

Nayera Moftah  
May El Samahy  
Nadia Abd El Wadood  
Monira Waseef

# Atlas of Common and Rare Genodermatoses

---


# Atlas of Common and Rare Genodermatoses

---

Nayera Moftah • May El Samahy  
Nadia Abd El Wadood • Monira Waseef

# Atlas of Common and Rare Genodermatoses

 Springer

Nayera Moftah   
Dermatology and Venereology Department  
Faculty of Medicine for Girls  
Al-Azhar University  
Cairo, Egypt

Nadia Abd El Wadood  
Dermatology, Venereology and Andrology  
Al-Haud Al-Marsoud Hospital  
Cairo, Egypt

May El Samahy  
Dermatology and Venereology Department  
Faculty of Medicine  
Ain Shams University  
Cairo, Egypt

Monira Waseef  
Dermatology, Venereology and Andrology  
Al-Haud Al-Marsoud Hospital  
Cairo, Egypt

ISBN 978-3-031-60787-5      ISBN 978-3-031-60788-2 (eBook)  
<https://doi.org/10.1007/978-3-031-60788-2>

© The Editor(s) (if applicable) and The Author(s), under exclusive license to Springer Nature Switzerland AG 2024  
This work is subject to copyright. All rights are solely and exclusively licensed by the Publisher, whether the whole or part of the material is concerned, specifically the rights of translation, reprinting, reuse of illustrations, recitation, broadcasting, reproduction on microfilms or in any other physical way, and transmission or information storage and retrieval, electronic adaptation, computer software, or by similar or dissimilar methodology now known or hereafter developed.

The use of general descriptive names, registered names, trademarks, service marks, etc. in this publication does not imply, even in the absence of a specific statement, that such names are exempt from the relevant protective laws and regulations and therefore free for general use.

The publisher, the authors and the editors are safe to assume that the advice and information in this book are believed to be true and accurate at the date of publication. Neither the publisher nor the authors or the editors give a warranty, expressed or implied, with respect to the material contained herein or for any errors or omissions that may have been made. The publisher remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

This Springer imprint is published by the registered company Springer Nature Switzerland AG  
The registered company address is: Gewerbestrasse 11, 6330 Cham, Switzerland

If disposing of this product, please recycle the paper.



---

## Preface

The fast-moving world of genetic research inspired us to present an atlas containing common and rare genodermatoses. It provides the dermatologists, pediatricians, and internists with about 1000 photos of more than 200 different genodermatoses collected from multicenter medical institutions in Egypt since 2010, some of which very rare.

Consanguinity is high in Egypt; hence, many different varieties of genodermatoses with different presentations are encountered. In this atlas, the reader is presented with photos of affected family members at different ages.

The diagnosis of genodermatoses is not an easy task; key points for a correct diagnosis of each disease are mentioned in a concise manner, while a wealth of photographs will assist the practitioner's review, through their colorful presentation, in giving the most accurate diagnosis of the different genodermatoses and counseling families and patients.

With the advances in genetic studies, further research will be of invaluable support to those studying the expected affected gene, to build what may be the basis of gene therapy.

It is the hope of the authoring team that this atlas will, in the meantime, contribute to a better understanding of genodermatoses, their variability, and thus to sound medical decisions and safer, more effective treatments for patients facing a life with these complex conditions.

Nayera Moftah  
May El Samahy  
Nadia Abd El Wadood  
Monira Waseef

---

## Acknowledgments

We would like to thank all the co-authors who contributed to writing the main criteria of the genodermatoses published in this atlas and to the revision of its chapters.

### Co-authors

**Nermeen S.A. Abdel Fattah, MD**

Professor of Dermatology and Venereology  
Faculty of Medicine, Ain Shams University, Cairo, Egypt

**Noha H. Moftah, MD**

Professor of Dermatology, STDS, and Andrology  
Faculty of Medicine, Minia University, Al-Minia, Egypt

**Shaimaa Hassan Mohamed, MD**

Assistant Professor of Dermatology and Venereology  
Faculty of Medicine for Girls, Al-Azhar University, Cairo, Egypt

We would like to thank all the dermatologists who contributed clinical photographs of their patients to this atlas, after obtaining their parents' consent for publication, and who assisted in preparing the chapters.

### Contributors (Alphabetically)

**Abeer Mostafa, MD**

Dermatology and Venereology Department, Faculty of Medicine for Girls, Al-Azhar University,  
Cairo, Egypt

**Ahmed Kamal, MD**

Al-Haud Al-Marsoud Hospital, Cairo, Egypt

**Ahmed Said Alkasbi, EFB**

Al-Haud Al-Marsoud Hospital, Cairo, Egypt

**Alfallooji, EFB**

Al-Haud Al-Marsoud Hospital, Cairo, Egypt

**Aliaa El-Said, MSc**

Dermatology and Venereology Department, Faculty of Medicine for Girls, Al-Azhar University

**Amjad Saad, EFB**

Al-Haud Al-Marsoud Hospital, Cairo, Egypt

**Ammar Aldujalli, EFB**

Al-Haud Al-Marsoud Hospital, Cairo, Egypt

**Asmaa Hamdy, EFB**

Al-Haud Al-Marsoud Hospital, Cairo, Egypt

**Ayat A. Abo Oun, EFB**

Al-Haud Al-Marsoud Hospital, Cairo, Egypt

**Belal Muwafak, EFB**

Al-Haud Al-Marsoud Hospital, Cairo, Egypt

**Doaa Atef, MSc**

Al-Haud Al-Marsoud Hospital, Cairo, Egypt

**Eman Fathy Gomaa, EFB**

Al-Haud Al-Marsoud Hospital, Cairo, Egypt

**Fady Waheed, MSc**

Al-Haud Al-Marsoud Hospital, Cairo, Egypt

**Fatma Abd El Salam, MD**

Dermatology and Venereology Department, Faculty of Medicine for Girls, Al-Azhar University,

Cairo, Egypt

**Ghada Osama Elshahat, EFB**

Al-Haud Al-Marsoud Hospital, Cairo, Egypt

**Ghada Raslan, MD**

Al-Haud Al-Marsoud Hospital, Cairo, Egypt

**Hala Fayed, MSc**

Al-Haud Al-Marsoud Hospital, Cairo, Egypt

**Hanan Hamdy, MSc**

Al-Haud Al-Marsoud Hospital, Cairo, Egypt

**Hayder Al-Darraj, EFB**

Almatareya Educational Hospital

**Husham Adnan Abbas, EFB**

Al-Haud Al-Marsoud Hospital, Cairo, Egypt

**Khadega Husien Fata, EFB**

Al-Haud Al-Marsoud Hospital, Cairo, Egypt

**Maged Farid, MD**

Consultant of Dermatology, Venereology and Andrology

Al-Haud Al-Marsoud Hospital, Cairo, Egypt

**May Farook, MD**

Consultant of Dermatology, Venereology, and Andrology

Al-Haud Al-Marsoud Hospital, Cairo, Egypt

**Mohamed Samir, MSc**

El Sinbelaween Hospital, El Sinbelaween, Egypt

**Monira Waked, MD**

Consultant of Dermatology, Venereology, and Andrology

Al-Haud Al-Marsoud Hospital, Cairo, Egypt

**Mostafa Kadry, MD**

Consultant of Dermatology, Venereology and Andrology, Al-Haud Al-Marsoud Hospital,

Cairo, Egypt

**Muath Abkar AL Ahdal, EFB**

Al-Haud Al-Marsoud Hospital, Cairo, Egypt

**Nada Shaaban Mohamed, MSc**

Dermatology and Venereology Department, Faculty of Medicine for Girls, Al-Azhar University,

Cairo, Egypt

**Rasha Saeed Awad, EFB**

Al-Haud Al-Marsoud Hospital, Cairo, Egypt

**Samar Ashry, MSc**

Al-Haud Al-Marsoud Hospital, Cairo, Egypt

**Samir Sabry, MSc**

Al-Haud Al-Marsoud Hospital, Cairo, Egypt

**Shaimaa Farouk, MSc, EFB**

Al-Haud Al-Marsoud Hospital, Cairo, Egypt

**Shamil Aljobory, MD**

General Mosul Hospital, Iraq

**Shaymaa Hosny Elgabry, MSc**

Al-Haud Al-Marsoud Hospital, Cairo, Egypt

**Wafaa Abd Elbaset, MSc, EFB**

Al-Haud Al-Marsoud Hospital, Cairo, Egypt

**Younna El-Sayed, MSc**

Dermatology and Venereology Department, Faculty of Medicine for Girls, Al-Azhar University,  
Cairo, Egypt

**Lastly, we would like to thank the Springer team, especially Mrs. Juliette R. Kleemann and Ms. Sharon Spears for their great support during the preparation of this atlas.**

---

# Contents

<b>1 Ichthyoses and Ichthyotic Syndromes</b> . . . . .	1
Hereditary (Primary) Ichthyosis . . . . .	1
Common Ichthyosis . . . . .	1
Autosomal Recessive (AR) Ichthyoses . . . . .	2
Keratinopathic Ichthyoses . . . . .	12
Ichthyosiform Syndromes . . . . .	22
Keratitis, Ichthyosis, and Deafness (KID) Syndrome . . . . .	22
Hystrix-Like Ichthyosis with Deafness (HID) Syndrome (AD) . . . . .	22
Chanarin-Dorfman Syndrome (AR) Neutral Lipid Storage Disease with Ichthyosis . . . . .	22
Refsum Syndrome (AR) . . . . .	24
Sjögren-Larsson Syndrome (AR) . . . . .	25
Netherton Syndrome (AR) . . . . .	25
Tay-Sachs Syndrome (PIBIDS) (AR) (Congenital Ichthyosis with Trichothiodystrophy) . . . . .	26
Rud Syndrome (AR) . . . . .	28
Laurence-Moon-Bardet-Biedl Syndrome (AR) . . . . .	28
MEDNIK Syndrome (AR) . . . . .	29
Conradi-Hünemann-Happle Syndrome (XLD) (XLD Chondrodysplasia Punctata) . . . . .	29
CHILD Syndrome (XLD) . . . . .	31
References . . . . .	38
<b>2 Erythrokeratodermas and Palmoplantar Keratoderma</b> . . . . .	39
Erythrokeratoderma . . . . .	39
Erythrokeratoderma Variabilis (AD) . . . . .	39
Progressive Symmetric Erythrokeratoderma (AD) . . . . .	39
Palmoplantar Keratodermas (PPK) . . . . .	42
Punctate PPK Type 1 (AD) (Buschke-Fischer Syndrome) . . . . .	42
Acrokeratoelastoidosis of Oswald Costa (AD) (Inverse Papular Acrokeratosis) . . . . .	42
Punctate Keratosis of Palmar Creases . . . . .	45
Cole Disease (AD) . . . . .	45
PPK Striate (AD) . . . . .	47
PPK Areata (AD) . . . . .	47
Carvajal Syndrome (AD) (Cardio-Cutaneous Syndrome) . . . . .	47
Howel-Evans Syndrome (AD) (Tylosis with Esophageal Cancer) . . . . .	47
Richner-Hanhart Syndrome (AR) (Tyrosinemia Type II) (Oculocutaneous Tyrosinemia) . . . . .	47
Pachyonychia Congenita Type 1 (AD) . . . . .	49
Diffuse Palmoplantar Keratoderma (PPK) . . . . .	49
Transgradient Keratodermas . . . . .	53

Mal de Meleda PPK (AR) (Keratosis Extremitatum Hereditaria Trangrediens et Progrediens) . . . . .	53
Greither's Disease (AD) (Trangrediens et Progrediens PPK) . . . . .	56
Papillon-Lefèvre Syndrome (AR) . . . . .	58
Vohwinkel Syndrome (AD) (Keratoderma Hereditaria Mutilans) (PPK with Honeycomb Pattern) . . . . .	63
Bart-Pumphrey Syndrome (AD) . . . . .	64
Olmsted Syndrome (AD/R, XLR) (Diffuse Mutilating Keratoderma with Periorificial Plaques) . . . . .	65
Huriez Syndrome (AD) (Sclerolyosis) . . . . .	66
Non-Transgredient Keratodermas . . . . .	66
Unna-Thost Syndrome (AD) . . . . .	66
Vorner Syndrome (AD) . . . . .	68
Naxos Disease (AR) . . . . .	68
References . . . . .	70
<b>3 Epidermolysis Bullosa</b> . . . . .	71
Epidermolysis Bullosa Simplex (EBS) . . . . .	73
Acral Peeling Skin Syndrome (APPS) (AR) . . . . .	73
Skin Fragility Syndrome . . . . .	75
Epidermolysis Bullosa Simplex (EBS), Localized Subtype (AD) . . . . .	75
Epidermolysis Bullosa Simplex (EBS), Generalized Subtype (AD) . . . . .	75
Epidermolysis Bullosa Simplex (EBS), Severe Subtype (AD) . . . . .	78
Epidermolysis Bullosa Simplex (EBS) with Mottled Pigmentation (AD) . . . . .	78
Epidermolysis Bullosa Simplex (EBS)-Ogna (AD) . . . . .	78
Junctional Epidermolysis Bullosa (JEB) . . . . .	80
Junctional Epidermolysis Bullosa (JEB)-Severe Subtype (AR) . . . . .	80
Junctional Epidermolysis Bullosa (JEB)-Intermediate Subtype (AR) . . . . .	80
Dystrophic Epidermolysis Bullosa (DEB) . . . . .	83
Recessive Dystrophic Epidermolysis Bullosa (RDEB), Severe Subtype . . . . .	83
Dominant Dystrophic Epidermolysis Bullosa (DDEB), Intermediate Subtype . . . . .	86
Dystrophic Epidermolysis Bullosa (DDEB) Pruriginosa . . . . .	86
Dominant Dystrophic Epidermolysis Bullosa (DDEB) Albopapuloid (AD) . . . . .	86
Kindler Epidermolysis Bullosa (AR) . . . . .	88
References . . . . .	93
<b>4 Pigmentary Genodermatoses</b> . . . . .	95
Hypomelanosis . . . . .	95
Hypomelanosis Related to a Defect of Embryological Development of Melanocytes . . . . .	95
Hypomelanosis Related to a Defect of Melanogenesis . . . . .	96
Hypomelanosis Related to a Defect of Biogenesis of Melanosomes . . . . .	100
Hypomelanosis Related to a Defect of Melanosomes Transport . . . . .	102
Other Hypomelanoses . . . . .	103
Hypermelanosis . . . . .	106
Incontinentia Pigmenti (XLD) . . . . .	106
Linear and Whorled Nevoid Hypermelanosis (LWNH) . . . . .	107
Dowling-Degos Disease (DDD) (AD) . . . . .	107
Reticulate Acropigmentation of Kitamura (RAK) (AD) . . . . .	108
Reticulate Acropigmentation of Dohi (RAD) (AD) . . . . .	109
Dyschromatosis Universalis Hereditaria (DUH) (AD/AR) . . . . .	109
Naegeli-Franceschetti-Adassohn Syndrome (NFJS) (AD) . . . . .	109
Familial Gigantic Melanocytosis (FGM) (AD) . . . . .	112

McCune–Albright Syndrome (MAS) . . . . .	113
Peutz–Jeghers Syndrome (AD) . . . . .	116
Laugier–Hunziker Syndrome . . . . .	116
References . . . . .	126
<b>5 Genodermatoses with Malignant Potential . . . . .</b>	<b>129</b>
Tuberous Sclerosis (AD) . . . . .	129
Neurofibromatosis (NF) (AD) . . . . .	137
Von Recklinghausen Syndrome . . . . .	137
Birt–Hogg–Dubé Syndrome (BHDS) (AD) . . . . .	145
Cowden Syndrome (AD) . . . . .	148
Gorlin Syndrome (AD) . . . . .	149
Nevoid Basal Cell Carcinoma Syndrome . . . . .	149
Bazex–Dupré–Christol Syndrome (XLD) . . . . .	150
Rombo Syndrome (AD) . . . . .	151
Reed Syndrome (AD) . . . . .	152
Brooke–Spiegler Syndrome (AD) . . . . .	153
References . . . . .	155
<b>6 Genodermatoses with Defective Excision Repair . . . . .</b>	<b>157</b>
Xeroderma Pigmentosum (XP) (AR) . . . . .	157
Pigmented Xerodermoid . . . . .	160
DeSanctis–Cacchione Syndrome (DSC) (AR) . . . . .	161
Cockayne Syndrome (CS) (AR) . . . . .	162
Dyskeratosis Congenita (DC) (Zinsser–Engman–Cole syndrome) (X-linked Recessive, AD or AR) . . . . .	163
Rothmund–Thomson Syndrome (AR) . . . . .	165
References . . . . .	167
<b>7 Vascular Disorders . . . . .</b>	<b>169</b>
Capillary Malformations . . . . .	169
Port-Wine Stain (Nevus Flammeus) . . . . .	169
Sturge–Weber Syndrome . . . . .	169
Klippel–Trenaunay Syndrome . . . . .	171
Proteus Syndrome . . . . .	172
Fabry Disease . . . . .	174
Venous Malformations . . . . .	180
Venous Lake . . . . .	180
Blue Rubber Bleb Nevus Syndrome (Sporadic/AD) . . . . .	180
Maffucci Syndrome . . . . .	181
Osler–Weber–Rendu Syndrome (AD) . . . . .	184
Hereditary Hemorrhagic Telangiectasia . . . . .	184
Hemangiomas . . . . .	186
PHACES Syndrome . . . . .	187
Lumbar (Sacral) Syndrome (XL) . . . . .	190
Pelvis Syndrome . . . . .	190
Lymphangioma Circumscriptum (LC) . . . . .	191
References . . . . .	193
<b>8 Acantholytic Genodermatoses . . . . .</b>	<b>195</b>
Darier Disease (Keratosis Follicularis) (AD) . . . . .	195
Hailey–Hailey Disease (Benign Familial Chronic Pemphigus) (AD) . . . . .	199
References . . . . .	199

<b>9</b>	<b>Dermal Disorders</b> .....	207
	Cutis Laxa (AD, AR, XLR) .....	207
	Ehlers-Danlos Syndrome (EDS) (AD, AR) .....	209
	Pseudoxanthoma Elasticum (PXE) (AR) .....	211
	Marfan Syndrome (AD) .....	213
	Buschke-Ollendorff Syndrome (AD) .....	214
	Lipoid Proteinosis (Hyalinosis Cutis et Mucosae) (AR) .....	215
	Focal Dermal Hypoplasia (Goltz syndrome) .....	220
	Juvenile Hyaline Fibromatosis (JHF) (AR) .....	226
	References.....	227
<b>10</b>	<b>Ectodermal Dysplasia</b> .....	229
	Hypohidrotic or Anhidrotic Ectodermal Dysplasia (Christ-Siemens-Touraine Syndrome) (XLR).....	229
	Hidrotic Ectodermal Dysplasia [3, 4] (Clouston Syndrome) (AD) .....	233
	Ankyloblepharon-Ectodermal Dysplasia-Clefting Syndrome (Hay-Wells Syndrome) (AD) .....	235
	Witkop's Syndrome (Tooth-and-Nail Syndrome) (AD) .....	237
	Hallermann-Streiff Syndrome (Oculo-Mandibulo-Facial Syndrome) (Sporadic/AD).....	238
	Monilethrix (AD) .....	239
	Atrichia with Papular Lesions (AR).....	240
	Uncombable Hair Syndrome (AD/AR) .....	241
	Björnstad Syndrome (AR) .....	242
	References.....	243
<b>11</b>	<b>Premature Aging Syndromes (Progeroid Syndromes)</b> .....	245
	Hereditary Conditions with Premature Aging.....	245
	Progeria (Hutchinson-Gilford Syndrome) (AD).....	245
	Adult Progeria (Werner Syndrome) (AR).....	245
	References.....	248
<b>12</b>	<b>Genetic Immunodeficiency Disorders</b> .....	249
	Chronic Mucocutaneous Candidiasis (CMC) (AD/AR).....	249
	Wiskott-Aldrich Syndrome (XLR).....	250
	Hyper-IgE Syndrome (Job Syndrome) (AD/AR) .....	251
	References.....	254
<b>13</b>	<b>Miscellaneous</b> .....	255
	Lesch-Nyhan Syndrome (X-Linked Recessive) .....	255
	GAP0 Syndrome (AR).....	256
	Phakomatosis Pigmentokeratolica (PPK) (AR) .....	257
	Aplasia Cutis Congenita (AD, AR).....	258
	Membranous Aplasia Cutis Congenita .....	258
	Bart Syndrome [15] (Aplasia Cutis + Epidermolysis Bullosa).....	259
	Adams-Oliver Syndrome (AD, AR or Sporadic) (Aplasia Cutis + Limb Defect) .....	260
	Prolidase Deficiency (Peptidase Deficiency) (AR).....	262
	Brauer Syndrome (Focal Facial Dermal Dysplasia) (AD, AD) .....	262
	H Syndrome (AR).....	263
	Epidermodysplasia Verruciformis (AR) (Tree-Man Disease).....	264
	Turner Syndrome .....	264
	References.....	265





Ichthyosis is commonly inherited as a single entity. However, it may be part of syndromes that induce abnormalities in organs other than the skin. These include KID, HID, Chanarin-Dorfman, Refsum, Sjögren-Larsson, Netherton, Tay-Sachs (PIBIDS), Rud's, Laurence-Moon-Bardet-Biedl, MEDNIK, Conradi-Hünemann-Happle, and CHILD syndrome.

## 1. Hereditary (Primary) Ichthyoses

- (a) Common Ichthyoses
  - Ichthyosis Vulgaris
  - X-linked Recessive (XLR) Ichthyosis
- (b) Autosomal Recessive (AR) Ichthyoses
  - Major Forms
    - Non-Bullous Congenital Ichthyosiform Erythroderma.
    - Lamellar Ichthyosis
    - Harlequin Ichthyosis
  - Minor Forms
    - Self-healing Collodion Baby
    - Acral self-healing Collodion Baby
    - Bathing-suit Ichthyosis
- (c) Keratinopathic Ichthyoses
  - Epidermolytic Ichthyosis
  - Superficial Epidermolytic Ichthyosis (of Siemens)
  - Ichthyosis Hystrix Curth-Macklin
  - Ichthyosis en Confetti

## 2. Ichthyosiform Syndromes

- (a) KID Syndrome
- (b) HID Syndrome
- (c) Chanarin-Dorfman Syndrome
- (d) Refsum Syndrome
- (e) Sjögren-Larsson Syndrome
- (f) Netherton Syndrome
- (g) Tay-Sachs Syndrome (PIBIDS)
- (h) Rud's Syndrome
- (i) Laurence-Moon-Bardet-Biedl Syndrome
- (j) MEDNIK Syndrome
- (k) Conradi-Hünemann-Happle Syndrome
- (l) CHILD Syndrome

## Hereditary (Primary) Ichthyosis

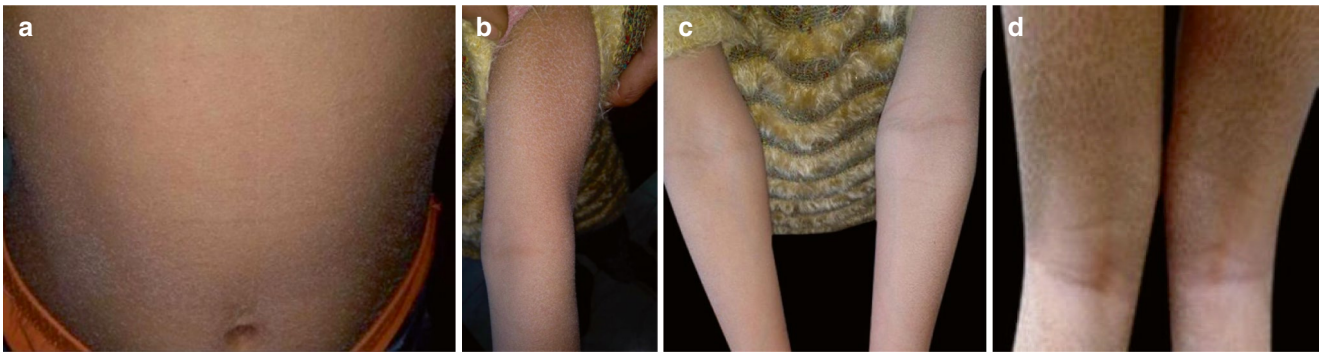
### Common Ichthyosis

#### Ichthyosis Vulgaris (AD) [1, 2] (Figs. 1.1, 1.2, and 1.3)

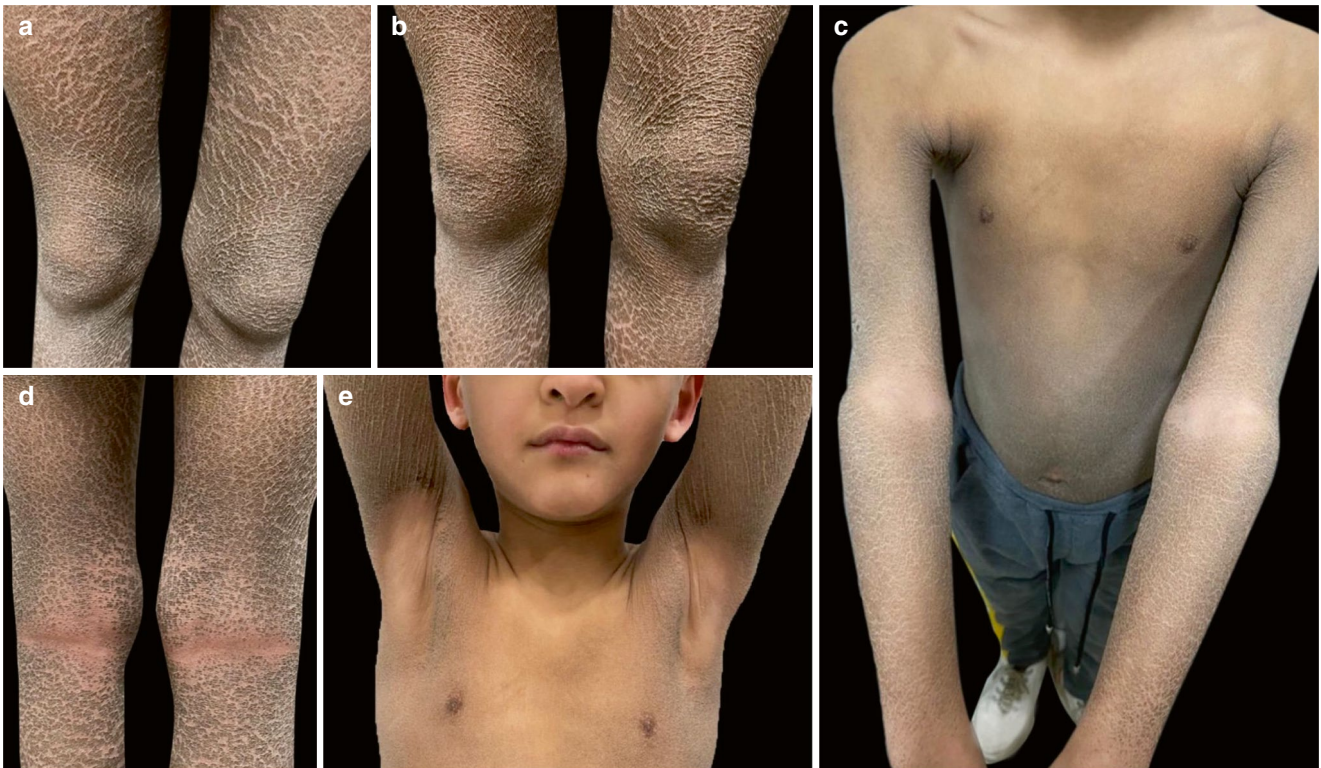
- The most common disorder of cornification.
- Autosomal dominant inheritance: mild ichthyosis with a heterozygous filaggrin (*FLG*) mutation and more severe ichthyosis with mutations in both *FLG* alleles.
- Onset: during infancy and most patients exhibit clear clinical manifestations by the age of 5 years.
- Clinical characteristics:
  - Skin: dry, fine, small, white, flaky scales. The extensor surfaces of the upper and lower extremities are the initial target with sparing of the flexural creases.
  - In most cases, no extracutaneous involvement of the eyes, ears, skeletal, and the nervous systems.
- Associations:
  - Atopic dermatitis, asthma, allergic rhinitis.
  - Palmoplantar hyperlinearity and hyperkeratosis (keratosis punctata).
  - Keratosis pilaris and furrowed heels.
- Prognosis: improves with age and summer.
- Treatment: emollients, humectants, and keratolytics (e.g., urea, lactic, and salicylic acids); the latter group may be irritating in patients with coexistent atopic dermatitis.

#### X-Linked Recessive Ichthyosis [3] (Figs. 1.4 and 1.5)

- Absence of steroid sulfatase (STS) activity due to the deletion of the entire *STS* gene.
- Almost exclusively affects boys and men, with transmission by asymptomatic female carriers.
- Onset: skin findings usually appear within the first year of life, 15–20% have manifestations at birth.
- Clinical characteristics:
  - Widespread polygonal large dark brown plate-like adherent scales on the anterior aspect of lower legs and trunk with fine-scale on the scalp.



**Fig. 1.1** Ichthyosis vulgaris. Fine white scales on the abdomen (a) on the limbs (b, c, d), sparing flexures (c, d)



**Fig. 1.2** Ichthyosis vulgaris. Large adherent scales, grayish tessellated (tile-like), similar to fish skin on the lower legs (a, b), sparing flexures (c-e)

- Dirty neck appearance and affection of axillae.
- Face (except pre-auricles), palms, and soles are spared. Flexor areas are variably involved.
- Associations:
  - Corneal opacities.
  - Cryptorchidism.
  - Prolonged labor due to low placental estrogen production (may result in birth via cesarean section).
- Prognosis: improves with summer, worsens with age.
- Treatment: topical humectants, keratolytics, and retinoids.

### Autosomal Recessive (AR) Ichthyoses

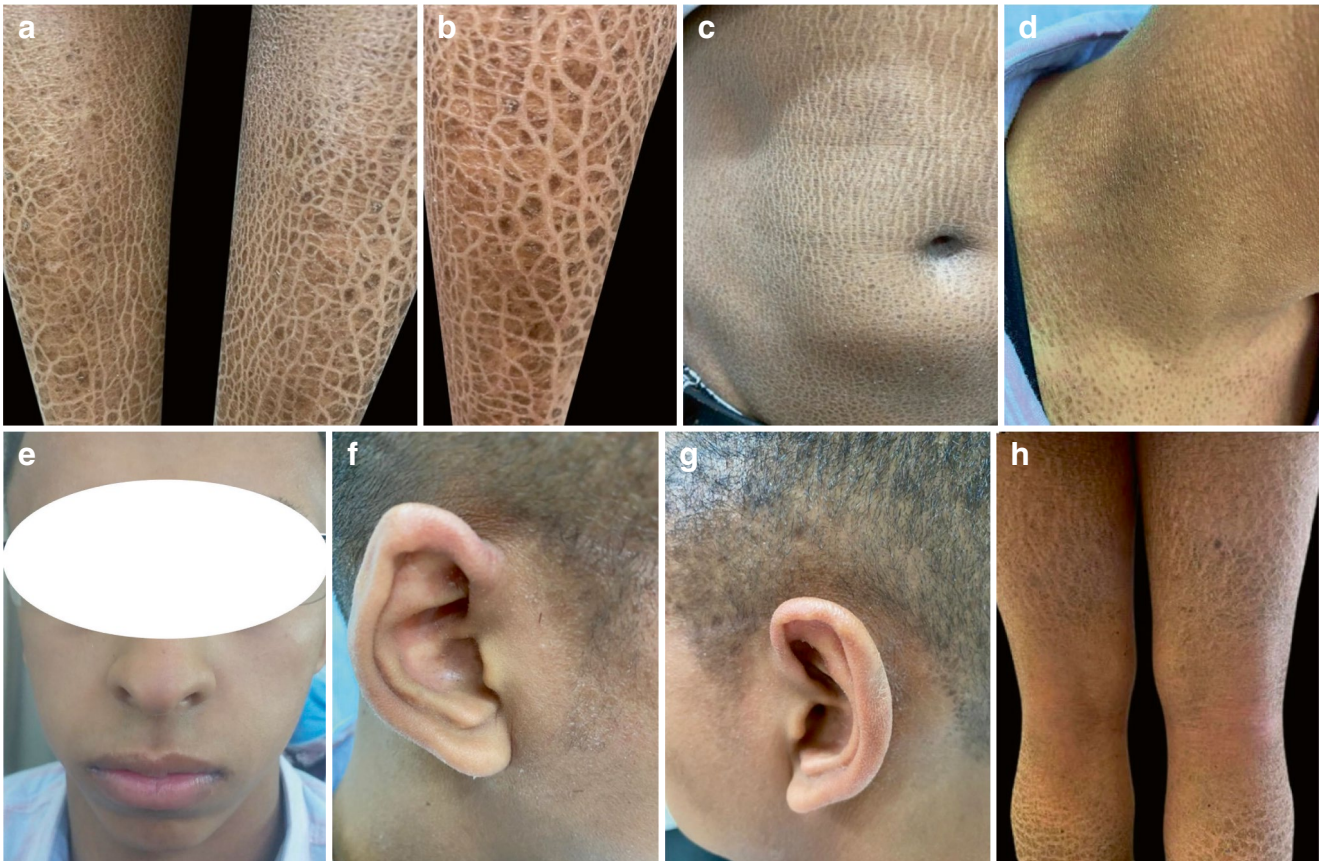
#### Non-Bullous Congenital Ichthyosiform Erythroderma (AR) [4] (Figs. 1.6 and 1.7)

- Mutations in Transglutaminase 1 (*TGM1*), *ALOXE3*, *ALOX12B*, and *NIPAL4* genes.
- Onset: at birth.
- Clinical Characteristics:
  - Scales: at birth with collodion membrane, generalized erythroderma with fine, flaky white, powdery scales. Flexures, face, palms, and soles are involved.





**Fig. 1.3** Ichthyosis vulgaris. Hyperlinearity of the palms (accentuated skin marking) (a), dorsum of feet (b), knees (c)



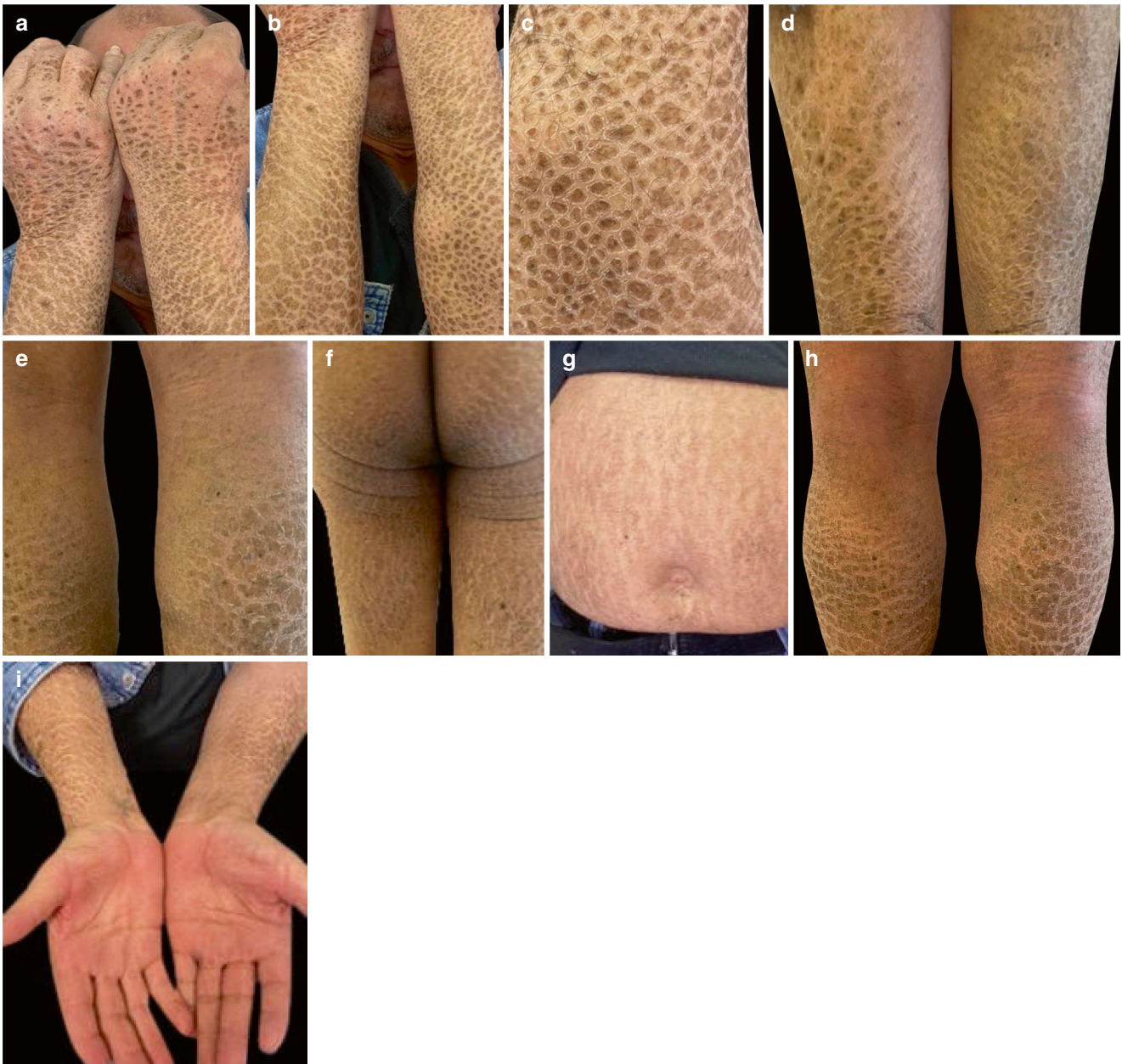
**Fig. 1.4** X-linked ichthyosis. Large prominent dark dirty brown scales on limbs (a, b) smaller light brown on trunk (c), Dark scales on the neck 'dirty neck' (d), face spare (except pre-auricles) (e-g), with sparing flexures (h)

- Mild form of lamellar ichthyosis.
- Hearing impairment due to accumulation of scales in external ear ± scarring alopecia.
- Hyperkeratotic lesions on joints.
- Ectropion, palmoplantar hyperkeratosis, heat intolerance, and hypohidrosis due to obstruction of sweat ducts and nail dystrophy may occur.
- Severe exfoliative erythroderma may cause metabolic stress or mild growth retardation.
- Treatment: oral retinoids are more beneficial for scaling than for the associated erythema; increased intake of

fluids, calories, and protein is required for erythrodermic patients.

#### **Lamellar Ichthyosis (AR) [5, 6] (Figs. 1.8, 1.9, 1.10, 1.11 and 1.12)**

- Mutation in *TGM-1* and *ABCA12* genes.
- Onset: at birth.
- Clinical Characteristics:
  - Usually a collodion-like membrane is present at birth.
  - During the first week of life, the membrane cracks and peels off in sheets then forms generalized large thick,



**Fig. 1.5** X-linked ichthyosis in adult male. Large prominent dark dirty brown scales on upper limbs (a–c), lower limbs (d, e), buttocks (f), abdomen (g). Flexor areas and palms are spared (h, i)

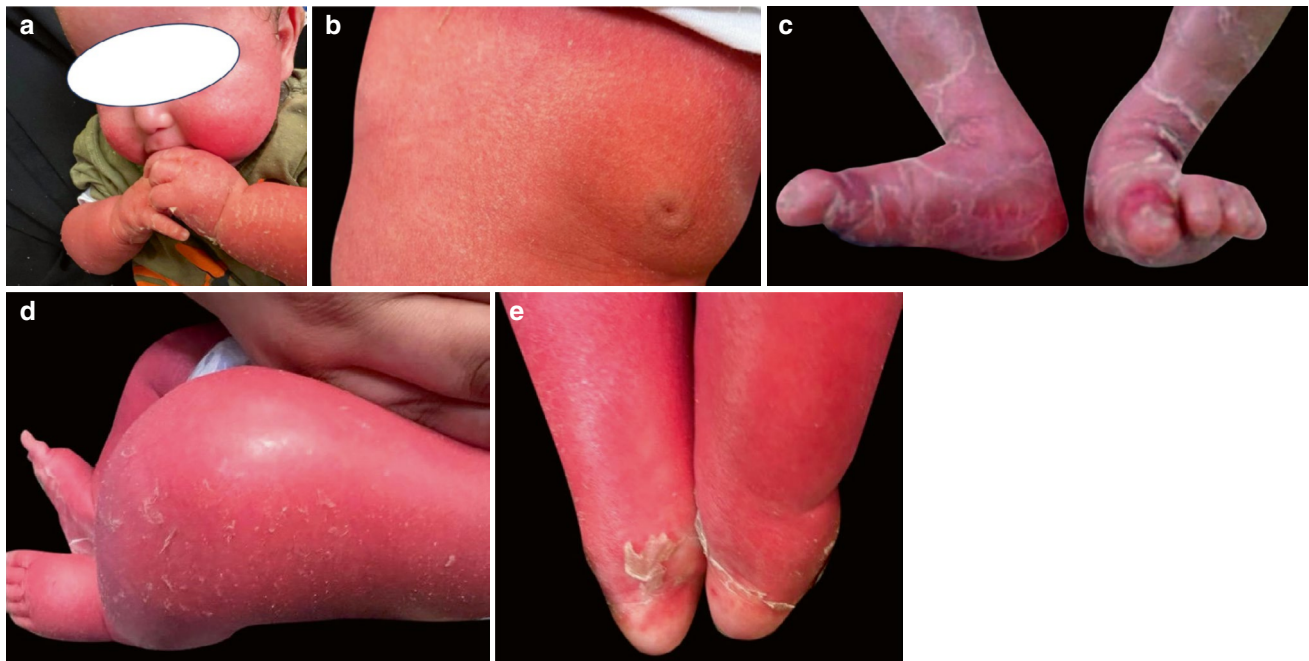
dark, brown plate-like adherent scales, which are quadrilateral, adherent in the center, and free at the edge with raised border often leading to superficial fissures, forming a mosaic or bark-like pattern. [Erythroderma](#) is either absent or minimal.

- Heat intolerance (heat stroke) and hypernatremia.
- Scarring alopecia especially at the periphery of the scalp (tautness of facial skin) and sparse scalp hair.
- Marked ectropion due to taut skin as well as plate-like scales around eyes associated with madarosis, conjunctivitis and keratitis, eclabium, hypoplasia of nasal and auricular cartilage (crumbled).
- Ears are small and deformed. Accumulation of scales in the ear may lead to recurrent infection.
- “Bathing-suit ichthyosis” caused by temperature sensitive *TGM-1* mutation affects primarily trunk and scalp with a higher incidence in the South African population.
- Palmoplantar hyperkeratosis range from accentuating skin markings to severe thickened skin with cracking and fissuring.
- Hypotrichosis and nail dystrophy with thickening and ridging.
- Prognosis: persistent.





**Fig. 1.6** Non-Bullous congenital ichthyosiform erythroderma. Generalized fine, flaky white, powdery scales with dry skin and persistent generalized erythroderma on face with ear affection (a, b), back (c), limbs with flexures (d, e), and palmoplantar hyperkeratosis (f, g)



**Fig. 1.7** Non-bullous congenital ichthyosiform erythroderma. Generalized fine, flaky white, powdery scales with dry skin and persistent generalized erythroderma on face (a), trunk (b) and limbs (c-e)



**Fig. 1.8** Lamellar ichthyosis. 2 weeks neonate with large, plate-like scales on face (taut skin causing ectropion), scalp, ear deformity and accumulation of scales in the ear (a–c), limbs and extremities (d, e)

- Treatment: acitretin use during early childhood is effective for hyperkeratosis and scaling. Acitretin improves ectropion and avoid eye complications and eyelid surgery.

#### **Harlequin Ichthyosis (AR) [7, 8] (Figs. 1.13 and 1.14)**

- Mutation in *ABCA12* gene.
- It is a severe and usually fatal form of ichthyosis.
- Onset: infant born premature.
- Tightly encased neonate.
- Encasement of hard thickened stratum corneum leads to hyperkeratotic cast (cracks).
- Scales: large, yellow, brown adherent plate, separated by broad deep intensely red fissures gives armor-like plaques. Baby is stillborn or dies soon after delivery. Acitretin may allow survival, with treatment may develop into lamellar ichthyosis or congenital ichthyosiform erythroderma-like phenotype.
- Complications in the neonatal period:
  - Tautness of facial skin with severe ectropion.
  - Eclabium and microcephaly.
  - Flat ears, rudimentary or absent, and deformities of the nose (all with taut skin lead to grotesque appearance and distortion).
  - Hands and feet are edematous and swollen leading to mitten hands and feet.
  - Autoamputation.
  - Eyelashes/eyebrows are usually missing (spare scalp hair).
  - Erythroderma.





**Fig. 1.9** Lamellar ichthyosis. Female patient with large, plate-like scales on face with obvious ectropion, scarring alopecia with ear deformity and accumulation of scales in ear (recurrent infection) (a–c),

plate-like scales with mosaic pattern on trunk (d), upper limb and extremities (e, f). Hyperkeratosis of the palms and nail dystrophy (f, g)



**Fig. 1.10** Lamellar ichthyosis. A male patient with large, plate-like scales on face with ectropion, scarring alopecia, eclabium (a). Large thick, dark plate-like adherent scales in the center and free at the edge

and form a mosaic pattern (reptilian scales) on trunk (b, c), limbs and extremities (d–f). Hyperkeratosis of the soles (g)

- Dies within days due to respiratory failure and sepsis.
- Taut facial skin prevents the infant from suckling.
- Treatment: systemic retinoid and advanced neonatal intensive care (life-threatening and often fatal disorder).

#### **Collodion Baby (AR) [9] (Figs. 1.15 and 1.16)**

- Onset: these babies are often premature with low birth weight.
  - Born covered with a taut, yellow, shiny, transparent membrane resembling plastic wrap, a cellophane-like membrane. Within 2–3 weeks, the membrane peels off in sheets, leading to erythema, mild scaling, ectropion, eclabium, and distortion of nose and ears (misshapen or crumbled ears), hypoplastic fingers, nose, and anonychia.
  - Complications: impaired suckling, restricted ventilation, fluid and electrolyte imbalances, dehydration, skin infection, and sepsis.
- Prognosis:
    - Collodion baby is the usual presentation for Harlequin ichthyosis and congenital ichthyosiform erythroderma. AD lamellar ichthyosis, Sjögren-Larsson syndrome, trichothiodystrophy, neutral lipid storage disease, Conradi-Hünemann-Happle syndrome, Hays-Wells syndrome, and ectodermal dysplasia may also occasionally present as collodion baby.
    - A subset of collodion babies with underlying mutations in *TGM1*, *ALOX12B*, or *ALOXE3* have a “self-healing” phenotype (self-healing collodion baby) where the skin is fairly normal in appearance when the membrane resolves.
  - Treatment: humidified incubator, emollients, and monitoring for complications; keratolytics and manual debridement of the membrane are not advised due to risk of systemic absorption and infection, respectively.





**Fig. 1.11** Lamellar ichthyosis. Large thick brown plate-like scales on face with obvious ectropion, scarring alopecia (periphery of scalp) (a). Large, plate-like scales forming a mosaic pattern on trunk (b, c), scalp (d), and limbs with significant flexural involvement (e–g)



**Fig. 1.12** Lamellar ichthyosis in an adult female. Adult patient with obvious ectropion with large, plate-like scales on face, scarring alopecia with ear deformity (a–c). Large, plate-like scales forming a mosaic pattern on neck, trunk, limbs, extremities (e–f), and palmar hyperkeratosis (g)



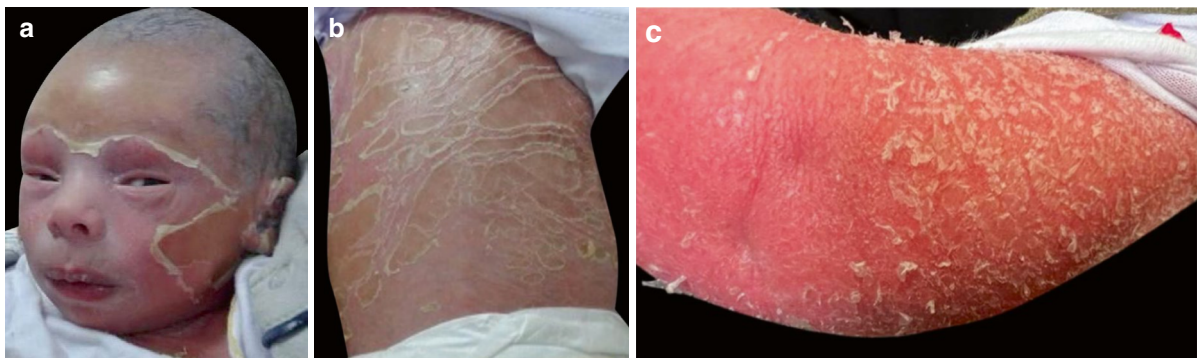
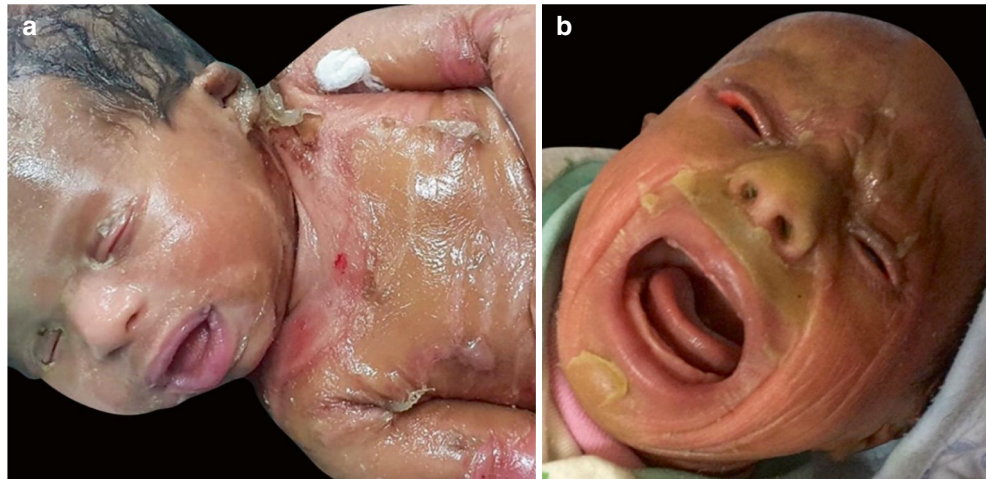
**Fig. 1.13** Harlequin Ichthyosis. Obvious ectropion with large, yellow, horny, extremely thickened armor-like plaques on face associated with eclabium and scarring alopecia (a), mitten hands and feet (b, c)





**Fig. 1.14** Harlequin Ichthyosis. Eclabium and obvious ectropion with extremely thickened scales with red deep fissures on face, neck, upper chest (a, b) and lower trunk (c)

**Fig. 1.15** Collodion baby. Day 1 with shiny, transparent membrane resembling plastic wrap, ectropion, eclabium with deformed ears (a). Day 5 with erythema, diffuse mild scaling, ectropion, eclabium (b)



**Fig. 1.16** Collodion baby. Baby with a taut, shiny, transparent membrane resembling plastic wrap with erythema on desquamation (a–c)

## Keratinopathic Ichthyoses

### Epidermolytic Ichthyosis (AD) [10] (Bullous Congenital Ichthyosiform Erythroderma) (Multiple-Ridged Hyperkeratosis) (Figs. 1.17, 1.18, 1.19, and 1.20)

- Mutation in Keratin (*KRT1*) gene is associated with severe palmoplantar hyperkeratosis while mutation in *KRT10* spare palms and soles.
- Onset: at birth.
- Clinical characteristics:
  - Erythroderma, peeling, erosions, denuded skin, and multiple blisters (misdiagnosed as epidermolysis bullosa in newborns).
  - Later (First few months): decrease skin fragility, with the development of widespread erythema, hyperkeratosis, and focal erosions that form yellow-brown, thick, warty, corrugated ridges and furrows on flexors, joints, and neck, also form cobblestone pattern on extensors surface of joints and dorsal surface of hands and feet.
  - Multiple blisters occur due to skin friction.
- Severe hyperkeratosis leads to the shedding of scales in the superficial epidermis revealing a tender erythematous base.
- Carpus-like scales and hyperkeratosis on the trunk, anterior neck, and flexors sometimes may outgrow into Ichthyosis Hystrix.
- Thickened horny warty or spine-like scales on creases causing palmoplantar hyperkeratosis.
- Complications:
  - Sepsis and electrolyte imbalance (hypernatremia).
  - Foul odor (a pungent body odor), secondary infection, angular cheilitis, hair loss, hypocalcemia, vitamin D resistance, severe palmoplantar hyperkeratosis leading to severe digital contractures and deformities, and gait posture abnormalities due to excessive keratinization.
- Histopathology: (Epidermolytic Hyperkeratosis) (Diagnostic).
  - Massive orthokeratotic hyperkeratosis.
  - Hypergranulosis.
  - Lysis of keratinocytes of the granular cell layer.
- Treatment: keratolytics, topical retinoid and vitamin D preparation with the treatment of secondary bacterial infection.



**Fig. 1.17** Epidermolytic ichthyosis. Hyperkeratosis with corrugated ridges and furrows on flexors (a). Hyperkeratosis with a cobblestone pattern on extensors surface of joints (b, c) on dorsa of feet (d), palmar hyperkeratosis (e), carpus-like scales on trunk with focal erosions (f, g)





**Fig. 1.18** Epidermolytic Ichthyosis. Male patient, showing hyperkeratosis with corrugated ridges and furrows on face (a), flexors (b, c), extensors (d, e) with palmar hyperkeratosis (f)



**Fig. 1.19** Epidermolytic ichthyosis. Male patient, showing hyperkeratosis with corrugated ridges and furrows on face (a), neck (b), extensors (c, d) with maceration (e) and palmar hyperkeratosis (f)





**Fig. 1.20** Epidermolytic ichthyosis. Female patient showing hyperkeratosis with corrugated ridges and furrows on trunk (a, b), limbs with increasing severity on elbows and knees (c, d). Maceration is marked in hands and flexures (e-i)