1 Pediculosis

- **Definition**: Pediculosis is caused by the three types of sucking lice including body louse (*Pediculus humanus humanus*), head louse (*Pediculus humanus capitis*), and pubic or crab louse (*Pthirus pubis*). The head louse is prevalent in all countries at all social levels (Maunder 1983).
- **Clinical feature**: The characteristic itching that accompanies infestation may be complicated by secondary bacterial infections (Forsman 1995). Most epidemiological studies have used direct visual inspection for diagnosis (Fig. 43); however, plastic comb detection is proven better (Balcioglu et al. 2008). Dermoscopy can help in diagnosis by visualizing eggs (nits) and/or lice (Fig. 44).
- **Pathological manifestation**: Because of severe itching, pathological manifestations of excoriation and secondary bacterial infection are seen. In addition, bite reaction and hypersensitivity dermatitis may be present (Takcı et al. 2012).

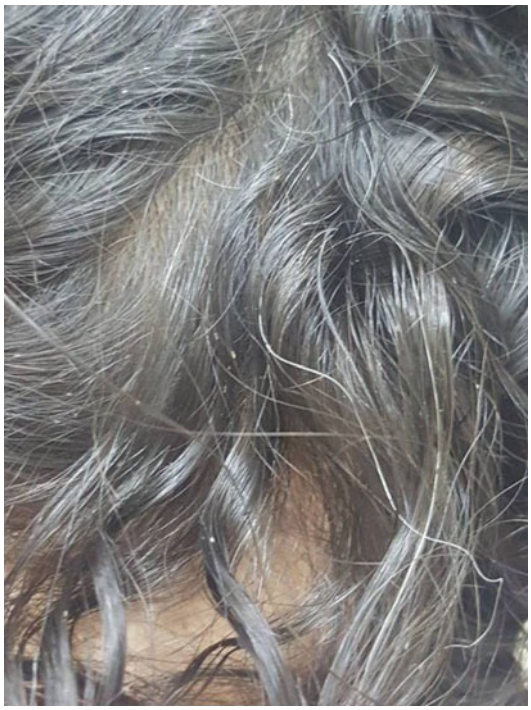

Fig. 43 Pediculosis capitis showing nits (eggs) firmly attached to the hair shaft close to the scalp. (Taken by Dr. Azza Mostafa, Dermatology, Venereology and Andrology Department, Faculty of Medicine, Ain Shams University, Cairo, Egypt)

- **Prognosis and treatment**: Removing lice by hand or lice comb, heating infested clothings, and shaving scalp were the oldest methods of controlling human lice. Despite the introduction of other treatments including cresol, naphthalene, sulfur, mercury, vinegar, petroleum, and insecticides, a number of new cases and resistance ones have increased (Sangaré et al. 2016). Treatments include organochlorines (DDT, lindane), organophosphates (malathion), carbamates (carbaryl), pyrethrins (pyrethrum), pyrethroids (permethrin, phenothrin, and bioallethrin), and oral ivermectin (Sangaré et al. 2016).
- **Differential diagnosis**: Itchy scaly scalp, dandruff/seborrheic dermatitis, psoriasis, and tinea capitis (Elewski 2005).

Fig. 44 Dermoscopy in pediculosis capitis showing (**a**) nits (eggs) firmly attached to the hair shaft close to the scalp and (**b**) head lice on the scalp, 1–3-mm-long, dorsoventrally flattened ectoparasite with three pairs of legs (×10). (Taken by Dr. Azza Mostafa, Dermatology, Venereology and Andrology Department, Faculty of Medicine, Ain Shams University, Cairo, Egypt)

3.2.2 Scabies

- **Definition**: Scabies is a common pruritic skin infestation caused by *Sarcoptes scabiei* mite (Hengge et al. 2006). The estimated worldwide annual prevalence is 300 million (Chosidow 2006). The main manifestations are mediated through hypersensitivity-like reactions and immune responses (Anderson and Strowd 2017).
- **Clinical feature**: Findings include serpiginous white lines indicative of mite burrows; these classically occur in interdigital web spaces, areolae of female breasts, and male genitalia, but they may be found on other body sites (Anderson and Strowd 2017) (Fig. 45). Visualizing burrows or mites on dermoscopy can assist in diagnosis (Dupuy et al. 2007) (Fig. 46).
- **Pathological manifestation**: Scabies mites burrow into the top layer of the skin where the adult female lays eggs (Fig. 47). The pathological manifestations are mediated through inflammatory and hypersensitivity-like reactions to mite products leading to different pruritic lesions (Anderson and Strowd 2017).
- **Prognosis and treatment**: If all close contacts are not treated simultaneously, patients may become re-infested. Nonadherence to treatment regimen is another cause of treatment failure. Patients should decontaminate all bedding, towels, and clothings at the time of treatment (Chosidow 2006). Topical permethrin is widely used, but it is associated with resistance, poor compliance, and allergic reactions. Other treatments include oral ivermectin and topical agents such as lindane, precipitated sulfur, malathion, and ivermectin (Thomas et al. 2015).
- **Differential diagnosis**: Eczema, papular urticaria, and irritant or contact dermatitis (Anderson and Strowd 2017).

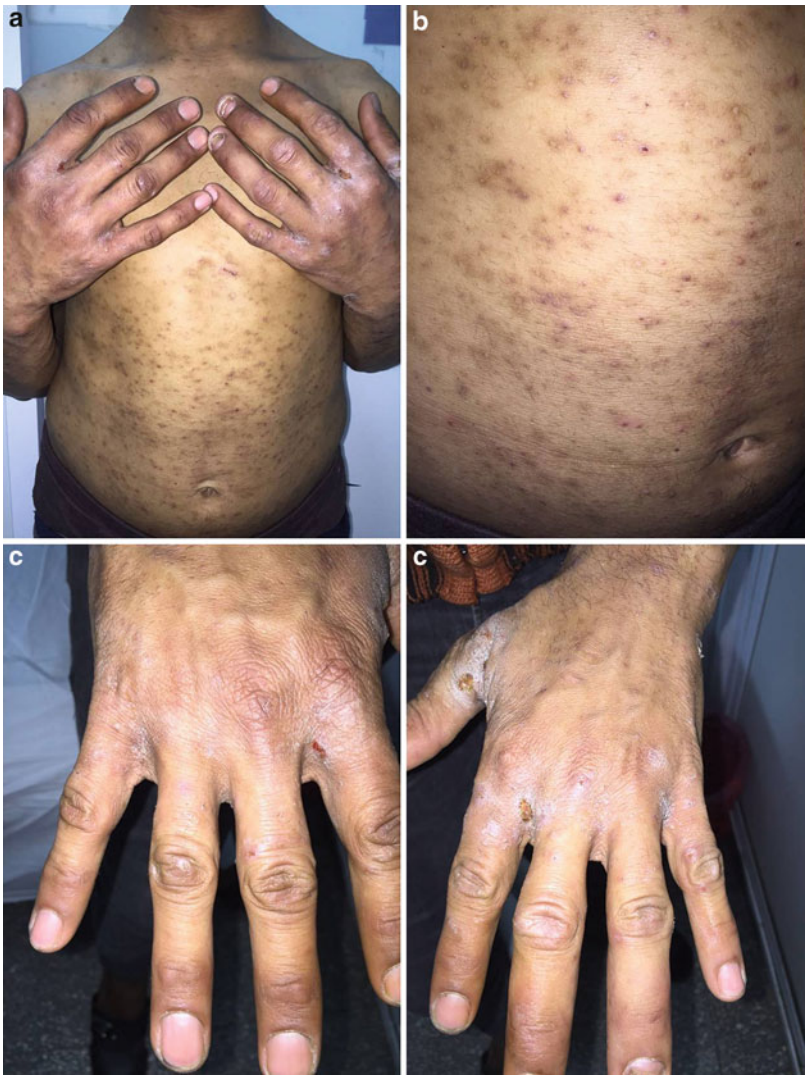

Fig. 45 Pleomorphic lesions of scabies on the trunk and interdigital areas with secondary infection of the interdigital area of the left hand. (Taken by Dr. Mona Atef, Dermatology, Venereology and Andrology Department, Faculty of Medicine, Ain Shams University, Cairo, Egypt)

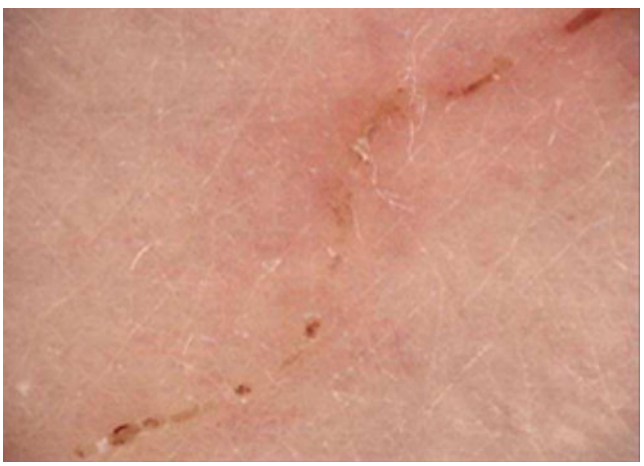

Fig. 46 S-shaped burrow with eggs (black dots) and a mite appearing as delta wing jet at its lower end in dermoscopic examination. (Taken by Prof. Enas Attia, Dermatology, Venereology and Andrology Department, Faculty of Medicine, Ain Shams University, Cairo, Egypt)

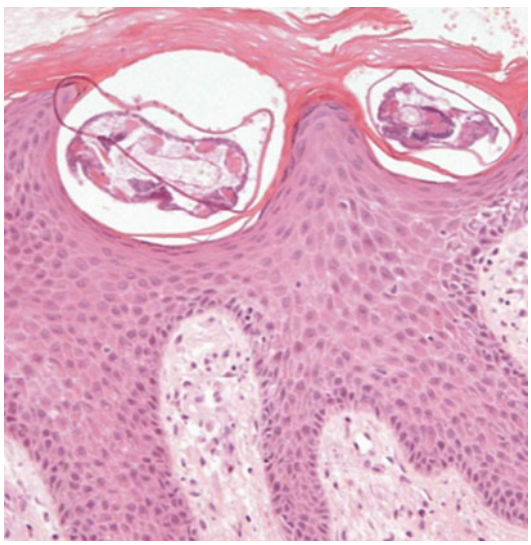

Fig. 47 Scabies mites burrow into the top layer of the skin. (Taken by Dr. Mona Atef, Dermatology, Venereology and Andrology Department, Faculty of Medicine, Ain Shams University, Cairo, Egypt)

4 Neoplastic Condition

4.1 Cutaneous T-Cell Lymphoma

- **Definition**: Cutaneous T-cell lymphoma is a heterogeneous group of lymphoproliferative disorders characterized by varying degrees of malignancy (Olek-Hrab et al. 2016). Histamine H4 receptor seems important in pathogenesis of pruritus in this condition (Zampeli and Tiligada 2009). In Sézary syndrome, enhanced Th2 cytokines contribute to pruritus (Dummer et al. 1996).
- **Clinical feature**: Mycosis fungoides is the most common type of cutaneous T-cell lymphoma, with a long time presentation of mild symptoms and limited patches. With progression, increased pruritus and skin manifestations develop (Fig. 48). Sézary syndrome is a progressive form of mycosis fungoides, characterized by erythroderma (Fig. 49), lymphadenopathy, and presence of Sézary cells in peripheral blood (Bagherani and Smoller 2016).
- **Pathological manifestation**: Histopathological findings include atypical T lymphocytes having cerebriform nuclei (marked enfolding of nuclear membrane) infiltrating the epidermis (epidermotropism) and dermis (Fig. 50). In immunohistochemical study, tumor cells show increased CD4/CD8 ratio (Bagherani and Smoller 2016) (Fig. 51).
- **Prognosis and treatment**: It is a lifelong disorder and can recur after discontinuation of therapy (Bagherani and Smoller 2016). Controlling disease may manage itch.

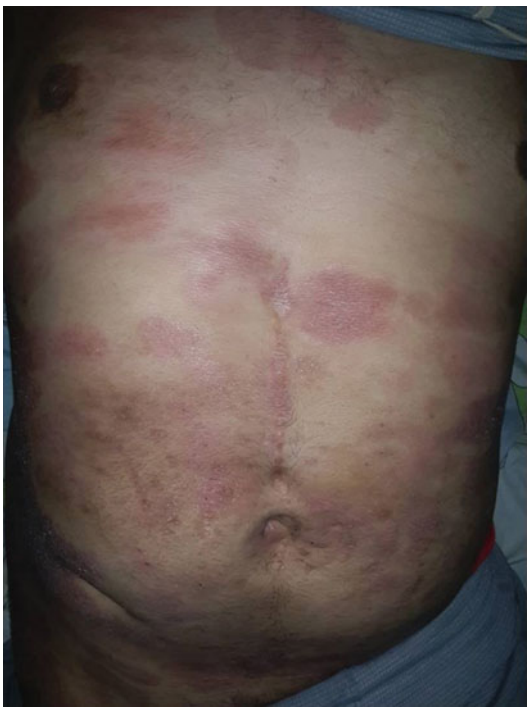

Fig. 48 Pruritic patches of mycosis fungoides. (Taken by Dr. Azza Mostafa, Dermatology, Venereology and Andrology Department, Faculty of Medicine, Ain Shams University, Cairo, Egypt)

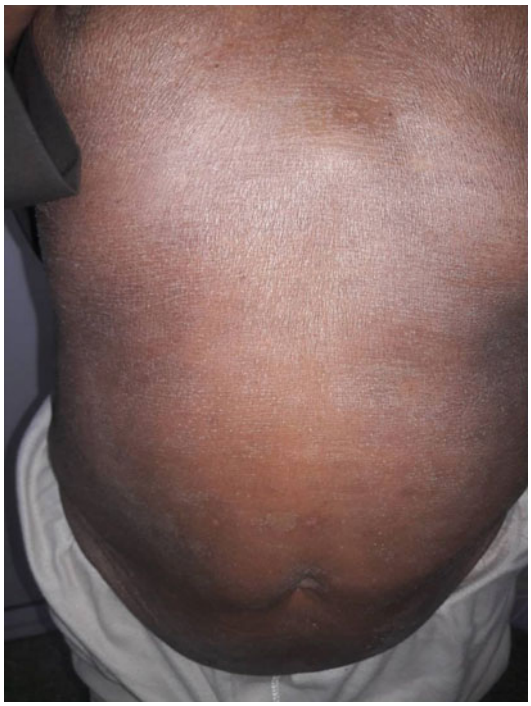

Fig. 49 Erythroderma in Sézary syndrome. (Taken by Dr. Azza Mostafa, Dermatology, Venereology and Andrology Department, Faculty of Medicine, Ain Shams University, Cairo, Egypt)

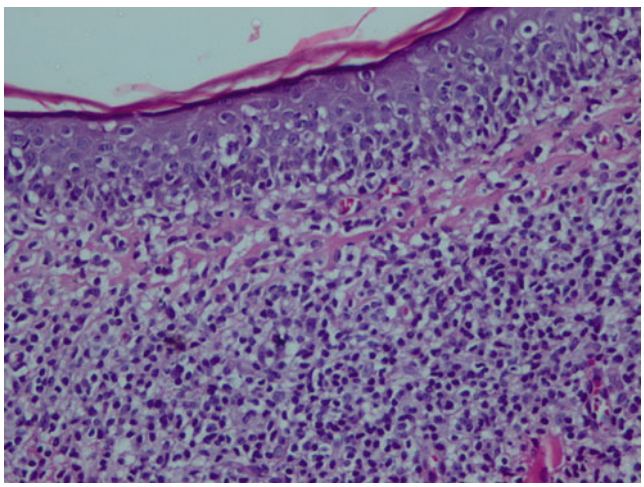

Fig. 50 Histopathology of mycosis fungoides showing diffuse lymphocytic infiltration of the papillary dermis, extensive epidermotropism of small- to medium-sized lymphocytes with cerebriform nuclear contour and perinuclear halo occurring singly and in clusters forming Pautrier microabscesses (hematoxylin and eosin stain x400). (Taken by Dr. Azza Mostafa, Dermatology, Venereology and Andrology Department, Faculty of Medicine, Ain Shams University, Cairo, Egypt)

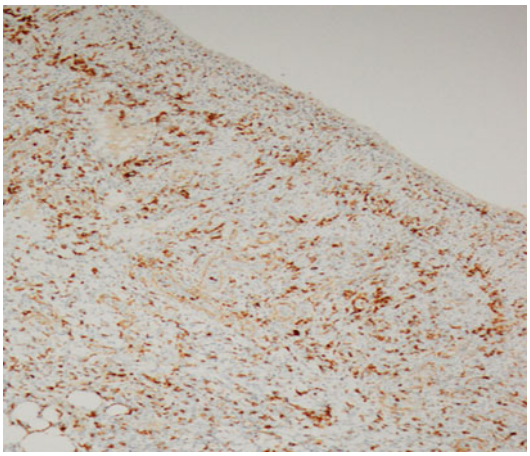

Fig. 51 Mycosis fungoides; immunohistochemistry staining with anti-CD4 antibody showing positively labeled cells in the epidermis and the majority of dermal infiltrate (anti-CD4 x200). (Taken by Dr. Azza Mostafa, Dermatology, Venereology and Andrology Department, Faculty of Medicine, Ain Shams University, Cairo, Egypt)

Skin-directed phototherapies and topical anti-lymphoma treatments including carmustine, retinoids, and mechlorethamine (nitrogen mustard) have demonstrated effectiveness in early stages but may exacerbate pruritus (Olek-Hrab et al. 2016). Romidepsin and vorinostat reduced pruritus (Field et al. 2016).

- **Differential diagnosis**: Parapsoriasis, eczema, and tinea corporis (Olek-Hrab et al. 2016).

5 Miscellaneous Pruritic Skin Condition

5.1 Primary Cutaneous Amyloidosis

- **Definition**: Primary cutaneous amyloidosis refers to the extracellular deposition of amyloid material in apparently normal skin without systemic involvement (Schreml et al. 2010). It seems to have association with various autoimmune/immune disorders (Dahdah et al. 2009).
- **Clinical feature**: Its major variants include (a) macular amyloidosis (Fig. 52), with mild to severely itchy lesions that may form patches of darkened skin commonly on the upper back, and (b) lichen amyloidosis (Fig. 53), with itchy, raised brown lesions discrete and coalescing to hyperkeratotic tan-brown papules commonly on the pretibial surfaces (Schreml et al. 2010). The condition is thought to be induced by scratching (Salim et al. 2005). On dermoscopy, the most common finding is a central hub surrounded by various configurations of brownish pigmentation (Chuang et al. 2012) (Figs. 54 and 55).
- **Pathological manifestation**: The key component is the deposition of amorphous amyloid material within the

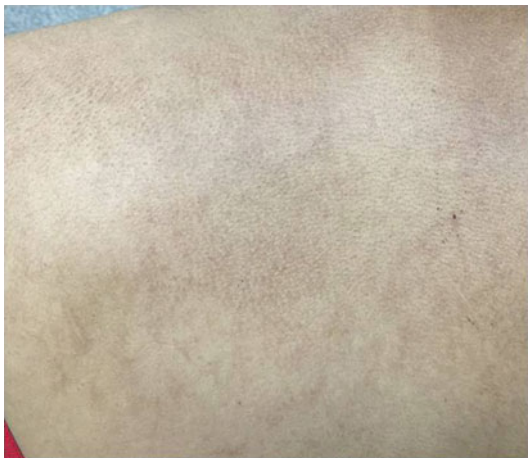

Fig. 52 Patches of darkened skin of macular amyloidosis. (Taken by Dr. Mona Atef, Dermatology, Venereology and Andrology Department, Faculty of Medicine, Ain Shams University, Cairo, Egypt)

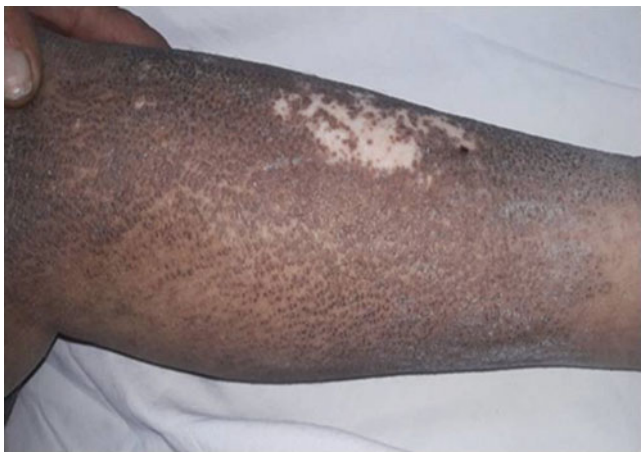

Fig. 53 Raised brown hyperkeratotic tan-brown papules of lichen amyloidosis. (Taken by Dr. Mona Atef, Dermatology, Venereology and Andrology Department, Faculty of Medicine, Ain Shams University, Cairo, Egypt)

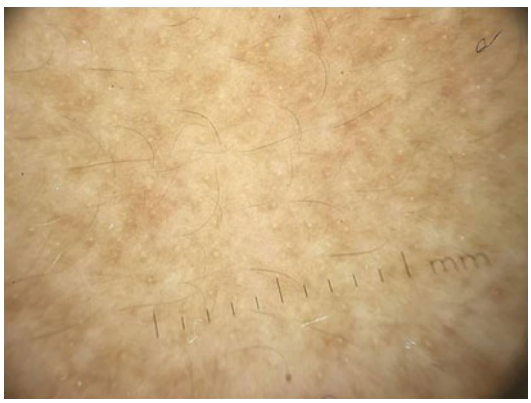

Fig. 54 Dermoscopy of macular amyloidosis showing central hub surrounded by various configurations of brownish pigmentation. (Taken by Dr. Azza Mostafa, Dermatology, Venereology and Andrology Department, Faculty of Medicine, Ain Shams University, Cairo, Egypt)

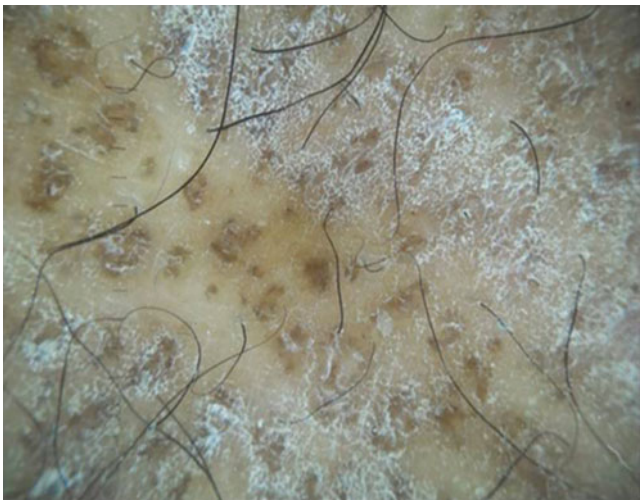

Fig. 55 Dermoscopy of lichen amyloidosis showing central hub surrounded by various configurations of brownish pigmentation. (Taken by Dr. Azza Mostafa, Dermatology, Venereology and Andrology Department, Faculty of Medicine, Ain Shams University, Cairo, Egypt)

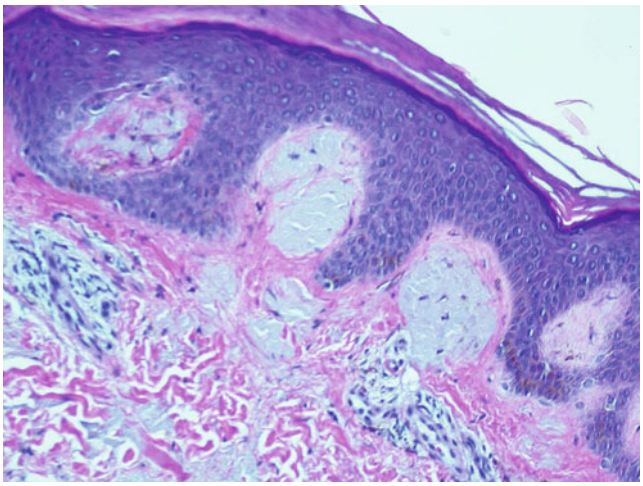

Fig. 56 Histopathology of lichen amyloidosis with deposition of amorphous amyloid material within the papillary dermis (H&E stain, X400). (Courtesy of Dr. Delaram Mohamed Mahmoud, Alborge Laboratories, Doha, Qatar)

papillary dermis (Fig. 56). Congo red highlights the deposits as red-orange material (Fig. 57) and under polarization takes on a bright apple-green birefringence. Cytokeratin (CK) NMF 116 staining can be used to identify the amyloid as epidermal in origin (Fig. 58) (Huilgol et al. 1998).

- **Prognosis and treatment**: It is a chronic condition without potential for malignant transformation.

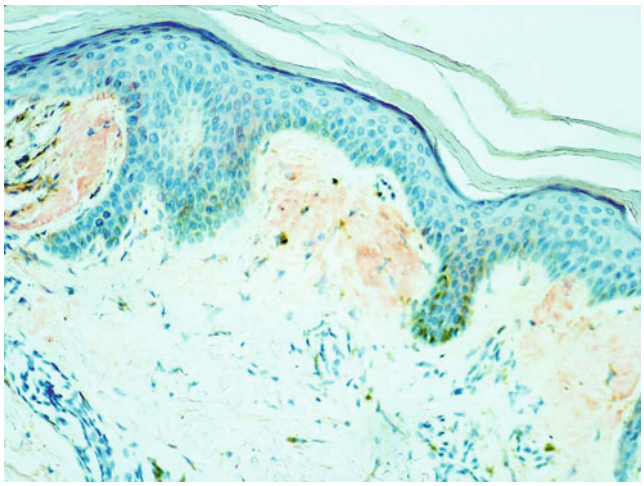

Fig. 57 Lichen amyloidosis; Congo red highlights amyloid deposits as red-orange amorphous material (Congo red stain, X400). (Courtesy of Dr. Delaram Mohamed Mahmoud, Alborge Laboratories, Doha, Qatar)

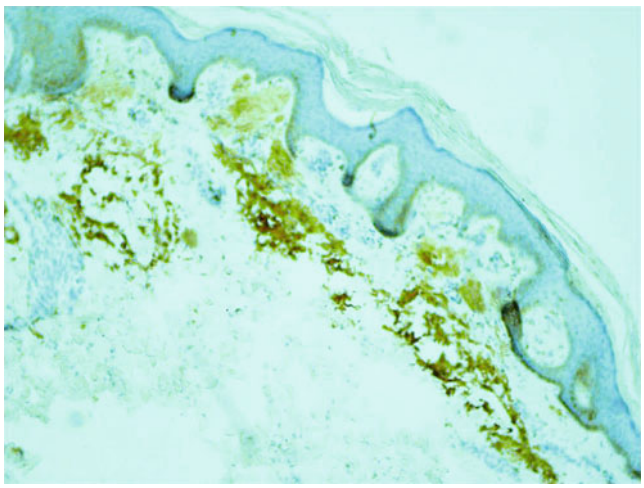

Fig. 58 Lichen amyloidosis; immunohistochemistry showing positive staining with anti- cytokeratin NMF 116 of dermal amyloid deposits (anti-NMF 116, X200). (Courtesy of Dr. Delaram Mohamed Mahmoud, Alborge Laboratories, Doha, Qatar)

Treatment is not required unless for symptomatic or cosmetic complaints. Success has been reported with corticosteroids, antihistamines, ultraviolet light, laser, dermabrasion, scalpel scraping, and retinoid agents (Salim et al. 2005).

- **Differential diagnosis**: Lichen simplex chronicus, lichen sclerosus et atrophicus, and prurigo nodularis (Salim et al. 2005).

References

Aberer W (2014) Angioedema is not just 'deep urticaria' but an entity of its own. Allergy 69(5):549–552

Agarwal US, Besarwal RK, Gupta R, Agarwal P, Napalia S (2014) Hand eczema. Indian J Dermatol 59(3):213–224

Aly R (1994) Ecology and epidemiology of dermatophyte infections. J Am Acad Dermatol 31(3 Pt 2):S21–S25

Amar SM, Dreskin SC (2008) Urticaria. Prim Care 35(1):141–157

Anderson KL, Strowd LC (2017) Epidemiology, diagnosis, and treatment of scabies in a dermatology office. J Am Board Fam Med 30 (1):78–84

Antiga E, Caproni M (2015) The diagnosis and treatment of dermatitis herpetiformis. Clin Cosmet Investig Dermatol 8:257–265

Bagherani N, Smoller BR (2016) An overview of cutaneous T cell lymphomas. F1000Res 5:pii: F1000 Faculty Rev-1882

Balcioglu C, Burgess IF, Limoncu ME, Sahin MT, Ozbel Y, Bilaç C, Kurt O, Larsen KS (2008) Plastic detection comb better than visual screening for diagnosis of head louse infestation. Epidemiol Infect 136(10):1425–1431

Barzilai A, Sagi L, Baum S, Trau H, Schvimer M, Barshack I, Solomon M (2017) The histopathology of urticaria revisited-clinical pathological study. Am J Dermatopathol 39(10):753–759

Bautista DM, Wilson SR, Hoon MA (2014) Why we scratch an itch: the molecules, cells and circuits of itch. Nat Neurosci 17(2):175–182

Bickle K, Roark TR, Hsu S (2002) Autoimmune bullous dermatoses: a review. Am Fam Physician 65(9):1861–1870

Bussmann C, Hagemann T, Hanfland J, Haidl G, Bieber T, Novak N (2007) Flushing and increase of serum tryptase after mechanical irritation of a solitary mastocytoma. Eur J Dermatol 17(4):332–334

Campalani E, Barker JNWN (2005) The clinical genetics of psoriasis. Curr Genomics 6(1):51–60

Caproni M, Antiga E, Melani L, Fabbri P, Italian Group for Cutaneous Immunopathology (2009) Guidelines for the diagnosis and treatment of dermatitis herpetiformis. J Eur Acad Dermatol Venereol 23 (6):633–638

Chorzelski TP, Jablouska S (1979) IgA linear dermatosis of childhood (chronic bullous disease of childhood). Br J Dermatol 101 (5):535–542

Chosidow O (2006) Clinical practices. Scabies. N Engl J Med 354 (16):1718–1727

Chuang YY, Lee DD, Lin CS, Chang YJ, Tanaka M, Chang YT, Liu HN (2012) Characteristic dermoscopic features of primary cutaneous amyloidosis: a study of 35 cases. Br J Dermatol 167(3):548–554

Clayion YM (1992) Clinical and mycological diagnostic aspects of onychomycoses and dermatomycoses. Clin Exp Dermatol 17 (Suppl 1):37–40

Dahdah MJ, Kurban M, Kibbi AG, Ghosn S (2009) Primary localized cutaneous amyloidosis: a sign of immune dysregulation? Int J Dermatol 48(4):419–421

Di Zenzo G, Calabresi V, Grosso F, Caproni M, Ruffelli M, Zambruno G (2007) The intracellular and extracellular domains of BP180 antigen comprise novel epitopes targeted by pemphigoid gestationis autoantibodies. J Invest Dermatol 127(4):864–873

Di Zenzo G, Della Torre R, Zambruno G, Borradori L (2012) Bullous pemphigoid: from the clinic to the bench. Clin Dermatol 30(1):3–16

Dummer R, Heald PW, Nestle FO, Ludwig E, Leine E, Hemmi S, Burg G (1996) Sézary syndrome T-cell clones display T-helper 2 cytokines and express the accessory factor-1 (interferon gamma receptor beta-chain). Blood 88(4):1383–1389

Dupuy A, Dehen L, Bourrat E, Lacroix C, Benderdouche M, Dubertret L, Morel P, Feuilhade de Chauvin M, Petit A (2007) Accuracy of standard dermoscopy for diagnosing scabies. J Am Acad Dermatol 56(1):53–62

Elewski BE (2005) Clinical diagnosis of common scalp disorders. J Investig Dermatol Symp Proc 10(3):190–193

Errichetti E, Stinco G (2016) Dermoscopy in general dermatology: a practical overview. Dermatol Ther (Heidelb) 6(4):471–507

Fahad AS, Ammar AR (2011) Unusual clinicopathological and immunological presentation of chronic bullous dermatosis of childhood (linear IgA dermatosis). Indian J Dermatol 56(5):573–575

Field H, Gao L, Motwani P, Wong HK (2016) Pruritus reduction with systemic anti-lymphoma treatments in patients with cutaneous T cell lymphoma: a narrative review. Dermatol Ther (Heidelb) 6 (4):579–595

Forsman KE (1995) Pediculosis and scabies. What to look for in patients who are crawling with clues. Postgrad Med 98(6):89–100

Foster KW, Ghannoum MA, Elewski BE (2004) Epidemiologic surveillance of cutaneous fungal infection in the United States from 1999 to 2002. J Am Acad Dermatol 50(5):748–752

Frigas E, Park MA (2009) Acute urticaria and angioedema: diagnostic and treatment considerations. Am J Clin Dermatol 10(4):239–250

Fry L (2002) Dermatitis herpetiformis: problems, progress and prospects. Eur J Dermatol 12(6):523–531

Goncharova Y, Attia EA, Souid K, Protzenko O, Koktishev I (2015) Dermoscopic features of clinically inflammatory dermatoses and their correlation with histopathologic reaction patterns. Arch Dermatol Res 307(1):23–30

Gorouhi F, Davari P, Fazel N (2014) Cutaneous and mucosal lichen planus: a comprehensive review of clinical subtypes, risk factors, diagnosis, and prognosis. ScientificWorldJournal 2014:742826

Griffiths CE, Barker JN (2007) Pathogenesis and clinical features of psoriasis. Lancet 370(9583):263–271

Habashy J, Elston DM (2017) Mastocytosis. Resource document. Medscape. http://emedicine.medscape.com/article/1057932-overview. Updated 15 May 2017. Accessed 23 May 2017

Heide R, Beishuizen A, De Groot H, Den Hollander JC, Van Doormaal JJ, De Monchy JG, Pasmans SG, Van Gysel D, Oranje AP, Dutch National Mastocytosis Work Group (2008) Mastocytosis in children: a protocol for management. Pediatr Dermatol 25(4):493–500

Hengge UR, Currie BJ, Jager G, Lupi O, Schwartz RA (2006) Scabies: a ubiquitous neglected skin disease. Lancet Infect Dis 6(12):769–779

Hide M, Francis DM, Grattan CE, Hakimi J, Kochan JP, Greaves MW (1993) Autoantibodies against the high-affinity IgE receptor as a cause of histamine release in chronic urticaria. N Engl J Med 328 (22):1599–1604

Hiragun M, Hiragun T, Mihara S, Akita T, Tanaka J, Hide M (2013) Prognosis of chronic spontaneous urticaria in 117 patients not controlled by a standard dose of antihistamine. Allergy 68(2):229–235

Horny HP, Sotlar K, Valent P (2007) Mastocytosis: state of the art. Pathobiology 74(2):121–132

Huilaja L, Mäkikallio K, Tasanen K (2014) Gestational pemphigoid. Orphanet J Rare Dis 9:136

Huilgol SC, Ramnarain N, Carrington P, Leigh IM, Black MM (1998) Cytokeratins in primary cutaneous amyloidosis. Australas J Dermatol 39(2):81–85

Jenkins RE, Hern S, Black MM (1999) Clinical features and management of 87 patients with pemphigoid gestationis. Clin Exp Dermatol 24(4):255–259

Joly P, Courville P, Lok C, Bernard P, Saiag P, Dreno B, Delaporte E, Bedane C, Picard C, Sassolas B, Plantin P, D'Incan M, Chosidow O, Pauwels C, Lambert D, Loche F, Prost C, Tancrede-Bohin E, Guillaume JC, Roujeau JC, Gilbert D, Tron F, Vaillant L, French Bullous Study Group (2004) Clinical criteria for the diagnosis of bullous pemphigoid: a reevaluation according to immunoblot analysis of patient sera. Dermatology 208(1):16–20

Kaplan AP (2002) Clinical practice. Chronic urticaria and angioedema. N Engl J Med 346(3):175–179

Kneisel A, Hertl M (2011) Autoimmune bullous skin diseases. Part 2: diagnosis and therapy. J Dtsch Dermatol Ges 9(11):927–947

Krause K, Spohr A, Zuberbier T, Church MK, Maurer M (2013) Up-dosing with bilastine results in improved effectiveness in cold contact urticaria. Allergy 68(7):921–928

Lallas A, Kyrgidis A, Tzellos TG, Apalla Z, Karakyriou E, Karatolias A, Lefaki I, Sotiriou E, Ioannides D, Argenziano G, Zalaudek I (2012) Accuracy of dermoscopic criteria for the diagnosis of psoriasis, dermatitis, lichen planus and pityriasis rosea. Br J Dermatol 166 (6):1198–1205

Lear JT, Smith AG (1998) Multiple blisters in a young boy. Linear IgA disease of childhood (LADC). (Chronic bullous dermatosis of childhood). Arch Dermatol 134(5):625, 628

Li RY, Wang AP, Xu JH, Xi LY, Fu MH, Zhu M, Xu ML, Li XQ, Lai W, Liu WD, Lu XY, Gong ZQ (2014) Efficacy and safety of 1% terbinafine film-forming solution in Chinese patients with tinea pedis: a randomized, double-blind, placebo-controlled, multicenter, parallel-group study. Clin Drug Investig 34(3):223–230

Lisi P (2007) Differential diagnosis of psoriasis. Reumatismo 59(Suppl 1):56–60

Liu YD, Wang YH, Ye YC, Zhao WL, Li L (2017) Prognostic factors for mortality in patients with bullous pemphigoid: a meta-analysis. Arch Dermatol Res 309(5):335–347

Mansi M, Zanichelli A, Coerezza A, Suffritti C, Wu MA, Vacchini R, Stieber C, Cichon S, Cicardi M (2015) Presentation, diagnosis and treatment of angioedema without wheals: a retrospective analysis of a cohort of 1058 patients. J Intern Med 277(5):585–593

Marsden RA, McKee PH, Bhogal B, Black MM, Kennedy LA (1980) A study of benign chronic bullous dermatosis of childhood and comparison with dermatitis herpetiformis and bullous pemphigoid occurring in childhood. Clin Exp Dermatol 5(2):159–176

Maunder JW (1983) The appreciation of lice. Proc R Inst GB 55:1–31

Maurer M, Magerl M, Metz M, Siebenhaar F, Weller K, Krause K (2013) Practical algorithm for diagnosing patients with recurrent wheals or angioedema. Allergy 68(6):816–819

Menter A (2016) Psoriasis and psoriatic arthritis treatment. Am J Manag Care 22(8 Suppl):s225–s237

Mihályi L, Kiss M, Dobozy A, Kemény L, Husz S (2012) Clinical relevance of autoantibodies in patients with autoimmune bullous dermatosis. Clin Dev Immunol 2012:369546

Nakamura M, Toyoda M, Morohashi M (2003) Pruritogenic mediators in psoriasis vulgaris: comparative evaluation of itch-associated cutaneous factors. Br J Dermatol 149(4):718–730

Nanda A, Dvorak R, Al-Saeed K, Al-Sabah H, Alsaleh QA (2004) Spectrum of autoimmune bullous diseases in Kuwait. Int J Dermatol 43(12):876–881

Navarini AA, Feldmeyer L, Töndury B, Fritsche P, Kamarashev J, French LE, Braun RP (2011) The yellow clod sign. Arch Dermatol 147(11):1350

Nicolas ME, Krause PK, Gibson LE, Murray JA (2003) Dermatitis herpetiformis. Int J Dermatol 42(8):588–600

Olek-Hrab K, Hrab M, Szyfter-Harris J, Adamski Z (2016) Pruritus in selected dermatoses. Eur Rev Med Pharmacol Sci 20(17):3628–3641

Oschatz C, Maas C, Lecher B, Jansen T, Björkqvist J, Tradler T, Sedlmeier R, Burfeind P, Cichon S, Hammerschmidt S, Müller-Esterl W, Wuillemin WA, Nilsson G, Renné T (2011) Mast cells increase vascular permeability by heparin-initiated bradykinin formation in vivo. Immunity 34(2):258–268

Phelps RG, Miller MK, Singh F (2003) The varieties of "eczema": clinicopathologic correlation. Clin Dermatol 21(2):95–100

Pires CA, Cruz NF, Lobato AM, Sousa PO, Carneiro FR, Mendes AM (2014) Clinical, epidemiological, and therapeutic profile of dermatophytosis. An Bras Dermatol 89(2):259–264

Salim T, Shenoi SD, Balachandran C, Mehta VR (2005) Lichen amyloidosus: a study of clinical, histopathologic and immunofluorescence findings in 30 cases. Indian J Dermatol Venereol Leprol 71 (3):166–169

Sampogna F, Gisondi P, Melchi CF, Amerio P, Girolomoni G, Abeni D, IDI Multipurpose Psoriasis Research on Vital Experiences Investigators (2004) Prevalence of symptoms experienced by patients with different clinical types of psoriasis. Br J Dermatol 151(3):594–599

Sangaré AK, Doumbo OK, Raoult D (2016) Management and treatment of human lice. Biomed Res Int 2016:8962685

Schaefer P (2017) Acute and chronic urticaria: evaluation and treatment. Am Fam Physician 95(11):717–724

Schreml S, Szeimies RM, Vogt T, Landthaler M, Schroeder J, Babilas P (2010) Cutaneous amyloidoses and systemic amyloidoses with cutaneous involvement. Eur J Dermatol 20(2):152–160

Siegfried EC, Hebert AA (2015) Diagnosis of atopic dermatitis: mimics, overlaps, and complications. J Clin Med 4(5):884–917

Simons FE, Ardusso LR, Dimov V, Ebisawa M, El-Gamal YM, Lockey RF, Sanchez-Borges M, Senna GE, Sheikh A, Thong BY, Worm M, World Allergy Organization (2013) World Allergy Organization Anaphylaxis Guidelines: 2013 update of the evidence base. Int Arch Allergy Immunol 162(3):193–204

Takcı Z, Tekin O, Karadağ AS (2012) A pediculid case: autosensitization dermatitis caused by pediculosis capitis. Turkiye Parazitol Derg 36(3):185–187

Thomas J, Peterson GM, Walton SF, Carson CF, Naunton M, Baby KE (2015) Scabies: an ancient global disease with a need for new therapies. BMC Infect Dis 15:250

Tsunemi Y (2016) Oral antifungal drugs in the treatment of dermatomycosis. Med Mycol J 57(2):J71–J75

Twycross R, Greaves MW, Handwerker H, Jones EA, Libretto SE, Szepietowski JC, Zylicz Z (2003) Itch: scratching more than the surface. QJM 96(1):7–26

Usatine RP, Tinitigan M (2011) Diagnosis and treatment of lichen planus. Am Fam Physician 84(1):53–60

Valent P (2006) Diagnostic evaluation and classification of mastocytosis. Immunol Allergy Clin North Am 26(3):515–534

Venzor J, Lee WL, Huston DP (2002) Urticarial vasculitis. Clin Rev Allergy Immunol 23(2):201–216

Weinstein A, Berman B (2002) Topical treatment of common superficial tinea infections. Am Fam Physician 65(10):2095–2102

Weston G, Payette M (2015) Update on lichen planus and its clinical variants. Int J Womens Dermatol 1(3):140–149

Wojnavrouska F, Marsden RA, Bhogal B (1988) Chronic bullous disease of childhood, childhood cicatricial pemphigoid and linear IgA disease of adults. J Am Acad Dermatol 19(5 Pt 1):792–805

Wong RC, Fairley JA, Ellis CN (1984) Dermographism: a review. J Am Acad Dermatol 11(4 Pt 1):643–652

Zampeli E, Tiligada E (2009) The role of histamine H4 receptor in immune and inflammatory disorders. Br J Parmacol 157(1):24–33

Zanichelli A, Bova M, Coerezza A, Petraroli A, Triggiani M, Cicardi M (2012) Icatibant treatment for acquired C1-inhibitor deficiency: a real-world observational study. Allergy 67(8):1074–1077

Zhao CY, Murrell DF (2015) Advances in understanding and managing bullous pemphigoid. F1000Res 4:pii: F1000 Faculty Rev-1313

Zuberbier T, Aberer W, Asero R, Bindslev-Jensen C, Brzoza Z, Canonica GW, Church MK, Ensina LF, Giménez-Arnau A, Godse K, Gonçalo M, Grattan C, Hebert J, Hide M, Kaplan A, Kapp A, Abdul Latiff AH, Mathelier-Fusade P, Metz M, Saini SS, Sánchez-Borges M, Schmid-Grendelmeier P, Simons FE, Staubach P, Sussman G, Toubi E, Vena GA, Wedi B, Zhu XJ, Nast A, Maurer M, Dermatology Section of the European Academy of Allergy and Clinical Immunology, Golbal Allergy and Asthma European Network, European Dermatology Forum, World Allergy Organization (2014) Methods report on the development of the 2013 revision and update of the EAACI/GA2LEN/EDF/WAO guideline for the definition, classification, diagnosis and management of urticaria. Allergy 69(7):e1–e29