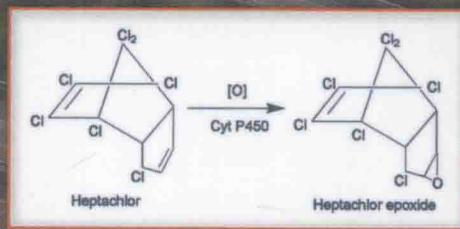
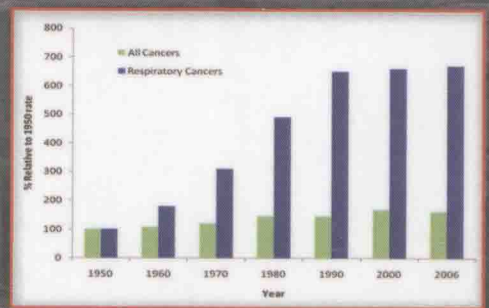
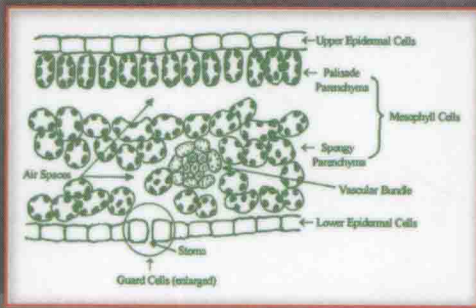


Third Edition

ENVIRONMENTAL TOXICOLOGY

Biological and Health Effects of Pollutants



Ming-Ho Yu
Humio Tsunoda
Masashi Tsunoda



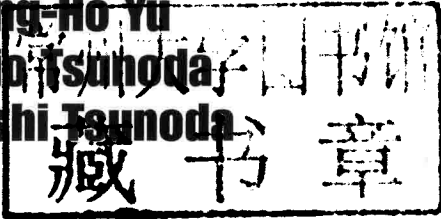
CRC Press
Taylor & Francis Group

Third Edition

ENVIRONMENTAL TOXICOLOGY

**Biological and Health Effects
of Pollutants**

Ming-Ho Yu
Humio Tsunoda
Masashi Tsunoda



CRC Press

Taylor & Francis Group
Boca Raton London New York

CRC Press is an imprint of the
Taylor & Francis Group, an **informa** business

CRC Press
Taylor & Francis Group
6000 Broken Sound Parkway NW, Suite 300
Boca Raton, FL 33487-2742

© 2011 by Taylor & Francis Group, LLC
CRC Press is an imprint of Taylor & Francis Group, an Informa business

No claim to original U.S. Government works

Printed in the United States of America on acid-free paper
Version Date: 20110617

International Standard Book Number: 978-1-4398-4038-2 (Hardback)

This book contains information obtained from authentic and highly regarded sources. Reasonable efforts have been made to publish reliable data and information, but the author and publisher cannot assume responsibility for the validity of all materials or the consequences of their use. The authors and publishers have attempted to trace the copyright holders of all material reproduced in this publication and apologize to copyright holders if permission to publish in this form has not been obtained. If any copyright material has not been acknowledged please write and let us know so we may rectify in any future reprint.

Except as permitted under U.S. Copyright Law, no part of this book may be reprinted, reproduced, transmitted, or utilized in any form by any electronic, mechanical, or other means, now known or hereafter invented, including photocopying, micro-filming, and recording, or in any information storage or retrieval system, without written permission from the publishers.

For permission to photocopy or use material electronically from this work, please access www.copyright.com (<http://www.copyright.com/>) or contact the Copyright Clearance Center, Inc. (CCC), 222 Rosewood Drive, Danvers, MA 01923, 978-750-8400. CCC is a not-for-profit organization that provides licenses and registration for a variety of users. For organizations that have been granted a photocopy license by the CCC, a separate system of payment has been arranged.

Trademark Notice: Product or corporate names may be trademarks or registered trademarks, and are used only for identification and explanation without intent to infringe.

Library of Congress Cataloging-in-Publication Data

Yu, Ming-Ho, 1928-

Environmental toxicology : biological and health effects of pollutants / Ming-Ho Yu, Humio Tsunoda, Masashi Tsunoda. -- 3rd ed.
p. ; cm.

Includes bibliographical references and index.

Summary: "Written primarily as a textbook for upper-level undergraduate and beginning graduate students, this book provides fundamental knowledge concerning the biological and health effects of pollutants on living systems. Also able to serve as a reference for professionals, the book stresses the chemical and biological characteristics of major pollutants found in the air, water, and soil, and their impacts on the health and wellbeing of humans, animals, and plants. This new edition is greatly expanded and updated, includes a color insert, and contains a new chapter on Occupational Toxicology"--Provided by publisher.

ISBN 978-1-4398-4038-2 (hardcover : alk. paper)

1. Environmental toxicology. 2. Environmental health. I. Tsunoda, Humio, 1930- II. Tsunoda, Masashi. III. Title.

[DNLM: 1. Environmental Pollutants--toxicity. 2. Environmental Exposure--adverse effects. WA 671]

RA1226.Y79 2012
615.9'02--dc23

2011020078

Visit the Taylor & Francis Web site at
<http://www.taylorandfrancis.com>

and the CRC Press Web site at
<http://www.crcpress.com>

Preface to the Third Edition

Many changes have occurred since the second edition of this book was published. Some of the changes include further global warming, growing world population, advancing technology and world economy, and expanding industrialization. Yet other changes include worsening air and water pollution, acid rain, and depletion of the ozone layer. In this volume, the information covered previously is updated or expanded.

I welcome Professor Humio Tsunoda and Dr. Masashi Tsunoda as coauthors. Together, they contributed a new chapter, “Occupational Toxicology” (Chapter 14). I am convinced that the material covered in the chapter enriches the content of this volume.

This book is written primarily as an introductory textbook for upper-level undergraduate and beginning graduate students majoring in environmental science, environmental toxicology, environmental health, and related fields. It is hoped that students as well as professionals interested in knowledge concerning the health and biological impacts of pollutants on living systems will find this volume a useful text or source book.

To assist with the students’ studies, review questions are placed at the end of each chapter. A *Solution Manual* has also been prepared separately.

Acknowledgments

I wish to express my sincere appreciation to my former advisers and mentors: the late Professor Ho Fang-Kai at National Taiwan University and Professor Gene W. Miller and the late Professor D.K. Salunkhe at Utah State University. Their guidance and kind help have contributed much to my teaching and research career. I am indebted to my wife, Ervena, for her support and encouragement, and I thank my three children, Albert, Christina, and Charlie, for their technical assistance. I thank Joseph Clements and his associates at CRC Press/Taylor & Francis Group for their patience and assistance.

Ming-Ho Yu

About the Authors

Dr. Ming-Ho Yu is professor emeritus at Huxley College of the Environment, Western Washington University. He taught environmental toxicology and environmental health at the university from 1970 to 1997. He received his BS from National Taiwan University in Taipei, Taiwan, and MS and PhD from Utah State University in Logan, Utah. He undertook postdoctoral study at Utah State University and the University of Alberta in Canada. While teaching at Western Washington University, Dr. Yu took a year of sabbatical leave and pursued research as a visiting professor at the Department of Hygiene and Public Health at Iwate Medical University in Japan. He also spent a summer as visiting professor to conduct research at the Institute of Whole Body Metabolism in Chiba, Japan.

Dr. Yu served as the vice president and president of the International Society for Fluoride Research (ISFR) from 1986 to 1996 and is the associate editor of *Fluoride*, the official publication of the society. He is a founding coeditor of *Environmental Sciences*, a journal published in Tokyo, Japan. He was also coeditor of *Environmental Fluoride 1985*, published by Elsevier Science in 1986. Dr. Yu is the author of *Environmental Toxicology—Impacts of Environmental Toxicants on Living Systems* and *Environmental Toxicology, 2nd Edition, Biological and Health Effects of Pollutants* and is coauthor of *Introduction to Environmental Toxicology*, editions 1–4, published by CRC Press.

Dr. Humio Tsunoda, professor emeritus at Iwate Medical University in Morioka, Japan, received his PhD from Hokkaido University in Japan. He received his MD by passing a national examination. He was a professor and chair in the Department of Hygiene and Public Health at Iwate Medical University for 27 years. Between 1997 and 2007, Professor Tsunoda served as a member of the Science Council of Japan, specializing in the area of environmental health. He received a Green Cross Award from the Japan Industrial Safety and Health Association, and awards for distinguished service from the Ministry of Construction; the Ministry of Labor; the Japanese Association of Rural Medicine; Japan Society for Atmospheric Environment; and Japanese Society for Occupational Health. In 2010, Professor Tsunoda received the Order of the Sacred Treasure, Gold Rays with Neck Ribbon from the government of Japan.

Dr. Masashi Tsunoda is an associate professor at the Department of Preventive Medicine and Public Health, Kitasato University School of Medicine in Japan. He received a PhD in social medicine from Niigata University in Japan, an MPH from the University of Pittsburgh, and a PhD in toxicology from the University of Georgia. He is a councilor of the Japan Society for Biomedical Research on Trace Elements; an editorial board member of the International Society for Fluoride Research; and a board member of the Japanese Society of Immunotoxicology. He is coeditor of *Kitasato Medical Journal* and a guest reviewer of *Toxicological Sciences*.

Contents

Preface to the Third Edition	xvii
Acknowledgments.....	xix
About the Authors.....	xxi
Chapter 1 Introduction	1
1.1 Study of Environmental Toxicology.....	1
1.2 Importance of Environmental Toxicology as an Area of Science	1
1.3 Introduction to This Book	1
Chapter 2 Environmental Changes and Health.....	7
2.1 Our Changing Environment	7
2.1.1 Introduction	7
2.1.2 World Population.....	7
2.1.3 Global Climate Changes: Global Warming	8
2.1.3.1 Impact on Plants	10
2.1.3.2 Impact on Birds and Animals.....	10
2.1.3.3 Impact on Tropical Species.....	12
2.1.3.4 Impact on Freshwater Fish.....	12
2.1.4 Impact on Marine Oxygen	12
2.1.5 Rising Acidity of Seawater.....	13
2.1.6 Rise in Diseases	15
2.2 Air Pollution	15
2.2.1 Introduction	15
2.2.2 Air Pollution and Developing Economies	16
2.3 Indoor Air Pollution	19
2.4 Water Pollution	19
2.5 Soil Pollution	23
2.6 The Changing Diseases	24
2.6.1 Cancer	24
2.6.2 Birth Defects and Child Mortality	30
2.6.3 Reproductive Damages.....	30
2.6.4 Respiratory Diseases	31
2.6.5 Endocrine Disruption	33
2.6.6 Diseases Induced by Metals	33
2.6.7 Foodborne Illnesses	34
Review Questions	35
References	36

Chapter 3	Occurrence of Toxicants.....	39
3.1	Introduction	39
3.2	Visible Smoke or Smog	39
3.3	Offensive Odors.....	40
3.4	Agricultural Damage.....	40
3.5	Intoxication of Animals.....	41
3.6	Injuries to Humans	41
3.7	Chronic and Acute Effects	42
3.7.1	Chronic Effects.....	43
3.7.2	Acute Effects	43
3.7.2.1	Donora, Pennsylvania, United States, 1948.....	44
3.7.2.2	Poza Rica, Mexico, 1950	44
3.7.2.3	London, England, 1952.....	44
3.7.2.4	New York, United States, 1953.....	45
3.7.2.5	Los Angeles, California, United States, 1954.....	45
3.7.2.6	New Orleans, Louisiana, United States, 1955.....	45
3.7.2.7	Worldwide Episode, 1962	45
3.7.2.8	Tokyo, Japan, 1970.....	45
3.7.2.9	Bhopal, India, 1984.....	45
3.7.2.10	Chernobyl, Soviet Union, 1986.....	46
3.7.2.11	Gas Leak on the Platform in the North Sea, 1988.....	47
3.7.2.12	Oil Spill in Alaska's Prince William Sound, 1989	47
3.7.2.13	Coal Mine Explosion in Western Virginia, United States, 2010.....	48
3.7.1.14	Gulf of Mexico Oil Spill, United States, 2010.....	48
3.7.2.15	Raspadskaya Coal Mine Explosion in Russia, 2010	49
3.7.2.16	Gas Explosion and Chemical Leak in Nanjing, China, 2010	49
3.7.2.17	Toxic-Sludge Spill in Hungary, 2010.....	49
3.7.2.18	Gas Explosion in Henan, China, 2010.....	50
3.7.2.19	Fukushima Nuclear Power Plant, Japan, 2011.....	50
	References	52
Chapter 4	Toxic Action of Pollutants.....	53
4.1	Introduction	53
4.2	Effects on Plants.....	53
4.2.1	Source of Pollutants	53

4.2.2	Uptake of Pollutants	53
4.2.3	Transport of Toxicant	55
4.2.4	Plant Injury	55
4.3	Mammalian Organisms	56
4.3.1	Exposure	56
4.3.2	Uptake	57
4.3.3	Transport	58
4.3.4	Storage	58
4.3.5	Metabolism	59
4.3.6	Excretion	59
4.4	Mechanism of Toxic Action	59
4.4.1	Disruption or Destruction of Cellular Structure	60
4.4.2	Direct Chemical Combination with a Cell Constituent	60
4.4.3	Effect on Enzymes	61
4.4.3.1	Enzyme Inhibition by Inactivation of Cofactor	62
4.4.3.2	Enzyme Inhibition by Competition with the Cofactor	62
4.4.3.3	Enzyme Inhibition by Binding to the Active Site	63
4.4.3.4	Inhibition of Enzyme Activity by Toxic Metabolite	64
4.4.4	Secondary Action as a Result of the Presence of a Pollutant	64
4.4.4.1	Allergic Response to Pollen	65
4.4.4.2	Carbon Tetrachloride	65
4.4.4.3	Chelation	65
4.4.4.4	Metal Shift	66
4.4.5	Free-Radical-Mediated Reactions	66
4.4.6	Endocrine Disruption	68
	Review Questions	69
	References	70

Chapter 5	Factors Affecting Xenobiotic Action	73
5.1	Introduction	73
5.2	Physiological Properties	73
5.3	Dose or Concentration	73
5.4	Duration and Mode of Exposure	74
5.5	Environmental Factors	75
5.5.1	Temperature	75
5.5.2	pH	76
5.5.3	Humidity	76
5.6	Interaction	76
5.6.1	Additive, Synergism, and Potentiation Effects	76

	5.6.2	Antagonism	77
5.7		Biological Factors	78
	5.7.1	Plants	78
	5.7.2	Animals and Humans.....	78
		5.7.2.1 Genetic Factors	78
		5.7.2.2 Developmental Factors	79
		5.7.2.3 Diseases	79
		5.7.2.4 Behavioral Factors	79
		5.7.2.5 Gender.....	80
5.8		Nutritional Factors.....	80
	5.8.1	Introduction	80
	5.8.2	Fasting and Starvation.....	80
	5.8.3	Proteins.....	81
	5.8.4	Carbohydrates.....	81
	5.8.5	Lipids.....	83
	5.8.6	Vitamin A.....	84
	5.8.7	Vitamin D.....	84
	5.8.8	Vitamin E (α -Tocopherol)	85
	5.8.9	Vitamin C.....	86
	5.8.10	Minerals	88
		Review Questions	89
		References	90
Chapter 6		Biotransformation: Metabolism of Xenobiotics	93
	6.1	Introduction	93
	6.2	Types of Biotransformation	93
	6.3	Mechanism of Biotransformation.....	94
	6.4	Characteristics of Biotransformation	94
	6.5	Consequence of Biotransformation	97
		6.5.1 Biotransformation of Endogenous Substances	97
		6.5.2 Activation of Xenobiotics.....	98
	6.6	Factors Affecting Biotransformation.....	100
	6.7	Characteristics of the Cytochrome P450s	101
		6.7.1 Induction.....	102
		6.7.2 Genetic Polymorphisms	103
		Review Questions	103
		References	104
Chapter 7		Responses to Environmental Toxicants.....	105
	7.1	Introduction	105
	7.2	Responses of Plants	105
	7.3	Responses of Humans and Animals.....	106
		7.3.1 The Respiratory Tract.....	106
		7.3.1.1 Nasopharynx.....	106

	7.3.1.2 Tracheobronchial Areas.....	106
	7.3.1.3 Alveoli	107
	7.3.2 Membranes	108
	7.3.3 Liver	110
	7.3.4 Kidneys.....	111
	Review Questions	113
	References	114
Chapter 8	Air Pollution: Inorganic Gases.....	115
8.1	Introduction	115
8.2	Sulfur Dioxide	115
	8.2.1 Sources of SO ₂	115
	8.2.2 Characteristics of SO ₂	116
	8.2.3 Effects on Plants.....	116
	8.2.4 Effects on Animals.....	120
	8.2.5 Health Effects.....	120
8.3	Nitrogen Dioxide	122
	8.3.1 Forms and Formation of Nitrogen Oxides	122
	8.3.2 Major Reactive Nitrogen Species in the Troposphere	122
	8.3.3 Effects on Plants.....	123
	8.3.4 Health Effects.....	124
	8.3.5 Biological Effects	124
	8.3.6 N ₂ O and Stratospheric O ₃ Layer Depletion	125
8.4	Ozone.....	128
	8.4.1 Sources of Ozone.....	128
	8.4.2 Photochemical Smog.....	129
	8.4.3 Effects on Plants.....	129
	8.4.4 Effects on Animals and Humans	131
	8.4.5 Biological Effects	132
8.5	Carbon Monoxide.....	134
	8.5.1 Introduction	134
	8.5.2 Formation	134
	8.5.3 Human Exposure.....	135
	8.5.4 Health Effects.....	135
	Review Questions	138
	References	139
Chapter 9	Air Pollution: Particulate Matter.....	143
9.1	Introduction	143
9.2	Characteristics of Particulate Matter.....	143
9.3	Formation of Particulates	144
	9.3.1 Physical Processes.....	144
	9.3.2 Chemical Processes.....	144

9.4	Health Effects	145
9.5	Silica	147
	9.5.1 Silicosis	147
	9.5.2 Pathogenesis	147
9.6	Beryllium.....	148
	9.6.1 Sources of Exposure to Beryllium	148
	9.6.2 Health Effects.....	150
	9.6.3 Biological Effects	150
	9.6.4 Therapy.....	151
9.7	Asbestos.....	151
	9.7.1 Chemical and Physical Properties.....	152
	9.7.2 Use.....	152
	9.7.3 Exposure.....	152
	9.7.4 Health Effects.....	153
9.8	Lead.....	154
	9.8.1 Sources of Lead.....	154
	9.8.2 National Lead Emissions.....	154
	9.8.3 Lead Air Quality Standards.....	155
	9.8.4 Effect of Lead on Health.....	155
	Review Questions.....	155
	References	156

Chapter 10 Environmental Fluoride

10.1	Introduction	159
10.2	Occurrence and Forms of Fluoride	159
	10.2.1 Introduction	159
	10.2.2 Airborne Fluoride.....	159
	10.2.3 Natural Waters.....	160
	10.2.4 Minerals and Soils.....	160
	10.2.5 Foods and Water.....	160
10.3	Industrial Sources of Fluoride Pollution	161
	10.3.1 Introduction	161
	10.3.2 Manufacture of Phosphate Fertilizers	162
	10.3.3 Manufacture of Aluminum	163
	10.3.4 Manufacture of Steel	163
	10.3.5 Combustion of Coal.....	163
	10.3.6 Other Sources.....	164
10.4	Effects on Plants.....	164
10.5	Effects on Animals.....	166
	10.5.1 Introduction	166
	10.5.2 Acute Effects	167
	10.5.3 Chronic Effects.....	167
10.6	Effects on Humans	170
	10.6.1 Daily Intake of F	170
	10.6.2 Absorption.....	170

10.6.3	Acute Effects	171
10.6.4	Chronic Effects.....	171
10.7	Biochemical Effect of Fluoride	172
10.7.1	In Plants.....	172
10.7.2	In Animals and Humans	175
10.8	Nutrition and Fluoride Toxicity	177
	Review Questions	178
	References	179
Chapter 11	Volatile Organic Compounds	181
11.1	Introduction	181
11.2	Sources	181
11.3	Petroleum Hydrocarbons	181
11.3.1	Alkanes.....	182
11.3.1.1	Health Effect.....	183
11.3.2	Alkenes.....	184
11.3.2.1	Health Effects	184
11.3.3	Aromatic Hydrocarbons	184
11.3.3.1	Benzene.....	185
11.3.3.2	Toluene.....	187
11.3.3.3	Xylenes.....	187
11.4	Polycyclic Aromatic Hydrocarbons	188
11.4.1	Sources	189
11.4.2	Physical and Chemical Properties.....	189
11.4.3	Transport	189
11.4.4	Exposure.....	189
11.4.5	Metabolism and Toxicity	191
	Review Questions	193
	References	193
Chapter 12	Soil and Water Pollution: Environmental Metals and Metalloids	195
12.1	Introduction	195
12.2	Lead	196
12.2.1	Characteristics and Use	196
12.2.2	Sources of Lead Exposure.....	196
12.2.2.1	Airborne Lead	196
12.2.2.2	Waterborne Lead	197
12.2.2.3	Lead in Food.....	198
12.2.2.4	Lead in Soils	198
12.2.3	Lead Toxicity.....	198
12.2.3.1	Lead Toxicity to Plants	198
12.2.3.2	Lead Poisoning in Animals and Fish.....	199
12.2.3.3	Health Effects of Lead in Humans	199

	12.2.4	Biological Effects of Lead.....	202
	12.2.5	Lead Toxicity and Nutrition	203
12.3		Cadmium	204
	12.3.1	Introduction	204
	12.3.2	Characteristics and Use of Cadmium.....	205
	12.3.3	Exposure to Cadmium.....	205
		12.3.3.1 Airborne Cadmium.....	205
		12.3.3.2 Waterborne Cadmium.....	206
		12.3.3.3 Cadmium Pollution of Soils.....	206
		12.3.3.4 Cadmium in Food.....	206
	12.3.4	Metabolism of Cadmium.....	207
	12.3.5	Cadmium Toxicity.....	208
		12.3.5.1 Toxic Effects on Plants	208
		12.3.5.2 Effects of Cadmium on Animals.....	209
		12.3.5.3 Effects of Cadmium on Humans	210
	12.3.6	Cadmium and Nutrition	212
12.4		Mercury	213
	12.4.1	Introduction	213
	12.4.2	Extraction and Uses of Mercury	213
	12.4.3	Sources of Mercury Pollution.....	214
	12.4.4	Biotransformation of Mercury	214
		12.4.4.1 Biomethylation of Mercury.....	215
		12.4.4.2 Demethylation of Methylmercury	215
		12.4.4.3 Methylmercury Biosynthesis and Diffusion into Cells	215
	12.4.5	Toxicity of Mercury.....	216
		12.4.5.1 Effects of Mercury on Algae	216
		12.4.5.2 Effects of Mercury on Plants.....	216
		12.4.5.3 Effects of Mercury on Animals.....	216
		12.4.5.4 Effects of Mercury on Human Health	217
	12.4.6	Biological Effects	219
	12.4.7	Mercury and Nutrition.....	221
12.5		Nickel.....	222
	12.5.1	Introduction	222
	12.5.2	Sources of Environmental Nickel Pollution.....	223
	12.5.3	Health Effect	223
12.6		Arsenic.....	225
	12.6.1	Occurrence and Properties.....	225
	12.6.2	Uses of Arsenic	225
	12.6.3	Sources of Exposure to Arsenic.....	226
	12.6.4	Human Exposure to Arsenic	226
	12.6.5	Animal Exposure to Arsenic.....	227
	12.6.6	Distribution of Arsenic in the Body	227
	12.6.7	Toxicity of Arsenic	227
		12.6.7.1 Toxicity to Plants	227

12.6.7.2	Toxicity of Arsenic to Animals and Humans	228
12.6.8	Biological Effects of Arsenic	229
	Review Questions	231
	References	232
Chapter 13	Pesticides and Related Materials.....	237
13.1	Introduction	237
13.2	Insecticides	237
13.2.1	Introduction	237
13.2.2	Chlorinated Hydrocarbons	237
13.2.2.1	Introduction	237
13.2.2.2	DDT	238
13.2.3	Organophosphorus Compounds	243
13.2.3.1	Introduction	243
13.2.3.2	Toxicity of Organophosphorus Compounds	244
13.2.3.3	Action of Acetylcholinesterase and Organophosphates.....	244
13.2.4	Carbamates	246
13.3	Herbicide	246
13.3.1	2,4-D and 2,4,5-T	246
13.3.2	Atrazine	248
13.4	Polychlorinated Biphenyls	249
13.4.1	Introduction	249
13.4.2	Properties of PCBs	249
13.4.3	Uses of PCBs.....	250
13.4.4	Environmental Contamination of PCBs.....	250
13.4.4.1	Wildlife Exposure to PCBs	251
13.4.4.2	Human Exposure to PCBs	252
13.4.5	Metabolism of PCBs	253
13.4.6	Toxicity of PCBs	253
13.4.7	Biological Effects of PCBs.....	254
13.5	Polybrominated Biphenyls.....	255
13.5.1	Introduction	255
13.5.2	Chemistry of PBBs.....	255
13.5.3	Toxicity of PBBs.....	256
13.5.4	Biological Effects of PBBs	256
13.6	Dioxin	256
13.6.1	Introduction	256
13.6.2	Exposure to PCDDs	257
13.6.3	Toxicity of Dioxins.....	257
13.6.3.1	Toxicity of Dioxins in Animals	257
13.6.3.2	Toxicity of Dioxins in Birds	258
13.6.3.3	Toxicity of Dioxins in Humans.....	259

13.6.4	Gene Regulation by Dioxins	260
13.6.5	Environmental Degradation of TCDD	261
	Review Questions	261
	References	262
Chapter 14	Occupational Toxicology	265
14.1	Introduction	265
14.1.1	Antiquity to Middle Ages: Diseases among Miners	265
14.1.2	After the Industrial Revolution: Metal Diseases	265
14.1.3	After the Nineteenth Century: Organic Compounds, Organic Metals, and Gases	267
14.1.4	Modern Era: Toxicology and Preventive Medicine	268
14.2	Changing Workplace Environment	269
14.3	Threshold Limit Values	270
14.4	Biological Exposure Indices	270
14.5	Respiratory Toxicity	271
14.5.1	Irritation of Airways and Edema	272
14.5.2	Occupational Respiratory Diseases	273
14.6	Other Occupational Diseases Caused by Toxic Substances	274
14.6.1	Metal Fume Fever	274
14.6.2	Fluorosis	275
14.6.3	Diseases Caused by Sensitizers	275
14.7	Recent Chemicals of Concern	276
14.7.1	Nanoparticles	276
14.7.2	Rare Metals	277
	Review Questions	277
	References	278
Chapter 15	Endocrine Disruption	281
15.1	Introduction	281
15.2	Review of Hormonal Function	281
15.3	Characteristics of Endocrine Disruptors	282
15.4	Mode of Action	285
15.5	Examples of Endocrine Disruption	287
15.5.1	Induction of Developmental Toxicity	288
15.5.2	Estrogen Mimics	288
15.5.3	Induction of Sterility	288
15.5.4	Antiandrogens	289
15.5.5	Induction of Imposex	290
15.5.6	Hypothyroidism	290
15.5.7	Changing Behavior	290

15.6	Hormonal Cancers.....	290
15.6.1	Introduction.....	290
15.6.2	Hormonal Cancers in Farmers.....	291
15.6.3	The Toxic Substance Control Act.....	292
15.7	Testing Estrogenicity.....	292
	Review Questions.....	293
	References.....	294
Chapter 16	Mutagenic Pollutants.....	297
16.1	Introduction.....	297
16.2	Types of Mutation.....	297
16.2.1	Chromosomal Aberrations.....	298
16.2.2	Gene Mutations.....	299
16.3	Effects of Mutation.....	299
16.4	Induction of Mutation.....	300
16.4.1	UV Light.....	300
16.4.2	Ionizing Radiations.....	301
16.4.3	Chemical Mutagens.....	302
16.4.3.1	Alkylating Agents.....	302
16.4.3.2	Intercalating Agents.....	304
16.4.3.3	Metals.....	304
	Review Questions.....	305
	References.....	305
Chapter 17	Environmental Cancer.....	307
17.1	Introduction.....	307
17.2	Causes of Cancer.....	307
17.3	Three Stages in the Development of Cancer.....	309
17.4	Metastasis.....	311
17.5	Classification of Carcinogens.....	311
17.5.1	Radiation.....	312
17.5.2	Chemical Carcinogens.....	312
17.6	Metabolism of Chemical Carcinogens.....	313
17.6.1	Free Radicals.....	314
17.6.2	DDT.....	315
17.6.3	Formaldehyde.....	315
17.6.4	Vinyl Chloride.....	315
17.6.5	Alkylating Agents.....	316
17.6.6	Trichloroethylene (TCE).....	317
17.6.7	Polycyclic Aromatic Hydrocarbons.....	317
17.6.7.1	Benzo(a)pyrene.....	318
17.6.7.2	Halogenated Aromatic Hydrocarbons.....	320
17.7	Respiratory Cancer Death Rates.....	320
17.8	DNA Repair.....	321
17.8.1	DNA Damage.....	321