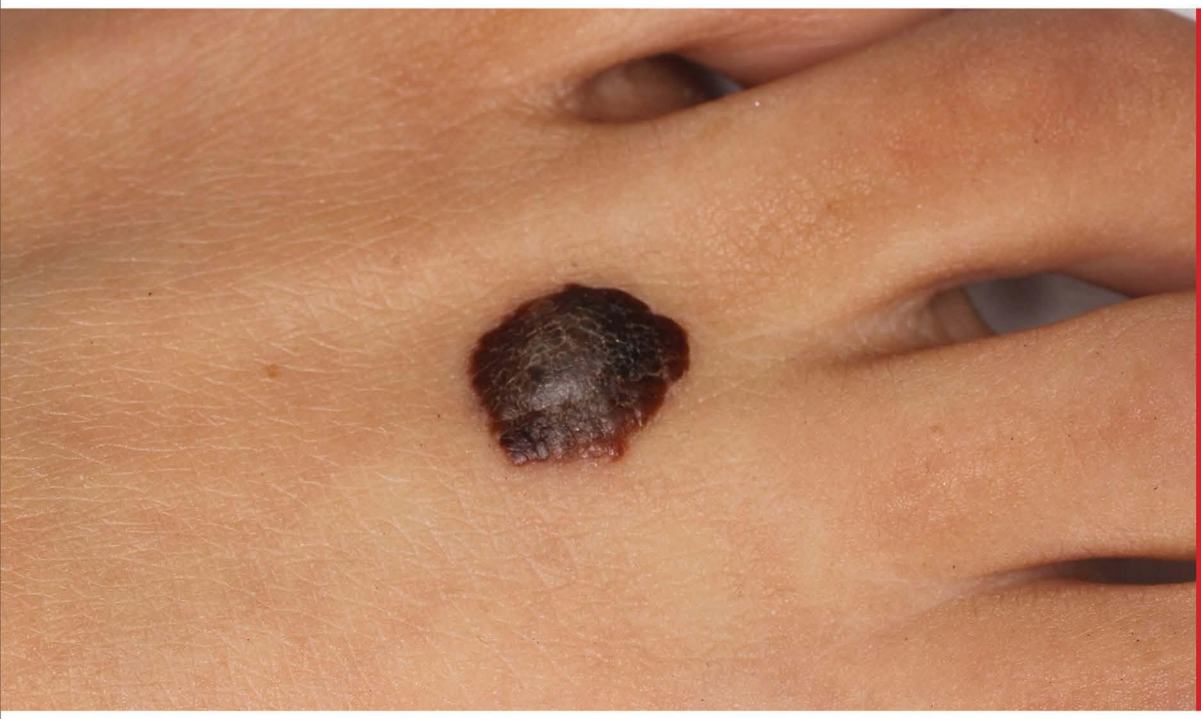
Roxburgh's Common Skin Diseases

19th Edition



EDITED BY
Ayşe Serap Karadag
Lawrence Charles Parish
Jordan V. Wang

CRC Press
Taylor & Francis Group

Roxburgh's Common Skin Diseases

19th Edition

Ayşe Serap Karadağ, MD

Department of Dermatology and Venereology
Istanbul Arel University, School of Medicine
Memorial Health Group Atasehir and Sisli Hospital
Istanbul, Turkey

Lawrence Charles Parish, MD, MD (Hon)

Department of Dermatology and Cutaneous Biology
Sidney Kimmel Medical College at Thomas Jefferson University
and Jefferson Center for International Dermatology
Philadelphia, PA, USA

Jordan V. Wang, MD, MBE, MBA

Department of Dermatology and Cutaneous Biology
Sidney Kimmel Medical College at Thomas Jefferson University
Philadelphia, PA
and Laser & Skin Surgery Center of New York
New York, NY, USA

CRC Press
Taylor & Francis Group
Boca Raton London New York

CRC Press is an imprint of the
Taylor & Francis Group, an **informa** business

Nineteenth edition published 2022
by CRC Press
6000 Broken Sound Parkway NW, Suite 300, Boca Raton, FL 33487–2742

and by CRC Press
2 Park Square, Milton Park, Abingdon, Oxon, OX14 4RN

Eighteenth edition published 2011

CRC Press is an imprint of Taylor & Francis Group, LLC

Library of Congress Cataloging-in-Publication Data
Names: Karadağ, Ayşe Serap, editor. | Parish, Lawrence Charles, editor. | Wang, Jordan V., editor. | Marks, Ronald. Common skin diseases.
Title: Roxburgh's common skin diseases / [edited] by Ayşe Serap Karadağ, Lawrence Charles Parish, Jordan V Wang.
Other titles: Common skin diseases
Description: Nineteenth edition. | Boca Raton : CRC Press, 2021. | Preceded by Common skin diseases 18th ed. / Ronald Marks, Richard Motley. 2011. | Includes bibliographical references and index.
Identifiers: LCCN 2021037604 (print) | LCCN 2021037605 (ebook) | ISBN 9780367614997 (hardback) | ISBN 9780367614980 (paperback) | ISBN 9781003105268 (ebook)
Subjects: MESH: Skin Diseases
Classification: LCC RL71 (print) | LCC RL71 (ebook) | NLM WR 140 | DDC 616.5—dc23
LC record available at https://lccn.loc.gov/2021037604
LC ebook record available at https://lccn.loc.gov/2021037605

ISBN: 978-0-367-61499-7 (hbk)
ISBN: 978-0-367-61498-0 (pbk)
ISBN: 978-1-003-10526-8 (ebk)

DOI: 10.1201/9781003105268

Typeset in Palatino
by Apex CoVantage, LLC

Contents

Preface

When Archibald Cathcart Roxburgh (1886–1954) created *Common Skin Diseases* in 1932,[1] we doubt that he had any idea that the book would now be in its 19th edition. Some later editions were edited by Peter Forbes Borrie (1918–1984),[2] John D. Kirby, and Ronnie Marks (1935–2020).[3] This may well be a record for a dermatology textbook and rivals such textbooks of medicine as those by Cecil[4] and Harrison.[5] There have been several dermatology books that have had multiple editions but none approaching two score.

What makes *Common Skin Diseases* such a perennial favorite among students and practitioners may be that it is not encyclopedic and that it is straightforward. It does not intend to be as all-encompassing as the works by Rook[6] or Bologna;[7] rather, it follows in the role of the *Manual of* Dermatology,[8] written during World War II for the medical corps, or the *Handbook of Diseases of the Skin* created by the Suttons.[9] Although it was once possible for a single physician to create an inclusive textbook, this is no longer feasible nor realistic. This was recognized by Donald M. Pillsbury (1902–1980) at the University of Pennsylvania in Philadelphia, who created the first modern multi-authored dermatology book in 1956. [10]

Roxburgh was an exacting author and sometime editor of the *British Journal of Dermatology*, where he seems to have been an equally exacting editor. According to one obituary, he wrote his textbook in the hours before breakfast, and he took all the pictures for his book himself, processing them as well.[11] *The Lancet* referred to his text as "a practical vade-mecum for the dermatologist."[12]

In creating this edition, we have built on the excellence of the previous versions. The contributors, whom we invited from several international centers, were asked to follow a suggested outline for the chapters. The mere complexities of modern medicine—and dermatology is no exception—often does not permit a uniform format nor did we wish to discuss every affliction of the skin. We have included color pictures where appropriate and have limited the additional reading to but ten items.

REFERENCES

1. Roxburgh AC. Common skin diseases, London: H. K. Lewis.1932.
2. Obituary: Peter Forbes Borrie, MD, MC Cantab, FRCP. Lancet. 1984; ii:415.
3. Finlay AY. Obituary: Professor Ronald Marks, 1935–2020. Br J Dermatol. 2020; 183:598–599.
4. Goldman L, Schafer AI, Cecil RL. Goldman-Cecil medicine. 26th edition/ed, Philadelphia, PA: Elsevier.2020: 2 volumes.
5. Harrison TR. Principles of internal medicine, Philadelphia, PA: Blakiston.1950.
6. Rook A, Wilkinson DS, Ebling FJG. Textbook of dermatology, Oxford; Edinburgh: Blackwell Scientific.1968.
7. Bolognia J, Jorizzo JL, Rapini RP. Dermatology, Edinburgh: Mosby.2003.
8. Pillsbury DM, Sulzberger MB, Livingood CS, et al. Manual of dermatology, Philadelphia, London: W.B. Saunders Company.1942.
9. Sutton RL. Handbook of diseases of the skin, St. Louis: C. V. Mosby Co.1949.
10. Pillsbury DM, Shelley WB, Kligman AM. Dermatology, Philadelphia, PA: Saunders.1956.
11. Obituary: Dr. A. C. Roxburgh. Br J Dermatol. 1955; 67:33–34.
12. Archibald Cathcart Roxburgh, MA, MD (Camb.), F.rRC.P. Lancet. 1954; ii:1237–1238.

Contributors

José Wilson Accioly Filho, MD, PhD
Sector of Dermatology
School of Medicine and University Hospital
Federal University of Ceará
Fortaleza, Brazil

Saira N. Agarwala, MD
Department of Dermatology
Lewis Katz School of Medicine at
Temple University
Philadelphia, PA, USA

Necmettin Akdeniz, MD
Department of Dermatology and
Venereology, Memorial Health Group
Şişli and Ataşehir Hospitals
Department of Dermatology
Istanbul, Turkey

Hasan Aksoy, MD
Department of Dermatology and
Venereology
Istanbul Medeniyet University
School of Medicine
Prof. Dr. Suleyman Yalcin City Hospital
Istanbul, Turkey

Christian Albornoz, MD
Department of Dermatology and Cutaneous
Biology
Sidney Kimmel Medical College at Thomas
Jefferson University
Philadelphia, PA, USA

Albert Alhatem, MD
Department of Pathology, Immunology, and
Laboratory Medicine
Rutgers-New Jersey Medical School
Newark, NJ
Department of Dermatology, St Louis
University School of Medicine
St Louis, MO

Sam Allen, FRCP, FFTM-RCPS(Glasg)
Infectious Diseases
NHS Ayrshire & Arran
Scotland, UK

Ozge Askin, MD
Department of Dermatology
Istanbul University
Cerrahpasa Medical Faculty, Fatih
Istanbul, Turkey

Laura Atzori, MD
Unit of Dermatology
Department of Medical Sciences and
Public Health
University of Cagliari, Italy

Robert Baran, MD
Nail Disease Centre
Cannes, France

Cynthia Bartus, MD
Department of Dermatology
Lehigh Valley Health Network
Allentown PA, USA

Mark Biro, MD
Department of Dermatology
Georgetown University School of Medicine
Washington, DC, USA

**Christopher B Bunker, MA(Hons)(Cantab),
MD(Cantab), FRCP**
Department of Dermatology
University College London and Chelsea and
Westminster Hospital
London, UK

Sueli Carneiro, MD, PhD
Department of Dermatology
School of Medical Sciences and University
Hospital
State of Rio de Janeiro University and Sector
of Dermatology
School of Medicine and University Hospital
Federal University of Rio de Janeiro
Rio de Janeiro, Brazil

Charles Cathcart, MBChB, PG, Med Ed Cert
Department of Dermatology
Liverpool University Hospitals NHS
Foundation Trust
Liverpool, UK

Emily Chea, DO
Department of Dermatology
Lehigh Valley Health Network
Allentown, PA, USA

Kayla A. Clark, BS
Department of Dermatology
University of Illinois at Chicago
College of Medicine
Chicago, IL, USA

Emily Correia, BS
Department of Dermatology and Cutaneous Biology
Sidney Kimmel Medical College at Thomas Jefferson University
Philadelphia, PA, USA

Annie Dai, BA
Department of Dermatology
Baylor College of Medicine
Houston, TX, USA

Razvigor Darlenski, MD, PhD
Clinic of Dermatology and Venereology
Acibadem-City Clinic, Tokuda Hospital
Sofia, Bulgaria

Abdullah Demirbaş, MD
Department of Dermatology and Venereology
Kütahya Health Sciences University
School of Medicine
Kütahya, Turkey

Kossara Drenovska, MD, PhD
Department of Dermatology and Venereology
Medical Faculty
Medical University
Sofia, Bulgaria

Robert Duffy, MD
Division of Dermatology
Cooper Medical School of Rowan University
Camden, NJ, USA

Ömer Faruk Elmas, MD
Department of Dermatology and Venereology
Kırıkkale University
School of Medicine
Kırıkkale, Turkey

Nurimar Conceição Fernandes, MD, PhD
Sector of Dermatology
School of Medicine and University Hospital
Federal University of Rio de Janeiro
Rio de Janeiro, Brazil

Caterina Ferreli, MD
Unit of Dermatology
Department of Medical Sciences and Public Health
University of Cagliari, Italy

Warren Heymann, MD
Division of Dermatology
Cooper Medical School of Rowan University
Camden, NJ
Department of Dermatology
Perelman School of Medicine
University of Pennsylvania
Philadelphia, PA, USA

Uta-Christina Hipler, PhD
Department of Dermatology
University Hospital
Jena, Germany

Madeline Hooper, BA
Department of Dermatology
Lehigh Valley Health Network
Allentown, PA, USA

Sylvia Hsu, MD
Department of Dermatology
Lewis Katz School of Medicine at Temple University
Philadelphia, PA, USA

Tara Jennings, MD
Division of Dermatology
Cooper Medical School of Rowan University
Camden, NJ, USA

Virginia A. Jones, MD, MS
Department of Dermatology
University of Illinois at Chicago College of Medicine
Chicago, IL, USA

Melek Aslan Kayıran, MD
Department of Dermatology and Venereology
Istanbul Medeniyet University
School of Medicine
Prof. Dr. Suleyman Yalcin City Hospital
Istanbul, Turkey

Jana Kazandjieva, MD, PhD
Department of Dermatology and Venerology
Medical University
Sofia, Bulgaria

Matthew Keller, MD
Department of Dermatology and Cutaneous Biology
Sidney Kimmel Medical College at Thomas Jefferson University
Philadelphia, PA, USA

Chelsea Kesty, MD
Department of Dermatology
Lehigh Valley Health Network
Allentown, PA, USA

Soo Jung Kim, MD, PhD
Department of Dermatology
Baylor College of Medicine
Houston, TX, USA

Wei-Liang Koh, MBBS, MRCP, FAMS
Department of Dermatology
Changi General Hospital
Singapore

Shalini Krishnasamy, MD
Department of Dermatology and Cutaneous Biology
Sidney Kimmel Medical College at Thomas Jefferson University
Philadelphia, PA, USA

Muriel W. Lambert, PhD
Department of Pathology
Immunology and Laboratory Medicine and Department of Dermatology
Rutgers-New Jersey Medical School
Newark, NJ, USA

W. Clark Lambert, MD, PhD, FRCP(Edin)
Department of Pathology
Immunology and Laboratory Medicine and Department of Dermatology
Rutgers-New Jersey Medical School
Newark, NJ, USA

Michael Joseph Lavery, MBBCh, BAO, MRCP(UK)
Division of Dermatology
Phoenix Children's Hospital
Phoenix, Arizona, USA

Jason B Lee, MD
Department of Dermatology and Cutaneous Biology
Sidney Kimmel Medical College at Thomas Jefferson University
Philadelphia PA, USA

Shari Lipner, MD, PhD
Department of Dermatology
Weill Cornell Medical College
New York, NY, USA

Erin McClure, BS
Department of Dermatology
Lehigh Valley Health Network
Allentown, PA, USA

Liam Mercieca, MD, MRCP(UK)
University Department of Dermatology
Mater Dei Hospital
Msida, Malta

Pietro Nenoff, MD
Laboratory for Medical Microbiology
Mölbis, Germany

Alexander V. Nguyen, BA
Department of Dermatology
Baylor College of Medicine
Houston, TX, USA

Neda Nikbakht, MD, PhD
Department of Dermatology and Cutaneous Biology
Sidney Kimmel Medical College at Thomas Jefferson University
Philadelphia, PA, USA

Ivy M. Obonyo, BS
Department of Dermatology
University of Illinois at Chicago College of Medicine
Chicago, IL, USA

Joseph Pace, MD, FRCP(Edin), FRCP(Lond), KM
University Department of Dermatology
Mater Dei Hospital
Msida, Malta

Allison Perz, BS
Division of Dermatology
Cooper Medical School of Rowan University
Camden, NJ, USA

Vesna Petronic-Rosic, MD, MSc, MBA
Department of Dermatology
Cook County Hospital
Chicago, IL, USA

Marcia Ramos-e-Silva, MD, PhD
Oral Dermatology Clinic and Sector of Dermatology
School of Medicine and University Hospital
Federal University of Rio de Janeiro
Rio de Janeiro, Brazil

Franco Rongioletti, MD
Unit of Dermatology
Department of Medical Sciences and Public Health
University of Cagliari, Italy

Kristen Russomanno, MD
Department of Dermatology
MedStar Washington Hospital Center and
Georgetown University Hospital
Washington, DC, USA

Robert A Schwartz, MD, MPH, DSc(Hon), FRCP(Edin)
Department of Pathology
Immunology and Laboratory Medicine and
Department of Dermatology
Rutgers-New Jersey Medical School
Newark, NJ, USA

Saloni Shah, BS
Department of Dermatology and Cutaneous Biology
Sidney Kimmel Medical College at Thomas Jefferson University
Philadelphia, PA, USA

Alexander Sherban, BM
Department of Dermatology and Cutaneous Biology
Sidney Kimmel Medical College at Thomas Jefferson University
Philadelphia, PA, USA

Nanette Silverberg, MD
Department of Dermatology
Icahn School of Medicine at Mount Sinai
New York, NY, USA

Rodney Sinclair, MBBS, MD
Sinclair Dermatology
Melbourne, Australia

Roselyn Stanger, MD
Department of Dermatology
Icahn School of Medicine at Mount Sinai
New York, NY, USA

Aspen R. Trautz, MD
Department of Dermatology
Lewis Katz School of Medicine at Temple University
Philadelphia, PA, USA

Nikolai Tsankov, MD, PhD
Clinic of Dermatology and Venerology
Acibadem-City Clinic
Tokuda Hospital, Sofia, Bulgaria

Maria M. Tsoukas, MD
Department of Dermatology
University of Illinois at Chicago College of Medicine
Chicago, IL, USA

Yalçın Tüzün, MD
Department of Dermatology
Istanbul University
Cerrahpasa Medical Faculty, Fatih
Istanbul, Turkey

Serap Utaş, MD
Department of Dermatology
Fulya Acıbadem Hospital
Istanbul, Turkey

Aarthy K Uthayakumar, BA(Hons)(Cantab), MBBS, MRCP
Department of Dermatology
University College London Hospitals NHS Foundation Trust
London, UK

Tugba Kevser Uzuncakmak, MD
Department of Dermatology
Istanbul University
Cerrahpasa Medical Faculty
Fatih, Istanbul, Turkey

Snejina Vassileva, MD, PhD
Department of Dermatology and Venereology, Medical Faculty
Medical University
Sofia, Bulgaria

Shyam Verma, MBBS, DVD, FRCP(London)
Department of Dermatology
Nirvana Skin Clinic
Vadodara, Gujarat, India

Shayan Waseh, BS, MPH
Department of Dermatology and Cutaneous Biology
Sidney Kimmel Medical College at Thomas Jefferson University
Philadelphia, PA, USA

Uwe Wollina, MD
Department of Dermatology and Allergology
Städtisches Klinikum Dresden
Germany

Sherry Yang, MD
Department of Dermatology and Cutaneous Biology
Sidney Kimmel Medical College at Thomas Jefferson University
Philadelphia, PA, USA

1 Glossary of Dermatologic Words and Terms

Lawrence Charles Parish

Each medical specialty has its own vocabulary, and dermatology is no different. Sometimes, the use of words or terms relating to the skin may seem different from those used in other fields. Other times, the Latinate form of the word may appear questionable.

Our purpose in creating this glossary is to make the chapters uniform and to be understandable to the reader being introduced to the field of dermatology. Where appropriate, we have used the American spelling and nomenclature. Synonyms are included, but an exhaustive listing is not provided.

Abscess: a tender, red 2–3 cm lesion that is inflamed with walled-off purulent material
Acantholysis: separation of epidermal cells due to loss of their connections
Acanthosis: diffuse thickening of the epidermis
Acneiform: resembling acne with somewhat pointed lesions that might include comedones, papules, and pustules
Allergic: an altered reaction to which the patient has been previously exposed
Alopecia: hair loss
Annular: ring-shaped, often with central clearing
Atopic: condition that includes asthma, hay fever, and atopic dermatitis
Atopy: strange-like
Auspitz sign: pinpoint bleeding when the scale is removed
Autoimmune: an altered reaction to one's own body
Barbae: relating to the beard
Biopsy: to take a living specimen for microscopic examination, as opposed to an autopsy (dead specimen)
Blaschko's line: the invisible lines of normal embryonic development that are whorls on the chest and flanks, "V" shaped on the back, and wavy appearance on the scalp
Bleb: a flaccid blister, as in a bulla
Blister: small (>0.5-cm) vesicle; larger (<0.5-cm) bulla
Bohn's nodule: a small nodule found in the ear canal or mouth of a newborn.
Bulla: a blister generally over 1.0 cm, as opposed to a small blister or vesicle and a pustule; bullae (plur)
Burow's solution: an astringent comprised of aluminum triacetate. It is usually diluted with water to make a 1:40 solution
Burrow: a superficial epidermal tunnel due to scabies
Café au lait: the color of coffee with milk or cream added
Carbuncle: an abscess with one opening
Casal's necklace: reddish pigmentation on the neck, resembling a collar, and due to pellagra
Cellulitis: redness, edema, and tenderness without a purulent opening
Chadwick's sign: bluish discoloration of the labia, vagina, or cervix that occurs during pregnancy
Chromonychia: abnormal discoloration of a nail except for white
Circinate: a round lesion-like circle
Clubbing: enlargement of the terminal digit of the fingers that creates a rounding down of the nail and may be associated with underlying disease, sometimes pulmonary malignancy
Comedo: occlusion of the pilosebaceous duct; comedones (plural)
Condyloma: a warty lesion found in the genital region
Confluent: lesions that have merged
Congenital: appearing at birth, not necessarily inherited
Crowe's sign: axillary freckling
Cutis marmarota: a red or blue mottled appearance of the skin due to cold exposure
Cyst: an elevated lesion with an epithelial lining
Dactylitis: sausage finger, swelling of an entire finger or toe, as found in psoriasis
Dandruff: scurf, white scale on the scalp
Darier sign: swelling of the skin after scratching the skin
Decubitus: lying down leading to loss of skin and subcutaneous material, that is, decubitus ulcer
Defluvium: flowing or falling off
Dermatitis: inflammation of the skin; dermatitides (plural)

DOI: 10.1201/9781003105268-1

Dermatographism: a red elevation of the skin due to scratching the skin
Desquamation: peeling of the skin, often in sheets, as occurs following a sunburn
Diascopy: a test that shows the vascular or non-vascular characteristics of a lesion when pressure is applied
Discoid: a round or nummular lesion
Eczema: inflammation of the skin; dermatitis is the preferred American term
Eczematoid: resembling eczema, that is, dermatitic-like
Ecchymosis: black and blue, due to bleeding under the epidermis
Eclabium: a deformity of the lips with the outward turning
Ectropion: an abnormal outward turning of either the upper or lower eyelid
Edema: swelling of tissue due to abnormal amounts of fluid
Emperipolesis: inclusion of a cell within the cytoplasm of another cell
Ephelids: freckles
Epithelioma: an older term used for describing basal cell carcinoma or squamous cell carcinoma
Eponym: use of a proper name to describe a disease
Epstein's sign: small elevated lesions in a newborn 's mouth
Eruption: a rapidly appearing lesion
Erosion: wearing away of the surface
Erythroderma: redness and subsequent shedding of scales, affecting most of the body's surface area
Erythronychia: reddish discoloration of the nail
Excoriation: picking or scratching to eliminate a lesion or an imaginary lesion
Exudate: fluid that has leaked from blood vessels into the surrounding tissue; when due to an infectious process, it is considered a purulent process or pus
Exfoliation: peeling off the skin
Factitial: artificial, self-created lesion
Familial: occurring within family members; not necessarily due to heredity
Flaccid: soft, no longer firm
Folliculitis: inflammation of the hair follicle
Freckle: a small brown lesion, that is, ephelids
Furuncle: an abscess with several openings
Fusiform: spindle-shaped
Futcher's line: also known as Voight's line; a normal demarcation between a darker and lighter area
Genodermatosis: disease with abnormal skin findings due to heredity
Goodell's sign: softening of the cervix, occurring after four weeks of gestation
Goosebump: horripilation, piloerection of the hair follicles due to emotions, temperature change, or fright, frequently observed on the forearms
Granuloma: packed collection of inflammatory cells
Granulomatous: resembling a granuloma
Gulliver's sign: an indication in a patient with pyoderma gangrenosum that the inflammation is being con trolled.
Gyrate: round or circular
Hematoxylin and eosin stain: abbreviated as H&E, where hematoxylin stains the nuclei purplish-blue and eosin stains the cytoplasm pinkish
Hereditary: inherited, as opposed to acquired
Herpetic: a group of lesions with central pustules, resembling the lesions of *Herpes simplex* or *Herpes zoster* infection
Hive: a reddish elevated lesion, that is, urticaria
Horripilation: see *goosebump*
Hutchinson's sign: vesicular eruption on the nose preceding eye involvement due to viral infection of the trigeminal nerve
Ichthyosiform: resembling ichthyosis or fish scale–like
Impetiginized: resembling impetigo with oozing, crusting, and scaling
Id reaction: development or stimulation of acute dermatitis or lesions in a distant location from the initial site, usually on the hands induced by most often due to a superficial fungal infection on the feet
Immunofluorescence: using fluorescence to stain the antibody. Direct immunofluorescence stains the antibody. Indirect immunofluorescence permits the antigen to react with the antibody, after which the non-antibody globulin is washed away, and the tissue is bathed with fluorescein-labeled anti-rabbit globulin
Impetiginization: superficial bacterial infection superimposed upon an underlying dermatitis

Isomorphic response: creation of additional lesions of the same characteristics as the original lesion, that is, Koebner phenomenon
Itch: an irritable feeling that can be associated with hives or many other skin conditions causing one to scratch
Jacuemier's sign: purplish discoloration of the vagina occurring early in the pregnancy
Kamino bodies: dull pinkish bodies found at the tip of the dermal papillae
Keratinization: creating additional skin or scale
Keratolysis: separation of sheets of epidermal cells
Keratosis: excessive horny material
Koebner phenomenon: see *isomorphic response*
Koilonychia: spoon-shaped nails
Lamellar: sheets of cells
Lentigo: a small brown lesion
Lesion: a characteristic change in the structure of the skin
Leukonychia: white streaks or dots in the nail
Lichenified: thickening of the skin, as in lichens
Linea: formation of a line
Lisch nodule: an elevated tannish nodule on the iris
Livedo: bluish color due to venous congestion
Lunula: the whitish half-moon area often seen at the base of the nail
Lupus: wolflike appearance
Maceration: softening of the skin leading erythema, oozing, and scaling
Macrophage: a cell that surround bacteria or other organisms. It can provide antigens to T cells that release cytokines that can start an inflammatory process
Macular: resembling a macule
Macule: a lesion that is flat with color change
Melanotic: a dark, blackened appearance
Melanonychia: brown or black streaks or dots in the nail
Microbiome: the bacteria, viruses, or fungi found in areas of the body
Morbilliform: red lesions resembling measles
Mottled: irregular discoloration
Multiforme: many different shapes
Nikolsky's sign: slight rubbing of the skin leading to peeling of the superficial layers
Nodule: a larger elevated lesion
Nummular: coin-shaped
Onychodystrophy: defective nail formation
Onychomadesis: shedding of the nail
Onychorrhexis: longitudinal ridging of then ail
Ophiasis: hair loss at the edges of the scalp
Palmar: pertaining to the ventral surface of the hand
Papular: resembling a papule
Papule: a smaller elevated firm lesion, varying in area up to 1 cm
Paraneoplastic: signs and symptoms occurring elsewhere in the body due to chemical signaling from a malignancy
Paronychia: inflammation of the nail fold that leads to a painful, sometimes, pruritic area
Patch: a large macule
Pathergy: an exaggerated response to an injury that exacerbates the underlying condition and may create new lesions
Pautrier microabcess: an accumulation in the epidermis of at least four atypical lymphocytes as found in mycosis fungoides
Peau d'orange: resembling the peel of an orange
Pityriasis: a scaly condition
Plantar: pertaining to the sole
Plaque: a small thickened area
Polymorphic: many different shaped lesions
Prurigo: an older term for an itching condition
Pruritic: an itchy condition
Pruritus: itching
Purpuric: extravasated red blood cells giving a purplish color

Pustule: a lesion containing white to yellow, somewhat viscous fluid
Rash: a term that should be avoided when possible, eruption
Reticulated: resembling a net
Retiform: netlike
Russell's sign: callouses on the dorsal aspect of the hand, associated with self-induced vomiting
Scale: exfoliated skin
Scaling: a lesion containing scale
Seborrheic: a term whose original meaning had to with the sebaceous gland
Serous: a watery yellowish fluid
Serpiginous: having a wavy appearance, like a snake moving
Sisaipho: ophiasis spelled backward to reflect a reversed hair pattern loss with the hair remaining at the edges of the scalp
Sign: a clinical manifestation that can be seen or elicited on examination
Syndrome: a group of signs and/or symptoms to describe a condition
Symptom: an abnormal feeling experienced by the patient that cannot be seen
Stria: a superficial atrophic line
Targetoid: resembling a target shape
Test results: a positive test result, such as pathogenic growth on a bacterial culture, confirms the diagnosis, whereas a reactive serologic test result only suggests the diagnosis
Tinea: a scaling fungal eruption
Trachyonychia: longitudinal ridging with brittle grayish nails, split ends, and a rough surface
Transudate: an edematous process due to increased pressure on blood vessels causing fluid to accumulate in the surrounding tissue leading to swelling of the tissue
Trichodystrophy: defective hair growth often leading to alopecia
Trichomalacia: distorted hair shafts due to repeated twisting, occurring in trichodystrophy
Tumor: abnormal skin growth, often connoting a skin cancer
Tzanck smear: a smear taken from moist tissue that is stained with Giemsa or toluidine blue that will show nucleic bodies; that is, in *Herpes simplex* or *Herpes zoster* infection with multinucleated giant cells that have ballooned
Ulcer: a defect that descends from the skin surface
Ulcerated: the result of an ulcer, a depression from the surface
Ungual: related to the nail
Verrucous: wartlike
Vesicle: a small blister
Voight's line: see *Futcher's line*
Xeropthalmia: decrease in tears
Xerotic: resembling dry skin
Xerostomia: decrease in saliva
Wart: a verruca
Wheal: a red elevated lesion, that is, hive
Welt: a red elevated lesion, that is, hive
Wood light: a diagnostic tool that uses long-wave ultraviolet light appearing as a black light to diagnose skin infections and disorders
Woronoff ring: a round, blanched area surrounding a psoriatic lesion in the shape of a girdle, resembling the lesions of *Herpes zoster* infection

ADDITIONAL READINGS

Burgdorf WH, Hoenig LJ. Favorite Animal Names in Dermatology. JAMA Dermatol. 2013;149:997.
Buxton PK. ABC of Dermatology. Introduction. Br Med J (Clin Res Ed). 1987;295:830–834.
Griffith RD, Falto-Aizpurua LA, Nouri K. Dermatologic Etymology: Primary morphology of skin lesions. JAMA Dermatol. 2015;151:69.
Grzybowski A, Parish LC. The Dermatologist and Color. Skinmed. 2018;16:376–378.
Leider M, Rosenblum M: A Dictionary of Dermatological Words, Terms and Phrases. New York, McGraw-Hill, 1968, 440 pp.
Milam EC, Mu EW, Orlow SJ. Culinary Metaphors in Dermatology: Eating Our Words. JAMA Dermatol. 2015;151:912.
Parish LC, Wallach D. Cutaneous Morphology: The basic tool of dermatology. Skinmed. 2003;2:76–77
Parish LC, Witkowski JA. Updating the Dermatologic Nomenclature: Names that are good or bad. Skinmed. 2010;8:199–200.
Parish LC, Lambert WC. Speaking Good (and Safe) Dermatologic English. Skinmed. 2019 29;17:90–91.
Sprecher E. What's in a Disease Name? Br J Dermatol. 2014;170:1005–1007

2 Diagnosing Skin Disease

Shayan Waseh and Jason B. Lee

CONTENTS

DIAGNOSING SKIN DISEASE

Skin diseases represent a vast and heterogeneous body of disorders that can vary greatly in their clinical presentations, manifesting signs, and associated symptoms. Adopting a systematic and methodic approach is essential to the effective and accurate diagnosis of skin disease. This systematic approach, when combined with the responsible utilization of appropriate diagnostic aids, can serve to secure the diagnosis in a wide variety of dermatologic conditions.

SIGNS AND SYMPTOMS

Signs

Many of the characteristics that define skin diseases are fundamentally visual in nature given the externality of the skin. The distribution, color, and morphology of skin lesions are all integral components of the description of dermatologic conditions and serve as a foundational component of the diagnostic process.

Color

The color of the skin is determined by the interaction of a variety of internal and exogenous factors, including the production of melanin pigment by resident melanocytes, the functional activity of skin vasculature, and many external forces, such as ultraviolet radiation and manipulation of the skin. Color changes related to these factors often manifest as hyperpigmentation, hypopigmentation, or erythema. Discoloration can be a source of significant distress for patients, especially when widespread or highly visible areas, such as the face, are involved. This is particularly true in dark-skinned patients, in whom the contrast between normal and affected skin may be dramatic, such as the depigmentation of vitiligo and hyperpigmentation of resolved lichen planus.

The pigmentation of the skin is primarily determined by the function of skin melanocytes in the production and distribution of melanin pigment. This process is responsible for the determination of skin type in normal skin, but it is also implicated in the pigmentary changes associated with many dermatologic conditions. Inflammation, ultraviolet radiation, and cryotherapy all can cause significant changes to skin color (Figure 2.1). Melanocytes are highly sensitive to cold temperatures, and cryotherapy may lead to post-treatment hypopigmentation, particularly in patients with darker skin. Inversely, exposure to ultraviolet radiation activates melanocytes to produce and

DOI: 10.1201/9781003105268-2

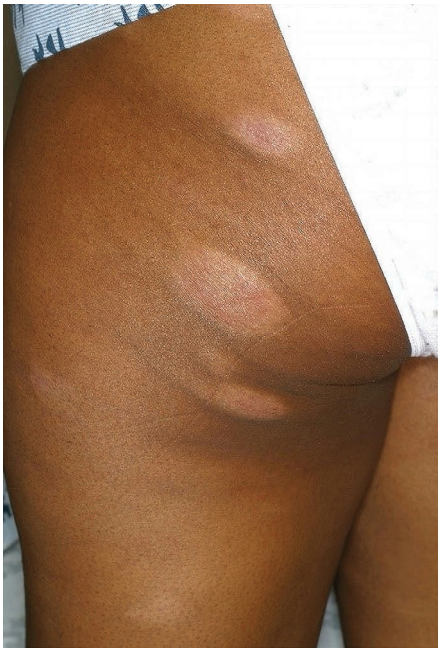


Figure 2.1 Hypopigmented and subtle erythematous plaques of sarcoidosis in a dark skin patient.

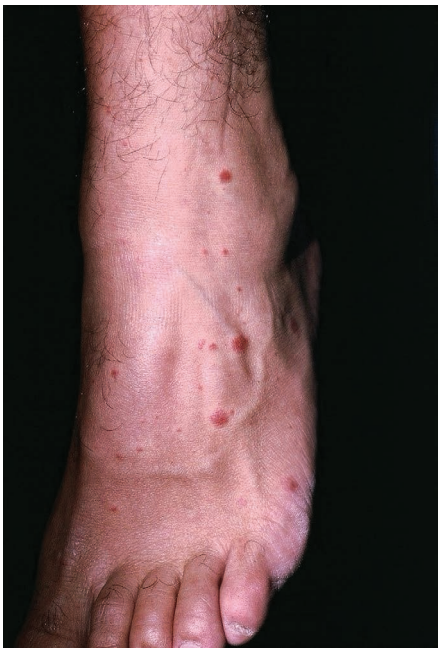


Figure 2.2 Non-scaly erythematous papules of early lesions of psoriasis.

distribute melanin granules more effectively, which can lead to skin tanning as part of an evolutionarily honed response.

A variety of other pigments can less commonly contribute to changes in skin color at a localized or generalized level. Systemic disorders in metabolic or endocrine function can cause generalized changes in skin pigmentation. For example, the buildup of homogentisic acid in connective tissue and cartilage in alkaptonuria leads to skin darkening, especially on the ears where cartilage is closely opposed to the skin. Prolonged systemic therapy, such as hydroxychloroquine, may result in widespread slate-gray discoloration.

Erythema is a visual manifestation of most inflammatory skin diseases, which is determined by the number, caliber, flow rate, oxygenation status, and body site of the skin's blood vessels. Other factors that determine the specific hue and shade include the density of the inflammatory infiltrate and epidermal changes. In turn, the specific characteristics of erythema, such as shade of color and border definition, can provide significant clinical insight into the disease process unfolding within the skin (Figure 2.2). A plaque of psoriasis, for example, has a characteristic, bright red hue that is well circumscribed (Figure 2.3), while a plaque of pityriasis rubra pilaris has a characteristic erythema with an orange hue that is less well-circumscribed. Additionally, the extravasation of red blood cells from the vasculature can lead to striking changes in skin color, referred to as purpura. This presence of palpable purpura is associated with a variety of vasculitides and vasculopathies. In darker skin individuals, erythema may be subtle, harder to detect than in fair skin individuals, and often have a duskier hue (Figures 2.4 and 2.5).

Texture

The texture of healthy skin should mostly be smooth and soft. When the normal function and life cycle of skin cells are disturbed, their texture can become profoundly altered. Coarseness, excessive scale, and dryness can each indicate a disruption of normal functioning and serve to indicate the presence of an underlying pathologic process.

The replacement rate of the cornified cells in the stratum corneum, the outermost layer of the epidermis, is approximately 2 weeks with some variation by body site and age. This turnover normally occurs incrementally through the shedding of individual cornified cells throughout the

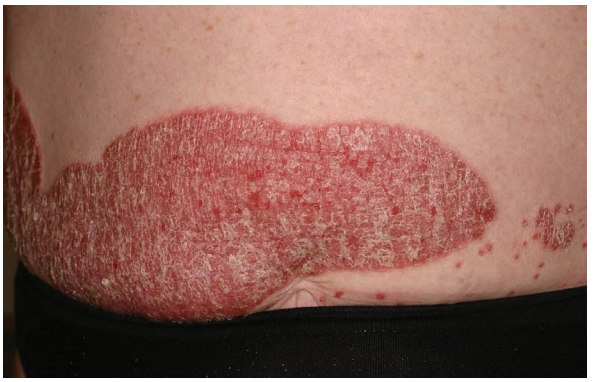


Figure 2.3 Scaly large erythematous plaque of psoriasis.

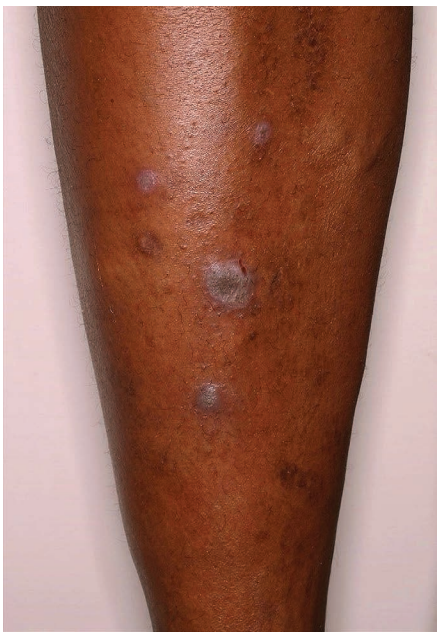


Figure 2.4 Flat-topped hyperpigmented papules with the violaceous border of lichen planus.

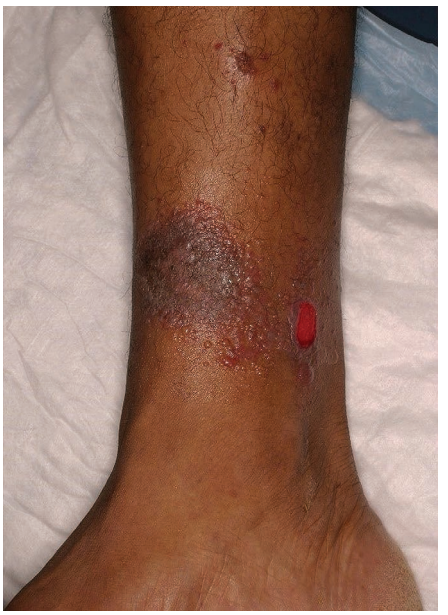


Figure 2.5 Hyperpigmented plaque surrounded by a cluster of vesicles due to allergic contact dermatitis from using an antibiotic ointment.

course of daily life. This process is largely imperceptible in healthy skin, but it can become apparent when the process of normal keratinization is disrupted. Should this occur, a significant scale can form on the surface of the skin, which results in visual and textural changes. This disruption of skin function can be the result of a variety of underlying conditions that can range from genetic abnormalities, such as ichthyosis, to inflammatory changes, such as psoriasis, to the exogenous influence of factors, such as medication application and repetitive friction.

Morphology: Primary and Secondary Skin Lesions

An appreciation of the essential attributes of color, size, shape, and thickness is vital to the process of describing and understanding skin lesions and, in turn, underlies the accurate diagnosis of dermatologic conditions. Traditionally, skin lesions have been divided into primary and secondary lesions, where a primary skin lesion represents the initial or primary appearance before any treatment, manipulation, or changes due to the natural history of the disease process. A secondary lesion represents the appearance after the evolution of the skin disease process, treatment, or manipulation of the primary lesion.

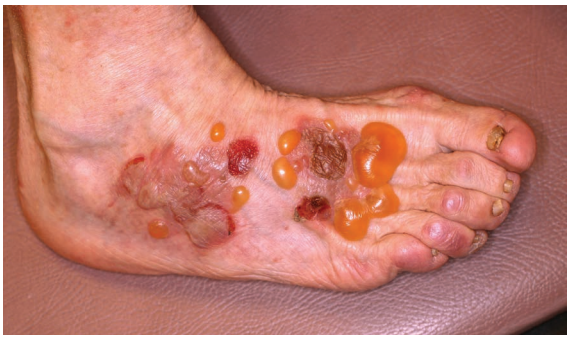


Figure 2.6 Tense vesicles and bullae of bullous pemphigoid.

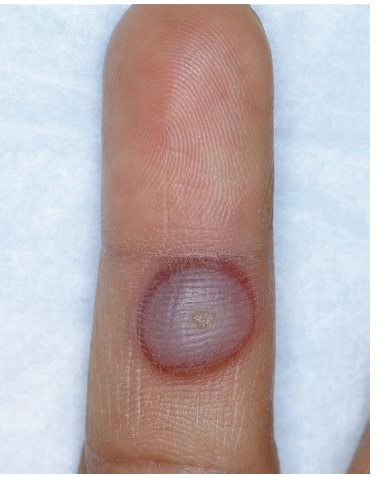


Figure 2.7 Tense hemorrhagic vesicle from cryotherapy of a wart.

Primary lesions have been categorized predominantly based on size and palpability. Although different size references have been applied, a 10-mm size threshold rather than 5 mm has been consistently applied. For example, macules, papules, and vesicles are 10 mm or less in diameter.

- *Macule/patch:* Flat, usually nonpalpable skin lesion
- *Papule/plaque:* Mesa or table-like elevated skin lesion
- *Vesicle/bulla:* Blisters that can be intraepidermal, subepidermal, or both

Some contour descriptors of a papule and plaque—flat-topped, dome-shaped, acuminate, papillated, digitated, and umbilicated—are strongly associated with specific skin conditions, such as the flat-topped papules of lichen planus (Figure 2.4), acuminate vesicles of dyshidrotic dermatitis, and the umbilicated papules of molluscum contagiosum. In addition, nodule (1–2 cm) and tumor (>2 cm) have been referred to as primary lesions that are larger and more elevated than plaques.

A variety of causes are associated with blistering dermatosis, including autoimmune, infectious, and inflammatory etiologies. Autoantibodies against desmogleins 1 and 3, which are components of desmosomes that keep keratinocytes attached to one another, resulting in acantholysis, or a loss in intercellular connections, and can lead to intraepidermal blisters. In contrast, autoantibodies against components of hemidesmosomes of the dermo-epidermal junction in bullous pemphigoid result in subepidermal blisters (Figure 2.6). Herpesvirus infection of the epidermis may result in acantholysis and varying degrees of epidermal necrosis, which can lead to intraepidermal or subepidermal blisters. Significant intercellular edema in allergic contact or nummular dermatitis results in intraepidermal blisters. Any process that weakens the dermo-epidermal junction may result in a subepidermal blister (Figure 2.7). Severe dermal edema from a variety of sources may also result in a subepidermal blister (e.g., lymphedema blister, bullous insect bite, and bullous Sweet syndrome). Depending on the severity and acuity, most interface dermatitides, which are associated with a variable degree of necrosis of keratinocytes at the dermo-epidermal junction, have a subepidermal bullous expression. Examples include bullous erythema multiforme, bullous lichen planus, and bullous fixed-drug eruption.

The location of these blisters within the epidermis determines their behavior and longevity. Intraepidermal blisters tend to be flaccid and evolve into erosions in a short amount of time, while subepidermal blisters tend to be tense and generally last longer before rupturing (Figure 2.6). Whether a blister is tense or flaccid, however, will ultimately depend on the size and speed at which it forms.

Secondary skin lesions include impetiginization, pigmentary changes, scale-crust that can be purulent and/or hemorrhagic, lichenification, fissures, erosion, ulceration, and scar formation. A patient with atopic dermatitis may manifest a variety of secondary skin lesions, all of which are due to manipulation of the skin, including rubbing, scratching, and picking by the patient due to persistent pruritus. The presence of secondary changes offers insight into the symptomatology

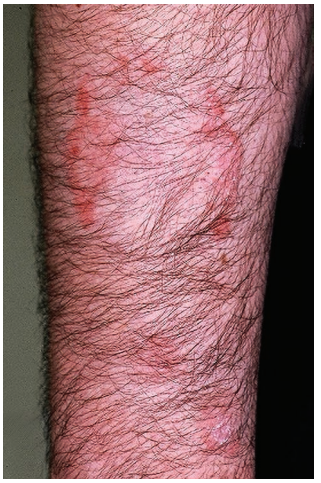


Figure 2.8 Scaly annular patch of tinea corporis.

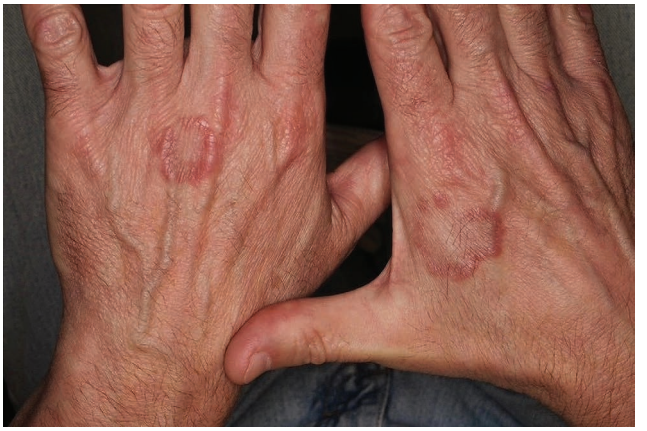


Figure 2.9 Annular non-scaly plaques of granuloma annulare.

of the patient's disease and provides useful information on the clinical course and characteristics of the condition. Inversely, they may also obscure the primary findings that would help identify the underlying skin disease; therefore, an awareness of the presence of secondary skin changes is important to adjusting clinical expectations during the assessment of primary lesions.

Dermatologic disorders can manifest in any variety of shapes, from the linear configuration associated with allergic contact dermatitis to polygonal papules with lichen planus (Figure 2.4) to scaly and non-scaly annular plaques associated with tinea corporis (Figure 2.8) and granuloma annulare (Figure 2.9). The demarcation of shape can be well-defined, such as psoriasis (Figure 2.3) and vitiligo, or it can be ill defined and blend into the surrounding normal skin, such as nummular dermatitis. Additionally, it is important to be aware that shape is not only limited to external skin changes but also includes depth of involvement, particularly in malignant skin conditions. This includes melanoma, where the depth of extension has profound prognostic implications, and basal cell carcinoma, where the insidious process of infiltration can cause significant distortion of surrounding tissue over time.

Distribution

The distribution of skin findings in dermatologic disorders is an important diagnostic tool. Diseases of the skin can present in a generalized manner or be localized to one or several specific body sites. Although the varicella-zoster virus causes the appearance of vesicles in both chickenpox disease and shingles, these two clinical entities vary considerably, as the former is characterized by a generalized eruption, and the latter is typically limited to the localized dermatome. Skin cancer is most commonly found on chronically sun-exposed sites, while necrobiosis lipoidica is almost always localized to the shin. Additional examples include erythema multiforme characteristically involving the palms and bilateral extremities (Figure 2.10), dermatitis herpetiformis involving bilateral elbows, knees, buttocks, and scalp, and warfarin-induced skin necrosis usually involving fatty areas, such as the abdomen and thigh. When encountering a hospitalized patient with a suspicion of drug reaction, the presence of mucosal involvement can be a clinically significant indicator of life-threatening diseases, such as Stevens-Johnson syndrome or toxic epidermal necrolysis requiring a higher acuity of care. In sum, careful assessment of the overall distribution of skin lesions should be performed routinely since it can provide important diagnostic information.

SYMPTOMS

Dermatologic conditions are often associated with a variety of subjective symptoms, including pruritus, pain, and discomfort. Awareness of the presence of these symptoms is an important component of clinical care, because these symptoms play a significant role in influencing the patient's quality of life and well-being.

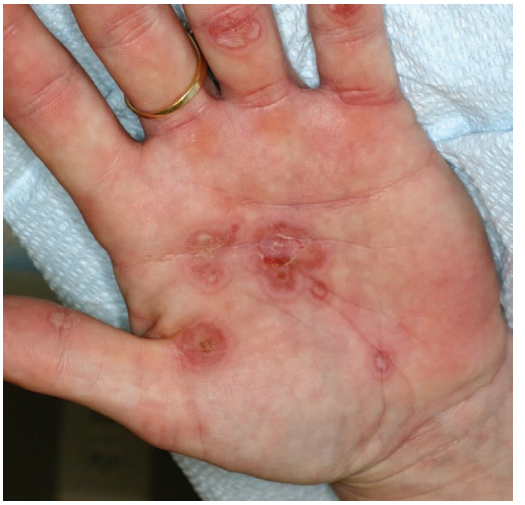


Figure 2.10 Targetoid macules and patches of erythema multiforme.

Pruritus

Pruritus, or itch, is a common symptom found in a wide variety of dermatologic disorders, including atopic dermatitis, urticaria, allergic contact dermatitis, nummular dermatitis, scabies, and dermatitis herpetiformis.

Pruritus is fundamentally characterized as an uncomfortable sensation linked to a desire to scratch. The degree of pruritus associated with these dermatologic conditions and other systemic disorders can vary from mild to debilitating. The presence of pruritus can be associated with significant skin changes, or it can be found in seemingly normal skin. Pruritus can be exacerbated by many different factors, including low humidity, frequent bathing, aging skin, and irritating substances. These factors can aggravate underlying skin disease, since they can incite pruritus, particularly in the diseases listed earlier.

Pruritus can also lead to the development of new skin lesions through the traumatic effect of scratching. For example, atopic dermatitis has been colloquially referred to as the "itch that rashes." Sites of repetitive scratching can also become infected, which can further exacerbate the disease. In some cases, new lesions of the underlying dermatologic disease can occur focally at the site of scratching, which is known as the Koebner phenomenon.

In addition to recognizing the impact that pruritus has on the quality of life and well-being of patients, a focused evaluation of the chronicity and behavior of pruritus symptoms can be a helpful diagnostic clue in the workup of dermatologic conditions. As an example, the pruritus in urticaria is typically transient and migratory, while it can be more chronic and exacerbated by drier seasons in atopic dermatitis.

Pain

The presence or absence of pain can be an important differentiating factor in the diagnosis of dermatologic disorders. Pyoderma gangrenosum and calciphylaxis are both classically characterized as being extremely painful. Additionally, the subjective symptom of pain is often associated with the presence of acute inflammation as seen in cellulitis, panniculitis, infected cysts, and even seborrheic keratoses when they become irritated. In the case of skin malignancies, the presence of pain may indicate perineural invasion.

Importantly, pain can be a significant detractor in the quality of life of patients with chronic dermatologic conditions. In severe atopic dermatitis and other diseases, fissuring of the skin can lead to significant pain and discomfort. In patients with irritant contact dermatitis from workplace exposure, pain can sometimes necessitate alterations in their workplace or work habits; therefore, pain represents a significant source of morbidity for patients with painful dermatologic diseases.

Disability

Dermatologic disorders can carry a profound degree of disability and morbidity into the lives of patients in a variety of ways. Many skin disorders are associated with significant cosmetic

concerns that can interfere with physical and mental well-being. There is a nearly universal human aversion to diseased skin, and it is challenging to prevent and overcome these feelings. One theory proposes that this aversion is rooted in the infectious nature of some dermatologic conditions and, therefore, serves as an evolutionarily protective mechanism. In the modern era, these prejudices are maladaptive and can interfere with interpersonal relationships and even employment. As examples, acne can be a significant stressor in the lives of adolescents and adults, and the nail and scalp changes seen in psoriasis can be embarrassing for patients who work in occupations requiring social contact. An appreciation of the impact that dermatologic disorders can have on the physical and mental well-being of patients is an integral component of providing patient-centered care.

The location of dermatologic disease can also be an important determinant of the degree of disability that it causes. Although the severity of most dermatologic conditions is correlated with the body surface area of involvement, even small and localized lesions on the palms and soles can be debilitating given their functional importance. For example, patients with dactylitis in psoriasis and psoriatic arthritis may be unable to work with their hands as effectively, if at all. Plantar warts and clavus can likewise cause discomfort during ambulation, which can limit mobility. Diseases, such as atopic dermatitis, can also cause fissuring around joints, which can result in discomfort with movement and subsequent immobilization.

Additionally, lesions affecting the face and other exposed areas of the skin can significantly impact self-esteem and self-confidence in patients who interact with others daily. The treatment of choice for various skin conditions may also vary based on the site of involvement. High-potency steroids are often prescribed for plaques on the body but seldom for the face and other areas of thin skin. Therefore, an appreciation of the distribution of lesions on a patient's skin is an important factor in understanding the patient's experience with their disease and in providing effective and appropriate clinical care.

Importantly, the impact of dermatologic conditions on health and well-being on a global and societal scale cannot be understated. Dermatologic conditions represent the fourth-leading cause of disability worldwide among nonfatal conditions. In the United States, one in four people are impacted by skin disease, and the estimated annual cost for medical care alone approaches $100 billion each year. The global health burden of some dermatologic disorders, such as psoriasis, has continued to rise over recent decades, which indicates a greater need for public and global health efforts to address dermatologic disease.

Common aids: The foundation of diagnosis in dermatologic disease is the clinical history and physical examination. An appreciation of the patient's demographic factors, history of present illness, and general medical status are all important components in understanding the patient's disease process. The presence or absence of associated systemic symptoms is an important data point that may indicate an urgent need for more acute and comprehensive care. Additionally, an informed and focused physical examination that accurately defines and describes the lesions of concern is a uniquely powerful diagnostic tool in the practice of dermatology; however, dermatologic diseases can manifest in a variety of ways, and even a single condition can have multiple different presentations that may overlap with other clinical entities. An armamentarium of diagnostic aids and tools has been developed to assist in the often-challenging endeavor of identifying skin lesions when history and physical examination alone are unable to definitively do so.

Lighting

The availability of bright and consistent environmental lighting is essential in evaluating skin disorders. Sunlight from examination room windows as a source of lighting should be avoided because it provides a highly variable lighting that depends on the time of day, weather conditions, and room orientation. Bright overhead ambient lighting provides more consistent and standardized illumination for skin examinations, while the additional implementation of sidelights can assist with minimizing light distortion and shadow.

More complicated light-based tools are also readily available in many clinical settings. The Wood's lamp is one such valuable tool that has found use in a variety of dermatologic conditions, such as vitiligo and bacterial and fungal infections. A Wood's lamp, which emits wavelengths in the 320–450-nm range, can assist in differentiating pigmentary changes, highlighting fungal and bacterial infections, such as tinea versicolor and erythrasma, and identifying systemic diseases, such as porphyria.

BEDSIDE DIAGNOSTIC TESTS

Diascopy

Diascopy is a useful technique that assesses the blanchability of a skin lesion through the application and pressing of a glass slide over the lesion. This simple test allows for the differentiation of erythema into vascular etiologies related to blood vessel dilation, which are blanchable, and hemorrhagic etiologies, which do not exhibit blanching. Diascopy can also be used in other clinical contexts, such as the identification of lupus vulgaris involving the skin, which exhibits an apple jelly color on testing.

Magnification

Although the naked eye can collect a significant amount of information regarding the morphology of a skin lesion, magnification tools can yield meaningful additional information. A simple magnifying glass can highlight features not readily seen on gross examination, such as small telangiectasias in a lesion suspicious for basal cell carcinoma.

Evaluation of skin scrapings prepped with potassium hydroxide under simple light microscopy is the classic diagnostic test utilized in the diagnosis of dermatophytosis. Using a blue stain, such as toluidine blue, microscopic evaluation of vesicle scrapings—referred to as the Tzanck smear—can be performed to diagnose herpesvirus infection. A mineral oil prep involves the examination of skin scrapings of burrow under light microscopy to identify the presence of scabies mites.

Skin Testing

The unique accessibility of the skin allows for the utilization of a variety of tests that can be readily carried out in the clinical setting. Manipulation of the skin by a clinician is one such test that can yield useful diagnostic information. In the case of Darier's sign, vigorous rubbing of the patient's skin can support the diagnosis of mastocytosis when it results in significant swelling, itch, and erythema. The presence of Auspitz's sign, which is the appearance of punctate bleeding after the scraping of scaly lesions, can be indicative of psoriasis. Additionally, the shearing of skin with rubbing, known as the Nikolsky sign, can be a clinically useful diagnostic finding in the evaluation of blistering skin disorders, such as pemphigus and toxic epidermal necrolysis.

More complex forms of skin testing are also available and can serve to either support or refute a variety of diagnoses. In the case of allergic contact dermatitis, the application of potential causative agents to the surface of the skin through a patch test can yield a hypersensitivity reaction that supports the suspicion of hypersensitivity to a certain substance. The clinical application of this test allows for it to be carried out in a more supervised and controlled setting with lower concentrations of the suspected allergen than otherwise possible.

A similar principle is applied in prick testing for anaphylactic reactions, which involves piercing the skin with a needle laden with a low concentration of the suspected allergen in a controlled and closely monitored setting with anaphylaxis treatment readily available. Additionally, the application of various biochemically active substances to the skin can help in identifying a variety of skin lesions; for example, acetic acid is commonly applied to suspected warts on genital areas and can result in significant whitening that serves to highlight the lesion of concern.

Dermatoscopy

With the advent of portable handheld dermatoscopes, the practice of dermatoscopy has become ubiquitous in dermatology. The technique involves rendering the cornified layer translucent either by using polarized light or immersion contact with the skin, thereby exposing subsurface structures that can be better visualized (Figure 2.11). The most widely utilized dermatoscope consists of polarized light capable of 10× magnification. Special attachments and adaptors for cameras and smartphones allow easy capture and sharing of dermatoscopic images.

Dermatoscopic diagnostic criteria have been developed for a variety of skin diseases, which include inflammatory, neoplastic, and infectious diseases. Its utility has been promoted for evaluating pigmented lesions, especially in the early detection of melanomas and their simulators, such as melanocytic nevi, seborrheic keratoses, dermatofibromas, and solar lentigines. In melanocytic lesions, assessment of subsurface structures, such as typical and atypical pigment networks, dots, and globules, allows for differentiating a nevus from a melanoma. Additionally, a variety of nonmalignant pigmented skin lesions exhibit characteristic appearances under dermatoscopy. A seborrheic keratosis, which can occasionally be difficult to distinguish from melanoma, often exhibits characteristic comedo-like openings on dermatoscopic evaluation. In vascular lesions, dermatoscopy allows for a greater definition of the specific vascular structures (e.g., lagoons) and

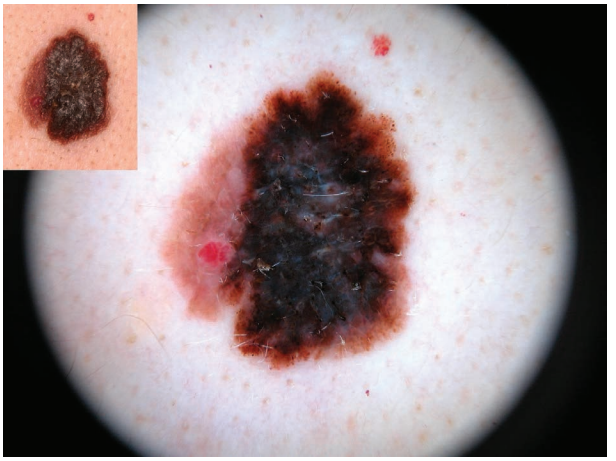


Figure 2.11 Dermatoscopy of melanoma showing multicomponent pattern: blue-gray veil, dark blotch, and asymmetric peripheral distribution of globules.

morphology present within the lesion. Since significant time and effort are needed to become proficient in dermatoscopy, early and strategic immersion in mastering this technique is recommended. Sources of learning material include books, internet sites, and courses.

Medicine is entering the era of artificial intelligence-augmented practice, and dermatology is expected to fully embrace this transformative technology. This is particularly true within the domain of skin cancer detection, where the application of artificial intelligence and machine learning has been increasingly developed. As dermatoscopes and other forms of visualization assist dermatologists in diagnosing skin conditions, advanced machine learning algorithms can process digital macroscopic or dermatoscopic images to identify patterns that differentiate lesions. The deployment of these technologies as diagnostic aids and supplementary tools has been shown to increase the diagnostic accuracy of dermatologists in the differentiation of skin cancers. The era of artificial intelligence–augmented practice is expected to provide more efficient and accessible care of skin diseases.

Laboratory studies: Although the externality of skin allows for the unique ability of clinicians to evaluate conditions through visual inspection and physical manipulation, there are a variety of contexts in which laboratory studies are indicated in the evaluation, diagnosis, and management of skin diseases. Laboratory studies can assist in the initial workup of dermatologic conditions, especially in cases where there is systemic involvement or potential involvement of internal organs. They may be helpful in the initial evaluation of symptoms, such as generalized pruritus when there are no readily apparent dermatologic causes. Laboratory studies are often indicated to monitor adverse reactions of high-risk systemic medications, such as isotretinoin and methotrexate, requiring baseline and serial laboratory studies to monitor the functional status of the liver, kidneys, and other organs.

A variety of laboratory tests are available for dermatologists to establish or confirm a specific diagnosis. In women with hirsutism, hormone levels can be obtained to confirm hyperandrogenism. Venereal disease research laboratory or rapid plasma reagin tests may be obtained in patients suspected of syphilis. Antinuclear antibody testing and tissue antibodies are often reported through titers and can support the diagnosis of diseases, such as systemic lupus erythematosus and a variety of vasculitides. The clinical interpretation of these tests can often be challenging when patients present in an atypical manner or results are borderline. Enzyme-linked immunosorbent assay tests are available to aid in the diagnosis of several autoimmune blistering diseases, such as pemphigus, pemphigoid, and dermatitis herpetiformis. In the case of pemphigus, the detection and level of anti-desmoglein antibodies can contribute to confirming a diagnosis and monitoring the disease course.

There are many examples of dermatologic diseases in which comorbid or associated diseases may need to be excluded via laboratory studies. A patient with alopecia areata may require a check of thyroid disease status, while a patient with oral lichen planus may require checking of viral hepatitis status. A diagnosis of Sweet syndrome requires the exclusion of some time-associated leukemias.

Dermatopathology: The function of dermatopathology—that is, the microscopic examination, description, and interpretation of skin biopsies—is essential to the practice of dermatology.

Through the use of microscopy in conjunction with a variety of histochemical and immunochemical stains, dermatopathology can offer significant insight into the underlying pathology for a wide variety of dermatologic conditions.

Biopsy of the skin is a necessary initial step in the process of dermatopathology evaluation. The selection of the biopsy site is an important decision that can have a profound impact on the utility and sensitivity of histologic evaluation. Depending on the suspected disease process, factors influencing the selection of an ideal biopsy site include lesion age, stage of development, and morphology.

Skin biopsy techniques include shave, punch, incision, and excision. In shave biopsies, a thin superficial portion of the skin is shaved off with a blade, whereas punch biopsies involve the use of a cylindrical cutting device that is rotated down to the level of the subcutaneous tissue before the base of the tissue is cut with scissors to release the specimen. Although a shave biopsy or removal is better suited for superficial epidermal skin lesions, such as superficial basal cell carcinomas, a punch biopsy allows for a more complete microscopic evaluation of the various layers of the skin, which is better suited for inflammatory dermatoses. Finally, an excisional biopsy typically involves the creation of an elliptical excision around the lesion of concern and can result in the greatest quantity of tissue removed for evaluation, which is particularly suited for suspected melanomas. A less optimal incisional biopsy may be warranted when lesions are too large for an excisional biopsy. The most appropriate method of biopsy is directly related to the clinical entity under investigation.

Since errors in the procurement of a skin biopsy specimen are not uncommon, steps to minimize the common errors should be implemented. This should include verification of patient name and site, especially when multiple sites are involved. An appropriate volume of fixative is matched for the size of the sample, for which the ratio of fixative to the specimen should be 15–20:1. The most common stain used in pathology and dermatopathology is the hematoxylin and eosin stain, also known as the H&E stain. This stain highlights the nuclei, cytoplasm, and extracellular matrix, which allows for visualization of individual cells forming the various components of the skin, including their nuclei.

Ancillary stains are often utilized when H&E-stained slides do not provide sufficient diagnostic information. In modern dermatopathology, the development of immunohistochemical stains has allowed for precise evaluation of specific epitopes within the skin. Immunohistochemical stains that target specific protein epitopes are available, which include those used to detect syphilis spirochetes and human herpesvirus 8 associated with Kaposi sarcoma.

For neoplasms that may be benign or malignant, a skin biopsy can often help provide a specific diagnosis, such as seborrheic keratosis, basal cell carcinoma, and melanoma. For inflammatory dermatoses, a biopsy can often demonstrate a histopathologic pattern that is associated with more than one disease, thus requiring clinical pathologic correlation. A spongiotic dermatitis, for example, is associated with nummular or allergic contact dermatitis, so the clinician should correlate this with the clinical findings to arrive at a specific diagnosis. A histologic description of the subepidermal blister with numerous neutrophils, which pattern observed in dermatitis herpetiformis, linear IgA dermatosis, and bullous lupus erythematosus, narrows the differential diagnosis and guides the clinician to pursue specific additional testing (Figure 2.12). In other instances,

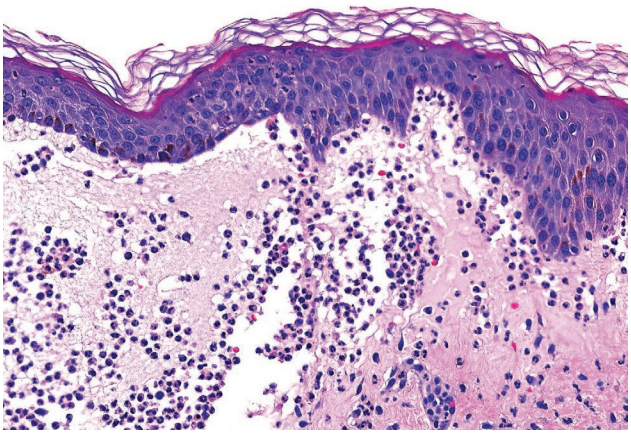


Figure 2.12 A subepidermal blister with neutrophils that may be seen in bullous lupus erythematosus, linear IgA dermatosis, and dermatitis herpetiformis.

a skin biopsy may show nonspecific changes. In these cases, depending on the clinical context, either additional biopsy or watchful waiting for more specific lesions to develop can be a reasonable course of action.

FINAL THOUGHT

As a visual specialty, physical examination in dermatology continues to play a critical role in diagnostic assessment. Accurate assessment of color, texture, morphology, and distribution is essential in the evaluation of dermatologic diseases. Becoming proficient in diagnosing skin diseases requires exposure to the wide spectrum of presentations of dermatologic disorders, especially those that are common, with follow-up and feedback—the necessary required steps toward expertise. An experienced dermatologist will rarely require additional diagnostic aids other than a physical examination. If further diagnostic confirmation is needed, a variety of diagnostic tests are available that include dermatoscopy, skin biopsy, and, shortly, artificial intelligence–augmented assessment of skin diseases.

ADDITIONAL READINGS

Elston DM, Stratman EJ, Miller SJ. Skin biopsy: biopsy issues in specific diseases. J Am Acad Dermatol. 2016;74:1–16.

Grzybowski A, Parish LC, Wollina U. The color of skin. Clin Dermatol. 2019;37:389–606.

Happle R, Kluger N. Koebner's sheep in Wolf's clothing: does the isotopic response exist as a distinct phenomenon? J Eur Acad Dermatol Venereol. 2018;32:542–543.

Jackson R. Morphological Diagnosis of Skin Disease: A Study of the Living Gross Pathology of the Skin. Grimsby, ON, Canada: Manticore; 1998.

Lee JB. Diagnostic and therapeutic instrumentation in dermatology. Clin Dermatol. 2021;39.

Micali G, Lacarrubba F. Alternative use of dermatoscopy. Dermatol Clin. 2018;36:345–502.

Tintle SJ, Cruse AR, Brodell RT, et al. Classic findings, mimickers, and distinguishing features in primary blistering skin disease. Arch Pathol Lab Med. 2020;144:136–147.

Trayes KP, Savage K, Studdiford JS. Annular lesions: diagnosis and treatment. Am Fam Physician. 2018;98:283–291.

Tüzün Y, Wolf R. Fold dermatoses. Clin Dermatol. 2015;33:411–508.

Wolf R, Parish LC, Parish JL. The rash: part I. Clin Dermatol. 2019;37:85–172. The rash: part II. Clin Dermatol. 2020;38:1–121.

Yang TB, Kim BS. Pruritus in allergy and immunology. J Allergy Clin Immunol. 2019;144:353–360.

3 Adnexal Diseases

Hasan Aksoy, Jordan V. Wang, and Ayşe Serap Karadağ

CONTENTS

ACNE

Definition: Acne vulgaris (acne) is a chronic, inflammatory disorder of the pilosebaceous unit, which affects about 85% of adolescents and young adults. The disease may result in permanent scars and often causes immense psychologic burdens, such as poor self-image, anxiety, and depression.

Overview: Four cardinal pathogenic factors of acne are follicular hyperkeratinization, sebum overproduction, bacterial colonization by *Cutibacterium acnes*, and inflammation.

Clinical presentation: Acne lesions arise on the sebaceous gland–rich areas of the face, chest, shoulders, and back. The primary lesions include open and closed comedones, papules, pustules, and abscesses or cysts. Plugging of the follicles with sebum and keratin can form skin-colored lesions that can oxidize to create blackheads.

Inflammation associated with the rupture of follicles can cause papules and pustules to form (Figure 3.1). Nodules (abscesses) are larger, deep-seated, and tender lesions that can be seen as the inflammation progresses. In severe cases, there may be deep, fluctuant, cystic lesions, which contain liquefied material (e.g., pus, blood), called pseudocysts. Lesions may subsequently evolve into transient erythema, post-inflammatory hyperpigmentation, and persistent scarring. Acne scars can be atrophic (e.g., icepick, rolling, boxcar), hypertrophic, and keloidal.

ACNE CONGLOBATA AND ACNE FULMINANS

Acne conglobata is a severe form of acne presenting with numerous inflamed papules, grouped comedones, painful nodules, cysts, sinus tracts, and severe scars, which predominantly involve the face and trunk. Acne conglobata is a component of the follicular occlusion tetrad, which is also composed of hidradenitis suppurativa, dissecting cellulitis of the scalp, and pilonidal sinus.

DOI: 10.1201/9781003105268-3

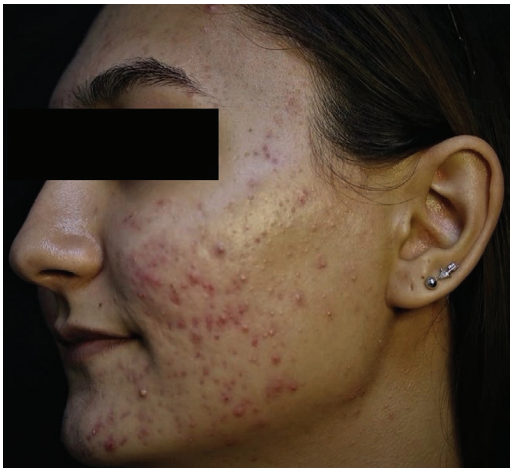


Figure 3.1 Multiple closed comedones, papules, and pustules on the cheek, chin, and forehead.

Source: Courtesy of Istanbul Medeniyet University Dermatology Clinic.

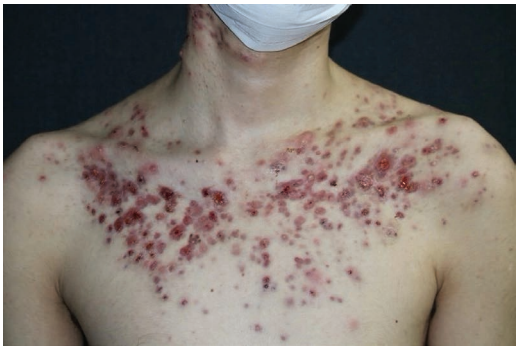


Figure 3.2 Acne fulminans; ulcerating, hemorrhagic, and crusted papules and nodules with scars on the chest and neck.

Source: Courtesy of Istanbul Medeniyet University Dermatology Clinic.

Acne fulminans is a rare and severe variant of acne, which presents with painful, ulcerating, hemorrhagic, crusted, necrotizing, and destructive papules, pustules, and nodules that eventually heal with scarring (Figure 3.2). This variant primarily affects male adolescents. Unlike acne conglobata, it is typically accompanied by systemic symptoms, such as fever, arthralgia, myalgia, and weakness, and systemic findings, including leukocytosis, anemia, and osteolytic bone lesions of the sternum and clavicles.

DRUG-INDUCED ACNE

Drug-induced acne is an acneiform eruption caused by medications, dietary supplements, herbal products, and systemic steroids (Table 3.1). It often has a good prognosis, which may not require cessation of the culprit drug. Development of lesions due to epidermal growth factor inhibitors (e.g., cetuximab, erlotinib, lapatinib) is often an indicator for successful treatment response.

Laboratory studies: Patients with post-adolescent acne or accompanying clinical signs of hyperandrogenism can be screened for potential alteration in serum levels of dehydroepiandesterone

Table 3.1 Common Culprits of Drug-Induced Acne

Topical, oral, systemic steroids
Hormones containing progesterone
Antiepileptic drugs (e.g., carbamazepine, phenytoin, phenobarbital)
Isoniazid
Lithium
Cyclosporine
Azathioprine
Halogens (iodides and bromides)
Disulfiram
Propylthiouracil
Quinidine
B vitamins (B6 and B12)
Tumor necrosis factor (TNF)-inhibitors
Epidermal growth factor receptor (EGFR) inhibitors

Table 3.2 Common Treatment Regimens for Acne Vulgaris

	Comedonal acne	Mild Papulopustular Acne	Moderate Papulopustular Acne	Severe Papulopustular Acne	Severe Nodulocystic Acne
First step	• Topical retinoid • Benzoyl peroxide	• Topical antibiotic and topical retinoid and/or benzoyl peroxide	• Topical antibiotic and topical retinoid and/or benzoyl peroxide • Oral antibiotic and topical retinoid and/or benzoyl peroxide	• Oral antibiotic and benzoyl peroxide and/or topical retinoid	• Oral isotretinoin • Oral antibiotic and topical retinoid and/or benzoyl peroxide
Second step	• Alternative topical retinoid • Azelaic acid • Salicylic acid	• Alternative topical combination therapy • Azelaic acid • Salicylic acid • Topical dapsone	• Alternative topical combination therapy • Consider a change in oral antibiotic	• Oral isotretinoin	

sulfate (DHEA-S) total and free testosterone, luteinizing hormone/follicle-stimulating hormone (LH/FSH) ratio, prolactin, and 17-OH progesterone. Acne fulminans may requires testing for inflammatory markers and blood counts. Histopathologic examination is rarely required.

Differential diagnosis: Acne is typically diagnosed clinically with relative ease; however, acneiform eruptions may sometimes be confused with acne.

Management: This is based on the severity of the disease and type of lesions (Table 3.2).

TOPICAL TREATMENT

Topical Retinoids

Topical retinoids regulate follicular keratinization, which can reduce microcomedo formation and offer comedolytic activity. They are also anti-inflammatory and can reduce pigmentation and scar formation. Topical retinoids include tretinoin, isotretinoin, tazarotene, adapalene, and trifarotene.

Benzoyl Peroxide

Benzoyl peroxide is not an antimicrobial, but it has bactericidal effects and can reduce the bacteria within follicles. It can help prevent antibiotic resistance from topical and systemic antibiotic therapy.

Other Topical Agents

Topical antibiotics include clindamycin and erythromycin, which can reduce the bacterial load; however, the resistance of up to 80% of *C. acnes* strains to erythromycin has been reported. These should be used in combination with other topical agents to prevent resistance. Azelaic acid can also inhibit bacterial overgrowth, regulate hyperkeratinization, and lighten post-inflammatory hyperpigmentation. Dapsone is another topical that works through anti-inflammatory and antibacterial effects, which can help with inflammatory lesions.

SYSTEMIC TREATMENT

Oral Antimicrobials

Systemic antibiotics are indicated in severe scarring acne or when topical treatment is difficult to apply. Tetracyclines (e.g., doxycycline, minocycline) are preferred due to their antibacterial and anti-inflammatory effects and lower antibiotic resistance. Doxycycline is often the first choice, with traditional dosing ranging from 100–200 mg/day. Recent evidence suggests that sub-antimicrobial

dose may also be sufficient. The most important side effects are photosensitivity and gastrointestinal upset.

Oral Isotretinoin

Isotretinoin is mainly used for the treatment of recalcitrant, severe papulopustular, and nodular acne. Isotretinoin is regarded as the most effective acne treatment; however, recurrence may develop in one-fourth of cases. Recent evidence has suggested higher cumulative doses than the traditional 120–150 mg/kg in more severe cases. Isotretinoin has many mucocutaneous side effects, including cheilitis and xerosis. Serum levels of cholesterol, triglycerides, and transaminases can elevate. The most important side is teratogenicity; therefore, effective contraception and frequent pregnancy testing are important in women of childbearing potential.

Hormonal Therapies

Hormonal therapies (i.e., antiandrogens) can be helpful in women with acne, regardless of whether hyperandrogenism is present. The most commonly used agents are combined oral contraceptive pills and spironolactone. Spironolactone can cause irregular menses, breast tenderness, headaches, nausea, and hypotension. Hyperkalemia is rare, and monitoring serum potassium is not indicated in low-risk individuals.

MAINTENANCE TREATMENT

In some patients, cure can be achieved with isotretinoin. Despite appropriate treatment, acne is a chronic and recurrent disease, and therefore, maintenance treatment is often required. The most suitable agents are topical retinoids and benzoyl peroxide.

Course: Acne vulgaris is a chronic disease that commonly manifests in adolescence. The disease has a relapsing-remitting course and may persist into adulthood. Although it has a good prognosis and usually is not associated with systemic involvement, severe acne variants should be considered in the presence of accompanying systemic symptoms or signs.

Final comment: This is a chronic disease that can manifest with visible lesions, dyspigmentation, or scarring; therefore, it has a psychosocial impact and should be treated appropriately. Although its use is limited by teratogenicity, oral isotretinoin is the most effective therapeutic agent.

FOLLICULITIS

Definition: This is inflammation of the hair follicle, which presents with erythematous papules or pustules in hair-bearing areas. It has superficial and deep forms, and it is typically caused by infectious agents, irritants, or medications.

Overview: Based on etiology, common forms of folliculitis include superficial bacterial folliculitis, gram-negative folliculitis, fungal folliculitis, viral folliculitis, and *Demodex* folliculitis.

Clinical Presentation

Bacterial Folliculitis

Overview: Clusters of pustules surrounded by an erythematous rim can manifest on the head (scalp and beard area), neck, trunk, groin, and extremities (Figure 3.3). Lesions usually heal in

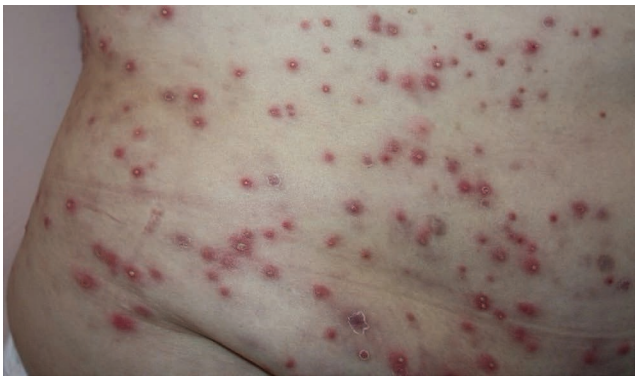


Figure 3.3 Bacterial folliculitis with numerous pustules with an erythematous rim on the trunk.

Source: Courtesy of Istanbul Medeniyet University Dermatology Clinic.

7–10 days but may also transform into furuncles. Nasal carriage of the most common pathogen, *Staphylococcus aureus*, is an important predisposing factor.

Management: Treatment with tetracyclines, especially for acne, may cause gram-negative folliculitis, which can be due to *Klebsiella*, *Enterobacter*, *Escherichia*, and *Proteus* species. It usually involves the face and is confused with acne. Hot-tub folliculitis is caused by *Pseudomonas aeruginosa* and primarily involves the trunk. This develops due to exposure to contaminated water.

Fungal Folliculitis

Overview: Dermatophytic folliculitis typically presents with follicular pustules on the surface of a red, firm, exudative, and extending plaque. It can develop in association with tinea barbae, tinea capitis, or tinea corporis. Lesions of folliculitis in tinea barbae involve the beard or mustache area. Trichophytic (Majocchi) granuloma classically occurs in women shaving their legs or when tinea corporis is first treated with topical corticosteroids. *Malassezia* (Pityrosporum) folliculitis commonly affects young males and presents with follicular papules and pustules involving the trunk, shoulders, neck, or extensor aspects of the arms. Candidal folliculitis appears as satellite pustules around the flexural lesions of candidiasis, especially in diabetics.

Demodex *Folliculitis*

Overview: *Demodex* normally lives in the pilosebaceous unit, but overgrowth can be associated with folliculitis. *D. folliculorum* and *D. brevis* can cause rosacea-like eruption, perioral dermatitis, or pityriasis folliculorum, especially on the zygomatic, periorbital, and nasal regions.

Laboratory studies: Histologically, superficial bacterial folliculitis demonstrates neutrophilic infiltration enclosing the follicular infundibulum and subcorneal/infundibular abscess formation. In KOH examination, hyphae and spores can be seen. *Demodex* mites can be demonstrated by direct microscopy of both superficial skin biopsy and KOH preparation.

Differential diagnosis: The differential diagnosis of folliculitis is listed in Table 3.3. The conditions mentioned in this chapter can easily mimic each other.

Management

Bacterial Folliculitis

Topical antibiotics, such as mupirocin, are used as first-line treatment. Oral antibiotics, such as dicloxacillin or cephalexin, are often required for furuncles or carbuncles. Nasal/skin decontamination can be achieved with a 5-day course of intranasal mupirocin application (twice daily) and chlorhexidine gluconate bathing. In gram-negative folliculitis, culprit antibiotics should be stopped, and oral isotretinoin has been shown to offer help.

Table 3.3 Differential Diagnosis of Folliculitis

- Bacterial folliculitis
- Gram-negative folliculitis
- Dermatophytic folliculitis
- *Malassezia* folliculitis
- Candidal folliculitis
- Herpetic folliculitis
- *Demodex* folliculitis
- Irritant folliculitis
- Ofuji disease
- Immunosuppression-associated eosinophilic folliculitis
- Eosinophilic pustular folliculitis of infancy
- Acne vulgaris
- Papulopustular rosacea
- Perioral dermatitis
- Drug-induced folliculitis
- Hidradenitis suppurativa
- Scabies
- Disseminate and recurrent infundibulofolliculitis
- Pseudofolliculitis barbae
- Acne keloidalis
- Folliculitis decalvans
- Keratosis pilaris
- Fox-Fordyce disease
- Idiopathic follicular mucinosis
- Perforating folliculitis

Fungal Folliculitis

Dermatophytic folliculitis is treated with oral antifungals such as terbinafine, griseofulvin, or itraconazole. Antifungal shampoo (e.g., ketoconazole) can be used to prevent the spread of spores. *Malassezia* folliculitis usually responds well to topical azoles or shampoos with selenium sulfide. In patients with candidal folliculitis, the use of steroids or antibiotics should be discontinued. Topical azoles and/or oral fluconazole can be used.

Demodex *Folliculitis*

Therapeutic options for *Demodex* folliculitis include topical permethrin 5% cream, topical ivermectin 1% cream, and oral ivermectin. Permethrin cream can be considered as initial treatment, and in recalcitrant cases, oral agents can be added.

Course: Most forms of folliculitis are curable conditions with a good prognosis. Recurrence of infective folliculitis can be prevented by proper hygienic measures and skin decontamination.

Final comment: Folliculitis refers to a heterogeneous group of conditions that may occur due to infection or irritation or as a manifestation of inflammatory skin disease. Different types of folliculitis should be properly diagnosed to clarify preventive and therapeutic recommendations.

ROSACEA

Definition: This is a chronic, inflammatory skin disease that typically affects the central face. It is characterized by persistent erythema, papules, pustules, telangiectasias, and recurrent flushing.

Overview: Rosacea commonly affects middle-aged women who are Fitzpatrick skin types I–III. Proposed pathophysiologic mechanisms include activation of the cutaneous innate immune system, neurovascular dysregulation, and increase in density of *Demodex* mites. Ultraviolet radiation is a contributing factor.

Clinical presentation: Rosacea has four clinical subtypes: erythematotelangiectatic, papulopustular, phymatous, and ocular (Table 3.4). Rosacea often presents earlier on as the erythematotelangiectatic subtype, which is characterized by persistent erythema, recurrent flushing, and telangiectasias on mid-face (Figure 3.4). Flushing can be triggered by physical, nutritional, or psychologic factors.

In the papulopustular subtype, patients have several small, dome-shaped erythematous papules and pustules on the mid-face. Unlike acne, rosacea is not typified by comedones (Figure 3.5).

Overview: In the phymatous form, sebaceous gland hypertrophy and fibrosis are present (Figure 3.6). Phyma primarily occurs in men and commonly affects the nose (rhinophyma) but may also be seen on the chin, ears, forehead, and eyelids.

Ocular involvement is present in 50–60% of patients who have rosacea, which can manifest with nonspecific symptoms, such as dryness, tearing, gritty sensation, styes, blepharitis, and itching.

Table 3.4 Summary of Clinical Subtypes of Rosacea

Clinical Subtype	Characteristics
Erythematotelangiectatic rosacea	• Recurrent flushing and fixed centrofacial erythema • Midfacial edema and/or telangiectasia • Skin sensitivity
Papulopustular rosacea	• Fixed centrofacial erythema, intermittent red papules, and pustules • No comedones • Persistent midfacial edema caused by intermittent inflammation
Phymatous rosacea	• Sebaceous gland hypertrophy and fibrosis • Flesh-colored, soft, irregular nodules • Nose: Rhinophyma; Chin: Gnathophyma; Ear: Otophyma; Forehead: Metophyma; Eyelid: Blepharophyma
Ocular rosacea	• Strongly suggestive: Lid margin telangiectasia, interpalpebral conjunctival injection, spade-shaped infiltrates in the cornea, scleritis, and sclerokeratitis • Nonspecific: Burning, stinging, light sensitivity, and foreign object sensation

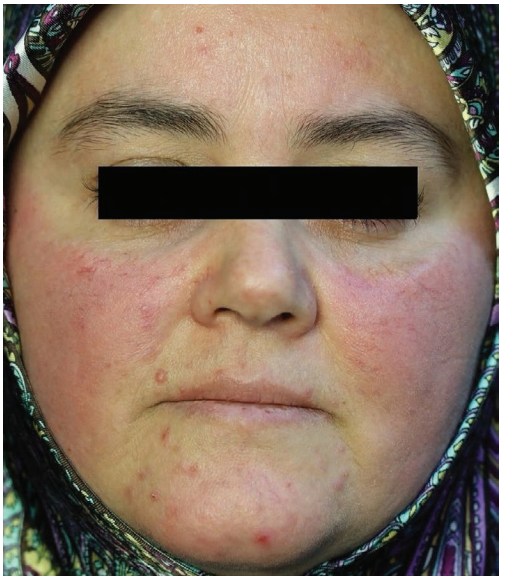


Figure 3.4 Erythematotelangiectatic rosacea. Erythema and telangiectasias are seen on the cheeks with a few papules in the perioral region.

Source: Courtesy of Istanbul Medeniyet University Dermatology Clinic.

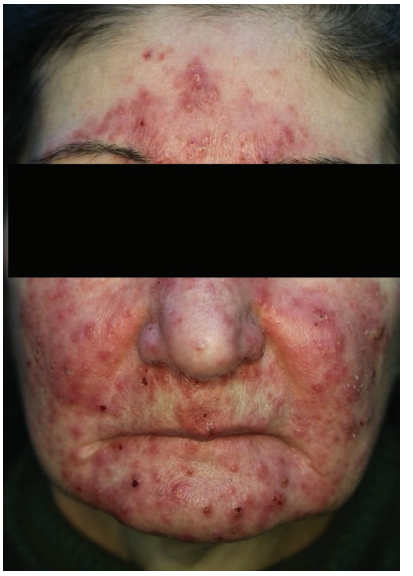


Figure 3.5 Severe papulopustular rosacea. Numerous papules and pustules with crust on an erythematous base can be seen on the forehead, nose, cheeks, and chin.

Source: Courtesy of Istanbul Medeniyet University Dermatology Clinic.

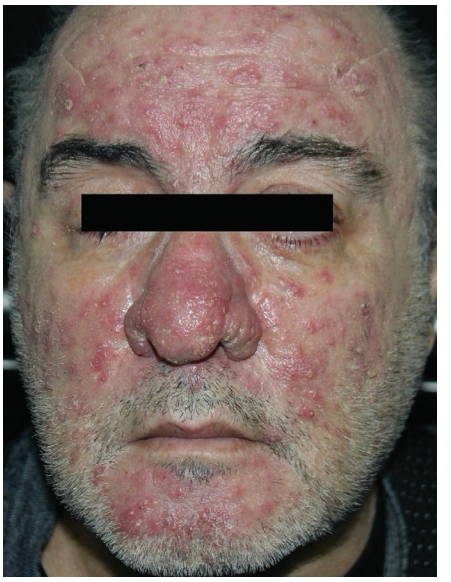


Figure 3.6 Papulopustular and rhinophymatous rosacea.

Source: Courtesy of Istanbul Medeniyet University Dermatology Clinic.

There is no correlation between the presence of ocular involvement and the severity of skin disease. Ocular rosacea is historically underdiagnosed.

Rosacea fulminans (i.e., pyoderma faciale, rosacea conglobata) is a severe form that is more common in young women. In addition to diffuse facial erythema, there is sudden onset, and coalescing papules, pustules, purulent nodules, and sinuses are often seen. Short-term use of systemic corticosteroids can be helpful.

Granulomatous rosacea is a clinical variant that presents with monomorphous, 1–3-mm-sized yellow-brown or red papules or nodules on the cheeks or periorificial areas. There is an

Table 3.5 Differential Diagnosis of Rosacea

Erythematotelangiectatic rosacea	Actinic damage
	Photoaging with telangiectasias
	Seborrheic dermatitis
	Contact dermatitis
	Keratosis pilaris rubra
	Malar rash
	Flushing
Papulopustular rosacea	Acne
	Demodex folliculitis
	Acneiform eruption
Phymatous rosacea	Lupus pernio
	Discoid lupus erythematosus
	Lupus vulgaris
Ocular rosacea	Seborrheic dermatitis
	Drug-induced ocular rosacea

Table 3.6 General Skin Care Measures in the Management of Rosacea

Avoidance of triggers, such as environmental factors (e.g., cold, heat, humidity), exercise, stress, diet, spices, histamine-rich food, alcohol, hot food
Use of broad-spectrum sunscreen with ultraviolet-A, ultraviolet-B, and visible-light protection
Cleansing using lukewarm water and soap-free cleansers
Moisturizing using non-oily moisturizers
Avoidance of topical corticosteroids
Avoidance of cosmetic products, such as waterproof make-up, skin toners, astringents, and abrasive exfoliators
Avoidance of cosmetic ingredients, such as sodium lauryl sulfate, strong fragrances, fruit acids, glycolic acids, alcohol, menthols, camphor, witch hazel, peppermint, and eucalyptus oil

"apple-jelly" appearance on diascopy as in sarcoidosis or lupus vulgaris, and dermal noncaseating granulomas are present histologically. This variant may cause permanent scarring.

Laboratory studies: Skin biopsy is rarely required for diagnosis and can be nonspecific.

Differential diagnosis: This can be organized according to subtype (Table 3.5). Papulopustular rosacea may resemble acne, but there are typically no comedones or scarring in rosacea. Some clinical features of acne, such as truncal distribution, hyperseborrhea, and adolescent-onset are not observed in rosacea. Actinic damage can be confused with erythematotelangiectatic rosacea; however, actinic damage commonly affects the periphery of the face and neck, upper chest, and postauricular region.

Management: Management of rosacea involves general skincare practices listed in Table 3.6 and pharmacologic intervention.

In patients with erythematotelangiectatic rosacea, topical α-adrenergic agonists, such as brimonidine (α_2) or oxymetazoline ($\alpha_{1A}+\alpha_2$), can help improve erythema by causing peripheral vasoconstriction. Carvedilol is a nonselective beta-blocker and is effective in the treatment of flushing and persistent erythema. Vascular lasers (e.g., pulsed dye laser) and intense pulsed light (IPL) can also be used to treat telangiectasias and erythema.

Papulopustular rosacea should be treated with topical agents, systemic antibiotics, or oral isotretinoin. First-line topicals include metronidazole, ivermectin, and azelaic acid. Topical metronidazole is often initially preferred. Ivermectin cream demonstrates slightly higher efficacy than metronidazole in terms of reduction in inflammatory lesions. Other topical options are listed in Table 3.7.

In patients with moderate to severe inflammatory lesions, systemic antibiotics, such as doxycycline, tetracycline, or azithromycin can be used. Low-dose (0.3 mg/kg/day) oral isotretinoin is recommended for patients with moderate to severe recalcitrant papulopustular rosacea. Systemic treatments are outlined in Table 3.8.

Table 3.7 Topical Agents Used in the Treatment of Rosacea

Drug	Mechanism	Subtype
Metronidazole	Anti-inflammatory Antioxidant Antibacterial Antiparasitic	Papulopustular Erythematotelangiectatic
Azelaic acid	Anti-inflammatory Antioxidant Antibacterial Anti-keratinizing	Papulopustular Erythematotelangiectatic
Ivermectin	Anti-inflammatory Antioxidant Antiparasitic	Papulopustular Erythematotelangiectatic *Demodex* mite
Brimonidine	α-2 adrenergic receptor agonist Vasoconstriction	Persistent erythema
Oxymetazoline	α-1 adrenergic receptor agonist Vasoconstriction	Persistent erythema
Sodium sulfacetamide + sulfur	Antibacterial Anti-inflammatory	Papulopustular
Permethrin	Antiparasitic	*Demodex* mite
Pimecrolimus	Inhibits T-cell activation	Granulomatous rosacea
Tacrolimus	and proinflammatory cytokines	Steroid-induced rosacea
Tretinoin	Anti-inflammatory Anti-keratinizing Inhibits TLR2	Erythematotelangiectatic Papulopustular

Table 3.8 Systemic Medications Used in the Treatment of Rosacea

Drug	Mechanism	Subtype
Doxycycline	Reduction of MMPs	Papulopustular
Tetracycline	Preventing kallikrein-5	Granulomatous
	Reduction of ROS and NO	Ocular
	Vasoconstriction	Phymatous
	Anti-inflammatory	
Ivermectin	Reduction of MMPs	Papulopustular
	Preventing kallikrein-5	Granulomatous
	Reduction of ROS and NO	Ocular
	Anti-inflammatory	Phymatous
	Antiparasitic	
Isotretinoin	Anti-inflammatory	Papulopustular
	Antioxidant	Granulomatous
	Anti-keratinizing	Ocular
	Reduction of sebaceous gland volume	Phymatous
Carvedilol	α1, β1, β2 antagonist	Erythematotelangiectatic
	Vasoconstriction	
	Antioxidant	
	Anti-inflammatory	
Metronidazole	Anti-inflammatory	Papulopustular
	Antioxidant	Granulomatous
	Antibacterial	Ocular
	Antiparasitic	

Abbreviations: MMPs, matrix metalloproteinases; ROS, reactive oxygen species, NO: nitric oxide.

Phyma may respond to low-dose isotretinoin if it is inflamed. In rhinophyma, isotretinoin may reduce the nasal volume and prevent progression. Severe and fibrotic forms can only be treated with physical modalities, such as surgical excision, electrosurgery, ablative lasers, and dermabrasion.

For ocular rosacea, lavage of eyelids twice daily with warm water and baby shampoo, use of eye drops, and referral to an ophthalmologist are recommended. Oral antibiotics, such as doxycycline, are helpful in most cases.

Course: It is a benign skin disease with a good prognosis that has no systemic complications. Since its chronic and recurrent nature, treatment is often required for both exacerbations and maintenance.

Final comment: This is an inflammatory syndrome affecting the midface with or without eye involvement. Management of rosacea aims to prevent symptoms, improve cosmesis, and maintain remission and involves patient education, appropriate skincare, avoidance of sunlight, and topical/oral anti-inflammatory medications, as well as interventions.

PERIORIFICIAL DERMATITIS

Overview: It is characterized by multiple papules and pustules localized around the mouth, nose, or eyes. It is commonly seen in young women and children. It is often associated with topical, nasal, or inhaled steroids, fluorinated toothpaste, mouthwashes, soaps, and cosmetics. It can be more common in atopic individuals. The exact cause is not understood.

Clinical presentation: There are many tiny pustules and pink papules, or thin plaques with desquamation in perioral, perinasal, and/or periocular areas (Figure 3.7). Lesions can spread around the lip, but there is typically an unaffected zone of 5 mm from the vermilion line.

Management: Periorificial dermatitis is usually treated with topical medications, which can include metronidazole, erythromycin, clindamycin, tacrolimus, and pimecrolimus. Systemic tetracyclines (e.g., doxycycline, minocycline) can be used for initial improvement. Any topical steroid use should be stopped.

HIDRADENITIS SUPPURATIVA

Synonym: Acne inversa

Definition: Hidradenitis suppurativa (HS) is a chronic, inflammatory disorder characterized by deep-seated and tender nodules, cysts, sinus tracts, and scarring in intertriginous areas. It is often misdiagnosed as folliculitis, furuncles, or carbuncles in the early stages. The disease shows female predominance and commonly arises in the second or third decade.

Overview: Aggravation of the disease is strongly associated with two major risk factors: smoking and obesity. Hyperkeratosis, occlusion, and destruction of the follicle and inflammation of the apocrine glands are implicated in the pathogenesis.

Clinical presentation: HS lesions are primarily located in the apocrine gland–bearing areas, such as axillae and inguinal folds. Further localizations include anogenital, gluteal, sternal, mammary, submammary, and retroauricular regions. Inflamed and noninflamed nodules can progress into the characteristic multiheaded comedones or coalesce to form sinus tracts with scarring

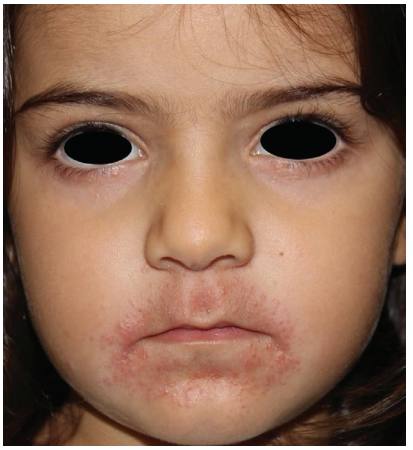


Figure 3.7 Multiple tiny papules and pustules in perioral and periocular regions.

Source: Courtesy of Istanbul Medeniyet University Dermatology Clinic.

(Figure 3.8). Deep-seated nodules can extend to develop abscesses in which suppuration drains to the skin surface (Figure 3.9). The discharged fluid consists of serous exudate, blood, and pus. As the disease progresses, bridged scars, fibrosis, contracture, and hardening of the skin may develop. Secondary infections can cause malodor.

Patients often report stinging, burning, itching, and warmth a few days before active lesions appear. Inflamed nodules, cysts, and sinuses are usually painful. Disease severity can be assessed with grading systems, such as the Hurley staging system.

HS is a component of the follicular occlusion tetrad in addition to acne conglobata, dissecting cellulitis, and pilonidal cyst. The disease is associated with several systemic conditions, such as Crohn's disease, pyoderma gangrenosum, diabetes mellitus, metabolic syndrome, polycystic ovary syndrome, and arthritis.

Laboratory studies: Diagnosis of HS is made clinically. Histopathology demonstrates a mixed inflammatory cell infiltrate in the deeper dermis, poral occlusion, inflammation, and fibrosis of the follicles and sweat glands. Later stages can show abscesses draining to the skin surface through a channel, tract formation containing inflammatory cells and keratin, and granulation tissue. As the disease progresses, fibrosis becomes more prominent.

Differential diagnosis: In the early stages, HS may be confused with furunculosis; however, nodules of furuncles have a central punctum and are not interconnected to form tracts. Acne, pilonidal disease, and dermoid/epidermoid cysts are also included in the differential of early lesions. Cutaneous Crohn's disease can present with perianal/genital fistulae, abscesses, and scars similar to HS, but there are no comedones, and the fistulae are linked to the gastrointestinal tract.

In advanced stages, the nodular, draining, ulcerating, indurated, and scarring lesions of HS may resemble infectious/granulomatous skin diseases, such as cutaneous tuberculosis, syphilis, granuloma inguinale, lymphogranuloma venerium, tularemia, actinomycosis, nocardiosis, and cat-scratch disease.

Management: This includes lifestyle modifications, treatment with topical or systemic pharmacologic agents, and surgical or laser interventions. The severity of the disease determines the therapeutic approach.

General measures include weight reduction, smoking cessation, reducing friction by wearing loose clothing, and skin decontamination using antiseptic scrubs or antibacterial soaps. Warm compresses can be beneficial. Patients should be screened for accompanying metabolic conditions.

Topical clindamycin is preferred as a first-line treatment in cases with mild to moderate inflammatory lesions. Topical dapsone or resorcinol can be used for their anti-inflammatory effects. Oral antibiotics (e.g., doxycycline, tetracycline, clindamycin, rifampin) are another first-line treatment option, and combination therapy is commonly required.

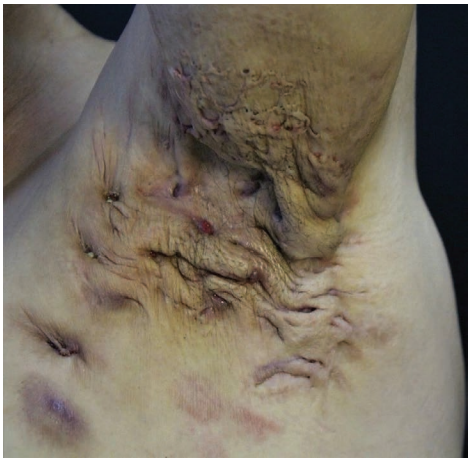


Figure 3.8 Multiheaded comedones, sinus tracts, draining sinuses, and scarring in the axilla.

Source: Courtesy of Istanbul Medeniyet University Dermatology Clinic.

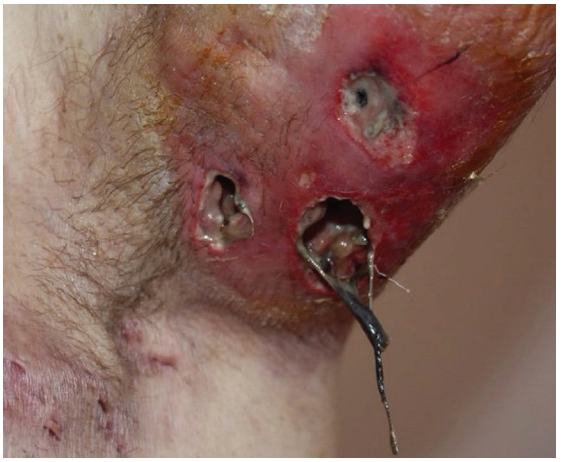


Figure 3.9 Abscess with sinus tracts that drain to the skin surface.

Source: Courtesy of Istanbul Medeniyet University Dermatology Clinic.

Antiandrogenic therapy is considered second-line treatment, especially for women with mild or moderate HS. Spironolactone can be used in women who experience hormonal flares. Metformin can inhibit the production of pro-inflammatory cytokines, reduce insulin resistance, and exert anti-androgenic effects.

Intralesional triamcinolone acetonide injection is an effective adjunctive therapy for individual lesions when inflamed. Oral retinoids do not appear to be effective enough. The results of the case series regarding the use of isotretinoin in HS have been disappointing.

Biologic agents can be considered in moderate to severe cases that are recalcitrant to conventional therapies. TNF-α inhibitors used for the treatment of HS include adalimumab and infliximab. Other biologic therapies have been utilized with varying degrees of success.

Surgery involves either limited or extensive excision and aims to improve the quality of life. It is non-curative and does not replace medical treatment, but it can offer benefit in severe, recalcitrant disease that includes scarring and sinus tracts. Deroofing of the sinus tracts, cysts, or abscesses is associated with fewer overall complications; however, wide excision has been shown to have lower rates of recurrence. Nd: YAG and carbon dioxide laser treatment have offered significant improvement in several studies.

Course: HS is a chronic, recurring, and debilitating disorder that is associated with poor quality of life and significant psychosocial morbidity. HS has many complications, including secondary amyloidosis, anemia, fistulae to the urinary or gastrointestinal tract, and lymphedema. Squamous cell carcinoma can rarely arise in sites of chronic lesions.

FINAL THOUGHT

HS is an unpleasant disease for both the patient and the physician. Lesions are often tender, draining, suppurating, and malodourous. Because HS is incurable, treatment is often difficult; however, proper disease management can offer improvement, especially in the quality of life.

ADDITIONAL READINGS

Alikhan A, Lynch PJ, Eisen DB. Hidradenitis suppurativa: a comprehensive review. J Am Acad Dermatol. 2009;60:539–563.

Dessinioti C, Antoniou C, Katsambas A. Acneiform eruptions. Clin Dermatol. 2014;32:24–34.

Gallo RL, Granstein RD, Kang S, et al. Standard classification and pathophysiology of rosacea: the 2017 update by the National Rosacea Society Expert Committee. J Am Acad Dermatol. 2018;78:148–155.

Goldburg SR, Strober BE, Payette MJ. Hidradenitis suppurativa: current and emerging treatments. J Am Acad Dermatol. 2020;82:1061–1082.

Laureano AC, Schwartz RA, Cohen PJ. Facial bacterial infections: folliculitis. Clin Dermatol. 2014;32:711–714.

Lee GL, Zirwas MJ. Granulomatous rosacea and periorificial dermatitis: controversies and review of management and treatment. Dermatol Clin. 2015;33:447–455.

Luelmo-Aguilar J, Santandreu MS. Folliculitis: recognition and management. Am J Clin Dermatol. 2004;5:301–310.

Saunte DML, Jemec GBE. Hidradenitis suppurativa: advances in diagnosis and treatment. JAMA. 2017;318:2019–2032.

van Zuuren EJ. Rosacea. N Engl J Med. 2017;377:1754–1764.

Williams HC, Dellavalle RP, Garner S. Acne vulgaris. Lancet. 2012;379:361–372.

4 Papulosquamous Diseases

Melek Aslan Kayıran, Jordan V. Wang, and Ayşe Serap Karadağ

CONTENTS

PSORIASIS

Definition: This is a chronic, systemic inflammatory disease that affects the skin and is the most common papulosquamous disease. Numerous systemic effects, such as hyperlipidemia, cardiovascular disease, diabetes mellitus, depression, inflammatory bowel disease, nonalcoholic fatty liver disease, and metabolic syndrome may accompany it.

Overview: Psoriasis can be seen in every age, gender, and race; however, it peaks between 16–22 and 57–60 years of age. Although its frequency varies by country, it is estimated to be between 0.09–11.8% of the general population.

Psoriasis is a multifactorial genetic disease that has been associated with many genes and pathways, especially HLA-CW*06, interleukin (IL)4, IL23/17 axis, and NF-κB signaling. Stress, humid and cold weather, trauma, smoking, obesity, HIV infection, beta-blockers, lithium, antimalarials, antidepressants, antivirals, and nonsteroidal anti-inflammatory medications are among the potential triggers. Streptococcal pharyngitis is known to initiate guttate psoriasis, especially in pediatric patients.

Clinical presentation: Psoriasis has different forms, such as psoriasis vulgaris (PV), pustular psoriasis, guttate psoriasis, inverse psoriasis, erythrodermic psoriasis, and palmoplantar psoriasis, which can be associated with psoriatic arthritis.

The most common form is PV and accounts for 80–90% of all cases. Lesions are often symmetric, well-demarcated, pink, scaly plaques (Figure 4.1). Lesions may differ in size and shape. Knees, elbows, scalp, and sacral region are frequently involved; however, lesions can be observed in all areas of the body (Figure 4.2).

There are a number of phenomena that can help to diagnose PV. For the "wax spot phenomenon," when the lesion is scraped with the blunt tip of a scalpel, the scale sheds in thin white layers, which indicates parakeratotic hyperkeratosis. If the lesion continues to be scraped, a sticky and wet layer is reached; this is the lowest layer of the dermal papillae, and this finding is called as the "last membrane phenomenon." When the lesion is scraped even further, bleeding foci are seen

Table 4.1 Pathogenesis of Psoriasis

Keratinocyte Hyperproliferation	Vasodilation in Dermal Capillaries	Proinflammatory Mediator Release
• Acceleration in cell turnover • Rapid desquamation of keratinocytes • Abnormal maturation and thickening of the stratum corneum	• Angiogenesis • Lymphocyte and neutrophil penetration into the skin	• Increased release of interleukin, endothelin, IFN-ϒ, TNF-α, and vascular endothelial growth factor • T-cell activation • Immune response onset

DOI: 10.1201/9781003105268-4

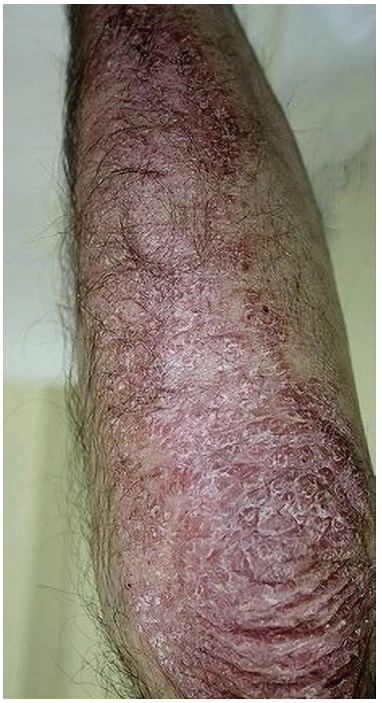


Figure 4.1 Psoriasis vulgaris with erythematous scaly plaques on the elbow and arm.

Source: Courtesy of Istanbul Medeniyet University Dermatology Clinic.

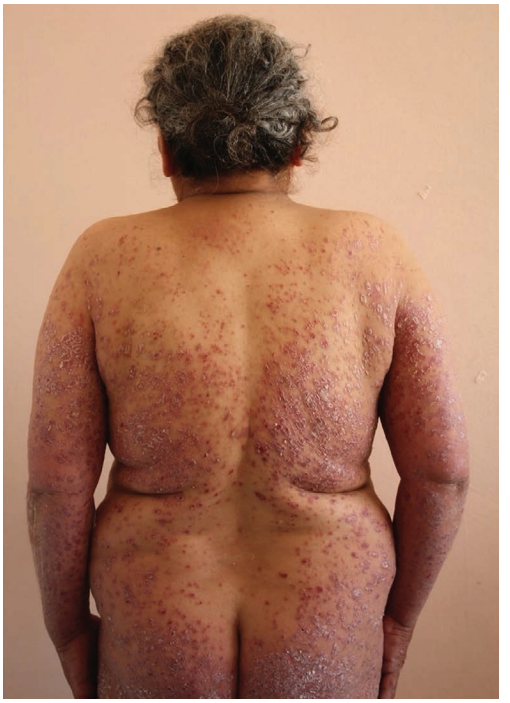


Figure 4.2 Psoriasis vulgaris with erythematous scaly papules and plaques on the back and arms.

Source: Courtesy of Istanbul Medeniyet University Dermatology Clinic.

as tiny pinheads. This finding is the "Auspitz sign" and indicates papillomatosis in the dermal papilla. While the lesions are healing, they can be surrounded by a hypopigmented ring, called the "Woronoff ring."

Guttate psoriasis is more common in children and young adults. Lesions are in the form of multiple, small, erythematous, scaly plaques that are 0.5–1.5 cm in diameter. Streptococcal throat infection is believed to precede many cases. A relationship has been found with HLA-CW*0602.

Inverse psoriasis is a variant that involves the retroauricular region, axillae, inframammary, inguinal, and intergluteal areas. It can be seen alone or together with other forms of psoriasis. It appears as well-defined, wet, erythematous plaques, and scale is not expected.

Pustular psoriasis is a clinical variant in which pustules are located on erythematous areas, which can be generalized or localized. It is seen at the rate of 1.2–1.8% among all forms of psoriasis. Its acute generalized form is also called von Zumbusch disease (Figure 4.3). Patients typically have fever, and pustules appear suddenly. It is more common between 30–50 years and in women. Its etiology includes drugs, such as terbinafine, amoxicillin, sulfonamides, and lithium, as well as infection, pregnancy, hypoparathyroidism, hypocalcemia, and ultraviolet radiation. Occasionally, it can emerge as a result of the sudden discontinuation of treatments in patients with psoriasis. Eye and nail involvement, along with a geographic tongue, can be observed. Fever, arthralgia, myalgia, malaise, and abdominal pain are common.

In localized pustular forms, fingers are typically involved (Figure 4.4), which has been called acrodermatitis continua of Hallopeau, acropustulosis, pustular acrodermatitis, acrodermatitis perstans, and dermatitis repens. It is common in middle-aged women. It starts in the form of sterile pustules in the nail folds and beds. The pustules combine to form pustule ponds that may open and form painful erosions. Onychodystrophy and anonychia may develop due to nail bed and matrix involvement. It usually starts on a few fingers and then extends onto the hands, forearm, and feet over time. Hand involvement is more common.

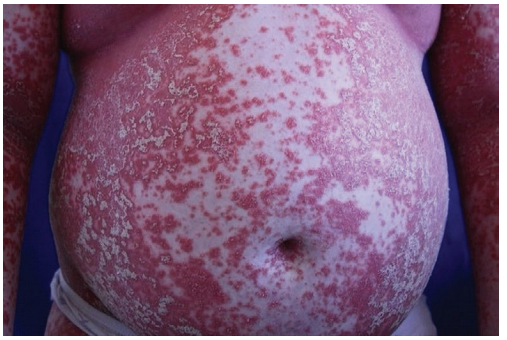


Figure 4.3 Pustular psoriasis with multiple pustules located on erythematous plaques on the chest, abdomen, flanks, and arms.

Source: Courtesy of Istanbul Medeniyet University Dermatology Clinic.

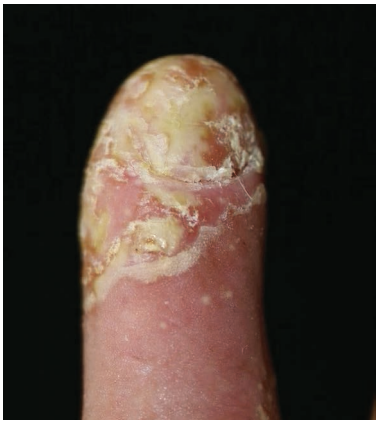


Figure 4.4 Localized pustular psoriasis, acropustulosis.

Source: Courtesy of Istanbul Medeniyet University Dermatology Clinic.

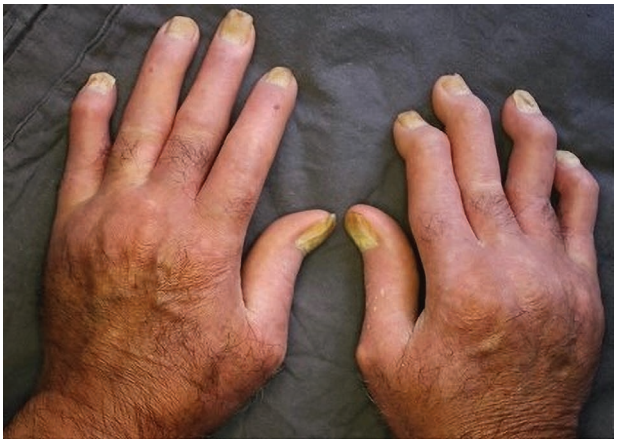


Figure 4.5 Psoriatic arthritis with asymmetric oligoarthritis of the hands.

Source: Courtesy of Istanbul Medeniyet University Dermatology Clinic.

Palmoplantar psoriasis can be encountered alone or in combination with other forms. Lesions are well-defined, hard, and thick scaly plaques, especially in the plantar region, which are sometimes accompanied by thick fissures. Erythema can be seen but is not always expected. It may be painful.

The most common comorbidity is psoriatic arthritis. which is a seronegative arthritis (Figure 4.5). It accompanies 5–7% of patients and can reach nearly 30% in those with severe psoriasis. It is seen equally in both genders. Although it can be positive, HLA-B27 is typically negative. Asymmetric oligoarthritis is the most common clinical presentation, and dactylitis and enthesitis can be seen. Joint pain and swelling, heel pain, and morning stiffness are common symptoms, and nail involvement is common.

Laboratory studies: Clinical findings are generally sufficient for diagnosis. In ambiguous cases, histopathologic examination can be helpful, which shows an elongation of the rete ridges and dermal papillae, edema of the dermal papillae, enlargement of blood vessels, thinning of the suprapapillary plates, parakeratosis, compact orthokeratosis, spongiform pustules, microabscesses caused by neutrophil accumulation in the upper portion of the epidermis, and regular acanthosis. Dilated capillaries and keratinocyte proliferation are expected in all stages.

Dermatoscopy can reveal red dot and globules; diffuse, patched, polygonal, and twisted vessels; and diffuse, patched, central, or peripheral scale.

Table 4.2 Nail Changes Seen in Psoriasis

Inflammation of the nail matrix	Inflammation in the nail bed	Hyponychium and proximal nail fold
Pitting	Onycholysis	Irregularly dispersed and tortuous veins
Onychomadesis	Splinter hemorrhages	
Leukonychia	Subungual hyperkeratosis	
Beau's lines	Oil-drop (salmon) patches	
Red spots on lunula		
Separation in nail plate		

Blood tests may be abnormal due to comorbidities, but laboratory findings are generally normal. Hyperuricemia can be seen in patients with extensive lesions. In psoriatic arthritis, C-positive protein (CRP) and erythrocyte sedimentation rate (ESR) can be elevated. In the generalized form of pustular psoriasis, leukocytosis, hypoalbuminemia, hypocalcemia, and elevated CRP and ESR can be observed.

Patients should be screened at regular intervals for comorbidities, such as metabolic syndrome, diabetes mellitus, hypertension, cardiovascular disease, inflammatory bowel disease, and liver dysfunction.

Differential diagnosis: This includes nummular dermatitis, seborrheic dermatitis, pityriasis rosacea, pityriasis rubra pilaris, syphilis, atopic dermatitis, pityriasis lichenoides chronica, parapsoriasis, and mycosis fungoides. In pustular forms, acute generalized exanthematous pustulosis, IgA pemphigus, and pustular drug eruption should be considered. In localized pustular forms, bacterial paronychia, herpetic whitlow, chronic candidiasis, and acrodermatitis enteropathica can be considered.

Management: Treatment decision depends on the clinical type, severity, extent, duration, response to previous treatments, and psychosocial status of the patient.

Topical Treatment

Topical treatments are typically sufficient in mild to moderate cases. Corticosteroids are anti-inflammatory, antiproliferative, and immunosuppressive. Treatment with high-potency corticosteroids is often started initially followed by lower potency formulations for maintenance as needed. Stronger corticosteroids should generally not be used for more than a few weeks at a time. For thick scaly plaques, it is useful to combine them with a keratolytic agent, such as salicylic acid, urea, or a retinoid (e.g., tazarotene), in order to increase penetration. Low- or medium-potency steroids should be used in inverse areas and on the face.

Anthralin and coal tar have been used with some benefit, but they have largely been replaced with topical steroids and steroid-sparing agents, such as calcipotriol and calcineurin inhibitors. Anthralin is mostly preferred in plaque psoriasis and used in short-term contact or combined preparations. Coal tar can be effective in reducing the thickness of scale in scalp psoriasis. Calcipotriol is a vitamin D analogue that suppresses inflammation and reduces the proliferation of epidermal keratinocytes in psoriasis. It is available alone or in combination with corticosteroids. Topical calcineurin inhibitors include tacrolimus and pimecrolimus. They can be particularly effective as maintenance treatment and in children.

Systemic Treatment

Systemic treatments are preferred in moderate to severe cases and those resistant to topical therapy or phototherapy. Agents include acitretin, methotrexate, cyclosporine, biologic agents, and steroids.

Acitretin can be used in all types of psoriasis and can be especially helpful in pustular psoriasis. Response can be observed after 4–6 weeks, but maximal effect is typically seen after 3–4 months. Once the disease stabilizes, the dose can be reduced for maintenance. Side effects are generally dose dependent and include skin dryness, cheilitis, palmoplantar desquamation, irritation, myalgia, hair loss, increased triglycerides, and increased liver function markers. Acitretin should not be used in women of childbearing age due to its teratogenicity.

Methotrexate works by inhibiting DNA synthesis through affecting dihydrofolate reductase. It reduces keratinocyte proliferation and has anti-inflammatory and immunomodulatory effects. Generally, 7.5–25 mg/week is sufficient for psoriasis treatment. It is helpful in PV, pustular, erythrodermic, and arthropathic psoriasis and affects nail findings. Patients should be given 1 mg/day of folate supplementation 48–72 hours after taking the medication to reduce gastrointestinal side effects. Before treatment, hepatitis markers, blood count, liver and kidney function tests, chest radiography, and complete urinalysis can be examined. Testing can be performed regularly for monitoring.

Cyclosporine suppresses IL-2 production and has immunosuppressive effects. It can be preferred in cases, where rapid remission is desired or in cases recalcitrant to other therapies. It is started by dividing 2.5 mg/kg/day into two doses and can be increased up to 4–5 mg/kg/day. In erythrodermic forms, treatment can be initiated with higher doses. Recurrence is common with discontinuation, especially abrupt cessation. Maintenance treatment is recommended, and patient can be slowly transitioned. Cyclosporine is nephrotoxic; if serum creatinine increases by 30% and glomerular filtration rate decreases below 30%, the treatment is discontinued. Side effects include hypertension, hyperlipidemia, electrolyte disturbance, myalgia, paresthesia, headache, flu-like syndrome, nausea, and vomiting. Blood pressure should be checked regularly.

Various biologic agents can target specific molecules and pathways in the psoriasis pathway. They generally have more systemic side effects and risks than other systemic immunosuppressant regimens. Common biologic agents include tumor necrosis factor-alpha inhibitors (e.g., adalimumab, etanercept, certolizumab), IL-17 inhibitors (e.g., secukinimab, ixekizumab, brodalumab), IL-12/23 inhibitors (e.g., ustekinumab) and IL-23 inhibitors (e.g., guselkumab, risankizumab). Biologic treatments are mainly approved for psoriasis vulgaris and psoriatic arthritis and are generally not as effective for pustular psoriasis.

Systemic corticosteroids are not routinely used in the treatment of psoriasis. Despite rapid response from treatment, flaring can be rapid and severe when the steroid is discontinued; however, in severe erythrodermic psoriasis and generalized pustular psoriasis, prednisone 30–60 mg/day can be considered for a short time to allow for improved control, especially as a biologic agent is administered and begins to take effect. Systemic steroids should be slowly decreased and discontinued as soon as possible.

Phototherapy

Overview: Phototherapy can be helpful in moderate to severe cases of plaque psoriasis and guttate psoriasis, where topical treatments may be impractical. It can reduce epidermal hyperproliferation and suppress T-cell apoptosis and cytokines. Phototherapy is typically administered three days a week and continued for an average of 6–8 weeks with titration. The most common regiments use narrowband ultraviolet (UV) B (311–313 nm), which is believed to be the most effective spectrum in the treatment of psoriasis. UVA (320–400 nm) can be effective, especially in extremity-localized thick plaques; however, it comes with greater risk of carcinogenesis and cannot be used in pregnancy and childhood.

Course: Psoriasis is a chronic and recurring disease without cure. With appropriate use of topical and systemic agents and thorough patient education regarding treatment strategies, psoriasis can be managed. Severe forms, such as pustular psoriasis and erythrodermic psoriasis, may be life-threatening if not treated appropriately. In these patients, appropriate treatment should be initiated as soon as possible.

Final comment: Psoriasis is a lifelong disease that is associated with various comorbidities. When treating patients, it is important to not only treat skin findings but also to screen for other related systemic conditions. When indicated, a multidisciplinary approach should be adopted.

LICHEN PLANUS

Definition: Lichen planus (LP) is a chronic and often recurring inflammatory skin disease that can involve skin and mucosa. The most common presentation is characterized by small, itchy papules. The cause is not yet fully understood.

Overview: While the prevalence of skin involvement varies between 0.2–1%, oral involvement is more common (1–4%); however, both are commonly seen together. The mean age at diagnosis is 50–60 years for oral lesions and 40–45 years for skin lesions. LP is 1.5 times more common in women compared to men. There is a strong association between hepatitis C infection and LP. HCV seropositivity is detected five times more in LP than the normal population.

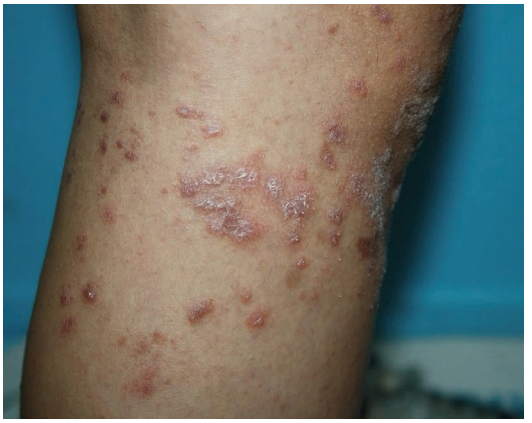


Figure 4.6 Lichen planus with lattice-like white lines, termed Wickham striae, on the papules.

Source: Courtesy of Istanbul Medeniyet University Dermatology Clinic.

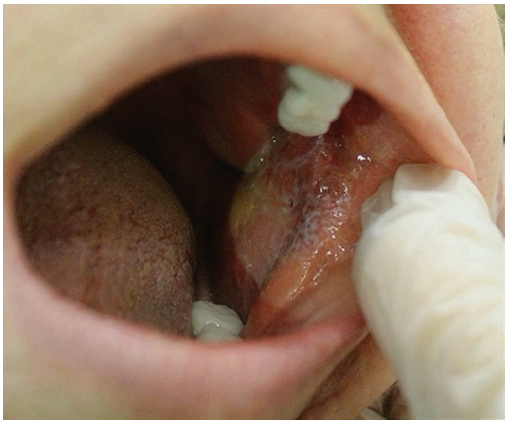


Figure 4.7 Mucosal involvement of lichen planus with reticular lesions on the buccal mucosa.

Source: Courtesy of Istanbul Medeniyet University Dermatology Clinic.

Clinical presentation: Generally, the flexural part of the wrists, the dorsum of hands, ankles, and waist are involved, but lesions can also be seen on the hips, trunk, and neck. When the axillae, inguinal, and inframammary areas are involved, it is called inverse LP. Lesions are typically violaceous, flat-topped, polygonal papules, which can have lattice-like white lines, termed Wickham striae (Figure 4.6). Although the disease can be significantly pruritic, itching is not observed in 20% of patients. As lesions resolve, they usually leave behind a gray to brown hyperpigmentation, especially in dark-skinned individuals.

Mucosal involvement is often in the form of reticular lesions on the buccal cheeks, which have a white lattice-like appearance (Figure 4.7). Other lesion types include erosive, papular, plaque-like, atrophic, ulcerative, and bullous. Erosive and ulcerative lesions are considered to be premalignant, and squamous cell carcinoma (SCC) development has been reported in 1% of patients.

Nail involvement alone is rare, but nails are affected in 25% of lichen planus patients (Table 4.3).

LP has clinically different types. These include the actinic form in sun-exposed areas, annular form in which papules combine to form plaques, linear form in which papules are aligned linearly due to the Koebner phenomenon, hyperpigmented form in which the lesions are darker and brownish purple, and inverse form that involves the intertriginous areas.

Laboratory studies: LP can often be diagnosed clinically; however, a biopsy may be necessary. Histopathologically, LP is characterized by hyperkeratosis without parakeratosis, apoptotic bodies

Table 4.3 Nail Changes Seen in Lichen Planus

Nail Plate	Matrix	Nail Bed	Bad Prognosis
Longitudinal streaking	Trachyonychia	Onycholysis	Nail bed anomalies
Fragmentation on nail plate	Pitting	Chromonychia	Longitudinal streaking
Onychatrophy	Pterygium	Splinter hemorrhages	Nail loss
Nail loss	Erythema of the lunula	Subungual hyperkeratosis	
	Irregularly dispersed and tortuous veins		

(Civatte bodies), and wedge-shaped hypergranulosis with a sawtooth appearance in rete ridges. There can also be vacuolar degeneration of keratinocytes, a characteristic band-like lymphocytic accumulation at the dermo epidermal junction, and pigment incontinence. In cases that do not improve despite treatment, a biopsy should be performed to exclude dysplasia and SCC. Patients can be screened for hepatitis C, especially if they have oral lesions or are at risk.

Differential diagnosis: LP can often be difficult to differentiate from lichenoid drug eruption, in which lesions are more frequently symmetrically distributed in sun-exposed areas with less oral involvement and without Wickham striae. Medication history in the last 2 years should be questioned. Common drugs include gold salts, antimalarials, beta-blockers, angiotensin-converting-enzyme inhibitors, penicillamine, nonsteroidal anti-inflammatory drugs, thiazide diuretics, spironolactone, and furosemide.

The differential also includes lupus erythematosus, guttate psoriasis, erythema dyschromicum perstans, secondary syphilis, pityriasis rosea, lichen amyloidosis, graft versus host disease, and pityriasis lichenoides chronica. For oral lesions, the differential includes leukoplakia, candidiasis, and morsicatio buccarum.

Management: This varies according to the number and localization of lesions. Because lesions tend to heal spontaneously, topical corticosteroids can be administered to hasten resolution and relieve itching. In oral involvement, potent topical corticosteroids are recommended as first-line treatment. When topical corticosteroids are insufficient, systemic corticosteroids can be used for several weeks. After improvement, slow tapering is often necessary in order to prevent abrupt recurrence of lesions. In resistant cases, other options include phototherapy and systemic retinoids.

Course: In the majority of patients, skin lesions resolve spontaneously within 1–3 years. Systemic steroids can lead to resolution with several weeks in many cases; however, recurrence is common. As lesions resolve, they typically leave behind transient hyperpigmentation. Spontaneous recovery is rare in oral involvement. Patients with chronic or ulcerative oral cases should be closely followed to monitor for potential malignancy, such as squamous cell cancer.

Final comment: LP is an inflammatory skin disease that can involve both skin and mucosa. Although skin lesions can improve spontaneously, treatment can hasten improvement. Mucosal involvements should be monitored for squamous cell cancer development.

PITYRIASIS RUBRA PILARIS

Definition: Pityriasis rubra pilaris (PRP) is an inflammatory and papulosquamous skin disease characterized by follicular and palmoplantar hyperkeratosis and orange-pink scaly plaques.

Overview: This appears in men and women at nearly equal rates. Although it peaks in childhood (1–10 years old) and adulthood (50–60 years old), it can be seen at any age.

Its etiology is not yet fully understood. Viral or bacterial infections and autoimmune diseases may be potential triggers.

Clinical presentation: PRP is divided into 6 groups according to age of onset, clinical manifestations, morphologic characteristics, and prognosis.

Type I (classic adult type): The majority of patients (55%) are type I. This type typically starts in the upper half of the body with a cephalocaudal spread (Figure 4.8). It begins as perifollicular papules with keratotic plugs, and diffuse salmon-colored plaques appear over time (Figure 4.9). Between these plaques, there are unaffected skin islets. After a few weeks to months, palmoplantar keratoderma in the form of thick orange scale emerges (Figure 4.10). Nail involvement may accompany. The condition can acutely turn into erythroderma. Within 3 years, about 80% of patients with this type regress spontaneously.

Type II (atypical adult type): In this type, there is no cephalocaudal progression. Palmoplantar involvement is accompanied by ichthyosiform dermatitis and lamellar scaling is seen. Alopecia can be seen on the scalp. Only 20% of patients regress within 3 years, and most conditions continue for many years.

Type III (classic juvenile type): This type is seen in children, who are 5–10 years old. It constitutes 10% of all cases. It has a clinical presentation similar to Type 1. Type III typically regresses spontaneously within 1 year.

Type IV (circumscribed juvenile type): This is the most common type in the 3–10-year age range. Sharply circumscribed, follicular, hyperkeratotic areas and erythema, especially on the knees and elbows, are observed. Of all cases, 25% are from this group. Remission can be seen within 3 years; however, relapse is frequent.

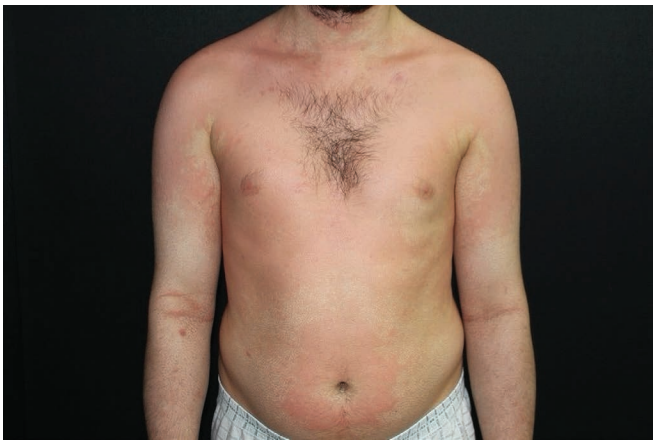


Figure 4.8 Pityriasis rubra pilaris with diffuse salmon-colored plaques and islands of sparing.

Source: Courtesy of Istanbul Medeniyet University Dermatology Clinic.

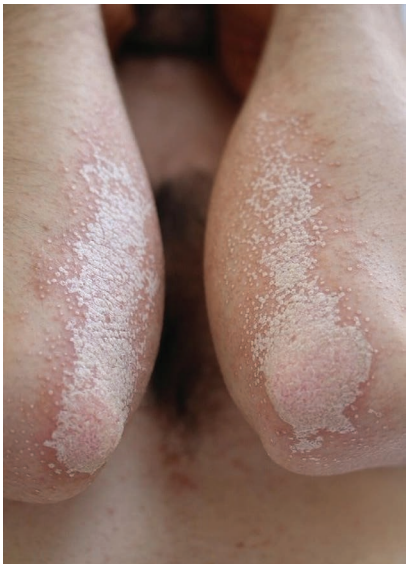


Figure 4.9 Pityriasis rubra pilaris with perifollicular papules with keratotic plugs, so-called nutmeg grater papules.

Source: Courtesy of Istanbul Medeniyet University Dermatology Clinic.

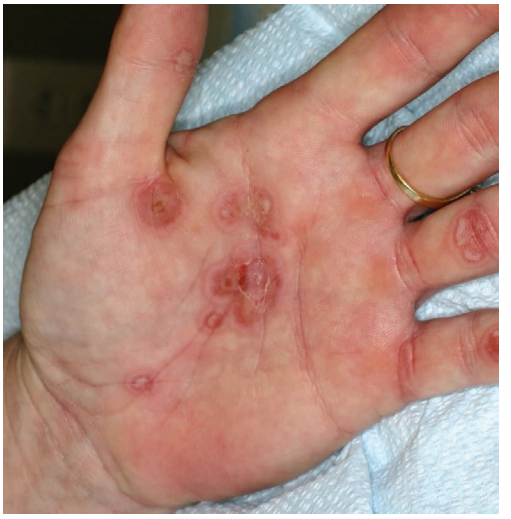


Figure 4.10 Pityriasis rubra pilaris with orange-colored palmoplantar keratoderma appearing as if it was dipped in wax.

Source: Courtesy of Istanbul Medeniyet University Dermatology Clinic.

Type V (atypical juvenile type): This type is seen between the ages of 0–4 years. It constitutes 5% of all cases. Hereditary forms are generally of this type. Follicular hyperkeratosis and ichthyosiform dermatitis are seen. Type V has an early onset and a chronic course.

Type VI (HIV-associated type): Similar to type 1, follicular plugs with spicules are seen. Erythroderma frequently develops. Lesions can be seen together in the setting with acne conglobata, hidradenitis suppurativa, and lichen spinulosus. It is often chronic.

PRP can sometimes be observed together with seronegative arthritis, alopecia, ectropion, and loss of sweating. Of all patients with PRP, more than 80% of cases have palmoplantar keratoderma, and 45% can progress to erythroderma.

Laboratory studies: Histopathologic examination demonstrates irregular psoriasiform acanthosis of the epidermis, parakeratosis and orthokeratosis in "checkerboard" pattern, follicular plugs

accompanied by shoulder parakeratosis, thickening and neutrophil loss in the stratum corneum, and mild superficial perivascular lymphohistiocytic infiltration. Epidermal spongiosis and focal acantholytic dyskeratosis are rare but can be seen.

HIV infection must be investigated in generalized and rapid erythrodermic types.

Differential diagnosis: Classic psoriasis and pityriasis lichenoides should be considered. When erythroderma develops, psoriasis, atopic dermatitis, drug reactions, cutaneous T-cell lymphoma, congenital ichthyosis, paraneoplastic phenomenon, and graft versus host disease should be excluded.

Because ichthyosiform changes are observed in types II and V, which are atypical forms, PRP is differentially diagnosed with acquired and congenital ichthyosis and lichen spinulosus. Keratosis pilaris should also be considered when spiny follicular papules are seen.

Management: Because most cases are self-limiting and asymptomatic, treatment may not be required.

Topical moisturizers, keratolytic agents (e.g., urea 5–10%, salicylic acid 1–3%, alpha hydroxy acid), corticosteroids, retinoids, calcineurin inhibitors, and calcipotriol can be used to help with inflammation and scaling.

For systemic treatment, high-dose vitamin A (200,000–1,000,000 U/g) and acitretin (0.5 mg/kg/day) can be used in children, while isotretinoin (0.5–1 mg/kg/day) and UVB phototherapy can be used those older than age 12. Methotrexate, cyclosporine, azathioprine, and TNF-alpha inhibitors can be administered in resistant cases. Acitretin (0.5 mg/kg/day), isotretinoin (1–1.5 mg/kg/day), and methotrexate (5–30 mg/week) are first line treatments in adults. UVB and UVA1 or photochemotherapy (PUVA) can be tried. In resistant cases, cyclosporine (<5 mg/kg/day), TNF-alpha inhibitors, azathioprine (50–200 mg/day), secukinumab, ustekinumab, infliximab, fumaric acid, and intravenous immunoglobulin treatment can be trialed.

Antiretroviral treatment should be given in association with HIV.

Course: In most cases, PRP is a self-limiting and asymptomatic disease that does not require treatment. Of all type I PRP cases, 80% recover spontaneously within 3 years. Although types II and V have a chronic course, type III often enters remission after 1 year. The course of types IV and VI is uncertain.

Final comment: PRP, which has distinctive findings, such as follicular involvement, orange color, waxlike keratoderma, and islands of sparing, is generally a self-limiting disease. Due to its atypical forms, erythroderma, and thick scaling, it can often cause significant disruption to a patient's life and difficulties in diagnosis and treatment.

PITYRIASIS LICHENOIDES

Definition: According to the clinical features, course, and response to treatment, pityriasis lichenoides includes a group of inflammatory skin diseases classified as pityriasis lichenoides et varioliformis acuta (PLEVA) and pityriasis lichenoides chronica (PLC).

Overview: The etiology, prevalence, and incidence of pityriasis lichenoides (PL) are not fully clarified. Disease has been shown to peak in the third decade, and the majority of cases are diagnosed before the age of 50 years. PL typically appears in late childhood and young adulthood; however, it can be seen in all ages, races, and geographic regions. It is thought to be slightly more common in men. Cases of PLEVA can also be seen during pregnancy.

Clinical presentation: PLEVA has an acute-subacute onset. Multiple 2–3-mm erythematous macules rapidly evolve into papules and then into polymorphic lesions (Figure 4.11). Papules have a thin mica-like scale that thicken over time, moves away from the periphery, and clings to the center. In time, the middle of the papules collapses and vesiculopustules (papules covered with hemorrhagic crusts and superficial necrotic ulcers) can be seen. They heal within weeks and months and can leave hypo/hyperpigmentation or varioliform scars. Lesions tend to involve the trunk's anterior aspect, flexural surfaces, and proximal extremities, but they can also be generalized. Skin lesions may rarely burn or itch and be accompanied by systemic symptoms, such as fever and fatigue.

PLC is the most common disease in the PL group. The lesions begin as erythematous, maculopapular lesions, which gradually evolve into small, dull erythematous-brown papules with shiny mica-like scale in the center (Figure 4.12). Necrotic lesions are not expected. The lesions regress within weeks and heal with hyperpigmentation. As in PLEVA, lesions can be polymorphic. The proximal trunk and extremities are involved, but acral or segmental involvement may also occur. It is generally asymptomatic.

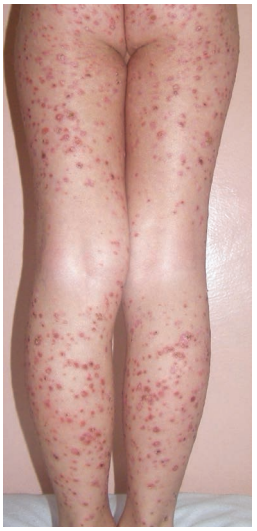


Figure 4.11 Pityriasis lichenoides et varioliformis acuta with polymorphic lesions consisting of macules, papules, and plaques with some covered with hemorrhagic crust.

Source: Courtesy of Istanbul Medeniyet University Dermatology Clinic.

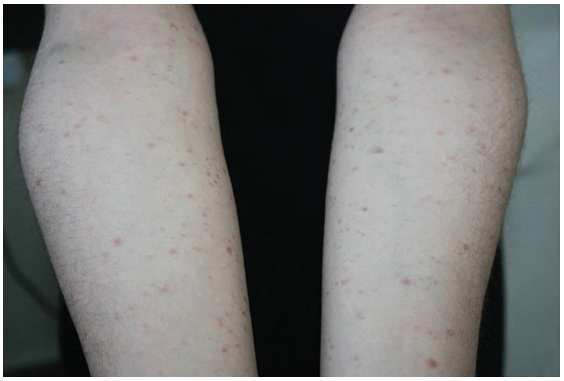


Figure 4.12 Pityriasis lichenoides chronica with maculopapular lesions on the arms.

Source: Courtesy of Istanbul Medeniyet University Dermatology Clinic.

Febrile ulceronecrotic Mucha-Habermann disease (FUMHD) is a rarely seen type. It may have sudden onset or develop gradually from PLEVA or PLC. It is more common in males between the ages of 10–30 years. In the aggressive and generalized form, purpuric-black, ulceronecrotic and crusted plaques can suddenly appear and tend to merge. Hemorrhagic bullae and pustules may accompany them. Painful, extensive skin necrosis and secondary infection of ulcers can be observed. As a result, fulminant sepsis and hypertrophic and atrophic scars can develop. It may involve oral and genital mucosa. Pain, itching, high fever, weakness, fatigue, sore throat, diarrhea, abdominal pain, pneumonia, splenomegaly, arthritis, and conjunctival ulcers can be observed.

Laboratory studies: For PLEVA, histopathologic features include parakeratosis, spongiosis, dyskeratosis, acanthosis, lymphocytic exocytosis in the basal layer, erythrocytes in the epidermis, apoptotic and necrotic keratinocytes, neutrophilic inclusions, vacuolization in the basal layer, and focal necrosis in the form of diffuse peripheral necrosis in the dermis. Subepidermal vesicles and dermal sclerosis may accompany previous lesions.

In PLC, histopathology can reveal focal parakeratosis, acanthosis, focal spongiosis, minimal keratinocyte necrosis, hemorrhage and minimal vacuolar degeneration of the basal layer, lymphocyte and erythrocyte focal invasion, and superficial, band-like perivascular lymphocytic infiltration covering the dermo epidermal junction locally.

With FUMHD, biopsy can demonstrate a deep and intense inflammatory infiltration, epidermal and dermal ulceration, leukocytoclastic vasculitis, and apoptotic and necrotic keratinocytes. Leukocytosis, anemia, hyperalbuminemia, and hypoalbuminemia can be seen, as well as elevated erythrocyte sedimentation, C reactive protein, lactate dehydrogenase, liver enzymes, and IL-2 receptor levels.

Differential diagnosis: This can include lymphomatoid papulosis, guttate psoriasis, LP, tinea versicolor, Gianotti-Crosti syndrome, pityriasis rosea, drug eruptions, varicella and other viral eruptions, generalized arthropod bite, erythema multiforme, small vessel vasculitis, secondary syphilis, papulonecrotic tuberculid, polymorphous light eruption, generalized folliculitis, dermatitis herpetiformis, toxic epidermal necrolysis, and graft-versus-host disease.

Management: There is no current standard treatment protocol for PL; however, treatments are generally selected based on type of lesions, distribution, scarring, and systemic symptoms. Phototherapy (UVB, narrow-band UVB, PUVA, UVA1) can be considered as first-line treatment, especially in PLC and generalizes presentation. UVB is effective in the pediatric age group. If an underlying etiology is detected, treatment of this is recommended. Tetracyclines, erythromycin, dapsone, and acyclovir may be considered especially in infections. Tetracyclines and erythromycin can also provide benefit with their anti-inflammatory effect, but it is recommended to be discontinued gradually due to recurrence following cessation. Antiretroviral treatment should be given in HIV-positive cases.

Topical corticosteroids can reduce inflammation and itching in mild to moderate cases. Antihistamines and moisturizers can also be added. Although these treatments provide symptomatic relief, they do not change the course of the disease.

In severe cases, including those with fever, arthritis, and myalgia, systemic corticosteroids (prednisone 40–60 mg/day started and slowly reduced), methotrexate, oral calciferol, pentoxifylline, thiobendazole, dapsone, 4-diaminodiphenyl-sulfone, intravenous γ-globulin, cyclosporine, and retinoids can be used. Systemic corticosteroids and methotrexate have proven to offer benefit in FUMDH, especially in children. Tumor necrosis alpha inhibitors may be useful.

Course: PLEVA is generally self-limiting within weeks to occasionally years, but remissions can be seen. In PLC, generalized lesions typically heal within months, but they can continue for years. FUMHD can be serious. Mortality can occur in up to 25% of cases, especially in immunosuppressed and elderly individuals; therefore, the disease should be treated as soon as it is diagnosed.

Final comment: PL is a disease group with an undefined etiology, and its treatment has not yet been clarified. Although PLC is a chronic but milder form, FUMHD can be serious; therefore, patients should be followed closely with particular clinical presentations.

PITYRIASIS ROSEA

Definition: Pityriasis rosea (PR) is a skin disease with sudden onset, which is characterized by papulosquamous lesions. Although its etiology has not been clearly elucidated, it has been associated with human herpesvirus (HHV-6 and HHV-7) infections.

Overview: The incidence of PR is estimated to be between 0.5–2%. Of all cases, 75% are diagnosed between the ages of 10–35 years. PR is less common under 10 years of age and peaks between the ages of 20–29 years. It is relatively more common in women. Although PR is generally more frequent in winter months, there are also a few studies reporting no seasonal variation. In some patients, there may be a recent history of upper respiratory tract infection before lesions appear.

Clinical presentation: Although PR generally has a typical presentation, an atypical presentation can be seen in 20% of cases. Atypical morphology is seen in papular, urticarial, erythema multiforme-like, vesicular, purpuric, hemorrhagic, follicular, hypopigmented, circinata and marginata, and irritated types, while atypical distribution is seen in inverse, unilateral, extremity dense, mucosal, and acral forms.

In typical PR cases, annular lesions are prominent. The first emerging lesion is called the "herald patch," which is frequently seen on the trunk. The herald patch is an ovoid, erythematous, scaly annular plaque with slightly raised edges and a diameter of 2–10 cm (Figure 4.13). After this lesion present, erythematous, ovoid plaques with a diameter of 5–10 mm emerge after 3–4 days in children and 1–2 weeks in adults. These lesions have a slightly gray peripheral collarette of scale (Figure 4.14). These typically form along the Langer's lines of the trunk and proximal extremities, which can resemble a pine tree of a *Christmas tree* pattern. Pruritus can be seen in 25% of patients. Before skin lesions appear, some patients may experience weakness, anorexia, mild fever, and enanthema.

In pregnant women, some complications may develop with PR. It has been reported that intrauterine fetal infection, and, consequently, congenital defects, fetal hydrops, and fetal death, can be seen with PR in pregnancy. Pregnant women with high HHV-6, especially those with PR lesions starting before the 15th gestational week and those with enanthema, are considered in the major risk group for fetal complications, while those with constitutional symptoms and involvement of more than 50% of the body surface area are considered in the minor risk group.

Laboratory studies: Histopathologic examination may be helpful in cases that cannot be clinically diagnosed. Perivascular superficial dermatitis with lymphocytes, histiocytes, and eosinophils, hyperplasia, focal spongiosis, focal parakeratosis, irregular acanthosis, elongated rete ridges, endothelial and papillary dermal edema, and extravascular erythrocytes can be seen.

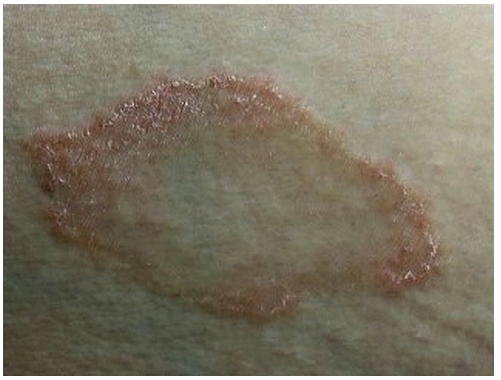


Figure 4.13 Pityriasis rosea with herald patch.

Source: Courtesy of Istanbul Medeniyet University Dermatology Clinic.

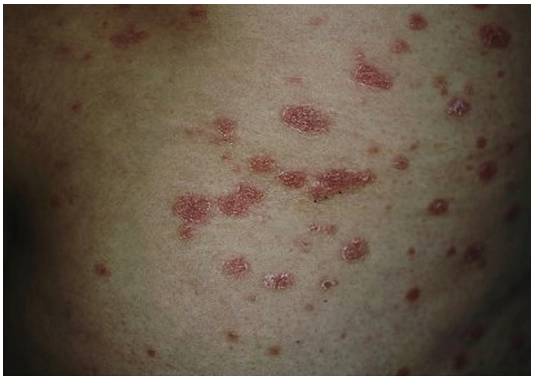


Figure 4.14 Pityriasis rosea with erythematous ovoid plaques with grayish peripheral collarette.

Source: Courtesy of Istanbul Medeniyet University Dermatology Clinic.

Differential diagnosis: This includes tinea corporis, nummular dermatitis, and erythema annulare centrifugum for single lesions, while secondary syphilis, guttate psoriasis, annular lichen planus, tinea versicolor, tinea corporis, parapsoriasis, erythema dyschromicum perstans, and erythema multiforme are considered for generalized lesions.

Management: Even if the disease is not treated, PR is self-limiting. Oral antihistamines and topical corticosteroids may help with pruritus. Systemic corticosteroids, phototherapy, acyclovir, or cidofovir may be useful in severe and resistant cases. Low-dose acyclovir (800 mg/day, three times daily for 1 week) treatment can be used in high-risk pregnant women with early onset of disease and systemic symptoms. Bed rest should be recommended for these pregnant women.

Course: The lesions typically resolve in 6–8 weeks without any scarring. In some patients, it can take 5–6 months. Temporary hypopigmentation or hyperpigmentation can be seen as lesions heal. Although recurrence is not often expected, this can be seen by 1.8–3.7% of cases.

Final comment: PR is a papulosquamous disease that is often seen in adolescents and young adults. It is generally self-limiting. In treatment-resistant cases, it is useful to confirm the diagnosis. PR is believed to be associated with HHV-6 and HHV-7 infections.

ERYTHRODERMA

Synonym: exfoliative erythroderma

Definition: Thesis defined by diffuse erythema or edema covering more than 90% of body surface area. In erythroderma, anatomic, physiologic, barrier, and metabolic functions of the skin are impaired. There are various causes, including inflammatory diseases, infections, drug eruptions, and underlying malignancy. Because there are high rates of morbidity and mortalities, it should be promptly diagnosed and with rapid initiation of treatment.

Overview: The incidence is not clearly known and varies according to geography. It has been reported as very different rates of approximately between 1–44/100,000. It is rare in the neonatal period and is more common between the ages of 40–60 years. It is two to four times more common in men.

Clinical presentation: Erythroderma may emerge due to primary skin diseases, infections, drug use, and malignancies. In approximately half of cases, it is idiopathic.

The most common cause of erythroderma is psoriasis. Other cutaneous diseases, such as atopic dermatitis, seborrheic dermatitis, contact dermatitis, PRP, LP, acquired ichthyosis, subacute lupus erythematosus, bullous pemphigoid, pemphigus foliaceus, actinic dermatoses, sarcoidosis, dermatomyositis, and graft versus host, are among other causes. Infections include staphylococcal scalded skin syndrome, toxic shock syndrome, crusted scabies, dermatophytosis, and congenital cutaneous candidiasis. In 1% of patients, there is an underlying malignancy. This can include mycosis fungoides, cutaneous T-cell lymphoma, diffuse cutaneous mastocytosis, B-cell chronic

Table 4.4 Common Causes of Erythroderma

Neonatal-Infant	Childhood	Adult
Congenital • Ichthyoses • Omen syndrome • Congenital cutaneous candidiasis • Diffuse cutaneous mastocytosis • Staphylococcal scalded skin syndrome	Infections • Staphylococcal scalded skin syndrome • Crusted scabies • Dermatophytoses	Inflammatory skin diseases • Psoriasis vulgaris/pustular psoriasis • Contact dermatitis • Atopic dermatitis • Pityriasis rubra pilaris • Lichen planus • Chronic actinic dermatitis • Acquired ichthyosis
	Drugs*	
	Existing dermatologic diseases • Atopic dermatitis • Psoriasis vulgaris/pustular psoriasis • Pityriasis rubra pilaris	
Non-congenital • Seborrheic dermatitis • Psoriasis vulgaris • Atopic dermatitis • Staphylococcal scalded skin syndrome		Drugs* Malignancies • Cutaneous T cell lymphomas (Sezary syndrome, Mycosis fungoides) • Internal malignancies (often gastric, esophageal, colon, liver, prostate, renal, lung cancer) • Leukemias
Drugs*		Infections • Staphylococcal scalded skin syndrome • Crusted scabies • Dermatophytoses • Toxic shock syndrome
Metabolic diseases		Bullous diseases • Pemphigus foliaceus • Bullous pemphigoid • Paraneoplastic pemphigus
		Connective tissue diseases • Dermatomyositis • Subacute lupus erythematosus)
		Blood disorders • Hypereosinophilic syndrome • Mastocytosis • Graft versus host disease

Note: *Most common drugs: Vancomycin and ceftriaxone in neonatal; antiepileptics, amoxicillin, sulfonamide, and antituberculosis drugs in childhood; antiepileptics, antibiotics, and nonsteroidal anti-inflammatory drugs in adults

lymphocytic leukemia, and solid organ cancers. In newborns, ichthyosiform diseases may result from primary immune deficiencies and metabolic diseases. It is accepted to be idiopathic when the cause cannot be determined.

In erythroderma, the skin is generally covered with bright red erythematous patches and/or plaques, and a yellowish-white scale can emerge over time (Figure 4.15). The patient may feel hardening of the skin due to edema and lichenification. Itching often accompanies it. Patients may experience fever, weakness, fatigue, muscle and joint pain, nausea, and vomiting. There may be lymphadenopathy, splenomegaly, and hepatomegaly. Hair loss and nail findings, such as subungual hyperkeratosis, onycholysis, and dry and brittle nails can be observed.

Clues related to the underlying disease may be seen in patients. The presence of psoriatic plaques due to psoriasis and the presence of intact islets of skin are in favor of PRP and mycosis

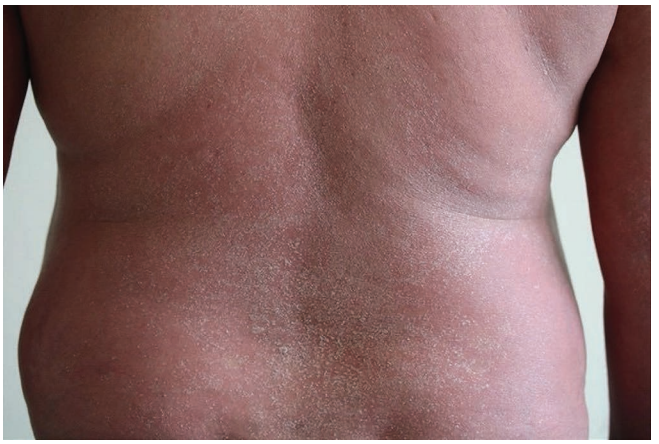


Figure 4.15 Erythroderma with bright red erythematous plaques covering the body.

Source: Courtesy of Istanbul Medeniyet University Dermatology Clinic.

Table 4.5 Clinical Clues to Possible Causes of Erythroderma

Disease	Scale of Skin Lesions	Early Involved Sites	Primary Lesion	Tips
Psoriasis	Diffuse Erythematous Thin or thick Pustular ponds	Groin and periumbilical regions in newborns Knee/elbow in adults	Papule Plaque Pustule	Typical nail findings History of psoriasis Existing psoriatic plaques
Pityriasis rubra pilaris	Bran-like Small husk-like Dry	Scalp, face, palmoplantar area	Follicular hyperkeratotic papules	Islands of sparing Thick, waxy keratoderma Nutmeg-grater-like lesions
Staphylococcal scalded skin syndrome	Exfoliation Perioral radial crust-fissures	Face and flexural folds	Erythema	Skin sensitivity Positive Nikolsky sign
Pemphigus foliaceus	Raised edges Cornflake-like	Seborrheic regions	Vesicle Bulla	Malodorous intertriginous areas Positive Nikolsky sign
Drug reactions	Exfoliation	Any location	All lesion types	Facial edema Purpuric rash Sudden onset
Seborrheic dermatitis	Yellow-colored Oily	Seborrheic regions	Papule Plaque	Frequent in Neonatal, HIV+ patients
Mycosis fungoides	Gray-colored	Hips Legs Bathing-suit distribution	Infiltrated plaque Nodule	Slow development Lymphadenopathy
Atopic dermatitis	Thin	Flexural regions in adults Face, extensor regions in children	Plaque	Flexural areas in children Pruritic intertriginous and groin areas in newborn
Crusted scabies	Hyperkeratotic Fine	Interdigital Finger and toe webs Wrists Periumbilical Periareolar Penis	Excoriated papule	Pruritus Excoriations Burrows

fungoides (MF). Drug etiology should be investigated in erythroderma with sudden onset; it typically improves rapidly after discontinuation of the offending agent. Cutaneous T-cell lymphomas and visceral malignancies should be considered in erythroderma that develops slowly over an extended duration of time.

Laboratory studies: Histopathologic examination frequently does not reveal the underlying cause. Commonly observed findings include perivascular dermal infiltration, acanthosis, hyperkeratosis, and parakeratosis. Direct immunofluorescence can be useful in determining whether there is an underlying bullous disease or connective tissue disorder. KOH, mineral oil, and gram-staining can be considered to look for possible infectious etiologies.

In the majority of patients, the levels of ESR and CRP are elevated. Anemia, leukocytosis, eosinophilia, and disturbances in serum protein levels and fluid electrolyte balance can be seen.

Necessary testing for malignancy should be checked if clinically indicated, including peripheral smear, chest radiography, and abdominal ultrasonography (USG).

Differential diagnosis: It is easy to diagnose erythroderma, but finding the underlying cause is not always easy. Help can be obtained from the patient's history, clinical presentation, histopathologic and immunofluorescent examination, and laboratory findings.

Management: Finding the responsible disease process is important for prompt treatment and follow-up. If the underlying cause can be detected, then the appropriate treatment should be initiated based on the diagnosis. If it is thought to result from drugs, then all potential culprits should be stopped, if possible. Because it is a severe condition, there should be a low threshold to hospitalize patients. The hemodynamics of patients should be checked, and fluid and electrolyte balance should be maintained. Wet dressings, topical corticosteroids, and moisturizers may be recommended. Oral antihistamines can have benefit for pruritus, and systemic antibiotics can be administered for secondary infections. Systemic corticosteroids, methotrexate, azathioprine, and phototherapy can be administered in idiopathic cases when there are no contraindications.

Course: Erythroderma often has high morbidity and mortality. Mortality often results from related causes, such as heart failure due to fluid–electrolyte imbalance, sepsis, and pneumonia from secondary infection. Response to treatment varies according to the underlying cause and time of initiation for treatment. In drug-related cases, discontinuation of the culprit can help to quicken recovery. In erythroderma that is secondary to malignancy, is necessary to identify and treat the underlying cause, but the erythroderma is generally more severe and progressive. Oftentimes, skin disease may progress parallel to the course of the underlying malignancy. Idiopathic erythroderma may recur. In recurrent cases, malignancy screening should be repeated.

FINAL THOUGHT

This is one of the frequent emergencies in dermatology. As soon as the cause of the disease is established, it is important to intervene and start treatment as soon as possible. Clues regarding the underlying primary disease must be reviewed in order to offer better treatment and prevent recurrence with necessary precautions.

ADDITIONAL READINGS

Bellinato F, Maurelli M, Gisondi P, et al. A systematic review of treatments for pityriasis lichenoides. J Eur Acad Dermatol Venereol. 2019;33:2039–2049.

Halper K, Wright B, Maloney NJ, et al. Characterizing disease features and other medical diagnoses in patients with pityriasis rubra pilaris. JAMA Dermatol. 2020:e203426.

Husein-ElAhmed H, Gieler U, Steinhoff M. Lichen planus: a comprehensive evidence-based analysis of medical treatment. J Eur Acad Dermatol Venereol. 2019;33:1847–1862.

Inamadar AC, Ragunatha S. The rash that becomes an erythroderma. Clin Dermatol. 2019;37:88–98.

Mahajan K, Relhan V, Relhan AK, et al. Pityriasis rosea: an update on etiopathogenesis and management of difficult aspects. Indian J Dermatol. 2016;61:375–384.

Rapalli VK, Waghule T, Gorantla S, et al. Psoriasis: pathological mechanisms, current pharmacological therapies, and emerging drug delivery systems. Drug Discov Today. 2020;25:2212–2226.

Roenneberg S, Biedermann T. Pityriasis rubra pilaris: algorithms for diagnosis and treatment. J Eur Acad Dermatol Venereol. 2018;32:889–898.

Rothe MJ, Bialy TL, Grant-Kels JM. Erythroderma. Dermatol Clin. 2000;18:405–415.

Svoboda SA, Ghamrawi RI, Owusu DA, et al. Treatment goals in psoriasis: which outcomes matter most? Am J Clin Dermatol. 2020;21:505–511.

Wolf R, Parish LC, Parish JL. Emergency Dermatology. 2nd ed. London: CRC Press; 2017.

5 Dermatitides

Allison Perz, Tara Jennings, Robert Duffy, and Warren Heymann

CONTENTS

Definition: The dermatitides are a group of eczematous disorders characterized by inflammation of the epidermis. They present clinically as a spectrum of acute, subacute, and chronic lesions, including pruritic vesicles, erythematous papules, and/or lichenified plaques (Table 5.1). While *eczema* is the preferred term in the United Kingdom, *dermatitis* is used in the United States.

ATOPIC DERMATITIS

Synonyms: Eczema

Definition: Atopic dermatitis (AD) is a complex immune-mediated skin disorder that presents with intense pruritus and, most commonly, erythematous, often-lichenified papules and plaques on the face and flexural surfaces of infants and children. The word *atopy* means strange.

Overview: The etiology of AD is complex and not yet fully elucidated. There is a strong genetic component with contributing environmental factors. AD is characterized by elevated IgE levels, impaired epidermal barrier function, immune dysregulation with an imbalance of suppressive and inflammatory T-cell subtypes, and alterations in the skin microbiome. Impaired skin barrier function, oftentimes due to mutations in the filaggrin protein, results in penetration of the stratum corneum by environmental irritants and allergens. This leads to an abnormal immune response and both acute and chronic inflammation. Transepidermal water loss aggravates the xerosis, and changes of the acid mantle result in abnormal cutaneous bacterial colonization. Intense pruritus leads to scratching and further impairment of the skin barrier, which puts patients at greater risk for skin infection, specifically with *Staphylococcus aureus*.

AD is part of the "atopic triad" of asthma, AD, and allergic rhinitis, which are thought to share similar hypersensitive immunologic etiology. AD typically presents first, followed by asthma in childhood and allergic rhinitis in adolescence. This is referred to as the *atopic march*. AD is also often comorbid with food allergies; however, the association between the two is unclear. Food allergies are generally not considered a cause or trigger of AD even when allergen-specific IgE tests are positive.

Clinical presentation: Patients typically present in infancy and childhood with pruritus and erythematous papules and plaques on the face and flexural surfaces, including the wrists, forearms, antecubital fossae, neck, and popliteal fossae. Infants are more likely to present with lesions on the face and extensor surfaces. Patients experience intense pruritus and typical rub and scratch their skin, which causes lesions to become excoriated. Chronic lesions of AD are often lichenified and may demonstrate post-inflammatory hyper- or hypopigmentation. In patients with darker skin tones, follicular papules may be the dominant morphology (Figures 5.1–5.4).

DOI: 10.1201/9781003105268-5

Table 5.1 Types of Dermatitis

Type	Synonyms	Age Group	Classic Clinical Findings	Distribution
Anogenital pruritus	Pruritus ani, pruritus vulvae	Adults	Erythema and lichenification with excoriation	Perineal, perianal, and genital skin
Ashy Dermatitis	Erythema dyschromicum perstans	Adults and children	Blue-grey macules and patches	Trunk, neck, and extremities
Atopic dermatitis	Atopic eczema	Children > Adults	Acute: Erythema, vesicles, weeping and crusting Subacute: Erythematous plaques or patches with overlying scale Chronic: Lichenified plaques with hyper/hypopigmentation	Infants: Face, scalp, extensor surfaces of extremities Children/ adults: Flexural aspects of extremities All ages: Generalized disease possible
Id reaction	Autoeczematization	Children and adults	Pruritic, erythematous papules, and/or vesicles	Extensor surfaces of the arms, face, trunk, and legs
Contact dermatitis	Occupational dermatitis	Children and adults	Well-demarcate, geometric erythema with weeping vesicles in the early stages and lichenification in chronic disease	Anywhere on the body
Dyshidrotic dermatitis	Pompholyx, palmoplantar eczema	Adults and children	Pruritic pustules	Hands and feet, particularly the lateral surfaces
Keratosis pilaris	Gooseflesh	Children, young adults > Adults	Small monomorphic skin-colored papules	Proximal arms and legs, buttocks
Lichen simplex chronicus	Circumscribed neurodermatitis	Adults	Well-demarcated leathery plaques of thickened skin with accentuated skin markings	Shins, scalp, nape, wrists, vulva, scrotum
Nummular dermatitis	Discoid eczema	Children and adults	Coin-shaped scaly plaques possibly with erosions or crusting	Trunk and extremities
Prurigo nodularis		Adults > children	Hyperpigmented to violaceous papules and nodules with scaling or crusted centers; the center of lesions is often excoriated and can appear dark gray or hypopigmented	Extremities > trunk
Seborrheic dermatitis		Children and adults	Erythematous, fine, greasy scaling patches and plaques	Scalp, eyebrows, nasolabial folds, chest, ears
Stasis dermatitis	Venous eczema, gravitational eczema	Adults	Erythematous, scaly, fissured patches and plaques that may demonstrate a “woody” edema and brown pigmentation secondary to hemosiderin deposition	Legs
Xerosis	Eczema craquelé, winter itch	Adults	Erythematous, polygonally cracked skin with horizonal and vertical fissuring	Trunk and extremities