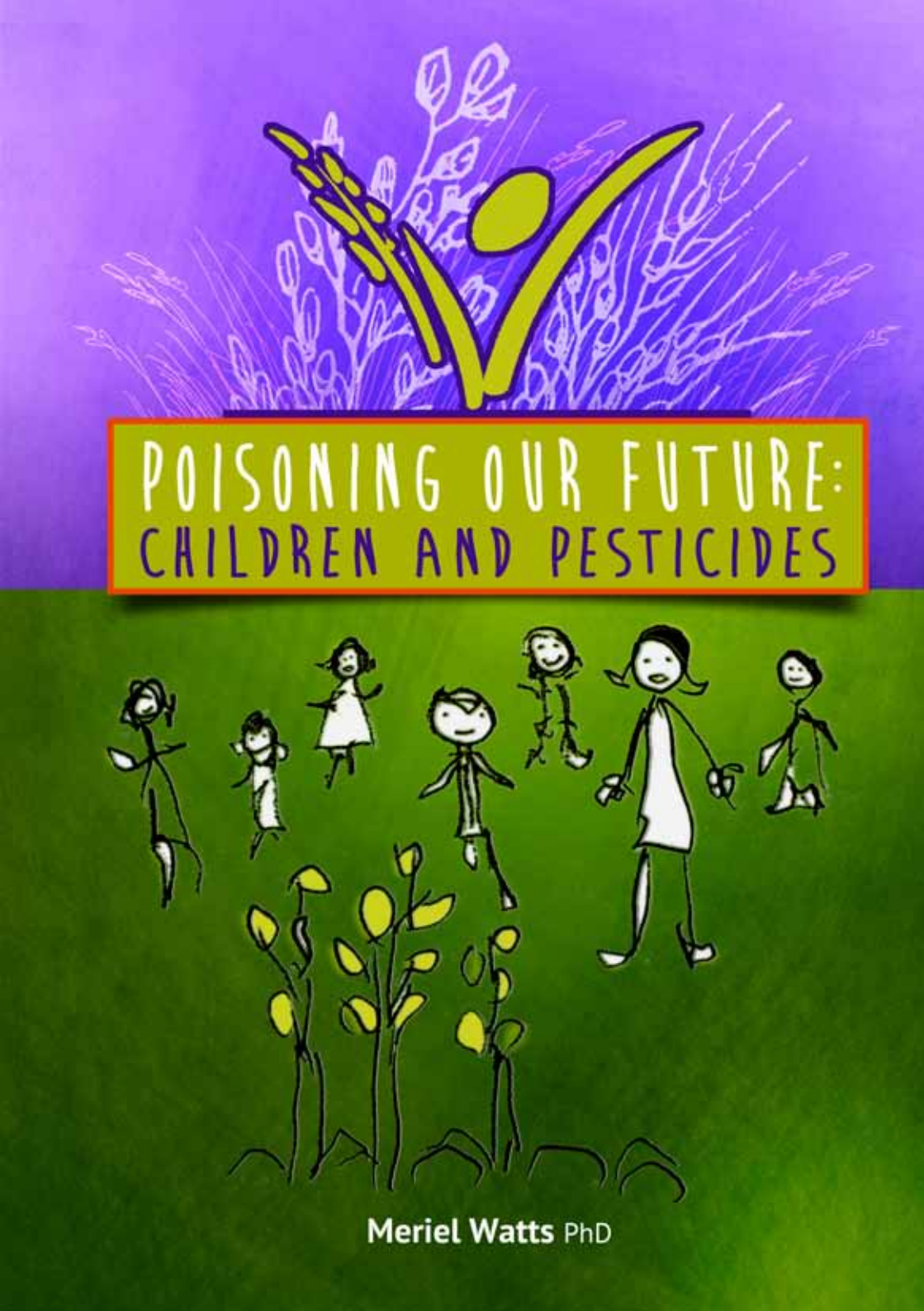
POISONING OUR FUTURE: CHILDREN AND PESTICIDES



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If we are to teach real peace in this world, and if we are to carry on a real war against war, we shall have to begin with the children.

~ MAHATMA GANDHI

1 Introduction

"What matters is that our children's bodies have become garbage cans! Everyday, I cry because of those diseases simply caused by the environment. More people have died because of chemicals than during World War II. Those who don't want to see any cause for concern in our studies will have to answer for their serious dishonesty." | Giles-Eric Seralini 2013[1]

There are many factors that determine the health and well being of children– genetic, nutritional, social, economic, cultural, and environmental. All are important and all interact with each other in ways barely understood at times. This book is about one very important facet of that complex mix–the effects of pesticide exposures on children.

A number of writers (e.g. Muncke 2009) have drawn attention to the pattern of worsening human health shadowing the increase in chemical use in everyday life and chemical pollution of the environment since the wide- spread introduction of industrial chemicals and industrialised agriculture post-World War I. There has been a growing awareness of the potential impact of these synthetic chemicals on child health over the last two decades. In part that has arisen from the observations of the worsening burden of child disease including infectious diseases, cancer, respiratory diseases, as well as behavioural and developmental problems. In 2010, Dr Gina Solomon,[2] gave the following evidence to a US Senate hearing about protecting children from environmental threats:

> *Some childhood diseases and abnormal conditions are on the rise. For example, childhood leukaemia and brain tumours—the two most common childhood cancers—have increased by more than 20% since 1975. Asthma approximately doubled in prevalence between 1980 and 1995 and has stayed at the elevated rate. Certain birth defects of the penis and testes, such*

[1] Professor and research scientist in molecular biology at the University of Caen. On GMOs and Roundup. Interview by Maryvonne Ollivry, Paris Match. 17 January 2013. http://gmoseralini.org/the-price-of-truth/

[2] Director of the National Resources Defense Council, Associate Director, Pediatric Environmental Health Specialty Unit, and Associate Clinical Professor of Medicine, University of California, San Francisco.

as cryptorchidism (undescended testes), have increased 200% between 1970 and 1993. And, of course, there is autism, the diagnosis of which has increased by more than ten-fold in the last 15 years.[3] | *Solomon 2010*

Observations such as these have stimulated a growing concern about children's exposure to toxic chemicals, and this in turn has fuelled an intense round of scientific investigation that has unravelled some startling information about just how vulnerable a child, and especially the developing foetus in its mother womb, is to exposures of even very low levels of chemicals, especially those that affect the immune, endocrine and neurological systems. Alongside this has emerged an understanding that what ails adults can often be traced back to the womb – that the exposure of the unborn foetus leads to chronic and debilitating conditions in the old-aged, termed the **foetal origins of disease**, or **developmental origins of adult disease**.

A seminal publication in this process was the USA's National Research Council report *Pesticides in the Diet of infants and Children* (NRC 1993), which clearly spelled out that "children are not little adults" and that they are especially vulnerable to the effects of pesticides.

Pesticide poisoning is a serious health problem that disproportionately affects infants and children. | *Goldman 2004*

…there is now sufficient evidence to indict low level exposures to pesticides as a serious threat to health and well-being of children…

This book pieces together just some of the research showing how children are being born pre-polluted, affected by pesticides in the home, in their food, in the rural environment, even in schools — and not forgetting those hundreds of thousands of children born into poverty that are forced to work with pesticides in order for their families to survive. It examines evidence that children thus exposed face significant risks of birth defects, childhood cancer, Autism Spectrum Disorders, neurodevelopmental delays, asthma, middle ear infections, and other diseases. It also examines some of the mounting evidence that child exposures to pesticides may be a factor contributing to the explosion of adult diseases such as obesity, type 2 diabetes, other metabolic diseases, and cardiovascular problems, as well as cancer, neurological diseases and immune disorders.

Most types of pesticides are implicated—organochlorines (OCs), organophophates (OPs), carbamates, and synthetic pyrethroids; insecticides, herbicides,

[3] These figures are for the United States.

fungicides, and others. Many are endocrine disruptors.

Analysis of metabolites in the urine of children in the US has led researchers to calculate that as many as 40% of the children in that country have had cumulative exposures to OPs that put them at risk of neurological impacts (Payne-Sturges et al 2009). Pesticide residues are not alone in children's bodies. Body burden studies in North America (e.g. Schmitt et al 2007; CDC 2009) show they are in the company of polybrominated diphenyl ethers (PBDEs), polychlorinated biphenyls (PCBs), perfluorinated chemicals (PFCs) and polyaromatic hydrocarbons (PAHs), and heavy metals—each of which carries significant risks including endocrine disruption, developmental disruption, neurotoxicity, and cancer, among others, adding to the dangers of pesticide exposure.

Whilst the science is not yet complete, and may never be, there is now sufficient evidence to indict low level exposures to pesticides as a serious threat to health and well-being of children, condemning them to life-long health problems that can also affect their own children, and hence travel down through future generations. But it is not just individuals that are affected—society as a whole is being undermined by these exposures—by a reduction in IQ, and by an increase in behavioural problems and problems of socialisation, as well as by a burgeoning health burden and associated costs.

Why is this problem allowed to continue in the face of international conventions such as the 1989 United Nations Convention on the Rights of the Child? Because our institutional and regulatory systems are completely inadequate to the task. For the most part, they do not even recognise the special vulnerability of children and they fail to require the appropriate sorts of testing that would reveal the real effects of pesticides. Worse, government, and even many scientists, make the unfounded assumption that pesticides are necessary to grow food, to feed the world, for farmers to

make a decent living. These assumptions are challenged and recommendations provided for improving regulatory systems and government policies so that children can truly be protected from the effects of toxic pesticides, enabling them to live lives in which they can achieve their potential in health, learning and well-being.

"It is already well established that the in utero and perinatal "environment" and maternal and early childhood circumstances play major roles in the risk of later life disease". | Cooper et al 2011 ■

Children's talent to endure stems from their ignorance of alternatives.

~ MAYA ANGELOU

2 Exposure

In 1993, the USA's National Research Council published the report *Pesticides in the Diet of Infants and Children,* with the oft-quoted conclusion "children are not 'little adults'" (NRC 1993). Headed by paediatrician Philip Landrigan, the Committee on Pesticides in the Diets of Infants and Children drew attention to the fact that pesticide regulatory systems are premised on the effects on adults, yet children are more vulnerable to pesticides than adults. One reason for this increased vulnerability is that children have greater exposure to pesticides than do adults not involved in occupational use.

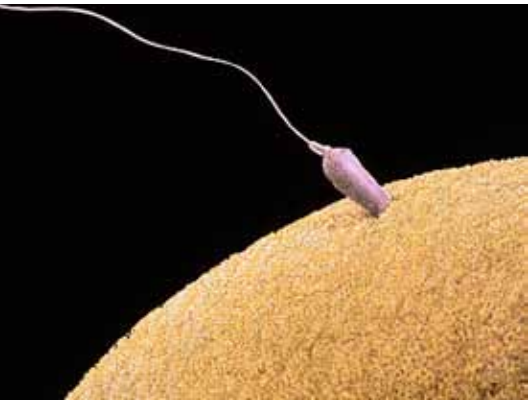
2.1 Inhaling and ingesting more

Children eat and drink more than adults in relation to their body weight, and so take in relatively more residues. US figures show that, generally, children in the first six months of life consume seven times more water per kg of body weight than does the average adult (Landrigan et al 1999). In the US, and for people with westernised diets, children tend to consume relatively more processed foods such as fruit juices and baby foods which may concentrate residues; infants in particular also have a much higher intake of vegetables, which often have relatively higher levels of residues than do meats. Pesticides found in baby food in the US included eight that are toxic to the nervous system, five that affect the endocrine system, and eight that are potential carcinogens (Landrigan et al 1999).

They also inhale a relatively greater quantity of air: the breathing rate over the first 12 years of life is about double that of adult breathing rates (Miller et al 2002), so they can take in double the amount of inhaled pesticide as an adult under the same situation of exposure. When the breathing rate is taken into account relative to lung surface area, the amount of airborne contaminants reaching the lung surface is likely to be about 3-4 times higher in 3-month old children than in adults (WHO 2006). This makes children more vulnerable to the effects of spray drift and household insecticides. In fact, inhalation from household use of pesticides exceeds food residues as a source of pesticide exposure for many children in the US (Landrigan et al 1999).

Children often have a closer association with the environment that may be contaminated with pesticides: they live closer to, and sit, lie and play on the floor, exposing themselves to contaminated surfaces and house dust. They put into their mouths, particularly when they are teething, various objects that may have spray residues on them especially if household insecticides are used. Children's play raises dust that may hold residues and be inhaled (CPCHE 2005). They will also be more exposed to volatile pesticide vapours, particularly those that have densities heavier than air, in indoor situations—children have died from playing on grain fumigated with aluminium phosphide (Garry 2004). Semi-volatile pesticides such as chlorpyrifos have long persistence on rugs, furniture, soft toys, pillows and other absorbent surfaces particularly in closed apartments (Landrigan et al 1999). Levels of chlorpyrifos in the air following indoor household use in the US were significantly higher in the infant breathing zone than in the adult sitting zone (Fenske et al 1990). This avenue of greater exposure is confirmed by significantly higher levels of the metabolites of pyrethroid insecticides, commonly used in households, in the urine of children than in that of adolescents or adults in the USA (Barr et al 2010a).

Children also sit, lie and play on the lawn and bare earth, and put earth into their mouths—again a potential exposure route if pesticides have been used outdoors, or spray drift occurs (NRC 1993). Soil from outdoor play areas in homes in an agricultural area of Washington State, USA, contained residues of azinphos-methyl, phosmet, chlorpyrifos and ethyl parathion (Simcox et al 1995).



2.2 Born pre-polluted

Yet exposure begins long before children get to play in the dirt: it begins from the very first moments in the womb when the embryo is being formed from the father's sperm and the mother's egg.[4] Many pesticides can be readily transferred from the mother across the placenta to the developing foetus during pregnancy (Daston et al 2004), and so children are

[4] It could be argued that it begins even before that: pre-conception, with father's exposures (Perera & Herbtsman 2011). Semen samples from farmers have been found to contain alachlor, atrazine, 2,4-D, diazinon, metolachlor and a metabolite of chlorpyrifos; and the semen from urban men has been found to contain chlordane, DDE, heptachlor and HCB (Colborn 2006). In the section on cancer in the next chapter, evidence is provided that fathers' exposure to some pesticides is linked to certain childhood cancers.

born already carrying a significant load of pesticides, even of so-called 'non-persistent' ones such as organophosphates. In a New York study of newborn infants, seven pesticides and pesticide metabolites were detected in the umbilical cord blood of up to 83% of the children (Whyatt et al 2003). The levels found generally matched mother's use of household insecticides, or treatment of the home by a pest exterminator, during pregnancy. Various organochlorine pesticides have been found in umbilical cord blood in China, India, Japan, Thailand, Kazakhstan and Kyrgyzstan.[5] Other pesticides have been found in the placenta and amniotic fluid, the liquid layer that protects and nourishes the foetus, providing the nutrients needed to make it grow and develop (refer Table 1).

Babies will continue to be born pre-polluted as long as pregnant women are exposed to pesticides...

These are not just random finds: many studies have reported such contamination and the frequency can be very high: in one US study, 100% of cord blood samples contained DEET, 94% contained chlorothalonil and 63% contained chlorpyrifos (Barr et al 2010b); and in another study 100% contained OP metabolites (Whyatt & Barr 2001).

Some pesticides are found in higher levels in cord blood than in the mother. Chlorpyrifos was found in 70.5% of samples of maternal blood and 87.5% of cord blood, in a study in the US, attributed to mothers' greater levels of the detoxifying enzyme paraoxonase 1 (PON1). Diazinon was present in 33.3% of maternal blood and 47.3% of cord blood (Huen et al 2012).

The presence of pesticide residues in the meconium (first faeces) of newborn infants is added evidence that the foetus has been exposed *in utero* to pesticides. Meconium is formed by the foetus from around the 12th week of pregnancy. It accumulates throughout pregnancy and is then excreted by the newborn after birth. Chemicals that cross the placenta are deposited in the meconium throughout pregnancy, and the meconium thus provides a cumulative 'catalogue' of the chemicals to which the foetus has been exposed during its development (Ostrea et al 2006). Samples of meconium taken in the Philippines have shown foetal exposure to a range of pesticides. In one study, even though the mothers were exposed to agricultural use, it was predominantly the home use pesticides propoxur and the pyrethroids cypermethrin, cyfluthrin, and bioallethrin that were found in the meconium. Other studies have found a wide range of pesticides in meconium, and in the plasma of newborn infants (neonates).

5 China (Zhao et al 2007), India (Nair et al 1996), Japan (Fukata et al 2005), Thailand (Asawasinsopon et al 2006), Kazakhstan and Kyrgyzstan (UNEP 2002).

Table 1: Pre-polluting pesticides

Pesticide	Cord blood[1]	Placenta[2]	Amniotic fluid[3]	Meconium[4]	Neonate plasma[5]	Urine in Pregnancy[6]	Mother's blood[7]
acephate						●	
acetochlor	●				●		
alachlor	●				●		
aldrin		●					
atrazine	●				●		
bendiocarb	●						
bifenthrin				●			
Bt toxin	●						●
captan	●						
captafol	●						
carbaryl						●	
carbofuran	●				●		
chlordane	●	●	●	●			
chlorothalonil	●				●		
chlorpyrifos	●			●		●	
cypermethrin	●			●			
cyfluthrin	●			●			
dacthal	●						
2,4-D						●	
DDT/DDE	●	●	●	●			●
DEET	●					●	
diazinon	●			●		●	
dicloran	●				●		
dieldrin		●					
dichlorvos					●		
endosulfan	●	●	●				
endrin		●					
folpet	●						
fonofos	●				●		
glufosinate-ammonium	●						●
HCB	●	●	●	●			●

Pesticide	Cord blood[1]	Placenta[2]	Amniotic fluid[3]	Meconium[4]	Neonate plasma[5]	Urine in Pregnancy[6]	Mother's blood[7]
HCH	●	●	●				●
heptachlor		●	●				●
lindane	●	●	●	●			●
linuron	●						
malathion	●			●	●		
metalaxyl	●				●		
methoxychlor		●					
metolachlor	●				●	●	
methyl parathion	●				●		
mirex	●	●	●				●
parathion	●			●	●		
pentachloro-phenol	●			●			
permethrin	●				●		
phorate					●		
piperonyl butoxide	●						
pretilachlor				●			
profenofos	●						
propoxur	●			●			
terbufos	●				●		
trifluralin	●				●		
vinclozolin	●						
Metabolites of:							
carbamates						●	
dithiocarbamate fungicides						●	
OPs	●		●			●	
pyrethroids	●					●	

1 Whyatt & Barr 2001; Whyatt et al 2003; Barr et al 2007; Pathak et al 2008; Barr et al 2010b; Herrero-Mercado et al 2010; Neta et al 2010; Liao et al 2011; Wickerham et al 2012
2 Shen et al 2007; Fukata et al 2005; Freire et al 2011
3 Luzardo et al 2009; Tzatzarakis et al 2009
4 Ostrea et al 2006; Barr et al 2007; Ostrea et al 2009; Huen et al 2012
5 Whyatt et al 2003
6 Castorina et al 2010
7 Röllin et al 2009; Aris & Leblanc 2011

Babies will continue to be born pre-polluted as long as pregnant women are exposed to pesticides, whether it is from household use, agriculture, or disease vector control. Eighty eight percent of pregnant women in an inner city New York study used pesticides in their homes during pregnancy (Williams et al 2008). Nearly 100% of indoor air samplers in the homes of pregnant women in New York contained chlorpyrifos, diazinon and propoxur, with piperonyl butoxide in up to 68.5% (Whyatt et al 2007). More than 78% of pregnant women in a rural area of California, USA, had detectable levels of OP metabolites in their urine (Castorina et al 2010), giving some indication of the extent of pregnant women's exposure to pesticides, at least in that country. Thirty-four different metabolites were measured in the pregnant women. In South Africa, a number of organochlorines were detected in the plasma of women delivering babies. The levels of DDT were particularly high in women from regions in which it is sprayed for malaria control (Röllin et al 2009).

Even dietary exposure of the mother results in residues in the infant. In the first of its kind, a study by Aris & Leblanc (2011) showed that consumption of genetically modified foods, such as soybeans, corn and potatoes, was resulting in residues of the pesticides for which those crops had been modified in women in urban Canada. A metabolite of glufosinate-ammonium (3-MPPA) was found in 100% of pregnant women and the cord blood of their babies, whilst the Bt toxin Cry1Ab was found in 93% of pregnant women and 80% of their babies. The women had had no contact with pesticides. Glufosinate is reported to be associated with increased risk of birth defects in humans.

2.3 Contaminated breast milk

> *Almost all studies throughout the world have shown DDT to be present in the milk of 100% of lactating mothers.* | *Spicer & Kereu 1993*

Already carrying a load of pesticides when they are born, infants are then exposed to further contaminants through their mothers' milk. This intake is significant and several studies have shown it is the major determinant of children's body burdens, especially of organochlorines like DDT and its metabolite DDE: babies that are bottle-fed have significantly lower levels of these OCs, the difference still apparent several years after breast feeding is discontinued (Karmaus et al 2001a; Carrizo et al 2006). Female children appear to accumulate higher levels than male children (Grimalt et al 2010).

A survey of infants in Bhopal, India, revealed they were consuming, through breast milk, 8.6 times more endosulfan than the 'tolerable daily intake' levels recommended by the World Health Organization (WHO), as well as

chlorpyrifos, HCH, malathion, and methyl parathion (Sanghi et al 2003). A more recent study, in Assam in the north-east of India, revealed high levels of HCH in breast milk, with 100% of samples exceeding the WHO guideline; recent extensive use of technical HCH (illegal) and lindane (legal) in agriculture, particularly paddy cultivation, is believed to be the cause of contamination. The breast milk also contained high levels of DDT and DDE (21-24% of samples exceeded WHO guidelines), thought to result from ongoing use for malaria vector control and illegal use in agriculture. The authors of the study concluded that infants in the region are at high risk from these contaminants (Mishra & Sharma 2011).

There are numerous studies from around the world detailing the levels of DDT/DDE in women's breast milk; such is the extent of global contamination with DDT/DDE that it's hard to conceive of any child not receiving a dose of it in their first feeds. DDT was first identified in breast milk in 1951—and still the problem persists. As long as DDT is used for malaria vector control, residues will continue to accumulate in breast milk, not just in the women of those countries that use it, but also in the women of the Arctic regions where persistent organic pollutants such as DDT congregate and accumulate. Many other pesticides have also been found in breast milk, including synthetic pyrethroids—refer Table 2.

There is also evidence that these residues in breast milk are accumulating in children: a study conducted in Spain found that the levels of DDE and HCB in infants' blood were twice that of their mothers, despite their cord blood having been slightly lower than maternal levels (Verner et al 2010).

Table 2: Pesticides found in breast milk

atrazine	diazinon	heptachlor
bendiocarb	dichlorvos	endosulfan
bifenthrin	dicofol	lindane
chlorpyrifos	dieldrin	malathion
chlorpyrifos-methyl	dimethoate	methyl parathion
chlordane	disulfoton	mirex
cyfluthrin	esfenvalerate	permethrin
lambda-cyhalothrin	ethion	propoxur
cypermethrin	fenvalerate	tetramethrin
dacthal	fonofos	toxaphene
DDE/DDT	HCB	tralomethrin
deltamethrin	HCH	

Sources: Wandji et al 1998; Gandhi & Snedeker 1999; Karmaus et al 2001a; Porter et al 2002; Sanghi et al 2003; Poon et al 2005; Bouwman et al 2006; Bradman et al 2007; Carrizo et al 2006; Ntow et al 2008; Polder et al 2008; Haraguchi et al 2009; Fujii et al 2011; Srivastava et al 2011; Weldon et al 2011; Corcellas et al 2012; Feo et al 2012.

Though contaminated by environmental poisons, breastfeeding is still highly recommended over formula milk. A breastmilk free from poisons is a fundamental right that must be protected by ending the use of pesticides and industrial toxins. In 2004, the World Alliance for Breastfeeding Action (WABA) and the International POPs Elimination Network (IPEN) issued a joint statement stating that:

"The contamination of breastmilk is one symptom of the environmental contamination in our communities. Responsibility for this problem belongs to the industrial sources of contamination, not to breastfeeding women. The individual decision to breastfeed must be promoted and protected while we work collectively towards eliminating the chemicals that contaminate the food we eat, the water we drink, the air we breathe, and the products we use.

Studies have shown that breastfeeding, even in a contaminated environment, has a positive impact on the development of children as compared to those who are artificially fed. Breastfeeding supports infant growth and health as well as maternal health in ways that breastmilk substitutes cannot. Indeed, breastmilk contains sub-stances that help the child develop a stronger immune system and other protections against environmental pollutants and pathogens."

Source: WABA & IPEN. 2004. Joint Statement – World Alliance on Breastfeeding Action and International POPs Elimination Network. http://www.waba.org.my/whatwedo/environment/pdf/Joint.pdf

In many countries in which the persistent pesticides, like dieldrin, DDT, HCB, HCH, and mirex are no longer used, women will continue to be exposed for years to come as the chemicals linger in the environment, and these exposures are difficult to avoid. However, Table 2 reveals that a number of pesticides still in common usage are also contaminating breast milk. These include herbicides like atrazine and insecticides like malathion and permethrin, the use of which is virtually endemic, globally. The ongoing use of DDT for malaria control in Africa and some Asian countries is also condemning more generations of children to carrying body burdens of toxic chemicals that affect them through out their lives. It is the responsibility of international organistaions such as the UN, national governments, the pesticide industry, farmers organisations, scientists, and all users of pesticides to stop this contamination of breast milk and babies' bodies.

2.4 Residues of pesticides in food

> *"For many children diet may be the most influential source [of exposure to pesticides]."* | *Statement by American Academy of Pediatrics (CEH 2012)*

Residues in food and drink are an important source of ongoing every-day low-level exposure to mixtures of pesticides, particularly residues in fresh fruit and vegetables, and drinking water. The average person in the US is said to be exposed to 10 to 13 pesticides each day via food, beverages, and drinking water (Benbrook 2008). One survey of food being consumed by urban US children found that 14% contained at least one OP and 5% contained at least one pyrethroid insecticide. Eleven different OPs and three pyrethroids were measured in the food (Lu et al 2010). However, a more recent review of US studies of children's exposure to pyrethroids reported 7 different pyrethroids (permethrin, cypermethrin, bifenthrin, esfenvalerate, cyfluthrin, deltamethrin, phenothrin and tetramethrin) in fruit and vegetables, concluding that dietary exposure was the dominant type of exposure, except in houses with frequent pesticide applications (Morgan 2012).

Metabolites of OPs have been found in the urine of 99% of urban pre-school children in Seattle, USA. Although levels were higher in children whose parents used pesticides in the garden, the metabolites were still present in those whose parents did not, indicating that at least some of them came from diet (Lu et al 2001).

Australian children have a much higher intake of chlorpyrifos, the most frequently found OP residue, than children in the USA or Japan: the Australian estimated dietary intake for 2-5 year-olds is 0.6 µg/kg bw/day, compared with

children aged 3-6 in Japan (0.007 µg/kg bw/day) and in the US (age not given) of 0.03 µg/kg bw/day (Babina et al 2012).

Finally, as further proof of the exposure resulting from pesticide residues in conventionally-produced food, there is now compelling evidence that organic diets dramatically reduce children's exposure to organophosphate insecticides. Children eating organic diets in Seattle had six times lower levels of metabolites of OPs in their urine compared with children eating a conventional diet (Curl et al 2003). When children changed to organic fruit and vegetables, their urinary levels of chlorpyrifos and malathion metabolites fell to undetectable almost immediately (Lu et al 2006, 2008), indicating that their previous exposure was solely dietary.

2.5 Health treatments

The application of shampoo containing permethrin to treat head lice can result in elevated levels of pyrethroid metabolites in children's urine (Naeher et al 2009). Other highly hazardous pesticides used to treat head lice or scabies in children include pyrethrins with piperonyl butoxide, lindane, carbaryl, phenothrin, and malathion, with the chemical being applied directly to the scalp in the case of head lice or the skin in the case of scabies (PAN UK 1999; CDC 2010; DermNet NZ 2011). All are likely to result in the absorption of some of the chemical into the child's body.

Children in malaria-prone areas where insecticides are used for indoor residual spraying are also exposed, including prenatally. A study of 255 delivering women from areas of South Africa where DDT is used in this manner were found to have significantly higher levels of DDT, DDE and DDD in their blood than those women from areas were it is not used (Channa et al 2012). Children will also be exposed to synthetic pyrethroids used on insecticide-treated bed nets that are distributed throughout malaria-prone regions and also used in other areas. Children may be exposed by touching, or sucking on the netting.

2.6 Contamination of the home and school environment

Although few studies are available for pesticide contamination of the home in Asia or the Pacific, many studies have been carried out in the USA, and it is reasonable to assume they will be somewhat indicative of the situation elsewhere. At the least, they provide an illustration of where problems may lie. The US studies demonstrate that homes are commonly contaminated with pesticides, particularly synthetic pyrethroids and organophosphates used for indoor pest control, but also herbicides used on the lawn and tracked inside, wood preservatives and organochlorines in the timber used to build the house (Eskenazi et al 1999), and in agricultural areas a whole host of pesticides used on the farm. Where the house is contaminated, so too are the children who live in it.

Urban children

Urban exposure can be significant, largely as a result of the use of insecticides for the control of flies, fleas, cockroaches and other pests in the home, whether they are from household sprays or pesticides applied by professional exterminators. One study in Minnesota, USA, even found higher exposure in urban children from homes with frequent pesticide use than non-urban children from homes where well-water was used. Over a five-day period, metabolites of chlorpyrifos was detected in the urine of 98% of the urban children, and malathion in 46%. The levels were higher in children than adults (Adgate et al 2001).

Exposures are likely to be highest where household insecticide use or pest extermination occurs.

Exposures are likely to be highest where household insecticide use or pest extermination occurs, where pesticides are used on lawns or home garden, or where public health fogging is done to control human disease-bearing vectors such as mosquitoes, or for control of unwanted horticultural pests (such as Mediterranean fruit flies in the USA or painted apple moth in New Zealand). One of the main sources of pyrethroid residues in children is household applications (Lu et al 2006; Naeher et al 2010). This exposure is likely to be greatest where there is poverty, particularly for children living in crowded low quality housing prone to insect infestation.

A recent study in Australia found that there was widespread chronic exposure of preschool children to organophosphate and pyrethroid insecticides and that, although most exposures were higher in the

rural area, urban children's exposure to chlorpyrifos and bifenthrin was just as great, probably because they are used widely in domestic situations as well as in agriculture. Australian children have substantially higher exposures to a wide range of OPs and pyrethroids than children in both USA and Germany (Babina et al 2012).

Following the application of 2,4-D herbicide to lawns in the US, residues of the herbicide have been found in indoor air, and on all surfaces within the home including table tops, mainly tracked-in by the homeowner applicator or dogs. Children were ingesting up to 30 µg/day from contact with table-tops (in comparison with estimated dietary ingestion of about 1.3 µg/day) (Nishioka et al 2001).

House dust, especially in older houses, can contain residues from pesticides used in treating wood from which the house was built, such as chlordane, DDT, dieldrin, heptachlor and lindane; these banned persistent organochlorines have been found widely distributed in indoor air and surfaces in the US (Landrigan et al 1999; Abb et al 2010). Uptake through skin contact can exceed 'acceptable daily intake' levels (Landrigan et al 1999). Other pesticides found in urban house dust in USA include bifenthrin, cyfluthrin, cyhalothrin, cypermethrin, deltamethrin, esfenvalerate, fenpropathrin, fenvalerate, permethrin, phenothrin, resmethrin, and tetramethrin (Morgan 2012). One study of 199 households in the US state of North Carolina found the following pesticides in house dust: permethrin (99%), o-phenylphenol (95%), chlorpyrifos (82%), chlordane (71%), DDT (38%), heptachlor (36%), diazinon (33%), DDE (28%), methoxychlor (26%), carbaryl (21%), dieldrin (17%), lindane (5%), 2,4-D (3%), and alachlor (1%) (Anthopolos et al 2012).[6]

Rural Children

The situation can be even worse for farm children and especially the children of farmworkers. The latter may be exposed *in utero* when their mothers spray or are in contact with pesticides. They often play in the

[6] This study may have also included rural households.

fields or accompany their parents when they work. Their parents track pesticide-contaminated soil and dust into their homes and vehicles, their clothes and skin may be contaminated, and washing those clothes may spread the residues to the children's clothes. Children are likely to be exposed to short-range drift and ambient levels of residues in the air, and their drinking water may contain greater levels of residues than those to which urban children are exposed, especially if using well-water (GAO 2000). They may also eat food directly from fields that have recently been sprayed.

One study, which quantified exposure estimates for a population of young farmworker children in the USA, found that 95% of 115,000 different exposure scenarios and dose estimates posed a risk to children's health from chlorpyrifos exposure (Beamer et al 2012).

As could be expected, residue levels are generally highest in the houses of pesticide applicators, then farmworkers' homes and then non-farmworker rural homes (Loewenherz et al 1997; Fenske et al 2002), with the levels in the dust of agricultural homes being as much as 7 times the levels in non-agricultural homes (Lu et al 2000). In the USA, chlorpyrifos has been detected in the house dust of 100% of applicator houses that were tested (Fenske et al 2002); and chlorpyrifos, diazinon, chlorthal-dimethyl (DCPA), and permethrin in up to 90 % of dust samples in farmworker houses (Bradman et al 2007). Atrazine was found in all but 2 of 230 dust samples from the homes of 29 pesticide applicators in Iowa, USA (Lozier et al 2012). Other pesticides found in the dust of rural households include allethrin, azinphos-methyl, carbaryl, chlorthal-dimethyl, cypermethrin, 2,4-D, glyphosate, iprodione, malathion, methyl parathion, metolachlor, parathion, phosmet, piperonyl butoxide and simazine (Lu et al 2000; Curl et al 2002; Fenske et al 2002; Harnly et al 2009; Gunier et al 2011; Quirós-Alcalá et al 2011; Golla et al 2012).

Contamination of dust in vehicles used by farmworkers to get to and from work can be even greater than in their homes—in one study in the US state of Washington an average of 0.75 µg/gm for azinphos-methyl was found in vehicle dust compared with 0.53 µg/gm in house dust. Eighty five percent of houses and 87% of vehicles were contaminated; and 88% of child urine samples contained residues of dimethyl DAP, a metabolite of azinphos-methyl. Malathion, methyl parathion, phosmet, chlorpyrifos and diazinon were also found in vehicles (Curl et al 2002).

Pesticide residues in the urine of children follow a similar pattern to those of houses, with the highest levels in the children of pesticide

applicators (Fenske et al 2002), and with the youngest children having the highest level of contamination within the same family (Loewenherz et al 1997). A study of school children aged 12-13, in Chiang Mai province of Thailand, found that those whose parents were farmers or engaged in agricultural work had higher levels of pyrethroid metabolites and 2,4-D in their urine than those whose parents did not have agricultural exposures. The residues of all other pesticides, including chlorpyrifos, were surmised by the authors to have come from dietary exposure (Panuwet et al 2009). Metabolites of OPs were found in 93% of the children of apple and pear orchard workers in Washington State, USA, with similar frequency of detection in house dust and vehicles (Coronado et al 2006). A study of children living in an agricultural community along the US/Mexican border found OP metabolites in 100% of urine samples and on the hands of 50% of the children, and OPs in the house dust of 76% of the houses sampled (Shalat et al 2003). Other pesticides, or their metabolites, detected in the urine of US farmworker children include 2,4,5-T, 2,4-D, acetochlor, atrazine, chlorpyrifos, coumaphos, DEET, diazinon, glyphosate, isazophos, malathion, metolachlor, parathion, pirimiphos-methyl, and pyrethroid metabolites (Arcury et al 2007; Curwin et al 2007).

Not surprisingly, risk of exposure to pesticides is increased during spray seasons: the levels of OP metabolites in the urine of children from an agricultural community in Washington State, USA, were considerably elevated during the months when pesticides were sprayed in the regions' orchards compared with the non-spray months, irrespective of whether or not parents had contact with pesticides (Koch et al 2002). During these months, exposure can exceed regulatory guidelines: children of orchard or field workers were estimated to be receiving doses of azinphos-methyl above the US EPA chronic dietary reference dose (RfD) for 56% of exposures during spray season; for children of non-agricultural workers it was for 44% of exposures.

Yet, it is not just those rural children living on farms or near fields that are affected: ambient community (i.e. away from the fields) air monitoring data from agricultural regions of California showed that short-term chlorpyrifos exposure estimates exceeded the 'acute reference dose' (another way of saying

an 'acceptable dose') for 50% of children; and non-cancer risks were higher for children than adults (Lee et al 2002).

In the Bang Rieng agricultural community in Thailand, 94% of farm and non-farm children had OP metabolites in their urine, at similar levels in the non-spraying season but significantly elevated in the farm children during the spraying season (Petchuay et al 2006). The level of metabolites in the urine of Thai children across three studies is about double those found in US children (Panuwet et al 2012).

A study of child exposure in banana and plantain plantations in Costa Rica revealed multiple routes of exposure. Houses were on average only 17m from the plantations, and schools and play areas were even closer, at only 12m distance. Violations of legally-established aerial spraying buffer zones occurred. When aerial spraying was carried out, people, houses, playgrounds, clothes hung out to dry, and toys in the gardens got wet from the pesticide mist; cars, roofs and school tables turned yellow. Children ate the fruit growing round the houses without washing them. Children would also play in the plantations, barefoot. They worked too, placing chlorpyrifos-treated bags around bunches of plantain. When parents came home from spraying in the plantations, they would hug their babies and toddlers without removing contaminated clothes. Contaminated clothing was washed with children's clothing. As well as the occupational use of pesticides, parents also used pesticides in the home against rats, cockroaches and mosquitoes, and sprayed their yards with paraquat. Diarrhoea was very common after parents' backpack spraying especially amongst 6-12 year old children who were usually present on the farm when it was done. Other common symptoms during and after spraying included headaches, dizziness, nausea and vomiting (Barraza et al 2011). A second study found that, for more than half the children, estimated intake of chlorpyrifos from the treated bags used on bananas and plantain exceeds US EPA chronic reference doses. Chlorpyrifos was detected in more than half the hand and foot wash samples (Van Wendel de Joode et al 2012).

In Nicaragua, children living in a community in the path of rainwater run-off from a large crop-dusting airfield had depressed cholinesterase activity, thought to be caused by playing barefoot in puddles of water. Pesticides found in their well-water included toxaphene, chlordimeform, DDT and organophosphates such as fenthion, methyl parathion and chlorpyrifos (McConnell et al 1999).

Poisoned school children - USA

"Agricultural land surrounds Mound Elementary School in Ventura County [California USA], with a lemon grove across the street and strawberries grown not far away. Complaints by neighbors about careless pesticide applications went unheeded by the County Agricultural Commissioner, until one day in November 2000 when a cloud of chlorpyrifos (Lorsban), an organophosphorus insecticide, drifted onto the school grounds from the lemon grove. Dozens of students and teachers complained of dizziness, headaches, and nausea following the early morning application. The grower did a second application later that week that also drifted onto the school grounds. Samples from the kindergarten room (45 feet from the grove), desks and play areas (hundreds of yards distant), and other campus locations tested positive for organophosphates." | Kegley et al 2003

Poisoned School children – Sri Lanka

In November 2010, Vikalpani National Women's Federation carried out a case study in Nuwara Eliya District, Sri Lanka. They found that 119 schoolchildren, from a school of 519, had been admitted to hospital for pesticide poisoning, with nausea, vomiting, dizziness, fainting, and stomach pain. The school is next to a carrot plantation, where an organophosphate called Ocron had been used (the container label did not identify the active ingredient) (Vikalpani 2011).

NUWARA ELIYA DISTRICT HIGHLIGHTED ON MAP OF SRI LANKA

Poisoned school children - Benin

"On August 24, 1999, in the village of Maregourou [Benin], three boys between the age of 12 to 14 went to weed the cotton field of their father. The cotton crop was cultivated together with maize. The day before, the father had sprayed the field with endosulfan and the boys did not know. After the work, they were hungry and they took a few maize cobs to eat. Fifteen minutes later they started vomiting. They were taken to the hospital of Bembereke where one boy of 12 died. The two others survived." (Ton et al 2000)

2.7 Schools

Children at school can be subjected to pesticide exposures both from use in the schools and from nearby operations. In the USA, 2593 people, mainly children, were identified with acute pesticide exposure at school between 1988 and 2002. Sixty nine percent of cases arose from application of pesticides on the school grounds–diazinon, chlorpyrifos and malathion were commonly implicated. Thirteen percent of cases arose from spray drift from neighbouring operations–chlorothalonil, chlorpyrifos, cyfluthrin, dicofol, glyphosate, malathion, mancozeb, methamidophos, and propargite, were the main pesticides involved (Alarcon et al 2005).

Acute effects are not the only concern with exposure via spray drift, with a growing number of epidemiological studies linking exposure to pesticide drift to chronic conditions in children such as autism spectrum disorders (Roberts et al 2007) and childhood acute lymphoblastic leukaemia (Rull et al 2009).

In the study in Costa Rica referred to in the previous section, such is the level of exposure of school children in the banana and plantain plantation areas drift from aerial applications close-by that teachers are meant to keep children inside during spraying. However, they frequently didn't (Barraza et al 2011).

2.8 Accidental ingestions

Children may also be exposed to pesticides stored in the home, both rural and urban, particularly where pesticides are stored in soft drink or other beverage bottles, still a common practice in some parts of Asia. Reuse of pesticide

containers makes children think the containers are safe even when they contain pesticides. Looting of grain baited with rodenticides can result in poisoning of children from families living in poverty (Goldman 2004).

Most accidental ingestion cases occur in children under the age of five-six years. More than 60% of 709 pesticide poisoning cases reported to a toxicological information centre in Brazil from 2004 to 2007 involved children up to four years old, mainly with domestic pyrethroid insecticides (Caldas et al 2008). In Cape Town, South Africa, where pesticide poisoning of children is increasing every year, more than 91% of the 306 cases of pesticide poisoning and exposure cases presenting at the children's hospital from 2003 to 2008 were under six years of age; the main problems were OPs and carbamates (Balme et al 2010). In Pakistan, pesticides accounted for 17% of the child poisonings treated at a Karachi hospital, with OPs accounting for most of these (Manzar et al 2010). Forty-eight percent of pesticide poisonings referred to the poison centre in Milan, Italy, during 1995-7, were children under the age of 5, and most commonly involved OPs and pyrethroids in the home (Davanzo et al 2001). Figures from Zimbabwe and Israel indicate that ingestion of insecticides is the most common form of acute poisoning in children under the age of five (Dong & Simon 2001; Weissmann-Brenner et al 2002). In the USA, 50% of child poisoning cases occurred below the age of 3, and were mostly caused by insecticides. Of all the hospitalisations for acute pesticide poisoning in the states of North and South Carolina, 30% were for children (Garry 2004). These are assumed to be accidental ingestion. There were 6,040 domestic pesticide poisonings under the age of 15 in China, between 1997 and 2003, with 243 deaths (Zhang et al 2011) – some of these may have been intentional ingestion.

Children may also be exposed to accidental contamination of food or water. Five students died, and 39 were hospitalised, after drinking milk contaminated with endosulfan at a school in Ranchi, Jahrkand, India, in November 2008 (Prasad 2008). In the remote Peruvian village of Tauccamarca, 24 of the village's 48 children died after consuming a powdered milk substitute, part of their school lunch that had been accidentally contaminated with the organophosphate insecticide methyl parathion (Rosenthal 2003). In Benin, four children died after work clothes left on the roof of a house after spraying were exposed to overnight rain that leached out the endosulfan into the vessel used for drinking water (Glin et al 2006). These accidents continue to happen: in 2011, three children died and 50 were hospitalised in Peru after eating their school lunch. The lunch of rice and fish, provided by the government's national food assistance programme, had been placed in a container which had previously held rat poison (BBC 2011).

2.9 Working children

Around 215 million children are engaged in 'child labour' worldwide. This is over 7% of all children. Nearly 70% of child labourers work in agriculture—around 150 million children. In some countries, children under the age of 10 make up 20% of the rural child labour force (ILO 2006, 2011).

These figures include children on family farms, commercial farms and plantations, bonded labour[7], and trafficking and forced labour or slavery. The children begin work as young as 5 years of age (ILO 2006, 2011). In Africa, South and Central Asia[8], children work in cotton fields in conditions that expose them to highly hazardous pesticides, during or immediatly after spray applications, even doing the spraying[9]—on top of the ardous labour, overwork, beatings, violence, harassment, abuse, sexual harassment and rape, lack of pay, and the loss of education they also suffer. They are employed because they can be made to work for longer hours, for less pay, and are easier to abuse in terms of their employment rights. Child trafficking and bonded labour situations add to their misery. In Mali, as much as 50% of the work force in some cotton areas are children; in Kazakhstan, that figure rises to 60%; and, in Egypt, as many as 1 million children between the ages of 7 and 12 are employed to help with pest management in cotton crops (EJF 2007).

> In all these situations, and many more, the children are exposed to highly hazardous pesticides even if they are not actually using them.

Eighteen years of age is the dividing line between childhood and adulthood according to the International Labour Organization (ILO). Under ILO Convention 138, the minimum legal age for children to be employed in hazardous work, which includes exposure to pesticides, is 18 years of age; it is 13 years for light work, with developing countries having the option to set their minimum one year lower. ILO Convention 182 forbids children

[7] Bonded labour is a type of forced labour where labourers are tied to their employee often through indebtedness. It is a form of modern slavery, with a person forced to offer their labour and/or that of their child in return for a cash advance or credit until the debit is repaid. Often the debt is fraudulently imposed, and workers may be subject to violence or threats. Most common amongst landless and migrant families, and with tenancy or share cropping arrangements (ILO 2006).

[8] Primarily China, India, Pakistan, Brazil, Uzbekistan, and Turkey; but also Egypt, Kazakhstan, Tajikistan, Turkmenistan, Benin, Burkina Faso, Cote d-Ivoire, and Mali (EJF 2007).

[9] Especially in Uzbekistan, Pakistan, India, and Turkey (EJF 2007).

being involved in:

a. *"slavery or practices similar to slavery, such as the sale and trafficking of children, debt bondage and serfdom and forced or compulsory labour,"*

b. "work which, by its nature or the circumstances in which it is carried out, is likely to harm the health, safety or morals of children" (ILO 2011).

Both Fairtrade and certified organic standards prohibit child labour (EJF 2007), but outside these audited schemes, illegal child labour is rife in agriculture in the developing world.

Asia

In India, many mothers have no place to leave their children when they work picking tea so they carry them on their backs. Soon the child is also picking tea with its small nimble fingers, handling recently sprayed foliage.

A former chairman of the Tea Board in West Bengal describes how a child becomes a worker:

"The workers are as attached to the land as the tea bushes. They were born in the tea estates. They live there all their lives. They die there. The mother who works in the tea gardens has no place to leave her children. She puts her child on her back and brings the child with her when she works. What is more natural than that the child wants to know what the mother is doing and wants to help her pluck the tea. That is how the child becomes a worker. It is easy for children to pluck. Their fingers are nimble and the bushes are at their height. The child plucks the leaves and puts them in her mother's basket. Whatever the child plucks increases the pay of the mother. I would not say that the children are employed. They are helping their parents. Then, when the child is twelve, she is given a basket of her own and earns her own wages. She is paid half of what an adult is given."

Source: US Department of Labour: By the Sweat and Toil of Children, Volume II; The Use of Child Labor in US Agricultural Imports and Forced and Bonded Child Labor. A Report to the Committee on Appropriations, 1995, p. 48. In: ILO 2006.

Cottonseed production in India has the highest percentage of child labour of any sector. Although the numbers employed have fallen in recent years because of the concerted efforts of a number of organisations, still in 2009-2010 an estimated 169,900 children below the age of 14, and 211,600 aged 14-18 years, worked in cottonseed production, constituting about 32% of the labour force. Of these, approximately 70% are girls (Venkateswarlu 2010). They are exposed for long periods to highly hazardous pesticides (ILO 2006).

Elsewhere in Asia, similar practices occur: in the Philippines, children work on vegetable farms, ten hours per day, six and a half days per week. In Sri Lanka, children on tea estates are exposed to pesticides (ILO 2006). Bangladesh children are involved in collecting rose flowers that have been sprayed every second day for 45 days out of a 90-day production period with pesticides such as malathion (Wittstock & Quinto 2008).

Latin America

Latin American children routinely work on coffee, sugar cane, cardamom and cotton plantations (ILO 2006).

In Ecuador's flower industry, children are exposed to methyl bromide fumigation of seedbeds and to other pesticides on flowers they pick (ILO 2006). And even those children who do not work in the industry but live with parents that do, are exposed: one study found that their acetycholinesterase levels were lower compared with children whose parents do not work in the industry (Suarez-Lopez et al 2012).

In Costa Rica, during the 1980s, 72 out of every 100,000 child agricultural labourers were hospitalised for pesticide poisoning (Wesseling et al 1993). Children from the age of 10 place chlorpyrifos-treated bags over plantain bunches in Costa Rican plantations (Barrazza et al 2011).

In El Salvador, young boys spray pesticides in the sugar cane fields without protective clothing and only a few wear shoes (ILO 2006).

The annual occupational pesticide poisoning rate for children in Nicaragua over a 12 year period was 3 per 100,000, mainly in tobacco cultivation but also in grain and vegetable cultivation. It is believed that about 5.8% of Nicaraguan children work in agriculture. An estimated 18,516 children aged between 5 and 14 years old were poisoned over the period 1995 to 2006, even though children are not legally allowed to work there until the age of 14. Six children aged between 12 and 15 died from highly hazardous pesticides either from spraying crops (boys) or cutting recently fumigated tobacco leaves (girls). Children carry, mix and prepare pesticides, apply them by hand or leaking backpack sprayer, plant

treated seeds and apply fumigants in a closed environment. Sixty-one percent of the pesticides involved in the poisoning incidents were WHO Classes I and II, meaning that 33% of the pesticides that poisoned are regarded by WHO as only moderately or slightly hazardous. Yet they poison children. They included atrazine, benomyl, carbendazim, carbofuran, diazinon, fluazifop, malathion, mancozeb, and pendimethalin (Corriols & Aragón 2010)—all rated as highly hazardous by PAN International.[10] In Mexico, children working on tobacco plantations and frequently exposed to OPs and carbamates were found to have depressed levels of the enzyme acetylcholinesterase, which is indicative of OP and carbamate exposure. For some children, the levels were depressed by as much as 190%, and many had anaemia (Gamlin et al 2007).

Table 3: Pesticides reported to have caused acute poisoning of children in Nicaragua

aldicarb	diazinon	metalaxyl
aluminium phosphide	DDT	methamidophos
atrazine	deltamethrin	methomyl
Bt	dimethomorph	methyl parathion
benomyl	endosulfan	paraquat
carbendazim	edifenphos	pendimethalin
carbofuran	ferbam	phorate
carbosulfan	fosetyl	profenofos
chlorpyrifos	fluazifop	propineb
cyanamide	glyphosate	propoxur
cypermethrin	malathion	terbufos
cyproconazole	mancozeb	thiocyclam
2,4-D		

Source: Corriols & Aragón 2010

Africa

In Africa, children work on cocoa, coffee, cotton, floriculture, and sisal plantations. Children apply pesticides without protective clothing in the cocoa plantations of Cameroon, Côte d'Ivoire, Ghana and Nigeria. In Tanzania, girls aged between 10 and 13 are spraying pesticides on the coffee crops, without protective clothing—some for 3 hours per day. In Uganda, children are exposed to pesticides in sugar cane production. Also, in Tanzania, they are exposed to herbicides in tea fields, and they also apply pesticides with bare hands in the tobacco fields (ILO 2006).

[10] http://www.pan-germany.org/download/PAN_HHP-List_1101.pdf

Table 4: Some child poisonings in Latin America 2010-11

Country	Date	Incident
El Salvador	Jul 9 2010	Two children died and five other family members were hospitalised after eating maize tortillas made from treated seed destined for planting. Maize seed treated with carbamate insecticides is distributed by the government for planting by peasant farmers, but not for human consumption. Doctors confirmed this was not the first such poisoning case. Relatives recalled how the father told his wife to cook the treated maize seed, as they had nothing else to eat.
Colombia	Aug 12 2010	At least 42 children suffered acute inhalation symptoms (nausea, headache, sore eyes, stomach cramps) after a potato field was sprayed next to their school. Two were hospitalised.
Dominican Republic	Sep 2010	Three children died from methomyl poisoning, confirmed by post-mortem. Police are investigating whether food was accidentally or deliberately laced.
Dominican Republic	Oct 6 2010	13-year-old boy died in hospital from OP poisoning, after eating possibly contaminated rice pudding.
Paraguay	Jan 13 2011	Ten people including children from the Yeruti neighbourhood presented symptoms of pesticide inhalation, with abnormal blood tests; five were hospitalised for further examination. Three days earlier a young man was brought dead to the hospital after suffering high fever, stomach pain and vomiting. Families blame the spraying of the nearby soy fields.
Chile, Valparaiso	Jan 17 2011	Residents of Hijuelas suffered poisoning symptoms several hours after pesticides were sprayed by helicopter on Chuico Blanco avocado farm. Adults and children suffered eye and throat irritation, vomiting, headache and respiratory difficulties. Methoxyfenozide was identified as one of the compounds applied, but other pesticides are suspected to be in the spray mix.

Source: Williamson 2011

In Egypt, boys aged between 9 and 19 routinely spray pesticides in the cotton fields (Abdel Rasoul et al 2008).

In South Africa, poverty drives many youths, even as young as 12-14 years of age, to sell pesticides illegally on the streets, at rail stations and even door-to-door. Highly hazardous pesticides like aldicarb, methamidophos, and chlorpyrifos are decanted into drink and medicine bottles and sold unlabelled for unregistered mainly domestic uses. The youths are at risk from spillage and contamination. Children also purchase these pesticides for parents and use them at home. This problem has also been documented in Zimbabwe, Tanzania, Mozambique, United States, Brazil, the Dominican Republic and Israel (Rother 2010). 'Street selling' in Cape Town resulted in at least 44 child exposures and poisonings from 2003 to 2008 (Balme et al 2010).

Conclusion

In all these situations, and many more, the children are exposed to highly hazardous pesticides even if they are not actually using them. Poverty drives this situation of abuse in which children, such as those bonded, may be working up to 17-18 hours per day, 365 days per year for little or no pay. In fact, a 1996 survey found that over 80% of the agricultural households with working children were below the poverty line (ILO 2006).

Factors that drive rural poverty also then drive children into working with or being exposed to highly hazardous pesticides – factors such as globalisation of trade, structural adjustment programmes and intensive export-oriented agriculture, land grabbing, and the global dominance of agribusiness with its control of seeds, water and other inputs, all conspire to drive input costs out of the reach of small farmers, land out of their hands, and profits out of their reach. Child labour and poverty is a vicious cycle: children are deprived of education and their health, become trapped in low-paid hazardous work with weak bargaining power, their communities lose resilience, their ability to produce deteriorates, and poverty is intensified, driving yet more children into heartbreakingly soul-destroying lives blighted by exposure to highly hazardous pesticides. ■

We owe our children, the most vulnerable citizens in our society, a life free of violence and fear.

~ NELSON MANDELA

Children's special vulnerability

The previous chapter described the many ways in which children are exposed to pesticides including through hazardous working conditions, and their greater intake of pesticides via food, drink, and the environment. In this chapter, we look at biological aspects that make children so much more vulnerable to the effects of those pesticides than the adults upon which regulatory standards are based.

Children often react differently to chemicals than do adults.

Understanding the toxicity of pesticides in relation to child development requires an understanding of the constantly changing interaction between development processes and the environment in all its dimensions (physical, biological, chemical, social and spiritual). From the early stages of foetal life, environmental factors may already alter the genetic make-up of the individual to produce a different phenotype and, as the phenotype changes, it may alter the environment and be further altered by the environment. For example, genetically determined development of enzyme function may alter the responses to toxic substances in immature organisms, and exposure to such substances may further modify responses at a later time or throughout the life span. Thus, environmental exposures may impair or delay the development of biochemical or physiological systems fatally, temporarily, or permanently.

Children (from the prenatal period through adolescence) often react differently to chemicals than do adults because, compared to adults, they have different exposures, different vulnerabilities determined by critical windows of development, and a longer life ahead of them. *"To protect children's environmental health (especially for the foetus and the small child), it is important to understand when and how they can be particularly vulnerable to chemical exposures. Understanding the rapidly changing nature of the child is essential to understanding vulnerability to chemicals"* (IFCS 2003).

Children are different from adults in composition and metabolism as well as in physiological and biochemical processes. In a period of 26 weeks, the

foetus grows from microscopic size to recognizable human form, weighing about 500 gm. Physical growth and the maturing of function continues from birth to adolescence, with development rates varying from system to system, organ to organ, and tissue to tissue. Thus, not only do infants and children differ from adults, but at any point during development, each child differs in structure from herself or himself at any other age (NRC 1993).

3.1 Greater absorption and tissue permeability

The unborn foetus and young children have a greater ability to absorb pesticides and other chemicals than do adults. Absorption of pesticides occurs primarily through the lungs, skin, and gastrointestinal tract. Since the functional determinants of these uptake processes vary with age, the uptake of pesticides is also likely to vary between specific age groups. For example, the respiratory ventilation rate in infants is significantly larger relative to lung surface compared with adults. Therefore, infants potentially receive a greater exposure of lung surface to airborne compounds on a body weight basis (Bennett & Zeman 2004). The particle dose in the pulmonary region is also likely to be two to four times higher in three-month old children than in adults, particularly for sub-micrometer size particles (Ginsberg et al 2005).

The skin surface area relative to body weight is greater in children than in adults, such that the potential dose received following dermal exposure is likely to be about three times greater in infants than in adults. The permeability of the epidermal barrier is poorly developed in the preterm infant, resulting in greater absorption of chemical agents through the skin. The skin of newborn infants and young children is more permeable than adult skin because of its increased hydration; and this, together with a much higher surface area of skin relative to body weight, means that children are likely to absorb more pesticides through their skin (Miller et al 2002; WHO 2006). It is even worse for infants born before the full term of pregnancy because the 'stratum corneum', the outermost layer of the skin, is not fully developed until just before full term (WHO 2006).

...children are more likely to accumulate chemicals in their bodies.

Gastric absorption may also be altered because adult levels of gastric acid in the stomach are only reached at about 2 years of age. This means that for infants under the age of two, absorption of alkaline pesticides may be increased and of acidic ones decreased (WHO 2006).

However, since most pesticides are highly lipid soluble and are formulated for easy penetration of membrane barriers, absorption through the oral route is usually rapid. Nevertheless, the over-all bioavailability of pesticides will likely be determined by a combination of other factors such as gastric emptying time and intestinal motility, interactions with food and other substances, intestinal metabolism, enzymatic activity, bacterial flora, intestinal and liver blood flow, physico-chemical characteristics of the chemical, pre-existing conditions, and other factors.

The blood-brain barrier,[11] which provides some protection to the adult brain and nervous system from toxic substances by at least partially preventing them from being absorbed by the brain, is not fully developed at birth and continues to mature until about 6 months of age (Schwenk et al 2003; WHO 2006). Thus the developing foetal brain is relatively defenceless against chemicals in the mother's blood stream that cross the placenta and invade the foetal blood supply.

3.2 Vulnerability in metabolism and excretion

Children's metabolic pathways, especially in the first months after birth, are immature compared to those of adults. They are less able to deal with most toxic chemicals, such as OPs, and thus are more vulnerable to them (Landrigan et al 1999).[12] The liver and kidneys are still developing, reducing the child's ability to metabolise, detoxify, and excrete chemicals, often leading to greater concentrations and longer half-lives in the body compared with adults (Suk et al 2003; Daston et al 2004). Some metabolizing enzyme systems develop within a few months of birth but oxidative demethylation can take up to 2 years (WHO 2006). Generally, renal function is less developed in neonates and young children compared with that in older children or adults, and therefore less able to eliminate pesticides through the urinary tract. Glomerular filtration and renal tubular function are less mature in neonates than in adults. Renal blood flow increases with age. The blood flow to kidney normalized to tissue weight, however, remains fairly constant after about the age of one year and renal maturity is attained during the second year of life (WHO 2006). There can be a 3-fold difference in the half-life of

[11] "The blood-brain barrier refers to the multiple anatomic and physiological factors that prevent or slow the entry of toxicants and drugs into the central nervous system." (Miller et al 2002).

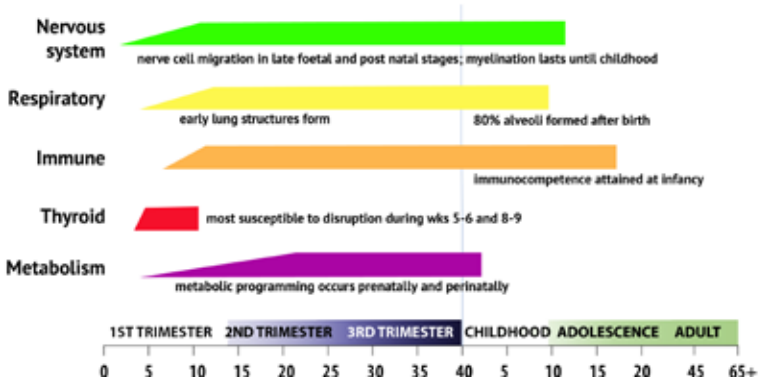
[12] Some chemicals are less toxic to children because the metabolised form is actually more toxic than the original, and they do not metabolise them easily into this form (Landrigan et al 1999).

chemicals between newborns and adults (Daston et al 2004). Hence children are more likely to accumulate chemicals in their bodies.

Newborn children can be 65 to 164 times more vulnerable than adults to the OPs chlorpyrifos, diazinon, and parathion (Furlong et al 2006). This is because the paraoxonase 1 (PON1) enzyme responsible for detoxifying chlorpyrifos is present at very low levels in children under the age of two (Furlong et al 2005), three-to-four-fold lower than those of their mothers (Holland et al 2006). Activity of PON1 increases up until the age of seven (Huen et al 2009) so it is not until this age that children have the same ability as adults to detoxify OPs. PON1 levels are even lower in the unborn foetus (Huen et al 2009). There is also a huge variation in the levels of PON1 between people because of genetic polymorphisms (variations in genes) and, as a result, the range for chlorpyrifos sensitivity can be as much as 14-fold among mothers and as much as 26-fold among newborns (Furlong et al 2006).

3.3 Developmental vulnerability: critical windows

Throughout the first years of life, children undergo rapid growth and development, and their complex, delicate developmental processes may be easily interrupted and derailed by pesticides. A single pesticide may affect multiple processes and multiple pesticides may affect a single process (Miller et al 2002). Exposures are especially damaging during critical windows of vulnerability in which children are particularly susceptible to damage.



CRITICAL WINDOWS OF VULNERABILITY FOR SELECTED SYSTEMS AND ORGANS

These windows occur from the period around conception until adolescence, depending on the organ system; organ systems undergo rapid change and extensive growth both prenatally and in the first few months after birth, in some cases even for years. But the unborn foetus and newborn are at greatest risk, and interference with their developmental processes can lead to lifelong alterations in behaviour, growth anddevelopment, and disease occurrence. Body structures are being formed and the nervous, endocrine and reproductive systems developed. The immune system is immature. Exposures to pesticides at the prenatal stage can have very different outcomes than if the same exposure were experienced later in life, especially if the pesticide is an endocrine disruptor (Landrigan et al 1999; Selevan et al 2000; Schettler 2002; Suk et al 2003).

Nervous system

The body continues to grow and develop throughout childhood, but up to the age of one year growth is particularly rapid. There is extensive growth of the brain and nervous system after birth but these are not fully developed until the age of 10-12. This is a broad window of vulnerability. During this period the development follows a precise step-by-step sequence involving a number of complex processes that involve up to 100 billion neuronal cells with trillions of connections (CHE 2008). In some parts of the brain, nerve cells that will ultimately be near the surface of the brain migrate from more central locations during late foetal and early infant life. The process of myelination of nerve tracts continues throughout childhood, and incomplete myelination of nerve fibres alters the responses to neurotoxins. These are just two of the many developmental processes taking place in the brain that could be disrupted by neurotoxic pesticides (NRC 1993). The brain, unlike other organs, cannot repair cells that have been damaged. So during these years, children are especially vulnerable to those toxins that pass through the blood-brain barrier and damage the nervous system (Landrigan et al 1999; Eskenazi et al 1999). Endocrine disruptors that alter growth, thyroid, steroid and sex hormones also play critical roles in the development of the brain (Schettler et al 2000). Exposure to even very

small amounts of neurotoxins during critical days of foetal development can change the architecture of the brain forever (Selevan et al 2000).

> *"Slight decrements in brain function may have serious implications for future social functioning and economic activities, even in the absence of mental retardation or obvious disease. Each neurotoxic contaminant may perhaps cause only a negligible effect, but the combination of several toxic chemicals, along with other adverse factors, such as poor nutrition, may trigger substantial decrements in brain function."* (Grandjean et al 2008)

Respiratory system

The development of the respiratory system is also a complex process stretching from conception to early adulthood, passing through distinct phases of growth and maturation. Exposure of the respiratory system during critical windows of foetal life can significantly affect growth and function of the lungs, having profound effects that may not be seen if the same exposure occurred in an adult. About 80% of the alveoli[13] in adult lungs are formed after birth, affecting neonates' ability to clear chemicals from their bodies via respiration (Pinkerton & Joad 2000).

Immune system

Development of the immune system begins early in foetal life and continues through infancy and adolescence, with immunocompetence attained at about one year and immune memory established at about 18 years of age.

… foetal and early childhood exposure to pesticides that damage the immune system is of critical concern.

Exposure to pesticides may result in immunosuppression, altered resistance to infectious and carcinogenic agents, auto immunity, hypersensitivity, or carcinogenicity. Evidence suggests that the outcome of exposure to pesticides depends on the window of immune development when the exposure occurs, and so the developmental status of the immune system is a key factor in determining the resulting effects on health (WHO 2006). Foetal exposure, in particular, to immunotoxic chemicals that cross the placenta may permanently damage the development of the immune system leading to deficient immunity and consequent conditions such as asthma, decreased resistance to infectious disease, reduced ability to fight tumours, autoimmune disease, hypersensitivity reactions, and chronic diseases later in life (Peden 2000; Miller et al 2002; Winans et al 2011). A number of pesticides are known to cause developmental

[13] Air sacs in the lungs where oxygen and carbon dioxide are exchanged.

immunotoxicity including atrazine, carbofuran, chlordane, DDT, diazinon, HCB, and HCH (Holladay & Smialowicz 2000; Winans et al 2011). Malnourishment, especially inadequate protein and zinc, leads to immune deficiency (Holladay & Smialowicz 2000). Thus malnourished children exposed to pesticides, a situation so common in poverty-stricken rural Asia, are doubly at risk of lifelong lack of immunity and hence vulnerability to infectious diseases and cancer. Since infectious diseases are four of the top five causes of death in developing countries (Winans et al 2011), foetal

The prenatal and perinatal periods are also the times at which metabolic programming occurs

Table 5:
Pesticides for which immunotoxic effects have been documented in the scientific literature

2,4-D	dinitrocresol	naled
acephate	diquat	nickel sulphate
aldicarb	diuron	paraquat
allethrin	endosulfan	parathion
arsenic	endothall	PCNB (quintozene)
arsenic trioxide	endrin	pentachlorophenol
atrazine	EPN	permethrin
azinphos-methyl	EPTC	phenthoate
barban	fenitrothion	phorate
captan	fenthion	phosalone
carbaryl	fenpropathrin	piperonyl butoxide
carbofuran	fluometuron	pirimicarb
carbophenothion	formaldehyde	propanil
chlordane	glyphosine	propham
chlordecone	heptachlor	propoxur
chlordimeform	HCH	s-bioallethrin
chlorfenethol	hexachlorobenzene	simazine
chlorfenvinphos	lindane	sodium arsenite
chlormequat	malathion	tetrachlorvinphos
chloride	maleic hydrazide	thiram
chlorpyrifos	mancozeb	toxaphene
chlorobenzilate	maneb	tributyltin
chlorpropham	mercuric chloride	tributyltin chloride
copper	metam sodium	tributyltin oxide
crufomate	methiocarb	trichlorfon
cycloheximide	methoxychlor	trichloroethane
cypermethrin	methyl dithiocarbamate	trichloroethylene
DDT	methyl parathion	triisopropylphosphate
diazinon	metribuzin	triphenyltin chloride
dichlorvos	mevinphos	triphenyltin hydroxide
dieldrin	mirex	zineb
dimethoate	molinate	ziram
dimethyl sulfoxide	monocrotophos	

Source: PAN UK undated

and early childhood exposure to pesticides that damage the immune system is of critical concern.

Metabolism

The prenatal and perinatal periods are also the times at which metabolic programming occurs, laying down the foundation for a number of metabolic functions later in childhood and adulthood, that can contribute to conditions such as diabetes and obesity, including the development of fat cells and mechanisms of weight homeostasis (WHO 2010; La Merrill & Birnbaum 2011).

Vulnerability to OP pesticides depends in part on levels of the PON1 enzyme. This enzyme is involved in protection against OPs and oxidative stress. As mentioned earlier, children are born with low levels of the enzyme and the low levels persist up until the age of seven, so children remain particularly vulnerable to OP pesticides up to this age (Huen et al 2009).

A closer look at endocrine disruptors

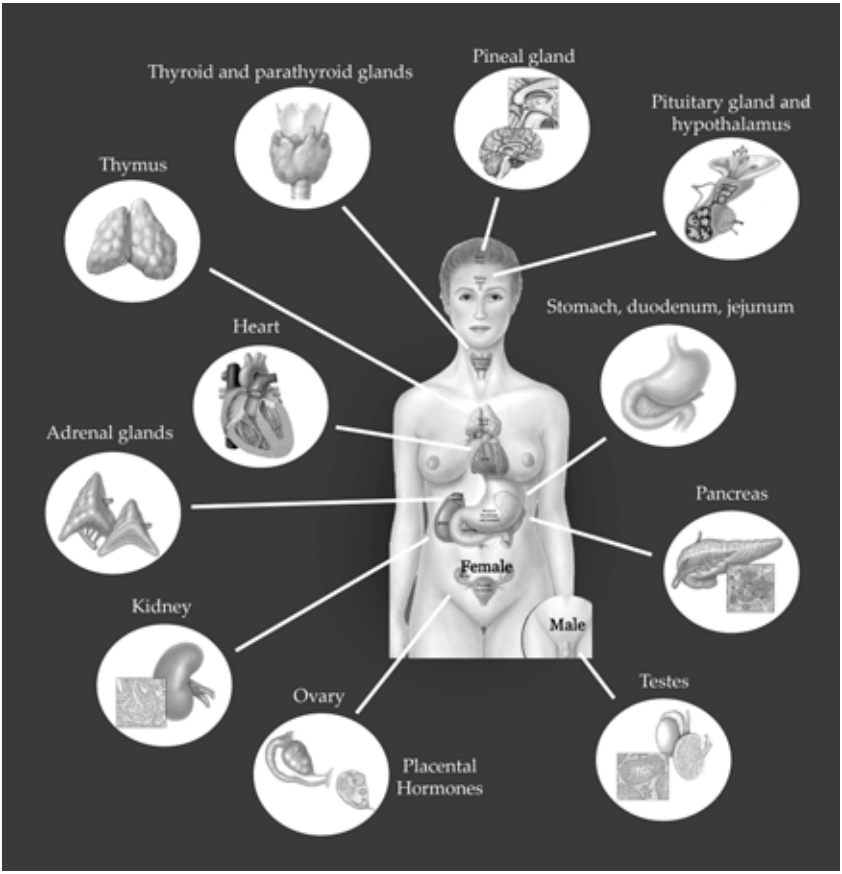
…data used to register pesticides utterly fails to reflect the reality of exposure of the unborn foetus or newly born child to low levels of endocrine disrupting pesticides.

The endocrine system is a delicately balanced system of glands and hormones that maintain homeostasis[14] and regulate metabolism,[15] growth, responses to stress, the function of the digestive, cardio-vascular, renal and immune systems, sexual development and reproduction, and neurobehavioural processes including intelligence. In fact, it governs "virtually every organ and process in the body" (Birnbaum 2010). Exposures to chemicals that interfere with the development of the endocrine system during early life stages can have severe health consequences throughout childhood and into adulthood, and even for subsequent generations, the effects continuing long after the exposure to the endocrine disrupting chemical has ceased. For example, disruption of the growth hormone can result in osteoporosis later in life (WHO 2006).

All of the health problems described in the next chapter can be precipitated by

[14] Regulation of the internal environment to maintain a balanced, constant, stable condtion within the body.

[15] Chemical reactions within the body that provide for growth and activity, including the conversion of food to energy.



ENDOCRINE SYSTEM

endocrine disruption in the foetal and early childhood stages—birth defects; brain development and behavioural problems including attention deficit hyperactivity disorder; cancer including breast, prostate and non-reproductive cancers; diabetes, obesity, and cardiovascular disease; immune effects including allergies and asthma; and reproductive disorders including those of fertility and fecundity, precocious puberty, and endometriosis (Myers et al 2009; Birnbaum 2010).

Maternal exposure to endocrine-disrupting chemicals, in particular, appears to increase the risk of developmental abnormalities in the reproductive organs of female and male foetuses, as well as affecting the brain, skeleton, thyroid, liver, kidney and immune system (Colborn et al 1993).

Thyroid hormones are particularly important for development of the central nervous system and alterations to thyroid form and function can result in physical and mental retardation, and congenital birth defects. Disruption to the thyroid hormone can result in "lowered IQ, poor word discrimination, decreased reading comprehension, and learning deficits". During weeks 5-6 and 8-9 in human gestation, the thyroid is particularly susceptible to disruption by chemicals (WHO 2006). In Kasargod, prenatal exposure to endosulfan resulted in an increase in cases of goitre[16] especially amongst female children, as well as congenital birth defects and mental retardation, lowered IQ and other neurodevelopmental deficits (NIOH 2002).

Because the endocrine system operates on tiny amounts of hormones, endocrine disruption occurs at levels of exposure far lower than those normally considered toxic (Birnbaum 2010). Additionally, hormones and hormonally

Table 6: Endocrine Disrupting Pesticides

Each of the 221 pesticides in this table is considered by the European Union to be an endocrine disruptor or has one or more verified citations to published, accessible, primary scientific research demonstrating effects on the endocrine system, and is cited in one or more of the sources given below the table.

2,4,5-T	bromopropylate	cycloprothrin	diuron
2,4-D	bromoxynil	cyhalothrin	dodemorph
2,4-DB	butamifos	cyfluthrin	endosulfan
abamectin	bupirimate	cypermethrin	endrin
acephate	captan	cyproconazole	epichlorohydrin
acetochlor	carbaryl	DBCP	epiconazole
acrifluorfen-methyl	carbendazim	dacthal/DCPA	EPN
alachlor	carbofuran	DDT	EPTC
aldicarb	chloranil	deltamethrin	esfenvalerate
aldrin	chlordane	diazinon	ethion
ametryn	chlordecone	dibromochloropro-	ethiozin
amitraz	chlordimeform	pane	ethoxyquin
amitrole	chlorfenvinphos	dichlorprop	ethylene dibromide
anilofos	chlormethoxyfen	dichlorvos	ethylene dichloride
atrazine	chlorobenzilate	dichlofenthion	ethylene oxide
bendiocarb	chloronitrofen	diclofop-methyl	etofenprox
benomyl	chloropropham	diclone	etridiazole
bentazone	chloropropylate	dicofol	fenarimol
bifenox	chlorothalonil	dieldrin	fenbuconazole
bifenthrin	chlorotoluron	difenoconazole	fenchlorphos
biphenyl	chlorpyrifos	diflubenzuron	fenitrothion
bitertanol	clofentezine	dimethoate	fenoxycarb
bioallethrin	clotrimazole	dimoxystrobin	fentin acephate
boric acid	copper oxychloride	dinitrophenol	fenvalerate
bromacil	cyanophos	dinocap	fenthion
bromophos	cyanazine	dinoseb	ferbam
bromophos-ethyl	cyanofenphos	diquat	fipronil

[16] Swelling of the thyroid gland indicative of thyroid dysfunction; often caused by iodine deficiency but also by exposure to environmental chemicals such as DDT (Tebourbi et al 2010).

active chemicals can cause different effects at different levels of exposure, and low dose exposure commonly experienced by humans can have profoundly serious effects even when the high dose exposures normally tested on rats in laboratories may not have an effect (Myers et al 2009; Birnbaum 2010). This means that the data used to register pesticides utterly fails to reflect the reality of exposure of the unborn foetus or newly born child to low levels of endocrine disrupting pesticides.

"The soaring health crisis unfolding in countries around the world demands that the regulatory apparatus of governments move into the 21st century. Blind obedience to 16th-century dogma[17] will not solve the problem. Unless and until regulatory agencies incorporate modern endocri-

fluazifop-butyl
flucythrinate
flufenacet
flusilazole
flutriafol
fluvalinate
glyphosate
heptachlor
hexachlorobenzene (HCB)
HCH
hexaconazole
imazalil
ioxynil
iprodione
isofenphos
iosproturon
isoxathion
ketoconazole
lambda-cyhalothrin
leptophos
lindane
linuron
malathion
mancozeb
maneb
MCPA
mecoprop
menfenacet
metam-sodium
methiocarb
methomyl
methoprene
methoxychlor
methyl bromide
metiram
metolachlor
metribuzin
mevinphos
mirex
molinate
monocrotophos
myclobutanil
nabam
nitrobenzene
nitrofen
nuarimol
omethoate
oryzalin
oxadiazon
oxamyl
oxine-copper
oxyfluorfen
paraquat
parathion
parathion methyl
penconazole
pencycuron
pendimethalin
pentachlorophenol
pentachlorobenzene
permethrin
phenthoate
phosalone
phosphamidon
picloram
piperonyl butoxide
piperophos
pirimicarb
pirimiphos-methyl
pretilachlor
prochloraz
procymidone
prodiamine
profoxydim
prometryn
pronamide
propamocarb
propanil
propazine
propiconazole
propoxur
prothiophos
pyrazoxyfen
pyrethrins
pyridate
pyrifenox
pyrimethanil
pyriproxifen
quinalphos
quintozene
resmethrin
simazine
sumithrin
tebuconazole
tepraloxydim
terbutyrn
tetramethrin
thenylchlor
thiobencarb
thiram
tolclofos-methyl
toxaphene
triadimefon
triadimenol
tribenuron-methyl
tributyltin compounds
triphenyltin
trichlorfon
triclopyr
triflumizole
trifluralin
vinclozolin
zineb
ziram

Sources:
(1) TEDx List of Potential Endocrine Disruptors, updated July 18, 2011 http://www.endocrinedisruption.org/endocrine.TEDXList.overview.php
(2) PAN International List of Highly Hazardous Pesticides, PAN Germany, http://www.pan-germany.org/download/PAN_HHP-List_1101.pdf
(3) Watts 2007
(4) Mnif et al 2011

[17] The 16th century dogma referred to is the principle developed by physician Paracelsus that "the dose makes the poison" which is interpreted to mean that the higher the level of chemical, the worse the effect, a 'positive dose-response relationship'.

nologic principles into their risk assessment paradigms, they will continue to provide false assurances of "safety" and fail to recognize the actual health risks posed by chronic low-level exposure to an increasing number of chemicals found in commonly used products." | *(Myers et al 2009)*

3.4 More time to develop chronic diseases

Because most children have a longer life ahead of them than do adults, they have more time in which to develop chronic diseases initiated by early exposures (Landrigan et al 1999). This is particularly relevant for diseases such as cancer that have a long latency period, i.e. that require years or even decades to evolve from the initiation of the disease to its actual manifestation. In addition, deficits such as in the immune system, which develop at an early age, may persist throughout life constantly undermining the person's health (Suk et al 2003).

There is also increasing evidence of what has become known as 'the developmental, or foetal, origins of adult disease'. Many diseases are now thought to be triggered by exposure to environmental chemicals early in life, especially

AN INUIT GRANDMOTHER AND HER GRANDCHILD ARE HIGHLY EXPOSED TO PERSISTENT ORGANIC POLLUTING PESTICIDES.

in the foetal and neonatal periods (Newbold et al 2007; Gillman et al 2007). These early exposures are more likely to lead to disease than similar exposures encountered later in life. There is evidence that foetal and infant exposures to pesticides increase risk of childhood cancer. There is also concern that early exposures to neurotoxic pesticides may increase risk in later life of chronic neurologic diseases such as dementia, Parkinson's disease, and amyotrophic lateral sclerosis[18] (Landrigan et al 1999; Suk et al 2003); and to metabolism, appetite and endocrine function disorders leading to obesity and diabetes (Lassiter et al 2008). Exposure to endocrine disruptors during critical windows can result in irreversible effects on reproductive, nervous and immune systems, whereas similar exposure in adulthood might only result in reversible changes (Cal EPA 2010).

...permanent reprogramming of a heritable trait. The effect can last over a number of generations...

3.5 Future generations - epigenetic effects

Exposure to toxic chemicals during embryonic[19] and foetal development can result in chemical modification of the operation of some genes in the offspring, i.e. the DNA itself is not damaged so there is no mutagenic damage, but the way in which the genes are 'turned off' and 'turned on', or gene expression, is affected. This is known as an epigenetic alteration, and it means that the effects of the chemical last beyond the normal transient direct effect, causing "lasting functional changes in specific organs and tissues and increased susceptibility to disease that may even affect successive generations" (Grandjean et al 2008), if it is the 'germ cells'[20] that are affected (Skinner et al 2011). In other words, it results in permanent reprogramming of a heritable trait, sometimes called foetal programming. The effect can last over a number of generations—at least four in studies carried out by Anway et al (2006) using the fungicide vinclozolin on rats. Exposure to vinclozolin during critical windows of development of rat embryos resulted in breast tumour development in subsequent generations of adult rats. A consistently high incidence of breast tumours occurred across all for generations that were monitored, as did prostate disease, kidney disease, abnormalities of the immune system, testes and blood, and changes in behaviour and learning capacity (Anway et al 2006; Skinner et al 2011). These

[18] Also called Lou Gehrig's disease, this is a form of motor neuron disease with rapid progressive and fatal weakness, muscle atrophy and other conditions.

[19] Embryonic development takes place when the sperm fertilises the egg to form the embryo, which then develops into the foetus.

[20] Reproductive cells - responsible for the formation of gametes (sperm and eggs)

epigenetic effects were apparently passed down through epigenetic alterations in the male germ line.

Other conditions that may be passed on through epigenetic mechanisms after exposure to endocrine disruptors include metabolic disorders such as diabetes, cancer, and reproductive abnormalities (Grandjean et al 2008).

There is also evidence that social stresses and nutritional factors can interact with and exacerbate epigenetic changes (Perera & Herbstman 2011), so that children living with the social stresses and nutritional deprivation of poverty in developing countries are once again most vulnerable to the epigenetic effects of embryonic and foetal exposure to highly hazardous pesticides.

3.6 Multiple and cumulative risks

Children are also generally more vulnerable to multiple and cumulative risks. Invariably, a child is not exposed to a single environmental contaminant or stressor or by means of a single exposure pathway, especially in

...these stressors affect a child's response to a toxic pesticide exposure; yet none of these are factored in when determining 'acceptable' levels of exposure for children.

developing countries where children may be exposed to multiple pollutants at varying concentrations, vector-borne and infectious diseases, poor nutrition, and poor sanitation all at the same time. The combined risk resulting from multiple exposures from various toxic substances and stressors that accumulate over time, pathways, sources, or routes is magnified to undetermined levels in children compared to adults.

Because of the special characteristics of children, they are more vulnerable to the combined effects of pesticides and other toxic chemicals in food and water, inside and outside the house, at school, and their immediate environment, especially in agricultural plantation areas. Wood in the home is often treated with pesticides. Even passenger aircraft are pesticide-sprayed in flight, despite the irrationality and obvious risks. On top of these, children are exposed to radiation from the sun, medical X-rays, radioactive fall-out from previous nuclear weapons tests, radiation released by nuclear power stations, especially from disasters such as Three-mile Island, Chernobyl and, recently, Fukushima. As if these were not enough, children are also exposed to depleted uranium used in the Gulf War and other wars of aggression in the Middle East and elsewhere. Add to that burden the electromagnetic radiation from microwave ovens, televisions, computers and now the widespread use of mobile phones and the transmitters that serve them. All of these stressors affect a child's response to a toxic pesticide exposure; yet none of these are factored in when determining 'acceptable' levels of exposure for children.

The current understanding of the health risks arising from mixed exposures to specific chemicals is quite limited. However, over the past several years, efforts have been made to assess the risks to multiple and cumulative exposures to two or more dissimilar agents such as radiation and one or more chemical agents, including pesticides such as paraquat. Apart from *a priori* reasoning, some evidence is emerging that mixed radiation/chemical exposures, when evaluated in aggregation, were linked to chronic health endpoints such as cancer and intermediate health outcomes such as chromosomal aberrations and reproductive anomalies (Chen & McKone 2001; Shirangi et al 2009; Savitz et al 1989). For example, paraquat acted in a greater than additive fashion with radiation to increase formation

of tumour cells in mice (Geard et al 1984); 2,4-D increased chromosomal aberrations when exposure was combined with radiation (Riabchenko et al 1995); and atrazine increased the effect of electromagnetic fields on an immune parameter (Rajkovic et al 2010).

Despite the general lack of understanding, multiple contaminants and stressors are always at play, and so multiple and cumulative risks must always be taken into account when considering the effects of pesticides on children In the absence of complete knowledge, a precautionary approach must be taken to exposure of pregnant women and children to hazardous pesticides. ■

If I had influence with the good fairy who is supposed to preside over the christening of all children, I should ask that her gift to each child in the world be a sense of wonder so indestructible that it would last throughout life.

~ Rachel Carson

4 Effects of pesticides on children

"Epidemiological evidence demonstrates associations between early life exposure to pesticides and pediatric cancers, decreased cognitive function, and behavioural problems…Chronic toxicity end points identified in epidemiological studies include adverse birth outcomes including preterm births, low birth weight, and congenital anomalies, pediatric cancers, neurobehavioural and cognitive deficits and asthma."
Statement by American Academy of Pediatrics (CEH 2012)

4.1 Acute poisoning

Symptoms of acute poisoning in children vary with the type of pesticide, but for the commonly used organophosphorus and carbamate compounds, they include fatigue, dizziness, blurred vision, nausea, vomiting, dry throat and difficulty breathing, stinging eyes, itchy skin, and a burning nose; and muscular symptoms, such as stiffness and weakness. Death can occur rapidly, or over the course of a few weeks (Goldman 2004).

Other symptoms that may occur can be found in Table 7 below.

Table 7: Some acute symptoms of pesticide poisoning

numb lips and tongue	itching	memory loss
sore throat	blisters	difficulty in walking
blurred vision	nausea, vomiting	anxiety, restlessness
tears	abdominal cramps	involuntary twitching
headache	diarrhoea	rapid pulse
salivation	uncontrolled urination	drop in blood pressure
nose bleed	weakness, fatigue, lethargy	muscular pain, stiffness
swelling	dizziness	muscle weakness
chest pain, tightness	disorientation, confusion	back pain
wheezing	agitation	seizures
difficult breathing	inarticulate speech	paralysis
sweating	depression	coma
burning skin		death

Source: Watts 2010

4.2 Birth defects and congenital conditions

Chemicals that cause birth defects are known as teratogens. There is no way we can be absolutely sure which pesticides cause birth defects and which do not. However, some of the offending pesticides can be identified with a reasonable degree of certainty by means of two types of scientific study: laboratory studies in which animals are exposed to the pesticide and birth defects observed, and epidemiological studies which measure any increase in occurrence of birth defects amongst people who have been exposed to certain pesticides relative to people amongst similar populations that have not been exposed.

Pesticides that are known from animal studies to be teratogenic include the organophosphate insecticides like dimethoate; carbamate insecticides such as carbaryl; fungicides like benomyl, captan, maneb, mancozeb, propiconazole; and herbicides such as paraquat and 2,4-D (Garry et al 1996; García 2003). There are many more.

Numerous epidemiological studies have been carried out to determine whether or not pesticides are causing birth defects in humans. Some studies have not shown any relationship with exposure to pesticides, but many have. Because of the inherent difficulties in epidemiological studies, negative findings should not be interpreted to mean that a pesticide does not cause birth defects. Negative findings are more likely than positive findings even in the most carefully designed studies. The number of observations necessary to elicit a statistically significant result is often extremely difficult to achieve if the incidence rate is relatively low and diagnosis difficult to establish, such as with cancer, neurologic, reproductive and immunologic disorders. Firm conclusions are often difficult to arrive at because of the variety of different birth defects and possible causes, problems in obtaining wide exposure contrasts against a background of pervasive low-level exposure, and the difficulty in accurately determining exposure to pesticides. Many studies have failed to take into account the importance of exposure during the critical windows of vulnerability, which can be a matter of only a few weeks (Kogevinas & Sala 1998), and so effects that might have occurred because of such exposure have been blurred by more crude exposure scenarios. For example, some birth defects may only occur as a result of exposure to particular pesticides during the first trimester of pregnancy. Nevertheless. there is now considerable evidence indicating that exposure to pesticides

Many studies have failed to take into account the importance of exposure during the critical windows of vulnerability.

has been causing, and continues to cause, birth defects in many countries. This unacceptable situation is still denied by some and is likely to continue until the pesticides implicated are withdrawn from use.

General parental exposure

Many studies have made links between parental exposure to pesticides in general and birth defects.

They have found that families of pesticide applicators have more birth defects (Garry et al 1996), as much as 10.1%, compared with the average rate of birth defects in the USA of 3.7%, with some families having more than one child with birth defects (Garry et al 2002). Families of male pesticide applicators in cotton fields in India suffered increased congenital defects such as anencephaly, cleft palate, harelip, club foot, limb malformations, eye deformities and extra fingers or toes, as well as stillbirths and neonatal deaths (Rupa et al 1991). Paternal occupational exposure to pesticides has also been linked to neural tube defects in England (Fear et al 2007).

Families living in agricultural areas are more likely to have birth defects (Schreinemachers 2003). Parental exposure has been associated with congenital abnormalities (Magoon 2006; de Siqueira et al 2010) including congenital hypospadias[21], cryptorchidism[22] (Kristensen et al 1997; Carbone et al 2006; Rocheleau et al 2009) and micropenis (Gaspari et al 2011a); missing or reduced limbs (Schwartz et al 1986, Schwartz & LoGerfo 1988);

[21] Hypospadias is the abnormally placed urinary opening on penis.
[22] Cryptorchidism is the absence of one or both testes.

anencephaly[23] (Lacasaña et al 2006); spina bifida (Brender et al 2010); and congenital heart disease (Yu et al 2008).

Sometimes the studies have found links between maternal exposure and congenital malformations, including cleft palate, neural tube effects, heart defects and limb defects, spina bifida, anencephaly, hypospadias, and cryptorchidism (Blatter et al 1996; Shaw et al 1999; Engel et al 2000; Medina-Carrilo et al 2002; Rojas et al 2000; Calvert et al 2007; Rocheleau et al 2009; Brender et al 2010; Dugas et al 2010; Gabel et al 2011).

Sometimes exposure is premised upon maternal occupation, showing a link between employment in the floriculture industry in Colombia and congenital defects and birthmarks (Restrepo et al 1990a, 1990b; Idrovo & Sanin 2007); occupation in gardening and cryptorchidism (Weidner et al 1998); exposure in orchards or greenhouses and spina bifida and hydrocephaly; in grain farming with missing or reduced limbs (Kristensen et al 1997); and employment in glasshouses and cryptorchidism (Andersen et al 2008). One study found an association between maternal exposure to pesticides used in the home and neural tube defects.

Exposure during critical periods

Some studies have linked exposures to pesticides during particular time periods with certain birth defects: for example maternal exposure preconception with spina bifida (White et al 1988); maternal exposure during the period from the month before conception and the first trimester with multiple anomalies including nervous system defects and oral clefts (Nurminen et al 1995; García et al 1998); use of insect repellents during the first trimester with hypospadias (Dugas et al 2010); and paternal exposure in greenhouses producing vegetables and flowers during the 3 months prior to conception with hypospadias (Brouwers et al 2007) and cryptorchidism (Pierik et al 2004).

Specific pesticides

Still other studies have linked exposures to specific pesticides with birth defects:

- maternal exposure to DDT though living in a village where it is sprayed to combat malaria was associated with a 33% greater chance of having male children born with one or more external urogenital birth defects (Bornman et al 2010).

[23] Anencephaly is the absence of a major part of the brain and skull, caused by failure of the neural tube to close, usually between the 23rd and 26th days of pregnancy. It may also involve facial distortions and heart defects.

- the herbicides 2,4-D, MCPA, atrazine, and trifluralin are associated with anomalies of the central nervous system, circulatory, respiratory, urogenital, and musculoskeletal systems, particularly in male children (Garry et al 1996, 2002; Schreinemachers 2003);
- maternal exposure to atrazine is also associated with gastroschisis[24] (Waller et al 2010);
- four of fourteen children born to fathers who applied phosphine had defects of the central nervous system, and there was also an above average rate of eye cataracts in girls (Garry et al 2002);
- maternal exposure to diclofop-methyl during pregnancy is associated with increased risk of hypospadias (Meyer et al 2006);
- maternal exposure to oxydemeton-methyl at 4 weeks of pregnancy is associated with congenital defects of heart, eye, face and brain (Romero et al 1989);
- maternal residence near pesticide application, in particular the use of benomyl and methomyl, is associated with neural tube defects; elevated risks of neural tube defects, anencephaly and spina bifida were also associated with use of benzimidazole, methyl carbamate, or OPs (Rull et al 2006);
- maternal exposure during the second trimester to malathion from aerial spraying for Mediterranean fruit fly in the San Francisco area is associated with gastrointestinal anomalies (Thomas et al 1992);
- elevated maternal plasma levels of HCB is associated with hypospadias in offspring (Giordano et al 2010);
- possible paternal exposure to glufosinate is associated with birth defects (García et al 1998);
- there was a slight association between New Zealand 2,4,5-T sprayers and congenital defects (Smith et al 1982);
- parental exposure to both cyanazine and dicamba is associated with congenital abnormalities (Weselak et al 2008);
- maternal exposure to herbicides or rodenticides is associated with congenital heart defects (transposed aorta and pulmonary artery) (Loffredo et al 2001).

One study showed that people from an area of frequent pesticide spraying in Southeast Mexico who have a PON1 polymorphism, which makes

[24] Gastroschisis is a birth defect in which the baby's intestines protrude through a hole in the abdominal wall.

them more vulnerable to the effect of OPs, had an increased risk of spina bifida (Gonzalez-Herrera et al 2010).

Other studies have drawn links between levels of pesticides in surface waters and birth defects (Winchester et al 2009), including levels of atrazine with abdominal wall defects (Mattix et al 2007).

Parental body burden

Some studies have used the presence of pesticides in tissues as a surrogate measure of foetal exposure to pesticides and found the following associations with birth defects:

- hexachlorobenzene (HCB) in body fat with undescended testicles (Hosie et al 2000);
- OC pesticides in breast milk with cryptorchidism (Damgaard et al 2006);
- maternal serum levels of DDE with cryptorchidism and an extra nipple in sons (Longnecker et al 2002);
- DDE in cord blood and colostrum with cryptorchidism (Brucker-Davis et al 2008);
- paternal exposure to Agent Orange (2,4,5-T and 2,4-D) with spina bifida (Ngo et al 2010);

CONGENITAL DEFECTS FROM ENDOSULFAN RANGE FROM DEFORMITIES AND HEART DISEASE TO MENTAL RETARDATION AND EYE PROBLEMS.

- breast milk levels of DDT and HCB with congenital hypothyroidism or cretinism (Nagayama et al 2007);
- DDT, HCH and endosulfan in cord blood with neural tube defects (Ren et al 2011);
- Elevated placental DDT, its metabolites and HCH with neural tube defects in rural China (UNEP 2012).

Endosulfan in India

But perhaps the most striking evidence that pesticides cause birth defects comes from the villages of Kasargod, a region in the southern Indian state of Kerala, where 20 years of aerial application of endosulfan to cashew nut plantations exposed successive generations of villagers to a single pesticide. Many pregnant women and their unborn children were exposed.

Congenital defects experienced as a result of the endosulfan exposure included malformations of the male reproductive tract such as cryptorchidism,

Birth defects in Immokalee

Immokalee is a city in the heart of the tomato-growing region of Florida, USA. In the small Towers Cabin labour camp just south of Immokalee, three babies were born within seven weeks of each other a few years ago. Carlos had no arms or legs; Jesus had a deformity of the lower jaw causing his tongue to fall back down his throat with a constant threat of choking; and Violeta, at first thought to be a boy, had one ear, no nose, a cleft palate, one kidney, no anus, and no visible sexual organs. She survived only 3 days. The three mothers all worked in the vast tomato fields of Ag-Mart Produce. A sign at the entry to the fields told that they had been sprayed with 32 different pesticides during the season, including metribuzin, mancozeb and avermectin, all known to cause birth defects. The women had been told to pick the tomatoes before the restricted entry interval was up. *"When you work on the plants, you smell the chemicals,"* said Herrera, mother of Carlos. She had worked in a field recently sprayed 24-36 days after conception. She said she felt sick the entire time she worked in the field, with dizziness, nausea, vomiting, light-headedness, burning eyes and nose, skin rashes and open sores. She described being coated in pesticides.

Source: Estabrook 2011.

hydrocele, and inguinal hernia; deformities of hands and feet including stag horn limbs and other skeletal abnormalities; congenital heart disease; congenital mental retardation and cerebral palsy; and congenital eye problems such as cataracts and retinopathy. The congenital problems were more prevalent in girls (NIOH 2002; Quijano 2002).

Other congenital conditions

One study found that agricultural workers exposed to OPs had significantly increased sperm chromosome nullisomy[25] involving the sex chromosomes. It is thought that this might increase the risk of genetic syndromes such as Turner syndrome (Garry 2004).[26]

4.3 Other birth outcomes

Stillbirths, neonatal death

Both paternal and maternal exposure to pesticides, including occupational and home use, has been linked to stillbirths (Goulet & Theriault 1991; Rupa et al 1991; Taha & Gray 1993; Nurminen et al 1995; Pastore et al 1997; Medina-Carrilo et al 2002), with one study linking it particularly to exposure during the second trimester (White et al 1988), and one to paternal exposure to DDT (Cocco et al 2005).

Foetal death has been found to be higher following maternal occupational exposure to pesticides round the time of conception (Ronda et al 2005), and to maternal residence in areas using endocrine disrupting pesticides (such as endosulfan and methoxychlor), and halogenated hydrocarbon pesticides[27] (Bell et al 2001). In the latter study, foetal death was caused by congenital defects.

Neonatal death because of congenital anomalies has also been associated with parental pesticide exposure (Schreinemachers 2003; de Siqueira et al 2010).

A study in India found increased stillbirths and neonatal deaths amongst the families of workers exposed to endosulfan and other pesticides in India's cotton fields (Rupa et al 1991).

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[25] Nullisomy is a lethal genetic condition involving the lack of one of the normal chromosomal pairs.

[26] Turner syndrome occurs in girls and is characterised by short stature, swelling, broad chest, low hairline, low set ears and webbed neck, with non-working ovaries, no menstrual cycle and sterility. It is often accompanied by congenital heart disease, hypothyroidism, diabetes, vision and hearing problems, autoimmune diseases, and cognitive defects.

[27] Included in the list of halogenated hydrocarbons were endosulfan, dicofol, methoxychlor, methyl bromide, and chloropicrin.

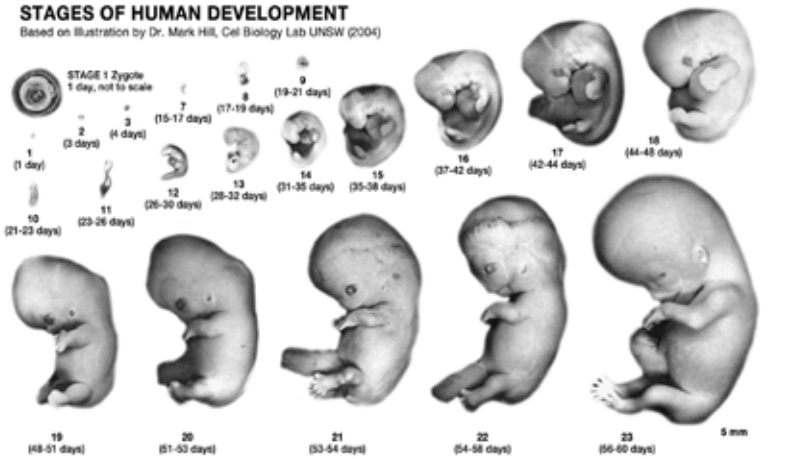
Hospital and community-based case control studies in central Sudan reveal a significant and consistent two-fold elevated risk in perinatal mortality associated with pesticide exposure, with the risk increasing to three-fold amongst women employed in agriculture (UNEP 2012).

Sex ratio

Exposure to certain pesticides can alter the ratio of female to male children, often increasing the relative number of female births. The analysis of births of the spouses of male DDT applicators in Italy during a 1946-1950 anti-malarial campaign found an elevated rate of female/male births (Cocco et al 2005). Exposure to HCB in Turkey elevated the female/male ratio (Jarrell et al 2002), as did exposure to the nematicide 1,2-dibromo-3-chloropropane or DBCP in Israel (Goldsmith 1997) and Latin America (Garry 2004), and fungicide use amongst pesticide applicators in Minnesota, USA (Garry et al 2003). However, amongst the same pesticide applicators in Minnesota exposure to other pesticides, apart from fungicides, favoured increased male births (Garry et al 2002). In Australia, elevated levels of DDE in mothers was associated with increased male births (Khanjani & Sim 2006).

Foetal growth, birth weight, pre-term birth

It is now well recognised that intrauterine growth, birth weight, and birth size can have a profound effect on health in later life—for example, lower birth weight has been associated with increased risk of adult onset cardiovascular disease, type 2 diabetes, osteoporosis, depressive disorders and some cancers.



Intrauterine growth influences other adult metabolic disorders such as high blood cholesterol, fatty liver and obesity, and non-metabolic disorders such as chronic lung disease (Perera & Herbstman 2011). Intrauterine growth retardation is also associated with increased infant mortality (Pathak et al 2011).

Numerous studies have been carried out to determine whether or not pesticides affect foetal growth, birth weight, head size, and other birth measurements, which may in turn indicate future health and development. The picture is somewhat unclear, for some studies show no effect from pesticide exposure whilst others do show an effect. As with other epidemiological studies on pesticides, it is notoriously difficult to properly identify exposure. Nevertheless, the studies that do show pesticides may be causing reduced foetal growth, lower birth weight or altered size must be taken seriously and not dismissed simply because not all studies confirm their findings:

- A study in Brazil found an association between pesticide use and low birth weight (de Siqueira et al 2010).
- In China, maternal pesticide use was linked with smaller size at birth (Zhang et al 1992).
- In France, associations were found between maternal exposure to insecticides from household use or nearby agricultural activity, and decreased birth weight and head circumference (Petit et al 2012).

More detailed studies have linked exposure to organochlorine insecticides with altered birth outcomes:

- Reduced birth weight and length correlated with exposure during pregnancy to wood preservative chemicals including lindane and pentachlorophenol in Germany (Karmaus & Wolf 1995).
- In India, higher levels of lindane and other isomers of HCH (Pathak et al 2011) and DDT (Sharma et al 2012) were associated with reduced intrauterine growth, whilst elevated levels of HCH, DDT, and DDE in cord blood and/or placenta were correlated with reduced birth weight, length at birth, head circumference, ponderal index (measure of leanness), and chest circumference in newborns (Dewan et al 2013).
- In Saudi Arabia, the presence of DDT residues in placental tissues, maternal and cord blood was associated with reduced head circumference, crown-heel length, birth weight and birth height (Al-Saleh et al 2012).
- In New Jersey, USA, higher levels of metolachlor in maternal cord blood were linked to decreased birth weight; and higher cord blood levels of dichloran were linked to increased abdominal circumference at birth (Barr et al 2010b).

- In Spain, lowered birth weight was associated with elevated levels of DDT, DDE, HCB, and HCH in cord blood; decreased birth length was associated with increased HCB; and decreased head circumference with DDT (Lopez-Espinosa et al 2011).
- Elevated levels of DDE in maternal blood were associated with lower birth weight in Inuit women (Wojtyniak et al 2010).
- Elevated levels of HCB in breast milk were associated with impaired foetal growth in Norwegian women (Eggesbø et al 2009).
- Elevated levels of HCB correlated with reduced head circumference in France (Brucker-Davis et al 2010).
- Post-natal infant growth was slightly diminished in infants whose mothers had elevated levels of HCB (and other chemicals) in their milk (Brucker-Davis et al 2010).
- Babies born in the US in the early 1960's whose mothers had elevated levels of DDE during pregnancy were more likely to have lower birth weight and to have been born preterm. Those with the smallest exposures had a 50% increased chance of being born prematurely, but those with the highest levels had a 200% chance of premature birth. The authors concluded that DDT exposure is likely to contribute significantly to infant mortality (Longnecker et al 2001).

Prenatal exposure to pesticides may be contributing to a "silent pandemic" of developmental neurotoxicity.

Although most of the evidence above points to organochlorines as problems, organophosphates have also been associated with altered birth outcomes. Residential chlorpyrifos exposure *in utero*, as measured by levels in umbilical cord blood, was associated with decreased birth weight and birth length in a New York study, and significantly poorer mental and motor development at three years of age. Exposure to diazinon and propoxur also impaired foetal growth, although to a lesser extent (Whyatt et al 2004). This confirmed findings of an earlier study, of African-American women, in which high levels of prenatal exposure to chlorpyrifos correlated with reduced birth weight and body length (Perera et al 2003; Whyatt et al 2004). Elevated levels of organophosphate metabolites in maternal urine have been associated with shortened gestation and decreased birth length (Rauch et al 2012). There was a tentative association between exposure to organophosphate insecticides and smaller head size in newborns of women living in pea, potato and wheat-growing areas in France (Petit et al 2010).

The PON1 genotype influences the effects of organophosphate exposure on birth outcomes: among pregnant women with measureable levels of chlorpyrifos in their blood, those with lower PON1 levels had children with smaller infant head circumferences at birth, in a New York study. Smaller head size is predictive of subsequent reduced cognitive ability and IQ (Berkowitz et al 2004).

Other current use pesticides may also be causing adverse birth outcomes. In an analysis carried out in rural China, in which 20 non-persistent pesticides were measured in cord blood, reduction in birth weight was associated with increased levels of total pesticides, and with individual levels of vinclozolin and acetochlor (Wickerham et al 2012).

Pre-term births have been associated, in epidemiological studies, with pesticides generally (Cremonese et al 2012), use of herbicides especially atrazine and 2,4-D and OPs (Colborn & Carroll 2007), and maternal exposure to DDT, endosulfan or HCH (Wigle et al 2008; Pathak et al 2010).

Intrauterine growth retardation or low birth weight have been associated with atrazine, metolachlor, cyanazine, HCH, and lindane (Colborn & Carroll 2007; Pathak et al 2011), including in the case of atrazine as residues in drinking water (Villanueva et al 2005; Ochoa-Acuña et al 2009). Atrazine is also associated with smaller head circumference (Chevrier et al 2011). A Polish study found that triazine herbicides in combination with other pesticides were associated with low birth weights (Dabrowski et al 2003).

4.4 Neurodevelopmental and behavioural effects

> *"Prospective contemporary birth cohort studies in the United States link early-life exposures to organophosphate insecticides with reductions in IQ and abnormal behaviors associated with attention-deficit/ hyperactivity disorder and autism."* | *Statement by American Academy of Pediatrics (CEH 2012)*

Most neurodevelopmental effects, such as lowering of IQ, cannot be seen at birth and often are not evident until later in life. They may be expressed in changes in behaviour and ability throughout childhood and into adulthood, and can range from mild to totally debilitating. Most of these effects are missed by normal regulatory processes for pesticides (Colborn 2004).

Developmental, learning and behavioural disabilities are regarded as having reached epidemic proportions in the USA (Schettler et al 2000). These disabilities have an enormous impact on families and on society, as well as on the individual child. About 17% of US school-age children suffer from

one or more learning, developmental or behavioural disabilities. This includes attention deficit / hyperactivity disorder (ADHD), autistic spectrum disorders, epilepsy, Tourette syndrome,[28] mental retardation, reduced IQ, dyslexia,[29] and cerebral palsy, but it does not include conduct disorders.[30] All of these conditions are believed to be the outcome of abnormal processes that occurred as the brain was developing in the foetus or in early childhood (Szpir 2006). They result in reduced learning, reduced employment, and increased social alienation (Schettler et al 2000). Rates of mental illness and suicide are higher in these children, with increased likelihood of substance abuse and committing crimes later in life (Szpir 2006). These risks are enhanced if the person is from lower socio-economic status.

Genetic–environment interaction

Current thinking is that these disorders, once thought to be largely genetic, may in fact be at least partly a result of growing levels of environmental contamination and chemical body burden. Genetic influences are still important, not least because they interact with environment influences. Some children with a genetic susceptibility to developing ADHD, autism or another of the neurobehavioural conditions may escape it in the absence of chemical insult (Szpir 2006). Additionally, certain genetic variations may make some children more susceptible because their particular expression of genes for key metabolic enzymes makes them less able to detoxify chemicals. About 4% of the US population carries a gene that reduces levels of the enzyme acetylcholinesterase,[31] increasing vulnerability to OPs especially for the prenatal developing brain. About 30-40% carry the PON1 variation of a gene that reduces the levels of the enzyme paraoxonase, which detoxifies OPs (Schettler et al 2000; Eskenazi et al 2010). PON1 variations have been implicated in adult onset Parkinson's and Alzheimer's diseases (Eskenazi et al 2010). Variations of another gene, encoding for the enzyme family glutathione S-transferases, makes children vulnerable to prenatal exposure to DDT causing adverse effects on cognitive functioning, memory and verbal skills (Morales et al 2008).

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[28] Repeated and uncontrolled rapid movements and sounds called tics.

[29] Dyslexia is a specific learning disability involving difficulty with written language, particularly with reading and spelling, but it is not an intellectual disability. Most people with dyslexia have average or above-average intelligence.

[30] Conduct disorders include repetitive patterns of at least three or more of the following: aggression, fighting, stealing, vandalism, blaming others, low self-esteem, poor tolerance, irritability, temper tantrums, lying, truancy, and substance abuse (Schettler et al 2000).

[31] An enzyme found throughout the nervous system that is responsible for breaking down the neurotransmitter acetylcholine; a genetic deficiency characterised by reduced levels of the enzyme results first in over-activation and then in dysfunction of the nervous system (Schettler et al 2000).

Environmental chemicals

There is a burgeoning literature on the influence of environmental chemicals on neurodevelopment and behaviour. Most of this relates to chemicals toxic to the nervous system (neurotoxicants) including heavy metals such as lead, mercury and cadmium, polychlorinated biphenyls (PCBs), polybrominated diphenyl ether flame retardants (PBDEs), and pesticides (Szpir 2006). However, chemicals may also adversely affect neurodevelopment through their endocrine disrupting effects on the thyroid gland, as thyroid hormones are critical in regulating brain development. Any lowering of thyroxine levels or other interference with thyroid hormone action, even minor transitory reductions, is likely to reduce IQ (Schettler et al 2000). Many pesticides are known to adversely affect the thyroid, including 2,4-D, mancozeb, endosulfan, malathion, dimethoate, and fenvalerate (Colborn 2004), and organochlorine pesticides like endrin, endosulfan, DDT, and HCB (Freire et al 2011). A study of children in Mexico, from a community contaminated by a pesticide factory, found a consistent increase in levels of thyroid hormone T3 with serum concentrations of OC pesticides. Other epidemiological studies have found a variety of different relationships between OC pesticides and levels of various thyroid hormones, including a negative association with T3 levels (Freire et al 2012).

PON1 variations and neurobehavioural outcomes

Elevated levels of OP metabolites in the urine of pregnant women in an agricultural community in the Salinas Valley of California, USA, have been linked to abnormal reflexes in the neonate period (Young et al 2005);[32] and to poorer mental development and symptoms of 'pervasive personality disorder'[33] in 2 year-old children. Every 10-fold increase in the level of metabolites resulted in a doubling of pervasive personality disorder (Eskenazi et al 2007). A subsequent study of the same group found that certain variations in the PON1 gene involved in detoxifying OPs were linked with poorer mental and psychomotor development (Eskenazi et al 2010).

Another study found that elevated levels of OP metabolites in a woman's urine during the third trimester of pregnancy resulted in reduced cognitive development at 12 months of age, particularly perceptual reasoning, and these effects were increased in those who carried certain PON1 genotypes (Engel et al 2011).

[32] A subsequent study in urban children also found that prenatal exposure to OPs increased abnormal reflexes in newborns, with any detectable level of malathion metabolites in maternal urine resulting in a 240% increase in risk (Engel et al 2007).
[33] Also referred to by the authors as autism-like behaviour.

Prenatal exposure to pesticides—at levels not producing adverse health outcomes in the mother—may be contributing to a "silent pandemic" of developmental neurotoxicity (Harari et al 2010). Numerous studies on animals have shown that *in utero* or neonate exposure to OPs affects neurodevelopment (Eskenazi et al 1999, 2007). Some show that inhibition of chlolinesterase can interfere with brain development leading to permanent brain damage (London et al 2012). Now there is also a gathering number of studies showing that children exposed to highly hazardous pesticides, especially OPs, *in utero* or during early critical development phases, face significant risks of an array of developmental disorders including poor memory, learning disabilities, impaired mental development, reduced motor performance, ADHD, autism spectrum disorder, neurodevelopmental delays, and other neurobehavioural problems and deficiencies (Guillette et al 1998; Eskenazi et al 2007, 2008; Roberts et al 2007; CHE 2008; Jurewicz & Hanke 2008; Searles Nielsen et al 2010; London et al 2012). In adolescents, the effects of OP exposure are mainly seen as mental and emotional problems (Jurewicz & Hanke 2008). An analysis of the urinary levels of OP metabolites in children indicates that as many as 40% of US children may be at risk of neurological impacts from cumulative exposures to OP pesticides (Payne-Sturges et al 2009). Given that the urinary metabolite level in Thai children is double that of US children (Panuwet et al 2012), they are even more at risk.

- Several studies of children in Ecuador, with high potential prenatal exposure to OPs and carbamates, because their mothers had worked in the cut-flower industry during pregnancy, found reduced motor skills, poorer communication, reduced memory, and poorer visual performance compared with children whose mothers had not worked in the industry, indicating delayed neurodevelopment amongst young children ranging from 3 months to 8 years, with the delay being as much as 1.6 years amongst the older children. Malnutrition, manifesting as stunted growth, made the effects worse (Grandjean et al 2006; Handal et al 2007, 2008; Harari et al 2010).
- Children from agricultural communities in the US showed poorer response speed and slower learning in neurobehavioural tests than children from non-agricultural communities (Rohlman et al 2005).
- Boys spraying OP pesticides in Egypt's cotton fields did significantly worse in neurobehavioural tests than boys not working in agriculture, with increasing cognitive deficits associated with increased years of spraying (Abdel Rasoul et al 2008). More neuromuscular disorders were also identified in the boys who sprayed (Ismail et al 2010).

- A study of Hispanic children living in an agricultural community in Arizona, USA, showed that short-term OP exposure reduced children's cognitive and behavioural functioning, including speed of attention, sequencing, mental flexibility, visual search, concept formation, and conceptual flexibility (Lizardi et al 2008).
- Prenatal exposure to the carbamate propoxur in the Philippines, as measured by residues in the meconium, was associated with poorer motor development in children at two years of age (Ostrea et al 2012).

Malnourishment is thought to increase the vulnerability to neurobehavioural effects of pesticides on children (Handal et al 2007). Malnourishment is a perennial problem for the global poor, who are also often those most at risk of exposure to the pesticides that cause neurobehavioural effects.

Attention Deficit / Hyperactivity Disorder (ADHD)

ADHD is a complex disorder in which a great variety of behavioural symptoms are exhibited and brain functions affected. It is characterised by hyperactivity, impulsive behaviour, and lack of ability to sustain attention (Aguiar et al 2010). Other characteristics include defiant behaviour, anxiety, inability to sit still or listen; children are easily distracted, forgetful, make careless mistakes, don't follow instructions, have difficulty organising, avoid or dislike mental effort, lose things, and interrupt others. Often learning is impaired (CDC 2011).

ADHD is estimated to affect 3 to 7% of all school children in the US, with diagnosed rates having increased, on average, 5.5% each year from 2003 to 2007 (CDC 2011), although one report in 2012 outs the figure at 14% (Landrigan et al 2012). Rates are higher in boys than in girls. Another 5% of children have learning disabilities without ADHD (Pastor & Reuben 2008). Rates in Asia may be similar: one review of data in 2006 concluded that rates there were 3-10% (Byun H 2006). The global prevalence is estimated to be 5.29% of under 18-year olds (Polanczyk et al 2007).

Although ADHD has been generally regarded as being of genetic origin, there is now increasing evidence implicating environmental chemicals as a causative factor (Aguiar et al 2010). For a start, children with low birth weight are more likely to have ADHD (Pastor & Reuben 2008), and as we saw earlier in this chapter there is considerable evidence linking exposure to some pesticides with reduced birth weight.

Neurotoxic organophosphate insecticides may be a key factor in ADHD. Animal studies have shown OPs cause cognitive deficits and hyperactivity. Biological plausibility is demonstrated by OPs' effects on neurochemical targets, growth factors, secondary messenger systems, DNA replication, neuron growth, and oxidative stress (Bouchard et al 2010; Marks et al 2010).

Typical levels of OP metabolites common among children in the USA—mainly arising from eating pesticide-treated fruit and vegetables—have been linked to prevalence of ADHD (Kuehn 2010). Each 10-fold increase in urine levels of OP metabolites was associated with a 55 to 72% increase in the likelihood of ADHD in children aged 8 to 15 years, in one study. For the most-commonly detected OP metabolite, di-methyl thiophosphate, children with levels higher than the median had twice the likelihood of ADHD compared to children with undetectable levels (Bouchard et al 2010). In a second study, prenatal exposure to organophosphates led to increased levels of attention problems in children once they reached five years of age, especially in boys. Each 10-fold increase in a pregnant mother's urinary concentration of OP metabolites led to a 500% increased risk that her child would be diagnosed with ADHD by age five (Marks et al 2010).

Low-level parental exposure to organochlorine pesticides like DDT may also be implicated in causing ADHD, although very little research has been done on this association so far. A recent US study found that children born with an elevated level of DDE and PCB in their cord blood had an increased risk of ADHD, up to 70% more for those with the lowest levels (Sagiv et al 2010). This is supported by a case in Sweden reported by Hardell et al (2002), in which a child with ADHD and his mother were both found to have elevated levels of DDE in their body fat. Further work by Sagiv et al (2012) corroborated these findings but only in relationship to male children.

Garry et al (2002) found an association between children borne to pesticide applicators exposed to glyphosate and neurobehavioural deficits; and between those exposed to the grain fumigant phosphine and neurological and neurobehavioural deficits, including ADHD and autism. Forty-three percent of children with ADHD had fathers who used glyphosate.

Autism

'Autism Spectrum Disorders' (ASD) is a set of neurodevelopmental disorders characterised by impaired social interaction, restricted communication, and repetitive stereotypic behaviours. Mental retardation is associated with about 40-55% of cases (Newschaffer et al 2006). It is generally believed that ASD arises from alterations to specific brain structures during critical windows of vulnerability in foetal development. It may be caused by genetic or environmental factors or a combination of the two (Roberts et al 2007).

Prevalence is hard to establish and estimates have varied widely, although in 2006 they were reported to be around 0.6% of the population, with one recent UK estimate of 1.1%. In a recent survey of 7 to 12-year-old children in South Korea, the prevalence of ASD was found to be a surprisingly high 2.64% (Kim et al 2011). In 2012, the rate in the US was reported as 11% (Landrigan et al 2012).

Prevalence has increased dramatically in recent years: in the US state of California the number of children on the autism register increased by 210% between 1987 and 1998 (Schettler et al 2000); and a 600% increase was observed between 1990 and 2001 in children under 5 years of age (Shelton et al 2012). Boys are 4-5 times more likely to have ASD than girls (Shelton et al 2012).

Pesticides are now regarded as leading causes of autism with both OPs and OCs listed in the top ten causes, along with heavy metals such as lead and mercury, and industrial chemicals such as PCBs, flame retardants and fluorinated compounds (Landrigan et al 2012).

An investigation of the influence of pesticide drift into homes near agricultural fields in the US found a strong association between ASD in children and their mothers residing near fields where endosulfan and/or dicofol were sprayed in the periods just before and during foetal development of the central nervous system (weeks 1-8). The risk of ASD increased with the quantity of pesticide used and with proximity to the fields. Children whose mothers were living within 500m of these fields had a more than 600% increased risk of ASD (Roberts et al 2007).

Eskenazi et al (2007) found a 230% increased risk of Pervasive Developmental Disorders, which include autism, for each 10 nanomole/litre increase in urinary metabolites of OPs.

Other work has shown that variations in the levels of PON1 enzymes and variations in PON1 genetic expression are associated with ASD, further

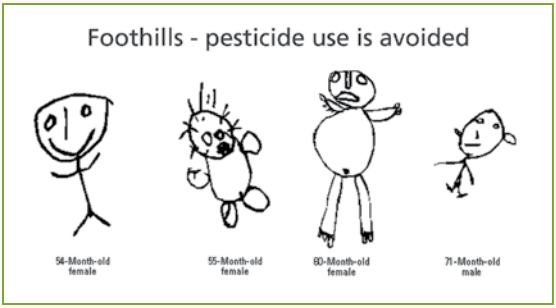
implicating exposure to organophosphate pesticides in the development of ASD (Eskenazi et al 2010).

Mechanism thought to be involved in the development of autism include inhibition of acetylcholinesterase during neuronal development, disruption of GABA signalling pathways, oxidative stress, and prenatal disruption of immune development—implicating a number of pesticides (Shelton et al 2012).

Intellectual development

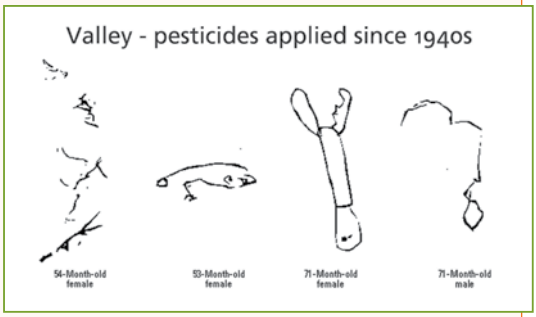
In a startling new piece of research, Dr David Bellinger of the USA's Children's Hospital Boston concluded that the impact of organophosphate insecticides on children is responsible for a significant lowering of IQ across the whole US population. After reviewing published data, he concluded that OPs were responsible for lowering the country's IQ level by 17 million points, not much less than the 23 million points lost to lead poisoning, and considerably more than that caused by ADHD, autism and a number of other childhood conditions. An effect, often dismissed as 'clinically unimportant' in the individual becomes very significant across a whole society, including in terms of declining intellectual ability, and extra costs for education and health care. As Bellinger (2012) points out, because of the ubiquitous nature of exposure to chemical such as OPs, "a risk assessment that focuses solely on individual risk, and fails to consider the problem in a public health context is potentially misleading".

Pesticides and child development - the Yaqui Indians of Mexico



Elizabeth Guillette and colleagues (1998) carried out a study among the Yaqui people of Mexico. They compared two groups of children sharing genetic, cultural and social backgrounds, one exposed to heavy pesticide use, and the other from an area where pesticide use was avoided.

When chemical pesticides and fertilisers were embraced by many of the residents in the Yaqui valley in the late 1940s, other residents moved into the foothills in protest at the change, and stayed there. In the valley, up to 90 separate applications of pesticides were made per year, including multiple organochlorine and organophosphate mixtures and pyrethroids. As well as this agricultural use, household insecticides were used throughout the year. In contrast, the ranching lifestyle of the highlands required no pesticide use, and the government DDT applications each spring for malaria control were their only contact with pesticides. The survey revealed no differences in physical growth or other outward manifestations, but it did reveal significant differences in functional abilities.



In the following areas, the valley children showed a marked decrease in function relative to the highland children: physical stamina, ability to catch a ball, fine eye-hand coordination, ability to draw a person (the valley children providing only random undifferentiated lines in comparison with the highland children's easily recognisable human figures), recall after 30 minutes, although immediate recall was equivalent, and group play—

Three recent studies have confirmed that children exposed to OPs in the womb have lower IQs, memories, and perceptual reasoning by the time they start school than children that are not exposed, with implications for longer-term learning and academic success (Gray & Lawler 2011). The studies all began in the later 1990s and followed the children through until the age of seven. The first study found that elevated levels of OP metabolites in a woman's urine during the third trimester of pregnancy resulted in reduced cognitive development in her child at 12 months of age, particularly perceptual reasoning (Engel et al 2011). The second study found that prenatal exposure to OPs, again assessed by the levels of OP metabolites in pregnant women, significantly reduced IQ in children at the age of 7 and by as much as 7 points, as well as reducing their working memory, processing speed, verbal comprehension, and perceptual reasoning (Bouchard et al 2011). The third study found that as little as 4.6 picograms of chlorpyrifos per gram of cord blood during gestation resulted in a drop of 1.4% of a child's IQ and 2.8% of its working memory (Rauh et al 2011).

Three recent studies have confirmed that children exposed to OPs in the womb have lower IQs, memories, and perceptual reasoning by the time they start school than children that are not exposed.

the valley children were less creative, roaming aimlessly or swimming in the irrigation canals with minimal group interaction.

Additionally, the valley children were observed to be more aggressive, hitting siblings and becoming more upset by minor corrective comment by a parent. The researchers concluded that the differences they found in mental/neurological functioning were indicative of brain dysfunction and held implications for learning ability and social behaviour. Whether the effects were the result of one chemical, or one class of chemicals, or a whole mixture of chemicals that may have been working additively, synergistically or independently, remains unknown.

Adult onset neurological disease

In 1980, David Barker and colleagues published a study showing that infants with low birth weight and small head circumference are more likely to develop coronary heart disease, hypertension, stroke, insulin resistance, and diabetes as adults (Landrigan et al 2005).

This study stimulated a lot of interest in what became known as foetal (or developmental) onset of adult disease (Stein et al 2008). Most attention was given to nutritional factors in cancer, heart disease, and metabolic disease, but more recently attention has turned to neurological diseases such as Alzheimer's disease and Parkinson's disease, and in particular to the effects of early exposure to neurotoxicants.

Child development in India

Kavitha Kuruganti carried out a similar study of the effects of high exposure to pesticides on child development, using an approach adapted from that of Guillette et al (1998), and the results confirmed those of the earlier study. Kuruganti's (2005) study was carried out in regions of cotton cultivation where pesticide use is high, across six states in India.[34] Three study villages were selected in each state, as were three control villages where pesticide consumption was much lower. Twenty five 4 to 5 year-olds and twenty five 9 to 13 years-olds were selected from each village. In all 1,648 children were tested for memory, stamina, analytical, motor, and tactile perception abilities through various games and activities such as making shapes with wooden blocks, solving jigsaw puzzles, drawing human figures, ball catching, dropping peanuts onto a bottle cap, jump exercises, standing on one leg, walking a plank, and recall tests.

Overall children heavily exposed to pesticides performed worse in 80% of the tasks. In both age groups, they displayed lower abilities in cognition, memory, stamina, motor skills and concentration (significantly lower in some abilities, and marginally so in some others). In the 4 to 5 age group, the results were strikingly different in the areas of mental ability (wooden blocks), cognitive ability (drawing human figure), stamina, eye-hand coordination, and concentration. For the 9 to 13 year-olds, the most significant differences were analytical ability (jigsaws), stamina, fine motor skills involved in eye-hand coordination and nose tapping, and concentration.

[34] Andra Pradesh, Karnataka, Punjab, Gujarat, Maharashtra, Tamil Nadu.

There is now a gathering body of evidence that neurotoxicity as a result of developmental exposures can remain "silent" for many years but eventually result in adult onset neurological diseases such as Parkinson's and Alzheimer's diseases.

Parkinson's Disease

Early life use of pesticides has been associated with a 7-fold increased risk of Parkinson's disease (Golbe et al 1990).

The California Environmental Protection Agency, in a recent reassessment of paraquat, expressed concern about the effects of the herbicide on the developing brains of children, in particular drawing attention to its potential effect on the mechanism underlying Parkinson's disease, the nigrostriatal dopaminergic system:

> *"OEHHA identified the brain as a sensitive target of paraquat's toxic effects, particularly in children. There is direct evidence that paraquat can penetrate the central nervous system. Paraquat may affect different systems of the brain including the nigrostriatal dopaminergic system. The developing brain may be particularly sensitive to oxidative insults, a mechanism of action of paraquat."* | *(Cal EPA 2010)*

Several animal studies have linked adult onset Parkinson's disease to neonatal exposure to paraquat. Such exposure, even at low doses can induce permanent brain function changes, and neurochemical and behavioural changes in the adult mouse, including reduced dopamine (Fredriksson et al 1993). Previous exposure, and particularly developmental exposure, to paraquat enhances vulnerability to neurotoxins, and there is progressive neurotoxicity with continuing exposure leading to earlier onset of Parkinson's disease than is the norm (Zhou et al 2011).

Other animal studies have linked additional pesticides to increased risk of Parkinson's disease. Perinatal exposure to OC pesticides caused changes to the nigrostrial system of the brain in male offspring, with effects on the dopaminergic system that appeared likely to last into adulthood, suggesting a link with Parkinson's disease (Cooper et al 2011). Prenatal exposure to diazinon, but not chlorpyrifos, caused transcriptional changes in gene expression in mice associated with Parkinson's disease (Slotkin & Seidler 2011).

Early life use of pesticides has been associated with a 7-fold increased risk of Parkinson's disease.

Chlorpyrifos damage to foetus causing neurodevelopmental effects

Chlorpyrifos is the most widely studied pesticide in terms of neurodevelopmental effects, most of those studies coming from the USA. The studies appear to have been stimulated, at least in part, by the widespread exposure of US children to chlorpyrifos through its use in homes to exterminate household pests. Home use was banned in the US in 2002, but not agricultural use. It is given special attention here because its effects are indicative of those of other organophosphates, less well studied, and to which children are also exposed, especially in developing countries.

Child exposure

As reported in the chapter on exposure, chlorpyrifos has been found in umbilical cord blood, the meconium of newborns, indoor air samplers of pregnant mothers in urban USA, breast milk in India, children's urine, rural house and vehicle dust, on the hands of toddlers, and in rural air monitoring. Chlorpyrifos has been ubiquitous in the USA: a metabolite was found in the urine of over 80% of adults and 90% of children from representative population samples (Schettler et al 2000). Exposure to chlorpyrifos is also widespread in other countries, particularly amongst rural populations and working children.

Known effects on children

Epidemiological studies of pregnant mothers exposed to chlorpyrifos through home pesticide use demonstrated a link between *in utero* exposure to chlorpyrifos and low birth weights and/or reduced head circumference of newborns, especially for mothers whose genetic makeup is such that they produce low levels of PON1, the enzyme responsible for detoxifying chlorpyrifos in the body. Reduced head circumference is indicative of subsequent reduced cognitive ability (Whyatt & Barr 2001; Whyatt et al 2004; Berkowitz et al 2004).

Newborn infants in New York, exposed *in utero* to chlorpyrifos from household use, were found to have delayed cognitive and psychomotor development. Those most exposed had significantly more attention problems, attention-deficit/hyperactivity disorder problems, and pervasive developmental disorder problems at 3 years of age (Rauh et al 2006; Gulson 2008). A second study found that these effects were independent of socio-economic factors (Lovasi et al 2011). In a separate study, as little as 4.6 picograms of chlorpyrifos per gram of cord blood during gestation resulted in a drop of 1.4% of a child's IQ and 2.8% of its working memory (Rauh et al 2011).

> *"These findings indicate that prenatal exposure to the insecticide chlorpyrifos not only increases the likelihood of developmental delay, but may have long-*

term consequences for social adjustment and academic achievement," said lead author and investigator on the study [Rauh et al 2006], Virginia Rauh, ScD. "Relatively speaking, the insecticide effects reported here are comparable to what has been seen with exposures to other neurotoxicants such as lead and tobacco smoke." | (CCCEH 2006)

The latest study from Virginia Rauh (Rauh et al 2012), demonstrates that prenatal exposure to chlorpyrifos is altering children's brain structure, the effects being visible at least 11 years after birth. At levels observed with routine non-occupational use and below the threshold for any signs of acute exposure, they found significant abnormalities in the cerebral surface, enlargements derived from enlargements in the underlying white matter. These abnormalities occurred in regions of the brain associated with attention, receptive language, social cognition, reward, emotion and inhibitory control. They also linked the abnormalities with reduced IQ. Their findings support those from laboratory studies, and previous epidemiological studies linking chlorpyrifos exposure with child cognitive impairment.

Prenatal exposure to chlorpyrifos is altering children's brain structure

Laboratory studies

A series of studies beginning in 1999 showed that foetal exposure to low levels of chlorpyrifos, lower than those inhibiting cholinesterase,[35] interfere with the development of the foetus in mammals. They showed that the foetus is more sensitive to chlorpyrifos than adult rats, that it alters prenatal development of the brain and behaviour, that chlorpyrifos has a wide range of activity in the brain quite apart from inhibiting cholinesterase and that this wide range of activity makes chlorpyrifos far more toxic than previously thought. They showed that, as the brain and nervous system develop, there are numerous points in time and sites at which chlorpyrifos interferes.

At the early stages, it attacks neurons, which process information and are the transmitters of the nervous system. Neural cell replication is affected and the number of neural connections is reduced. This damage is not expressed until years later, causing neurobehavioural alterations during adolescence and adulthood. Glial cells, which develop later than neurons, are even more susceptible to chlorpyrifos. Glial cells have many functions including providing nutrition to neurons and linking with the immune system. Whilst effects on the forebrain of the rat, which reaches its peak of development during gestation, are bad enough, the effects on the cerebellum, which reaches its peak two weeks after

[35] Inhibition of cholinesterase has traditionally been taken as the indication of OP poisoning.

birth, are even more severe. As animals mature, damage is evident in a wide variety of brain regions – the most vulnerable being the hippocampus—resulting in behavioural abnormalities. Chlorpyrifos also disrupts serotonin, a neurotransmitter that provides essential signals during brain development, and which in turn has been linked to appetite and mood disorders (Slotkin 2004; Colborn 2006; Slotkin et al 2006).

To add to the complexity of chlorpyrifos' effects, it appears that there are sex-related differences in effects on the brain, and subsequent cognitive function in adolescence and adulthood, with females affected more than males by prenatal exposures and vice versa for postnatal exposures (Slotkin 2004). Confirming that link, researchers at the University of Wisconsin Madison found that female mice exposed *in utero* to chlorpyrifos are slow learners, but male mice are not affected (Haviland et al 2010). Perinatal exposures to ongoing low doses of chlorpyrifos also resulted in anxiety in adult female mice (Braquenier et al 2010).

Making things even more complicated, it seems that chlorpyrifos' developmental effects extend beyond those involving neurotoxicity, to involve both heart and liver in ways that can result in the onset of cardiac and metabolic diseases (including diabetes and obesity) long after the end of chlorpyrifos exposure. Again, prenatal exposure to low doses that do not inhibit cholinesterase result in alteration of adult function, this time cardiac and liver function. There is a complex dose-response relationship: whereas with acute poisoning a higher dose gives a worse effect, here in some instances effects do not occur at anything but a low dose, and in some cases there were larger alterations at low doses than seen at high doses (Meyer et al 2004).

Together these studies demonstrate that adult models of toxicity do not work for the foetus, and do not predict the vulnerability of the foetus to the effects of chlorpyrifos, and probably other organophosphates (Slotkin 2004; Colborn 2006).

> *'The ever-changing state of the embryo makes it a more sensitive model for toxicity and a better predictor of long-term, delayed effects."* | *Colborn 2006*

Other organophosphates

Organophosphates other than chlorpyrifos also have neurodevelopmental and behavioural effects, although laboratory studies on animals suggest that these effects differ as they do not depend on the suppression of acetylcholinesterase, the common mechanism of OPs (Slotkin et al 2008b).

Doses of OPs given to newborn rats at levels below those that trigger changes to acetylcholinesterase were sufficient nevertheless to cause changes in the developing brain:

- Diazinon—the effect was on emotional responsiveness and cognitive function with changes in the developing brain that correspond to neuro-developmental delays (Slotkin et al 2008a).
- Parathion—caused changes in the brain likely to manifest as learning related deficits. As with other OPs, effects were much more widespread in males than females (Slotkin et al 2008b).

Diazinon, like chlorpyrifos, interferes with sexual differentiation of the brain, narrowing or eliminating many of the normal sex differences in behavioural and/or neurochemical parameters. Additionally, subsequent repair processes differ substantially, with females showing a greater general capacity to offset damage (Slotkin et al 2008b).

During the 1990s, there were numerous incidents of illegal indoor spraying with methyl parathion in the US states of Mississippi and Ohio, resulting in a number of poisonings. In a subsequent investigation of long-term neurological effects, some of the exposed children were found to have impaired short-term memory and attention, and more behavioural and motor skill problems. Behavioural problems included anger, misbehaving, impulsiveness, sadness, shyness, and difficulty relating to other children (Ruckart et al 2004).

Other pesticides

Although OPs are the leading contenders for neurological effects on children, there are a number of other pesticides involved as well. Laboratory studies have shown that 2,4-D, chlordane, methoxychlor, endosulfan, and vinclozolin, amongst others, can cause neurodevelopmental effects (Colborn 2004). Paraquat has already been discussed under adult-onset disease for its potential to cause Parkinson's disease after developmental exposures.

Pyrethroids

Pyrethroids and pyrethrins interfere with nerve cell function, either increasing or decreasing excitability of nerve cells resulting in repetitive firing or prolonged inactivity. They can permanently alter neuroreceptors in the brain and as a result cause behavioural changes. Some pyrethroids cause permanent hyperactivity in animals exposed to small doses on a single critical day of development (Schettler et al 2000).

Exposure to piperonyl butoxide[36] in the third trimester of pregnancy, and as measured by personal air samplers for their pregnant mothers, has been found to delay mental development in children at 3 years of age (Horton et al 2011).

Organochlorines

The effects of OCs on nerve cells and brain neuroreceptors are similar to those of pyrethroids (Schettler et al 2000). Prenatal exposure to the DDT metabolite DDE has been linked with neurodevelopmental delays in children, especially movement or muscular activity associated with mental processes (psychomotor) (Eskenazi et al 2006; Torres-Sánchez et al 2007) and poor attention (Sagiv et al 2008). It seems that at least part of the effect may be mediated by effects on the thyroid. A study published in 2011 showed that levels of OC compounds, including HCB, DDE and trans-nonachlor (metabolite of chlordane) in maternal serum and breast milk were associated with reduced levels of the hormone T3RU in women and newborns, and this in turn was associated with reduced performance in neuropsychological tests (Julvez et al 2011).

A number of studies have shown an association between prenatal exposure to organochlorines and developmental problems, including the following:

- Exposure *in utero* to DDT, but not DDE, is associated with adverse effects in preschoolers including on general cognitive functioning, memory and verbal skills (Morales et al 2008).
- A study of Mexican farm workers' children in California, USA, found that prenatal exposure to DDT, measured in the serum of their mothers when they were pregnant, was associated with neurodevelopmental delays during early childhood (Eskenazi et al 2006).
- Prenatal exposure to endosulfan from aerial spraying of cashew plantations in Kasargod, India, resulted in congenital mental retardation, cerebral palsy, delayed mental and psychomotor development, learning disabilities, low IQ, and epilepsy (NIOH 2002; Quijano 2002).
- Prenatal exposure to DDT, as determined by maternal residues, was associated with a decrease in psychomotor and mental development at one month of age (Bahina-Medina 2011), decreased cognitive skills at 4 years of age (Ribas-Fitó et al 2006b).
- Elevated levels of DDE in placental cord blood was associated with decreased alertness, quality of alert responsiveness, cost of attention, and other potential attention-associated measures including self-quieting and motor maturity, in 2 week old infants (Sagiv et al 2008).

[36] A synergist that potentiates pyrethroid insecticides.

Summary

The findings of the two comprehensive studies in Mexico and India described earlier imply grave consequences for the future of the child, the family, and society as a whole; and these two studies are supported by a raft of other studies demonstrating the neurodevelopmental effects of pre- and post-natal exposure to a wide range of pesticides but especially organophosphates. As Schettler (2000) pointed out:

> *"A loss of 5 points in IQ is of minimal significance in a person with an average IQ. However, a shift of 5 IQ points in the average IQ of a population of 260 million increases the number of functionally disabled by over 50% (from 6 to 9.4 million), and decreases the number of gifted by over 50% (from 6 to 2.6 million)."*

That translates to a serious reduction in intellectual capacity across the entire population, and this does not even take into account all the behavioural problems such as aggression and lack of sociability, and other adverse social effects resulting from these, that cascade from disrupted neurobehavioural development.

4.5 Cancer

Child cancer rates have been steadily increasing around the world. In Britain, they increased by 35% between the years 1962 and 1998, with an annual increase of 0.8%. Across 15 countries in Europe, the annual increase was 1.1% over the years 1978-1997 (Lyons & Watterson 2010). In the USA, whilst the overall childhood cancer incidence rates increased 13% from 1973 to 1997 the rates of increase for some specific childhood cancers were much higher: 30% for non-Hodgkin's lymphoma, 21% for brain cancer and 21% for acute lymphocytic leukaemia (CEC 2006). Similar increases were seen in young adults in Canada, especially non-Hodgkin's lymphoma and thyroid cancer in both men and women, lung and brain cancer in women, and testicular cancer in men, the latter with an average rate of 1.7% increase per year between 1987 and 1996 (CEC 2006). Health experts warn that child cancer rates are rising in China, too (Anon 2011). Some cancers in adults may well result from contributing factors that occurred during prenatal development and childhood, given that cancer generally has a long latency period.

As childhood cancer rates have grown, attention has turned to pesticides as one of the potential causative factors. There is an increasing amount of epidemiological evidence that both direct childhood exposures and parental exposures to pesticides are associated with childhood cancer. Leukaemia (Van Maele-Fabry et al 2010), and child cancer in general, are most consistently associated with maternal exposures (Infante-Rivard & Weichenthal 2007; Lyons & Watterson 2010). Exposure of the father, pre-conception, can also result in childhood cancer, particularly leukaemia (Infante-Rivard & Weichenthal 2007) and brain cancer (Vinson et al 2011). These exposures occur through both occupational and household uses. A large international study across seven countries identified an association between childhood brain tumours and maternal farm exposure to pesticides during the five years preceding the diagnosis (Efird et al 2003). A high rate of brain cancer was found in children playing in orchards in Kashmir, India (Bhat et al 2010).

Table 8: Types of child cancers associated with different exposure scenarios

Type of Exposure	Cancer
parental occupational exposure as farmer, pesticide applicator, landscaper, grounds-keeper	leukaemia, brain cancer, neuroblastoma, Wilm's tumour, Ewing's sarcoma, soft-tissue sarcoma, colorectal cancer, germ cell (testes), Hodgkin's disease, non-Hodgkin's lymphoma, eye cancer
maternal occupation as farmer or florist	leukaemia, neuroblastoma, soft-tissue sarcoma, Wilm's tumour
living on farms	non-Hodgkin's lymphoma, brain cancer, Ewing's sarcoma
rural residence associated with high pesticide use	Ewing's sarcoma, leukaemia, neuroblastoma and other nervous tissue tumours, non-Hodgkin's lymphoma, Wilm's tumour, renal carcinomas, liver tumours, thyroid carcinomas, soft tissue sarcomas, rhabdomyosarcomas (muscle and connective tissue), melanoma, germ cell sarcomas, bone cancer
preconception exposure of the father to pesticides	leukaemia, brain cancer, Wilm's tumour
maternal exposure during pregnancy (occupational and home use)	leukaemia, brain, neuroblastoma, non-Hodgkin's lymphoma, Wilm's tumour, liver tumour
household use	leukaemia, brain cancer, neuroblastoma, non-Hodgkin's lymphoma, Wilm's tumour
use on pets	brain cancer
professional pest control in home	leukaemia, non-Hodgkin's lymphoma, Wilm's tumour, Ewing's sarcoma, soft-tissue sarcoma, brain cancer
gardens and lawn care	leukaemia, brain cancer, bone cancer, Wilm's tumour, neuroblastoma, Hodgkin's disease, non-Hodgkin's lymphoma, Ewing's sarcoma, soft tissue sarcoma

Source: Zahm & Ward 1998, Infante-Rivard & Weichenthal 2007; Carozza et al 2008; Thompson et al 2008; Ferris I Tortajada et al 2008.

The childhood cancers most commonly associated with pesticide exposures are leukaemia, brain cancer, non-Hodgkin's lymphoma, neuroblastoma (a tumour in nerve tissue), Ewing's sarcoma (a tumour of bone tissue), and Wilm's tumour (kidney). Others include soft-tissue sarcoma, colorectal cancer, germ cell cancer, Hodgkin's disease, eye cancer, renal and liver tumours, thyroid cancer, and melanoma.

There is also a set of adult cancers associated with exposure to pesticides: breast, lung, multiple myeloma, ovary, pancreas, prostate, stomach, and testicular—and of these, at least breast, prostate, and testicular cancer are thought to have origins in early developmental exposures to environmental hormone disruptors (Cooper et al 2011).

Types of pesticides implicated

Studies have linked childhood cancers to exposure to herbicides, insecticides and fungicides, but few have linked them to specific pesticides because of the difficulties in determining exposure. For leukaemia, the greatest risks are household insecticide use and prenatal exposure to insecticides, and for neuroblastoma it is herbicides (Infante-Rivard & Weichenthal 2007), but many pesticides are implicated. One study in India found an association between elevated levels of endosulfan in bone marrow and leukaemia in children from areas of Karnataka and Kerala where endosulfan had been used (Rau et al 2012). A recent study in China found a nearly 3-fold increase in acute lymphocytic leukemia in children with pyrethroid metabolites in their urine (Ding et al 2012).

In many cases, children are exposed to an array of different pesticides, and this in itself may make the risk of cancer worse. One study of pesticides and fertilisers in groundwater found that the risk of child cancers was elevated when the ground water was contaminated with atrazine, simazine, metolachlor, alachlor or nitrates from fertiliser; but when atrazine, metolachlor and nitrates were all elevated there was a 750% increase in cancer risk (Thorpe & Shirmohammadi 2005).

Genetic variations in the ability to metabolise OPs and carbamates again come into play, as they did for the effects on neurodevelopment. Elevated rates of brain cancer in children whose mothers reported home treatment for insects were associated with genetic variations in the paraoxonase enzyme PON1, with those leading to reduced ability to detoxify OPs and carbamates associated with higher levels of brain cancer (Searles Nielsen et al 2005, 2010).

Cancer later in life

It is clear that prenatal and childhood exposure to a number of pesticides may result in childhood cancer. However, there is an emerging scientific consensus that the critical window of exposure to carcinogens is *in utero* and in early childhood, and that exposures during this time may also result in cancer that does not manifest until later in life, leading to an increased risk of cancer over a lifetime. In fact, research from Sweden concludes that adult cancer risk is largely established during the first 20 years of life (Czene et al 2002; Hemminki & Li 2002).

Table 9: Pesticides linked to cancers and windows and/or types of exposure

Pesticide	Cancer	Window/type of Exposure
carbaryl	brain	ever
diazinon	brain	ever
heptachlor	brain	pregnancy and breastfeeding
lindane	brain leukaemia[1]	age 7 months through to diagnosis use for head lice treatment
atrazine[3]	bone, leukaemia	in well water
metolachlor[3]	bone, leukaemia	in well water
chorothalonil, PCNB	leukaemia[5]	
dichlorvos	leukaemia	childhood
endosulfan	leukaemia[8]	
permethrin	leukaemia[7]	pregnancy
propoxur	leukaemia	childhood
propargite	leukaemia[6]	
Baygon[37] [2]	leukaemia	pregnancy
DDT	Wilm's tumour	at birth
ethylene dibromide	Wilm's tumour	at birth
endrin	Wilm's tumour	at birth
chlordane	neuroblastoma leukaemia	pregnancy, childhood childhood
flea collars	brain	birth to diagnosis
flea bombs	brain	pregnancy; 7 months to diagnosis
lice treatment	brain	pregnancy, childhood
fungicides	brain	pregnancy, childhood
herbicides	astrocytoma, tumour of glial cells in brain[9]	2 year period before birth
termiticides	brain	pregnancy, ever
pest strips	brain non-Hodgkin's lymphoma leukaemia	pregnancy to diagnosis pregnancy to 2 years pregnancy, childhood
herbicides	brain leukaemia[4]	birth to diagnosis pregnancy
pyrethroid head lice shampoo[1]	leukaemia	childhood
triazine herbicides	leukaemia[5]	
chlorinated phenol herbicides (2, 4-D, diclofop, MCPA, MCPB)	leukaemia[5]	
azole fungicides	leukaemia[5]	
organophosphates	leukaemia[5, 10]	
fumigants	leukaemia[5]	
pyrethroids	acute lymphocytic leukaemia[11]	

Source: Zahm & Ward 1998, except:

1 Menegaux et al 2006
2 Infante-Rivard & Weichenthal 2007
3 Thorpe & Shirmohammadi 2005
4 Turner et al 2010
5 Rull et al 2010
6 Reynolds et al 2002
7 Ferreira et al 2012
8 Rau et al 2012
9 Shim et al 2009
10 Soldin et al 2009
11 Ding et al 2012

[37] Baygon products contain the pyrethroids cyfluthrin and transfluthrin, the carbamate propoxur, and the OP chlorpyrifos.

Prenatal exposure to synthetic oestrogens is associated with increases in breast and vaginal tumours in humans later in life (Birnbaum & Fenton 2003). Such exposure appears to imprint breast cells making them more sensitive to subsequent exposures to carcinogens and hormonally active compounds (Davis et al 1998). It is thought that the same situation occurs with prenatal exposure to xenoestrogens, or oestrogen-mimicking chemicals.

Breast development affects subsequent risk of breast cancer. A number of pesticides are known to affect prenatal mammary gland development in rodents in ways that increase susceptibility to carcinogens or hormonally active agents, such as by increasing the number or density of terminal buds (the least mature ductal structures in the mammary gland and the most susceptible to carcinogens) (Rudel et al 2011). These include atrazine, DDT, endosulfan, malathion, methoxychlor, and permethrin (Watts 2007).

Exposures during childhood and early adolescence can also result in cancer in later years. A study by Cohn et al (2007) found a five-fold increase in the risk of breast cancer among young American women who were under the age of 14 in 1945 when widespread use of DDT began in the USA, and mostly under the age of 20 when that use peaked. They used blood samples obtained from young women from 1959 to 1967. This was the period of peak DDT use in America and these women were exposed during the vulnerable periods of childhood and adolescence. The median time to diagnosis was 17 years, and the mean age at diagnosis was 44 years.

4.6 Obesity, diabetes and metabolic disease

Our knowledge of the insidious effects of pesticides is continually unfolding and in recent years connections have been made between exposure to pesticides and some of society's most rapidly escalating health problems, such as diabetes, obesity and metabolic disease, the latter a condition associating obesity with hypertension, type 2 diabetes, and cardiovascular disease (Lee et al 2006, 2007; Rignell-Hydbom et al 2007; Jones et al 2008; Montgomery et al 2008).

Obesity and diabetes are rising at epidemic rates in many countries. The worldwide prevalence of obesity has doubled since 1980, even increasing in pets and laboratory animals (Thayer et al 2012). Obesity is a known risk factor for diabetes so the two go hand-in-hand. Whilst most attention has been focused on lifestyle factors such as diet and exercise, there is now a little glimmer of light being shed on the role of environmental chem-

icals in both conditions, and particularly prenatal and early childhood exposure, as causative factors (Newbold et al 2007; La Merrill & Birnbaum 2011; Slotkin 2011). In fact, weight-gain from low dose exposure to chemicals was showing up in animal tests way back in the 1970s, but it was Paula Baillie-Hamilton of Stirling University in Scotland who is credited with exposing the significance of this in 2002, and formulating the hypothesis that chemical toxins may be causing the global obesity epidemic (Holtcamp 2012).

In 2008, Leon Lassiter from Duke University, USA, and colleagues observed:

> *"It is increasingly evident that adverse events in fetal or neonatal life, including chemical exposures like those studied here [parathion] can lead to misprogramming of metabolism, appetite, and endocrine status contributing ultimately to morbidities such as obesity and diabetes."*

Other scientists have commented that the epigenetic changes leading to overweight, obesity and diabetes, as a result of exposure to environmental factors during foetal development, called foetal programming, are caused by endocrine disruption, and that these effects can be passed on to subsequent generations (e.g. Newbold et al 2007; Valvi et al 2011).

Pesticides implicated in obesity, diabetes and metabolic disease

Low-level exposure to organochlorines such as DDT, endrin, lindane and HCB, organophosphates and carbamates can all cause weight gain (Newbold 2010).

Organochlorines

Organochlorines may cause weight gain by interfering with most of the mechanisms involved in weight control by:

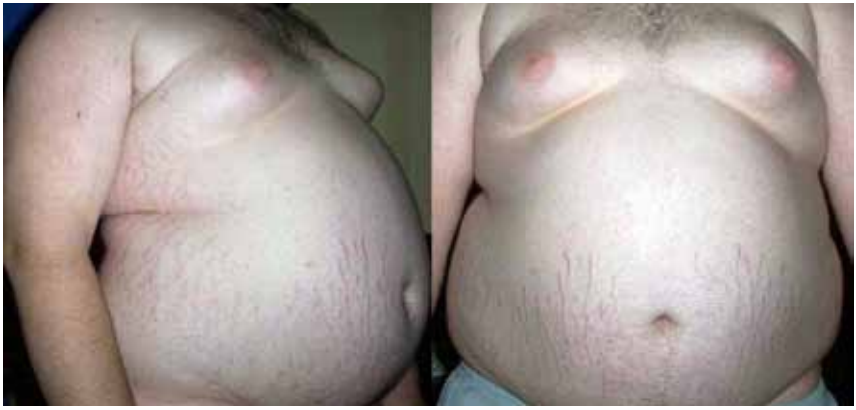
- disrupting the weight-controlling hormones such as catecholamines, thyroid hormones, estrogens, testosterone, corticosteroids, insulin, growth hormone, and leptin;
- altering the levels of and sensitivity to the neurotransmitters dopamine, noradrenaline, and serotonin;
- interfering with metabolic processes; and
- damaging nerve and muscle tissues (Baillie-Hamilton 2002).

There is evidence that pre- and post-natal exposure to these chemicals may be particularly problematic. One of the most recent studies found that *in utero* exposure to DDE was strongly associated with two indicators of early obesity: rapid weight gain in the first 6 months and elevated body mass index at 14 months. There is substantial evidence that rapid weight gain in the first

few months of life gives rise to obesity or related metabolic disorders later in life, and that BMI at 1-2 years is strongly predictive of later obesity. This Spanish study found that babies born to normal-sized mothers with higher than average blood levels of DDE were twice as likely to grow rapidly during the first six months of life than those born to mothers with the lowest levels of DDE. By 14 months of age, those from the mothers with the highest level were four times more likely to be overweight (as measured by BMI) (Mendez et al 2011).

A number of other studies have also shown that exposure to DDE may affect postnatal growth:

- one study showed that high prenatal exposure to DDE decreases height in children (Ribas-Fitó et al 2006a);
- one found that higher childhood DDE concentrations were associated with reduced height of girls but not boys (Karmaus et al 2002);
- another found that higher prenatal exposure to DDE was associated with greater height around the time of puberty in boys but not girls (Gladen et al 2000);
- babies born in Belgium with elevated levels of DDE in their cord blood had slightly elevated body mass indexes in the first 3 years of their lives (Verhulst et al 2009);
- a study in Spain found that cord blood concentrations of DDE were associated with overweight in girls, and of DDT with overweight in boys, at 6.5 years of age (Valvi et al 2011);
- a number of other studies have shown elevated body mass index and/or body weight from exposure to DDT or DDE prenatally across the placenta (La Merrill & Birnbaum 2011).



- However, results are not consistent and a recent study of boys in Russia found elevated levels of organochlorine pesticides (HCH, HCB, DDE) in boys at age 8-9 were associated with reduced growth and reduced body mass index during the prepubertal period (Burns et al 2012).

Exposure to HCB is also implicated in obesity: children in Spain whose mothers were exposed to HCB during pregnancy had a higher risk of being overweight and obese at 6 years of age (Smink et al 2008).

Currently-used pesticides

However, it is not just the largely obsolete organochlorines that are a problem. A Danish study published in 2011 found that children exposed prenatally to currently used pesticides—their mothers worked in greenhouses during early pregnancy—were not only born with lower birth weight but by the ages of 6 to 11 years they had significantly higher body mass index and body fat percentage, the latter being nearly one third higher (Wohlfahrt-Veje et al 2011).

Of the currently used pesticides, OPs are particularly implicated in obesity and diabetes because of their ability to disrupt glucose metabolism, and cause insulin resistance, insulin deficiency and 'dyslipidemia'[38] (Cooper et al 2011). Laboratory studies have implicated a number of specific OP pesticides, including chlorpyrifos, parathion and diazinon:

- foetal and neonatal rats exposed to chlorpyrifos had excessive weight gain and leptin dysfunction (leptin is a hormone that regulates appetite) (Lassiter & Brimijoin 2008);
- neonatal rats exposed to parathion had increased weight gain and signs of a pre-diabetic state (such as elevated serum glucose and impaired fat metabolism) (Lassiter et al 2008);
- neonatal male rats exposed to sub-toxic levels of chlorpyrifos produced, in adulthood, a "metabolic pattern for plasma lipids and insulin that resembles the major adult risk factors for atherosclerosis and type 2 diabetes mellitus", i.e. elevated cholesterol and triglycerides, and insulin after eating (Slotkin et al 2005);
- neonatal exposure of both male and female rats to diazinon resulted in diabetes-like metabolic dysfunction in adult rats (Adigun et al 2010);

[38] High levels of blood cholesterol and triglycerides.

- developmental exposures to chlorpyrifos cause appetite disorders in adulthood (Aldridge et al 2004).

Thayer et al (2012), reporting on a workshop of scientists gathered to discuss the role of environmental chemicals in diabetes and obesity, commented that "the general findings are that early-life exposures to otherwise subtoxic levels of OPs result in pre-diabetes, abnormalities of lipid metabolism, and promotion of obesity in response to increased dietary fat".

Thayer et al (2012) also identified sulfonylurea herbicides and imidazole fungicides as potentially implicated in obesity and diabetes, because of their effects on weight gain, blood sugar levels, or the pancreas.

4.7 Immune function, allergies, asthma

> *Immune cells reside in virtually every tissue in the body and exert regulatory influences over the function of those organs. If the immune cells are dysfunctional the organs are usually dysfunctional as well…Adult exposure immunotoxicity data have little to no relevance for the developing immune system.* | *(Dietert 2011)*

Any disruption to the normal development of a child's immune system can result in childhood afflictions such as respiratory allergy, type 1 diabetes, recurrent otitis media[39], and paediatric coeliac disease[40] (Dietert 2011), but it can also have far reaching consequences to that person's health throughout life including their ability to deal with viruses, bacteria, parasites, tumour cells, and to avoid chronic allergic, inflammatory and autoimmune conditions and cancers.[41] For example, disruption by chemicals to the complex balances between the T helper cells 1 & 2 (Th1 and Th2), which are types of lymphocytes, can result in such things as allergies, asthma, reduced ability to ward off infections, development of leukaemia, and development of autoimmune disease (Hertz-Picciotto et al 2008). It is claimed that the incidence of infectious disease in childhood is elevated following exposure to contaminants during pregnancy or through breastfeeding (Richter-Reichhelm et al 2002).

[39] Middle ear infection.

[40] Disease of the small intestine causing gas, diarrhoea, distended tummy, irritability, depression, failure to thrive, intolerance to gluten in grains, etc.

[41] These can include conditions as seemingly unrelated as multiple sclerosis, atherosclerosis, psoriasis, asthma, Alzheimer's Disease, Parkinson's Disease, Graves Disease, myalgic encephalomyelitis, coeliac disease, acute myocardial infarction, inflammatory bowel disease, type 1 diabetes, hearing loss, rheumatoid arthritis, lupus, infertility, endometriosis, loss of taste, alopecia, fatty liver, and kidney disease. Some of the inflammatory conditions can lead to cancers later in life including lymphoma, leukaemia, and thyroid, colon, lung, and skin cancers (Dietert 2011).

Because the balance of Th1 and Th2 during foetal life changes after birth, the effects of chemicals on immune development during critical windows of the pre- and early post-natal periods are not the same as effects on adult immune systems (Dietert & Piepenbrink 2008).

Chemicals can induce increased (hypersensitivity) and decreased (suppression) immune response, including autoimmune and inflammatory responses (Hertz-Picciotto et al 2008). Additionally, it seems that there is a strong connection between the development of the immune system and that of the central nervous system, such that disruption to critial events in the development of the immune system may result in neuro-behavioural and psychiatric disorders (Hertz-Picciotto et al 2008).

The immunotoxicity of a wide range of pesticides has been established in laboratory and epidemiological studies, but there is little data on the effects of these pesticides following prenatal and early childhood exposures. Early childhood exposure to pesticides and particularly herbicides has been found to increase risk of asthma (Salam et al 2004). Other studies show that prenatal exposure to pesticides can result in increased lung and middle ear infections as well as asthma (Wigle et al 2008). One study in the US found significantly elevated allergies and hay fever in male children who had been exposed while still in the womb to pesticides, particularly 2,4-D or organophosphates (Weselak et al 2007).

Organochlorines

Some studies have however found links between organochlorine exposure and immune problems in children. One study found an increase in the incidence of middle ear infection (otitis media) in Inuit children in their first year of life with elevated prenatal exposure to DDE, dieldrin and HCB (Dewailly et al 2000). Another found an increase in lower respiratory tract infections in children in Spain, whose mothers had elevated levels of DDE in their blood during pregnancy (Sunyer et al 2010). Children exposed to DDT in Germany had significantly higher risk of asthma (Karmaus et al 2001b). Another study in Germany found that children aged 4-7 exposed to chlordane and heptachlor through fumigation of homes for termites, experienced increased allergies, skin problems and upper respiratory tract infections. Analysis

of their blood showed abnormalities in a number of immune biomarkers, such as cytokines and neuropeptides, indicating problems with T-cell regulation, inflammation, and hypersensitivity (Phillips 2000). Animal studies also show that the developing immune system is especially vulnerable to organochlorines such as chlordane, HCB, DDT, and kepone (Dewailly et al 2000).

A study in Egypt found that elevated levels of chlorinated pesticides (DDT, HCH, endosulfan, heptachlor, aldrin, endrin, dieldrin) in the blood of breast-fed infants and their mother's milk was significantly correlated with increased bleeding tendency in the infants, together with decreased white blood cell count, lymphocytes and cytokines, described by the authors as "an organochlorine-induced immunotoxicity" (Schaalan et al 2012).

Other studies have shown that low-level childhood exposure to DDE altered immune system biomarkers such as increased IgE levels and reduced eosinophilic granula (Karmaus et al 2005). In animal studies, exposure to heptachlor and methoxychlor during gestation, lactation or early juvenile stage results in suppression of the immune system but the same doses do not cause immunotoxicity in adults (Richter-Reichhelm et al 2002).

Organochlorines are also associated with reduced ability to suppress tumours, thus increasing the risk of cancer:

- A US study found that elevated levels of chlordane in cord blood were associated with reduced levels of a cytokine that is involved in tumour suppression (Neta et al 2011).
- A Canadian study found that higher levels of DDE, HCB, and PCBs were associated with reduced levels of tumour necrosis factor (Bilrha et al 2003).

Synthetic pyrethroids

Synthetic pyrethroid insecticides also cause problems for the developing immune system. Elevated levels of permethrin in cord blood were associated with reduced levels of an anti-inflammatory cytokine which is part of the immune mechanism involved in asthma and allergy: reduced levels increase asthma and allergy (Neta et al 2011).

Perversely, insecticide-treated bed nets (ITN) used to protect children from malaria, appear to lower children's immunity to the disease (Guyatt et al 1999). In a study in Tanzania, children using the ITNs had lower levels of antibodies against 'variant surface antigens' which are important to the development of natural immunity to the malaria parasite *Plasmodium falciparum*

(Askjaer et al 2001). ITNs are treated with pyrethroid insecticides, commonly permethrin or deltamethrin, but also other pyrethroids. The study did not identify which insecticide was used originally on the bed nets but did state that the nets had been retreated annually with alpha-cypermethrin.

Any disruption to the normal development of a child's immune system... can have far reaching consequences to that person's health throughout life.

Allowing pregnant women and newborn children to be exposed to immunotoxic pesticides unacceptably increases the risks of the children developing asthma, type 1 diabetes and a raft of chronic conditions including cancer that significantly reduce the quality of life (Dietert 2011).

A note about asthma

Respiratory problems due to pesticide exposure may be related to immune system dysfunction, direct irritation effects, or other mechanisms (Bernstein et al 1999; Upton & Caspar 2008). Many pesticides are powerful respiratory irritants and may directly damage the bronchial mucosa making the airways sensitive to allergens or other irritants, and causing non-immunological reactive airways dysfunction. They can exacerbate existing asthma or trigger attacks. Exposure can involve inhaling soil or liquid aerosols or vapour. Respiratory toxicity, including wheeze, may even occur with dermal absorption of pesticides such as OPs, carbamates, and paraquat (Hernández et al 2011). One study in New Zealand concluded that the bioaerosol effect of inhaling an aerially sprayed formulation of *Bacillus thuringiensis kurstaki* (Btk) might be responsible for an increase in childhood asthma (Hales et al 2005). The hospital admission rate for childhood asthma increased by 40% during the period of aerial spraying, and it was more than 50% for male children aged 0-4 (Gallagher 2005).

4.8 Reproductive

Foetal exposures to endocrine-disrupting pesticides have been linked to a number of problems with the reproductive system, ranging from birth defects such as hypospadias and cryptorchidism which were discussed earlier in this chapter, through early onset puberty and other effects on sexual maturity, to a whole raft of hormone-related problems in adulthood, including menstrual irregularities, uterine fibroids, endometriosis, and infertility (Crain et al 2008). Although these latter problems are largely adult conditions rather than those of childhood, their genesis often lies in exposures to endocrine disrupting substances during foetal development and early childhood.

Girls

Prenatal and early childhood exposure to endosulfan in the South Indian region of Kasargod resulted in a wide variety of birth defects, neurodevelopmental conditions, endocrine and reproductive problems. In girls, the latter included endometriosis, early menarche, frequent menstrual disorders including excessive flow and irregular cycle, and altered levels of hormones, particularly higher levels of luteinising hormone, progesterone and oestradiol (NIOH 2002). Subsequent laboratory research has shown that neonatal exposure to endosulfan disrupts development of the uterus (Milesi et al 2012).

Early puberty

The age that girls go through puberty varies, but generally that age has been decreasing over the last 40 years, at least in industrialised countries, with breasts appearing one or two years earlier than in the past. Early puberty[42] puts girls at increased risk of depression, sexual victimization, obesity, polycystic ovarian syndrome, breast cancer, and social problems such as experimenting with sex, alcohol, or drugs at a younger age (Barrett et al 2009).

There may be a number of factors involved in stimulating early onset puberty, including low birth weight,[43] obesity,[44] and exposure to endocrine-disrupting pesticides (Krstevska-Konstantinova et al 2001; Steingraber 2007; Schoeters et al 2008). Extremely precocious puberty in a 4-month-old girl in France is thought to have resulted from oestrogenic activity caused by exposure of both parents to a number of pesticides. The baby girl had breast enlargement, 3 episodes of menstruation, markedly increased uterine length and maturation, and "dramatically high oestrogenic activity"—5 times higher than expected (Gaspari et al 2011b). The father also reported decreased libido. DDT, DDD, lindane and endosulfan sulphate were all found in her blood, that of her mother, and in the soil of the farm where they lived. Only endosulfan sulphate was found in her father's blood. Twenty-two tonnes of DDT, lindane and endosulfan were stored, and had been for many years, on the farm.

High levels of DDT metabolites were also found in girls in Puerto Rico experiencing early expression of secondary sex characteristics (Guillette et al 2006).

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[42] Early, or precocious, puberty is described as "initial breast and pubic hair development before 7 years of age for Caucasian-American girls and 6 years of age for African-American girls" (Guillette et al 2006).

[43] Low birth weight, reduced intrauterine growth, and premature birth are linked to exposure to a number of pesticides – see section 4.3.

[44] Obesity is also linked to exposure to a number of pesticides – see section 4.6.

In a study on Chinese textile workers, for each 10ng/g increase in serum total DDT, there was a reduction of 0.2 years in daughter's age of reaching menarche.[45] In another study, the authors estimated for each 15 µg/L of DDE increase in the mothers' serum, the daughters' age of menarche was reduced by one year (Colborn & Carroll 2007).

Currently used pesticides are also associated with early puberty: in a study of women greenhouse workers in Denmark, the daughters of those exposed to pesticides (a total of 124 different active ingredients) during the first trimester of pregnancy showed earlier breast development (mean onset was 8.9 years compared with 10.4 years for the unexposed) (Wohlfahrt-Veje et al 2012a).

There is evidence also from laboratory studies that some pesticides may contribute to delayed puberty, for example short-term exposure of juvenile female rats to low doses of the synthetic pyrethroid esfenvalerate delayed the onset of puberty (Pine et al 2008).

Breast development

A comparison of two similar and genetically-related populations in the Yaqui valley of Mexico[46] revealed the effects of pesticide exposure on breast development in girls. When chemical pesticides and fertilisers were introduced into the Yaqui valley in the late 1940s, there was a philosophical split between those of the Native American inhabitants who embraced them and those who did not—the latter group shifting into the hills where they stayed. In the valley, up to 90 separate applications of pesticides were made per year, including multiple organochlorine and organophosphate mixtures and pyrethroids. As well as this agricultural use, household insecticides were used throughout the year. In contrast, the ranching lifestyle of the highlands required no pesticide use, and the government DDT applications each spring for malaria control were their only contact with pesticides. In comparison, the pesticide-exposed girls in the valley developed larger breasts but a "poorly-defined relationship between breast size and mammary gland development", with less mammary tissue and more fat tissue. Cord blood samples taken from this town two years before the girls in this study were born had high levels of DDT metabolites, lindane, heptachlor, aldrin, endrin and dieldrin (Guillette et al 2006).

Studies on rats show that prenatal exposure to environmentally relevant levels of atrazine can delay development of the mammary gland

[45] First menstruation.
[46] This is the same population referred to in the section on neurodevelopment.

during puberty and into adulthood, and decrease later milk production and duration of lactation. The authors of the study proposed that "embryonic exposures alter breast architecture, as supported by the discovery that pesticide-exposed girls exhibit breast development that is associated with adipose deposition and not ductal or glandular growth" (Crain et al 2008), referring to the Guillette study described above.

Female adult reproductive disorders

UTERINE FIBROIDS

Uterine fibroids are non-cancerous tumours of the uterus that cause pain, heavy periods and abnormal bleeding, infertility and complications during pregnancy, and may necessitate a hysterectomy. Animal studies have shown that pre-natal and neonatal exposure to endocrine disruptors can induce uterine fibroids later in life, and that adult exposures to endosulfan, kepone, toxaphene, dieldrin and methoxychlor all contribute to their growth (Barrett et al 2009; Crain et al 2008).

ENDOMETRIOSIS

Endometriosis is a chronic, painful, inflammatory condition that occurs in women when the tissue that normally lines the inside of the uterus (the endometrium) grows outside the uterus on, for example, the ovaries, abdomen, or pelvis. It is a major contributor to female infertility. There is overwhelming evidence from animal studies that links endometriosis with exposure to organochlorine pesticides including DDT and methoxychlor, as well as other organochlorines such as dioxin and PCBs, and the suggestion is that prenatal exposures to organochlorines can "program uterine tissue in such a way that it is more likely to develop endometriosis following secondary exposures in adulthood" (Barrett et al 2009).

POLYCYSTIC OVARIAN SYNDROME (PCOS)

Polycystic ovarian syndrome is a disorder affecting metabolism and reproduction. It commonly involves diabetes, high cholesterol, high blood pressure, high androgen production, premature pubic hair growth, irregular periods, abnormal bleeding, pelvic pain, ovarian cysts, and excessive facial and body hair. It arises during prenatal development and particularly from exposure to high androgen levels during the development of the ovary and follicles. It is reasonable therefore to assume that exposure to pesticides that increase the levels of, or mimic androgens such as testosterone, may be implicated in the development of this syndrome. There appears to be little research on this, but one study has linked PCOS with exposure to the plastic ingredient bisphenol A (Barrett et al 2009; Crain et al 2008).

MENSTRUAL CYCLE PROBLEMS

Altered menstrual cycles can interfere with the ability of women to conceive (fecundity). There seems to be some evidence that exposure to endocrine disruptors, such as bisphenol A and dioxins, during foetal development can lead to menstrual cycle irregularities after puberty. Some studies have shown that exposure to organochlorine pesticides shortens the menstrual cycle and exposure to hormonally active pesticides such as lindane, atrazine, mancozeb or maneb increases the length of the cycle, and causes missed periods and bleeding between periods (Farr et al 2004; Crain et al 2008). It is reasonable, therefore, to suspect that prenatal exposure to some endocrine disrupting pesticides may also influence the menstrual cycle. This is supported by the finding that elevated levels of DDT in mothers' blood, just after the birth of their daughters, correlated with their daughters decreased probability of getting pregnant 28-31 years later (Cohn et al 2003).

FERTILITY

Whilst there is little information about foetal or childhood exposures to pesticides on subsequent fertility, it is known from laboratory tests that the exposure of pregnant rats to the pesticides chlorpyrifos and methoxychlor results in changes to the gonadotrophin-releasing hormone, which is suggested by the authors of the study "to have long-lasting consequences to the fertility of the animal" (Miller et al 2004).

In a study in China, male rats were exposed to a mixture of the OPs dichlorvos, dimethoate and malathion before mating with females, who were subsequently exposed to the same pesticides during gestation and lactation. The offspring, when sexually mature, had abnormal levels of progestin, estradiol, testosterone, and luteinizing hormone. Females had enlarged uteruses and males enlarged testes and epididymis, and there was a reduction in rates of pregnancy and live births (Yu et al 2011).

Boys

Prenatal exposure to pesticides that have oestrogenic (feminising) or anti-androgenic (anti-masculinising) effects can result in disrupted male reproductive development that affects not only boys but also adult reproductive function, particularly causing hypospadias, undescended testes, smaller testes, testicular cancer, epididymal cysts, lowered sperm counts, decreased sperm quality, and poor fertility (Toppari et al 1996). Numerous pesticides have been found in laboratory studies to reduce testosterone production (e.g. linuron, diuron, iprodione) or block its action, (e.g. vinclozolin, procymidone, chlorpyrifos-methyl). Diuron also damages the testes. Numerous other

pesticides have anti-androgenic effects, including DDE, fenitrothion and prochloraz; or oestrogenic effects, including DDT, methoxychlor, lindane, and chlordecone. Prenatal and neonatal exposure to any of these can adversely affect a boy's reproductive development (Toppari et al 1996; Sharpe 2009). Even exposure during puberty can be a problem: mice exposed during puberty to cypermethrin suffered decreased testosterone levels (Jin et al 2011).

A study of boys born to women occupationally exposed to pesticides in greenhouses in Denmark found that maternal exposure had adverse effects on reproductive development of their sons. The boys had shorter penises and smaller testes. Follicle-stimulating hormone and the ratio of luteinizing hormone to testosterone were increased (Andersen et al 2008). These effects persisted when the same boys were re-measured at 6-11 years of age: boys whose mothers were in the highest exposure group had 24.7% smaller testes and 9.4% shorter penises compared with unexposed mothers, but pituitary and testicular hormones did not differ between exposed and unexposed (Wohlfahrt-Veje et al 2012b).

Diminished reproductive health in boys has also been associated with exposure to pesticides in South Africa: farm boys highly exposed to pesticides had lower serum luteinizing hormone and higher oestradiol and follicle stimulating hormone, as well as reduced height and weight, compared with non-farm boys with lower pesticide exposures (English et al 2012).

Endosulfan is one pesticide found to adversely affect boys' development. In Kasargod, South India, where villagers were exposed to repeated aerial spraying with endosulfan, boys suffered delayed sexual development (significantly reduced development of pubic hair, testes, and penis), reduced synthesis of testosterone and higher levels of luteinising hormone (NIOH 2002; Saiyed et al 2003). These findings correlate with animal studies that show endosulfan caused a number of adverse effects on male reproductive parameters in rats, reducing fertility: degeneration of seminiferous tubule epithelium, reduced sperm count, altered spermatogenesis, increased abnormal sperm, testicular necrosis, and aspermatogenesis (Dalsenter et al 1999; ATSDR 2000; Sinha et al 2001). Effects were reported to be greater if exposure occurred during the developmental phase (adverse effects on male offspring have occurred even at dose levels that were not toxic to the mother (Sinha et al 2001). ATSDR (2000) concluded that, for humans, exposure during the period of testicular maturation may result in disturbed spermatogenesis at sexual maturity (ATSDR 2000).

Exposure to atrazine during lactation can result in damage to the prostate

gland: the herbicide suppressed suckling-induced increases in prolactin secretion in lactating rats which then resulted in elevated prolactin levels in the male offspring at puberty and subsequent persistent inflammatory changes in the prostate (WHO 2006).

Transient exposure of female rats to the fungicide vinclozolin during the period of gestation when sex determination is occurring resulted in the male offspring having decreased sperm production and viability in adulthood, and increased infertility; and these effects were passed on to male offspring through the next three succeeding generations (Anway et al 2005). ■

MOTHER AND CHILD INUIT SCULPTURE DONATED TO THE STOCKHOLM CONVENTION SERVES AS A PRECAUTIONARY REMINDER OF THE CONVENTION'S GOAL TO PROTECT HEALTH AND THE ENVIRONMENT.

There can be no keener revelation of a society's soul than the way in which it treats its children.

~ NELSON MANDELA

5

Regulatory and policy failure

"Government policies guided by supposedly 'science-based' risk assessment methodology have proven to be more effective at protecting vested interests than in protecting health and the environment. In fact, 'science-based' risk assessment is not the decisive factor in determining the regulatory status of a toxic chemical. The reality is that corporate interests and political expediency are the dominant considerations influencing regulatory decisions pertaining to toxic chemicals, especially in Southern countries where financial, technical, human and other resources are sorely lacking and where socio-political circumstances are conducive for powerful chemical companies to exert influence and manipulate public policy. The unequal power relations between the strong and the weak, between the rich and the poor, and between the First World and the Third World is very much in the decision-making processes of government. Decisions that tend to protect health and environment are allowed only in so far as these do not threaten significantly the dominant economic interests or only when strong public pressure is exerted on government. It is not unusual, for example, that bureaucrats ignore the recommendations of a government appointed toxicology committee or even abolish the committee itself rather than ban or restrict the toxic chemicals that the committee has deemed to be too dangerous to be allowed into the market. Even intergovernmental bodies are not immune to corporate influence as technical committees are packed with corporate scientists or scientists under their influence." | *(Quijano 2003)*

It is clear from the preceding chapters that international chemicals conventions, national pesticide regulatory processes, and government policies are all failing to protect children from the harmful effects of pesticides. As the years unfold, scientists are learning more and more about the manifold ways in which seemingly innocuous exposures to low levels of pesticides, such as are commonly found as residues in food or drift on the wind, are undermining the health and well-being of our children, and leaving them with a lifetime legacy of damage and failed potential. With the increasing incidence of neurodevelopmental problems and chronic diseases, independent scientists and civil society organisations have been trying to draw the attention of those same institutions to the problems pesticides are causing. But by-and-large the ears are deaf, the eyes are blind and the attention is turned away.

Why?

International chemicals conventions, being based on consensus, are sadly weakened by vested interests – witness the continued failure of the Rotterdam Convention on Prior Informed Consent to list chrysotile asbestos because exporting countries like Russia and previously Canada simply block agreement; and the long drawn-out battle with India, the main manufacturer of endosulfan, to list the pesticide under the Stockholm Convention on Persistent Organic Pollutants for a global phase-out, even though that country has seen the worst of the effects of endosulfan. But international conventions and national regulations are inter-linked—the former can facilitate change at the national level, and strong national policies can promote strong leadership in international conventions to make them truly effective in protecting children.

There are three main ways in which national regulatory processes and government policies are failing to protect children from pesticides:

1. Pesticide registration processes fail to assess the real effects of pesticides on children.
2. Pesticide registration processes and government policies and practices fail to provide protection to children from the pesticides that they have registered, let alone those that are used illegally.
3. Governments fail to question the received 'wisdom' that pesticides are necessary and to look beyond them at highly sustainable methods of managing pests, weeds, and diseases.

All of these areas of failures stem from a primary failure to apply the precautionary principle, despite its widespread inclusion, in some form or other, in a number of international conventions and treaties, such as the Stockholm Convention on Persistent Organic Pollutants.[47]

[47] Others include World Charter for Nature, adopted by the UN General Assembly in 1982; [Montreal] Protocol on Substances that Deplete the Ozone Layer (1987); Second North Sea Declaration – Calling for Reduction of Pollution (1987); Nordic Council's International Conference on Pollution of the seas (1989); Paris convention for the Prevention of Marine Pollution from Land-based sources (PARCOM) (1989); Bergen Declaration of Sustainable Development (1990); Second World Climate Conference – Ministerial Declaration (1990); Bamako Convention on Transboundary Hazardous Waste into Africa (1991); Rio Declaration on Environment and Development (1992); Helsinki Convention on the Protection and Use of Transboundary Watercourses and International Lakes (1992); Framework Convention on Climate change (1992); Maastricht Treaty on the European Union (1994); 4th North Sea Conference of Ministers (1995); Barcelona Convention; United Nations Agreement on the Conservation and Management of Straddling Stocks and Highly Migratory Fish Stocks (1995); UN Intergovernmental Panel on Climate Change (IPCC 1995); Article 10 of the Cartagena Protocol on Biosafety to the Convention on Biological Diversity (2000); the Strategic Approach to International Chemicals Management (SAICM) (2006).

5.1 Applying the precautionary principle to protect children

The precautionary principle was designed to deal with situations exactly such as children face with ongoing low doses exposures to multiple pesticides. It provides a framework, procedures, and policy tools for situations of scientific complexity, uncertainty and ignorance, where there is a need to act before there is strong proof of harm in order to avoid, or reduce, potentially serious or irreversible threats to health or the environment.

Application of the precautionary principle is particularly appropriate for the protection of children's health because:

- the science underlying the impacts of pesticides on children is more complex, less researched and less understood than that of the impacts on adults;
- the likelihood of serious harm to children is greater than for adults because of their greater exposure and developmental vulnerabilities;
- children are involuntarily exposed to a greater proportion of the risks caused by society's activities than adults, yet they have less power to avoid them; and
- children benefit proportionally less than adults from society's risk-generating activities (Martuzzi & Tickner 2004).

pesticides are inherently hazardous and should be presumed harmful until proven otherwise

Applying the precautionary principle entails recognition that pesticides are inherently hazardous and should be presumed harmful until proven otherwise. It acknowledges that, historically, most hazardous chemicals have eventually been shown to cause serious and irreversible damage to human health and the environment. It accepts the reality that the long-term impacts of toxic chemicals are difficult to predict and often impossible to prove. It is not dependent, as is risk assessment, on the generation of extensive scientific data and exhaustive quantitative analysis of risks as pre-conditions to decision-making, policy formulation, and action. This is particularly important for third world countries lacking the resources needed to characterize the risks of pesticide exposure (Quijano 2003).

Professor Romeo Quijano of the University of the Philippines sets out the following essential elements of the precautionary principle (Quijano 2003):

1. ***P****revention – This is the first essential element of the precautionary principle. Prevention is the major activity, not mitigation. Avoidance of exposure is the major concern, not defining the limits of exposure as in*

the risk assessment approach. The question asked is not how much exposure is allowable but whether the exposure is necessary in the first place.

2. ***R**everse onus – This means putting the burden of proof of safety on the polluters and not putting the burden of proof of harm on the potential victims.*
3. ***E**limination – The ultimate goal under the precautionary principle is the elimination of toxic chemicals, not just the management of risks. Especially for persistent organic pollutants (POPs), elimination is the only long-term option because risks are considered unmanageable.*
4. ***C**ommunity-oriented – The health of communities is a primary concern of the precautionary principle. The people's basic right to health and to a healthful environment takes precedence over corporate and proprietary rights to profit from those communities.*
5. ***A**lternatives assessment – More often than not, the need that chemicals are supposed to address can be addressed more effectively and safely over the long term by non-chemical alternatives.*
6. ***U**ncertainty is a threat – "Absence of evidence is no evidence of absence (of harm)". To be meaningfully protective, therefore, an assessment process looking into the potential environmental and health impacts of a chemical should consider uncertainties as a warning signal.*
7. ***T**echnically/scientifically sound – The evaluation process using a precautionary approach is not just an arbitrary procedure based on mere speculations and unfounded fears. It is based on the best available scientific evidence and guided by technically sound analytical procedures.*
8. ***I**nformation unrestricted – The application of the precautionary principle would require full disclosure and accessibility of information relevant to the appraisal of potential threats that a chemical brings to human health and the environment. The appraisal process made subordinate to corporate interests [e.g. confidentiality of corporation-generated data] would be tantamount to the violation of people's fundamental right to health and a healthful environment.*
9. ***O**pen – A risk appraisal system based on the precautionary principle is an open, democratic and participatory process. It is not the exclusive domain of elite scientists and government regulators. It is the people's right to participate in the decision-making processes relevant to the protection of their health and their environment.... The people have the right to determine for themselves what chemicals they need and which they don't need, what risks are acceptable and what are not acceptable. This right is also an extension of the right to health, since without it, the right to health is unattainable.*

10. ***N**eed-based – Assessing the need for the chemical as part of a comprehensive and integrative approach to risk appraisal before it is allowed to be released into the market. The benefits that the chemical brings to people must be reasonably clear and more important than the potential threats of harm.*

5.2 Pesticide registration

industry tests are biased towards conclusions of safety

Most current pesticide regulatory processes are the exact antithesis of the precautionary principle. They are based on a risk assessment model with its underlying assumption that "there is a 'safe' level below which a toxic pesticide is not toxic" (Antoniou et al 2011); and that the 'safe' level can be determined by the manufacturer carrying out a series of laboratory tests on animals, using high doses of a single pesticide looking for prescribed effects, and then reporting the results faithfully to the regulator. There are many problems inherent in this approach.

Conflict of interest

There is an obvious conflict of interest in industry providing its own studies for registration of a pesticide. "*Every time industry studies are compared with those from the independent scientific literature, the same verdict is reached: industry tests are biased towards conclusions of safety*" (Antoniou et al 2011). There are also many cases of data from industry and their associated laboratories being found to be fraudulent, for example:

- Eleven animal tests carried out on chlordane and heptachlor between 1959 and 1972 were withheld from the US EPA until a court ruled that the studies be released. The studies were purported to conclude that the pesticides posed no significant threat to the unborn but, when the raw data were re-analyzed, the opposite was found to be true, according to Dr Kate Short (1994). A later review found "a high incidence of unequivocal liver cancer, which in most cases were statistically significant" (Epstein 1990).
- In the late 1970s, Industrial Bio-Test, the USA's then largest independent testing laboratory, was found to have routinely falsified data on 140 different pesticides. The US EPA reviewed 801 of its studies on the pesticides and found 74% to be invalid. In 1981, four employees were indicted and charged with falsification of data (Short 1994).

- In 1991, the US EPA placed Craven Laboratories[48] in Texas under investigation for falsifying residue data for at least seventeen pesticides. They were convicted in 1992 (Short 1994).
- In 1995, the federal judge in Columbus, Georgia, fined pesticide manufacturer DuPont USD 101 million for withholding research data and misrepresenting results during a trial over the fungicide Benlate. Judge Elliot said that "put in layman's terms, DuPont cheated. And it cheated consciously, deliberately and with purpose" (Bane 1995).

It is clear then that the pesticide industry and its data cannot be relied upon to protect the health and well-being of children.

'Good Laboratory Practice'

The tests required for registering pesticides in many countries must adhere to the rules of what is termed 'Good Laboratory Practice' (GLP). GLP was originally developed by the US Food and Drugs Administration in 1978, apparently in an unsuccessful attempt to end fraudulent industry tests such as the Industrial Bio-Test scam. Eventually the intergovernmental trade and development organisation OECD (Organisation for Economic Cooperation and Development) developed guidelines for GLP, with the aim of facilitating trade by establishing a standardised set of rules for tests for all WTO member countries. Note: the purpose of GLP is to facilitate trade, not to protect children from harmful pesticides. The GLP guidelines determine the animals to be experimented upon, the number of animals required for the tests, how long they should be exposed and the doses of pesticides that should be used. They specify how the studies are to be planned, carried out, monitored, recorded and reported. "*GLP is a management system. It is not a guarantee of 'good science'*" (Antoniou et al 2011).

Many regulatory bodies rely on industry-generated data and reject studies from independent scientists

Many regulatory bodies, from the European Food Safety Authority in the north to New Zealand's Environmental Protection Agency in the south, rely almost exclusively on industry-generated data from GLP tests for pesticide assessment, determining it to be the "highest quality data" and steadfastly rejecting studies from independent scientists reported in open peer-reviewed literature, because they have not been carried out according to GLP (Antoniou et al 2011).

There are good reasons that many independent, often government-funded,

[48] Both Industrial Bio-Test and Craven Laboratories carried out trials on pesticides for chemical companies, such as Monsanto, which they then submitted as registrational data.

scientists choose not to use GLP tests: the test protocols are antiquated, mostly focussed on a narrow range of gross effects such as birth defects and tumours that occur at high dose rates, assume there is a 'safe dose' below which effects do not occur, demand a positive-dose response, and terminate the animals before old age is reached. So they often miss the functional changes (such as in immune, endocrine and metabolic functions) which usually occur at lower doses than those prescribed by GLP, doses that are more in line with normal human exposures; and they miss the conditions that develop in old age after earlier exposures (Antoniou et al 2011). It is evident from the material presented in Chapter 4 that these functional changes are of the utmost significance, not only in terms of the child's health, but also its lifelong chances of disease and chronic ill health, and potential for sociability, learning and quality of life. Since the early 1990s, independent government-funded scientists have been publishing studies showing that chemicals, including pesticides, at doses thousands of times lower than those generally considered toxic, interfere with normal human development.

Harassment of Independent Scientists

The Permanent People's Tribunal hearing on Agrochemical Transnational Corporations (TNCs) in Bangalore, 2011 found that "The undermining of independent science and research and silencing of uncomfortable truth by powerful TNCs is widespread."

"Poisoning with atrazine, a herbicidal pesticide (produced by Syngenta): Atrazine is another endocrine disrupter that caused severe health effects, including demasculinisation and feminisation of males both in humans and in animals. This is widely reported in animal studies internationally. Its use in areas in the US can, for example, be correlated with the feminisation of amphibians. Whilst banned in the European Union, atrazine remains a widely used herbicide in many parts of the world. Despite well documented proof to its endocrine disrupter effects in the scientific literature, Syngenta chooses to harass and discredit scientists involved in research rather than stop its production and use."

Source: PPT 2011

"GLP is a 'shield' that industry uses to protect itself from inconvenient findings in the independent scientific literature", and they use this to dismiss the findings of independent studies as unvalidated and irrelevant. Regulatory authorities that demand GLP tests are complicit in this fraud, according to Antoniou et al 2011.

Specific ways in which regulatory protocols fail include:

- The positive-dose response requirement fails to take into account endocrine disruption that can be stronger at very low doses than at high doses (Colborn & Carroll 2007).
- There is a concomitant assumption of a threshold below which there is no significant toxicity, but this is challenged by findings in independent scientific studies (Colborn & Carroll 2007; Antoniou et al 2011). Indeed, "the historical record shows that 'safe thresholds' for known neurotoxicants have been continuously revised downward as scientific knowledge advances. For example, the initial 'safe' blood lead level was set at 60 micrograms/deciliter (ug/dl) in 1960. This was revised down to 10 ug/dl in 1990. Current studies suggest that lead may have no identifiable exposure level that is 'safe'" (Schettler et al 2000).
- The high dose protocols fail to consider exposures that are environmentally relevant especially to the unborn and newborn, and fail to target various organ systems at critical stages of development from foetal life through to adulthood (Colborn & Carroll 2007).
- Early life exposures, i.e. during critical windows of foetal development, are not generally included in the tests required for regulatory purposes. "Current US EPA and OECD guidelines do not specify that the animals placed on study be exposed to the test chemical during *in utero* or preweaning development; most are placed on study as young adults of 5–6 weeks of age" (Makris 2011).
- Testing for the neurotoxicity of organophosphates usually only requires consideration of one mechanism, that of cholinesterase inhibition, and fails to test for developmental neurotoxicity despite the considerable and expanding literature illustrating the non-cholinergic neurotoxic effects (Schettler et al 2000).
- Animal studies tend to underestimate human vulnerability to neurotoxicants: "Regulatory decisions that rely largely on toxicity testing in genetically similar animals under controlled laboratory conditions will continue to fail to reflect threats to the capacities and complexity of the human brain as well as important gene-environment interactions" (Schettler et al 2000).
- Testing for developmental immunotoxicity is generally not carried out, and allergic, inflammatory and autoimmune effects are not looked for (Dietert 2011).
- Risks are estimated for a single chemical at a time as if it were the only one in the world, when in reality children are exposed to complex

chemical mixtures, with some of the chemicals having additive effects and others synergistic interactions to magnify the damaging effects or even cause new kinds of harm (Schettler et al 2000).

- Risks are estimated for a single chemical at a time and generally fail to consider the impact of ubiquitous exposure on society as a whole (Bellinger 2012).
- Existing body burdens of chemicals and cumulative effects are ignored in determining safe exposures (Antoniou et al 2011).
- Damaging effects of pesticides on mammary gland development are not tested for (Rudel et al 2011).
- The developmental origins of cancer and the increased carcinogenic risks to the foetus and newborn are generally not reflected in regulatory testing (US EPA 2005).

"The historical record clearly reveals that our scientific understanding of the effects of toxic exposures is not sufficiently developed to accurately predict the impact of toxicants, and that our regulatory regime has failed to protect children." | *(Schettler et al 2000)*

Overhauling the regulatory system

For all these reasons, many scientists, academics, policy-makers and civil society organsations believe that a drastic overhaul of the pesticide regulatory process is long overdue.

Many scientists, academics, policy-makers and civil society organisations believe that a drastic overhaul of the pesticide regulatory process is long overdue

At the very least, the time has come to replace the out-dated and industry-supportive risk assessment process with one based on hazard analysis and cut-off criteria for certain hazardous qualities, such as carcinogenicity, mutagenicity, developmental neurotoxicity, developmental immunotoxicity, and endocrine disruption. Unlike the old risk assessment model, this approach does not assume that when a hazard exists the risk can be managed. Instead it is based on the view that if a particular hazard exists, a less hazardous alternative should be used. Europe has instituted such a system, to a limited extent, although the hazard cut-off criteria are still insufficient to protect children. Industry is fighting tooth and nail to prevent hazard assessment gaining ground against risk assessment (Antoniou et al 2011), but it is vital that the old industry-protective regime be replaced with a new one supportive of public health and particularly children's health.

5.3 Government policies

"Recommendation to [US] government: advance less toxic pesticide alternatives."

"Recommendation to [US] government: aid in identification of least toxic alternatives to pesticide use internationally, and unless safer alternatives are not available or are impossible to implement, ban export of products that are banned or restricted for toxicity concerns in the United States."
| Statement by American Academy of Pediatrics (CEC 2012)

However, simply replacing the regulatory system is not enough. National governments must develop policies based on protecting children from exposures to pesticides that will undermine their health throughout their lifetime. Even when pesticides are known to be immunotoxic, for example, nothing is done to prevent the exposure of pregnant women and children to them (Dieter 2011). Protecting children requires a precautionary approach. Government must institute policy to stop the use of highly hazardous pesticides, as a starting point. However this also is not enough. Even the PAN International List of Highly Hazardous Pesticides does not include all the pesticides that may cause developmental neurological, immunotoxic or endocrine damage to children—because the list is based on existing regulatory outcomes. Until such time as regulatory systems are capable of identifying those pesticides which cause damage at critical development stages, all pesticides should be regarded as suspected developmental toxins, and their use be replaced by sustainable, nontoxic agroecological methods of pest, disease and weed management, and food and fibre production. And until such time as governments do this, every institution, organisation and member of society has a responsibility to ensure that pregnant women and children are not exposed to any pesticide, including as residues in food, that may cause them harm, through either acute poisoning or chronic effects that only become apparent later but cause lifelong impairment. Even that is not enough, for evidence shows that when fathers are exposed preconception to some pesticides, harm can still occur to the child.

Every institution, organisation and member of society has a responsibility to ensure that pregnant women and children are not exposed to any pesticide

Are pesticides really necessary?

In the final analysis, the only real way to protect children from the harm done to them by pesticides is go back to first principles and ask the question: do

we really need to use these pesticides? This is a question seldom asked at a policy level, the assumption is simply made that pesticides are necessary. It is even written so in the introductions of many scientific papers, but not one of them provide any proof to back this statement. Where attempts are made to justify a need for pesticides, they usually rely on comparing yields under pesticide use with those of the same system but with the pesticides removed, instead of comparing them with the yields of modern, sustainable agroecological production. There is a wealth of scientific and evidential data showing that crops can be grown perfectly well without using pesticides. In fact, the World Bank report on Community Managed Sustainable Agriculture (CMSA) in the Indian state of Andra Pradesh (Kumar et al 2009) shows that farmers' financial returns are much improved with the shift to sustainable non-pesticide management of their crops based on agroecological approaches. Over a period of 4 years in the mid 2000's, 300,000 farmers converted to CMSA on 1.36 million acres of farmland, 5.1% of the total farmland of Andra Pradesh. Since that report was published, many more farmers in Andra Pradesh have switched to bring the total to more than 10 million, farming more than 10 million hectares, according to Ramanjaneyulu & Raghunath (2011). Not only have these farmers' costs dropped and income increased, they have relief from debt and mortgages, they have improved food security, improved health, and improved soil ecology and environment. This is proof that the original presumption that pesticides are necessary is fundamentally flawed and that a major rethink of pesticide and agricultural policy is urgently required, at national and international levels. Farmers are demonstrating the way forward, but

ECOLOGICAL RICE FARMING IN VIETNAM.

national policy is slow to follow although at the international level, there is now high level support for the need to adopt agroecological practices in order to combat hunger and malnutrition. For example:

- In 2009, the International Assessment of Agricultural Knowledge, Science and Technology for Development (IAASTD)[49] answered the question it had posed in 2003: *How can we reduce hunger and poverty, improve rural livelihoods, and facilitate equitable, environmentally, socially and economically sustainable development through the generation, access to, and use of agricultural knowledge, science and technology?* (IAASTD 2003). The Assessment concluded that it is necessary to shift from current farming practices to sustainable agriculture systems capable of providing both significant productivity increases and enhanced ecosystem services. "'Business as usual' is not an option if we want to achieve environmental sustainability," that the food security challenge is likely to worsen if market-driven agricultural production systems continue to grow in 'a business as usual mode,' and that sustainable development can be promoted through reduced agrochemical inputs and use of agroecological management approaches (IAASTD 2009).
- In 2010, the UN Special Rapporteur on the Right to Food, Olivier De Schutter reported to the UN Human Rights Council that, in order to combat hunger and malnutrition, "*States should implement public policies supporting the adoption of agroecological practices*." His report found that agroecology raises productivity at the field level, reduces rural poverty, contributes to improving nutrition, and contributes to adapting to climate change, concluding that "*States can and must achieve a reorientation of their agricultural systems towards modes of production that are highly productive, highly sustainable and that contribute to the progressive realization of the human right to adequate food*." (De Schutter 2011)
- In August 2011, UNEP published a guidebook on agricultural adaptation to climate change, based primarily on the agroecology approach to agricultural production encompassing sustainability and biodiversity (Clements et al 2011).

[49] The IAASTD was a global assessment of the impacts of agricultural knowledge, science and technology on hunger, poverty, nutrition, human health, and environmental and social sustainability in relation to both the past and the future. The Assessment process was initiated in 2002 by the World Bank in partnership with a multi-stakeholder group of organisations, including FAO, GEF, UNDP, UNEP, WHO and UNESCO, and representatives of governments, civil society, private sector, and scientific institutions from around the world (IAASTD undated).

- In 2010, the Food and Agriculture Organization of the United Nations (FAO) published a report which concluded that "in order to meet the related challenges of food security and climate change" agriculture must adopt an ecosystem approach. The FAO website 'Save and Grow' (FAO 2011) further elaborates on this: "The present paradigm of intensive crop production cannot meet the challenges of the new millennium." Their new paradigm is 'ecosystem-based', focussed on developing a healthy soil and healthy agroecosystem, and whilst it does not actually eschew all pesticide use it sees them as a last resort.
- In addition, a slew of recent NGO reports provide evidence that the agroecological approach to agriculture, rather than the chemical approach, is the best way for farmers to meet the changes of poverty, rising food prices and climate change, for example those by Christian Aid (Hobbs & Powell 2011), the Institute for Agriculture and Trade Policy and the Asian Farmers Association for Sustainable Rural Development (Hansen-Kuhn et al 2011), and ActionAid (Chung 2012).

There is a wealth of scientific and evidential data showing that crops can be grown perfectly well without using pesticides.

The principle of minimum harm

Instead of asking the questions—what pesticides are available, how much harm from them is acceptable, how do we protect children, what is a safe level of exposure, which pesticides need protective equipment, what studies do we need to prove they are safe—the first question that should be asked is 'how do we manage our pests, weeds and diseases in crops in ways that minimise harm to people and to the environment?' This is an expression of the principle of minimum harm (Watts 2000), a principle that has been around in one form or another for many years. It was spelled out by environmental philosopher Paul Taylor, in 1986, in his book *Respect for Nature*. The principle acknowledges that humanity necessarily causes damage to the environment in pursuit of its basic and non-basic needs, but prescribes that this damage should be minimised. Even the World Bank acknowledged it in 1993: "To be ethical the project with the least environmental impacts should be selected" (Montague 1996). To be ethical, management of pest, weeds, and diseases must also minimise damage to humans, especially children.

Alternatives assessment/substitution

Applying the principle of minimum harm to pesticides is simple: all that is needed is an assessment of alternatives (O'Brien 1999, 2000). Compare the hazardous

effects of the pesticide proposed for registration with those of all other effective alternatives available, including pesticides and non-pesticide methods of management. If there are existing effective, less harmful alternatives, the pesticide should not be registered. If there are not, then the next step is to determine whether the pesticide meets the cut-off criteria for hazardous properties. Is it highly acutely toxic, carcinogenic, mutagenic, a reproductive toxin, a developmental neurotoxin, immunotoxin, or an endocrine disruptor? If so it should not be registered. If it does not have any of these properties, then it can be registered and used, with caution.

This process is really just an improved version of the substitution principle which came into operation first in Swedish pesticide policy in 1985.

> *"According to the Swedish Act on Chemical properties (SFS 1985, p 426) section 5 'anyone handling or importing a chemical product must take such steps and otherwise observe such precautions as are needed to prevent or minimize harm to human beings or to the environment. This includes avoiding chemical products for which less hazardous substitutes are available.'" | Bergkvist et al 1996*

CHILDREN JOIN PROTEST MARCH IN MINDANAO, PHILIPPINES.

Sweden's National Board of Agriculture did recognise the need to assess non-chemical methods:

> *"If equally effective, non-chemical methods are available for a certain control a pesticide will be banned for that control." | Liden 1989*

However, neither the Swedish nor the recently implemented European chemical legislation REACH, which also includes the substitution principle, actually included non-chemical management in their registration processes. It is time that registration processes do. This is the precautionary approach in action. In summary, in order to protect children from the developmental effects of hazardous pesticides, government policies and practices including pesticide registration processes, need to change dramatically—to adopt the precautionary principle and the principle of minimum harm; and implement alternatives assessment and substitution. A pesticide should only be registered and used if there is no less harmful, effective way of managing the particular pest, weed or disease, including by non-chemical methods, and only if the pesticide is not acutely toxic, does not cause carcinogenicity and mutagenicity, and is not a reproductive toxin, developmental neurotoxin or immunotoxin, nor an endocrine disruptor. Rachel Carson put it very simply way back in 1962: "chemical pesticides should not be used where there are acceptable substitutes" (Norton 1991). Why has the World been so slow to learn? ■

Children are one third of our population and all of our future.

~ SELECT PANEL FOR THE PROMOTION OF CHILD HEALTH, 1981

6 Conclusion

Children are now born pre-polluted—their mothers absorb pesticides from exposure to agricultural use, household pesticides and even residues in food, and these pesticides cross the placenta, appear in the amniotic fluid surrounding the unborn foetus, and turn up in the meconium of new born infants. The newborn are then exposed to more contaminants through their diet, firstly in their mothers' breast milk, and then as residues in the food they eat particularly fruit and vegetables, unless they eat organic food. If pesticide treatments are used for head lice or scabies control, children are further exposed. They are also exposed to pesticides used for household insect control and home garden use, the latter tracked into the house and lingering in household dust and on surfaces such as tables. Children are generally more exposed to pesticides than adults, apart from occupationally exposed adults, because they inhale and ingest more relative to their body size and therefore take on relatively more residues. They are also closer to contaminated environments such as house dust on carpets, residues in outdoor soil, and because they put into their mouths objects that may have residues on them especially when teething.

The situation is particularly problematic for farm children and especially the children of farmworkers. They often play in the fields or accompany their parents when they work. Their parents track pesticide-contaminated soil and dust into their homes and vehicles, their clothes and skin possibly contaminated, and washing those clothes may spread the residues to the children's clothes. Rural children are likely to be exposed to short-range drift and ambient levels of residues in the air, and their drinking water may contain greater levels of residues than those to which urban children are exposed, especially if using well-water. They may also eat food directly from fields that have recently been sprayed.

Children get poisoned at school by drifting pesticides from nearby operations. They accidentally ingest pesticides left in the home, and through accidentally contaminated food and water.

Children also get exposed to pesticides, and poisoned, through their work—on family farms, commercially employed, or as bonded or forced labour. Children

begin work as young as 5 years of age in some developing countries and many are exposed to pesticides, even though the international legal minimum age for light work is 13 and 18 for highly hazardous work, which includes exposure to pesticides. Around 150 million children work in agriculture—most of these will be at risk of exposure to pesticides. Poverty is the overwhelming factor that drives this situation of exploitation and abuse. Many parents are forced into this situation by the global forces that make the rich richer and the poor, and especially the rural poor of developing countries, poorer.

Children are more vulnerable to pesticides than adults because their absorption through skin and gut is greater and they are less able to metabolise toxic chemicals. Their developing bodies, and particularly their immune, neurological and endocrine systems, are acutely sensitive to the effects of pesticides during critical windows of vulnerability, and the effects of exposures during these periods can last a lifetime, and even beyond: the epigenetic mechanisms triggered by some pesticide exposures, especially endocrine disruptors, mean that the effects can be felt down through succeeding generations. Children also have a longer life span ahead of them, generally, to manifest chronic diseases and conditions as a result of early exposures to pesticides.

There is a wealth of evidence that maternal or paternal exposure to pesticides can result in birth defects, still births, pre-term births, altered sex ratio of births, and alterations in birth outcomes such as birth weight and size. Alterations to birth weight and size can increase the risk later in life of conditions such as cardiovascular disease, type 2 diabetes, osteoporosis, depressive disorders and some cancers.

Prenatal exposure to pesticides is now implicated in what has been termed 'a silent pandemic' of developmental toxicity. There is a burgeoning body of evidence that prenatal and early childhood exposure to pesticides that are toxic to the nervous system, especially organophosphates, are causing serious developmental, learning and behavioural disorders in children, many of which may last throughout life. These include reduced IQ, learning disabilities, poor memory, poor communication, reduced motor ability, reduced response speed, poor visual performance, and behavioural problems including emotional problems, autism, and attention deficit hyperactivity disorder. The result is reduced learning and increased social alienation, with profound consequences for society as a whole, including significantly reduced intellectual capacity and increased behavioural problems such as aggression and other social effects that cascade from these. Early exposure to neurotoxic pesticides is also implicated in adult onset neurological diseases such as Parkinson's and Alzheimer's diseases.

Prenatal parental exposure to a variety of pesticides has been linked to a variety of childhood cancers, most commonly leukaemia, lymphoma, and brain cancer. A number of adult cancers, especially those with a hormonal basis such as breast, prostate, and testicular are thought to have origins in early developmental exposures to environmental hormone disruptors.

Our knowledge of the insidious effects of pesticides is continually expanding and now connections have been made between exposure to pesticides and some of society's most rapidly escalating health problems, such as diabetes, obesity and metabolic disease, the latter a condition associating obesity with hypertension, type 2 diabetes, and cardiovascular disease. There is evidence that low level exposure, especially prenatal and early childhood exposures, to organochlorines, organophosphates and carbamates may all interfere with weight-controlling mechanisms, glucose metabolism, and insulin maintenance, and may alter early childhood growth rates to predispose to obesity.

Pesticides are also implicated in disruptions to the normal development of children's immune systems which can result in childhood afflictions such as respiratory allergy, type 1 diabetes, recurrent otitis media, and paediatric coeliac disease. Additionally, disrupted immune system development can have far reaching consequences for health throughout life including the ability to deal with viruses, bacteria, parasites, tumour cells, and to avoid chronic allergic, inflammatory and autoimmune conditions and cancers.

Foetal exposures to endocrine disrupting pesticides have been linked to a number of problems with the reproductive system, ranging from birth defects such as hypospadias and cryptorchidism, through early onset puberty and other effects on sexual maturity, to a whole raft of hormone-related problems in adulthood, including menstrual irregularities, uterine fibroids, endometriosis, and infertility. Although these latter problems are largely adult conditions, their genesis often lies in exposures to endocrine disrupting substances during foetal development and early childhood.

Yet despite the wealth of good science illustrating these problems, children are still being exposed. International conventions are useful but without national polices backed by strong political will to ensure implementation, this situation will not improve. Pesticide registration processes are fraught with problems: industry conflicts of interest, adherence to outdated scientific protocols termed Good Laboratory Practice and failure to act on good independent science based on more up-to-date scientific techniques, failure to recognise the critical nature of prenatal and early childhood exposure to pesticides that are developmental neurotoxins, immunotoxins and endocrine disruptors,

failure to recognise functional effects on metabolism, and failure to recognise the prenatal origins of many adult diseases such as cancer. Add to that the harassment of independent scientists whose study results displease the pesticides industry, and the latter's active campaigns to undermine the validity of the results, and to ensure that regulatory processes suit their needs rather than those of children.

Every institution, organisation and member of society has a responsibility to ensure that pregnant women and children are not exposed to any pesticide, including as residues in food, that may cause them harm, through either acute poisoning or chronic effects that only become apparent later but cause lifelong impairment.

Pesticide regulatory systems and policies need a drastic overhaul. As a first step, governments must institute a policy to stop the use of pesticides that are highly hazardous, for if they are used, children will be exposed to them. Registration processes must move from an industry supportive model of risk assessment to a more public health supportive model of hazard assessment, with cut-off criteria that prevent the registration of pesticides that are carcinogenic, mutagenic, developmental neurotoxins or immunotoxins, or endocrine disruptors, and which embraces the precautionary principle. However registration must also include alternatives assessment, based on the Principle of Minimum Harm: the least harmful method of managing pests,

WOMEN CALLS FOR END TO PESTICIDE USE IN SRI LANKA

weeds and diseases should be used. Where effective non-chemical methods or less toxic chemicals exist, a toxic pesticide should not be registered or used.

The problems we have today with children's lives being blighted by pesticides are because of an institutional failure to acknowledge that pesticides are not necessary. Most governments and many scientists assume, without any evidence, that pesticides are necessary. But good science and a wealth of observational data have shown repeatedly that farmers can make more money, and improve their food security and the health of their families and the environment by not using pesticides and practising instead biodiversity-based ecological agriculture. Many farmers already know this and they are leading the way forward, but governments are very slow to follow. ■

Be the change that you want to see in the world.

~ MAHATMA GANDHI

7 Recommendations

Pesticide Action Network Asia and the Pacific provides the following recommendations to address the problems of children's exposure to highly hazardous pesticides:

Governments and relevant others should:

1. adjust agricultural policy and practice to remove the assumption that pesticides are necessary;
2. encourage farmers to change to agroecology, biodiversity-based ecological agriculture, or organic agriculture;
3. ensure that pest, weeds, and diseases are managed by the methods that cause the least harm to humans and the environment (Principle of Minimum Harm);
4. in pesticide registration, replace risk assessment with alternatives assessment and hazard assessment, using the precautionary principle as the framework, such that pesticides are only registered if there is no effective less harmful alternative, including non-chemical methods of management;
5. in pesticide registration, institute cut-off criteria such that pesticides that are carcinogenic, mutagenic, developmental neurotoxins or immunotoxins, or endocrine disruptors are not registered or used;
6. remove the requirement that studies used to register pesticides must meet the guidelines for GLP;
7. ensure the registration process is based on studies from independent scientists not industry science, but require industry to reveal all it knows about the toxic effects;
8. remove the assumption of a safe threshold for pesticides;
9. ensure studies include low doses, and dose-responses other than positive dose-response;
10. ensure the studies include prenatal and developmental exposures, and effects in old age;
11. ensure the studies include allergic, inflammatory and autoimmune

effects, and effects on the developing mammary gland;

12. ensure the studies reflect additive and synergistic effects with other pesticides; and
13. ensure that policy decisions include assessment of multiple and cumulative exposures and risks with other potentially hazardous toxic agents.

Whilst these changes are being made to the pesticide registration process, government and others should:

1. build individual and community awareness of the pathways of exposure for children, and the potential effects on their health; and
2. ensure that pregnant women and children are not exposed to highly hazardous pesticides, or pesticides that have the potential for developmental toxicity or endocrine disruption, including through residues in food. ■

Glossary

acceptable dose – a level of exposure that is regarded by the regulatory agency as posing a level of risk that is acceptable to the agency.

acetylcholinesterase – an enzyme found throughout the nervous system that is responsible for breaking down the neurotransmitter acetylcholine. *Also see cholinesterase inhibition.*

acute lymphoblastic leukaemia – a form of blood cancer involving the overproduction of immature white blood cells in the bone marrow and prevention of the production of normal blood cells.

agroecology – the science of applying ecological concepts and principles to the design and management of sustainable agroecosystems. It includes the study of the ecological processes in farming systems and processes such as: nutrient cycling, carbon cycling/sequestration, water cycling, food chains within and between trophic groups (microbes to top predators), lifecycles, herbivore/predator/prey/host interactions, pollination, etc. Agroecological functions are generally maximized when there are high species diversity/ perennial forest-like habitats.

acute reference dose – an estimate of the amount of a substance in food or drinking water, normally expressed on a body weight basis, that can be ingested in a period of 24 hours or less without appreciable health risks to the consumer on the basis of all known facts at the time of the evaluation (JMPR 2002).

anencephaly – the absence of a major part of the brain and skull, caused by failure of the neural tube to close, usually between the 23rd and 26th days of pregnancy. It may also involve facial distortions and heart defects.

autism spectrum disorders – developmental brain or cognitive disorders characterised by impaired social interaction, restricted communication, and repetitive stereotypic behaviours; symptoms range from mild to severe disabilities. *Also see Pervasive Developmental Disorder.*

bioavailability – the degree of activity or amount of pesticide that becomes available for biological activity; the uptake and activity of a pesticide in the body.

cholinesterase inhibition – the inhibition of the enzyme acetylcholinesterase from breaking down acetylcholine thereby disrupting neural signalling functions by prolonging or magnifying activity of acetylcholine. *Also see acetylcholinesterase*.

chromosomal aberration – disruption in the normal chromosomal content of cells, which can lead to cancer.

chronic reference dose - an estimate of the amount a substance in food or drinking water, normally expressed on a body weight basis, that can be ingested every day without appreciable health risks to the consumer on the basis of all known facts at the time of the evaluation.

coeliac disease – autoimmune disorder of the small intestine triggered by gluten, a protein in wheat and some other grains.

conduct disorders – include repetitive patterns of at least three or more of the following: aggression, fighting, stealing, vandalism, blaming others, low self-esteem, poor tolerance, irritability, temper tantrums, lying, truancy, and substance abuse (Schettler et al 2000).

cryptorchidism – a male birth defect involving the absence of one or both testes.

DDT – dichlorodiphenyltrichloroethane, an organochlorine insecticide.

DDE – main metabolite of DDT.

dyslexia – a specific learning disability involving difficulty with written language, particularly with reading and spelling, but not an intellectual disability. Most people with dyslexia have average or above-average intelligence.

dyslipidemia – high levels of blood cholesterol and triglycerides.

endocrine disruption - interference, by a exogenous chemical (i.e. one not naturally in the body), of any aspect of hormonal action.

epigenetic – heritable changes in gene expression or cellular phenotype caused by mechanisms other than mutations.

epidemiological study – a study that tries to determine if any factor, such as pesticide exposure, is associated with a particular health effect by comparing two groups of people who are alike except for the factor under study.

epidermal barrier – in the outer layer of the skin, it helps prevent infection, water loss, and absorption of toxic substances. It starts to develop from about week 24 of gestation.

GABA – gamma aminobutyric acid, the principle inhibitory neurotransmitter in the mammalian system; it acts as the main inhibitor of neural excitations in the central nervous system; also regulates development of neural cells.

gastroschisis – a birth defect in which the baby's intestines protrude through a hole in the abdominal wall.

glomerural filtration – the filtration of blood plasma in the glomerulus of the kidney, the first step in urine formation.

HCB – hexachlorobenzene, an organochlorine insecticide, now banned globally.

HCH – hexachlorocyclohexane, an organochlorine insecticide, now banned globally.

hydrocele – fluid-filled sac in the scrotum.

hypospadias – a male birth defect involving the abnormally placed urinary opening on the penis.

immunocompetence – ability of the body to produce a normal immune response.

immunotoxicity – adverse effects on the functioning of the immune system of exposure to a chemical.

meconium – earliest faeces of a new-born infant.

metabolite – the breakdown product of a pesticide as the result of metabolism.

myelination – the formation of the insulating myelin sheath around the axon of nerve cells, normally beginning in the 14th week of foetal development.

neural tube defect – a group of common birth defects of the brain and spinal cord, resulting from the failure of the neural tube to close properly during

the formation of the brain and spinal cord that occurs very early in human development.

neurodevelopmental delay – delays in development of a child's neurological pathways, usually manifested in delays in developing reflexes and processing of sensory information, resulting in deficient balance, motor control, eye functioning, eye-hand coordination, perceptual skills, and learning; can result in behavioural symptoms such as frustration, hyperactivity and hypersensitivity, and failure to match performance to ability.

neurotoxicity – toxicity of pesticides (and other chemicals) to the nervous system, altering some aspect if its structure or function.

nullisomy – a lethal genetic condition involving the lack of one of the normal chromosomal pairs.

OCs – organochlorine pesticides

OPs – organophosphate pesticides

perinatal – the period around childbirth usually from five months before and one month after.

Pervasive Developmental Disorder – a broad category of social, communication and behavioural problems. Includes autism spectrum disorders, Rett syndrome, and childhood disintegrative disorder. *Also see autism spectrum disorder*.

phenotype – the totality of an organism's observable traits or characteristics.

PON1 – human enzyme paraoxonase which detoxifies various organophosphate pesticides.

prenatal – the period before childbirth.

recurrent otitis media – middle ear infection

respiratory ventilation rate – the rate at which gas enters or leaves the lung.

spina bifida – a birth defect involving the neural tube resulting in the incomplete development of the brain, spinal cord and their coverings.

spray drift – the physical movement of pesticide droplets from the spray nozzle

through the air at the time of application or soon after, to any site other than that intended for application.

Tourette's Syndrome – repeated and uncontrolled rapid movements and sounds called tics.

Turner syndrome – a genetic condition among females not having the usual pair of X chromosomes. Symptoms include short stature, premature ovarian failure, and difficulty in imagining spatial-temporal relations among objects, nonverbal memory and attention.

US EPA – United States Environmental Protection Agency

WHO – World Health Organization

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POISONING OUR FUTURE: CHILDREN AND PESTICIDES

Meriel Watts PhD

ABOUT PAN AP

Pesticide Action Network Asia and the Pacific (PAN AP) is one of the five regional centres of Pesticide Action Network (PAN), a global network primarily dedicated towards the elimination of harm caused to humans and the environment by pesticides and towards promoting biodiversity-based ecological agriculture.

PAN AP's vision is a society that is truly democratic and culturally diverse; based on the principles of food sovereignty, gender justice and environmental sustainability. It has developed strong partnerships with peasants, agricultural workers, indigenous peoples, fisherfolks, rural women movements and other small food producers in the Asia Pacific region. Guided by the strong leadership of these grassroots groups, PAN AP has become a strong advocacy network with a firm Asian perspective.

Its mission lies in strengthening people's movements to advance and assert food sovereignty; promote biodiversity-based ecological agriculture and the empowerment of rural women; protect people and the environment from highly hazardous pesticides; defend the rice heritage of Asia; and resist the threats of corporate agriculture and neo-liberal globalisation.

Currently, PAN AP comprises 108 network partner organisations in the Asia Pacific region and links with about other civil society and grassroots organisations regionally and globally.

WORLD WITHOUT POISONS

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