Proceedings of a Conference on

THE EFFECT OF HORMONAL DISRUPTERS ON THE HEALTH & DEVELOPMENT OF CHILDREN

June 25, 1999
University of Toronto

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June 25, 1999
Koffler Institute for Pharmacy Management
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University of Toronto

Funded by:

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http://www.utoronto.ca/chp/

Table of Contents

Foreword

Planning for this Conference began more than a year ago when I was approached by a member of the Centre's Cancer Prevention Interest Group who had spoken with Neil MacLusky. Neil had suggested that it might be very useful if someone organized a conference which explored the current state of knowledge and attempted to develop a consensus statement on the developmental and health consequences of exposure to human-made chemicals in the environment. Our Centre volunteered to take the lead on this and we formed a committee, whose members are noted in Appendix A, to assist with the planning.

As we proceeded with the planning, we agreed that we should narrow our focus somewhat by concentrating on hormonal disrupters in the environment and their relationship to child health and development. Our goal was to hold a one-day open conference with a subsequent day devoted to trying to develop a consensus statement which might be presented to relevant policy-makers in Canada. Unfortunately however, in spite of substantial attempts to do so, we were unable to raise the funds required to hold such a double-barreled event and in the end we decided to simply hold a one-day event open to the interested public.

As we hope you will agree on reading these proceedings, this conference was successful in that it did present interesting and useful information regarding the topic and identified some themes which cut across all of the presentations summarized by Monica Campbell in her closing remarks reproduced here. We hope that this summary helps to guide future action by a range of stakeholders on these important issues.

For our part, the committee intends to meet to consider the report and formulate its next steps in the near future. Anyone who would like to participate in the process, should contact either me (irv.rootman@utoronto.ca) or Joanne Lacey (joanne.lacey@utoronto.ca).

In closing, I'd like to thank our funders, speakers, members of the planning committee and sponsoring organizations. But I would especially like to thank Joanne Lacey who took care of the organizational details, Monica Campbell who chaired the conference and Anna Pancham who prepared these proceedings.

Irving Rootman
Director, Centre for Health Promotion,
University of Toronto and Chair, Conference Planning Committee

Background, Objectives & Programme

Background

A growing body of evidence has suggested that the health of human and wildlife populations may be adversely affected by increased amounts of chemicals that have been released into the environment. Such chemicals are found in human populations from the Arctic to the tropics and, because of their persistence in the body, can be passed from generation to generation. The consequences of this increasing chemical burden remain uncertain.

Because some pollutants mimic the effects of hormones that are involved in regulating normal development, particularly the brain and the reproductive organs, a number of studies have speculated that recent increases in the incidence rates of diseases affecting these organ systems may be the direct, or indirect result of chemical exposure. It is thought that such exposures may be especially damaging in sensitive periods (e.g. pre- and post-natal) and populations (e.g. children). Despite seemingly disturbing trends, the extent of the threat to human health presented by environmental chemical exposure remains difficult to assess.

Objectives

The objectives of the proposed conference were: (1) to explore the current state of knowledge and action regarding exposure to hormonally active chemicals, particularly in relation to children; and (2) to examine the steps needed to reduce the effects of these chemicals on the development and health of children. A principal aim of the conference was to bring scientists in the field, together with representatives from governmental regulatory authorities, to share knowledge and compare the different testing and regulatory approaches now being used.

Programme

The conference consisted of four expert presentations, each of which was followed by a brief Question and Answer period. After all the speakers presented, a Panel Discussion was held to provide an opportunity for the speakers to elaborate on key themes from the day and address additional questions from the participants.

Conference Agenda

Time	Agenda Item
8:30 am	Registration - Lobby, Koffler Institute for Pharmacy Management
9:00 am	Welcome **Dr. Irving Rootman**, Director, Centre for Health Promotion
	Opening Remarks **Dr. Neil MacLusky**, Professor, Center for Reproductive Sciences Columbia-Presbyterian Medical Center
9:15 am	What do we Know? "Chemicals of Concern" **Dr. Chris DeRosa**. Director, Division of Toxicology, U.S. Agency of Toxic Substances & Disease
10:15 am	Refreshment Break
10:30 am	"Reproductive Consequences of Environmental Chemical Exposure: The Challenge for Future Research" **Dr. Neil MacLusky**
11:15 am	"Hormonal Effects of Perinatal Exposure to PCBs and DDT – Studies in North Carolina and Mexico" **Dr. Walter Rogan**, Clinical Investigator, National Institute of Environmental Health Science
12:00 noon	Lunch
1:30 pm	"RTHS & Implications for Environmental Contaminants" **Dr. Peter Hauser**, Professor of Psychiatry & Internal Medicine University of Maryland
2:30 pm	Refreshment Break
2:45 pm	Panel featuring all presenters, and questions from the floor Chair: **Ms. Barbara McElgunn,** Health Liaison Officer Learning Disabilities Association of Canada
3:45 pm	Closing Remarks **Dr. Monica Campbell**, Environmental Health Specialist, Toronto Public Health Department, Education, Research & Development

Welcome, Introduction And Opening Remarks

(The following are excerpts from remarks by Dr. Irving Rootman, Director of the Centre for Health Promotion.)

Welcome

On behalf of the organizing Committee and the sponsors I would like to welcome you to this conference on the Effect of Hormonal Disrupters on the Health and Development of Children. We have an excellent program for you today and I am sure that everybody will go away a lot more knowledgeable about these issues. We are really pleased that you are here and we hope that it will be an opportunity for you to hear some of the leading people in this field and to have some exchange with them.

Introduction

(The following are excerpts from remarks by Monica Campbell, Manager of the Health *Promotion and Environmental Protection office for the Department of Public Health in Toronto.)*

It is an honour and a privilege to be asked to chair this session. I am really looking forward to today. I am looking forward to the comments and getting a nice distillation of what the latest research is showing on the effect hormonal disrupters on the health and development of children.

Opening Remarks

(The following are excerpts from remarks by Neil MacLusky, Professor and Scientific Director at the Centre for Reproductive Science, Faculty of Medicine, Columbia University.)

I am a reproductive endocrinologist who's worked a lot on sexual differentiation, not in toxicology and not in dealing with environmental chemicals. I was attracted into this field because I perceived a growing problem that needed a good scientific investigation. The causes for concern are that a lot of the chemicals that we as a species have been pouring into the environment since the beginning of the industrial era are known to interact with the normal mechanisms in our bodies and in animal's bodies that respond to hormones. They are hormonal mimics or hormonal antagonists. So the normal physiological endocrine mechanisms that we are vitally dependent upon for development as well as functioning for adults are affected by these chemicals.

We know from animal studies that there is potential for harm. If you take these chemicals, put them into animals -- bad things happen. We also know from wildlife and studies on the environment that the things that have happened to laboratory animals have happened and are continuing to happen to animals in the wild. Of particular concern is that many of

these man-made chemicals differ from the natural environmental compounds. We live in an environment where there naturally exists hormonally active chemicals. There are many things that we eat that contain hormonal activation. Many things in our environment, not just man-made, can interact with hormone receptors. But the one thing that is really troubling about many of the man-made chemicals is that they are long lived and they bio-accumulate in tissues in contrast to the things that are out there naturally. And lastly, clinical epidemiological studies suggest there are long-term increases in the incidence of just those problems that you would predict based on the animal work. We know from animal work that certain things go wrong when you expose animals to environmental chemicals. If you look for the same kinds of defects in humans you can see an increase in the last 20-40 years in exactly those kinds of defects. That is the problem in a nutshell.

Not surprisingly, this problem has gathered a great deal of attention politically and journalistically. This is a quote from American Vice President Al Gore in a foreword to one of Theo Colborn's books:

> *"Human beings in such remote locations as Canada's far northern Baffin island, now carry traces of persistent synthetic chemicals in their bodies including such notorious compounds as PCB's, DDT and dioxin. Even worse in the womb and through breast milk mothers pass this chemical legacy on to the next generation ".*

What Do We Know? "Chemicals Of Concern

Christopher DeRosa "

In recent years much attention has been focused on the potential for a wide range of xenobiotic chemicals to interact with and disrupt the endocrine systems of animal and human populations. An overview of the chemicals that have been implicated as endocrine disruptors is presented. The ubiquity in the environment and associated body burdens of these chemicals in human populations are described. Potential mechanisms of action are reviewed, including the role of specific intracellular receptors and their interactions with endogenous and exogenous materials. The subsequent up regulation or down regulation of physiological processes at critical stages of development is discussed.
The potential for joint toxic action and interaction of chemical mixtures is also discussed. The acknowledged role of wildlife populations as sentinels of potential human health effects is reviewed, and the weight of evidence for the role and impact of endocrine disruptors is presented. The implications of exposure to endocrine-disrupting chemicals for human health are reviewed, with special emphasis on the potential for transgenerational effects in at risk populations. Recommendations for future research include the development of (1) structural activity and in vivo and in vitro functional toxicology methods to screen chemicals for their endocrine-disrupting ability, (2) biomarkers of exposure and effect, and (3) in situ sentinel systems.

Table 1. Variety of health effects observed in creatures in the Great Lakes Basin

	Effect									
Creature	Reproductive effects	Eggshell thinning	Generational effects	Deformities	Organ damage	Behaviour changes	Hormonal changes	Metabolic changes, "wasting"	Immune suppression	Tumors
Bald eagle	•	•	•	•		•		•		
Beluga whale	•			•	•		•		•	•
Black-crowned night heron	•	•		•						
Caspian tern	•		•	•		•		•		
Chinook coho salmon	•				•		•			•
Common tern	•				•	•		•		
Double-crested commorant	•	•	•	•	•	•		•		
Forster's tern	•		•	•	•	•		•		
Herring gull	•	•	•	•	•	•	•	•	•	
Lake trout	•		•		•	•		•		
Mink	•		•		•			•		
Osprey	•	•								
Otter										

Note: From Hileman (1993).

Table 2. Chemicals associated with reproductive and endocrine-disrupting effects

Insecticides	Industrial Chemicals	Fungicides	Herbicides	Nematocides
Carbaryl	Bisphenol A	Benomyl	2,4-D	Aldicarb
Chlordane[o]	Benzo-[a]pyrene[o]	Hexa-chlorobenzene[o]	2,4,5-T	Dibromo-chloropropane[o]
Dicofol	Cadmium[o]	Mancozeb	Alachlor	
Dieldrin[o]	Dioxin (2,3,7,8-TCDD)[o]	Metiram complex	Amitrole	
DDT and metabolites (DDE)[o]	Lead[o]	Tributyl tin[o]	Atrazine	
Endosulfan[o]	Mercury[o]	Zineb	Metribuzin	
Heptachlor and heptachlor epoxide[o]	PBBs[o]	Ziram	Nitrofen	
Hexa-chlorocyclohexane[o]	PCBs[o]		Trifluralin	
Hexa-chlorocyclohexane[o]	Penta-chlorophenol[o]			
Methomyl	Penta- to nonylphenols			
Methoxychlor[o]	Phthalates			
Mirex[o]	Styrenes[o]			
Oxychlordane				
Parathion				
Synthetic pyrethroids				
Toxaphene[o]				
Transnonachlor				

Note: Adapted from Colborne et al. (1993)
[o]Chemicals that are the subject of toxicological profiles

Table 3. Breast milk[o] pesticide concentrations

Compound	Range of reported means (ppm milk fat)
p,p' - DDT	0.2 – 4.3
p,p' - DDE	1.2 – 14.7
Dieldrin	0.05 – 0.24
Hexachlorocyclohexane (HCH)	0.008 – 0.08
HCH	0.003 – 0.02
HCH	0.27 – 0.53
Hexachlorobenzene	0.04
Hepatachlor and heptachlor epoxide	0.035 – 0.13
Oxychlordane and chlorodane	0.05 – 0.12
PCBs	0.8 – 1.5

Note: Adapted from Mattison and Cullen (1994)
[o] U.S. breast milk

Dr. DeRosa's presentation was based on the above research. Table numbers reflect those as they appear in the original article. Notes and references that appear in the table refer to the references cited in the article. For a complete list of references or clarification please see the original article or contact the author.

DeRosa, C., Richter, P., Pohl, H., and D. Jones (1998) "Environmental Exposures That Affect The Endocrine System: Public Health Implications", **Journal of Toxicology and Environmental Health**, Part B, 1:3-26.

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Reproductive Consequences of Environmental Chemical Exposure: The Challenge for Future Research

Neil MacLusky

The mechanisms involved in making us male or female are entirely dependent on hormones. Anything that interferes with the production or actions of hormones will influence the differentiation mechanisms including cognitive, metabolic and reproductive functions.

There is a range of chemicals that are structurally similar to natural steroidal hormones. Examples of these agents include insecticides, herbicides, fungicides, over the counter and prescription drugs and plastics. These chemicals, which are present in everyday items, mimic natural hormones. These agents are not as strong as natural hormones, but nevertheless their interaction with the reproductive system has been noted.

This problem is huge. There are numerous agents that have been shown to be hormonally active that are going to be around for a long time. As opposed to the natural steroidal hormones which are easy to clear from the system, these chemicals bioaccumulate. Top predators tend to bioaccumulate these agents within body fat.

The entire field of reproductive toxicology owes an enormous debt to wildlife biologists. Wildlife biologists presented the initial evidence suggesting the negative impact of environmental chemicals on the reproductive system. There have been a variety of wildlife and animal laboratory studies that reveal an increase in breast and testicular cancer, behavioural changes and a decrease in male fertility. It is very difficult however to translate those studies into the implications for humans. While it may be possible to locate a group with increased exposure to an agent, establishing a control group is virtually impossible. Human studies have shown a relationship between environmental chemicals including decreased sperm count and an increase of cases of undescended testes, hypospadias and testicular and breast cancer.

It is clear that there is an effect of these agents on reproductive development. However, regardless of the amount of research currently available, drawing conclusions is problematic. It is difficult to tease out the effect of one hormone against the background of hormones that exist in our bodies and in our environment. The current research available is suggestive evidence that is highly vulnerable to confounding variables. Consequently, confirming causality is complicated.

However, sufficient cause for concern has been established. There are a lot of chemicals in the environment and they have been there for a long time. It has been clearly established that these compounds have an impact of the reproductive process in lab and wildlife studies. In humans, a cause and effect relationship has yet to be verified. We need to further develop the weight of evidence idea and do more careful epidemiological studies with human at risk populations to provide the weight of evidence needed to determine the

extent to which environmental chemicals impact on normal pre and post natal reproductive function.

Hormonal Consequences of Background Exposure to PCBs and DDE – Studies in North Carolina and Mexico

Walter Rogan

Objectives

Polychlorinated biphenyls (PCBs) and dichlorodiphenyl dichloroethene (DDE) are ubiquitous toxic environmental contaminants. Prenatal and early life exposures have been shown to affect pubertal events in experimental animals. We studied whether prenatal or lactational exposures to background levels of PCBs or DDE were associated with pubertal growth and development in humans.

Study Design

Follow up of 594 children from existing North Carolina cohort whose prenatal and lactational exposures had previously been measured. Height, weight and stage or pubertal developmental were assessed through annual mail questionnaires.

Results

Height and weight of boys at puberty increased with transplacental exposure to DDE; adjusted means for those with the highest exposures (maternal concentration 4+ppm fat) were 6.3cm and 6.9kg larger than those with the lowest (0-1ppm). There was no effect of the ages at which pubertal stages were attained. Lactational exposures to DDE had no apparent effects; neither did transplacental or lactational exposure to PCBs. Girls with the highest transplacental PCB exposures were heavier than other girls by 5.4kg, but differences were significant only if the analysis was restricted to whites.

Conclusion

Prenatal exposures at background levels may impact body size at puberty.

Background Information

Dr. Rogan's presentation was based on the following 2 research articles. For complete versions, please contact the author:

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Table numbers reflect those as they appear in the original article. Notes and references that appear in the table refer to the references cited in the article. For a complete list of references please see the original article.

Rogan, W et al, (1987) "Polychlorinated Biphenyls (PCB's) and Dichlorodiphenyl Dichloroethene (DDE) in Human Milk: Effects on Growth, Morbidity and Duration of Lactation", **American Journal of Public Health**, October, Vol 77, No. 10, pp 1294-1297.

Gladen, B., Rogan, W., (1995)"DDE and Shortened Duration of Lactation in a Northern Mexican Town" **American Journal of Public Health**, April, Vol. 85, No. 4, pp. 504-508.

Polychlorinated Biphenyls (PCBs) and Dichlorodiphenyl Dichloroethene (DDE) in Human Milk: Effects in Growth, Morbidity and Duration of Lactation.

Abstract

We followed 858 children from birth to one year of age to determine whether the presence of Polychlorinated Biphenyls (PCBs) and Dichlorodiphenyl Dichloroethene (DDE) in breast milk affected their growth or health. Neither chemical showed an adverse effect on weight or frequency or physician visits for various illnesses, although differences were seen between breast-fed and bottle-fed children with bottle-fed children being heavier and having more frequent gastroenteritis and otitis media. Children of mothers with higher levels of DDE were breast-fed for markedly shorter times, but adjustments for possible confounders and biases did not change the findings. In absence of any apparent effect of the health of the children, we speculate that DDE may be interfering with the mother's ability to lactate, possibly because of estrogenic properties.

Table 1. Duration of Lactation and Percentage of Women with Lactation Failure by Chemical Levels*

Chemical Levels	No. of Women	Median Weeks	% with Lactation Failure
DDE			
0.31- 0.99	54	26	5
1.00- 1.99	205	26	6
2.00- 2.99	217	23	6
3.00- 3.99	135	24	8
4.00- 4.99	48	18	15
5.00-5.99	27	9	24
6.00-23.80	48	10	10
PCBs			
0.49- 0.99	43	26	5
1.00- 1.49	192	25	8
1.50- 1.99	232	24	9
2.00- 2.49	134	23	7
2.50- 2.99	60	18	10
3.00- 3.49	31	26	10
3.50- 3.99	18	26	0
4.00- 15.80	24	13	13

*Amounts of DDE and PCBs are estimated concentrations in mother's milk fat at birth in parts per million. Weeks represent number of weeks child was mostly breast-fed.

Table 2. Results of Regression of Duration of Lactation on Chemicals Level and Other Factors in All Lactations and First Lactations

	All Lactations		First Lactations Only	
	Coefficient	95% Confidence Interval	Coefficient	95% Confidence Interval
Maternal age (yrs)	0.9	(0.5, 1.2)	0.8	(0.3, 1.3)
Maternal race				
White	0	--	0	--
Black	-2.3	(-9.3, 4.8)	-5.6	(-14.4, 3.1)
Other	3.1	(-20.5, 26.7)	1.7	(-21.8, 25.2)
Maternal Education (yrs)	1.1	(0.3, 1.9)	1.0	(0.1, 2.0)
Maternal Occupation				
While Collar	-12.2	(-19.5, -5.0)	-15.3	(23.4, -7.2)
Professional	-10.0	(-17.0, -3.1)	-10.7	(-18.4, -3.1)
Labourer/Farmer	-9.6	(-19.3, 0.1)	-8.9	(-19.6, 1.8)
Paraprofessional	-5.3	(-13.3, 2.7)	-9.8	(-18.7, -0.9)
Housewife	-1.6	(-9.0, 5.9)	-5.2	(-14.1, 3.7)
Student	0	--	0	--
Maternal Smoking				
No	4.8	(1.4, 8.3)	3.9	(-0.3, 7.9)
Yes	0	--	0	--
Maternal Alcohol				
< one drink/wk	0.9	(-1.7, 3.5)	1.2	(-2.0, 4.4)
> = one drink/wk	0	--	0	--
Study area				
Pitt	-3.5	(-6.6, -0.5)	-2.4	(-6.0, 1.3)
Durham	-2.3	(5.2, 0.6)	-1.3	(-4.9, 2.3)
Wake	0	--	0	--
PCBs (ppm in milk fat)	-1.1	(-2.2, 0.1)	-0.7	(-1.9, 0.6)
DDE (ppm in milk fat)	-1.1	(-1.7, -0.5)	-0.9	(-1.7, -0.1)

Dependent variable in regression is number of weeks mostly breast-fed. Independent variables are the factors listed. For categorical factors, the reference category is shown with a coefficient of zero and no confidence interval.

Table 3. Per Cent of Children Ever Having Upper Respiratory Infection (URI). Otitis Media (Ear), or Gastroenterititis (GI) in Various Age Intervals by Feeding Method and Contaminant Amounts.

0-3 Months						3-6 Months						6-12 Months					
			% Ever Having						% Ever Having						% Ever Having		
	mg	**No. of children**	**URI**	**Ear**	**GI**		**mg**	**No. of children**	**URI**	**Ear**	**GI**		**mg**	**No. of children**	**URI**	**Ear**	**GI**
Bottle-feeders Ex-breast-feeders		80	16	18	24	Bottle-feeders Ex-breast-feeders		80	28	33	13	Bottle-feeders Ex-breast-Feeders		80	48	58	25
Breast-feeders		--	--	--	--	Breast-feeders		172	35	39	14	Breast-Feeders		321	54	63	29
		689	21	11	11			503	24	22	6			353	49	52	17

of children ever having the disease during the time period. Diseases are upper respiratory infections (URI), otitis media (ear) and gastroenteritis (GI).

DDE and Shortened Duration of Lactation in a Northern Mexican Town

Abstract

Objectives

Worldwide declines in the duration of lactation are cause for public concern. Higher levels of dichloethene (DDE) have been associated with shorter durations of lactation in the United States. This study examined whether this relationships would hold in an agricultural town in Northern Mexico.

Methods

Two hundred twenty nine women were followed every two months from childbirth until weaning or until the child reached 18 months of age. DDE was measured in breast mild samples taken at birth, and women were followed to see how long they lactated.

Results

Median duration was 7.5 months in the lowest DDE group and 3 months in the highest. The effect was confined to those who had lactated previously, and it persisted after statistical adjustment for other factors. These results are not due to overtly sick children being weaned earlier. Previous lactation lowers DDE levels, which produces an artifactual association, but simulations using best estimates show that an effect as large as that found here would arise through this mechanism only 6% of the time.

Conclusions

DDE may affect women's ability to lactate. This exposure may be contributing to lactation failure throughout the world.

Table 2. Relationship between DDE Levels and Durations of Lactation, 229 Mexican Women and 722 US Women

	Mexico[a]		United States°	
p, p' – DDE, ppm, fat basis	% of Women	Median Duration, mo	% of Women	Median Duration, mo
0-2.5	13	7.5	51	7.8
2.5-5.0	26	5.0	39	6.1
5.0-7.5	29	3.0	6	3.5
7.5-10.0	14	3.5		…
10.0-12.5	9	4.0	4	3.8
12.5	9	3.0		…

Note: DDE levels are from the breast milk sample collected at birth
[a]Data from the present study.
°Data from study described in Rogan et al.

Table 4. Relationship between DDE and Duration of Lactation

	First Lactation		Later Lactations	
p, p' – DDE, ppm, fat basis	% of Women (n=95)	Median Duration, mo	% of Women (n=134)	Median Duration, mo
0-5.0	32	3.0	43	8.8
5.0-7.5	36	2.5	24	4.1
7.5-10.0	14	1.5	15	5.0
10.0	19	4.0	18	2.8

Please note that Tables 1 and 3 were omitted from these proceedings, but do appear in the original article.

RTHS & Implications for Environmental Contaminants

Peter Hauser

A thyroid disruptor is an exogenous substance that disturbs thyroid homeostasis through alterations in synthesis, secretion, transport, metabolism, binding action or elimination of endogenous thyroid hormones. Examples of synthetic thyroid disruptors include flavanoids, phthalate esters, polycyclic aromatic hydrocarbons, polyhydroxyphenols, phenol derivatives, dioxin and dioxin-like compounds (DLC). The most notable dioxin-like compound is Polychlorinated Biphenyls (PCBs). These compounds either act as hormonal mimics or block the hormone.

Numerous chemicals are reported to disrupt the endocrine and thyroid hormones, the most common being dioxin-like compounds. In 1994, 68,000 synthetic compounds were being used in the United States. 1,500 new chemicals are produced every two years. The American Federal Government only tests about 15 new chemicals each year. These are very potent compounds and there are more and more of them each day.

These chemicals have a primary effect on children. Thyroid hormones are essential for normal brain and behavioural development. It is essential that there is no disruption of thyroid hormone homeostasis.

The primary source of fetal thyroid hormone is the mother. Studies have shown that dioxin/TCDD crosses the placental barrier. The brain, which is primarily fat, acts as a reservoir for these chemicals. The concentration of TCDD chemicals in the fetal brain is above those of the maternal concentrations. The fetal brain acts as a reservoir for the maternal TCDD. This is particularly concerning.

There are also recent public concerns. In North Providence, Rhode Island there are areas where children are not allowed to play because of contamination of dioxin and PCBs. In New Jersey there are autism clusters in areas where leukemia clusters were found years ago. In California there is an increased incidence of congenital hypothyroidism in areas with increased perchlorate in the groundwater. Of particular concern is that some companies are creating buffer zones around their chemical plants.

There is evidence that dioxin and dioxin-like compounds and other synthetic compounds are thyroid disruptors, that dioxin-like compounds produce adverse effects on brain and behavioural development and abnormalities on in-utero brain and behavioural development of thyroid hormone action. What has yet to be confirmed is if the adverse effects of dioxin-like compounds on brain and behavioural development are mitigated through the thyroid hormone system.

Studies show that perinatal exposure to dioxin-like compounds has a variety of implications. For example in animal studies: mice studies show increased hyperactive behaviour and decreased coordination; rats studies show hypo- or hyperactivity (with decreased hyperactivity after amphetamine administration) reduced grip strength and

impaired t-maze learning; monkey studies reveal hypo- or hyperactivity, delayed spatial alteration, and delayed discrimination- reversal learning on the Wisconsin apparatus as a result of exposure to synthetic chemicals. In humans, hypoactivity, lower IQ, impaired attention, hypotonia, hyporeflexia at birth and poor scores on habituation tasks are associated with synthetic chemicals. In fact one study found a 6 point drop in IQ associated with maternal consumption of fish equal to 2lbs/month (~1 serving of fish/week) during pregnancy.

Thyroid hormone is produced by the thyroid gland and there is feedback inhibition at the pituitary level. The pituitary gland is responsible for making thyroid stimulating hormone, which then induces the thyroid gland into making thyroid hormone. It is a negative feedback loop. In resistance to thyroid hormone, we find that concentrations are elevated at the level of the pituitary such that thyroid stimulating hormone continues to be made rather than cease, as it should when there are high levels of thyroid hormone and that the thyroid gland continues to make thyroid hormone. This is an anomaly of this feedback loop.

According to my research, the developmental consequences of resistance to thyroid hormones in humans include attention deficit, hyperactivity, a 10-12 drop in IQ (relative to family members who are non-resistant) and a lack of habituation to performance tasks. It is also not uncommon to see a short stature, bird-like face and lighter weight in resistant individuals. In addition, my research documents abnormal Sylvian tissue morphology and smaller corpus colossum in resistant subjects.

In my animal research, increased locomotor activity, increased travel time to locate objects and memory impairment were noted with transgenic mice as opposed to wild mice. Some of these effects could be normalized with amphetamine application. It is fair to hypothesize that these results could also be found in human studies with in-utero exposure to synthetic compounds. I expects to see these studies materialize in the next few years.

Scientists need to share information with the public to provide unbiased information to clarify the situation. Parents are extremely concerned about what is going on and we need to provide some answers. One goal should be to create a public that is activated and that seeks out information. It is also important to form partnerships between scientists, the public and the chemical companies to address these concerns.

Continuous Performance Task
(a measure of sustained auditory attention)

Measure	RTH (n=9)	Controls (n=11)	P
"Hits"	132.4 (32.5)	179.9	0.002*
False alarms	38.5 (56.8)	7.4 (7.9)	0.14*
Performance Accuracy	2.2 (1.7)	3.6 (1.2)	0.05

* analysis of data using log (x+1) for transformation
** log [hits/(false alarms +1)]

Mean IQ and Achievement Test Score: All Subjects

TEST	RTH+ (n=73)	RTH- (n=57)	
Verbal IQ*	88.9 ± 1.7	101 ± 2.0	p<0.001
Performance IQ	94.8 ± 1.6	104 ± 2.1	p<0.002
Full Scale IQ**	90.8 ± 1.5	103 ± 2.0	p<0.001
Reading Achievement	80.6 ± 2.3	91.6 ± 2.5	p<0.03
Math Achievement	81.4 ± 2.1	95.8 ± 2.5	p<0.01

* IQ scores are means ± Standard Error
** 3 RTH+ and no RTH- subjects had a Full scale IQ under 70

Mean Scores: Matched SIB Pairs

TEST	RTH+ (n=16)	RTH- (n=16)	
Verbal IQ*	87.1 ± 3.9	102 ± 3.6	p<0.002
Performance IQ	96.9 ± 3.3	107 ± 3.5	p<0.02
Full Scale IQ	91.0 ± 3.3	105 ± 3.6	p<0.001
Reading Achievement	78.4 ± 4.8	94.8 ± 4.9	p<0.03
Math Achievement	76.8 ± 3.9	90.7 ± 5.5	p<0.05

* IQ scores are means ± Standard Error

Sylvian Fissure Anomalies: Left Hemisphere

	RTH+ (n=49)	**RTH- (n=40)**	
All subjects	24/49 (49%)	14/40 (35%)	n.s.
Males	15/22 (68%)	7/21 (33%)	p</= 0.03
Females	9/27 (33%)	7/19 (37%)	n.s.

Note: No significant differences were found in the frequency of R Sylvian fissure anomalies

What is the future for this field and this research?

Panel Discussion

More research needed

- Create a lab setting that is more realistic
- Assess what results from combinations of chemicals rather than evaluating chemicals in isolation
- Conduct more research on plastics and food
- Evaluate herbal preparations

Develop a screening and testing program

- Identify hazardous chemicals and those that require further testing
- Parallel the effort in Europe
- Create a research inventory
- Collaborative efforts between academics, government and industry
- Limit what chemicals can be used and how

Increase interaction between scientists and the public

- Provide more information and be vigilant about disseminating information
- Make the issues more accessible to the public, reachable
- Create a venue so this information can be heard and acted upon (use buying power)

Increase availability of information

- What are we exposed to?
- How do we find out what we are exposed to?
- Implement ingredient lists for the packaging of products

Communication

- Emphasize common goals, concerns and interests
- Identify unifying issues
- Spreading the word by using credible sources: doctors, scientists
- Continue to think about and address the issue
- Increase environmental literacy

Closing Remarks

(The following are excerpts from remarks by Monica Campbell, Manager of the Health *Promotion and Environmental Protection office for the Department of Public Health in Toronto.)*

Today we have heard from key scientists about how hormonal disruptors in the environment raise serious concerns about the health of children. We have learned that a huge number and variety of chemicals exist. We have heard that these chemicals can be very potent, that they can persist in the environment much longer than endogenous or naturally occurring chemicals and that we are transferring both the chemicals and their effects to the next generation.

Some of the impacts of these chemicals include cognitive effects that may result in fewer gifted children and more children with developmental challenges. The weight of the evidence about potential adverse effects is strong in both laboratory studies on animals and wildlife studies.

The current research requires more epidemiological studies on humans that link individual exposures with individual effects. While further research is warranted to establish causal links between environmental exposures and adverse health effects, there is also a pressing need to implement precautionary actions now to minimize exposures to hormonally active environmental contaminants. As several of our speakers indicated, the next step must be translating our existing scientific knowledge on potential hormonal, developmental and reproductive impairments into health-protective policy.

The final themes that emerged during the panel discussion included the need for research, policy and education. All the presenters agreed that more research was necessary, but that more health protective policies need to be developed and integrated into the risk assessment process. And lastly, a stronger education initiative is necessary to give the public sufficient information by which to protect themselves and their families, and to empower the public to advocate for more health-protective policies. The public's right to know about environmental health risks needs to be addressed, and the work of environmental and health advocacy groups needs to be supported. The end result should be increased pressure on politicians to regulate the use of these chemicals to safeguard our health, our children's health as well as generations to come.

Appendix A

Members of Planning Committee

Daniel Desaulniers, Environment & Occupational Toxicology, Health Canada

Brian Gibson, Department of Public Health Sciences, University of Toronto

Joanne Lacey, Centre for Health Promotion, University of Toronto

Neil MacLusky, Columbia University

Barbara McElgunn, Learning Disabilities Association of Canada

Len Ritter, Canadian Network for Toxic Centres, University of Guelph

Irving Rootman, Centre for Health Promotion, University of Toronto

Beth Savan, Environmental Studies Proramme-Innis College, University of Toronto

Rodney White, Institute for Environmental Studies, University of Toronto

Appendix B

Biographical Statements

Monica Campbell is the Manger of the Health Promotion & Environmental Protection Office, Toronto Public Health Department, where she participates in applied research and provides continuing education to public health staff. Dr. Campbell is an Assistant Professor in the Department of Public Health Sciences at the University of Toronto and an Adjunct Professor in Ryerson University's School of Environmental Health. She holds a doctoral degree in Toxicology, and conducts research on soil contamination, drinking water, lead, pesticides, and state of the environment reporting, air quality, and children's environmental health issues.

Chris DeRosa is the Director, Division of Toxicology, Agency for Toxic Substances and Disease Registry (ATSDR). His current professional interests are centered on the interface of environmental health science and science policy, with emphasis on risk analysis as a synthetic construct for the risk assessment and disease prevention paradigms. He holds graduate degrees in biology from Miami University in Ohio. Prior to joining ATSDR, Dr. DeRosa worked with the Environmental Protection Agency (EPA) in a number of capacities, including Acting Director of Environmental Criteria & Assessment Office, Group Leader, and Acting Branch Chief of the Chemical Mixtures Assessment Branch. He has also held teaching positions with the University of Virginia and the University of Maine. Dr. DeRosa is a four-time recipient of the EPA Bronze Medal, a member of several toxicological and biological societies and the author of over 100 peer-reviewed publications.

Peter Hauser is a physician researcher with expertise in neuroendocrinology, molecular genetics and childhood learning disabilities. Before serving as Professor of Internal Medicine at the University of Maryland School of Medicine and Chief of Psychiatry at the Baltimore VA Medical Center, Dr. Hauser was at the National Institutes of Health. There, he coordinated a multidisciplinary team of scientists and basic scientists who studied patients with resistance to thyroid hormone, a thyroid disease caused by mutations in the thyroid receptor gene. He was responsible for elucidating the association of resistance to thyroid hormone with attention deficit hyperactivity disorder, which is a major consequence of this illness. More recently he has devoted his attention toward understanding the adverse effects of dioxin and dioxin-like compounds on the thyroid system and neurodevelopment. His publications have clarified the role of thyroid hormone and the thyroid receptor in brain, behavioural and intellectual development.

Neil MacLusky is currently a Professor and Scientific Director of the Center for Reproductive Science at the Columbia University Medical School. He received his Ph.D. from the University of London and has since held appointments there, as well as McGill, Yale and, until recently, at the University of Toronto, where he was the Director of Basic Research in the Division of Reproductive Science at the Department of Obstetrics and Gynecology. He is a member of a number of scientific societies, and has been honoured with several fellowships and awards. He is also the author or co-author of over 140 scientific publications as well as numerous review articles and book chapters.

Barbara McElgunn is a Health Policy Officer for the Learning Disabilities Association of Canada. Her background is in nursing, with a post-graduate specialty from the Montreal Neurological Institute. She is a member of the Research Committee of the Learning Disabilities Association of America, the Behavioural Toxicology Society, and the Pesticide Management Advisory Council. She has served on numerous national and international advisory committees and working groups on children's environment and health issues.

Walter Rogan is a clinical investigator with the Epidemiology Branch at the National Institute of Environmental Health Sciences (NIEHS), where he is a project officer for a 4 site, randomized, controlled clinical trail of oral chelation therapy to prevent lead-induced disorders of growth, behaviour, and cognitive development in toddlers. Dr. Rogan holds a MD from the University of California (UC) San Francisco and a MPH in Biostatistics from UC, Berkeley. After internship at San Francisco General Hospital he came to NIEHS, where has held several appointments including Chief of Epidemiology, and Associate Director of the Division of Biometry and Risk Assessment. His main research focus has been the effect of pollutant chemicals on the growth and development of children.

Irving Rootman is a Professor in the Department of Public Health Sciences at the University of Toronto and the Director of the University of Toronto's Centre for Health Promotion which is a World Health Organization Collaborating Centre in Health Promotion. Prior to joining the University of Toronto in 1990, he worked for Health and Welfare Canada as Director of the Program Resources Division, as Chief of Health Promotion Studies in the Health Promotion Directorate, and as Chief of Epidemiological and Social Studies in the Non-Medical Use of Drugs Directorate. He has acted as a Senior Scientist, consultant and technical advisor for the World Health Organization and is a member of the board of the International Union for Health Promotion and Education. He has published widely in the field of health promotion and is an author of a recent book entitled People-Centred Health Promotion. He has a Ph.D. in sociology from Yale University. He is the Chair of the WHO-EURO Working Group on Health Promotion Evaluation.

Appendix C

List of Participants

Laura Alexander, GE Canada

Virginia Anderson, Community

Danita Aziza, Community

Hilary Balmer, RAINET

Vivian Bertrand, Environment Canada–Policy & Community

Rose Bilotta, Community

Anne Birks, Toronto Public Health

Wayne Bowers, Health Canada

Gwen Burrows, Hospital for Sick Children Foundation

Monica Campbell, Toronto Public Health Department

Nita Chaudhuri, South Riverdale Community Health Centre

Karen Cowan, New Visions Toronto

Tina DeRita, Health Canada

Ria Demos, Health Canada–Policy & Programs

Manuella Federici, Health Canada

Trevor Fleck, Ontario Ministry of Health

Brenda Leach, Office of Karen Kraft Sloam, MP North York

Les Levine, Ontario Ministry of Health

Bruce Loquist, Community

Judith MacPhail, Toronto-Sunnybrook Regional Cancer Centre

Madha Malhotra, Environment Canada

Jill McDowell, Pollution Probe

Sue Millburn-Hopwood, Environment Canada–Policy & Community

Steven Narod, Centre for Research in Women's Health

Carolyn O'Brien, Food & Consumer Prod. Manufacturers. Of Canada

Laura Pascoe, Workers Health & Safety Centre

Peter Pennefather, Faculty of Pharmacy, University of Toronto

Sharon Rickard, Nutritional Sciences, University of Toronto

Lou Riklik, Occupational Health Clinic

Irving Rootman, Centre for Health Promotion, University of Toronto

Helen Samek, Heinz Canada

Kevin Semande, Ontario Ministry of Health

Peter Shin, Nutritional Sciences, University of Toronto

Cheryl Shour, Community

Christine Siambani, Community

Mimi Singh, Canadian Plastics Industry Association

Audrey Smargiassi, CINBOISE

Adam Socha, Health Canada-Standards Development Branch

Danielle Stein, Toronto Public Health Department

Joanne Taylor Lacey, Centre for Health Promotion

Shirley Thompson, Toronto Catholic District School Board

Lillian Thompson, Nutritional Sciences, University of Toronto

Wendy Ward, Nutritional Sciences, University of Toronto

Rodney White, Institute for Environmental Studies, University of Toronto

Hamish Wilson, CIUT Radio

Jane Ying, Toronto Public Health Department

Peter Zambrowicz, Toronto Public Health Department

Alena Zelinka, Workers Health & Safety Centre

Note: This list may be incomplete due to late registration.