

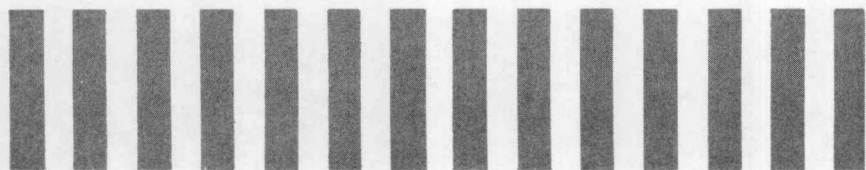
Dermato- toxicology

third edition

Francis N. Marzulli
Howard I. Maibach

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edited by

Francis N. Marzulli
National Research Council

Howard I. Maibach
*University of California
San Francisco Medical Center*



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contributors

Robert B. Armstrong, M.D.
Department of Dermatology, Columbia University, College of Physicians and Surgeons, 630 West 168th Street, New York, New York 10032

Susan M. Barlow, Ph.D.
Department of Health and Social Security, Hannibal House, Elephant and Castle, London SE1 6TE, U.K.

Monica C. Bischoff
Associate, Institute of Neurotoxicity, Albert Einstein College of Medicine, 1300 Morris Park Avenue, Bronx, New York 10461

Fred G. Bock, Ph.D.
Papanicolaou Comprehensive Cancer Center, 1155 N.W. 14th Street, Miami, Florida 33136

Robert L. Bronaugh, Ph.D.
Dermal and Ocular Toxicology Branch, Food and Drug Administration, 200 C Street, S.W., Washington, D.C. 20204

Edwin V. Buehler, Ph.D.
Hill Top Research, Inc., Cincinnati, Ohio 45242

Allen G. Collins, M.B., F.R.A.C.P., F.A.C.D.
52 Gurwood Street, Wagga Wagga, New South Wales 2650, Australia

†K. D. Crow, M.D.
Wiltshire Area Health Authority, Swindon Health District, Princess Margaret Hospital, Okus Road, Swindon SN1 4JU, England

Paul H. Dugard, Ph.D.
Central Toxicology Laboratory, Imperial Chemical Industries Limited, Alderly Park, Cheshire, England

Henry F. Edelhauser, Ph.D.
Department of Ophthalmology, Medical College of Wisconsin, Milwaukee, Wisconsin 53201

John H. Epstein, M.D.
Department of Dermatology, University of California, San Francisco Medical Center, 3rd Avenue and Parnassus, San Francisco, California 94143

†Deceased.

Gerald A. Gellin, M.D.

Department of Dermatology, University of California, San Francisco Medical Center, 3rd Avenue and Parnassus, San Francisco, California 94143

Albert Giles, Jr., B.S.

Division of Toxicology, Food and Drug Administration, 200 C Street, S.W., Washington, D.C. 20204

Richard D. Granstein, M.D.

Department of Dermatology, Massachusetts General Hospital, Boston, Massachusetts 02114

Leonard C. Harber, M.D.

Department of Dermatology, Columbia University, College of Physicians and Surgeons, 630 West 168th Street, New York, New York 10032

J. W. Hiddemen, Ph.D.

Alcon Laboratories, Fort Worth, Texas 76101

Niels Hjorth, M.D.

Department of Dermatology, Gentofte Hospital, DK-2900 Hellerup, Copenhagen, Denmark

W. E. Howe, Ph.D.

Alcon Laboratories, Fort Worth, Texas 76101

Kays Kaidbey, M.D.

Department of Dermatology, University of Pennsylvania, School of Medicine, 34th at Spruce, Philadelphia, Pennsylvania 19104

Georg Klecak, M.D.

Department of Biological and Pharmaceutical Research, F. Hoffman-La Roche & Company, Ltd., Basle, Switzerland

Albert M. Kligman, M.D.

Department of Dermatology, University of Pennsylvania, School of Medicine, 34th at Spruce, Philadelphia, Pennsylvania 19104

Andrija Kornhauser, Ph.D.

Division of Toxicology, Food and Drug Administration, 200 C Street, S.W., Washington, D.C. 20204

Arthur H. McCreesh, Ph.D.

U.S. Army Environmental Hygiene Agency, Toxicology Division, Aberdeen Proving Ground, Maryland 21010

T. O. McDonald, Ph.D.

Alcon Laboratories, Fort Worth, Texas 76101

Bertil Magnusson, M.D.

Department of Dermatology, University of Lund, Malmo, Sweden

H. C. Maguire, Jr., M.D.

Dermatology Department, Hahnemann Medical College, 230 North Broad, Philadelphia, Pennsylvania 19102

Howard I. Maibach, Ph.D.

Department of Dermatology, University of California, San Francisco Medical Center, 3rd Avenue and Parnassus, San Francisco, California 94143

Francis N. Marzulli, Ph.D.

National Research Council, 2101 Constitution Avenue, N.W., Washington, D.C. 20418

C. G. Toby Mathias, M.D.

Department of Dermatology, University of California, San Francisco Medical Center, 3rd Avenue and Parnassus, San Francisco, California 94143

Torkil Menné, M.D.

Department of Dermatology, Gentofte Hospital, DK-2900 Hellerup, Copenhagen, Denmark

John E. Milner, M.D.

Department of Environmental Health, SC-34, School of Public Health and Community Medicine and Department of Dermatology, School of Medicine, University of Washington, 1959 N.E. Pacific, Seattle, Washington 98195

Elvin A. Newmann

Procter & Gamble Company, Miami Valley Laboratories, Cincinnati, Ohio 45247

Alan W. Nichol, Ph.D.
*Riverina-Murray Institute of Higher
Education, Wagga Wagga,
New South Wales 2650, Australia*

Patrick K. Noonan, Ph.D.
*Pharmacokinetics and Drug Metabolism,
Key Pharmaceuticals, 4400 Biscayne Blvd.,
Miami, Florida 33137*

Darien Parker, Ph.D.
*Department of Pathology,
Royal College of Surgeons of England,
Lincoln's Inn Fields,
London WC2A 3PN, U.K.*

Ronald D. Parker
*Procter & Gamble Company,
Miami Valley Laboratories,
Cincinnati, Ohio 45247*

Madli Puhvel, Ph.D.
*Division of Dermatology, Department of
Medicine, UCLA School of Medicine,
Los Angeles, California 90024*

John R. T. Reeves, Ph.D.
*University of California, San Francisco
Medical Center 3rd Avenue and Parnassus,
San Francisco, California 94143*

S. M. Robertson, Ph.D.
*Alcon Laboratories,
Fort Worth, Texas 76101*

Edward L. Rongone, M.D.
*Department of Biochemistry, Creighton
University School of Medicine, 24th and
California, Omaha, Nebraska 68131*

Van Seabaugh, M.A.
*Consumer Product Safety Commission,
200 C Street, S.W., 5th Floor, Washington,
D.C. 20204*

John A. Shaddock, Ph.D.
*Department of Pathology, University
of Texas, Southwestern Medical School,
Dallas, Texas 75235*

Alan R. Shalita, M.D.
*Division of Dermatology, State University
of New York, Downstate Medical School,
New York, New York 11203*

Arthur J. Sober, M.D.
*Department of Dermatology, Massachusetts
General Hospital, Boston, Massachusetts
02114*

Peter S. Spencer, Ph.D.
*Institute of Neurotoxicology, Albert Einstein
College of Medicine, 1300 Morris Park
Avenue, Bronx, New York 10461*

Marshall Steinberg, Ph.D.
*Hazleton Laboratories America, Inc., 9200
Leesburg Pike, Vienna, Virginia 22180*

J. L. Turk, Ph.D.
*Department of Pathology,
Royal College of Surgeons of England,
Lincoln's Inn Fields,
London WC2A 3PN, U.K.*

Frederick Urbach, M.D.
*Center for Photobiology, Temple University
School of Medicine, 3401 North Broad,
Philadelphia, Pennsylvania 19140*

Geo von Krogh, M.D.
*Department of Dermatology, University of
California, San Francisco Medical Center,
3rd Avenue and Parnassus, San Francisco,
California 94143*

Wayne Wamer, B.S.
*Division of Toxicology, Food and Drug
Administration, 200 C Street, S.W.,
Washington, D.C. 20204*

Ronald C. Wester, Ph.D.
*Department of Dermatology, University of
California, San Francisco Medical Center,
3rd Avenue and Parnassus, San Francisco,
California 94143*

preface

This edition contains most of the material from the two previous editions as well as new chapters, updated references, and other materials. Among the new chapters is one that provides introductory information on skin hypersensitivity. It precedes nine chapters on special aspects of this subject. We have also included a chapter on reproductive hazards from skin-absorbed chemicals, because of the increased concern about such effects.

Additionally, current interest in replacing the Draize test for evaluating eye irritation has directed our attention to a need to discuss the developments occurring in this area. Requests for methods of testing for contact hypersensitivity of the vagina have led to the inclusion of this subject as well. The induction of porphyria cutanea tarda by chemicals has also been included.

We would appreciate readers' comments and suggestions for future editions.

Francis N. Marzulli
Howard I. Maibach

preface to the second edition

This edition updates many chapters of the first edition and eliminates certain topics found only in that edition (sweat and sebaceous gland toxicology, histologic and immunologic aspects of contact dermatitis, effects of drugs on cutaneous microbial flora, and cutaneous manifestations of food intolerance). The intent is to limit the size of this edition while increasing the scope of certain subjects.

We revised the order of presentation beginning with a brief description of the skin itself, its structure, function, and biochemistry. From this background information we proceed to a discussion of the barrier functions of skin and factors involved in dermal penetration with the thought that a topically applied substance must first penetrate the skin if it is to sensitize, irritate, or result in systemic effects. We present a more comprehensive treatment of this important subject with greater attention to practical and *in vitro* studies as well as theoretical considerations.

We follow this with an expanded section on skin sensitization, including a comparison of animal and human findings. Information on skin irritation has been up-dated.

We expanded our coverage of photobiology because of increasing recent interest and concerns in this area.

Finally, we introduce varied subjects of more than peripheral interest to many dermatotoxicologists, such as skin carcinogenesis, chloracne, pigmentation, eczema, urticaria, granulomas, hair, and sebaceous gland toxicology. Neurotoxic substances and toxicity from heavy metals are also discussed. Eye irritation is placed near the end of the book not because of a lack of

importance but simply because the eye, though it shares many anatomic similarities to skin, is a separate and distinctly unique organ.

Test methods suggested by the Interagency Regulatory Liaison Group (IRLG) and Organization for Economic Cooperation and Development (OECD) are provided as appendixes for those toxicologists interested in regulatory agency guidelines. The IRLG is no longer a functioning group, however, and their guidelines are included for interest only.

Recent activities by animal welfare groups have resulted in a reappraisal of animal test methods with interest in using tissues or cell cultures in place of animals. The development of the Ames test for predicting carcinogenic potential was a leading stimulus to this type of effort. However, the Ames test has its limitations and toxicologists have been concerned for years about the applicability of animal tests to humans. But there is an even greater divergence between *in vitro* systems and humans. Tests involving complicated mechanisms, such as those that occur in immunology, require intact animals and become exceedingly difficult to replace by *in vitro* methods. The rabbit eye test for eye irritation has received wide adverse publicity by animal welfare groups. Yet, even with its limitations, the rabbit eye has an important capacity not shared by tissue cultures—it offers a time-frame for recovery when injured. Also, it possesses anatomical structures such as the cornea, iris, and conjunctiva that are not unlike those of humans. If investigators treat the rabbit eye with the care used in human ocular experimentation this should substantially alleviate public concern for this issue.

In the future we may see a proliferation of *in vitro* test methods as pressures to replace animal testing develop. Only time will tell how useful they are.

Francis N. Marzulli
Howard I. Maibach

preface to the first edition

Dermatotoxicology, a relatively new discipline, is defined as a science that deals with adverse skin effects and the substances that produce them. This volume represents a first attempt at consolidating recent developments in various aspects of skin research of interest and concern to researchers in dermatotoxicology.

Three key subdisciplines are skin irritation, skin sensitization, and skin penetration. Skin metabolism and skin carcinogenesis are related important subdisciplines. Pharmacologic aspects of skin are for the most part concerned with skin appendages such as the eccrine glands and the pilosebaceous apparatus.

A section on immunology is included as the basis of understanding allergic contact dermatitis. The science of immunology has undergone an explosion of new developments, some of which provide a better understanding of the complicated mechanisms that may be involved in skin sensitization. Eye irritation is included in this volume primarily because of a traditional linkage of eye and skin irritation.

Different in scope from those texts that deal with clinical dermatology or cosmetic science, this volume attempts to provide useful background, reference, and up-to-date state of the art information in areas such as skin irritation, skin sensitization, and skin penetration. The contents should be of special interest to those engaged in evaluating toxicologic safety; much of the impetus to the development of dermatotoxicology as a separate discipline derives from government regulations suggesting and sometimes demanding that certain products applied to the skin should be evaluated for toxic hazard prior

to reaching the market place. This volume provides background information rather than specific test methodologies.

Because recent developments in some of these areas have been rapid and because of the time involved in the preparation of any such volume, some parts may be outdated by publication date. Certain chapters that were expected to have involved more extensive coverage were reduced in scope and others were eliminated in order to meet deadlines. We believe nevertheless that this represents a satisfactory beginning in this relatively new discipline and that it fulfills a need and provides a groundwork on which future authors can build.

We want to acknowledge the assistance in the review of manuscripts by Carl Bruch, John Lucas, Helen Reynolds, Joseph McLoughlin, Max Samter, Andrew Ulsamer, Robert Hehir, Van Seabaugh, Anne Wolven, Paige Yoder, William Markland, Leon Sanders, and Elizabeth Weisburger. We thank Mary Phillips, our editor at Hemisphere, for her valuable assistance in transforming our manuscript into a book.

Francis N. Marzulli

Howard I. Maibach

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