CHEMTrust

Protecting humans and wildlife from harmful chemicals

# No Brainer

## The impact of chemicals on children's brain development: a cause for concern and a need for action

A CHEM Trust Report

March 2017

CHEMTrust
Protecting humans and wildlife from harmful chemicals

This briefing was produced by CHEM Trust, a UK-based charity working at UK, EU and International level to protect humans and wildlife from harmful chemicals.

CHEM Trust's particular concerns are related to hormone disruptors, the cocktail effect of chemicals and the role of chemical exposures in the early life of wildlife and humans.

CHEM Trust engages with scientific, environmental, medical and policy communities to improve the dialogue concerning the role of adverse effects of chemicals in wildlife and humans and to harness a wide coalition to drive improved chemicals policy and regulation.

For more about our work, including our regularly-updated blog, see **www.chemtrust.org.uk**

Further copies of this briefing can be downloaded from **www.chemtrust.org.uk/brain**

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## About the Authors

The main review of the state of science was drafted by an experienced chemicals policy consultant, Dr Maricel V Maffini, and it was then peer reviewed by two of the most eminent scientists in this area, Prof Barbara Demeneix (Laboratory of Evolution of Endocrine Regulations, CNRS, Paris) and Prof Philippe Grandjean (Department of Environmental Medicine, University of Southern Denmark, Denmark & Department of Environmental Health, Harvard T.H. Chan School of Public Health, Boston, USA), who also provide answers in the Q&A section. The policy recommendations and advice for individuals are written by Dr Michael Warhurst and Dr Ninja Reineke of CHEM Trust, informed by the state of the science, the views of the scientists and our own experience of following chemicals policy development for more than two decades.

Dr Maffini, is an independent consultant based in Maryland, US. She has more than 20 years of research experience in the fields of carcinogenesis, reproductive biology and endocrine disruption. She has authored numerous peer-reviewed journal articles, including one in 2014 on *Brain drain: the cost of neglected responsibilities in evaluating cumulative effects of environmental chemicals*, as well as reviews and book chapters. Her current work focuses on environmental health issues related to chemical safety with special emphasis on chemicals in food, risk assessment and science policy. Her most recent position was as Senior Scientist with the US Natural Resources Defense Council; prior to NRDC she was a Research Assistant Professor at Tuft University School of Medicine.

## Acknowledgements

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# 2 Executive summary

Science has shown that many thousands of people have been exposed to now mostly banned chemicals such as lead and PCBs at high enough levels to have had their brain development negatively affected. This report finds that there are other chemicals which are still in routine use in our homes where there is evidence of similar developmental neurotoxic (DNT) properties, and also identifies huge gaps in our knowledge of the impacts of other chemicals on brain development. It also points out the unpleasant reality that we are constantly exposed to a cocktail of chemicals, something which is still largely ignored by chemical safety laws.

In spite of the lessons of the past, regulators are continuing to only regulate after harm is caused, instead of acting to effectively protect the most precious of things; children's developing brains.

> "Reported exposures to several neurotoxicants in the EU commonly exceed the levels that are associated with adverse effects on brain development." Philippe Grandjean

In June 2007 CHEM Trust wrote the briefing *Chemicals Compromising Our Children*, which highlighted growing concerns about the impacts of chemicals on brain development in children. Almost 10 years later, CHEM Trust has revisited the issue with this report, which includes contributions from two of the most eminent scientists in this area, Professor Barbara Demeneix (Laboratory of Evolution of Endocrine Regulations, CNRS, Paris) and Professor Philippe Grandjean (Department of Environmental Medicine, University of Southern Denmark, Denmark & Department of Environmental Health, Harvard T.H. Chan School of Public Health, Boston, USA), who also peer reviewed the report.

## Our brain and its development

Our brains are astoundingly complex, made up of over 85 billion neurons, which have grown, developed and interconnected during our lives. The brain is the organ that takes the longest to develop, with initial stages of cell division, creation of neurons and their migration taking place from the first hours after fertilisation and throughout the foetus' time in the womb. However, brain development does not stop at birth – it's not until our twenties that neurons are fully developed with their myelin coats.

Throughout this complex developmental process a range of signalling chemicals and other processes operate in order to control what happens. The thyroid hormone system is intimately involved in brain development and function, yet it is well established that this system can be disrupted – for example by a lack of iodine (essential to make thyroid hormone) or by certain chemicals. If developmental processes are disrupted, this most often creates permanent problems.

> "The report commissioned by CHEM Trust on developmental exposure to neurotoxic chemicals and correlated brain consequences is an excellent coverage of the literature."
> Barbara Demeneix

The complexity of brain development and function means that deficits can be very subtle – small reductions in IQ, disabilities that exist with a broad spectrum of seriousness such as autism, or in some cases conditions which do not have fully agreed diagnostic criteria.

## Disruption of brain development by chemicals

We are all exposed to hundreds of man-made chemicals in our daily life, coming from everyday products including food, furniture, packaging and clothes. Many of these chemicals will have no negative effects on us, but it is now well established that some are able to disrupt normal development of the brain. Chemicals with long established DNT properties such as lead, PCBs and methylmercury, have been joined by others where DNT effects have been identified more recently, and which are being used in everyday products. There are also rising concerns about chemicals that are very similar to chemicals that have had their use restricted, but which we continue to use as there isn't sufficient information about their toxic effects. We know even less about thousands of other chemicals in routine use, which have had no testing for DNT properties.

> "A variety of chemical agents can interfere with early brain development, and such chemical brain drain is most likely irreversible." Philippe Grandjean

Chemical exposures are so ubiquitous that experts have recognized that babies are born "pre-polluted". Scientific paediatric and gynaecology & obstetrics societies have consistently warned about chronic health implications from both acute and chronic exposure to chemicals such as pesticides and endocrine disruptors.

The report identifies evidence of DNT properties for the following chemicals:

- **Bisphenol A (BPA)**; a chemical that was used to make baby bottles, is currently being phased out of till receipts (in the EU), but is still used in the making of food can linings and many polycarbonate plastics. There are also concerns about closely related chemicals that are not restricted, including Bisphenol S.

> "Chemical exposure is now at unprecedented levels, is multiple, ubiquitous, and present from conception onwards." Barbara Demeneix

- **Brominated Flame Retardants (BFRs)**; a group of chemicals added to furniture, electronics and building materials. The evidence for neurodevelopmental effects is strongest for the PBDE (polybrominated diphenyl ether) group of BFRs, which are already banned or nearly banned in the EU, though they are still in furniture in our homes, and in dust. However, other BFRs are now being found in dust and human blood serum, with concerns that these BFRs might have similar effects.
- **Phthalates;** a group of chemicals used as plasticisers in PVC and in other products. Some chemicals in this group are now banned in the EU, but many others are still in use.
- **Per- and poly-fluorocarbons (PFCs);** used as non-stick coatings or breathable coatings, are a large group of chemicals, a few of which are in the process of being restricted by the EU. There is evidence that some PFCs can disrupt the action of the thyroid hormone. PFCs are very persistent in the environment, and many of them can accumulate in our bodies – they are routinely found in blood.
- **Perchlorate;** a contaminant of food, related to the use of certain fertilisers and hypochlorite bleach, and is known to disrupt the thyroid hormone system.

## Are we protected?

The EU has the most sophisticated regulations in the world for controlling chemical use. However, there are a number of key flaws in this system:

> “From human poisoning cases, we know of at least 200 chemicals that can enter the human brain and cause damage to the nerve cells…I would think that virtually all of them can also harm the development of the human brain, most probably at much lower levels than those that cause adverse effects in adults. About half of these chemicals are commonly used… and therefore present a high potential for exposures.” Philippe Grandjean

- There is often inadequate safety information about individual chemicals, including a lack of information about neurodevelopmental effects.
- The processes to ban chemicals are too slow, and the restrictions created often have big loopholes as a result of industry lobbying.
- Chemicals are addressed one at a time, so one chemical may have its use restricted, but closely related chemicals remain in use.
- We are always exposed to multiple chemicals, but regulations almost always assume we are only exposed to one at a time, even though numerous scientists have shown that chemical effects can add together in our bodies.

## Policy recommendations

It is clear that our children are not currently being protected from chemicals that can disrupt brain development. We have identified a range of policy measures that could improve the situation, including:

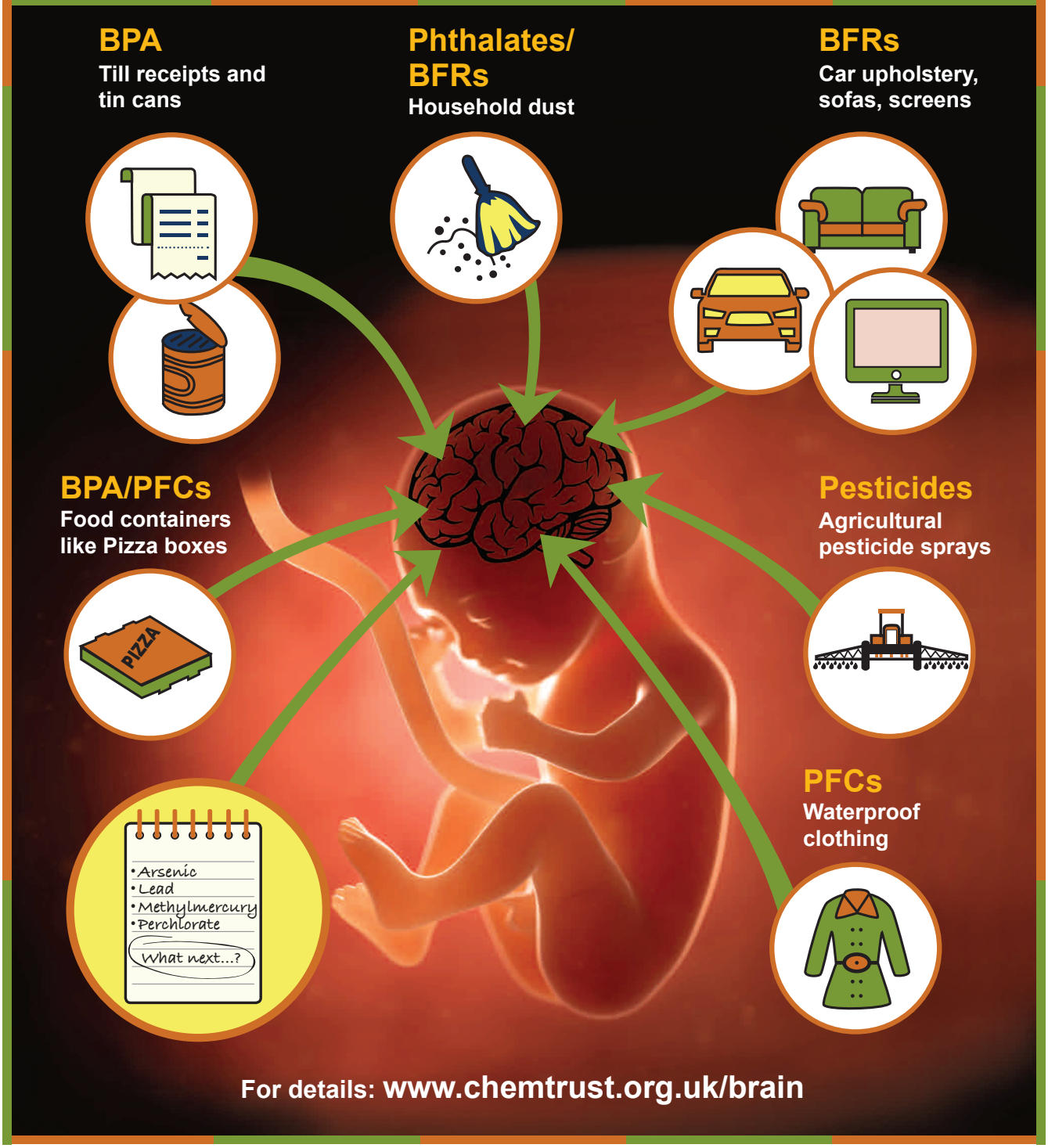
- **Acting faster to ban chemicals of concern**, including addressing groups of similar substances, not just those where we have the most information.
- **Ensuring that any safety testing of chemicals** includes evaluation of DNT effects.
- **Ensuring better identification and regulation of** neurodevelopmental toxic chemicals.
- **Ensuring that all uses of chemicals are properly regulated**; for example there is a lack of effective regulation of chemicals in food packaging including paper, card, inks, glues and coatings.
- **The UK and Ireland should remove the requirement for an open flame test for furniture.** This test is not required in the rest of the EU, and leads to increased use of flame retardant chemicals.

Finally, it is important to note that EU regulations have already controlled a number of chemicals of concern, and that EU laws provide a tool to address these problems. We therefore think it is vital for the UK Government to work to stay aligned with EU chemicals laws, whatever the eventual outcome of the UK’s Brexit process.

> “The current generation has the responsibility to safeguard the brains of the future.” Philippe Grandjean

Though full protection will only come from proper regulation of chemicals, the report also includes a chapter with tips for reducing your and your family’s exposures in daily life.

# Chemical threat to brain development



# 3 Introduction

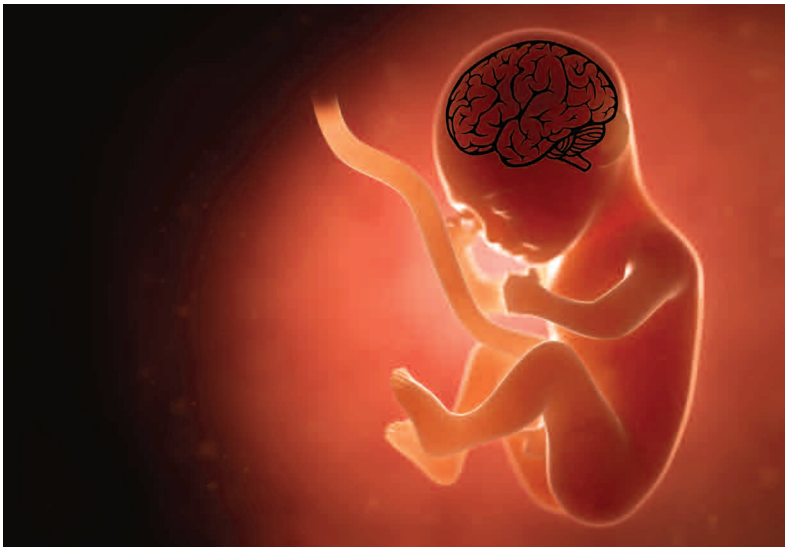
In June 2007 CHEM Trust wrote the briefing *Chemicals Compromising Our Children*[a], which highlighted growing concerns about the impacts of chemicals on brain development in children. Almost 10 years later, CHEM Trust has decided to revisit this issue.

We want this report to reflect the state of knowledge in this rapidly evolving field, and the views of two of the most eminent scientists in this area, Barbara Demeneix and Philippe Grandjean, and to have clear policy recommendations.

The main review of the state of science was drafted by an experienced chemicals policy consultant, Maricel Maffini, and it was then peer reviewed by both Barbara Demeneix and Philippe Grandjean. The report also includes a Q&A with these two scientists, to learn where they think the science in this area is going and what the priorities for public health should be. We then give policy recommendations from CHEM Trust, informed by the state of the science, the views of the scientists and our own experience of following chemicals policy development for more than two decades. Finally, some tips as to how people can reduce their exposure to chemicals of concern.

a http://www.chemtrust.org.uk/wp-content/uploads/neurotoxbriefing.pdf

# 4 Summary of the science



This report is focused on chemical exposures and their contributing role to certain neurological diseases and disorders. There is evidence for a wide range of other factors playing a role in these disorders, including genetics, low birth weight, premature birth, smoking or drinking during pregnancy, viral infections and brain damage in the womb or early years of life.[1]

It is estimated that, worldwide, 10 to 20% of children and adolescents suffer from mental health problems. In 2007, the global prevalence of just attention deficit hyperactivity disorder (ADHD) was 5.3%.[2]

In the United States, the prevalence of ADHD in children aged 3 to 17 years increased by 33% between 1997-1999 and 2006-2008.[3] In 2012, more than 5 million children in this age group had been diagnosed with ADHD (10% of children) and 4.9 million (8% of children) with a learning disability.[4]

The numbers in Europe, although lower, are also of grave concern. A snapshot report on child and adolescent mental health in Europe from 2009 reported that in the European Union, on average, 1 in every 5 children and adolescents suffers from developmental, emotional or behavioural problems and 1 in 8 have a clinically diagnosed mental disorder.[5] In England, for example, 5-16-year-old children are affected by various neurological disorders including anxiety (3.3%), ADHD (2.5%), learning disorder (4-8%) and conduct disorder (5.8%).[5] When combined, these pathologies affect approximately 16-20% of children in this age group.

A first study of neurological and neurodevelopmental disorders in Norway based on nationwide register data from 2012 determined that the incidence of ADHD was 3.4% in Norwegian 11-year-olds.[6]

A recent study on the prevalence of childhood psychiatric disorders in Denmark, Finland and Sweden found increases in hyperkinetic disorder[a] or ADHD and autism spectrum disorders in all three countries in a 10-year period.[7] As one example: between 2000 and 2008 the prevalence for hyperkinetic disorder in 10-year olds increased 4-fold in Denmark, nearly 3-fold in Finland and 8-fold in Sweden (see Figure 1).

a While the term ADHD is often used in the US, the term hyperkinetic disorder is widely used in the EU and requires that the clinician directly observes the symptoms (rather than relying only on parent and teacher reports). The World Health Organisation International Classification of Mental and Behavioural Disorders 10th revision (ICD-10) talks about attention-deficit hyperactivity disorder as hyperkinetic disorder (HKD). This classification system defined HKD as a persistent and severe impairment of psychological development, characterised by "early onset; a combination of overactive, poorly modulated behaviour with marked inattention and lack of persistent task involvement; and pervasiveness, over situations and persistence over time of these behavioural characteristics." ICD-10 notes that characteristic problems of lack of persistence, moving between activities without completion, and disorganised and excessive activity always arise early in development, but usually continue through school years and can persist into adult life. World Health Organization. *The ICD-10 Classification of Mental and Behavioural Disorders*. Available at: www.who.int/entity/classifications/icd/en/bluebook.pdf. Last updated 1993; 1: 1-263. The ADHD Institute (http://www.adhd-institute.com/assessment-diagnosis/diagnosis/icd-10/).

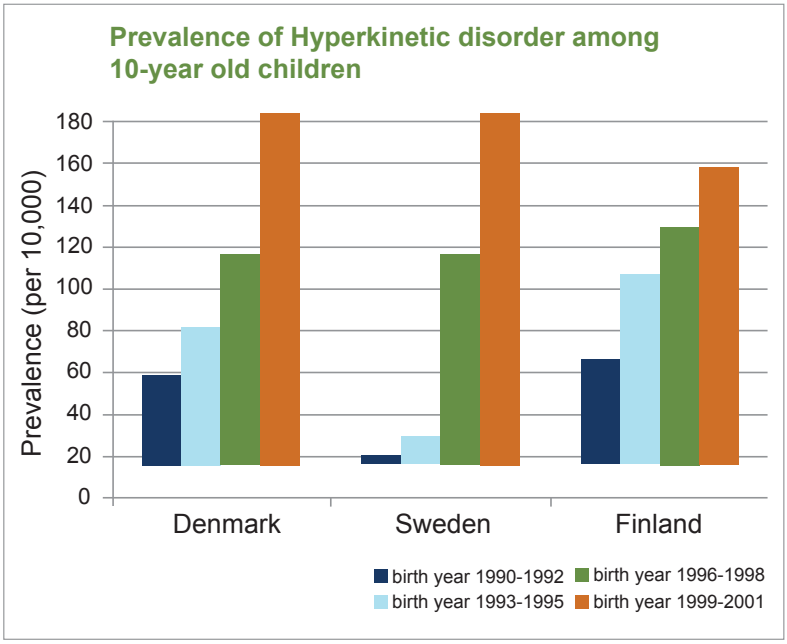



***Figure 1:*** *Prevalence of hyperkinetic disorder among 10-year old children in Denmark, Sweden and Finland for the birth cohorts 1990-1992, 1993-1995, 1996-1998, 1999-2001 adapted from: "The increasing prevalence of reported diagnoses of childhood psychiatric disorders: a descriptive multinational comparison." (Atladottir et al. European Child & Adolescent Psychiatry 24:173-183, 2015).*

For autism spectrum disorder, the increase in prevalence was equally concerning, with Sweden having the highest increase in cumulative prevalence (prevalence in 10-year olds) of 4.5-fold, followed by Denmark with almost 3-fold and Finland with almost double the prevalence in a decade. While at least some of the increase in hyperkinetic disorder/ADHD is thought to be due to increased awareness and increased diagnosis,[8,9] there is concern that exposure to certain chemicals could have contributed to some of the incidence.[60] Moreover, it is considered that there is probably an underlying true increase in the incidence of autism/autism spectrum disorder and researchers have suggested that some of the incidence of autism spectrum disorders might also be partially related to chemical exposures.[10-13] It is clear that given the importance of this issue, better standardised data needs to be collected in order to determine more precisely any trends over time in brain function both in children and in old age.

Understanding trends in diseases is crucial to increasing our understanding of contributory factors to disease origin. While genetics could explain some of the observed changes, the fast pace at which these trends have occurred are inconsistent with the much slower rate at which genetic changes take place, suggesting that environmental factors, chemical and non-chemical like the ones mentioned above, are probably responsible for shaping these disease patterns. It has been concluded that overall, genetic factors seem to account for no more than perhaps 30-40% of all cases of neurodevelopmental disorders, and therefore that non-genetic, environmental exposures, including chemicals are involved.

Advances in our understanding of brain development have added significant insight into the long-term health effects of environmental factors interfering with normal neurological developmental processes.[14] Substances used as industrial chemicals, pesticides, or food additives can all affect the same developmental mechanisms, leading to adverse consequences such as increased disease risk. A publication following the conference on Environmental Stressors in the Developmental Origins of Disease: Evidence and Mechanisms, (PPTOX III) held in Paris in 2012 concludes that:

"Early development (in utero and during the first years of postnatal life) is particularly sensitive to developmental disruption by nutritional factors or environmental chemical exposures, with potentially adverse consequences for health later in life".[15]

Exposures to chemicals with DNT properties which can be found in the environment and the food supply are preventable causes of impaired brain development. While several of these chemicals have been restricted, exposure can still take place as many of them are persistent (long-living) and some, like the PCBs can bioaccumulate, i.e. build up in our bodies over time. Additionally, we are exposed to numerous substances with similar properties which may act in an additive way and yet safety assessment is usually only focused on one substance at a time.

## 4.1 Brain development is uniquely vulnerable to disruption

Our brains are astoundingly complex, made up of over 85 billion neurons,[16] which have grown, developed and interconnected during our lives. The brain is the human organ that takes the longest to develop, with the initial stages of cell division, creation of neurons and migration to form the brain taking place from the first hours after fertilisation and throughout the foetus's time in the womb. However, brain development does not stop at birth – it's not until our twenties that neurons are fully developed with their myelin coats.[17]

Normal brain development is the result of an undisturbed harmonious interaction among cells, and between cells and hormones. Hormones play an important role in cell migration and differentiation, neuron-to-neuron communication and growth.[18] Experts in brain development state that "the prenatal brain develops under the influence of an ever-changing hormonal milieu" with inputs arising from the foetal, placental and maternal compartments.[19] However, external substances can interfere with the normal function of hormones. Endocrine disrupting chemicals (EDCs) are examples of substances that can alter this delicate balance, and as thyroid hormones play a vital role in brain development, thyroid disrupting chemicals are of particular concern.

Pregnancy, childhood and adolescence are periods of brain development that are considered critically sensitive to toxic chemicals. Rapid changes occurring during these life-stages render a child highly susceptible to environmental chemicals, with even small exposures at the wrong time altering the brain's developmental programming signals in an irreversible way. Impaired brain development may result in a broad range of human health effects: from altered reproduction, metabolism and stress response,[20] to mental retardation[21] and subtle, subclinical intellectual deficiencies.[22] In addition, foetal and early childhood life stages are particularly sensitive to heavy metals and EDCs and there are likely to be no safe levels which can be set with sufficient certainty. Indeed, the EU Endocrine Disrupter Expert Advisory group highlighted in a special report that thresholds of adversity from exposure to EDCs may be very low or non-existent during foetal development due to the immaturity of homeostatic mechanisms and absence of endocrine feed-back loops or immaturity of toxicokinetic defence/detoxification mechanisms as compared to adult life stages.[23]

As an example it mentions that "the entire cerebral cortex is produced by only 11 rounds of cell division of the founder population. Triggering premature differentiation of even a single cell early on could reduce the number of cells that would make up a particular region of the cortex."

Exposures to environmental chemicals during these susceptible times could therefore have dire and irreversible consequences to the individual's health in particular, and to public health in general. A detailed visualisation of the stages involved in the development of the brain can be found here: http://endocrinedisruption.org/prenatal-origins-of-endocrine-disruption/critical-windows-of-development/timeline-test/

Some nutritional deficiencies are also associated with impaired brain development. For instance, iodine deficiency,[24] an issue affecting almost 40% of the global population,[25] leads

to a decrease in thyroid hormone production and function. This underlying condition increases the vulnerability of these groups, especially pregnant women and children, to environmental chemicals with thyroid-disrupting properties such as perchlorate.[24] Exposure to these chemicals can occur via indoor air, dust and residues in food – see chapter 7, page 33 for tips on how to reduce your exposure.

## 4.2 Health consequences of impaired brain development

Just as important and concerning as the increase in clinically diagnosed diseases/ disorders are decreases in brain function. Borderline disabilities, while rarely recognized beyond the individual, present noticeable consequences when considered at the population level. This was emphasised in the review paper on *Neurobehavioural effects of developmental toxicity* published in the Lancet 2014 by Adjunct Professors of Environmental Health Philippe Grandjean, and Philippe Landrigan.[26] They aptly said that developmental disabilities;

"can have severe consequences—they diminish quality of life, reduce academic achievement, and disturb behaviour, with profound consequences for the welfare and productivity of entire societies."

Philippe Grandjean emphasised in his book *Only one chance*:

"If some disruption happens, brain development will be incomplete or abnormal, and there will be little, if any, time and opportunity for repair".[27]

Most clinical manifestations associated with impaired brain development can be placed into two major categories: behavioural and intellectual. However, as the brain is a collection of interconnected networks, these categories are closely related.

> "Preconception and prenatal exposure to toxic chemicals in food, water, air, and consumer products is a determinant of maternal, child and adult health."
>
> International Federation of Gynecology and Obstetrics. International Journal of Gynecology and Obstetrics 131:219-225, 2015

*Behavioural effects* comprise of behaviours associated with ADHD, hyperkinetic disorder, aggression, delinquency, anxiety and impaired social interactions in general. *Intellectual effects* include learning disabilities and impaired memory, verbal comprehension, reasoning and executive skills.

Environmental chemical exposures, especially during prenatal and early postnatal life are likely explanations for a part of these disabilities, among other causes. In the US, exposures to mercury, lead and organophosphate pesticides have been associated with the loss of around 40 million IQ points in a population of 25 million children up to 5 years of age.[28] European children born to mothers with borderline thyroid dysfunction exposed to perchlorate have been found to show signs of heightened risk of delayed neurodevelopment.[29] Normal production of thyroid hormone is crucial for foetal and early life brain development, and perchlorate inhibits thyroid hormone production.

Most if not all chemical exposures can be reduced by implementing policy measures such as bans and restrictions and strong mitigation strategies. One such successful strategy was removing lead from petrol. This change has demonstrated causality and the positive impact of chemical exposure reduction. In the US, children born after 2000 were estimated to have IQ scores 2.2-4.7 points higher than children born in the 1970s before the lead in petrol phase-out strategy was implemented.[30] Sadly, other chemicals with DNT properties are now on the market, such that lead is now just one of many chemicals associated with neurobehavioural problems.

A small reduction in IQ points might not necessarily affect the ability of an individual to live a productive life. However, looking at it from the perspective of the whole population,

impaired IQ values would shift the overall distribution and result in a reduced number of "gifted" people and an increase in individuals needing help to study, work or live a normal life. Deficits in IQ could therefore result in profound implications for society.[31]

## 4.3 From womb to tomb: What and where are these chemicals?

It has been known for many years that some chemicals have DNT properties, including lead, methylmercury and PCBs. For other chemicals the identification of DNT properties is more recent, while for others there are concerns from animal studies or because of their similarity to chemicals known to have this toxicity. Some chemicals with known or suspected DNT properties are in widespread use, and for example, can be found in products such as furniture, food packaging, toys, cosmetics, and paint. Some of these chemicals are a constant presence in our homes, our food (e.g. from pesticide residues) and our bodies from before we are born to the moment we die.

Chemicals such as PCBs and DDT/DDE have been largely banned for many years; however, their persistence means that children continue to be exposed to them – in addition to other chemicals that are still in use.[32]

### *a) Chemicals with long-established DNT effects*

The following list aims to provide a brief overview of chemicals with known neurodevelopmental effects. The use of these chemicals is now heavily restricted.

**Lead** has been well known to cause intellectual disabilities for many years, with no known safe blood concentration. Even blood lead concentrations as low as 5 µg/dl, once thought to be a "safe level", may result in decreased intelligence in children, behavioural difficulties and learning problems.[33] Lead exposure is believed to be responsible for the loss of more than 22 million IQ points in young children in the US.[28] New evidence also shows associations between blood lead levels and ADHD, inattention and hyperactivity.[34-36] Although mostly eliminated from petrol in the developed world, lead can still be present in paint in old houses and old water pipes. These ongoing low level exposures continue to damage the future of millions of children who may never reach their full intellectual potential.

**Mercury** is a pollutant from coal burning as well as historically having a range of uses, including in thermometers and fungicides. Methylmercury is formed from inorganic mercury in the environment and is a common contaminant of fish, in particular of predators like swordfish and tuna. Methylmercury's neurotoxic effects are well established, and exposure during development prevents neurons from finding their appropriate place in the brain, causing lower language, attention and memory scores, reduced cognitive performance and psychomotor deficiencies in children.[37,38] A global treaty, the Minimata Convention, has been agreed to address mercury pollution[a]. Even with current controls on mercury pollution, it will take many decades to bring down the level of pollution and therefore, dietary advisories are needed (see chapter 7 for details).

**Polychlorinated biphenyls (PCBs)** were banned from most uses in the late 1970s in many countries, but they can still be found in products made before they were taken off the market, including large electrical transformers and building sealants.[39] PCBs are persistent organic pollutants and endocrine disruptors linked to many health impairments, including neurological effects. They are now known to interfere with normal function of thyroid hormone, and growing evidence indicates PCBs adversely affect neurodevelopment.[40] Animal studies have found that new-born rodent pups simultaneously exposed to PCBs and other neurotoxins (e.g., mercury and PBDEs) showed exacerbated developmental neurotoxicity and this effect was observed at exposure levels that have been reported in children.[41,42]

a http://www.mercuryconvention.org

### *b) Chemicals that have more recently been identified as having suspected DNT effects*

The following list aims to provide a brief overview of chemicals with suspected neurodevelopmental effects, several of them are still in use and adding to the 'burden of the past'.

**Bisphenol A (BPA)** is a high-profile EDC due to both its current widespread use in consumer products as well as the extraordinary number of studies demonstrating its adverse health effects, often at low doses, in animals, as well as studies that associate exposure with health effects in people. BPA has been found in people's urine worldwide, with most studies showing a detection frequency of over 90%.[43] A study published by the German Environment Agency in 2009 found BPA in the urine of 591 out of 599 children between 3 and 14 of age.[44] BPA is a high-production volume chemical used to make plastics and polymers commonly used in food manufacturing, packaging and many consumer products. BPA's effects on animal behaviour have been reported for many years.[45,46] More recently, emerging human data suggests that similar adverse effects may occur in children. For example, it has been described that Spanish children with higher concentrations of BPA in urine had worse behavioural scores and social problems.[47] In the US, pre-teen and teenage children with higher BPA in urine had a higher prevalence of ADHD.[48] A 2016 systematic review of studies in children younger than 12 years found that prenatal exposure to maternal BPA was related to higher levels of anxiety, depression, aggression, hyperactivity, inattention, and conduct problems.[49]

**Phthalates** are a family of chemicals with multiple uses, the most common of which is as plasticizer to make hard plastic materials soft and flexible. Many consumer products including building materials, furnishings, clothing, paints, some toys, medical devices, and pharmaceuticals [50] contain phthalates. They are also widely used as food-contact materials in manufacturing and handling equipment[51] as well as packaging.[52] Many have been measured in processed foods[53,54] and infant formula.[55] Three members of this class of chemicals, dibutyl phthalate (DBP), benzylbutyl phthalate (BBP) and diethylhexyl phthalate (DEHP), are best known for their anti-androgenic properties and association with altered reproductive organ development in boys.[56] Emerging human evidence shows suggestive but not consistent data regarding the relationship between exposure to phthalates before birth and children's cognitive development. A US study showed persistent association between certain maternal urinary phthalates and IQ loss in children aged 7 years.[57] However, a European study found no association with cognitive, psychomotor or behavioural development.[58] Another US study found that urine levels of some phthalates in children were associated with increased odds of attention deficit disorder (ADD) and learning disabilities at ages 6-15 years.[59]

**Perchlorate** interferes with the normal functioning of the thyroid gland by competing with the uptake of iodine needed to make thyroid hormone.[60] Maternal thyroid dysfunction during gestation has been associated with impaired brain development in the child.[61] In the US almost all individuals tested have perchlorate in their bodies, with higher levels found in children.[62,63] European children born to mothers with

borderline thyroid dysfunction exposed to perchlorate have shown signs of heightened risk of delayed neurodevelopment.[61]Perchlorate is a contaminant released into the environment from both natural and anthropogenic sources. According to European Food Standards Authority (EFSA) it has been found in fresh fruits and vegetables potentially due to natural fertiliser.[64] In addition, drinking water can also be a source of exposure (water disinfection with chlorinated substances could lead to formation of perchlorate).[65,66] Moreover, both in the EU[52] and US,[67] perchlorate is an authorized additive for uses in plastic containers holding raw materials (e.g., flour, rice, sugar) and finished food. EFSA and the French Agency for Food, Environmental and Occupational Health & Safety (ANSES)[68] stressed that young children, especially those with mild to moderate iodine deficiency, are at high risk from perchlorate in the diet from contaminated fruits and vegetables, drinking water and infant formula. Neither agency included chemical exposure from bleach or packaging[69] in their calculations of the amount of perchlorate pregnant women and children can safely eat. The German Government has also drafted an evaluation of perchlorate as part of the EU chemicals regulation REACH (Registration, Evaluation, Authorisation and restriction of Chemicals), proposing that it should be considered an EDC for the environment.[70]

> "Evidence of neurodevelopmental toxicity of any type—epidemiological or toxicological or mechanistic—by itself should constitute a signal sufficient to trigger prioritization and some level of action." (The TENDR Consensus Statement. Environmental Health Perspectives 124: A118-A119, 2016)

**Polybrominated diphenyl ethers (PBDEs)** are widespread contaminants of the environment and the human body. Although octa- and penta-BDE are now banned, and deca-BDE is also being restricted in the EU, exposure to PBDEs is still widespread from their use as flame retardants in existing consumer products such as furniture, building materials, textiles and electronics – and their presence in house dust. These chemicals persist in the environment and some bioaccumulate, building up in the body over time. PBDEs induce neurodevelopmental effects in rodents,[71] and a recent Dutch review reported that PBDEs were associated with lower mental and psychomotor development and IQ in pre-school children, and poorer attention in those of school age.[72] Studies in US children also found decreases in attention, processing speed, fine motor coordination and cognition and poor working memory in pre-adolescent children.[73] Earlier studies in the US had already reported that younger children, 1-6 years, showed lower mental and physical development.[74] Researchers have also found a correlation between plasma PBDE levels and prevalence of hypothyroidism in Canadian women aged 30-50 years.[75]

**Organophosphate pesticides:** A recent systematic review concluded that prenatal and to a lesser extent postnatal exposure to organophosphate pesticides may contribute to neurodevelopmental and behavioural deficits in preschool and school children.[76] Chlorpyrifos is an organophosphate pesticide that has been widely used in the EU. Its residues have been found in grains (e.g. barley, wheat), fruits (e.g. peaches, strawberries, grapes) and vegetables (e.g. tomatoes, carrots, cabbage), and its metabolite has been found in the urine of the EU population.[77] Data on developmental neurotoxicity associated with chlorpyrifos mostly comes from the US. These findings associate exposure with poor working memory and

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overall IQ deficits in 7-year old children,[78] detrimental mental development as early as 1-2 years of age,[79] along with attention and ADHD problems at age 3[80] and 5[81] years. In 2015 the EU substantially reduced the Maximum Residue Level for chlorpyrifos, which has led to a ban on many uses from 2016.[82]

**Arsenic** is a widely found contaminant which occurs both naturally and as a result of human activity.[83] An EFSA opinion from 2009 estimated that dietary exposure to inorganic arsenic for children under three years of age is in general estimated to be from 2 to 3-fold that of adults. They examined the evidence for a range of health impacts, and concluded that "there is little or no margin of exposure and the possibility of a risk to some consumers cannot be excluded" for cancer and skin lesions. They also identified evidence from animal studies associating exposure during development with impacts on learning, memory behaviour and other aspects of early brain development.[84]

### *c) Chemicals with emerging evidence of DNT effects*

For the chemicals outlined above – along with others including toluene and ethanol[27] – the evidence of neurodevelopmental effects is compelling. However, there are other chemicals where there is evidence of concern. Chemicals where science is now raising concerns:

- **Per- and polyfluorinated compounds (PFCs)** are highly persistent and bioaccumulative chemicals with multiple industrial and food applications, in particular as non-stick or breathable coatings. Although some PFCs have been restricted, many are still in routine use. PFOA (perfluorooctanoic acid) and PFOS (perfluorooctane sulfonic acid) are the most researched members of this family, but there are a very large number of other PFCs in use. Human studies have found that certain PFCs interfere with normal thyroid hormone action.[60,85] As mentioned above, thyroid hormones play a fundamental role in brain development during gestation and early life, and a decrease in thyroid hormone levels during pregnancy has been associated with impaired brain development.

- **Other brominated flame retardants:** Hexabromocyclododecane (HBCD) is a brominated flame retardant (BFR) which has been used in building materials. It is now listed as a persistent organic pollutant (POP) under the United Nations Environment Programme (UNEP), so its use is restricted globally (with exemptions). Animal data indicate that prenatal exposure to HBCD may lead to behavioural changes in rodents, particularly motor activity and cognition, learning and memory.[86] Repeated exposures to HBCD also showed disruption of the thyroid hormone in rats.[87] Although no human epidemiological data have been collected, the DNT potential of HBCD observed in animal studies gives cause for concern, particularly for unborn babies and young children. It's worth noting that scientists are identifying further 'novel' or 'new' BFRs in dust in UK houses[88] and in blood serum in Sweden[89] – however, there tends to be less knowledge about the hazards of these chemicals, even though they are in our homes and bodies.

- **Organophosphorus flame retardants:** Tris (2-chloroethyl) phosphate or TCEP is used as a flame retardant plasticizer in furniture, textiles, the building industry, and in the manufacturing of cars and aircrafts.[90] It's already included in the list of substances of very high concern (SVHC) under the EU chemicals law REACH for its reproductive toxicity and studies also found that the brain appeared to be a target organ with effects including neuronal death and hippocampal lesions. An Austrian study found that TCEP present in indoor particulate matter and dust correlated with declined cognitive skills in children.[91] For other similar flame retardants there is insufficient DNT data to conclude whether they are similarly toxic to the brain.[92,93]

- **Bisphenols other than BPA:** For some uses, BPA has been replaced with bisphenol S (BPS), a substitution that may have similar or worse health effects. Recent studies have found that BPS and other similar bisphenols are found in humans, and research suggests they may exhibit developmental neurotoxicity in animals.[94-96] One study has found initial indications that BPS exposure during development may affect maternal behaviour in mice.[97]

Other substances, such as certain compounds functioning as UV filters in sunscreens have been shown to cause decreased motor activity and to affect auditory development in rats exposed during gestation.[98]

There is also evidence that other pesticides are of concern. For instance, of the 287 pesticide files reviewed by EFSA, 101 had data on thyroid disruption at some level and another 97 had effects on the developing nervous system.[124]

#### *d) Chemicals with unknown DNT effects*

As the bulk of chemicals have not been properly assessed with respect to neurotoxic or developmental neurotoxic effects, there are almost certainly many chemicals with undetected DNT effects that are in use. See "Chemical safety testing that doesn't adequately consider DNT", on page 18 for details.

## 4.4 How can developmental neurotoxic chemicals affect children?

Children exposed to environmental chemicals don't usually show any overt manifestation of impaired brain development. Changes effected by daily exposures to chemicals are not visually obvious; they are surreptitious. The result of the neurodevelopmental disruption will depend on when the exposure occurs, what area of the brain was affected and how the chemical interferes with normal developmental processes.

Compared to the adult nervous system, the impact of chemical exposure on children's brains can be fundamentally different depending on the precise timing, and can result in permanent alterations in the structure and/or function of the brain. A whole range of developmental processes occur which are specific to the developing brain and can be targets for disruption. They include stem cell proliferation, cellular differentiation and migration, and cellular maturation. In addition, experts at OECD and EFSA concluded that the child's brain processes for absorption, distribution, metabolism and excretion of chemicals are different from those of the adult brain.[99]

There is a wide range of mechanisms by which chemicals can negatively affect brain development. Although we know little about the specific modes of action of most of the chemicals of concern, the following are some examples that could lead to impaired brain development, and which are described below:

a) Hormone disruption
b) Neuronal death
c) Altered neuronal connectivity
d) Blocking of N-methyl-D-aspartate receptor (NMDA receptor)
e) Epigenetic effects.

### a) Hormone disruption

Different parts of the brain produce their own hormones as well as react to hormones produced by other organs (e.g. pituitary, thyroid, ovaries, testes). These specialized and sensitive areas react to incredibly small amounts of hormones triggering local (e.g. neuron to neuron communication) and long-distance (e.g. hormone released in the blood stream to induce ovulation) biological effects.

The scientific evidence indicates that EDCs exert their effects in many ways including:

- Binding to hormone receptors either triggering the same signal as the natural hormone or blocking the hormone from binding to it which stops the hormone from working as it should.
- Altering hormone distribution and metabolism, hormone production can be affected either locally within the brain or in other organs like the thyroid gland.
- Interfering with molecular epigenetic mechanisms (e.g. DNA methylation and histone modification) thus affecting the expression of genes needed at specific times during brain development, see 'Epigenetic effects' section below.

Consider PBDEs, BPA, phthalates and perchlorate: what they all have in common is that they are frequently found together in pregnant women,[100] they are associated with neurodevelopmental effects, and they interfere with the thyroid system. But the evidence indicates that they do not all affect the thyroid in the same way.

For instance, PBDEs affect hormone-receptor interaction and hormone metabolism (i.e. the rate at which the body processes the hormone).[101]

BPA has been postulated to antagonize thyroid hormone action by interfering with the binding of thyroid hormone to its receptor.[102]

Phthalates seem to affect several mechanisms including altering the transcriptional activity of the transporter needed to bring iodine into the thyroid cells to make the hormone, receptor-binding inhibition and inhibition of cell proliferation.[103]

Finally, perchlorate inhibits the transport of iodine into the thyroid cells.[104]

While the mechanistic underpinning of these chemicals is being sorted out, the effect is clear: thyroid insufficiency, which when occurring during foetal development can produce different long-lasting effects on the brain depending on the timing of the chemical exposure.[60]

### b) Neuronal death

Over-activation of glutamate ionotropic receptors in the brain can lead to death of neurons, with negative impacts on learning and memory impairment. The herbicide glufosinate can cause these effects, and the OECD has recently published an adverse outcome pathway (AOP) explaining the mechanism for this damage.[105] This and other AOPs, which aim to outline the key steps in a toxic response, are clearly promising tools for future screening of chemicals, and in the prediction of adverse effects. However, there is already evidence that AOPs can be misused. For example, Pesticide Action Network (PAN) Europe has argued in a recent report that they have been used, with inadequate justification, to overturn the results of animal tests making regulation less protective.[106]

### c) Altered neuronal connectivity

Neurons communicate with each other through the release of neurotransmitters including dopamine, serotonin, norepinephrine and glutamate. These neurotransmitters play key roles in modulating behaviour, cognition, learning and memory.[107] BPA has been shown to alter dopamine signalling leading to hyperactivity and attention deficits in humans. Exposures to PCBs and lead also disrupt the dopamine system.[108]

Acetylcholine and *gamma*-aminobutyric acid (GABA) are also important neurotransmitters during brain development. For instance, GABA regulates neuronal cell proliferation, migration and differentiation and the formation of synapses. One of the mechanisms by which the pesticide chlorpyrifos is associated with neurodevelopmental toxicity is by inhibiting GABA and acetylcholinesterase,[109] the enzyme needed to prevent accumulation of acetylcholine.

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### d) NMDA receptor effects

The NMDA receptor in neurons is important for learning and development, but its activity can be blocked by chemicals, including lead.

The OECD has recently published an adverse outcome pathway for this type of neuronal damage, which explains the biological steps that give rise to this impact.[110]

### e) Epigenetic effects

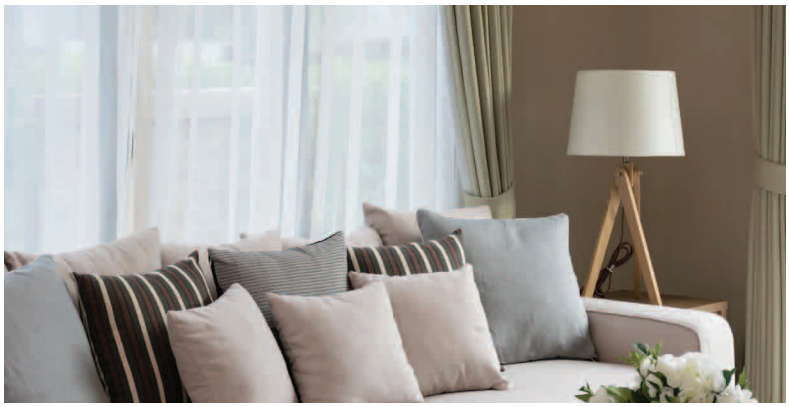
Our cells contain DNA (our genome), and associated with this DNA there is an epigenome. The epigenome is made up of: (i) chemical modifications to the DNA itself, such as methylation; and (ii) a number of histone proteins closely associated with the DNA. Changes in the epigenome can affect the expression or silencing of genes (sometimes also referred to as 'switching genes on and off') and thus controlling the production of proteins. Unlike the DNA that is the same in every cell in the body, the epigenome changes with cell differentiation and organ development, and can be altered by disease and environmental exposures. Sometimes these changes can be passed down from generation to generation.

Research has found that the developing brain undergoes substantial epigenetic modification during the foetal period and throughout life. Epigenetic processes respond to endogenous and environmental cues and are in part responsible for adult brain function and certain behaviours.[19] It has been suggested that even short exposure to environmental insults – chemical, physical, psychological – may have long-lasting effects on brain function.[111] Recent animal data suggested that prenatal exposure to BPA induces changes in the epigenome up to the fourth generation,[20] although the studies did not measure neurodevelopmental effects.

## 4.5 The failure of regulations to properly control DNT chemicals

Our understanding of the significance of early chemical exposures for children's health continues to develop. What we already know, including chronic disabilities and societies losing intellectual capital, is very concerning.

In reality we are all exposed to multiple chemicals through various routes (i.e. ingestion, dermal absorption, inhalation) and diverse sources such as food, dust, water and via consumer products. This complexity makes it difficult to unravel the impacts of individual substances and find solutions. However, one glaring roadblock to our poor understanding is the unprecedented lack of data on the chemicals in use today. A paper published in 2011 noted that less than 20% of high-production volume chemicals in widest use in consumer products in the US had been screened for their potential to disrupt human development or to cause disease in children.[30] In other words, chemicals produced at rates of more than 450 metric tonnes per year for use in clothing, building



materials, cleaning products and furniture have been given little to no scrutiny over their potentially damaging effects on our brains.

In the EU, toxicity data required under REACH has increased the amount of available toxicity data to some extent in recent years, but still the vast majority of substances used in even the highest tonnages have not been fully tested for the ability to derail brain function.

## 4.6 Chemical safety testing that does not adequately consider DNT properties

EU chemical and pesticide regulations require those entities registering chemicals, or applying for authorisation of pesticides, to provide certain safety testing information. However, few chemicals are actually tested for impacts on brain development. In addition, as recently emphasised by the International Society of Environmental Epidemiology, there are problems in using animal tests to assess likely DNT effects in people:[112]

"While some differences exist amongst organ systems between species, the human brain in particular differs radically from that of other species. Most likely, the complex brain development in humans makes it much more vulnerable to chemical hazards. Even small departures from optimal development may significantly affect higher cognition, behavior, and other brain functions."

These concerns are echoed in the TENDR statement (see Box 1) where the scientists state that "Only a minority of chemicals has been evaluated for neurotoxic effects in adults. Even fewer have been evaluated for potential effects on brain development in children."

### *1) Current neurotoxicity testing approaches do not adequately consider DNT*

The OECD guidance document for neurotoxicity testing from 2004,[113] delineates a roadmap to suggest when this testing is necessary. It is based on principles relying heavily on available data, chemical structure and effects on the nervous system following traditional toxicity evaluation using adult animals. If there is no evidence of very obvious neurotoxic effects (e.g. paralysis, convulsions, tremors and bizarre behaviour) at high doses and no evidence of macro or microscopic changes in the brain or nervous system, it is assumed that there is very low level of concern about potential neurotoxic effects for a particular chemical.

This testing approach means that in many cases there is no further testing for DNT effects. This is inadequate because:

a) the great majority of chemicals on the market lack sufficient safety information, and

b) the human brain is vastly more complex than the rodent brain, and thus much more vulnerable. Current procedures that look at decreased brain weight in rodent pups are not therefore sensitive to the kinds of effects that may occur in humans. While current OECD tests may be useful, they need to be interpreted prudently, as they do not reveal the extent of adverse effects that may occur in more complex brains like those of humans.

### *2) Sensitive testing methods are available but are seldom applied*

The OECD guideline study for developmental neurotoxicity from 2007[114] is designed to assess potential functional and morphological effects on the developing brain and nervous system. It measures the effects of prenatal exposure and exposure through lactation and

**Box 1: The Targeting Environmental Neuro-Developmental Risks(TENDR) Project**

In July 2016, over 40 leading US scientific and medical experts together with children's health advocates issued a call for action to reduce widespread exposure to chemicals that interfere with foetal and children's brain development.

In the statement, published in Environmental Health Perspectives, the authors conclude based on the available science that:

"children in America today are at an unacceptably high risk of developing neurodevelopmental disorders that affect the brain and nervous system"

at various life-stages, including young adulthood. The measurements include motor activity (hypo and hyper), motor and sensory functions (e.g. strength, coordination, reflex, hearing) and learning and memory (short- and long-term) performance. Unfortunately, these tests are not routinely done.

An OECD advisory group in 2014 concluded that there was a lack of in vitro tests for thyroid hormone disruption and more needed to be developed.[115]

In October 2016, OECD and EFSA organised a Workshop on Developmental Neurotoxicity which looked into the use of non-animal test methods for regulatory purposes.[a] This workshop emphasised that this is an important area in need of development of methods, as well as investigation of their use in regulatory decision-making. In future, predictive in-vitro test methods could be integrated in chemical-specific assessments and for prioritisation (for further testing) for the thousands of chemicals on the market for which there is no data at all on their potential to cause DNT.

### *3) Over reliance on Thresholds of Toxicological Concern (TTC)*

The TTC approach is a screening and prioritisation tool for risk assessment of chemicals when hazard data is unavailable and human exposure is estimated to be low. It requires knowledge of the chemical structure and information on human exposure, and then uses generic human exposure threshold values derived from substances grouped according to their chemical structure and likelihood of toxicity based on cancer and non-cancer health effects.[116] If a chemical exposure is estimated to be below the generic thresholds, no other risk assessment is necessary unless data is required for a specific regulation.

TTC is currently used by EFSA for evaluation of flavouring substances in food and pesticide metabolites in groundwater. It has also been proposed for assessment of consumer products; pesticide metabolites, degradation and reaction products; and for industrial chemicals assessment under REACH.

However, this approach uses only chemical structure and exposure estimates, and just looks at a limited range of toxic end points. There is therefore no adequate knowledge of whether the substance is an EDC or has other DNT properties since these are determined by experimental observations in cells or animals. This means the TTC approach is not appropriate for assessing such properties.

a https://www.efsa.europa.eu/en/events/event/161018b

> “Our failures to protect children from harm underscore the urgent need for a better approach to developing and assessing scientific evidence and using it to make decisions. We as a society should be able to take protective action when scientific evidence indicates a chemical is of concern, and not wait for unequivocal proof that a chemical is causing harm to our children.”
> (The TENDR Consensus Statement, Environmental Health Perspectives 124:A118-A119, 2016)

#### *4) Chemicals are tested one by one, and the toxicity of the mixtures we are really exposed to is generally ignored*

The toxicity of chemicals, when tested, is evaluated for each chemical individually. However, in reality humans are exposed to multiple chemicals from a wide variety of sources every day. Animal data show that exposure to a mixture of EDCs can cause adverse effects while exposure to the individual chemicals at the same dose, does not.[117] This research demonstrates that mixtures can have cumulative impacts, causing adverse effects. Prenatal exposure to mixtures has also been associated with the appearance of adverse effects later in life.[118] There are many studies which illustrate the need to consider the effects of simultaneous exposure to many chemicals, three examples of which are noted below:

- Virtually every pregnant woman in the US – and probably in the EU – has at least 43 chemicals in her body, from PCBs and PBDEs to phthalates and pesticides.[100,119]
- The UK Total Diet Study analysed 261 retail foodstuffs for 15 phthalates. Multiple food categories (bread, meats, cereal, fish, etc.) contained one or more phthalates.[120] Phthalates and BPA were found in all foods and beverages tested that are commonly consumed in Norway.[121]
- Between 43% and 96% of infant formula, both powder and liquid, tested in Italy, had two types of phthalates and BPA.[122]

The calculation of a chemical safe-dose in isolation (e.g. within one area of regulation) and without consideration of the full range of sources of exposure does not reflect the real world and fails to adequately protect public health.

## 4.7 A failure in the assessment of the risk of DNT effects

Risk assessment is routinely used to establish whether a chemical needs to be regulated in order to protect public health. However, risk assessment of DNT chemicals is subject to a number of crucial flaws:

#### *1) Over-reliance on inadequate data in risk assessment*

With little or no toxicity testing for developmental neurotoxicity and a lack of reliable exposure data for sensitive periods, it is impossible to perform a quantitative assessment of the risk of harm to the human brain and to adequately control exposures. Moreover, in the past, epidemiology has shown that harm to the human brain can occur at lower exposure levels than might be predicted from animal data,[123] and therefore a more precautionary stance is needed, pointing to elimination of exposure where possible rather than exposure reduction. See policy recommendations (6.2) for potential ways forward in this regard.

#### *2) Lack of assessment of cumulative biological effects of chemicals*

Assessing substances that act on the same organs or biological pathways that converge as a group rather than individually is a more accurate way to estimate the true health effects of chemical exposures. Except in a few instances, e.g. the pesticide evaluation performed by EFSA[124] and the cumulative risk assessment for a handful of phthalates conducted by EU Chemical Agency (ECHA),[125] risk assessment is conducted for an individual chemical based on the toxicity it causes to specific organs.

A health outcome such as a neurobehavioural disorder may seldom be the consequence of exposure to a single chemical; rather, the cumulative biological effects of multiple chemicals impacting brain development in different ways and at various life-stages are likely to contribute to the subclinical or clinical manifestation of the health problem. For example, PBDEs, PCBs, perchlorate and BPA are known to interfere with thyroid system potentially leading to impaired foetal and child brain development.

> "Our system for evaluating scientific evidence and making decisions about environmental chemicals is broken. We cannot continue to gamble with our children's health."
> (The TENDR Consensus Statement, Environmental Health Perspectives 124:A118-A119, 2016)

It is inadequate to estimate how much is safe to consume of each chemical individually when they could be having an additive effect. A more adequate approach would be to estimate the safe amount taking into consideration the toxicity and exposure data for all relevant chemicals. This tactic would more realistically reduce the risk of thyroid dysfunction. Also important to develop mitigation strategies to reduce the risk of health problems is to know which of these chemicals is a major contributor to thyroid dysfunction.

EFSA has developed a methodology to group pesticides causing effects on the nervous system and thyroid hormone system to deal with the cumulative effect of chemicals on these systems and reduce acute and chronic health effects caused by exposure to multiple chemicals. However, as noted above, this does not take into account other exposures to these and other chemicals with similar actions, including chemicals used in consumer articles, etc.

There is evidence for each of the chemicals mentioned above that by themselves they may cause neurodevelopmental toxicity. But there are many more[126] that both singly, and in combination, may cause equal or greater harm due to cumulative effects on the brain.

## 4.8 The cost of failure

The social and economic cost of mental disorders is huge, with the yearly cost associated with anxiety disorders and ADHD in children in the EU estimated at €74.4 and €21.3 billion, respectively, including direct health care, non-medical and indirect (production loss) costs.[127]

In 2010, the annual cost of learning disability per person was almost €10,000 in Spain and other child and adolescent behavioural and anxiety disorders cost approximately the same.[128] In the UK, child and adolescent disorders cost just under €5,000 per year per person affected by the disorder.[129]

These figures are overall costs of these conditions, not just those that are known or suspected of being due to chemical exposures. However, a recent study has estimated that:[130]

"EDC exposures in Europe contribute substantially to neurobehavioral deficits and disease, with a high probability of €150 billion costs/year."

This study focussed on costs from IQ loss, autism and ADHD which could be associated with EDC exposure – it therefore excluded the impacts of chemicals such as lead.

We know that people are exposed to a range of chemicals of concern, with knowledge increasing all the time. This should be sufficient incentive to design strategies aimed at significantly reducing exposure to thyroid disrupting chemicals and other developmental neurotoxicants, with the ultimate goal of eliminating, or at least decreasing, the contribution chemicals make to neurodevelopmental health problems.

# 5 Two top scientists answer our questions about DNT

## 5.1 Review of report

This report was reviewed by two eminent researchers in the field, both of whom have published extensively on the topic. The comments of both reviewers were addressed during the drafting and revision of the report.

In addition to reviewing our report, we asked both scientists a range of questions and their answers are shown below.

## 5.2 Barbara Demeneix

Barbara Demeneix holds a professorship in the Laboratory of Evolution of Endocrine Regulations, a CNRS mixed research unit within the Natural History Museum in Paris. Trained in the United Kingdom, France, Canada, and Germany, she is an internationally recognised expert on thyroid function and endocrine disruption and is the author of more than 160 scientific publications. She has received numerous awards for her work, notably the CNRS Medal for Innovation in 2014 and the Mentoring Award 2011 from the journal 'Nature'. Today, Barbara Demeneix maintains active roles in many EU research projects[a] and within the OECD representing France on different committees addressing endocrine disruption.

Her research focuses on evolution of thyroid hormone signalling: 1) Addressing the molecular basis of thyroid hormone action during amphibian metamorphosis. Within this context she developed an applied somatic and germinal transgenic technology that led to the creation of the start-up company WatchFrog[b] for screening and environmental monitoring. 2) Understanding thyroid hormone action on brain development and during aging, focusing on neural stem cells in adults. 3) Understanding thyroid hormone implication in hypothalamic control of metabolism.

Barbara is the author of *Losing our Minds: How Environmental Pollution Impairs Human Intelligence and Mental Health*, published by Oxford University Press, in 2014 and *Toxic Cocktail* which will be published by Oxford University Press in 2017.

***a) Why do you think neurodevelopment effects are of concern to current and future generations?***

Principally because chemical exposure is now at unprecedented levels, is multiple, ubiquitous, and present from conception onwards. We have recently learned of the highly sensitive period of early pregnancy as a window of vulnerability for changes in maternal thyroid hormone that can impact brain development (and hence IQ and neurodevelopmental disease risk). So given the number of chemicals that affect thyroid hormone signalling and that are found in pregnant women, there is major cause for concern.

In this context, contamination of amniotic fluid with a spectrum of xenobiotics presents a very worrying picture. Many of these xenobiotics are known thyroid hormone disruptors. The importance of too much or too little thyroid hormone in early pregnancy has recently been demonstrated, in terms of offspring IQ and brain structure.

a https://bdemeneix.wordpress.com/euprojects/
b WatchFrog: http://www.watchfrog.fr/

**b) *How certain are you that chemical exposures in the EU have affected children's brain function?***

As we developed in our 2015 paper we gave a "70-100% probability that polybrominated diphenyl ether and organophosphate exposures contribute to IQ loss in the European population. We concluded that EDC exposures in Europe contribute substantially to neurobehavioral deficits and disease, with a high probability of >€150 billion/year. These results emphasize the advantages of controlling EDC exposure."

**c) *How certain are you that some chemicals to which EU citizens are still exposed are actually affecting children's brain function today?***

We erred on the side of caution in the 2015 analysis. However, when I look at the data we now have on the effects of a mixture of common human amniotic fluid contaminants on thyroid hormone signalling in early embryogenesis, my disquiet deepens. The mixture was based on the most common chemicals found in US populations, including pregnant women, and effects were found on thyroid hormone signalling, neural lineage decisions, cell morphology and behaviour. Given that most of the substances are also ubiquitous in EU populations, I reiterate that this is cause for serious concern.

**d) *Given all the other potential causes of altered brain development, what sort of contribution do you think might be attributed to chemical exposures?***

It is clear that intense screen (computer, telephone etc.) usage is also changing communication of parents with children and that this is impacting children's post-natal development, possibly including brain development. However these factors do not directly impinge on in-utero growth and development, a period that has been shown repeatedly to be a vulnerable window for organ formation, particularly brain development. Other factors could include Wi-Fi signals and nanoparticles. However, the data is not anything like as strong as for chemicals (including atmospheric pollution). Hence, I'd say that given current data sets, chemical exposure is the environmental factor altering brain development for which we have the strongest evidence.

**e) *How would the effects of exposure to developmental neurotoxicant chemicals likely manifest themselves?***

- To measure effects one needs studies at the level of populations as it is exceedingly difficult to pinpoint effects of exposure in individuals. This is because there is always a large spectrum of abilities (that reflect different levels of intellectual ability) as is the case for neurodevelopmental disorders (overlap between symptoms and degrees of severity).
- This limitation was brilliantly illustrated (I cite this in both *Losing our Minds/ Toxic Cocktail*) by David Rall, a past director of the US National Institutes of Environmental Health Sciences (NIEHS), who referred to the case of thalidomide, the drug that was prescribed for pregnant women in the 1960s with a view to preventing morning sickness. It had no effect on the incidence of the symptoms, but it caused dreadful deformities in the limbs of the babies. Rall is quoted as asking the rhetorical question: "If thalidomide had caused a 10-point reduction in IQ, would its effects be known?" Today, would we notice it among the thousands of chemicals currently marketed? Of course the answer to Rall's question is 'no' – you have to look for effects at the level of populations.
- What's more, searching for correlations between exposure and effects on neurodevelopment is increasingly difficult as the numbers of chemicals increases and, by definition, the complexity of the mixtures to which we are all exposed.

*f) Which chemicals are most likely to be involved?*

Well as you know I've written a couple of books on this where I elaborate on my basic hypothesis:

- Many of the chemicals that are most likely to be involved are halogenated. Because of this structural similarity with thyroid hormone (TH), which is the most complex halogenated compound synthesized by vertebrates, such halogenated chemicals in our environment may disrupt the normal functioning of the thyroid and action of TH throughout our bodies at all ages.
- TH is essential for brain development. TH modulates all the processes implicated in brain development, proliferation, migration, differentiation, myelination, synaptogenesis and plasticity.
- TH signalling is thought to be the part of the endocrine system most prone to EDCs. Small variations in maternal TH affect children's IQ and brain structure.
- Iodine lack is increasing and iodine is needed to make TH – what's more many of these environmentally relevant chemicals interfere with iodine uptake by the thyroid gland (eg brominated molecules and perchlorate).
- Mercury, one of the most common and best-documented chemicals negatively affecting brain development, interferes with TH activation and metabolism.
- Other chemicals that are likely to be involved are covered in the above CHEM Trust report. Not all developmental neurotoxicants will be EDCs, but many will be. Moreover, it is also now known that many TH disrupting chemicals can be found in amniotic fluid.

*g) What should a member of the public do if they wish to reduce their risk – or the risk to their current/future children?*

See Table Four in Parent et al., 2016 – excellent tabular guide – usual ideas – eat organic, fresh food, etc. don't refurbish/repaint house if pregnant….avoid bottle water and microwaving in plastic containers etc.

*h) If you were in charge of the EU, what would you do to help solve this issue?*

By better testing and regulation of chemicals, with particular emphasis on taking into account biodegradability of chemicals during design and synthesis and avoiding regrettable substitutions as exemplified by BPA replacement with BPS. This latter example exemplifies the need for regulation of certain categories of chemicals.

*i) What do you think could be the role of grouping of similar chemicals in addressing the problem of neurotoxicity?*

Potentially very useful – the case of phthalates and their replacements would be an excellent case in point.

*j) Which groups would you prioritise?*

Phthalates (see above), phenols (BPA, triclosan etc.), iodine uptake inhibitors (perchlorate, nitrate and thiocyanate), flame retardants (brominated or chlorinated), perfluorinated compounds, heavy metals.

*k) What do you think should be done with chemicals in these groups?*

No substitutes allowed on the market until thoroughly tested.

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## 5.3 Philippe Grandjean

Philippe Grandjean was born in Denmark in 1950. He graduated as a medical doctor from the University of Copenhagen at age 23, and six years later he defended his doctoral thesis on the *Widening perspectives of lead toxicity*. He became Professor of Environmental Medicine at the University of Southern Denmark in 1982. A Fulbright Senior Scholarship award brought him to Mt. Sinai Hospital in New York, and he later served as Adjunct Professor of Neurology and Environmental Health at Boston University. In 2003, he became Adjunct Professor of Environmental Health at Harvard University. In 2015, he received the Bernardino Ramazzini Award for "his long career conducting and promoting environmental health research, especially his ground-breaking work on the effects of methylmercury and other environmental toxins affecting children and for his tireless advocacy of the need to protect future generations from the devastating effects of neuro- and developmental toxins."

He lives in Copenhagen, Denmark and in Cambridge, MA, and travels widely to study environmental problems and to examine children whose lives have been affected by pollution, more specifically, the delayed effects of developmental exposure to environmental chemicals.

Oxford University press published his book *Only One Chance: How Environmental Pollution Impairs Brain Development – and How to Protect the Brains of the Next Generation,* in July 2013. He also runs the "Chemical Brain Drain" web site, http://braindrain.dk

***a) Why do you think neurodevelopment effects are of concern to current and future generations?***

Our brains make us who we are, and we need optimal brain functions in order to enjoy the full benefits of the capacities that we inherited from our parents. But we have discovered that a variety of chemical agents can interfere with early brain development, and such chemical brain drain is most likely irreversible. We have only one chance to develop a brain, and that's the brain we will rely on for the rest of our lives. The current generation has the responsibility to safeguard the brains of the future.

***b) How certain are you that chemical exposures in the EU have affected children's brain function?***

I am as certain as one can be when relying on epidemiological studies. Experimental studies in laboratory animals strongly support the plausibility of adverse effects on brain development. Given that we cannot conduct human experiments with these toxic chemicals, we must rely on documented adverse effects observed in children with elevated exposures. However, current regulatory procedures usually ignore human studies due to possible flaws. However, if stronger documentation is demanded, we would have to study even larger numbers of children with neurotoxic effects – which seems paradoxical, as we would then postpone any effective prevention in the name of science, which to me is misleading and unethical.

**c) *How certain are you that some chemicals to which EU citizens are still exposed are actually affecting children's brain function today?***

We know the dose-related deficits from multiple studies on children in different countries, and reported exposures to several neurotoxicants in the EU commonly exceed the levels that are associated with adverse effects on brain development.

**d) *Given all the other potential causes of altered brain development, what sort of contribution do you think might be attributed to chemical exposures?***

Calculations in the United States show that IQ losses associated with chemical exposures are of a similar magnitude as the losses due to preterm birth and a variety of diagnoses, such as ADHD. I would therefore call the contribution by chemical brain drain very substantial.

**e) *How would the effects of exposure to developmental neurotoxicant chemicals likely manifest themselves?***

In most cases, the child will remain within the "normal" range of functions, but groups of children with elevated neurotoxicant exposures will show average functions that are below those in children who have escaped such exposures. Some research suggests that neurotoxic chemicals may contribute also to the development of ADHD, ASD, and other diagnoses, but these potential effects are still unclear.

**f) *Which chemicals are most likely to be involved?***

We only know about the most apparent ones that have been studied in at least some detail, currently about 12-14 chemicals. But several pesticides are suspected of causing adverse effects on brain development, as are some solvents, metals and other compounds. While lead, arsenic, methylmercury, and chlorpyrifos (a pesticide) may appear to be among the most serious hazards, other neurotoxic compounds are probably lurking, but haven't yet been documented. From human poisoning cases, we know of at least 200 chemicals that can enter the human brain and cause damage to the nerve cells (the chemicals are listed in my book *Only one chance*). I would think that virtually all of them can also harm the development of the human brain, most probably at much lower levels than those that cause adverse effects in adults. About half of these chemicals are commonly used (so-called high production volume) and therefore present a high potential for exposures.

**g) *What should a member of the public do if they wish to reduce their risk – or the risk to their current/future children?***

Based on what we know today, some limited advice can be given. In regard to lead, depending on the residence, consider having the drinking water at home tested for lead, as well as the paints that may peel and cause exposures. For arsenic, the drinking water in certain areas may be contaminated; filters are available to remove the arsenic. Fluoride can also be a water contaminant in certain areas; bottled water may be needed to avoid the water contaminants, though some brands are high in fluoride. In regard to mercury, pregnant women should avoid eating large, predatory fish, such as sushi tuna and canned albacore. Finally, I recommend that pregnant women avoid conventionally grown fruits and leafy vegetables, although those that can be peeled are less likely to be contaminated. The use of pesticides, paint thinners and the like at home or in the garden is also a bad idea, especially when exposures may involve pregnant women and small children.

**h) *If you were in charge of the EU, what would you do to help solve this issue?***

I would insist that the Precautionary Principle must be applied in order to protect the next generation's brains.

*i) What do you think could be the role of grouping of similar chemicals in addressing the problem of neurotoxicity?*

Grouping similar chemicals makes sense, but would probably have to be combined with computer-based prediction and high through-put testing in order to support classification as neurotoxic. We definitely need to move away from the current situation, where regulatory agencies rely on tests that do not reflect neurotoxic potentials, and where risks to children's brain development instead have to be established from evidence that chemicals are in fact damaging children's brains – a paradox, as that is exactly what we want to prevent.

*j) Which groups would you prioritise? What do you think should be done with chemicals in these groups?*

I think pesticides can be very problematic, especially those that are targeting insect nervous systems. Likewise, several solvents have the propensity to cross the blood-brain barrier, and that adds to the likelihood of a neurotoxic risk. Although certain types of toxicity, such as thyroid toxicity, may be of importance, we cannot rely on limited criteria like that, as we generally do not understand the mechanisms that make the known human neurotoxicants as dangerous as they are. It would be disingenuous to require knowledge on the mechanism before a proper prevention can be decided upon. Thus, intensive screening for toxicity to the brain is required for industrial chemicals in a more general sense, so that we can target our efforts to control substances and thereby protect the next generation's brains.

# 6 EU Policy context and recommendations

## 6.1 EU Policy context

One of the key objectives of the EU's 7th Environmental Action Programme (7th EAP), adopted in 2013 by all EU Member States and the EU Parliament, is to safeguard European citizens from risks to health and wellbeing. The 7th EAP also sets out a long-term vision of a non-toxic environment and proposes to address risks associated with the use of chemicals in products and chemical mixtures, especially those that interfere with the endocrine system.

The 7th EAP also includes a commitment to set out a comprehensive approach to minimising exposure to hazardous substances, and an EU Strategy for a non-toxic environment is currently being prepared for adoption in 2018. In addition, the EU is currently reviewing REACH, and in CHEM Trust's view there are important improvements that can be made to REACH in order to create stronger protection from chemicals with DNT properties.

> "Research indicates that some chemicals have endocrine-disrupting properties that may cause a number of adverse effects on health and the environment, including with regard to the development of children, potentially even at very low doses, and that such effects warrant consideration of precautionary action."
>
> EU's 7th Environmental Action Programme

In light of these policy aims, and the concerns laid out in this report, the overarching goal should be to eliminate exposure to chemicals which have DNT properties. To this end, chemicals with such properties should be identified and restricted. This will require action on many fronts, outlined below:

## 6.2 Recommendations

### *1) Action on chemicals identified as having evidence of developmental neurotoxicity: using available tools to act on existing knowledge*

- Given that in the case of developmental neurotoxic chemicals the brain development of future generations is at stake, it will be imperative to act on limited evidence rather than absolute proof. Final proof of causality in humans or through complete details of the mechanism of action are often impossible to achieve, and will in all likelihood require a large number of humans being harmed.
- In the assessment of the data it will be important to include results from academic studies even if they are not using internationally agreed test methods, so that a more comprehensive evidence base is used.
- All areas of chemical policy, including REACH, should develop approaches for assessing and controlling groups of chemicals with DNT potential, rather than just using a substance by substance approach.
- We call on the Commission and EU Member States to act where there is already evidence of DNT effects either in humans or animal studies, to ensure such industrial chemicals are regulated under REACH. If there is evidence for hormone disruption (i.e. thyroid disruption) these chemicals should be identified and regulated as EDCs, with the presumption that there is no safe threshold for exposure.
- Likewise, a precautionary approach to restricting pesticides and biocides with DNT properties should be adopted.

- Given the worrying research regarding DNT properties of perchlorate it should be identified as an EDC under REACH. Furthermore, a comprehensive assessment of sources is needed in order to then identify all available methods of reducing our exposure.
- In addition to the existing Commission recommendation for Member States to monitor levels of arsenic in food,[131] the EU should also develop specific measures and advice for reducing exposures to arsenic, in particular in pregnant women and small children.
- The possibility of creating a classification system for DNT chemicals should be investigated, as already exists for carcinogens, mutagens and reproductive toxins.

### 2) *Addressing the reality that we are all exposed to multiple chemicals all the time*

- The upcoming EU Strategy for a non-toxic environment, which is due in 2018, should include a focus on measures to improve the protection of children from combined exposures to neurodevelopmental toxic chemicals.
- In its Communication on 'The Combination effects on chemicals', 2012,[132] the Commission had promised a report reviewing the progress and experience associated with the actions on mixtures by the end of June 2015. However, the report has still not appeared and we recommend that it is published as soon as possible.
- The EU laws on food contact materials are very deficient, as they do not ensure EU regulation of chemicals in paper, board, ink, glues and coatings. Chemicals in food contact materials may be an important exposure route adding to the low level daily combined exposure of consumers, including children. Chemicals and chemical mixtures used for food contact materials should be adequately screened and tested for DNT properties.
- In the upcoming REACH review of 2017, the possibilities for authorities to act on known co-exposures to harmful chemicals needs to be strengthened. A risk assessment focusing on a single substance should no longer be used to decide on safe-use for substances reported to contribute to the same adverse outcome either because they have the same mechanism of action or mechanisms of action that converge. Therefore, a regulatory approach for cumulative risk assessment needs to be developed.
- EFSA has conducted some very useful work on the cumulative risk assessment of pesticides in combined assessments of those pesticides causing effects on the nervous system and thyroid hormone system.[124] However, to assess the overall daily exposure of a child to neurodevelopmental toxic chemicals it needs to be expanded to include chemicals from all other sources, e.g. indoor air pollution, dust and food contact materials.

### 3) *Ensuring proper identification of chemicals with DNT properties using existing screens and tests*

- Implement new and updated screens and test methods in the data requirements prescribed in EU laws, for example, including, but not limited to, those relating to industrial chemicals, pesticides and biocides, as soon as appropriate test methods become available.
- Ensure that the testing of chemicals for safety is not avoided by unjustified arguments. It should be made mandatory for all Extended One-Generation studies to include an assessment of DNT properties.

- For REACH substances which have already gone through registration, there is a need for revisiting them to see if they have the potential to cause effects on the brain development. The Commission should make it a priority to develop and fund in-silico and in-vitro screening of all those chemicals with known consumer uses. Where screening or lower-tier test data flag a concern, such chemicals should be subject to a more in-depth substance evaluation, where further higher-tier test data can be required and assessed.

### 4) Development of new tests and better screens to identify chemicals that can affect all aspects of brain development and function

- A well-resourced EU Expert Task Force on Protection of the Brain should be set up with the aim of identifying and developing better screens and tests for DNT properties. One key output of this group should be the development of a rapid screening framework, which includes in-silico and in-vitro rapid screening methods so that those chemicals which need more detailed examination can be identified and prioritised for agreement as OECD Guideline Studies.
- A second key goal of the EU Expert Task Force, as suggested by Grandjean and Landrigan,[26] would be to promote optimum brain health, inspiring, facilitating and co-ordinating research and public policies that protect brain health especially during the most sensitive life stages. One part of this would be to stimulate and coordinate new research to better understand brain development and function and how toxic chemicals interfere with brain development.
- There needs to be sufficient EU and national research funding for developing and improving rapid screening technologies and test methods for chemicals in use to identify those with potential to disrupt thyroid-related pathways or other potential neurodevelopmental toxicants.
- In the medium term, the test requirements in all relevant EU laws should be modified to include screens and tests for neurotoxicity. There is a need for a shift in emphasis from minimising the costs to industry to getting enough data to gain a reasonable assurance of safety.
- There is also a need for test methods to identify effects on brain function in old age which are due to early life exposures.

### 5) Better understanding of, and statistics on, neurodevelopmental disorders such as autism and ADHD

- The EU and Member States, need to improve data collection on neurodevelopmental disorders such as autism and ADHD, in order to determine more precisely any trends, over time, in brain function, both in children and in old age.
- More research is needed into neurodevelopmental disorders, focussing both on prevention and treatment.

### 6) Ensuring that the UK public is properly protected from hazardous chemicals

- Although the EU has not yet managed to fully address the issue of neurotoxic chemicals, it is important to note that EU regulations have already controlled a number of the chemicals of concern, and that EU laws provide a tool to address these problems.
- The UK has voted to leave the EU, which threatens to jeopardise UK public health unless the UK remains closely aligned with EU chemicals regulations.

- We would recommend that:

  a) The UK Government works to stay aligned with EU chemicals laws.

  b) The European Commission and the remaining EU27 Member States facilitate the UK's close alignment with EU chemicals laws, in the interest of public health and the environment.

- Efforts should be made to avoid flame retardant chemicals where possible. In particular, the UK and Ireland should remove the requirement for an open flame test for furniture. The rest of EU, and recently California, require only a smoulder test, which leads to reduced use of flame retardants whilst still providing effective protection against fires.[a]

**Box 2: Recommendations for the current 5-yearly review of the EU's main chemicals regulation, REACH**

The EU is currently reviewing its main chemicals regulation REACH, and in CHEM Trust's view there are important improvements that can be made to REACH in order to create stronger protection from chemicals with DNT properties.

- The European Chemical Agency (ECHA), the European Commission and EU Member States should work to ensure that REACH is able to assess and control groups of chemicals with DNT potential, rather than just using a substance by substance approach.
- REACH regulatory procedures, i.e. restriction and authorisation, should be considered for any industrial chemicals with evidence of DNT effects either in humans or animal studies. If there is evidence for hormone disruption (i.e. thyroid disruption) these chemicals should be identified and regulated as EDCs, with the presumption that there is no safe threshold for exposure.
- It is well known that many registration dossiers in REACH are of poor quality, and have not been updated. ECHA has suggested that there could be an implementing act clarifying the requirement to update dossiers.[133] We would suggest that this requirement could be combined with the results of rapid screening for DNT effects in order to identify those chemicals where dossiers should be updated – and potential evaluation undertaken – due to evidence of potential DNT effects.
- A regulatory approach for cumulative risk assessment needs to be developed for REACH. A risk assessment focusing on a single substance should no longer be used to decide on safe-use for substances reported to contribute to the same adverse outcome, either because they have the same mechanism of action or mechanisms of action that converge.




a http://www.chemtrust.org.uk/wp-content/uploads/chemtrust-response-beis-fr-nov16.pdf

# 7 What can you do to reduce your exposure?

The protection of future generations' brains requires proper policy measures, as laid out in Chapter 6 of this report.

You can help ensure that governments and the EU make these vital improvements by contacting your government and the politicians that represent you, including Members of the European Parliament, if you live in the EU. For details see: http://www.chemtrust.org.uk/takeaction-citizen/

However, in the meantime, individuals can reduce their own exposure to an extent; some ideas below:

## 7.1 Food

If you want to minimise your exposure to pesticides (some of which are known or suspected neurodevelopmental toxic chemicals), the best way to do this is to switch to organic food. PAN Europe has a useful consumer guide,[a] and the European Commission has a web site promoting organic farming[b] which has more information. You should also avoid the use of pesticides in your own house and garden.

Harmful chemicals can bioaccumulate up the food chain, with chemicals being stored in fat cells. Therefore if you eat meat, cut off the fatty parts and try to stick to lean meat.

Fish (particularly oily fish) can help brain development, but the oils in some fish also contain high levels of chemicals which have accumulated over time (for example methyl mercury and PCBs). The European Food Safety Authority has recently stated[c]:

Limiting consumption of fish species with a high methylmercury content is the most effective way to achieve the health benefits of fish whilst minimising the risks posed by excessive exposure to methylmercury...

EFSA recommends that individual Member States consider their national patterns of fish consumption and assess the risk of different population groups exceeding safe levels of methylmercury while obtaining the health benefits of fish. This particularly applies to countries where fish/seafood species with a high mercury content – such as swordfish, pike, tuna and hake – are consumed regularly.

a http://www.disruptingfood.info/en/cons-guide
b http://ec.europa.eu/agriculture/organic/
c http://www.efsa.europa.eu/en/press/news/150122.htm

### a) Food packaging

Food packaging uses a wide range of chemicals, and the regulation of packaging materials is not as good as it should be.[d] In particular, current EU laws do not properly control the chemicals used in paper, card, inks, glues and coatings.[e] To reduce your exposure, try to reduce your use of packaged food and instead buy more fresh products. Store cereals and rice etc in glass jars.

Do not use food packaging for purposes other than for what it was sold. For example, don't microwave in plastic boxes that aren't marked as microwave-safe, and microwave in glass if you can.

### b) Cooking food

Even when foods are sold stating they should be cooked in their packaging, this may not be the best option. For example, the Danish Co-op supermarket stopped selling microwavable popcorn as all brands contained PFC chemicals[f] – though now they have found alternatives.

### c) Cleaning products

In general, it is advisable to minimise the use of cleaning products. Use natural cleaning brands, in particular, look out for products with independent ecolabels such as the EU Ecolabel,[g] the Blue Angel[h] or the Nordic Ecolabel.[i]

### d) Soaps, shampoos and cosmetics

In the EU, all cosmetics must have an ingredients list, which makes it easier to avoid problem chemicals. Note that this list does not include identification of the chemicals in perfumes and fragrances.

### e) Till receipts and other thermal paper

Most thermal paper, such as till (cash) receipts, contain BPA, a known hormone disrupting chemical. The BPA can leach out and get into our bloodstream.[j] Minimise your handling of receipts or other thermal paper. The EU has agreed to ban this chemical, but this will take time to come into force, and there are concerns that similar chemicals will be used to replace BPA.[k] Don't let children play with receipts!

## 7.2 Dust

House dust has been found to have quite high levels of a range of problematic chemicals, including phthalates, brominated flame retardants and bisphenol A. It is generally a good idea to make sure you clean your home frequently in order to reduce the build-up of dust.

## 7.3 Asking companies

You can write to companies (or contact them on social media) to ask them about specific chemicals, about hormone disrupting chemicals in general or about chemicals that have been defined as being of very high concern under the EU's REACH chemicals regulation. Under REACH, a company must tell you if their product contains such a chemical – ECHA has a page explaining the process.[a]

d http://www.chemtrust.org.uk/chemicals-in-food-packaging-a-can-of-worms/
e http://www.chemtrust.org.uk/foodcontact/
f http://www.chemtrust.org.uk/pfcs/
g http://ec.europa.eu/environment/ecolabel/index_en.htm
h https://www.blauer-engel.de/en
i http://www.nordic-ecolabel.org/
j http://www.chemtrust.org.uk/hormone-disrupting-chemical-bisphenol-a-can-transfer-from-receipts-into-our-bloodstream/
k http://www.chemtrust.org.uk/eu-chemical-agency-committee-agrees-that-bisphenol-a-in-receipts-poses-risk-to-workers/

## 7.4 Finding out about chemicals

- ECHA's official database[b] has a simple 'info card' available for up to 120,000 substances.
- The European Trade Union Institute's Risctox database[c] gives information on a wide range of chemicals.
- ChemSec's 'Substitute it Now (SIN)'[d] list focusses on those chemicals with particularly problematic properties.

## 7.5 Other sources of advice about avoiding hazardous chemicals:

- Breast Cancer UK has a set of pages explaining how you can reduce your exposure to hazardous chemicals:
  http://www.breastcanceruk.org.uk/reduce-your-risk
- Project Nesting from Women in Europe for a Common Future, particularly aimed at those who are pregnant:
  http://www.projectnesting.org/start

a http://echa.europa.eu/chemicals-in-our-life/how-can-i-use-chemicals-safely/use-your-right-to-ask
b http://echa.europa.eu/information-on-chemicals
c http://risctox.istas.net/en/
d http://www.chemsec.org/what-we-do/sin-list

# 8 Glossary and Abbreviations

**7th EAP:** EU 7th Environmental Action Programme – a programme guiding the development of European environment policy until 2020, setting out a vision towards 2050

**ANSES:** Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail – French Agency for Food, Environmental and Occupational Health & Safety

**Anti-androgenic Properties:** Chemicals acting to block the effects of male sex hormones such as testosterone

**AOP:** Adverse outcome pathway – an analytical construct that describes a sequential chain of causally linked events at different levels of biological organisation that lead to an adverse health or ecotoxicological effect

**ADHD:** Attention deficit hyperactivity disorder – a group of behavioural symptoms including inattentiveness, hyperactivity, and impulsiveness

**ASD:** Autism spectrum disorder – condition that affects social interaction, communication, interests and behaviour

**Bioaccumulation:** The accumulation of a substance in an organism

**Biocide:** A non-pesticide substance intended to destroy, deter, render harmless, or exert a controlling effect on any harmful organism by chemical or biological means

**BPA:** Bisphenol A – a chemical used in the manufacture of clear polycarbonate plastic, and to manufacture other plastics, including the lining inside many food and drink cans. Known to have endocrine disrupting properties

**BFRs:** Brominated flame retardants – chemicals added to fabrics and plastics to make them less flammable

**CNRS:** Centre National de la Recherche Scientifique – National Centre for Scientific Research, France

**Cognitive Development:** Construction of thought processes, including remembering, problem solving, and decision-making, from childhood through adolescence to adulthood

**Cumulative Prevalence:** Probability that a particular event, such as occurrence of a particular disease, has occurred before a given age

**DDE:** Dichloro-diphenyl-dichloroethylene – breakdown product of the pesticide DDT

**DDT:** Dichloro-diphenyl-trichloroethane – synthetic insecticide developed in the 1940s

**DNT:** Developmental neurotoxic properties

**ECHA:** European Chemicals Agency

**EFSA:** European Food Safety Authority

**Embryogenesis:** Process by which the embryo forms and develops

**EDC:** Endocrine disrupting chemical – also known as hormone disrupting chemical
A chemical that can interfere with the endocrine or hormone system – the body's own sensitive chemical messaging system

**Endocrine System:** Collection of glands that produce hormones that regulate, among other things, metabolism, growth and development, tissue function, sexual function, reproduction, sleep, and mood

**Endogenous Hormones:** Hormones originating or produced within the organism

**Epidemiological Study:** Study and analysis of the patterns, causes, and effects of health and disease conditions in defined populations

**Epigenome:** Chemical changes made to DNA, affecting the expression of genes but not changing the DNA sequence

**Precautionary Principle:** Principle of EU law detailed that enables rapid response in the face of a possible danger to human, animal or plant health, or to protect the environment. In particular, where scientific data do not permit a complete evaluation of the risk

**EU Strategy for a Non-Toxic Environment:** A strategy currently being developed by the EU as part of its 7th Environment Action Programme

**Exposure, acute:** Single exposure (not lasting longer than a day) to a substance that causes severe harm, or even death

**Exposure, chronic:** Exposure occurring over a long period of time, with cumulative negative health effects

**GABA:** *gamma*-Aminobutyric Acid, a neurotransmitter

**Genome:** A full set of chromosomes, designating all the inheritable traits of an organism

**Halogenated Chemicals:** Chemicals that include halogens, a group of elements that include fluorine, chlorine, bromine and iodine

**HBCD:** Hexabromocyclododecane – a brominated flame retardant

**Homeostatic Mechanisms:** Mechanisms that maintain internal stability in an organism to compensate for changes in its environment

**Hyperkinetic Disorder:** The World Health Organisation International Classification of Mental and Behavioural Disorders 10th revision (ICD-10) describes attention-deficit hyperactivity disorder (ADHD) as hyperkinetic disorder (HKD), a term widely used in Europe. For a more detailed definition see footnote on page 10

**In Silico:** Scientific analysis using a computer model

**Iodine:** Chemical element that is an essential constituent of thyroid hormones

**Myelination:** The production of myelin, a fatty white substance that surrounds the axon of some nerve cells, forming an electrically insulating layer and is essential for the proper functioning of the nervous system

**Neurobehavioural Problem/Disorder:** Problem or disorder of or relating to the relationship between the action of the nervous system and behaviour

**Neurodevelopmental effect:** An effect on the growth and development of the brain or central nervous system

**Neuroendocrine:** The interactions between the nervous and endocrine systems

**Neurotoxic Chemical, Neurotoxins, Neurotoxicants:** Chemicals that are poisonous or destructive to nerve tissue

**Neurotransmitter:** Chemical substance which is released at the end of a nerve fibre in order to transfer the impulse to another cell

**NIEHS:** National Institute of Environmental Health Sciences, USA

**NMDA Receptor:** *N*-methyl-*D*-aspartate receptor (also known as the NMDA receptor or NMDAR), is a glutamate receptor and ion channel protein found in nerve cells which supports nerve cell function

**OECD:** Organisation for Economic Co-operation and Development – international organisation which aims to promote policies that will improve the economic and social well-being of people around the world.

**Organophosphate Pesticides:** Refers to a group of insecticides or nerve agents designed to act on the enzyme acetylcholinesterase, an enzyme essential to nerve function

**PAN Europe:** Pesticide Action Network Europe

**PBDEs:** Polybrominated diphenyl ethers – organobromine compounds used as flame retardants, and that have been restricted in the EU for many uses in recent years. However, exposure continues due to their persistent and bioaccumulative properties

**PCBs:** Polychlorinated biphenyls – group of chemicals that have been banned for over 30 years, but are still causing harm to health and the environment – including endocrine disruption – due to their highly persistent properties

**PFCs:** Perfluorinated compounds – group of chemicals used in products including waterproof clothing and non-stick pans. These highly persistent substances have been shown to have harmful effects on human health and the environment, including hormone disrupting properties

**Phthalates:** Group of ubiquitous chemicals (including DEHP, DBP, BBP) used in a wide range of products, including furnishings, clothing, and food packaging; and that are associated with a whole range of toxic effects, including hormone disruption

**POP:** Persistent organic pollutant

**Potency:** Potency in toxicology is a measure of how much of a chemical is required to create a particular adverse effect

**PPTOX:** A series of conferences on Prenatal Programming and Toxicity organised by the Endocrine Society

**REACH:** Registration, Evaluation, Authorisation and Restriction of Chemicals – the main EU Regulation covering industrial chemicals

**Reproductive Toxicity:** Ability of a chemical substance to interfere in some way with normal reproduction. It includes adverse effects on sexual function and fertility in adult males and females, as well as developmental toxicity in the offspring

**Steroidogenic Enzymes:** Enzymes involved in the production of steroid hormones

**SVHC:** Substance of Very High Concern – in the REACH chemicals regulation system

**Synaptogenesis:** Refers to the formation of connections (synapses) between neurons in the nervous system

**TCC:** Triclocarban – an antibacterial agent

**TCEP:** Tris (2-chloroethyl) phosphate – a flame retardant

**Thyroid Gland:** A gland located in the neck which secretes thyroid hormones which regulate growth and development

**TH:** Thyroid Hormone

**UNEP:** United Nations Environment Programme

**UV filters:** Chemicals that filter out certain ultraviolet light (sun screens)

**Xenobiotics:** Foreign chemical substances found within an organism that is not normally naturally produced by or expected to be present within it

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