HEALTH RISKS FROM EXPOSURE TO LOW LEVELS OF IONIZING RADIATION BEIR VII PHASE 2
HEALTH RISKS
FROM EXPOSURE TO
LOW LEVELS OF
IONIZING
RADIATION

BEIR VII PHASE 2

Committee to Assess Health Risks from Exposure to Low Levels of Ionizing Radiation

Board on Radiation Effects Research
Division on Earth and Life Studies

NATIONAL RESEARCH COUNCIL
OF THE NATIONAL ACADEMIES

THE NATIONAL ACADEMIES PRESS
Washington, D.C.
www.nap.edu
Contents

UNITS USED TO EXPRESS RADIATION DOSE xi

PUBLIC SUMMARY 1
Introduction, 1
How Ionizing Radiation Was Discovered, 1
How Ionizing Radiation Is Detected, 2
Units Used to Describe Radiation Dose, 2
What Is Meant by Low Doses of Ionizing Radiation, 2
Exposure from Natural Background Radiation, 3
Contribution of Man-Made Radiation to Public Exposure, 3
Scenarios Illustrating How People Might Be Exposed to Ionizing Radiation above Background Levels, 4
Evidence for Adverse Health Effects Such as Cancer and Hereditary Disease, 6
The BEIR VII Risk Models, 6
Research Reviewed by the Committee, 9
Conclusions, 10

EXECUTIVE SUMMARY 11
Introduction, 11
Evidence from Biology, 11
Estimation of Heritable Genetic Effects of Radiation in Human Populations, 12
Evidence from Epidemiology, 12
Integration of Biology and Epidemiology, 14
Estimating Cancer Risks, 14
Conclusion, 15
Recommended Research Needs, 15

1 BACKGROUND INFORMATION 19
Physical Aspects of Radiation, 19
Chemical Aspects of Radiation, 29
Molecular Mechanisms of DNA Repair, 32
Summary, 39
ANNEX 1A: Ionizing Radiation and Oxidative Damage—A Viewpoint from Saccharomyces cerevisiae, 40

xiii
2 MOLECULAR AND CELLULAR RESPONSES TO IONIZING RADIATION
   General Aspects of Dose-Response Relationships, 43
   Induction of Chromosome Aberrations, 45
   Induction of Gene Mutations in Somatic Cells, 46
   Radiation-Induced Genomic Instability, 47
   Cell Cycle Effects, 49
   Adaptive Response, 50
   Bystander Effects, 53
   Hyper-Radiation Sensitivity at Low Doses, 55
   Observed Dose-Response Relationships at Low Doses, 57
   Summary, 62

3 RADIATION-INDUCED CANCER: MECHANISMS, QUANTITATIVE EXPERIMENTAL STUDIES, AND THE ROLE OF GENETIC FACTORS
   Introduction, 65
   Mechanisms of Tumorigenesis, 66
   Radiation-Induced Genomic Instability in Radiation Tumorigenesis, 70
   Quantitative Studies in Experimental Tumorigenesis, 73
   Genetic Susceptibility to Radiation-Induced Cancer, 79
   Summary, 89

4 HERITABLE GENETIC EFFECTS OF RADIATION IN HUMAN POPULATIONS
   Introduction and Brief History, 91
   General Framework, 92
   Genetic Diseases, 92
   Risk Estimation Methods, 93
   Recent Advances with Respect to the Three Quantities Used with the DD Method of Risk Estimation, 94
   The Doubling Dose Estimate, 101
   Mutation Component of Genetic Diseases, 101
   MC Estimation for Chronic Multifactorial Disease, 105
   Other Potentially Relevant Data, 113
   Risk Estimation, 114
   ANNEX 4A: Models of Inheritance of Multifactorial Diseases in the Population, 120
   ANNEX 4B: The Doubling Dose, 122
   ANNEX 4C: Assumptions and Specifications of the Finite-Locus Threshold Model, 124
   ANNEX 4D: Differences Between Spontaneous Disease-Causing Mutations in Humans and Radiation-Induced Mutations in Experimental Systems, 124
   ANNEX 4E: Criteria Used to Assign Human Genes to One of Three Groups from the Standpoint of the Recoverability of Induced Mutations in Live Births, 125
   ANNEX 4F: Radiation Studies with Expanded Simple Tandem Repeat Loci in the Mouse and Minisatellite Loci in Human Germ Cells, 125
   ANNEX 4G: Doubling Doses Estimated from Genetic Data of Children of A-Bomb Survivors, 130

5 BACKGROUND FOR EPIDEMIOLOGIC METHODS
   Introduction, 132
   Collection of Epidemiologic Data, 133
   Analysis of Epidemiologic Data, 136
   Interpretation of Epidemiologic Data, 139
6 ATOMIC BOMB SURVIVOR STUDIES
   Introduction, 141
   Description of the Cohort, 142
   Statistical Methods, 143
   All Solid Cancers, 144
   Site-Specific Cancers, 147
   Cancers Resulting from Exposure In Utero, 151
   Benign Neoplasms, 151
   Nonneoplastic Disease, 152
   Life Shortening, 153
   Summary, 154

7 MEDICAL RADIATION STUDIES
   Introduction, 155
   Medical Uses of Radiation, 156
   Evaluation of Risk for Specific Cancer Sites, 173
   Discussion, 187
   Summary, 187

8 OCCUPATIONAL RADIATION STUDIES
   Introduction, 189
   Nuclear Industry Workers, 190
   Workers from the Mayak Facility, 201
   Chernobyl Cleanup Workers, 202
   Airline and Aerospace Employees, 204
   Medical and Dental Occupational Exposures, 204
   Summary, 205

9 ENVIRONMENTAL RADIATION STUDIES
   Introduction, 207
   Populations Living Around Nuclear Facilities, 208
   Populations Exposed from Atmospheric Testing, Fallout, or Other
   Environmental Release of Radiation, 212
   Populations Exposed from the Chernobyl Accident, 215
   Populations Exposed from Natural Background, 228
   Children of Adults Exposed to Radiation, 228
   Exposure to Radioactive Iodine 131, 233
   Discussion, 235
   Summary, 237

10 INTEGRATION OF BIOLOGY AND EPIDEMIOLOGY
    Introduction, 239
    DNA Damage Response and Cancer Risk, 239
    Projection of Risks Over Time, 239
    The Transport of Cancer Risk Between Different Populations, 240
    Form of the Dose-Response for Radiation Tumorigenesis, 245
    Dose and Dose-Rate Effects on Tumor Induction, 246
    Other Forms of Cellular and Animal Response to Radiation, 250
    Genetic Susceptibility to Cancer, 251
    Heritable Effects of Radiation, 252
    Summary, 252

ANNEX 10A: Application of the Moolgavkar and Knudson Two-Stage Clonal
   Expansion Model to the Transport of Radiation Cancer Risk, 253
ANNEX 10B: Evidence for the Connection Between Dose Effects and
   Dose-Rate Effects in Animal Experiments, 254
11 RISK ASSESSMENT MODELS AND METHODS
Risk Assessment Methodology, 259
Risk Models, 261
Variables That Modify the Dose-Response Relationship, 264

12 ESTIMATING CANCER RISK
Introduction, 267
Data Evaluated for BEIR VII Models, 267
Measures of Risk and Choice of Cancer End Points, 268
The BEIR VII Committee’s Preferred Models, 269
Use of the Committee’s Preferred Models to Estimate Risks for the U.S. Population, 274
Quantitative Evaluation of Uncertainty in Lifetime Risks, 278
Results of Risk Calculations, 278
Uncertainties in Lifetime Risk Estimates, 284
Coherence of Models with Other Studies, 286
Summary, 290
ANNEX 12B: Committee Analyses of Data on the LSS Cohort to Develop BEIR VII Models for Estimating Cancer Risks, 296
ANNEX 12C: Details of LAR Uncertainty Analysis, 308
ANNEX 12D: Additional Examples of Lifetime Risk Estimates Based on BEIR VII Preferred Models, 310

13 SUMMARY AND RESEARCH NEEDS
Evidence from Biology, 313
Genetic Effects of Radiation on Human Populations, 316
Epidemiologic Studies of Populations Exposed to Ionizing Radiation, 317
Integration of Biology and Epidemiology, 321
Models for Estimating the Lifetime Risk of Cancer, 322
Conclusion, 323

APPENDIXES

A BASIC BIOLOGICAL AND GENETIC CONCEPTS

B COMMENTARY ON “RADIATION FROM MEDICAL PROCEDURES IN THE PATHOGENESIS OF CANCER AND ISCHEMIC HEART DISEASE: DOSE-RESPONSE STUDIES WITH PHYSICIANS PER 100,000 POPULATION” 329

C ISSUES RAISED BY THE INSTITUTE FOR ENERGY AND ENVIRONMENT RESEARCH (IEER)

D HORMESIS

E FIFTEEN-COUNTRY WORKERS STUDY

REFERENCES

GLOSSARY

COMMITTEE BIOGRAPHIES

INDEX