A comprehensive, in-depth monograph such as this focused entirely on the subject of the cutaneous manifestations of lupus erythematosus (LE) is long overdue!

LE is increasingly being recognized as a more common autoimmune disorder than was previously thought, and the cutaneous manifestations of LE are among the most common clinical features of LE at its onset and throughout its course. The most commonly recognized environmental risk factor for LE, ultraviolet light exposure from sunlight and artificial sources, necessarily transduces its disease-exacerbating effect through the skin. Cutaneous LE can be a significant contributor to psychosocial and occupational disability. In addition, the universally recognized symbols of LE – the butterfly and the wolf – relate to different cutaneous manifestations of LE.

Yet, the skin has been the least well-studied organ system that is affected by LE. This has resulted from the relative “invisibility” of the skin and skin disease to non-dermatologists who deal with patients with LE. After all, “it’s only a rash.” Perhaps this would be less of a problem if nondermatologist physicians were better trained in the principles and practice of recognizing and managing skin diseases during their formal medical education. Also, contributing to this is the fact that expert management of LE and rheumatic skin disease in general are at risk of being lost from the dermatologist’s repertoire in some parts of the world, including the United States.

However, to a relatively small subset of academic dermatologists who subspecialize in the cutaneous manifestations of LE, the protean changes that can occur in the skin of patients with LE can be both fascinating and daunting. How a single disease process plays out so many different themes in a single organ system is truly amazing! This matrix becomes even more complex when one considers the relationships that exist between the various morphologic varieties of skin change in patients with LE and the various systemic manifestations of LE. Much is yet to be learned in this area!

We are indeed fortunate that Drs. Kuhn, Lehmann, and Ruzicka have assembled a highly experienced and expert group of individuals to address the various subjects presented in this monograph. From my perspective, this has been a wonderful, soup-to-nuts tour of our current understanding of all major aspects of LE skin disease. It is my hope that this effort will catalyze further thought and progress in this area.

Iowa City, Iowa, USA

Richard D. Sontheimer

June 2004
Lupus erythematosus (LE) is a chronic inflammatory autoimmune disease characterized by a wide spectrum of manifestations and a variable evolution. The skin is one of the most frequent sites of involvement, and thus it has long been central to the conceptual framework that physicians have used to deal with this disease. During the past few decades, the mechanisms of cutaneous LE have been under active investigation, and many clinicians and scientists around the world have spent considerable time studying the cutaneous manifestations of this disease. This research has led to the identification of subsets of LE defined by constellations of clinical and photobiological features, histologic and immunopathologic changes, and laboratory abnormalities. Besides the classic forms such as subacute cutaneous LE and discoid LE, there are uncommon variants that often lead to diagnostic difficulties. Therefore, there has long been a need for a book on the cutaneous manifestations of LE that provides not only a comprehensive description of the great variety of cutaneous abnormalities but also a synthesis of our knowledge of the relationship between cutaneous and systemic changes. Furthermore, the cutaneous manifestations of this disease are a reflection of very specific and also nonspecific immunopathologic events along with inflammatory responses, and major progress has been made in recent years in our knowledge of the skin as an immunologic organ. Many advances have also been made in understanding the induction of skin lesions of LE by ultraviolet light combined with alterations in selectins and adhesion molecules contributing to the accumulation of inflammatory cells in this disease. Animal models of LE have further provided insight into the contributing roles of various T-cell subsets. In addition, the management of cutaneous manifestations of LE is challenging, and although conventional topical and systemic therapy exists new treatment options have been introduced for patients with resistant disease.

_Cutaneous Lupus Erythematosus_ is written by leading clinicians and scientists in a multidisciplinary effort and includes chapters on the clinical aspects, pathologic characteristics, and management of this disease. The combination of the latest clinical and scientific data supplemented with colour reproductions of the clinical and pathologic changes of the skin provides a comprehensive summary of information on cutaneous LE. This book acquaints dermatologists, rheumatologists, and general physicians with the skin manifestations of LE, and we further hope that _Cutaneous Lupus Erythematosus_ will be a valuable resource for all clinicians who diagnose, treat, and manage patients with this disease. The editors would like to thank all authors for their significant contribution to accomplish this book. In addition, the editors dedicate this book to the memory of their mentor, colleague, and friend Dr. Günther...
Goerz, Professor of Dermatology, University of Düsseldorf, Germany, who taught them that LE is exciting, complex, and worth spending a lifetime studying.

Düsseldorf and Wuppertal, Germany
June 2004

Annegret Kuhn
Percy Lehmann
Thomas Ruzicka
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Andrade, Felipe, M.D., Ph.D.
Instituto Nacional de Ciencias
Medicas y Nutricion “Salvador Zubiran”
Department of Immunology
and Rheumatology
Vasco de Quiroga 15
Mexico, D. F. 14000
Mexico

Bacman, David, M.D.
University of Düsseldorf
Department of Dermatology
Moorenstraße 5
40225 Düsseldorf
Germany

Beissert, Stefan, M.D.
University of Münster
Department of Dermatology
Von-Esmarch-Straße 58
48149 Münster
Germany

Callen, Jeffrey P., M.D.
University of Louisville
School of Medicine
Department of Dermatology
310 East Broadway, Suite 200
Louisville KY 40202
USA

Casciola-Rosen, Livia A., Ph.D.
John Hopkins University
School of Medicine
Departments of Medicine and Dermatology
5200 Eastern Avenue
Baltimore, Maryland 21224
USA

Cervera, Ricard, M.D.
University of Barcelona
Hospital Clinic
Department of Autoimmune Diseases
Villarroel, 170
08036 Barcelona, Catalonia
Spain

Cuadrado, Maria J., M.D., Ph.D.
St. Thomas Hospital
The Rayne Institute
Lupus Research Unit
London SE1 7EH
United Kingdom

Flaig, Michael J., M.D.
Ludwig-Maximilians-University
Department of Dermatology
Frauenlobstraße 9–11
80337 München
Germany

Font, Josep, M.D.
University of Barcelona
Hospital Clinic
Department of Autoimmune Diseases
Villarroel, 170
08036 Barcelona, Catalonia
Spain

Fritsch, Peter, M.D.
University of Innsbruck
Department of Dermatology
Anichstraße 35
6020 Innsbruck
Austria
FURUKAWA, FUKUMI, M.D., PH.D
Wakayama Medical University
Department of Dermatology
811-1 Kimiidera
Wakayama 641-0012
Japan

HERNDON, THOMAS M., M.D.
Walter Reed Army Institute of Research
Department of Cellular Injury
Robert Grand Road, Building 503
Silver Spring, Maryland 20307-5100
USA

INGELMO, MIGUEL, M.D.
University of Barcelona
Hospital Clinic
Department of Autoimmune Diseases
Villarroel, 170
08036 Barcelona, Catalonia
Spain

JIMÉNEZ, SONIA, M.D.
University of Barcelona
Hospital Clinic
Department of Autoimmune Diseases
Villarroel, 170
08036 Barcelona, Catalonia
Spain

KARIM, YOUSUF, MRCP, MRCPath
St. Thomas Hospital
Department of Immunology
London SE1 7EH
United Kingdom

KIND, PETER, M.D.
Hautarztpraxis
Kleiner Biergrund 31
63065 Offenbach
Germany

KUHN, ANNEGRET, M.D.
University of Düsseldorf
Department of Dermatology
Moorenstraße 5
40225 Düsseldorf
Germany

LEE, LELA A., M.D.
University of Colorado
School of Medicine
Denver Health Medical Center
Department of Dermatology
660 Bannock Street
Denver, Colorado 80204
USA

LEHMANN, PERCY, M.D.
University of Witten-Herdecke
HELIOS Klinikum Wuppertal
Department of Dermatology
Arrenberger Straße 20
42117 Wuppertal
Germany

LUGER, THOMAS A., M.D.
University of Münster
Department of Dermatology
Von-Esmarch-Straße 58
48149 Münster
Germany

MEHLING, ANNETTE, PH.D
Cognis Deutschland GmbH and Co. KG
Henkelstrasse 67
40551 Düsseldorf
Germany

MEURER, MICHAEL, M.D.
University of Dresden
Department of Dermatology
Fetscherstraße 74
01307 Dresden
Germany

MILLARD, THOMAS P., M.D.
Gloucester Royal Hospital
Department of Dermatology
Gloucester, GL1 3NN
United Kingdom

NYBERG, FILIPPA, M.D., PH.D.
Danderyds Hospital
Department of Dermatology
18288 Stockholm
Sweden
List of Contributors

OCHSENDORF, Falk R., M.D.
University of Frankfurt
Department of Dermatology
Theodor-Stern-Kai 7
60590 Frankfurt
Germany

ORFANOS, Constantin E., M.D.
The Free University of Berlin
University Medical Center Benjamin Franklin
Department of Dermatology
Fabeckstraße 60-62
14195 Berlin
Germany

PRAMATAROV, Kyrill, M.D., Ph.D.
Medical University
Department of Dermatology
1, G. Sofiiski Street
1431 Sofia
Bulgaria

PROVOST, Thomas T., M.D.
P.O. Box 230
Milton, Delaware 19968
USA

ROSEN, Antony, M.D.
John Hopkins University
School of Medicine
Departments of Medicine, Cell Biology and Anatomy
5200 Eastern Avenue
Baltimore, Maryland 21224
USA

ROSENBAUM, Michele L., M.D.
University of Pennsylvania
School of Medicine
Department of Dermatology
2 Rhoads Pavilion, 36th and Spruce Sts.
Philadelphia, Pennsylvania 19104
USA

RUZICKA, Thomas, M.D.
University of Düsseldorf
Department of Dermatology
Moorenstraße 5
40225 Düsseldorf
Germany

SANDER, Christian A., M.D.
AK St. Georg
Department of Dermatology
Lohmühlenstrasse 4
20099 Hamburg
Germany

SCHNEIDER, Matthias, M.D.
University of Düsseldorf
Department of Rheumatology
Moorenstraße 5
40225 Düsseldorf
Germany

SCHNEIDER, Stefan W., M.D.
University of Münster
Department of Dermatology
Von-Esmarch-Straße 58
48149 Münster
Germany

SCHWARZ, Thomas, M.D.
University of Schleswig-Holstein
Campus Kiel
Department of Dermatology
Schittenhelmstrasse 7
24105 Kiel
Germany

SHINADA, Shuntaro, M.D.
University of Southern California Medical Center
Los Angeles County
1200 North State Street
Los Angeles, California 90033
USA

SONTHEIMER, Richard D., M.D.
University of Iowa
Carver College of Medicine
Department of Dermatology
200 Hawkins Dr. 2045BT-1
Iowa City, Iowa 52242-1090
USA

SPECKER, Christoph, M.D.
University of Düsseldorf
Department of Rheumatology
Moorenstraße 5
40225 Düsseldorf
Germany
Stephansson, Eija, M.D., Ph.D.
Karolinska Hospital Stockholm
Department of Dermatology
17176 Stockholm
Sweden

Sticherling, Michael, M.D.
University of Leipzig
Department of Dermatology
Stephanstraße 11
04103 Leipzig
Germany

Tebbe, Beate, M.D.
Praxis für Dermatologie und Allergologie
Hohenzollernstraße 91
14199 Berlin
Germany

Tsankov, Nikolai, M.D.
Medical University
Department of Dermatology
1, G. Sofiiski Street
1431 Sofia
Bulgaria

Tsokos, George C., M.D.
Walter Reed Army Institute of Research
Department of Cellular Injury
Robert Grand Road, Building 503
Silver Spring, Maryland 20307-5100
USA

Uetrecht, Jack, M.D., Ph.D.
University of Toronto
Faculty of Pharmacy
19 Russell Street
Toronto, M4G 3L5
Canada

von Mikecz, Anna, Ph.D.
University of Düsseldorf
Institut für Umweltmedizinische Forschung
Auf’m Hennekkamp 50
40225 Düsseldorf
Germany

Wallace, Daniel J., M.D.
Cedars Sinai Medical Center
UCLA School of Medicine
8737 Beverly Blvd., Suite 203
Los Angeles, California 90048
USA

Weber, Florian, M.D.
University of Innsbruck
Department of Dermatology
Anichstraße 35
6020 Innsbruck
Austria

Werth, Victoria P., M.D.
University of Pennsylvania
School of Medicine
Department of Dermatology
2 Rhoads Pavilion, 36th and Spruce Sts.
Philadelphia, Pennsylvania 19104
USA

Wetzl, Stefan, M.D.
Ludwig-Maximilians-University
Department of Dermatology
Frauenlobstraße 9–11
80337 München
Germany

Wollenberg, Andreas, M.D.
Ludwig-Maximilians-University
Department of Dermatology
Frauenlobstraße 9–11
80337 München
Germany

Yazdi, Amir S., M.D.
Ludwig-Maximilians-University
Department of Dermatology
Frauenlobstraße 9–11
80337 München
Germany
Abbreviations

ACA = anticardiolipin antibody
ACLE = acute cutaneous lupus erythematosus
ACR = American College of Rheumatology
ADCC = antibody-dependent cellular cytotoxicity
ANA = antinuclear antibody
APC = antigen-presenting cell
APS = antiphospholipid syndrome
ARA = American Rheumatism Association
BCR = B-cell receptor
BLE = bullous lupus erythematosus
CCLE = chronic cutaneous lupus erythematosus
cDNA = complementary DNA
CHLE = chilblain lupus erythematosus
CHS = contact hypersensitivity
CI = confidence interval
CLE = cutaneous lupus erythematosus
CR = complement receptor
cs = corticosteroids
CTLA-4 = cytotoxic T-lymphocyte activation molecule-4
DC = dendritic cell
DEJ = dermoepidermal junction
DIF = direct immunofluorescence
DLE = discoid lupus erythematosus
DM = dermatomyositis
ds-DNA = double-stranded DNA
DTH = delayed-type hypersensitivity
EADV = European Academy of Dermatology and Venereology
EBV = Epstein-Barr virus
ELISA = enzyme-linked immunosorbent assay
EM = erythema multiforme
ESR = erythrocyte sedimentation rate
FasL = Fas ligand
FITC = fluorescein isothiocyanate
G-6-PD = glucose-6-phosphate dehydrogenase
GC = glucocorticoid
GVH = graft-vs-host
XLVI  Abbreviations

HLA = human leukocyte antigen
HUUVS = hypocomplementemic urticarial vasculitis
ICAM-1 = intercellular adhesion molecule-1
ICLE = intermittent cutaneous lupus erythematosus
IFN = interferon
IL = interleukin
iNOS = inducible nitric oxide synthase
IPF = immune protection factor
LAT = linker for activation of T cells
LBT = lupus band test
LE = lupus erythematosus
LEP = lupus erythematosus profundus
LET = lupus erythematosus tumidus
LFA-1 = lymphocyte function-associated antigen-1
LFT = liver function test
LP = lichen planus
MHC = major histocompatibility complex
MMF = mycophenolate mofetil
MNC = mononuclear cell
MPF = mutation protection factor
mRNA = messenger RNA
NFAT = nuclear factor of activated T cell
NKT = natural killer cell
NLE = neonatal lupus erythematosus
NZB = New Zealand Black
NZW = New Zealand White
OR = odds ratio
PABA = p-aminobenzoic acid
p-ANCAs = antineutrophil cytoplasmic antibodies with a perinuclear pattern
PCT = porphyria cutanea tarda
PDC = plasmacytoid dendritic cell
PPD = purified protein derivative
PS = phosphatidylserine
PLE = polymorphous light eruption
PNM = papular and nodular mucinosis
RAR = retinoid acid receptors
REM = reticular erythematosus mucinosis
RES = reticuloendothelial system
RoRNP = Ro ribonucleoprotein
RXR = retinoid x receptors
SBC = sunburn cell
SCID = severe combined immunodeficient
SCLE = subacute cutaneous lupus erythematosus
SLAM = Systemic Lupus Activity Measure
SLE = systemic lupus erythematosus
SLEDAI = Systemic Lupus Erythematosus Disease Activity Index
snRNP = small nuclear ribonucleoprotein
SS = Sjögren’s syndrome
ss-DNA = single-stranded DNA
T4N5 = T4 endonuclease V
TCR = T-cell receptor
Th1 = T helper 1
Th2 = T helper 2
TNF = tumor necrosis factor
UV = ultraviolet
VCAM-1 = vascular adhesion molecule-1
VSV = vesicular stomatitis virus
Part I
Introduction