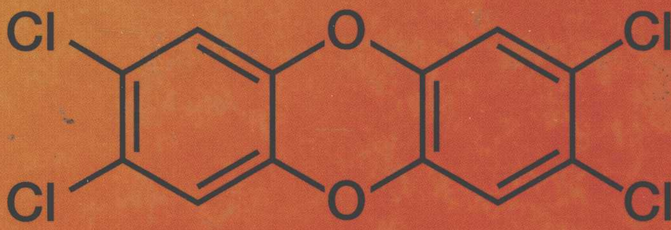

Dioxins and Health

Including Other Persistent Organic Pollutants and Endocrine Disruptors

Third Edition

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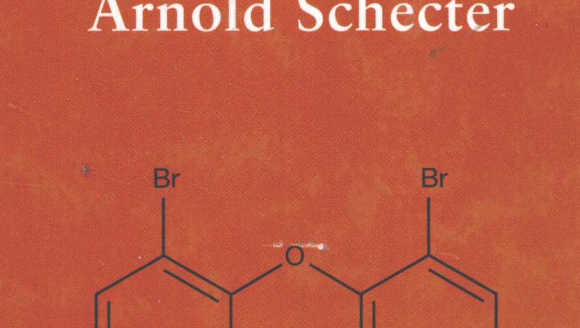
Arnold Schecter



WILEY

DIOXINS AND HEALTH

Including Other Persistent Organic Pollutants and Endocrine Disruptors
Third Edition

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To My Family

PREFACE

This is the third edition of *Dioxins and Health*, which includes other persistent organic pollutants (POPs) and endocrine disruptors (EDs). The series began in 1994 with the publication of the first edition, written in an attempt to describe many complex issues related to health effects of dioxins and similar compounds in a less technical manner for those in different academic, scientific, and professional disciplines, as well as for the general public. In 2003, a second edition of *Dioxins and Health* was published to highlight scientific advances regarding dioxin exposure, health effects, and mechanisms of action. In organizing the second edition, we again found a number of world-class scientists to describe updated methods and findings from their disciplines. We decided to prepare a medium-sized volume with many references to introduce scientists and the general public to major issues related to dioxin rather than attempt to prepare an encyclopedic text.

With the development of what was originally meant to be a third edition of *Dioxins and Health*, we decided to include other POPs and endocrine disrupters, some similar to dioxins. We selected brominated flame retardants, such as polybrominated diphenyl ethers (PBDEs) and hexabromocyclododecane (HBCD); perfluorinated chemicals (PFCs), such as perfluorooctanoic acid (PFOA) and perfluorooctanesulfonic acid (PFOS); and other endocrine disrupting chemicals similar to POPs in that they are found in human tissue at similar levels when measured, such as bisphenol A (BPA).

In the opening chapter, toxicologists Daniele Wikoff, Lauren Fitzgerald, and Linda Birnbaum introduce the readers to POPs, chemicals that are organic, toxic, persistent, and bioaccumulate. They review not only the classical POPs, such as dioxins, polychlorinated biphenyls (PCBs), and dichlorodiphenyl trichloroethane (DTT), but also emerging POPs, such as PBDEs and HBCD. The authors also provide the reader with a generalized overview of the history of POPs, the concepts of biomagnification and biomonitoring, and provide an introduction to many of the chemicals discussed in later chapters.

Following this introduction, the concept of evaluating the toxicity of mixtures of dioxins and dioxin like compounds, including dibenzofurans and some PCBs, is presented by Michael DeVito, an NIH toxicologist, who also works with the World Health Organization (WHO) and other dioxin committees. This chapter introduces dioxin toxic equivalency factors (TEFs) and toxic equivalency (TEQ), an approach used to estimate the toxicity of dioxins and dioxin-like compounds. TEFs are derived by assigning an estimated order of magnitude toxicity value to each congener. These values are multiplied by the measured amount of each congener, then summed to produce one number as an estimate of total dioxin toxicity (TEQ). This approach has been a major step forward in dealing with chemical mixtures, such as dioxins and dibenzofurans, which act by a similar mechanism of action.

The issue of chemical contamination in food is addressed by Janice Huwe, a senior chemist with the United States Department of Agriculture (USDA), whose work on measuring dioxins, PBDEs, and other pollutants in U.S. food is well known. She reviews classical POPs, as well as emerging POPs to which humans may be exposed through consumption of food, including seafood, meat, poultry, dairy, eggs, and grains. She also notes differences in chemical residue levels found in foods occasionally due to local environmental contamination.

PBDEs and replacement flame retardants for PBDE mixtures are discussed by environmental scientist Thomas Webster and chemist Heather Stapleton. PBDEs, widely used flame retardants in the United States, are being phased out because of their toxicity; however, they are being replaced by newer flame retardants, many of which have unknown chemical composition and may also be toxic. Despite this phase out, PBDEs are found in human populations, biota, and the environment. Details of this ongoing problem and problems originating with the use of new flame retardants are described in this chapter.

James Olson, a toxicologist who has conducted research on dioxins and related compounds for decades, discusses the pharmacokinetics of selected POPs. Olson reviews studies that show the disposition and kinetics of POPs in both human and selected animal models, providing the reader with information regarding factors that can help explain biological conditions to these compounds, such as dose-dependent and time-dependent tissue distribution.

An overview of immunology and immunotoxicology precedes a discussion of specific immunological aspects of dioxins and other POPs in the chapter written by Robert Luebke, Jamie DeWitt, Dori Germolec, Keith Salazar, and Nancy Kerkvliet. Some effects on the immune system are believed to be responsible for the toxicity of these compounds. Findings are presented that show that the sensitivity of the immune system is high during the perinatal period. Effects of POPs on the immune system include decreased ability to fight cancer and infectious diseases.

"Developmental Neurotoxicity of Dioxins," by Jean Harry and Pamela Lein, introduces the reader to neurogenesis and provides an overview of *in vitro* and *in vivo* studies that show adverse effects on brain development. The authors focus on several possible aryl hydrocarbon receptor (AhR) dependent mechanisms of dioxin neurotoxicity and describe certain adverse neurologic health outcomes associated with prenatal PCB exposure, including decreased IQ, psychomotor skills, and deficits in visual recognition, and memory.

Kyle Steenland, Tony Fletcher, and David Savitz describe their studies on the health effects of PFOA and their epidemiological findings in exposed and comparison populations in the chapter titled "Epidemiologic Evidence on the Health Effects of Perfluorooctanoic Acid (PFOA)." In the past, PFCs have been used to repel stains or water in clothing and carpets, and have also been used in nonstick coatings found in some cooking utensils. Although there is considerable evidence of health effects in animal models, including several types of tumors, neonatal death loss, and toxic effects on the immune, hepatic, and endocrine systems, the effects of PFCs are not well characterized in humans. Production of some PFCs in the United States has ended, but because they are persistent, depot sources will remain in the environment for many years and will subsequently continue to contaminate members of the general population.

Chemists Kurunthachalam Kannan, Chunyang Liao, and Hyo-Bang Moon introduce polybrominated dioxins (PBDDs) and dibenzofurans (PBDFs). These compounds are not as well known as their chlorinated cousins (PCDDs and PCDFs) because of the complex and costly analytical procedures needed to study them, and also because they are frequently found at lower levels than PCDD/Fs. However, they are believed to cause similar health effects as the chlorinated dioxins and dibenzofurans. The authors provide background information on these chemicals and their origins. They also discuss similarities and differences between PBDD/Fs and PCDD/Fs.

Cancer has long been a concern from exposure to dioxins, PCBs, and related POPs. Lennart Hardell and Mikael Eriksson review the literature on this subject, including their own groundbreaking research on dioxins and cancers in humans. The authors review epidemiological studies showing associations between POPs exposure and cancers, including soft tissue sarcomas, malignant lymphomas, multiple myeloma, leukemia, nasal and nasopharangeal cancers, hepatic cancer, and gastric cancer. The cancers considered by many to have the strongest associations with dioxin exposure are non-Hodgkin's lymphoma and soft tissue sarcoma, first linked to dioxin exposure in studies by these authors.

Reproductive and developmental effects of dioxins and other POPs are discussed by epidemiologists Anne Sweeney, Deborah del Junco, Marcella Warner, and Brenda Eskenazi. Inability to conceive, spontaneous abortion, altered menstrual periods, and endometriosis are possible reproductive effects of POP exposure. The authors review many studies regarding reproductive outcomes, including the Seveso Women's Health Study, paternal dioxin exposure, and environmental dioxin exposure.

The chapter on BPA, by Thaddeus Schug, Sarah Vogel, Laura Vandenberg, Joe Braun, Russ Hauser, Julia Taylor, Frederick vom Saal, and Jerold Heindel, provides an introduction to this endocrine disrupter. It has been commonly found in can linings and plastic bottles, such as baby bottles and water bottles. Although BPA has a short half-life in humans and is not persistent, it is sometimes considered similar to POPs because of its frequent intake. At the time of this book's preparation, there is a debate concerning what levels of BPA intake should be considered safe. Some scientists feel present government levels are too permissive. Epidemiological studies are not consistent with respect to BPA health; however, animal studies have shown obesity, decreased semen quality, cardiovascular disease, endocrine disruption, and cancer as health effects following BPA exposure.

Phthalate health findings are presented by John D. Meeker and Kelly K. Ferguson. Phthalates are found in many products, including perfumes, deodorants, cosmetics, and other personal care products, to which most in industrialized countries are regularly exposed. Phthalates are ubiquitous and have proven to be a challenge when measured in tissue, food, and other media. Laboratory contamination with phthalates has made analysis a major challenge. Data exists on phthalate levels in biota but quantification remains difficult. The endocrine-disrupting characteristics of phthalates may lead to reproductive and developmental effects in men and women, obesity, cancers, and possibly altered sex differentiation from fetal exposure.

The next chapters of the text focus on a number of incidents characterized by the presence of certain POPs. Epidemiologists Angela Cecilia Pesatori and Pier Alberto Bertazzi describe the well-known 1976 dioxin incident in Seveso, Italy. An explosion at a chemical factory released 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) on a residential population. In contrast to Vietnam and most other dioxin contaminated locations, the site of the Seveso contamination has been converted into a public park with precautions to reduce or prevent dioxin release from the soil underlying the park. A number of epidemiological studies, assessing cancer and other health effects, have been performed from this incident.

Susan Hammond, a social activist, and Arnold Schecter, a public health physician-researcher, each long active in Vietnam work, discuss Agent Orange and its dioxin contaminant, 2,3,7,8-TCDD, sprayed in Vietnam between 1962 and 1971. They describe major issues, including persistence of dioxin in the environment, people, and wildlife; social and legal issues arising from this controversial spraying; remediation efforts; and monetary issues involved in remediation.

Two of the most definitive incidents documenting human health damage from dioxin-like chemicals have been those of the rice oil contamination incidents in Japan and Taiwan, known as Yusho and Yucheng, respectively. Certain batches of rice oil used for cooking were contaminated with PCBs, PCDFs, and other toxicants in the 1960s in Japan and 1970s in Taiwan. Approximately 2000 people were classified as victims by government agencies for each incident. Professor Yoshito Masuda, the chemist who discovered and characterized PCDFs in the Japanese incident, describes both incidents in his Yusho and Yucheng chapter, which is coauthored by physician and scientific collaborator Arnold Schecter.

A fifth event involving dioxins is the 1981 Binghamton (New York) State Office Building (BSOB) incident, in which an electrical panel caught fire and subsequently heated PCBs and chlorinated benzenes in a nearby basement electrical transformer. The heated soot moved up air ducts and stairways to contaminate the entire office building. It took 13 years and approximately $50,000,000 to sufficiently clean the building and allow reoccupancy. This incident contributed substantially to the concept, validation, and implementation of TEFs and TEQs. In addition, the incident stimulated major advances in detection of individual dioxin and dibenzofuran congeners in environmental samples, human adipose tissue (fat tissue), and blood at low levels and hence, biomonitoring. The study of this incident unexpectedly found that all persons sampled, including those from the general population, had dioxins and dibenzofurans in their bodies. Before that time, it was believed that only certain individuals had dioxin contamination. Toxicologist Nancy Kim and physician Arnold Schecter, then working for the State of New York Department of Health and for the local county (Broome County) health department, respectively, review this incident from their unique perspectives as responders beginning at the time of the incident.

John Jake Ryan, a Canadian chemist formerly with Health Canada, describes the last major incident discussed in this book: The dioxin poisoning of former Ukrainian president Viktor Yushchenko, one of the better-known dioxin incidents worldwide. Victor Yushchenko was a politician running for the presidency of Ukraine when he mysteriously became ill. This was found to be a deliberate poisoning with pure 2,3,7,8-TCDD, the most toxic dioxin. Prior to the presidential election, he attended a late-night dinner with political opponents and abruptly became ill with symptoms now known to be from dioxin poisoning. Mr. Yushchenko continued his presidential campaign and became president of Ukraine despite health problems related to the dioxin poisoning.

The final chapter in the book, written by toxicologists David Szabo and Anne Loccisano, provides the reader with a summary of human health risk assessment focusing on many of the POPs that are currently of substantial concern. It serves to bring together in one self-contained chapter an overview of the chemicals covered in previous chapters, and some new chemicals, from the perspective of how to deal with and assess human health risk from these toxic compounds.

This book presents information on historical, social, and scientific aspects of dioxins and other related POPs. It endeavors to provide the reader with a concise yet relatively comprehensive overview of major compounds currently of interest with sufficient references to help the reader pursue issues of special interest in greater depth.

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ARNOLD SCHECTER

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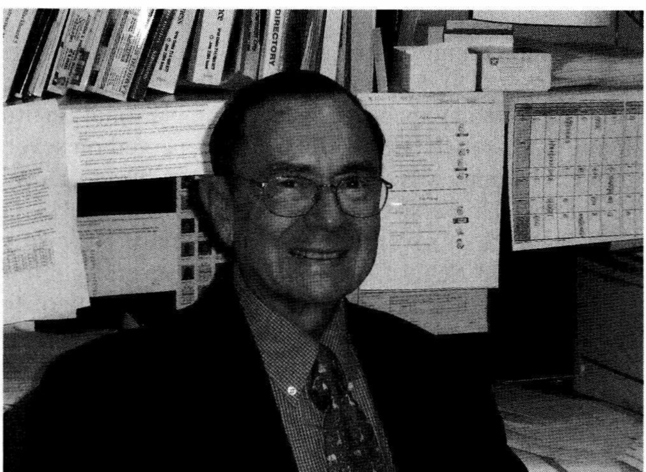
ABOUT THE EDITOR



Arnold Schecter is a public health and preventive medicine physician who specializes in research in biomonitoring to estimate exposure to various toxic chemicals. Collaborations include scientists in the United States, Germany, Finland, Canada, Vietnam, Cambodia, Laos, Japan, Russia, Israel, and other countries.

He began his work with dioxins by documenting dioxin and dibenzofuran formation from an electrical transformer fire in Binghamton, New York, collaborating with various expert chemists when they demonstrated that patterns found in fat tissue and blood of exposed workers were similar to those found in environmental samples from the fire. The U.S. Environmental Protection Agency (EPA) later decided to ban the use of PCBs in electrical transformers in public buildings based on this and other incidents.

Later, he studied dioxins from Agent Orange in Vietnamese and Americans. His research in Vietnam began in 1984 and continues to the present. His research documented elevated dioxin levels from Agent Orange in Vietnam, including elevated dioxin levels in Vietnamese food, blood, and milk and environmental samples from defoliation agents used in previous decades. The studies also documented dioxins from other sources in Vietnamese human tissues. He and his colleagues documented elevated dioxin levels in workers as much as 30–40 years after exposure.

More recently, with other scientists and physicians, his group documented PBDE levels in the milk of nursing American women. They also noted the levels were the highest to date by orders of magnitude compared with other then-published reports from various countries. This and other works were used to reduce PBDE manufacture and use. His recent work includes the study of human and food levels of HBCD, BPA, phthalates, and other persistent organic pollutants (POPs) and endocrine disruptors (EDs). Studies of home-based electrical waste recycling workers in less developed countries are some of the newest projects.

He enjoys communicating with a broad audience through various media. He served on EPA and ATSDR on dioxin and related chemicals expert panels and also served as a (dioxin) Special Expert at the National Institute of Environmental Health Sciences (NIEHS/NIH). He has served on several scientific editorial boards. His training was at the University of Chicago, Howard Medical School, and Columbia University School of Public Health. His employment has been on the faculties of several State University of New York campuses and New Jersey Medical School, as well as with several community-based health programs. He currently is a professor at the University of Texas School of Public Health, Dallas Campus.

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