
Springer

Berlin

Heidelberg

New York

Barcelona

Hong Kong

London

Milan

Paris

Singapore

Tokyo

G. Plewig • A.M. Kligman

ACNE and ROSACEA

3rd, Completely Revised and Enlarged Edition

With Contributions by
T. Jansen

With 216 Colored Plates



Springer

Prof. Dr. med. GERD PLEWIG
Ludwig-Maximilians-Universität München
Klinik und Poliklinik für Dermatologie und Allergologie
Klinikum München
D-80337 München
FRG

ALBERT M. KLIGMAN, M.D., Ph. D.
Department of Dermatology
University of Pennsylvania
226 Clinical Research Building
422 Curie Boulevard
Philadelphia, PA 19104-6142
USA

ISBN-13: 978-3-642-64096-4 e-ISBN-13: 978-3-642-59715-2
DOI: 10.1007/978-3-642-59715-2

Library of Congress Cataloging-in-Publication Data

Plewig, Gerd, 1939- Acne and rosacea / Gerd Plewig, Albert M. Kligman, in cooperation with Thomas Jansen -- 3rd, completely rev. and enl. ed. p. ; cm. Includes bibliographical references and index.

ISBN 3-540-66751-2 (hardcover : alk. paper)

1. Acne. 2. Rosacea. I. Kligman, Albert M., 1916- II. Jansen, Thomas, Dr. II. Title.

[DNLM: 1. Acne Rosacea--pathology. 2. Acne Rosacea--therapy. 3. Acne Vulgaris--pathology. 4. Acne Vulgaris--therapy. WR 430 P726a 2000] RL131 .P559 2000 616.5'3--dc21

This work is subject to copyright. All rights are reserved, whether the whole part of the material is concerned, specifically the rights of translation, reprinting, reuse of illustrations, recitation, broadcasting, reproduction on microfilm or in any other way, and storage in data banks. Duplication of this publication or parts thereof is permitted only under the provision of the German Law of September 9, 1965, in its current version, and permission for use must always be obtained from Springer-Verlag. Violations are liable for prosecution under the German Copyright Law.

Springer-Verlag is a company in the BertelsmannSpringer publishing group.

© Springer-Verlag Berlin Heidelberg 2000

Softcover reprint of the hardcover 1st edition 2000

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

Product liability: The publishers cannot guarantee the accuracy of any information about dosage and application contained in this book. In every individual case the user must check such information by consulting the relevant literature.

Production editor: W. Bischoff, Heidelberg

Cover design: de'blik Konzept & Gestaltung, Berlin

Data conversion: DTP by W. Bischoff

Printing and binding: Druckerei Stürtz, Würzburg

SPIN: 10708286 22/3134 - 5 4 3 2 1 0 - Printed on acid-free paper

Preface to the Third Edition

Twenty-five years have elapsed since the first publication of this book. The growth of basic knowledge since then has been both enormous and momentous. This has been a joyous enterprise for us. Our ability to treat acne and rosacea effectively has outpaced the vastly expanded understanding of their etiologies.

Acne today is not only an eminently treatable disease; in some cases, for example acne conglobata, it is actually curable. We think that no case is so severe as to be beyond help with the array of diverse drugs now available. Treatment failure is really physician failure. Prevention of acne in high-risk children has also become a promising possibility, now that it is possible to identify small comedones in prepuberty, as early as the age of 7 years. Topical comedolytic agents such as retinoids prescribed at the incipient stage might then prevent the evolution of the full-fledged disorder. This therapeutic maneuver could prevent the dreaded sequel of scarring.

We adhere firmly to the beliefs expressed in 1975 regarding our mission. This text is dedicated to the dermatologists and other practitioners who must diagnose and treat these disfiguring, remarkably protean, common disorders.

This is not a reference work for investigators, nor is it a scholarly review of the literature. The references we cite have been selected for their relevance to daily practice, for their educational worth, and for their readability. This called for a massive culling of the literally thousands of articles that have piled up in the past decades. We apologize to those authors whose contributions do not meet these particular qualifications.

A quote from the first edition epitomizes our current attitude: "We have sought to create a portfolio of still-life pictures of the gross and microscopic anatomy of acne (and rosacea). This will be a photographic record of what these maladies look like, their usual and unusual features, their archetypal as well as their recondite visages. We hope the reader will have the feeling of being in a theater, watching an unusual drama."

We declare forthwith that the views we present in respect to treatments are in the first place our own and much less constructed from the recommendations of other authorities. Some of our proposals will not meet the stringent requirements of what is now called evidence-based medicine. These are our best estimates, perhaps guesstimates, deriving from our long and concentrated experience. Since this is a practice-oriented text, we have taken on the hazardous responsibility of presenting our personal options and not the supernumerary alternatives which can be found throughout a contentious literature. The ambitious physician hoping to gain therapeutic speed by tapping into literature sources such as Medline or Internet is certain to become confused by the welter of divergent opinions.

On the other hand, we do not wish to pretend that no quandaries remain or that everything is as simple and straightforward as our didactic style might suggest.

There are so many acne-like and acneiform clinical pictures that diagnostic challenges are a commonplace. Then too, acne and rosacea frequently coexist with other disorders in overlapping mixtures. One has to consider how to deal with two or more diseases at the same time. For example, acne and rosacea may be present at the same time, one slowly disappearing, the other emerging. Furthermore, unpredictable fluctuations in the course of these chronic diseases can be maddening to the therapist.

We have said previously that the busy practitioner who does not have enough time for his patients should not take on patients with acne or rosacea. Listening is as important as looking. Even today, our better-educated patients hold a full bag of irrational folkloristic beliefs and myths which need to be dispelled. A good history is indispensable to understanding how the patient's disorder is impacting on the quality of life. The caring, compassionate physician will achieve more successful therapeutic outcomes for at least two reasons:

The placebo effect is prominent in these disorders. This explains why so many popular, unproved remedies seem to work. Even in properly controlled studies, it is astonishing how often the efficacy of the vehicle approaches that of the active drug. Psychological factors play an important, if often inscrutable, role in the response to treatment.

Showing a deep, empathetic interest engenders compliance with the therapeutic schedules, which are often uncomfortable and tiresome, and which interfere with other needs of daily life. Unlike some acute disorders, acne cannot be cured by one or two injections of a magic medicine. The best physician may have to keep changing his aim and therapeutic means.

We take pains to note some very important secular changes which have taken place in the last decades. Rosacea is steadily increasing among adult men and women and may last a lifetime – a dreadful prospect for many professional people. We speculate that these epidemiological changes reflect the environmental exposure and the impact of psychological forces that confront our patients.

Curiously, severe inflammatory acne, such as acne conglobata, seems to be on the wane. It is difficult to recruit such subjects for experimental studies. We suggest that this is the result of so many effective treatments such as oral isotretinoin and antibiotics.

Acne in black Afro-Americans has also come to the fore in the United States. It was formerly the conventional wisdom that acne was less common and less severe in blacks, expressed mainly as comedones. This turns out to be a misconception. The noticeable increase in acne among blacks is more apparent than real. Doctors who wrote and lectured about acne were white physicians who simply did not see black patients. With their increased access to medical care, it is becoming clear that acne is also a disease in blacks.

There has been much progress in the hormonal understanding and diagnosis of acne, with new syndromes arising. They have been included in this text.

Finally, there have been stunning advances in surgical interventions for the treatment of acne, especially in the end-stage of scars. Lasers have figured prominently in this development. Dermatologists have become masters in this field of surgery. It is outside the scope of this work to cover in detail these highly effective surgical treatments. The reader is referred to the most experienced authorities in this rapidly moving field.

Acne and rosacea are serious common diseases which can be ruinous to the quality of life in prosperous countries, where appearance is such a powerful force in psychosocial interactions. We bristle when third-party payers label acne a cosmetic problem, whose treatment they will not reimburse since they view acne as a mere nuisance rather than as an agonizing affliction.

We have written this book for those physicians who understand the deep sufferings of patients with chronic, disfiguring lesions of the face and body. We present herein the accumulated knowledge that will enable dedicated doctors to improve the quality of life for these long-suffering patients. Few disorders are more rewarding to treat.

GERD PLEWIG
ALBERT M. KLIGMAN

To
Helga and Lori,
two exceptional
women

Contents

| | |
|---|-----|
| History of Acne and Rosacea | 1 |
| Acne | |
| Etiology, Pathophysiology, and Nosology of Acne | 25 |
| Prevalence | 27 |
| A Précis of Pathogenesis | 28 |
| Anatomy of Follicles | 30 |
| Epidermal Lipids | 50 |
| Sebaceous Glands | 57 |
| Anatomy of Sebaceous Glands | 57 |
| Physiology of Sebaceous Glands | 58 |
| Micro-organisms | 83 |
| Cocci | 83 |
| Yeasts | 83 |
| Propionibacteria | 84 |
| Endocrinology of Acne | 96 |
| The Evolution of the Comedo | 99 |
| Dynamics of Primary Comedo Formation | 103 |
| Dynamics of Secondary Comedo Formation | 111 |
| Cysts | 111 |
| Fistuled Polyporous Comedones | 112 |
| Draining Sinuses | 112 |
| Dynamics of Inflammation | 146 |
| Inflammatory Lesions and Sequels | 149 |
| Pustules | 149 |
| Papules | 150 |
| Nodules | 150 |
| Draining Sinuses | 150 |
| Scope of Scars | 194 |
| Pitted, Crateriform, and Ice-Pick Scars | 194 |
| Atrophic Scars | 194 |
| Hypertrophic Scars | 194 |
| Perifollicular Papular Scars | 195 |
| Calcified Scars | 195 |
| Keloids | 195 |
| Fistulated Scars (Polyporous Comedones) | 196 |

| | |
|--|------------|
| Draining Sinus | 196 |
| Classification of Acne | 245 |
| Models of Acne | 251 |
| Acne in Animals: Canine and Feline Acne | 253 |
| Animal Models | 254 |
| Syrian Hamster | 254 |
| Rabbit Ear | 258 |
| Rhino Mouse | 265 |
| Human Sebocyte Cultures | 268 |
| The Acnes | 269 |
| Acne in Childhood | 271 |
| Acne Neonatorum | 271 |
| Acne Infantum | 271 |
| Acne Conglobata Infantum | 272 |
| Acne Venenata Infantum | 272 |
| Steroid Acne in Infants | 273 |
| Hippie Acne, Lip Balm Acne, McDonald Acne, and Kelp-Acne . . . | 273 |
| Chloracne in Children | 273 |
| Fetal Hydantoin Syndrome | 274 |
| Androluteoma Syndrome of Pregnancy | 274 |
| Acne in Puberty and Adulthood | 280 |
| Acne Comedonica (Comedonal Acne) | 280 |
| Acne Papulopustulosa (Papulopustular Acne) | 287 |
| Acne Conglobata | 294 |
| Acne Inversa | 309 |
| Acne Fulminans | 342 |
| SAPHO Syndrome | 352 |
| Solid Facial Persistent Edema in Acne | 354 |
| Acne Mechanica | 356 |
| Back Acne | 361 |
| Acne Tropicalis (Tropical Acne) | 363 |
| Postadolescent Acne in Women | 365 |
| Premenstrual Acne | 368 |
| Perimenopausal and Postmenopausal Acne | 369 |
| Polycystic Ovary Syndrome and SAHA Syndrome | 370 |
| Congenital Adrenal Hyperplasia | 374 |
| Cushing Syndrome | 376 |
| Androgen Excess | 377 |
| XYY Acne Conglobata | 377 |
| Body-Building Acne (Doping Acne) | 380 |

| | |
|---|------------|
| Excoriations..... | 381 |
| Acne Venenata..... | 385 |
| Occupational Acnes..... | 385 |
| Lip Balm Acne..... | 392 |
| Acne Cosmetica..... | 393 |
| Pomade Acne..... | 399 |
| Chloracne..... | 400 |
| Solar Comedones (Favre-Racouchot Disease)..... | 420 |
| Acne Aestivalis (Mallorca Acne)..... | 421 |
| Radiation-induced Comedones..... | 424 |
| | |
| Genetic Syndromes Associated with Acne or Acne-like Disorders..... | 425 |
| PAPA Syndrome..... | 425 |
| Ectrodactyly, Soft-tissue Syndactyly, and Nodulocystic Acne..... | 425 |
| Apert Syndrome..... | 425 |
| Familial Dyskeratotic Comedones..... | 428 |
| Haber Syndrome..... | 428 |
| Acne-free Nevus and Clonal Acne..... | 429 |
| Atrophoderma Vermiculata..... | 430 |
| | |
| Acneiform Diseases..... | 431 |
| Acneiform Eruptions..... | 432 |
| Steroid Acne..... | 440 |
| Amineptine Acne..... | 449 |
| Ecstasy Pimples..... | 454 |
| | |
| Rosacea | |
| Rosacea..... | 456 |
| Prevalence..... | 456 |
| Etiology and Pathogenesis..... | 456 |
| Clinical Findings..... | 459 |
| Histopathology..... | 465 |
| Laboratory Findings..... | 465 |
| Differential Diagnosis..... | 465 |
| Treatment..... | 466 |
| Topical..... | 466 |
| Systemic..... | 468 |
| Miscellaneous..... | 474 |
| Special Treatment Cases..... | 476 |

Acne-like Disorders

| | |
|---|-----|
| Perioral Dermatitis | 504 |
| <i>Demodex folliculorum</i> | 507 |
| Gram-negative Folliculitis | 513 |
| Necrotizing Lymphocytic Folliculitis (Acne Necrotica) | 525 |
| Sebaceous Gland Hyperplasia | 531 |
| Steatocystoma Multiplex | 537 |
| Steatocystoma Simplex. | 542 |
| Eruptive Vellus Hair Cysts | 543 |
| Nevus Comedonicus. | 545 |
| Dilated Pore. | 548 |
| Pilar Sheath Acanthoma | 549 |
| Omphalolith: The Ugly Navel Stone | 553 |
| Keratosis Pilaris. | 554 |
| Pseudofolliculitis Barbae | 555 |
| Osteoma Cutis. | 559 |
| Minocycline-induced Hyperpigmentation | 564 |

Treatment of Acne

| | |
|--|-----|
| History of Therapy: Post, Present and Future | 579 |
| Strategic Approaches to the Treatment of Acne | 581 |
| Diet. | 581 |
| Cleanliness. | 582 |
| Scalp Care | 583 |
| External Contactants | 583 |
| Emotions and Psychosomatic Factors. | 583 |
| How to Approach Acne. | 584 |
| Selection of Therapy. | 586 |
| Appraisal of Efficacy. | 586 |
| Topical Treatment | 589 |
| Tretinoin (all- <i>trans</i> -Retinoic Acid, Vitamin A Acid) | 589 |
| Other Topical Retinoids | 609 |
| Benzoyl Peroxide. | 611 |
| Topical Antibacterial Agents | 622 |
| Azelaic Acid. | 626 |
| Fusidic Acid. | 627 |
| Nicotinamide. | 628 |
| Salicylic Acid. | 629 |
| Systemic Treatment. | 634 |
| Antibiotics: Tetracyclines and Macrolides | 634 |
| Isotretinoin (13- <i>cis</i> -Retinoic Acid). | 649 |
| Vitamin A (Retinol) | 679 |
| Sulfonamides. | 680 |
| Sulfones | 681 |

| | |
|---|-----|
| Estrogens and Oral Contraceptives | 683 |
| Antiandrogens and Aldosterone Antagonists | 685 |
| 5 α -Reductase Inhibitors | 689 |
| Corticosteroids | 694 |
| Zinc | 696 |
| Physical Therapy | 697 |
| Ultraviolet Radiation | 697 |
| Cryotherapy | 698 |
| Abrasives | 699 |
| Chemical Peels | 703 |
| Lasers | 704 |
| | |
| Miscellaneous | |
| X-Ray Therapy: A Historical Note | 706 |
| Dermabrasion | 707 |
| Excision | 710 |
| Punch-Graft Elevation or Punch-Graft Transplant | 711 |
| Dermal Filler Substances: Collagen | 714 |
| Camouflage | 723 |
| Psychosocial Aspects of Acne | 727 |
| Spontaneous Involution of Acne | 731 |
| | |
| Subject Index | 733 |

Acknowledgements

Many highly skilled professionals have generously helped us to create this book. Our gratitude for their superb collaboration is acknowledged herewith. Our thanks are small recompense for their contributions.

We are especially grateful to the following colleagues, friends, and partners: Dr. THOMAS JANSEN, Department of Dermatology, Ludwig-Maximilians-University of Munich, has been indispensable in creating this third edition. He has added new chapters and has meticulously revised the entire text to spot erroneous statements. He is a specialist for sebaceous gland disorders, and without his expert advice the publication of this book would not have been possible.

Mr. PETER BILEK, a master of photography, Department of Dermatology, Ludwig-Maximilians-University of Munich.

Mr. WILFRIED NEUSE, photodesigner and enthusiastic artist with the camera, Department of Dermatology, Heinrich-Heine-University of Düsseldorf.

Prof. Dr. HELMUT H. WOLFF, Lübeck, Germany, and Miss. ELFRIEDE JANUSCHKE, Department of Dermatology, Ludwig-Maximilians-University of Munich, who contributed exquisitely beautiful examples of transmission electron microscopy. Mrs. GUDRUN KUTTER, Munich, a free-lance graphic designer, who from the very start has been extremely helpful with the artwork and reproduction of all illustrations. She contributed beautiful illustrations.

Mrs. CORNELIA HOFFMANN, Munich, a dedicated librarian, helped with the organization and citation of the historical bibliography.

The clinical photographs and the electron-microscopical pictures were superbly reproduced by Bros. CZECH & PARTNERS, a Munich offset company.

The histopathology plates were expertly set by REPRO TEAM PLC, a Munich lithographic studio.

Mrs. BRIGITTE FINGERHUTH and Dr. NANA MOSLER, Springer-Verlag Heidelberg, skillfully managed the printing of this book.

Mr. WILLI BISCHOFF, Springer-Verlag Heidelberg, once again expertly handled the many details during the preparation of the manuscript and the production of this book.

Mr. GERD GROSSMANN and Mrs. MARJA R. KALEVA, Galderma Laboratory, Freiburg, Germany, provided ample funding to support the many costly color photographs.

Many colleagues throughout the world allowed us to use their illustrations. They are acknowledged in the legends to the plates.

Finally, we acknowledge our indebtedness to a corps of collaborators who shared their thoughts with us on innumerable occasions. They are too numerous to name.

GERD PLEWIG, Munich

ALBERT M. KLIGMAN, Philadelphia