

NEOPLASMS OF THE SKIN AND MALIGNANT MELANOMA

*A Collection of Papers Presented at the
Twentieth Annual Clinical Conference on Cancer, 1975,
at The University of Texas System Cancer Center
M. D. Anderson Hospital and Tumor Institute,
Houston, Texas*



NEOPLASMS OF THE SKIN AND MALIGNANT MELANOMA

*A Collection of Papers Presented at the
Twentieth Annual Clinical Conference on Cancer, 1975,
at The University of Texas System Cancer Center,
M. D. Anderson Hospital and Tumor Institute,
Houston, Texas*



YEAR BOOK MEDICAL PUBLISHERS, INC.
35 East Wacker Drive, Chicago

Copyright © 1976 by Year Book Medical Publishers, Inc. All rights reserved. No part of this publication may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, recording, or otherwise, without prior written permission from the publisher. Printed in the United States of America.

Library of Congress Catalog Card Number: 76-9374

International Standard Book Number: 0-8151-0213-5

ON THE COVER: The electron micrograph shows a transversely sectioned dendritic process of a melanoma cell from a primary malignant melanoma on the right shoulder of a 41-year-old male patient. Within the cytoplasm of the process, a number of melanosomes and premelanosomes can be seen. Some are enclosed within a limiting unit membrane and the premelanosomes exhibit a fine periodicity.

Acknowledgments

FOR THEIR SUPPORT in making possible both the Twentieth Annual Clinical Conference and the publication of this monograph, the staff of M. D. Anderson Hospital and Tumor Institute of The University of Texas System Cancer Center gratefully acknowledges the assistance of the Texas Division of the American Cancer Society, American Cancer Society, Inc., and the Division of Continuing Education of The University of Texas Health Science Center at Houston.

The program was arranged and organized by a committee composed of the following staff members of M. D. Anderson Hospital: Charles M. McBride and J. Leslie Smith, co-chairmen; and members Marvin E. Chernosky, Jess F. Gamble, Evan M. Hersh, Eleanor J. Macdonald, William O. Russell, and H. Rodney Withers.

This volume was prepared for publication by the following members of the M. D. Anderson Hospital Department of Publications: Susan B. Freitag and Diane L. Culhane, editorial; Judith C. Demec, secretarial.

Many of the illustrations in this volume were prepared by members of the M. D. Anderson Hospital Department of Medical Communications.

Foreword

The Proceedings of the Twentieth Annual Clinical Conference, compiled here into monograph form, contain presentations made at the meeting.

In order to facilitate the earliest possible publication date of the monograph, citations in the reference lists generally were not verified by the editors but were, for the most part, published as furnished by the authors. The publisher has been most cooperative in scheduling the volume for rapid publication.

The material contained herein was submitted as previously unpublished material, except in the instances in which credit has been given to the source from which some of the illustrative material was derived.

THE EDITORS

Contents

WELCOME ADDRESS: BOARD OF REGENTS, <i>James E. Bauerle</i>	1
INTRODUCTION, <i>R. Lee Clark and Robert C. Hickey</i>	3
INTRODUCTION OF HEATH MEMORIAL AWARD RECIPIENT, <i>Robert C. Hickey</i>	7
HEATH MEMORIAL AWARD LECTURE: MALIGNANT MELANOMA IN CHILDREN, <i>Elson B. Helwig</i>	11
EPIDEMIOLOGY OF SKIN CANCER, 1975, <i>Eleanor J. Macdonald</i>	27
CARCINOGENESIS OF SKIN NEOPLASMS, <i>Robert G. Freeman</i>	43
CLASSIFICATION OF SKIN TUMORS, <i>Elson B. Helwig</i>	51
CLINICAL RECOGNITION OF SKIN NEOPLASMS, <i>G. Thomas Jansen</i>	57
SELECTED PRECANCEROUS SKIN AND MUCOCUTANEOUS LESIONS, <i>James H. Graham</i>	69
TREATMENT FOR PRECANCEROUS SKIN LESIONS, <i>Samuel F. Bean</i>	123
TREATMENT FOR EARLY SQUAMOUS CELL AND BASAL CELL CARCINOMA, <i>Marvin E. Chernosky</i>	129
RADIO THERAPY FOR BASAL AND SQUAMOUS CELL CARCINOMA OF THE SKIN, <i>Norah duV. Tapley</i>	155
CHEMOSURGERY FOR BASAL CELL AND SQUAMOUS CARCINOMAS OF THE SKIN, <i>Frederic E. Mohs</i>	173
TREATMENT OF ADVANCED BASAL CELL AND SQUAMOUS CARCINOMAS OF THE SKIN, <i>Don A. Gard</i>	189

MYCOSIS FUNGOIDES. TOPICAL ADMINISTRATION OF CHEMOTHERAPY AND IMMUNOTHERAPY, <i>Eugene J. Van Scott and Eric C. Vonderheid</i>	203
STEROIDS AND SURGERY IN THE MANAGEMENT OF CUTANEOUS ANGIOMAS, <i>Milton T. Edgerton</i>	211
PAGET'S DISEASE OF THE VULVA, <i>H. Stephen Gallagher, William T. Creasman, and Bruce Mackay</i>	231
DERMATOFIBROSARCOMA PROTUBERANS, <i>Richard G. Martin</i>	243
BIOLOGICAL ASPECTS OF PIGMENT CELLS AND MALIGNANT MELANOMA, <i>Marvin M. Romsdahl and Irene S. Cox</i>	251
INCIDENCE AND EPIDEMIOLOGY OF MELANOMA IN TEXAS, <i>Eleanor J. Macdonald</i>	279
HISTOPATHOLOGY AND BIOLOGIC BEHAVIOR OF MALIGNANT MELANOMA, <i>J. Leslie Smith, Jr.</i>	293
IMMUNOCOMPETENCE, IMMUNODEFICIENCY, IMMUNOPOTENTIATION AND PROGNOSIS IN MALIGNANT MELANOMA, <i>E. M. Hersh, J. U. Guttermann, G. M. Mavligit, C. M. McBride, and M. A. Burgess</i>	331
MALIGNANT MELANOMA OF THE HEAD AND NECK REGION, <i>Alando J. Ballantyne</i>	345
MALIGNANT MELANOMA OF THE TRUNK, <i>Charles M. McBride, Everett V. Sugarbaker, and Barry W. Brown</i>	363
MALIGNANT MELANOMA OF THE LIMBS: AN EVALUATION OF CHEMOTHERAPY BY REGIONAL PERFUSION, <i>Edward T. Krementz, R. Davilene Carter, Carl M. Sutherland, and Robert F. Ryan</i>	375
MALIGNANT MELANOMA OF THE VULVA, <i>Felix N. Rutledge</i>	401
CONSERVATIVE TREATMENT OF INTRAOCULAR MALIGNANT MELANOMA, <i>Milton Boniuk and Steven M. Bagan</i>	409
MALIGNANT MELANOMA OF THE GENITOURINARY TRACT, <i>R. B. Bracken, Edward M. Blight, and Douglas E. Johnson</i>	431

ANORECTAL MELANOMA, <i>Laurens R. Pickard and Charles M. McBride</i>	443
RADIOTHERAPY IN THE MANAGEMENT OF MALIGNANT MELANOMA, <i>H. R. Withers and David Harter</i>	453
SYSTEMIC CHEMOTHERAPY FOR MELANOMA, <i>Robert S. Benjamin, Jordan U. Gutterman, Eugene M. McKelvey, Laurence M. Einhorn, Robert B. Livingston, and Jeffrey A. Gottlieb</i>	461
CHEMOIMMUNOTHERAPY FOR MELANOMA: PRELIMINARY CLINICAL DATA AND DIFFICULTIES WITH IN VITRO MONITORING OF TUMOR-SPECIFIC IMMUNE REACTIONS, <i>Marion J. McMurtrey, Luis T. Campos, Joseph G. Sinkovics, Jimmy J. Romero, Kevin K. Loh, and Marvin M. Romsdahl</i>	471
SPECIFIC TUMOR IMMUNITY IN MALIGNANT MELANOMA, <i>Giora M. Mavligit, Jordan U. Gutterman, and Evan M. Hersh</i>	485
IMMUNOTHERAPY FOR MALIGNANT MELANOMA, <i>J. U. Gutterman, G. M. Mavligit, A. Kennedy, C. M. McBride, M. A. Burgess, and E. M. Hersh</i>	497
PROBLEMS IN HISTOPATHOLOGICAL DIAGNOSIS OF NEOPLASMS OF THE SKIN: SELECTED CASE MATERIAL, Moderator, <i>J. Leslie, Smith, Jr.</i>	533
INDEX	579

WELCOME ADDRESS:

Board of Regents

JAMES E. BAUERLE, D.D.S.

*Member, Board of Regents
The University of Texas System*

I AM HERE THIS MORNING to extend a welcome from The University of Texas System Board of Regents and from the central administration of The University. The University of Texas is a large system of higher education. There are 6 academic campuses and 5 health-science campuses, with a total of approximately 87,500 students. In the health-professional schools, medicine and dentistry, we have 2,926 students; there are 3,024 students in nursing as well as in the allied health schools and the School of Public Health. So, as a university system, we are very interested in health-related matters and health-related education.

The topic of this conference, *Neoplasms of the Skin and Malignant Melanoma*, is intriguing. I have looked over the titles of presentations to be made and have had the opportunity to examine some of the data that are to be presented. I have been especially fascinated by the data from my home community of San Antonio.

I was astonished to learn that squamous cancer of the skin occurs in San Antonio at the rate of 166 per 100,000 in white males, and that melanoma occurs at the rate of 9 per 100,000. The rate for women is considerably less for squamous cancer, but almost the same for melanoma. My interest also was aroused by finding the variation from one region of the state to another; in particular, the fact that melanoma occurs in San Antonio and in Houston at about the same rate, but is 3 times less frequent in El Paso. Further, I have a personal interest in this topic because of the plight of a professional colleague due to melanoma.

I believe that this will be an interesting conference on a health hazard with extensive ramifications, particularly in the Southwest.

Again, on behalf of The University of Texas System and its institutions hosting this conference, a sincere welcome.

Introduction

R. LEE CLARK, M.D., M.Sc., D.Sc. (Hon.)

President, The University of Texas System Cancer Center, and Professor of Surgery, The University of Texas M. D. Anderson Hospital and Tumor Institute, Houston, Texas

AND

ROBERT C. HICKEY, M.D.

Director, The University of Texas System Cancer Center M. D. Anderson Hospital and Tumor Institute, Houston, Texas

THIS CONFERENCE, entitled "Neoplasms of the Skin and Malignant Melanoma," is the Twentieth Annual Clinical Conference sponsored by The University of Texas System Cancer Center M. D. Anderson Hospital and Tumor Institute. Cosponsors are The University of Texas Health Science Center at Houston, through its Division of Continuing Education, and the American Cancer Society. The Texas Cancer Coordinating Commission is endorsing this publication.

The cochairmen of the conference are Drs. Charles McBride and J. Leslie Smith. The committee is listed elsewhere. Our appreciation is extended to them for their efforts.

It is important to note that the highest incidence of cancer of any site occurs in the skin. Some idea of the enormity of the problem may be gained through examination of the statistics collected during the past 23 years. In 56 Texas counties, there were 48,000 skin cancers, of which 65% were basal cell, 27% were squamous cell, 5% were melanoma, and 3% were of other histologic types. Of the 84,000 cancer patients registered at M. D. Anderson Hospital since 1944, 8,390 (9.9%) had cancer of the skin other than melanoma, and 4,286 (5.1%) had melanoma.

Collectively, tumors of the skin are unique in that some are very easy to treat while others are among the most complicated to diagnose, treat, and otherwise manage. These skin lesions may be the harbingers of other metabolic or visceral disturbances.

While cancers of the skin generally are more amenable to therapeutic measures than are cancers of other sites, accurate differential diagnosis presents many problems because of the variations in histological types, routes of metastasis, and different responses to therapy. The familiarity of the clinician with features of particular lesions makes a closer partnership with the pathologist, to assure correct diagnosis, more necessary than is the case for most other types of cancer.

Excluding melanoma, skin cancer should be the cancer most totally amenable to curative therapy. The innocuous appearance and the painless and slowly progressive nature of skin cancers, however, too frequently result in a loss of the opportunity for cure because of delay in seeking treatment as well as inadequate therapy. Education, especially of those ethnic groups most frequently affected and of individuals at risk because of exposure to environmental carcinogens, should produce immediate results for prevention and earlier diagnosis. These factors should greatly reduce the number of unnecessary deaths from skin cancer.

Historically, the first clear-cut study of carcinogenesis in man was the study, by Sir Percival Pott in 1775, of scrotal cancer, a condition that was referred to as "chimney sweep cancer." This tissue has since been a fertile field for animal studies in carcinogenesis. In the human being, the skin lends itself to studies of the influences on cancer exerted by genetics, nutrition, host resistance, endocrinology, geographic location, and sociologic factors. Recently, the intensified efforts to identify environmental factors acting as carcinogens appear to have brought us back to where Pott started.

There is a growing consensus that cancer is a set of complex diseases wherein orderly cellular processes are disrupted by genetic anomalies of one sort or another. These disruptions may be somatic or germinal, and of viral, chemical, or physical origin, but they must always be considered in terms of one or several environmental factors or inducers. The skin lends itself to such studies, and this system can contribute significantly to the definition and understanding of cancer.

With regard to cancer of the skin, continuing education and clinical attentiveness to incipient cancer already have yielded large dividends via earlier recognition and treatment. So also, clinical and basic research are being intensified in these areas. Cancer research has as its objectives the harvesting of new information to elucidate the origin,

nature, treatment and, finally, prevention of cancer. The great progress made since our last conference on tumors of the skin in 1962 has been reflected in this conference, and still better solutions to the problems of skin cancer are to be anticipated.

Introduction of Heath Memorial Award Recipient

ROBERT C. HICKEY, M.D.

Director, The University of Texas System Cancer Center M. D. Anderson Hospital and Tumor Institute, Houston, Texas

IT IS MY PRIVILEGE to introduce the 1975 Heath Memorial Award Recipient, Dr. Elson B. Helwig. The lecture, which has become a tradition at this Conference, this year is entitled, "Malignant Melanoma in Children."

The award, memorializing three brothers, Guy H., Dan C., and Gilford G. Heath, was made possible by the late William W. Heath, former Chairman of The University of Texas System Board of Regents.

The award honors, through careful selection, an individual who has made "outstanding contributions to the care of patients with cancer."

There is hardly a medical scientist in the world today whose contributions to the field of cutaneous pathology and skin neoplasms have been as significant as those of Dr. Elson B. Helwig. For almost 30 years he has lent leadership to the Armed Forces Institute of Pathology. Currently, he is Chairman, Center of Advanced Pathology; Chief, Skin and Gastrointestinal Pathology Division; and Associate Director for Consultation, Armed Forces Institute of Pathology in Washington, D. C.

Under Dr. Helwig's direction, the Institute's Skin and Gastrointestinal Pathology Division and its Center for Advanced Pathology have come to be considered among the most important resources for diagnostic consultation for both military and civilian physicians attempting to classify skin tumors.

Using the vast dermatologic specimen and slide volume available at

the Institute to its greatest advantage, Dr. Helwig and his collaborators have been able to study, collate, and report on large numbers of various skin tumor types which, because of their rarity of occurrence, previously were reported only in small numbers. This information has been shared with clinicians and cancer researchers throughout the world, and has fostered not only a better understanding of skin tumors but also more accurate diagnoses, which have led to improved treatment of patients with various types of cutaneous cancer.

Dr. Helwig and his colleagues have identified many specific skin tumor types and clarified the terminology that describes them. He is recognized for promoting the use of a uniform terminology and the categorization of skin tumors to facilitate and improve communications among cancer specialists throughout the world. Toward this goal, he served as coauthor of an international volume for the World Health Organization which lists skin tumors by classification and type. In addition, he has edited 2 texts on dermal pathology and has conducted more than 200 lectures and short courses on cutaneous pathology.

Dr. Helwig's influence served as an early stimulus to medical specialization. He helped form the American Society of Dermatopathology and served as the organization's third president. His work in training pathologists and dermatologists in cutaneous pathology led to the creation of a combined certificate of special competence in dermatopathology. The need to set standards for those who practice dermatopathology arose because of the increasing importance of this field in diagnosing and caring for patients with cutaneous disorders.

The Earl D. Osborne Fellows in Dermatopathology all have received their training under Dr. Helwig. This longstanding program, sponsored annually since 1951 by the American Academy of Dermatology, attests to the admiration and respect accorded our speaker by his peers.

Dr. Helwig is a native of Pierceton, Indiana. He earned his Medical Degree from Indiana University Medical School in 1932. After completing his residency in pathology in 1936, he joined the staff of New England Deaconess Hospital in Boston as an Assistant Pathologist. In 1939, he was certified by the American Board of Pathology and taught at Washington University School of Medicine until 1942, when he entered the Army Medical Corps. He served in the Pacific Theater during World War II and returned to join the Armed Forces Institute of Pathology in 1946 as a Senior Pathologist.

After release from the Army Medical Corps with the rank of Colonel in 1947, Dr. Helwig was appointed Chief of the Dermal and Gastroin-

testinal Pathology Branch of the Armed Forces Institute of Pathology, a title similar to the one he still holds. In 1955, he was appointed Chief of the Division of Pathology, and in 1963 he was named Associate Director for Consultation at the Institute.

His achievements have been acknowledged by numerous forms of recognition, including the President's Award for Distinguished Federal Civilian Service presented to him in 1966 by President Lyndon B. Johnson. This honor is the highest governmental citation which can be awarded a civilian.

Dr. Helwig has published more than 130 papers and 13 of his scientific exhibits have won awards. He is a member of the Editorial Boards of the *American Journal of Clinical Pathology*, *Cancer*, and *Year Book of Cancer*, and is a member or honorary member of numerous pathology and dermatology societies here and abroad.

Dr. Helwig's contributions to medical research and education have been invaluable in the diagnosis and treatment of patients with cancer. His forthright leadership and honest practice of medicine have earned him a reputation among his colleagues which has helped open avenues of international communication between cancer researchers and clinicians and has resulted in more competent treatment of patients with this disease.

It is with great pleasure that I introduce Dr. Elson B. Helwig, the 1975 Heath Memorial Award Recipient, on behalf of my colleagues from M. D. Anderson Hospital and Tumor Institute, the Division of Continuing Education of the Graduate School of Biomedical Sciences, The University of Texas Health Science Center, and the American Cancer Society.