CHAPTER 1

Introduction: Why Should We Care about Organic Chemicals and Human Health?

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ABSTRACT

Background: The last several decades have seen an enormous increase in the development and manufacture of different organic chemicals that have proven useful for many aspects of contemporary life. The question is the degree to which some of these chemicals cause harm to human beings.

Objective: This book is directed at the goal of identifying organic chemicals that, while useful in many regards, pose risks to human health because of their biological activity and often their persistence.

Discussion: The various chapters in this book are directed at the effects of organic chemicals on the various organ systems.

Conclusions: While recognizing the wonderful benefits that have come from the development and use of many organic chemicals, serious adverse human health effects have occurred because of inadequate testing prior to use and ineffective steps to prevent release of the chemicals into air, food, water, and the environment, resulting in exposure and disease in humans. It is urgent that more effective ways be found to ensure the safety of organic chemicals, no matter how useful they may be, before they are produced and released into the environment.
Organic chemicals are a major part of everyday life in the modern world. Without question, chemicals have made our lives much easier. But at the same time, it is important to recognize that there have been some downsides to the chemical revolution. This book is focused on the downsides, but that is not to indicate that the benefits of chemicals are ignored. The use of chemicals has resulted in increased food production and safety of food, safer drinking water, improvements in life expectancy from development of pharmaceuticals and antibiotics, and greater convenience to everyone.

It is quite remarkable how much has changed in our daily lives after the development of synthetic chemicals. In the past, our carpets, draperies, and clothes were all made from natural fibers such as wool, linen, or cotton. Today, many are made from synthetic products all derived from petroleum. Most carpets, draperies, and many clothes are treated with organic flame retardants. In the past, our cookware was made of glass, pottery, and various metals. Today, we store foods in plastic, and our cookware is lined with perfluorinated compounds to prevent food from sticking. We drive in cars that may have a metal motor and frame and have glass windows, but everything else is made from plastic and petroleum products. We spray our homes with pesticides and air fresheners. We bathe our bodies with personal care products (creams, cosmetics, deodorants, perfumes, polish for nails, etc.) containing many different chemicals, and often we have no idea what they are or what they might do to alter our health, no matter how beautiful they make us look and how good they make us smell. We dye our hair with chemicals and treat our hair with shampoos and conditioners that contain a variety of chemicals, often not even identified on the bottle because the mixture is proprietary.

We eat food that is often raised at distant places and depend on fossil fuels to get them to our local supermarket. Because we all like our fruits and vegetables to look perfect, they must be grown heavily treated with pesticides and fungicides, with herbicides added to keep the weeds under control. Since foods spoil over time, many fresh foods are treated with preservatives to make them look fresh even if they are not. Food additives are in almost every prepared product to reduce rate of spoilage and to improve color and flavor. There are some 3000 food additives in common usage. While our canned foods used to be in bare aluminum cans, we now line these cans with bisphenol A to avoid any metallic taste, assuming that the bisphenol A stays on the can. When we freeze our foods, we almost always place them in plastic, and we drink from plastic bottles and cups and assume that the plasticizers there, usually various phthalates or bisphenol A, do not leach into the food or drink.

It is not just fruits and vegetables that now contain chemicals that were not in them in earlier times. Now our meats come from animals treated with antibiotics and growth hormones. Our fish come from waters contaminated with persistent organic pollutants, such as bis[p-chlorophenyl]-1,1,1-trichloroethane (DDT) and its breakdown product, 2,2-bis(p-chlorophenyl)-1,1-dichloroethylene (DDE), other pesticides, polychlorinated biphenyls (PCBs), methyl mercury, and even pharmaceuticals that are discharged into the waste water through
human excretion and deposition of unused pharmaceuticals down the toilet. Many of the fish we eat come from fish farms, where fish are caged and fed food that often is contaminated with chemicals (Hites et al. 2004). In addition, in order to prevent infectious and fungal diseases in the enclosed, concentrated environment, antibiotics and fungicides must be used. Even the wild fish from lakes, streams, and the ocean contain organic chemicals, especially those that are lipophilic and persistent. The same contaminants, albeit usually at a lower concentration, are in our meats, eggs, and dairy products as a result of the contemporary practice of adding waste animal fats and products into the food fed to domestic farm animals. The feeding of waste animal fats to domestic animals that are not naturally carnivorous has resulted in the recycling of dangerous persistent chemicals like DDT and PCBs, which have not been produced in developed countries for more than 30 years, back into our food supply (IOM 2003).

Most people assume that the chemicals in carpets, in plastic food containers, and in drink bottles, and those sprayed under the kitchen sink to deal with insects stay put. However, it is clear that this is often not the case. Furthermore, most people assume that governments would not allow chemicals that might pose a hazard to health to be used. However, this also is often not the case. Unfortunately, chemicals volatilize from carpets and under-the-sink pesticide applications. They leach out of food and drink containers. Even before reaching the kitchen, there are chemicals in the food reflecting what the food animal ate or was treated with, and there are chemicals on the fruits and vegetables that are only partially removed by washing. So, a variety of organic chemicals are in the food and water we eat and drink and in the air we breathe, and are also absorbed through our skin.

Because infants and children are particularly vulnerable to harm from exposure to contaminants, there is special concern about the impact of pesticides in the diets of infants and children (NRC 1993). However, the mother’s body is the first environment for the child, and the contaminants in the mother’s body are passed to the fetus. Thus, efforts to reduce exposure to dangerous organics should focus on all women of reproductive age, not just infants and children.

Governments struggle to balance the promotion of new chemicals that will be useful to humankind with the protection of the public from hazards. The development and marketing of organic chemicals has increased enormously in a relatively brief period of time after World War II. In the United States, the Toxic Substance Control Act of 1976 (TSCA) is the law that presently regulates new chemicals. At present, there are more than 84,000 chemicals in this inventory, most of them organics. When the law was passed, most existing chemicals (62,000) were grandfathered into the inventory and were allowed to remain on the market without further study. Some chemicals were specifically identified to no longer be manufactured and used, as was the case with PCBs. New chemicals continue to be added to the inventory, but most of the testing of safety is dependent on the manufacturer. Figure 1.1 shows the
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Distribution of chemicals currently on the market. Most are organics, although there are also some metals. To date, only about 250 chemicals have been rigorously tested independent of the industry by the Environmental Protection Agency (EPA), and only 5 have been regulated. In addition, TSCA (and thus EPA) does not have regulatory authority over pesticides, tobacco and tobacco products, radioactive materials, foods, food additives, drugs, and cosmetics, all of which are regulated by different government agencies. While new legislation is needed, a number of steps have been taken to prioritize chemicals of high use and those that are the most worrisome in terms of impacts on public health.

In 1999, the Canadian government implemented a tiered approach to address chemicals of concern in their inventory under the Canadian Environmental Protection Act. They evaluated 23,000 chemicals with a screen including physicochemical properties that might relate to persistence and bioaccumulation, measures of toxicity to various organ systems with consideration of acute, subchronic, and chronic endpoints. They identified 500 chemicals of high priority and 193 that required regulatory action. The government is continually reviewing the high-priority chemicals.

Figure 1.1. Approximately 100,000 individual chemicals have been registered for commercial use in the United States over the past 30 years. Chemical classes that receive the majority of public attention (e.g., pharmaceuticals, cosmetics and food additives, and pesticides) constitute only a small percentage of this inventory. Analytical methodologies are currently limited to several hundred of these nonregulated chemicals. Adapted from Muir and Howard (2006) with permission.
In late 2008, the European Chemical Agency, in preparation for the implementation of Registration, Evaluation, and Authorization of Chemicals (REACH), preregistered about 150,000 substances (http://www.echa.europa.eu/). The stated goal of REACH is “to improve the protection of human health and the environment through the better and earlier identification of the intrinsic properties of chemical substances.” It gives greater responsibility to industry to manage risks from chemicals and to provide safety information. It also has a goal of obtaining progressive substitution of the most dangerous chemicals when less dangerous alternatives are available. The provisions of REACH are to be phased in over a period of 11 years.

These actions by various governments are all intended to prevent chemicals, especially organic chemicals, from being produced and used before it is certain that they will not escape into the environment, lead to exposure to animals and people, and pose significant hazards to human health. However, the reality is that to do so is very difficult. Premarket tests usually look at acute lethality in animal models or study animal or human cells in culture. Investigation of the subtle effects on the nervous or immune systems and the delayed elevated risk of developing cancer is much more difficult and much more expensive. Even if this long-term testing is done in animal models, there is no certainty that humans will respond exactly the same. Thus, we all become guinea pigs for the effects of exposure to chemicals.

Another major problem is that most testing and understanding of the hazardous effects of chemicals in animal and cellular models are done one chemical at a time. But in the real world, each of us is constantly exposed to a very great mixture of chemicals. There is a mixture of chemicals in the air we breathe, a different mixture in the water or other fluids we drink, yet a different mixture in the food we eat and then we put yet other chemicals on or in our body through medications, lotions, shampoos, and other personal care products. However, interactions between the effects of two or more chemicals have been very poorly studied. There are three major possibilities—the effects of two chemicals may be additive, less than additive, or synergistic (Carpenter et al. 1998). Of particular concern is when there are synergistic effects.

To make things even more complex, the above-mentioned discussion assumes that one chemical has only one site of action. DDT, for example, kills insects by blocking the action potential in insect nerves and causing paralysis. This is the mechanism of action that kills pests. However, in humans, DDT does not block action potentials but increases the risk of a great variety of human diseases, including cancer, cardiovascular disease, diabetes, nervous system effects, and changes in immune system function (detailed in the various chapters in this book). These different effects are certainly not mediated by actions at the neuronal sodium channel! And it is very unlikely that the effects on the different organ systems are mediated by the same mechanisms. This may involve different receptor binding sites or induction of different genes. Kiyosawa et al. (2008b) found that technical-grade DDT in
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rats induced genes associated with drug metabolism, cell proliferation and oxidative stress, and the nuclear receptors constitutive androstane receptor and pregnane X receptor. In another study, Kiyosawa et al. (2008a) reported that the pattern of gene induction in the mouse was significantly different from that in the rat to the same exposure. So one must conclude that any chemical that can induce genes regulating many different physiological functions has the potential to cause a great variety of different effects, but that there may be significant species differences which make extrapolation from animals to humans subject to errors.

These actions at different receptors and induction of a great variety of different genes likely explain the increasing frequency of demonstration of low-dose effects, nonlinear dose–response curves and what is commonly called “hormesis” (Calabrese 2008; Lee et al. 2010; Welshons et al. 2003). It has always been a tenant of toxicology that “the poison is in the dose.” This may well be true if the poison has a single binding site that leads to a single action, but it is clearly not true for the actions of many organics that have both multiple binding sites in different organ systems and also induce genes that alter many different physiological functions.

One book cannot hope to cover all organic chemicals or all possible biological effects. However, in this book, we have tried to consider effects on the major organ systems and the actions of representative chemicals for which there is at least some information. In many cases, the focus is on the persistent organic pollutants for the very practical reason that, because of their persistence, we have better exposure assessment and more information than is available for less persistent organics. As will be clear, our knowledge on the range of human health effects of organic chemicals is incomplete and much more research is needed.

REFERENCES


