Review article

CED
Clinical and Experimental Dermatology

CPD

Erythroderma (exfoliative dermatitis). Part 1: underlying causes, clinical presentation and pathogenesis

S. Tso,[1] F. Satchwell,[1] H. Moiz,[2] T. Hari,[3] S. Dhariwal,[1] R. Barlow,[4] E. Forbat,[4,5] H. Randeva,[6,7] Y. T. Tan,[8] A. Ilchyshyn,[4] M. M. Kwok,[9] T. M. Barber,[6,7] C. Thind[1] and A. C. Y. Tso[10]

[1]*Jephson Dermatology Centre, South Warwickshire NHS Foundation Trust, Warwick;* [8]*Department of Cardiology, South Warwickshire NHS Foundation Trust, Warwick, UK;* [2]*Department of Public Health, University of Warwick, Coventry, UK;* [3]*University of Buckingham Medical School, Buckingham, UK;* [4]*Department of Dermatology, University Hospitals Coventry and Warwickshire NHS Trust, Coventry;* [7]*Warwickshire Institute for the Study of Diabetes, Endocrinology and Metabolism, University Hospitals Coventry and Warwickshire NHS Trust, Coventry, UK;* [9]*Anaesthetics, Westmead Hospital, Sydney, Australia;* [10]*Department of Haematology, Tan Tock Seng Hospital, Singapore, Singapore;* [6]*Warwick Medical School, University of Warwick, Coventry, UK; and* [5]*Department of Dermatology, Worcestershire Acute Hospitals NHS Trust, Worcester, UK*

doi:10.1111/ced.14625

Summary

Erythroderma (exfoliative dermatitis), first described by Von Hebra in 1868, manifests as a cutaneous inflammatory state, with associated skin barrier and metabolic dysfunctions. The annual incidence of erythroderma is estimated to be 1–2 per 100 000 population in Europe with a male preponderance. Erythroderma may present at birth, or may develop acutely or insidiously (due to progression of an underlying primary pathology, including malignancy). Although there is a broad range of diseases that associate with erythroderma, the vast majority of cases result from pre-existing and chronic dermatoses. In the first part of this two-part concise review, we explore the underlying causes, clinical presentation, pathogenesis and investigation of erythroderma, and suggest potential treatment targets for erythroderma with unknown causes.

Introduction

Erythroderma (exfoliative dermatitis) is a dermatological emergency, and presents with extensive erythematous skin and scaling, affecting ≥ 90% of body surface area. First described by Von Hebra in 1868, erythroderma represents a cutaneous inflammatory state, with associated dysfunction of both the skin barrier and metabolic processes. Many diseases are associated with erythroderma, and most cases result from pre-existing and chronic dermatoses.[1] In Part 1 of this concise review, we explore the underlying causes, clinical presentation, pathogenesis and investigation of erythroderma, and suggest potential treatment targets for erythroderma of unknown cause.

Correspondence: Dr Simon Tso, Consultant Dermatologist, Jephson Dermatology Centre, South Warwickshire NHS Foundation Trust, Warwick, CV34 5BW, UK
E-mail: simontso@doctors.org.uk

Conflict of interest: the authors declare that they have no conflicts of interest.

Accepted for publication 22 February 2021

Underlying causes of erythroderma

Erythroderma is the result of severe skin dysmetabolism, reported in severe forms of a range of diseases, which can be broadly categorized into congenital, infective, inflammatory, immunobullous, neoplastic, iatrogenic and idiopathic causes. Table 1 shows the range of diseases associated with the clinical presentation of erythroderma, including the key clinical features and useful references for further reading. Commonly, erythroderma results from exacerbations of pre-existing dermatoses, such as psoriasis or eczema. Psoriatic erythroderma may result from sudden withdrawal of systemic or very potent topical corticosteroids. Drug-related erythroderma eruptions are often caused by anticonvulsants, antibiotics and topical

Table 1 Diseases associated with erythroderma and useful diagnostic features.

Category	Examples	Useful diagnostic features and investigations	Reading list of useful references
Congenital	Ichthyosis and keratinopathies Syndromic forms without skin blisters, such as: Netherton syndrome (AR) Sjögren–Larsson syndrome (AR) Dorfman–Chanarin syndrome (AR) Refsum syndrome (AR) KID syndrome (AR) Conradi–Hünermann–Happle syndrome (XLD) CHILD syndrome (XLD) IFAP syndrome (XLR and AD) X-linked ichthyosis (XLR) Nonsyndromic forms, such as: Lamellar ichthyosis (AR) Nonbullous congenital ichthyosiform erythroderma (AR) Harlequin ichthyosis (AR) Nonsyndromic forms with blistering such as: Epidermolytic ichthyosis (AD and AR) Other causes, such as: Immunodeficiency syndromes Omenn syndrome (AR) Hyper IgE syndrome Metabolic disorders Holocarboxylase synthetase deficiency (AR) Inherited form of acrodermatitis enteropathica (AR)	Clinical history Starts at birth. Inherited forms of acrodermatitis enteropathica may commence after the infant weans Clinical signs Collodion membrane may be present at birth in syndromic and nonsyndromic forms of congenital ichthyosis Recessive X-linked ichthyosis affects only males, and typically presents with generalized scale within 6 months of birth. May co-present with undescended testicles and corneal opacities Investigations Relevant gene panels Serum immunoglobulin level in Omenn syndrome Serum zinc level in inherited forms of acrodermatitis enteropathica	Hoeger and Harper, 1998;[17] Dhar *et al.*, 2012;[18] Louhichi *et al.*, 2019[19]
Inflammatory	Eczema Psoriasis PRP Seborrhoeic dermatitis	Clinical history Associated atopy; family history of atopy or psoriasis; previous clinical diagnosis of dermatosis. History of dystrophic nails and inflammatory arthropathy may favour a diagnosis of psoriasis PRP typically presents with palmoplantar keratoderma Clinical signs Palmoplantar keratoderma in PRP Nail pitting and dystrophy in psoriasis Investigations Full blood count (especially eosinophil count) and skin biopsy HIV screening in severe seborrhoeic dermatitis Total immunoglobulin E level in atopic dermatitis	Akhyani *et al.*, 2005;[20] Mathew and Sreedevan, 2017[21]

Table 1 continued

Category	Examples	Useful diagnostic features and investigations	Reading list of useful references
Immunobullous	Subcorneal: PF Intraepidermal: PV Subepidermal: BP	Clinical history Patients may not report any blisters in PV and PF. History of oral and genital ulceration is a key history in PV BP may present with a prebullous stage with widespread urticated pruritic plaques before blistering commences Clinical signs Scale, crust, erosion, typically confined to the skin in PF but sparing the mucosa Mucosal erosions and ulceration are a key feature in PV, and may or may not affect the skin Urticated plaques, larger intact and deroofed bullae in BP Investigations Skin histology: PF and PV show intraepidermal blistering; BP shows subepidermal blistering Skin direct IMF: PV and PF shows intercellular surface staining pattern; BP shows linear basement membrane zone pattern ELISA: key features are Dsg1 in PF; Dsg3 in PV; BP180 and BP230 in BP	Scrivener *et al*., 1998[22]
Infective	HIV Scabies SSSS	Clinical history and signs Opportunistic and recurrent infections in HIV Widespread pruritus and erythematous rash with burrows on dermoscopy in scabies Fever, malaise and widespread fluid-filled blistering rash in SSSS	Mathew and Sreedevan, 2017;[21] Bowles and Smirnov, 2019;[23] Paparizos *et al.*, 2019;[24] Lim *et al.*, 2019[25]
Neoplastic	Sézary syndrome Cutaneous T-cell lymphoma B-cell lymphoma Paraneoplastic pemphigus Malignancies, particularly, haematological and solid organ	Clinical history and signs Unexplained weight loss, lymphadenopathy, pruritus Investigations Blood test screening Flow cytometry Skin biopsy Lymph node/bone marrow biopsy	Lim *et al.*, 2018[25]

Table 1 continued

Category	Examples	Useful diagnostic features and investigations	Reading list of useful references
Immune	Hypersensitivity Contact dermatitis EMM Steven-Johnson syndrome (90% cases) Immunodeficiency GvHD Autoimmune SLE	Clinical history and signs EMM: about 90% cases caused by infections (particularly herpesvirus) and 10% caused by drugs; presenting as target-like erythematous lesions and polymorphous rash SJS: 90% cases associated with infections and typically presents with mucocutaneous skin erosions and conjunctivitis History of allogenic transplant in GvHD. Acute GvHD occurs within 3 months of transplantation and may be associated with gastrointestinal and liver dysfunction. Chronic GvHD may associate with dry eyes, scleroderma, hair loss, nail dystrophy, liver, lung and gastrointestinal dysfunction Extracutaneous features in SLE can include arthritis, pleurisy, pericarditis, kidney disease, neuropathy, etc. Investigations Blood test screening – autoantibodies. Skin biopsy. Patch testing in contact dermatitis	
Iatrogenic	Drugs such as antibiotics, anticonvulsants, antimalarials, allopurinol, lithium, barbiturates EMM (10% cases) DRESS Steven–Johnson syndrome (10% cases) Toxic epidermal necrolysis AGEP	Clinical history May present with systemic symptoms such as malaise, fever Clinical signs Lymphadenopathy and hepatosplenomegaly may present in DRESS syndrome. Pustular lesions developing at flexural sites may suggest AGEP or bacterial skin infection Investigations Blood test screening for eosinophilia and deranged liver function test. Skin biopsy	
Nutritional	Acrodermatitis enteropathica (inherited or acquired)	Clinical history Poor nutrition, excess alcohol, history of malabsorption Clinical signs and symptoms Triad of psoriasiform dermatitis of circumoral or periorificial areas, alopecia and diarrhoea Investigations Blood test screening for nutritional deficiencies	Hoeger and Harper, 1998[17]

Table 1 continued

Category	Examples	Useful diagnostic features and investigations	Reading list of useful references
Others	Cutaneous mastocytosis Hypereosinophilic syndrome Sunburn	Clinical history and sign Mastocytosis: rubbing an area of affected skin can activate mast cells leading to skin inflammation (Darier sign). Investigations Skin biopsy and haematological assessment in mastocytosis and hypereosinophilic syndrome	

AGEP, acute generalized exanthematous pustulosis; AR, autosomal recessive; AD, autosomal dominant; BP, bullous pemphigoid; CHILD, congenital hemidysplasia with ichthyosiform erythroderma and limb defects; DRESS, drug reaction with eosinophilia and systemic symptoms; Dsg, desmoglein; EMM, erythema multiforme major; GvHD, graft-versus-host disease; HIV, human immunodeficiency syndrome; IFAP, ichthyosis follicularis, atrichia and photophobia; KID, keratitis–ichthyosis–deafness; IMF, immunofluorescence microscopy; PF, pemphigus foliaceous; PRP, pityriasis rubra pilaris; PV, pemphigus vulgaris; SJS, Steven–Johnson syndrome; SLE, systemic lupus erythematosus; SSSS, *Staphylococcus* scalded skin syndrome; XLD, X-linked dominant; XLR, X-linked recessive.

preparations.[2] A detailed chronological history, including clinical improvement following drug cessation, are essential for the determination of the causative drug, which can often prove challenging.[2] Table 2 shows the distribution of the various causes of erythroderma. Despite the current knowledge and understanding of the many and varied causes of erythroderma, the precise cause may not be established in up to one in six cases.[2]

Clinical presentation of erythroderma

Erythroderma may present at birth, and develops either acutely (e.g. due to infection or drugs), or more gradually due to the progression of an underlying primary pathology, including dermatoses and malignancies.[2] Associated signs and symptoms may give further clues to the underlying aetiology of erythroderma.

Congenital

Congenital erythroderma may co-present with a diversity of cutaneous and extracutaneous clinical features at birth and later in life. In the case of autosomal recessive congenital ichthyosis, affected infants may co-present with collodion membrane, ectropion, eclabium and folded ears at birth, which may be further complicated, in the case of harlequin ichthyosis, by hair and nail abnormalities, hypohidrosis and skin contractures. In Netherton syndrome, the skin has the characteristic 'double-edged' ichthyosis linearis circumflexa appearance, the hair shaft is abnormal and brittle (trichorrhexis invaginata), and affected children have a predisposition to atopy. Developmental delays in children born with congenital erythroderma should always prompt the screening of syndromic forms of congenital ichthyosis and neutral lipid storage disease (e.g. Chanarin–Dorfman syndrome). In erythroderma due to primary acrodermatitis enteropathica, the presentation of perioral and perianal dermatitis may not present until after the affected infant begins to wean off breast milk. Congenital erythroderma may also co-present in severe combined immunodeficiency, a rare disease associated with alopecia, chronic diarrhoea, failure to thrive, lymphadenopathy and hepatosplenomegaly.

Acute

Acute erythroderma usually manifests clinically as widespread erythema, followed by exfoliative scaling over the subsequent 2–6 days.[3] The morphology of the

Table 2 Literature review of the differential causes of erythroderma from different geographical locations worldwide.

Reference	Description of study	Differential causes	Demographics (age and sex)
Akhyani *et al.*, 2005[20]	Case series of 97 patients with acquired erythroderma in Iran	Dermatoses 59.7% Drug reactions 21.6% Malignancies 11.3% Idiopathic 7.2%	Median age at diagnosis 46.2 years; male : female ratio 1.85 : 1
Leenutaphong *et al.*, 1999[26]	Case series of 49 patients with acquired erythroderma in Thailand	Drugs 38.77% Dermatoses 27.5%	Median age at presentation 51.7 years; male : female ratio 2 : 1
Miyashiro and Sanches, 2020[2]	Case series of 309 patients in Brazil	Eczema 20.7% Psoriasis 16.8% Sézary syndrome 12.3% Drug eruption 12.3% Atopic dermatitis 8.7% Mycosis fungoides 5.5% Others 6.8% Idiopathic 16.8%	Median age 57 years; male : female ratio 2.2
Sudho *et al.*, 2003[27]	Case series of 25 patients in Porur, India	Psoriasis 32% Drugs 24% Eczema 12% Hereditary disorders 8% PF 4% Other 12%[a]	Age range of 5 days to 72 years; peak incidence 21–30 years (24%); male : female ratio 1.5 : 1
Mathew and Sreedevan, 2017[21]	Case series of 370 patients in Kerala, India	Psoriasis 32.7% Contact dermatitis 15.9% Idiopathic 15.7% Chronic actinic dermatitis 8.1% Drugs 6.5% Atopic dermatitis 6.5% Malignancy 3.2% PRP 3.2% 1.4% PF Other 0.8%[b]	Mean age of onset of erythroderma 55.38 ± 16.67 years (range 3–91 years); male : female ratio of 3.6 : 1
Yuan *et al.*, 2010[28]	Case series of 82 patients in China	Pre-existing 72% dermatoses (psoriasis 30.5%) Drug reactions 17% Idiopathic causes 6.1% Malignancies 4.9%	–
Rym *et al.*, 2005[29]	Retrospective study of 80 erythrodermic adults in Africa	Psoriasis 51.25% Drugs 11.25% Malignancy 8.75% Idiopathic 7.5% PF 6.25% Contact dermatitis 2.5% PRP 1.25% PF 1.25%	Mean ± SD age 53.78 ± 18 years; male : female ratio 2.2 : 1.0
Pal and Haroon, 2002[30]	Case series of 90 patients in Pakistan	Psoriasis 37.8% Idiopathic 14.6% CIE 7.8% PF 5.6% Drugs 5.5% Malignancy 5.5% Atopic dermatitis 3.3% Contact dermatitis 3.3% Crusted scabies 2.2% PRP 2.2%	Mean age of onset 41.6 years; male : female ratio of 2.8 : 1

CIE, congenital ichthyosiform erythroderma; PF, pemphigus foliaceous; PRP, pityriasis rubra pilaris; SSSS, *Staphylococcus* scalded skin syndrome. [a]Including malignancy, dermatophytosis, SSSS and PRP; [b]including crusted scabies and CIE.

rash preceding the erythroderma varies markedly, depending on the underlying cause, and particular attention to co-presenting symptoms is required to aid in the diagnosis of the underlying cause. Viral exanthems typically present as an acute morbilliform macular and/or maculopapular eruption spreading in a cephalocaudal direction. Drug eruptions may begin as a morbilliform or urticarial rash, which can further develop into pustules at flexural sites (in acute generalized exanthematous pustulosis), lymphadenopathy (in drug reaction with eosinophilia and systemic symptoms) or mucocutaneous skin erosions and blistering (in Stevens–Johnson syndrome and toxic epidermal necrolysis). Patients presenting with erythrodermic psoriasis may co-present with severe nail dystrophy. Erythroderma due to underlying immunobullous disease may present with intact and deroofed mucocutaneous blisters or erosions. Erythroderma in the context of unexplained weight loss, lymphadenopathy and presence of atypical lymphocytes (in blood film) in the absence of pre-existing skin diseases should prompt consideration of underlying malignancies such as Sézary syndrome.

Associations and sequelae

Thermoregulatory disturbances (fever and chills), reactive lymphadenopathy and superimposed bacterial infections may occur concurrently with erythroderma from all causes. In extreme cases, sequelae of erythroderma include hypovolaemia (with reflex tachycardia), high-output cardiac failure, anaemia, electrolyte disturbance and acute respiratory distress syndrome.[3,4]

Pathogenesis of erythroderma

Congenital

Disorders of lipid metabolism underpin the pathogenesis of a range of differential causes of congenital erythroderma. Reviews by Elias *et al.*[5] and Radner *et al.*[6] extensively discuss the pathogenesis of genodermatoses secondary to abnormalities and dysregulation in fatty acid, cholesterol and triglyceride metabolism and in lipid transportation. In brief, disordered lipid metabolism leads to abnormal lipid organization within the stratum corneum, therefore interfering with the normal lateral packing of lipids, which is crucial for the barrier function of the skin.[7] This abnormality has been observed in lamellar ichthyosis and atopic dermatitis.[8]

Acquired

The pathogenesis of acquired erythroderma is poorly understood. Studies suggest that factors such as an increase in serum IgE, interleukin (IL)-4 and IL-10, associated with T helper (Th)1/Th2 imbalance in favour of Th2 differentiation and dysregulated angiogenic factors could have a role in the pathogenesis of erythrodermic psoriasis.[9] IL-4 and IL-13 signalling are central to the pathogenesis of atopic dermatitis and other atopic diseases through activation of downstream IgE-dependent processes, which lead to activation of mast cells and eosinophils and to the clinical presentation of skin inflammation.[10] Indeed, the presence of dermal eosinophilic infiltrates is a characteristic histological feature observed in skin biopsies from patients with erythrodermic atopic dermatitis,[11] and this finding may also be observed in allergic contact dermatitis, urticaria, immunobullous diseases and dermal hypersensitivity reaction patterns.[12] IL-4 and IL-13 are targets for blockade by dupilumab, a biologic licensed for treatment of moderate to severe atopic dermatitis.

The pathogenesis of erythroderma in patients with haematological malignancies is poorly understood, and changes to the cytokine signalling profile in this group of patients are highly complex. Nevertheless, there is an increase in the Th2 profile of cytokines such as IL-4, IL-5 and IL-10 in the skin and serum of patients with Sézary syndrome,[13] overexpression of IL-13 signalling in cutaneous T-cell lymphoma,[14] and upregulation of IL-4 signalling in the bone marrow in patients with acute myeloid leukaemia.[15] The link between IL-4 and IL-13 signalling in the pathogenesis of erythroderma in patients with haematological malignancies remains speculative, given the lack of relevant studies.

Final common pathway

Regardless of the underlying cause of erythroderma, there is an increase in expression of adhesion molecules (increased expression of vascular cell adhesion molecule-1, intercellular adhesion molecule-1, E- and P-selectin found on endothelium *in situ* in patients with erythroderma, mycosis fungoides and atopic dermatitis)[16] and proinflammatory mediators stimulating dermal inflammation and epidermal turnover rate, which shortens the keratinocyte transit time through the epidermis, resulting in exfoliation.[1]

Discussion

Our literature review identifies that globally, the most common cause of erythroderma is due to an underlying primary skin disease.[2] However, to our knowledge, there are no recent UK data about the differential causes of erythroderma. Therefore, advancement of the current clinical management of erythroderma is reliant upon developing current knowledge of the underlying pathogenesis in order to identify possible targets for therapeutic intervention. Identification of the specific molecular cytokines with raised levels in erythroderma may allow clinicians to subtype erythroderma cases and manage them accordingly. The pathogenesis of erythroderma remains unclear, but the IL-4 and IL-13 pathways appear to be an attractive potential treatment target for managing erythroderma with unclear cause.

Conclusion

A wide range of diseases can lead to erythroderma but its pathogenesis remains poorly understood.

Learning points

- Infants presenting with erythroderma at birth or within the first year of life should always prompt the consideration of inherited metabolic diseases.
- Pre-existing dermatoses (particularly psoriasis and eczema) underlie a significant proportion of cases of erythroderma, as shown in the current literature to date.
- Regarding the acute presentation of erythroderma, the morphological nature of the rash preceding erythroderma and co-presenting symptoms are of great significance to aid in the aetiological diagnosis.
- In erythrodermic psoriasis, studies have suggested factors such as increased serum IgE, IL-4 and IL-10, associated with favoured Th2 differentiation and dysregulated angiogenic factors, could have a role in the pathogenesis.

References

1 Okoduwa C, Lambert WC, Schwartz RA *et al.* Erythroderma: review of a potentially life-threatening dermatosis. *Indian J Dermatol* 2009; **54**: 1–6.

2 Miyashiro D, Sanches JA. Erythroderma: a prospective study of 309 patients followed for 12 years in a tertiary center. *Sci Rep* 2020; **10**: 9774.

3 Harper-Kirksey K. Erythroderma. In: *Life-threatening rashes*. (Rose E ed). Cham: Springer, 2018; 265–77.

4 Mistry N, Gupta A, Alavi A, Sibbald RG. A review of the diagnosis and management of erythroderma (generalized red skin). *Adv Skin Wound Care* 2015; **28**: 228–36; quiz 237–8.

5 Elias PM, Williams ML, Holleran WM *et al.* Pathogenesis of permeability barrier abnormalities in the ichthyoses: inherited disorders of lipid metabolism. *J Lipid Res* 2008; **49**: 697–714.

6 Radner FPW, Marrakchi S, Kirchmeier P *et al.* Mutations in CERS3 cause autosomal recessive congenital ichthyosis in humans. *PLoS Genet* 2013; **9**: e1003536.

7 Groen D, Poole DS, Gooris GS, Bouwstra JA. Is an orthorhombic lateral packing and a proper lamellar organization important for the skin barrier function? *Biochim Biophys Acta* 2011; **1808**: 1529–37.

8 Pilgram GS, Vissers DC, van der Meulen H *et al.* Aberrant lipid organization in stratum corneum of patients with atopic dermatitis and lamellar ichthyosis. *J Invest Dermatol* 2001; **117**: 710–17.

9 Singh RK, Lee KM, Ucmak D *et al.* Erythrodermic psoriasis: pathophysiology and current treatment perspectives. *Psoriasis (Auckl)* 2016; **6**: 93–104.

10 Gandhi NA, Pirozzi G, Graham NMH. Commonality of the IL-4/IL-13 pathway in atopic diseases. *Expert Rev Clin Immunol* 2017; **13**: 425–37.

11 Moy AP, Murali M, Kroshinsky D *et al.* Immunologic overlap of helper T-cell subtypes 17 and 22 in erythrodermic psoriasis and atopic dermatitis. *JAMA Dermatol* 2015; **151**: 753–60.

12 Fung MA. The clinical and histopathologic spectrum of "dermal hypersensitivity reactions," a nonspecific histologic diagnosis that is not very useful in clinical practice, and the concept of a "dermal hypersensitivity reaction pattern". *J Am Acad Dermatol* 2002; **47**: 898–907.

13 Saed G, Fivenson DP, Naidu Y, Nickoloff BJ. Mycosis fungoides exhibits a Th1-type cell-mediated cytokine profile whereas Sézary syndrome expresses a Th2-type profile. *J Invest Dermatol* 1994; **103**: 29–33.

14 Geskin LJ, Viragova S, Stolz DB, Fuschiotti P. Interleukin-13 is overexpressed in cutaneous T-cell lymphoma cells and regulates their proliferation. *Blood* 2015; **125**: 2798–805.

15 Gao A, Gong Y, Zhu C *et al.* Bone marrow endothelial cell-derived interleukin-4 contributes to thrombocytopenia in acute myeloid leukemia. *Haematologica* 2019; **104**: 1950–61.

16 Sigurdsson V, de Vries IJ, Toonstra J *et al.* Expression of VCAM-1, ICAM-1, E-selectin, and P-selectin on endothelium in situ in patients with erythroderma, mycosis fungoides and atopic dermatitis. *J Cutan Pathol* 2000; **27**: 436–40.

17 Hoeger PH, Harper JI. Neonatal erythroderma: differential diagnosis and management of the "red baby". *Arch Dis Child* 1998; **79**: 186–91.
18 Dhar S, Banerjee R, Malakar R. Neonatal erythroderma: diagnostic and therapeutic challenges. *Indian J Dermatol* 2012; **57**: 475–8.
19 Louhichi N, Bahloul E, Marrakchi S *et al*. Thyroid involvement in Chanarin-Dorfman syndrome in adults in the largest series of patients carrying the same founder mutation in ABHD5 gene. *Orphanet J Rare Dis* 2019; **14**: 112.
20 Akhyani M, Ghodsi ZS, Toosi S, Dabbaghian H. Erythroderma: a clinical study of 97 cases. *BMC Dermatol* 2005; **5**: 5.
21 Mathew R, Sreedevan V. Erythroderma: a clinicopathological study of 370 cases from a tertiary care center in Kerala. *Indian J Dermatol Venereol Leprol* 2017; **83**: 625.
22 Scrivener Y, Cribier B, Le Coz C *et al*. [Erythroderma with immunoglobulin deposits along the basal membrane. Pemphigoid erythroderma?] (in French). *Ann Dermatol Venereol* 1998; **125**: 13–17.
23 Bowles AA, Smirnov B. Erythrodermic psoriasis and HIV infection. *N Engl J Med* 2019; **380**: 80.
24 Paparizos V, Vasalou V, Velissariou E *et al*. Norwegian scabies presenting as erythroderma in HIV: a case report. *Infez Med* 2019; **27**: 332–5.
25 Lim PN, Fox CP, Pammi M, Patel A. Paraneoplastic erythroderma: unusual presentation secondary to diffuse large B cell lymphoma. *BMJ Case Rep* 2019; **12**: e228412.
26 Leenutaphong V, Kulthanan K, Pohboon C *et al*. Erythroderma in Thai patients. *J Med Assoc Thai* 1999; **82**: 743–8.
27 Sudho R, Hussain SB, Bellraj E *et al*. Clinicopathological study of exfoliative dermatitis. *Indian J Dermatol Venereol Leprol* 2003; **69**: 30–1.
28 Yuan XY, Guo JY, Dang YP *et al*. Erythroderma: a clinical-etiological study of 82 cases. *Eur J Dermatol* 2010; **20**: 373–7.
29 Rym BM, Mourad M, Bechir Z *et al*. Erythroderma in adults: a report of 80 cases. *Int J Dermatol* 2005; **44**: 731–5.
30 Pal S, Haroon TS. Erythroderma: a clinico-etiologic study of 90 cases. *Int J Dermatol* 1998; **37**: 104–7.

CPD questions

Learning objective

To understand the underlying causes, clinical presentation, pathogenesis, investigations and potential treatments for erythroderma.

Question 1

A 45-year-old man presents with erythroderma secondary to a drug reaction to an antibiotic. How many days later would subsequent exfoliative scaling be expected to occur?

(a) 0–1.
(b) 2–6.
(c) 10–14.
(d) 14–28.
(e) 28–56.

Question 2

After being weaned off breast milk, an infant develops perioral and perianal dermatitis, which gradually developed into erythroderma. The condition does not improve with regular emollients and moderate-potency corticosteroids. Which trace-element deficiency would be expected with the underlying disorder?

(a) Low potassium level.
(b) Low magnesium level.
(c) Low calcium level.
(d) Low sodium level.
(e) Low zinc level.

Question 3

A 66-year-old man with Type 1 diabetes presents with a 12-day history of a widespread erythematous rash that started on his face and spread to affect most of his body, along with diffusely thickened and yellowish palms and soles. There were areas of uninvolved skin on his chest. What is the likely cause for his erythroderma?

(a) Eczema.
(b) Pityriasis rubra pilaris (PRP).
(c) Psoriasis.
(d) Scabies.
(e) Sézary syndrome (SS).

Question 4

Which pathway appears to be an attractive potential treatment target for managing erythroderma with an unclear cause?

(a) Tumour necrosis factor (TNF)-α.
(b) Interleukin (IL)-17.
(c) IL-4 and IL-13.
(d) CD-20.
(e) IL-12 and IL-23.

Question 5

A 5-day-old girl present widespread erythema and scaling covering 95% of her body with blistering and skin fragility. What is the most likely diagnosis?

(a) Conradi–Hünermann–Happle syndrome.
(b) Epidermolytic ichthyosis.
(c) Lamellar ichthyosis.
(d) Netherton syndrome.
(e) Refsum syndrome.

Instructions for answering questions

This learning activity is freely available online at http://www.wileyhealthlearning.com/ced

Users are encouraged to

- Read the article in print or online, paying particular attention to the learning points and any author conflict of interest disclosures.
- Reflect on the article.
- Register or login online at http://www.wileyhealthlearning.com/ced and answer the CPD questions.
- Complete the required evaluation component of the activity.

Once the test is passed, you will receive a certificate and the learning activity can be added to your RCP CPD diary as a self-certified entry.

This activity will be available for CPD credit for 2 years following its publication date. At that time, it will be reviewed and potentially updated and extended for an additional period.

