Fundamentals of Cancer Epidemiology
Second Edition

Philip C. Nasca, PhD, MPH
Professor of Epidemiology
Dean, School of Public Health
State University of New York, Albany

Harris Pastides, PhD, MPH
Professor of Epidemiology
Arnold School of Public Health
Vice President, Research and Health Sciences
University of South Carolina
Dedication

This book is dedicated to my wife, Bonnie, who has been my greatest source of inspiration and support for the past 42 years, and to my children and grandchildren, who help to keep me young and on my best behavior.

P.N.

This book is dedicated to my family and to my students. Patricia, Katharine, and Andrew provided the inspiration and support to always go the extra mile in pursuing my career’s challenges; my students provided the challenging questions that required me to be as exacting as science would allow.

H.P.

Acknowledgments

I am indebted to Will Parson for his excellent research of the current literature and his ability to keep things organized.

P.N.

Revisions are not supposed to be as hard as first editions, but given the rapidly changing nature of the field, this work required significant updating. I am indebted to Alexa Gallagher and Pam Pope for pushing me and for checking me.

H.P.
Contents

Preface xi

Contributors xiii

Chapter 1 The Descriptive Epidemiology of Cancer 1
Harris Pastides
Sources of Information 3
The Magnitude of Cancer 4
Geographic Variation of Cancer 13
Cancer in Developing Nations 21
Migrant Studies 23
Summary 26

Chapter 2 Basic Terminology 29
Philip C. Nasca
Pathologic Features of Cancer 30
Benign and Malignant Neoplasms 32
Metastasis 33
Angiogenesis 34
Cancer Diagnosis 34
Molecular Pathology 36
Cancer Staging 39
Classification of Neoplasms 43
Case Identification Problems and Epidemiological Research 45
Summary 46

Chapter 3 Biology of Normal Cells 49
Kevin M. Pumiglia, James McSharry, and Paul J. Higgins
The Eukaryotic Cell 49
Gene Expression in Normal Eukaryotic Cells 51
DNA Replication and Cell Division in Normal Cells 58
Summary 66
Chapter 8  Occupation and Cancer  158
Harris Pastides
Landmarks in Occupational Cancer Research  160
The Magnitude of the Problem of Occupational Carcinogenesis  161
Sources of Information about Occupational Cancer Risks  162
The IARC Classification Scheme  162
The Use of Epidemiology in Identifying Occupational Cancer Risks  165
Biological Monitoring  170
Medical Surveillance  172
Cancer Clusters  173
Occupational Carcinogenesis in Developing Countries  174
Summary  174

Chapter 9  Tobacco and Cancer  178
Philip C. Nasca
Tobacco Use in the United States from 1880 to 1995  179
Health and Economic Impacts of Cigarette Smoking  181
Mutagens and Carcinogens in Tobacco Smoke  184
Measuring Human Exposure to Tobacco Products  187
Epidemiological Studies  189
Environmental Tobacco Smoke  203
Smokeless Tobacco  205
Interactions between Tobacco and Other Environmental Exposures  209
2002 IARC Review of Tobacco and Cancer  209
Impact of Tobacco on Global Health  212
Summary  215

Chapter 10  Alcohol and Cancer  225
Philip C. Nasca
Alcohol Consumption Patterns and the Economic Costs of Alcohol Abuse  226
Scientific Evidence Linking Alcohol and Selected Cancers  229
Measuring Alcohol Exposure in Epidemiological Studies  236
Chapter 11  Ionizing, Nonionizing, and Solar Radiation and Cancer  265
Harris Pastides
What Is Radiation?  266
Ionizing Radiation  267
Electromagnetic Radiation  278
Solar Radiation  279
Summary  281

Chapter 12  Infectious Agents and Cancer  286
Philip C. Nasca
Viruses and Cancer: General Principles  287
Hepatocellular Carcinoma and Hepatitis
Viruses B and C  289
Human Papillomaviruses  296
Epstein-Barr Virus  304
Human T-Cell Lymphotropic Virus and Adult T-Cell Leukemias  310

Helicobacter pylori Infection and Cancer  312
Parasites and Cancer  316
Summary  318

Chapter 13  Immunity and Cancer Risk  334
Philip C. Nasca
Inborn Immunodeficiency Disorders  336
Induced Immunosuppression  337
Possible Biologic Mechanisms  343
Other Cancers  344
Preventing Cancer in Immunosuppressed Individuals  344
Thymectomy, Splenectomy, and Tonsillectomy  346
Immunostimulation  348
Summary  351
Chapter 14  Endogenous Hormones and Cancer  359
Elizabeth R. Bertone-Johnson and Lisa Chasan-Taber
Breast Cancer  360
Application of the Etiologic Model  371
Summary  377

Chapter 15  Exogenous Hormones and Cancer  389
Elizabeth R. Bertone-Johnson and Lisa Chasan-Taber
Combined Oral Contraceptives  391
Postmenopausal Hormones  398
Tamoxifen and Raloxifene  404
Diethylstilbestrol  407
Summary  408

Chapter 16  Diet and Cancer  419
Harris Pastides
An Overview of Foods and Nutrients  421
Types of Studies Used to Investigate the Relationship
between Diet and Cancer  422
Methods for Determining Dietary Intake  425
Epidemiological Evidence Regarding Diet and
Cancer  430
Diet and Cancer: A Global Perspective  434
Decreasing the Burden of Cancer through Dietary
Modification  436
Summary  438

Chapter 17  Childhood Cancer  443
Colleen C. McLaughlin
Cancers That Occur among Children  444
Incidence Patterns  448
Cancer Survival  456
Framework for Understanding Etiology of Childhood
Cancers  458
Etiology  460
Study Design Issues  472
Summary  475

Chapter 18  Cancer Screening  484
Philip C. Nasca
Basic Concepts  485
Study Designs  489
Preface

Revising *Fundamentals of Cancer Epidemiology* was a “labor” of love. We emphasize labor because advances in our understanding of the etiology of cancer and associated benefits relative to cancer prevention have advanced rapidly. This revision has paid particular attention to updating information in this rapidly evolving field. Students and other readers will benefit from the concise summarization of technical information, especially related to our understanding of the biology of cancer, gene–environment interaction, opportunities for better cancer control, and associated topics.

Substantive changes are to be found in every chapter and two new chapters were added: Childhood Cancer (Chapter 17) and Cancer Screening (Chapter 18).

As we said in the preface of our first edition, as longtime teachers of cancer epidemiology courses in graduate schools of public health, we often face the difficulty of selecting a course textbook. Although there are numerous books that cover aspects of cancer biology or present the epidemiology of cancer from a site-specific perspective, we felt that no single book offered a treatment of cancer epidemiology at a level appropriate for first-time students. In *Fundamentals of Cancer Epidemiology*, we offer students and others wishing to learn more about cancer an introduction of the current understanding of what cancer is, how it develops biologically and genetically, the “who, when, and where” of cancer (its descriptive epidemiology), and the determinants of cancer.

Although this book is not a methods text *per se*, we have included discussions of pertinent methodological issues in order to provide students with an epidemiological framework for evaluating hypotheses concerning the etiologic role of various risk factors as well as for developing rational preventive measures.

The book is divided into two parts. The objective of the first part is to provide an overview of the definition and observed distribution of cancer and cancer risk factors as we know them today. The second part is devoted to cancer risk factors that, based on current evidence, have the potential to affect the incidence of various human cancers to a substantial degree.
add separate chapters on each major cancer site would have made the text too long for a standard introductory course.

In any case, site-specific information is widely accessible in monographs and via the Internet (note that Appendix B contains a list of cancer-related informational Web sites). Fundamentals of Cancer Epidemiology is intended for use in cancer epidemiology courses in schools of public health as well as in schools of medicine, dentistry, nursing, and allied health programs. It is also directed toward individuals who work in cancer prevention and control programs in local, state, and federal agencies and who need an overview of the field. We assume that readers will have completed an introductory course in epidemiology. If they have not, we suggest that an epidemiology text be used in conjunction with this book. Although our overall goal was to create a text suitable for a typical 15-week graduate course, in developing it we assumed that it would be supplemented by instructor-prepared course notes and selected readings from the literature. In any case, whether the readers are graduate students or workers in the field of cancer prevention, our hope is that this text will provide them with a basic understanding of cancer epidemiology and stimulate them to pursue their interest in this field as they continue their education or professional development.
Contributors

Elizabeth R. Bertone-Johnson, ScD, SM
Associate Professor of Epidemiology
University of Massachusetts, Amherst
Amherst, Massachusetts

Lisa Chasan-Taber, ScD, MPH
Associate Professor of Epidemiology
University of Massachusetts, Amherst
Amherst, Massachusetts

Paul J. Higgins, PhD
Professor and Director
Center for Cell Biology and Cancer Research
Albany Medical College
Albany, New York

Jirong Long, MD, PhD
Assistant Professor
Vanderbilt Epidemiology Center
Vanderbilt University School of Medicine
Nashville, Tennessee

Colleen C. McLaughlin, CTR, MPH, PhD
Research Scientist
New York State Cancer Registry
New York State Department of Health
and
Department of Epidemiology
School of Public Health
State University of New York, Albany
Albany, New York

James J. McSharry, PhD
Senior Scientist and Professor
Center for Emerging Infections and Host Defense
Ordway Research Institute
Albany, New York
CONTRIBUTORS

Philip C. Nasca, PhD
Professor of Epidemiology
School of Public Health and Health Sciences
and
Associate Dean for Research
School of Nursing
University of Massachusetts
Amherst, Massachusetts

Harris Pastides, PhD, MPH
Professor of Epidemiology
Arnold School of Public Health
Vice President for Research and Health Sciences
University of South Carolina
Columbia, South Carolina

Kevin M. Pumiglia, PhD
Associate Professor
Center for Cell Biology and Cancer Research
Albany Medical College
Albany, New York

Wei Zheng, MD, PhD
Professor and Director
Vanderbilt Epidemiology Center
Vanderbilt University School of Medicine
Nashville, Tennessee