

Contents

Preface.....	xi
Acknowledgments	xiii
What's New in the Second Edition.....	xv
SECTION I INTRODUCTION	
Chapter 1	
Toxicology and Its Roots as a Science	3
Introduction	3
Toxic Chemicals	5
Epidemiological Studies.....	6
Causality.....	7
The Roots of Toxicology	8
The Evolution of Toxicology	14
Bibliography	15
Chapter 2	
Chemical Properties and Hazardous	
 Chemicals Information Resources	17
Introduction	17
Elements, Atoms, and Compounds.....	17
Mixtures, Suspensions, and Aerosols	19
Identifying Chemicals.....	19
Physical Properties of Chemicals.....	24
Appendix 2-1: Some Web-Based Resources	27
Appendix 2-2: Regulatory Agencies That Maintain Lists for Hazardous Chemicals.....	31
Appendix 2-3: Regional Poison Control Centers.....	41
Chapter 3	
Toxicity and the Factors That Modify Toxic Responses.....	51
Cellular Basis of Toxicity	51
Spectrum of Adverse Effects.....	52

CONTENTS

Factors That Modify Toxicity	55
Toxicogenomics and Its Importance in Public Health.....	59
Bibliography	60

Chapter 4

Biological Poisons: Plant and Animal Toxins	61
Introduction	61
Bacterial Toxins	63
Fungal Toxins.....	66
Algal Toxins.....	72
Higher Plant Toxins	74
Animal Toxins	77
Bibliography	86

Chapter 5

Environmental Pollutants and Their Fate.....	89
Introduction	89
Unfortunate Lessons Learned.....	90
Pollution Versus Contamination.....	105
Environmental Chemistry.....	106
The Environment: Compartments and Ecosystems.....	108
Toxicity in a Population	112
Endocrine-Disrupting Compounds.....	112
Conclusion	115
Bibliography	115

SECTION II TOXICOLOGY PRINCIPLES

Chapter 6

Dose and Response.....	119
Introduction	119
Relating Dose to Response.....	121
Dose–Response Graphs.....	122
How Individuals May Respond in a Population.....	124
The Dose Must Be Referenced to Time	124
Dose Standardization Based on Body Weight	125
Toxicity Rating.....	125
Referencing Dose to Environmental Media.....	126
Bibliography	128

Chapter 7

Absorption of Toxicants and Models of Disposition.....	129
Toxicant Entry into the Body	129
Cell Membranes.....	130
Movement of Toxicants Across Cell Membranes	131
Skin Absorptiion	134
Gastrointestinal Absorption	135
Respiratory Absorption	137
Other Exposure Routes.....	138
Chemical Disposition and Toxicokinetics	139
Models of Disposition.....	141
Bibliography	144

Chapter 8

Distribution, Storage, and Elimination of Toxicants	145
Introduction	145
Body Water and Volume of Distribution.....	146
Plasma Binding, Blood Flow, and Barriers to Distribution.....	148
Toxicant Storage	148
Toxicant Elimination.....	150
Urinary Excretion	152
Fecal Elimination.....	154
Pulmonary Elimination.....	155
Minor Routes of Elimination.....	155
Bibliography	157

Chapter 9

Biotransformation.....	159
Introduction	159
Enzymes.....	160
Tissues Where Biotransformation Proceeds.....	164
Phase 1 Reactions and Cytochrome P450	165
Phase 2 Reactions.....	171
Bibliography	174

Chapter 10

Chemical-Induced Mutagenesis	175
DNA and Mutations.....	175
Mutations and Apoptosis	182
Tests for DNA Damage and Mutagenicity.....	184
Examples of Chemical Mutagens	186
Bibliography	188

Chapter 11

Chemicals and Cancer	189
Introduction	189
Mutations in Genes That Regulate Cell Growth and Differentiation.....	190
Oncogenes	193
History of Chemical Carcinogenesis	195
Characteristics of Cancer Cells.....	196
Benign and Malignant Tumors	197
Tumor Angiogenesis, Metastasis, and Staging.....	199
Classification Systems for Carcinogens by Agency.....	200
Carcinogen Classification.....	204
Exposure to Carcinogens.....	209
Chemical-Induced Carcinogenesis Is a Multistep Process.....	211
Informing the Public About Carcinogens.....	214
Bibliography	216

SECTION III SYSTEMIC TOXICITY

Chapter 12

The Role of the Immune System	219
Introduction	219
Chemical Exposures.....	220
Immune Responses	220

Organs of the Immune System.....	221
Cells of the Immune System	223
Antibodies	224
Immunological Disorders.....	227
Immunosuppression by Toxicants.....	228
Examples of Chemical-Induced Immunological Disorders.....	229
Experimental Immunological Testing	230
Bibliography	230
Chapter 13	
Skin.....	233
Introduction	233
Structure of the Skin	234
Skin Absorption of Chemicals.....	236
Skin Toxicity: Local Effects.....	238
Bibliography	242
Chapter 14	
The Liver and Kidneys	245
The Liver	245
The Kidneys	254
Bibliography	258
Chapter 15	
The Cardiovascular System	259
General Considerations.....	259
Cardiac Physiology	259
Cell Types.....	261
Cardiac Electrophysiology.....	261
Assessing Cardiac Function	263
Effects of Toxicants on the Cardiovascular System.....	264
Blood Vessels	268
Blood.....	270
Bibliography	274
Chapter 16	
The Respiratory System.....	277
General Considerations.....	277
Nomenclature of Airborne Toxicants.....	280
Functional Divisions of the Respiratory System	281
Respiratory System Injury	283
Exposures to Air Pollutants.....	284
Defense Strategies	288
Types of Injury	291
Bibliography	294
Chapter 17	
The Nervous System.....	297
General Considerations.....	297
Cells of the Nervous System.....	300
The Blood–Brain Barrier	302
Neuron Action Potential and Synaptic Function.....	304
Neurotoxicity.....	305
Bibliography	311

Chapter 18

The Endocrine System.....	313
General Considerations.....	313
The Parts of the Endocrine System	313
The Reproductive System	317
Bibliography	323

SECTION IV TOXICOLOGY PRACTICE**Chapter 19**

The Practice of Toxicology.....	329
Introduction	329
Categories of Toxicologists.....	329
Expectations and Requirements for Toxicologists	333
Toxicologists as Expert Witnesses	335
Websites	336
Bibliography	338

Chapter 20

Regulatory Considerations	339
Standards, Guidelines, and Regulatory Agencies	339
Public Awareness and Public Outrage	341
Regulatory and Nonregulatory Agencies: Their Role in Protecting the Public from Chemical Exposures	343
Industrial Versus Environmental Standards.....	357
The Agency for Toxic Substances and Disease Registry.....	359
The National Toxicology Program.....	360
Consumer Product Safety Commission.....	361
Websites	362
Bibliography	364

Chapter 21

Toxicity Testing	365
The Nature and Scope of Toxicity Testing	365
Toxicity Test Objectives and Considerations	366
Animal Use and Extrapolation to Humans.....	369
Practical Aspects of Measuring Toxicity Experimentally.....	372
Acute Local Toxicity: Tests for Irritancy and Corrosiveness	373
Acute Systemic Toxicity: Use and Limitations of LD ₅₀	374
Efficacy, Toxicity, and Lethality.....	376
Other Examples of Prechronic Toxicity Testing in Laboratory Animals.....	381
Chronic Toxicity Testing in Laboratory Animals	382
Human Studies	383
Alternative Toxicity Testing Methods.....	384
Examples of In Vitro Tests for Several Toxicological Endpoints	387
Conclusion	391
Websites	391
Bibliography	392
Appendix 21-1: Example of a Template for a Subchronic Toxicity Study in Rodents for FDA Review.....	393

CONTENTS

Chapter 22

Uses and Limitations of Product Labeling for Public Safety	399
The Purpose of Product Labeling.....	399
Use of Product Labels by Consumers.....	400
Limitations of Product Labels	400
Federal Requirements	400
FIFRA and Pesticides.....	402
Pesticide Product Labeling.....	402
Product Labels Are Not Material Safety Data Sheets.....	408
Federal Food and Drug Administration Requirements for Labeling.....	409
Websites	413

Chapter 23

Toxicology Principles in the Management of Acute Poisonings.....	415
Introduction	415
Management of Acute Poisoning	416
Route of Exposure Influences Toxicity: An Example Using Cocaine.....	419
Intentional and Unintentional Exposures in the American Population.....	419
Inhalant Use	420
Toxicities Associated with “Street Drugs”	421
Websites	423
Bibliography	424

Chapter 24

Risk Assessment and the Perception of Risk	425
Overview of Risk	425
Risk Assessment	426
Cancer Risk Assessment	432
Ecological Risk Assessment	436
Toxicant Interaction and Chemical Mixtures.....	437
Responding to Public Concerns	440
Websites	442
Bibliography	443

Chapter 25

Making Informed Decisions.....	445
Difficulties in Decision Making	445
Risk Assessment in the Federal Government: Managing the Process	446
Making the Best Decisions.....	448
The CRAM Report.....	449
Websites	450
Bibliography	451

Glossary of Terms	453
Index	497