ONLY ONE CHANCE

How Environmental Pollution Impairs Brain Development—and How to Protect the Brains of the Next Generation

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Introduction

Brain Matters

ONLY ONE CHANCE TO DEVELOP A BRAIN

The brain makes us who we are. "I think, therefore I am," French philosopher René Descartes wrote. We think, we read, we write, all due to this exceptional and complex organ called the brain. Still, our sophisticated brains evolved over thousands of generations to serve needs prevalent during prehistoric life conditions. Modern society provides highly different challenges and potentials for our paleolithic nervous system. And now our brains are being put to an extreme test. It is double-edged.

Problems that we create often demand an even greater ingenuity to control the consequences. This is particularly true of chemical pollution. We have been enormously successful in generating useful industrial chemicals, but some of them accumulate in the environment, contaminate our food, or leak into our drinking water, thereby creating exposures that may be dangerous—a problem we often discover with much delay.

In addition, some of that pollution can attack brain development—a form of toxicity that I call chemical brain drain. Such effects may damage the thinking that we will badly need to counter the very risks to brain development. Will managing chemical brain drain require a level of thinking that is no longer possible? This is the question that worries me, a worry that made me write this book.

Having studied brain toxicity for 30 years, and having become more and more concerned about the consequences of chemical brain damage, I realized that I must speak up. As I shall argue in this book, brain drain can be easily overlooked, and it may appear to be silent, as it is frequently not accompanied by a formal medical diagnosis.

My own perspective as a physician changed, because I met victims of different types of brain drain. Although many of them had one or more traditional medical diagnoses, none was identified by the diagnosis that they truly had in common—chemical brain drain.

When I was a medical student at the University of Copenhagen, Denmark, in the early 1970s, the word "environment" had just entered the common vocabulary.

The TV news began to feature pollution problems and showed crippled victims, whose nervous system had been damaged by chemicals. I became fascinated by the likely impact of pollution on human health. Physicians needed to play an active role beyond diagnosis and treatment, I thought. However, our discoveries on disease etiologies are only slowly being translated into prevention, if at all. Why is that? Should we not try to protect brains and not limit ourselves to diagnosis and treatment after the damage has already happened?

After graduation from medical school, I started a career in environmental medicine and epidemiology research. I wanted to understand better why the medical community failed to prevent chemical damage to children's brains. I soon encountered some surprises that medical school had not prepared me for, surprises that were fundamental to our understanding of human development and the frailty of the human brain. The human physiology that I was taught at the university specified that the fetus is well protected inside the pregnant mother's womb. Contrary to this comforting notion, however, the placenta does allow toxic chemicals to seep through. Once within the fetal circulation, some of these compounds can cause damage to the sensitive processes going on in the developing brain. The mother may escape completely unscathed, but for her child, the damage can be catastrophic. Early brain development molds the brain functions that will be available for the rest of one's lifetime. You get only a single chance to accomplish that.

Our understanding has improved only slowly through scattered studies on single chemicals, such as lead, mercury, and alcohol, now known to be toxic to the developing brain. From these bits and pieces of information, a more general pattern is now becoming apparent and is changing our perspective on the health risks brought on by environmental chemicals. This new knowledge developed only gradually, often hampered when narrow economic interests countered the emerging evidence that could hurt an industrial company's bottom line. Only recently has it become clear that the brain is both crucial for our being who we are and at the same time also extremely vulnerable, especially during its development. Brains need vigorous protection.

Understanding the implications is not just a matter of biochemistry and statistics. Real people, children, victims are affected. Their lives are changed forever. Early in my medical career, I had the benefit of being a Fulbright Fellow for two years at Mount Sinai Hospital in New York, where Professor Irving J. Selikoff was my mentor. He taught me this: "Never forget that the numbers in your tables are human destinies, although the tears have been wiped away." So this book is also meant as a tribute to the sufferers of chemical brain drain. Many were not recognized as pollution victims but instead endured stigmatism and lack of rehabilitation and compensation.

I am embarrassed that the medical profession—and society—have not risen to the challenge. The effects on brain development may often be silent, but they are serious and demand a loud response. This book is meant to be very loud!

The Human Brain Is Unique

Compared to body size, the adult human brain is the largest in the biosphere, taking up about 2% of our body weight. It is about four times the size of that of a gorilla or chimpanzee. Much of this size difference is due to an expansion of the cerebral cortex—the cell-rich outer layers of the brain. The human brain is not the largest in the animal world, though. Whales and elephants have brains up to five times greater in size. Much of that weight is occupied by the complex wiring that is needed by the formidable size of these animals. In contrast, primate brains are built in a space-saving manner that allows highly efficient packing of cells within the skull. Among primates, humans by far have the largest number of brain cells.[1] Hence, it is not the weight or the actual size that makes a difference (Einstein's brain weighed only 1,230 grams and was no bigger than an average brain).

So brain size alone does not determine our cognitive abilities. Nevertheless, the sheer number of cells in the human brain is unusually large. The exact number of nerve cells, or neurons, is unknown, but a fair estimate is that each of us probably has close to 100 billion nerve cells packed between the ears. That is a hundred times one thousand times one thousand times one thousand. If this number is not impressive, then consider that the brain also houses supporting glia cells that provide nutrients, general housekeeping, and the insulation of nerve fibers. The glia cells outnumber the nerve cells almost everywhere in the brain.

For comparison, many insects make do with less than 1 million neurons, and even that small number in a mosquito or a honeybee is sufficient for some quite sophisticated functions.[2] So despite our substantial superiority in terms of brain cells, our understanding even of the brain functions of insects is quite limited (and they do manage to bite).

As with other animals, your highly sophisticated brain started out as a tiny strip of cells. By a couple of weeks after conception, these cells were ready to multiply. At the peak, about 12,000 cells were generated every minute—200 per second. Most cells did not remain in the same place, but aimed to specific locations within the developing brain. Moving by themselves to their final positions, some cells had to find their way across a distance up to 1,000 times their own size. When settled at their destination in the brain cortex or elsewhere, they began to develop extensions of the cell membrane to establish contact with other cells, probably hundreds of such extensions, to set up joint functions.[3]

So the brain develops by multiplication, migration, maturation, and messaging—complex steps, each of which has to happen in a specific fashion, in the correct order, and at the right time. These biological processes are extremely complex and are only superficially understood so far. The morphological changes and biochemical mechanisms are portrayed in current textbooks in the field. But there is no authoritative review so far that highlights how environmental hazards can damage brain development and what we need to do to protect the vulnerable developmental processes. Still,

we are beginning to appreciate that the intricate timetable of closely connected and complex processes is very sensitive to interference and that obstacles can have serious consequences. If some disruption happens, brain development will be incomplete or abnormal, and there will be little, if any, time and opportunity for repair. Thus, brain functions will be curtailed, whether attention, spatial orientation, muscular coordination, memory, or some other crucial aspect. Thus, the final product, the mature brain, will not express the full potentials that we inherited from our parents.

Brains Are Vulnerable

We get only one chance to develop a brain. The damage that occurs to a brain of a fetus or child will likely remain for the rest of his or her life. The consequences can therefore be dire. Neurodevelopmental delay or neurological disease are thought to occur in about one of six children in the United States.[4] The adverse conditions range from serious diagnosed disease, such as mental retardation, cerebral palsy, and autism to less clearly defined disorders like attention deficit hyperactivity disorder (ADHD) and more subtle deviations like learning disabilities and sensory deficits. An estimated 2 million children in the United States suffer from ADHD, and about 1.7 million from autism spectrum disorder. Some of these conditions seem to be increasing in prevalence, thus probably not being of genetic origin. Although the causation in most cases is unknown, environmental factors are likely culprits. This book will discuss what we know and what we can reasonably infer about industrial chemicals as likely and suspected causes of brain damage. I refer to such damage as chemical brain drain, as it may be subtle and insidious, yet the overall effects can be devastating. I will summarize different types of research and their interpretations, and I shall also discuss how we may responsibly act to protect the developing brains of the next generation.

The brain is different from other organs. Our overall health and well-being will not be negatively affected by donating a kidney for transplantation. Also, we generally don't depend on the maximal capacity of the liver or most other organs. However, the complete and optimal function of the brain is essential to each and every individual. To keep the nerve cells functioning, we reserve 15% to 20% of our blood supply for the brain and 25% of the energy used at rest—a 10-fold higher need for calories and oxygen compared to the rest of the body. So the heart and blood vessels inherently favor the brain to deliver the nutrients and energy required by the nerve cells. However, something is clearly going wrong when neurodevelopmental disease in children is among the most common types of childhood disorders, apparently even increasing in prevalence. However, the less obvious decreases in brain function are not recorded by the medical statistics, although even small degrees of brain damage can negatively impact human welfare and income.

We care for a child's well-being and prospective success in life, and any parent would worry about a slight delay in the child's brain development. As adults and

parents, we want our children to get a head start, to develop and utilize their talents and to enjoy the benefits of life to the fullest possible extent. Yet, we are changing the environment and unwittingly exposing the next generation to chemicals that may change early brain development into a toxic head start.

Through evolution, our brains have developed to deal with acute dangers, whether saber cats or thunderstorms. Our nerve connections will ensure that we become aware of the dangers and react to them to protect ourselves, being alerted by their pungent smell, their threatening looks, or their scary noise. But nothing in our past has prepared us to deal with the insidious chemical threats that endanger the development of the next generation's brains. On the contrary, we are thoroughly enjoying the immediate benefits of attractive consumer goods, efficient technologies, and handsome profits that we generate from producing and disseminating hazardous chemicals. Our senses are not geared toward detecting the underlying dangers. The irony is that the resulting brain drain may wipe out some of those senses that we badly need to manage this very problem.

While we are polluting our food, drinking water, and air with chemicals that may harm brain development, we have been acting as if the risk of chemical brain drain is nonexistent. True, convincing proof is available for only a few well-researched chemicals. The best documentation available is in regard to lead pollution, which has ruined the lives of countless children. While we were slowly gathering detailed scientific documentation, a whole generation of Americans, and children around the world, suffered loss of brain function due to the pollution from our careless use of lead as an octane-booster in gasoline, as paint pigment, and as applications in myriads of consumer products. Only when the scientific evidence became truly overwhelming was a consensus finally reached that the public should be protected against this brain drainer.

We are now discovering similar evidence about other chemicals, such as mercury, polychlorinated biphenyls (PCBs), arsenic, some solvents, certain pesticides, and other industrial compounds. Again, we hesitate to act, because we prefer to have convincing proof before making restrictions against activities and products that are useful to society. In an attempt to translate the science into terms that may help priority-setting, economists have begun to calculate the costs to society due to chemical brain drain. In terms of lost income alone, the losses add up to billions of dollars per year. Despite the enormous costs, we have been reluctant to control the hazards that endanger brains.

Brain Drainers Are Not Easily Identified and Eliminated

We are up against substantial challenges when seeking information on chemical brain drain. One complication is that each toxic chemical may not appear by itself to cause any obvious or serious risk to our brains. The damage may only be detectable

from the effects of a combination of chemicals. Even so, only the most severe deviations from optimal development are likely to trigger a medical diagnosis, but they may nonetheless lead to fundamental deficits like learning or memory problems.

To make the situation even more difficult, our traditional research methods are inefficient tools to obtain the documentation we desire. Proper proof may take decades to gather for each individual chemical, one by one. Thus, useful knowledge has been accumulated only for a small number among the thousands of environmental pollutants. A few years ago, I scrutinized the scientific and medical literature to identify the industrial chemicals that had caused brain toxicity one way or another. I found that more than 200 industrial chemicals can be toxic to the human brain, although the majority of cases relate to poisonings of adults (see the updated Appendix list of known brain drainers).[5] These chemicals are obviously able to gain access to the nervous system and to exert damage to brain cells. It seems evident that these substances can also be hazardous to the brain during development. Due to the vulnerability of developing brains, chemicals that are toxic to adult brains are probably even more of a threat to young brains and at much lower doses.

Unfortunately, such evidence on damage to children's brains is available only for a handful of chemicals. This lack of information cannot be due to developing brains being resistant to toxic chemicals—in fact, they are more vulnerable. The reason is more likely the obstacles and time constraints in conducting research in this area. Our ignorance is further upheld because testing industrial chemicals for developmental brain toxicity is not mandatory. Further, scientists generally express their conclusions in a subtle language that tends to underestimate the risks. As a result of these three flaws (which I call the "triple whammy"), we do not know the potential of most environmental pollutants for causing brain drain. Without systematic evidence, we are left in the dark and at great risk.

Worse, we often require an unrealistic high level of understanding of each chemical and its adverse effects before we make decisions on restricting its use and initiating preventive efforts. A convincing proof is typically demanded by the affected industry that stands to lose revenue if a chemical is considered toxic with consequent loss of market. For 50 years, powerful economic interests resisted restrictions to the use of lead additives in gasoline, insisting that documentation did not exist that lead pollution was dangerous. True, regulatory agencies also have a desire for detailed documentation, and so do ambitious scientists, who aspire to disentangle the innermost secrets of biochemical mechanisms.

With time, regulatory efforts result in a gradual tightening of rule-making for an increasing number of toxic chemicals. Thus, the vast majority of official exposure limits have decreased as better information became available. Initial regulations are often found to be too lax and optimistic, so that adverse effects at lower levels of exposure are recognized only after the fact. Even worse, evidence on neurotoxicity is usually not available and is therefore not considered in regulatory decisions. And tightened regulations barely keep pace with the increasing complexity of

environmental pollution. Although the 200 known neurotoxicants are recognized as toxic hazards, only a few are regulated to protect developing brains.

It may take decades and substantial resources to generate the documentation that regulators desire before deciding to control a brain-draining chemical. Although lead poisoning and other brain toxicity have been extensively described, they are usually looked upon as a specific aspect of toxicology only related to individual substances, and not as a reflection of a hazard of general relevance. Again and again, doubt and skepticism, especially from the side of vested interests, pose obstacles to prudent protection of developing brains. Our insights are therefore only slowly being translated into prevention due to what journalism professor William Kovarik calls "historical amnesia."[6] While waiting for prevention policies to happen, exposures disseminate and increase, and persistent chemicals accumulate in food chains. As a result, our knee-jerk demand for detailed documentation leaves the brain power of the next generation in harm's way.

We are faced with a paradox. When we test new drugs, we conduct research studies on volunteers. But with environmental chemicals, we cannot conduct controlled clinical trials where children or pregnant women would be given a test chemical every day. Even if the high dose did not exceed the maximum exposure occurring in society, the study would certainly be considered unethical, especially in vulnerable populations, and would and could not be approved by ethical review boards. So while a controlled study of suspected brain drainers to support our documentation is not allowed, the insidious and undesirable exposures to children and pregnant women remain. In most cases, we do not even attempt to keep track of possible adverse health effects. And while we are pondering the research on a small number of chemicals that have been studied in some detail, action is being postponed for thousands of other substances that have not yet been evaluated.

The consequences, in regard to disease and organ dysfunction, may be subtle and hard to detect in the individual child. Most negative effects on brain development barely affect standardized, routine health statistics, and any changes are slow and can take many years to recognize. On the other hand, we are facing a massive prevalence of brain dysfunction, autism, and many other signs of ill health due to developmental insults. Because the exposures to toxic chemicals happen worldwide, the adverse effects are appearing now as a silent pandemic.[7]

Chemicals serve useful purposes in society, and we routinely have faith in modern technology as being inherently safe, a belief that is also supported by comforting statements from industry. This view is now being challenged, as we realize that many technologies have been introduced without proper attention to their risks. When new legislation on chemicals control was introduced in the late 1970s, existing chemicals in current use were not required to be tested for toxicity. Even the current European Union (EU) legislation does not require any specific tests for brain toxicity. This flawed rationale awarded all existing chemicals and production processes the right to be considered innocent or innocuous unless the opposite was

proven. This logic makes less and less sense, and it is especially dangerous in regard to adverse effects on the developing brain.

Confronting the Challenge

We need to raise the question "What should be done about it?" Because most chemicals have been poorly studied so far, we have a very incomplete understanding of the role of each of them in causing adverse effects. New chemicals introduced during the last 30 or so years must by law, at least within the European Union, be examined for toxic effects. However, we do not require such information for the majority of the currently used industrial chemicals because they were initially marketed before stricter laws were enacted. They were "grandfathered" in, according to regulatory slang, although this wording gives the false sense of comfort as if grandpa cares more about industrial chemicals than his grandkids' well-being.

Parents do not need to rely on official health statistics to decide that abnormal brain development should be curbed. But they are not well positioned to decide how to avoid poisoning by toxic chemicals in everyday life. We have certain options as consumers, such as choosing organic foods and healthy lifestyles thought to be beneficial, and we can try to avoid specific chemicals known to be toxic. However, most toxicants are not listed on the labels of consumer products, and you cannot see, taste, or smell them. One batch of toys may contain a large amount of toxic substances like phthalates, but the release of these substances when a child chews on the toy may be negligible compared to the release from another product with a lesser concentration. Some stores now require that the products they sell must be without toxic chemicals, such as phthalates or perfluorinated compounds, and this seems like a good approach from the viewpoint of the consumer. But what if the toy then contains an alternative or substitute of unknown potential toxicity?

These issues are complex and leave the parent or consumer with little chance of avoiding chemical risks by her own actions or choices. Therefore, industrial companies also need to make healthy choices as they produce and use chemicals, and they must make responsible decisions regarding toxicity testing and pollution abatement. Mechanisms are available to put such a strategy into place, should we choose to do so. But they may require a new way of thinking and of decision making, where health risks are taken into account even though they may as yet be considered unconfirmed. That would be in accordance with the so-called precautionary principle. Although often criticized in the United States, this decision rule is part of the EU treaty and allows policy choices to counter serious health risks in the absence of a complete proof of the hazard. Chemical brain drain should be considered a public health threat serious enough to evoke precautionary intervention with the aim of protecting the brains of future generations.

Prevention of chemical brain drain may seem costly in the short term, but I shall argue that it is cheaper in the long run and may be one of the best investments we can make. Moreover, if we don't act, our children and grandchildren may not forgive us. My hope is that this book will help to inspire more responsible decision making to protect the brains of the future. As a first step, we should allow no more grandfathering of chemicals that threaten brain development.

The Strategy

Having now given an overview of the book let me explain what the individual chapters will cover. Each chapter in the book can be read independently of the others, although together, they build toward the conclusions of the final chapter. Chapter 1 lays out the foundation for the book by explaining why the early stages of brain development are so vulnerable to the effects of toxic chemicals. Even medical textbooks do not discuss brain development from the point of view of vulnerability to toxic damage, so this summary will also contain something new for specialists.

Chapter 2 reveals how we optimistically counted on the placenta to protect the fetus, and how sad experience rectified that error. I focus on discoveries made in Australia and France and how they paved the way, very slowly, for a wider recognition of the vulnerability of the fetus, especially in regard to brain development. We now know that hundreds of industrial chemicals circulate in the fetal blood as a sign of chemical invasion. Thus, in hindsight, we were naïve and wrong to assume that the fetus was protected in the womb.

In the following chapters, I will highlight more mistakes, each chapter focusing on a specific brain drainer. Lead poisoning (chapter 3) was first thought of as a potentially life-threatening disease, which, in survivors, left no trace at all. Accordingly, lead exposure was not considered a hazard, unless clinical signs of poisoning developed. With time, research in the United States and elsewhere disclosed that brain drain is a continuous response, where the extent of the damage is proportional to the exposure, and that even small doses are hazardous.

Chapter 4 describes how early reports from Japan on brain toxicity due to mercury in seafood were ignored at first. The belief was that seafood was healthy and could therefore not be hazardous to anyone's health. Again, more refined research documented adverse effects at lower and lower exposure levels. However, public health action was delayed for several decades because healthy food items were considered resistant to pollution risks. Again, a naïve assumption hampered the interpretation of brain toxicity research and therefore delayed prevention.

It is not only during prenatal development that the brain is vulnerable to toxic chemicals. It took the poisoning of thousands of infants to make us recognize brain toxicity due to arsenic-contaminated milk powder (chapter 5). Although this discovery of life-threatening, acute effects must have been shocking, one untoward effect

of the embarrassing tragedy was that the long-term fate of the victims was never examined. Even recent, authoritative assessments of arsenic toxicity have ignored the effects of arsenic on brain development. But I have met victims, whose suffering clearly shows that the toxicity does not disappear simply because it is ignored by the perpetrators. This certainly also applies to persistent organic chemicals that resist breakdown (chapter 6). Once absorbed, they remain in our body, and they can be passed on to the next generation. This is particularly true for a highly successful industrial chemical called PCB, first produced in the 1920s in Anniston, Alabama. Now this community is one of the world's most polluted towns, and the residents carry some very high PCB burdens. The PCB will go away only very slowly, and the pollution will likely continue to affect developing brains in many years to come.

We should have learned from the blunders, misfortunes, and new insights on brain drain caused by lead, mercury, arsenic, and persistent chemicals. But brain drain is not just a matter of a few annoying substances, as I will describe in chapter 7. Pesticides are often designed to interfere with the neural functions of pests, especially insects. Unfortunately, the brain biochemistry differs little between species, and the pesticides can therefore cause neurotoxicity also in humans. There are many other brain toxicants. I have included as an Appendix the updated list of chemicals that are known to be toxic to the brain. This list is incomplete, to a great extent because brain toxicity is almost never tested. This lack of information is dangerous, as the vulnerability of the developing brain is a physiological characteristic that creates exceptional susceptibility toward toxic chemicals in general, not just toward lead, mercury, and a few other poisons.

Disrupted brain development can have severe consequences. Even subtle brain damage has a tremendous personal and societal dimension, which is often overlooked or ignored. Chapter 8 puts these costs into perspective. Such damage may not be recorded as a medical diagnosis, but affected children may need special education in school; they may become less successful in life, contribute less to society in terms of income and tax revenues, and become involved in delinquency, substance abuse, and other problems because of their deranged behavior. In terms of dollars, decreased IQ and loss of lifetime income due to brain drain costs us billions of dollars per year in the United States alone. These expenses are usually hidden and ignored, as the victims and the causation are generally unknown.

Chapter 9 discusses how inertia in science is a hurdle, but not the only one. Thousands, perhaps millions, of children may suffer adverse effects that could have been prevented while expert committees contemplated the evidence. This inertia is augmented by the chemical manufacturers and other companies that question the validity of the evidence and demand more documentation. These vested interests have repeatedly manipulated brain-drain research, and they have manufactured uncertainties to raise doubt about the conclusions and the credibility of scientists. There are of course uncertainties, but the costs of brain drain are

simply too enormous for us to accept that our incomplete understanding should allow continuing damage to the next generation's brains.

The final chapter outlines how chemical brain drain can be prevented. Test methods are available, although some need further validation, some are expensive, and they all have limitations, but they are helpful in identifying substances that are suspect. The consumers' own choice of a healthy lifestyle is only a partial solution. More to the point, there are healthy potentials in the use and production of chemicals. Cleaner production and safe products should take into account benefits to today's children and their children. We need to act as true parents and grandparents. Precautionary thinking and prudent intervention are needed. While we can't rely on technofixes, special diets, or neuroenhancers, we can choose green technologies and responsible innovation that do not put brains at risk.

I realize that any book on a hot neuroscience or public health topic may be outdated fairly soon. But to cover the research frontline is only one part of my purpose in writing this book. We already have plenty of evidence to support actions to protect against brain drainers. What we need most is therefore, as said by Gustave Speth, dean at Yale University, a new consciousness and a transformation in politics.[8] Such mechanisms may at first seem impossible, but they must nonetheless be implemented on behalf of our children and grandchildren. While chemical brain drain appears as a silent pandemic without impressive statistics on mortality or disease, the impacts are serious enough to demand a loud response. To promote discussion and exchange of information, a website has been generated at www.chemicalbraindrain.info, where news and reader comments will be gathered. I look forward to hearing from you. But I first want to share with you what I have found out.

CONTENTS