# Early dioxin exposure and later health effects

# Proof of evidence: Ringaskiddy-Indaver Pleanala Hearing

Gavin W. ten Tusscher, M.D., Ph.D., paediatrician

**Affiliation:**

Department of Paediatrics and Neonatology

Westfriesgasthuis

Maelsonstraat 3

1624 NP Hoorn

The Netherlands

Email: g.w.ten.tusscher@planet.nl

# Introduction

In the following I will strive to elucidate the tremendous impact that dioxins, formed as unwanted by-products of incineration processes, have on human health. I have limited myself to concentrating on health effects of exposure to dioxins, PCBs and furans because this is my field of research and experience. It must be borne in mind that many other substances found in waste incinerators also cause serious negative health effects, for example, small particles (particulate matter) and heavy metals (lead, mercury, etc). I refer the reader to experts on these substances for further information.

In 1980-1990 it was realised that incinerators spread highly toxic dioxins into the environment, polluting humans, including nursing children (via breast milk). In 1987 a cohort study was initiated in the Amsterdam/Zaandam region of the Netherlands to study possible effects of these chemicals on reproduction. Effects on thyroid hormone metabolism, liver, haematology and immunology, and retinol binding protein were found in neonates. Follow-up was performed at the age of 2½ years, 8-12 years and 13-18 years. Persistent effects were seen. Effects on haematological and immunologic parameters into preschool age, and negative effects on lung function and negative effects on brain development - both behavioural and cognitive - at the age of 8-12 years, were associated with perinatal exposure. The data of the follow-up study during puberty (13-18 years) show signs of endocrine disruption, including a delay in breast development in girls in association with higher prenatal dioxin exposure.
As a result of the alarming outcomes of the above mentioned studies, studies in other parts of the Netherlands and Europe were initiated. Similar outcomes were found. The

last two decades has seen an enormous increase in the available data regarding later health effects of early dioxin exposure. Furthermore, a number of studies in the vicinities of waste incinerators have shown negative health effects in the surrounding populations. In the following sections these and other studies will be elaborated on. In addition, recent waste incinerator accidents will be mentioned. It must be emphasised that the studies, and accidents, mentioned in this proof of evidence is not complete, but merely a selection of the overwhelming burden of proof, that even low dose background environmental dioxin exposure has negative health effects spanning many years and possibly generations.

Finally, it must be remembered that current filter standards have considerably reduced the emissions of dioxins and other substances via chimneys, the collection of these substances is in the flue gas or flue ash, which presents the next problem: what do we do with the extremely toxic flue gas/ash? These residues are often stored in large storage dumps, presenting a risk to the environment and population at large in the case of an accident. Furthermore, such storage facilities are not limitless. Experimentation with working the residues into other products such as tarmac has been tried. However, when the tarmac is broken up we are again presented with the toxins. In addition, products such as broken up tarmac are often used in landfills. In other words, the dioxins and such like are being produced by incineration processes but cannot be effectively destroyed – the problem is merely shifted and shifted until it is no longer visible, and then often ignored.

**What are dioxins?**

Polychlorinated dibenzo-p-dioxins (PCDDs), polychlorinated dibenzo-furans (PCDFs) and some polychlorinated biphenyls (PCBs), such as PCB-77, -126 and -169 (henceforth jointly referred to as dioxins) belong to the group of most toxic substances known. PCDDs consist of a family of 75 congeners, or structurally similar compounds. They are, in pure form, colourless crystals or solids. With the exception of small amounts for research purposes, they are not intentionally manufactured by industry (1). Dioxins are formed as waste products of combustion processes and municipal incinerators are amongst the primary sources of these compounds in Europe (2;3). Other sources of dioxins include the combustion of fossil fuels and wood, chlorine bleaching processes in pulp and paper mills, chlorination of drinking water and chlorinated organic chemical production. During the Vietnam War, an extensively used defoliant called Agent Orange, used during Operation Ranch Hand, was a major source of dioxin pollution in South East Asia (4;5).

PCBs are a family of 209 possible congeners, of which 13 are likely to be similar to tetrachloro-p-dioxin, TCDD, the most toxic dioxin congener.

Finally, there are 135 possible PCDF congeners. Heating of PCBs is a notable source of PCDFs.

**Why are dioxins a human health hazard?**

Dioxins are poorly degradable in nature and persist in the environment, accumulating in the human food chain mainly via fish-oils and animal fats (6;7). They do not dissolve

easily in water and hence settle to surfaces, such as river sediments or grass. Fish eat the plankton and other microscopic organisms on river bottoms, herbivores eat the grass. Larger animals in turn eat these aquatic organisms and animals and eventually the food chain, as it is called, leads to man eating the dioxin contaminated animals or plants, such as dairy products and meat (8).

The main contributors to dioxin intake in the European Union are milk and dairy products (16-39%), meat and meat products (6-32%) and fish and fish products (2-63%) (9). These chlorinated polyaromatic compounds are highly hydrophobic and are therefore difficult for an organism to metabolise. The accumulation results in increasing concentrations of dioxins in each higher step in the food chain. Dioxins in the human are primarily stored in adipose tissues and liver (10). Their lipophilicity allows them to readily pass the placenta, whereupon they are stored in foetal liver and adipose tissues (11;12). In 1986 relatively high background dioxin concentrations in the breast milk of Dutch mothers was first reported, followed by similar findings in other industrialised countries (13-16). As a result foetuses and breastfed children were exposed to relatively high “background” dioxin levels, averaging approximately 30 ng/kg fat, as measured in breast milk (13-15;17;18). One nanogram (ng) is one billionth of a gram. The half-life, or time it takes to remove half of the amount, of dioxins in the human body is estimated at 7 to 12 years (1).

Two Asian incidents of PCB and PCDF contamination of rice oils led to large numbers of people being poisoned. The 1968 accident in Japan, "Yusho", and the 1978 accident in Taiwan, "Yucheng", revealed direct toxicity effects, but also long-term effects and

even teratogenic effects (19-21). In 1976, in the Italian town of Seveso, a chemical plant exploded releasing a large amount of pure TCDD, or dioxin, into the atmosphere (22;23). The resulting health effects, in many ways similar to those seen in the Asian accidents, demonstrated that the toxic effects of dioxin exposure were varied and largely not understood. Studies done amongst industrial workers and Agent Orange exposed subjects during the Vietnam War, exposed in adulthood, have produced conflicting health effects (5;24-26).

However, all these subjects were exposed to high concentrations of dioxins and PCBs. The shocking finding of dioxins in human breast milk in women not living in "contaminated" areas led to growing concern over possible teratogenic and long-term health effects in children prenatally exposed to "background" concentrations. Background concentrations being the concentrations found in average, healthy people, not living in areas at extra risk for exposure. It was in this setting that a Dutch longitudinal cohort study was started in 1989, by Koppe and Pluim (17;27), which later became known as the Amsterdam/Zaandam study. Various abnormalities were seen, some of which had normalised by follow-up at 2½ years (28), but other abnormalities only presented themselves later. The number of subjects in the Amsterdam study was limited, yet the results seen in this group were alarming enough to prompt a larger cohort study, supported by a governmental institution, to re-evaluate the dioxin and PCB effects of perinatal exposure in children. The Rotterdam and Groningen group elicited similar findings to what the Amsterdam/Zaandam group had found, supporting the validity of the concerns (29-32).

Studies in various other countries have also shown childhood effects of perinatal exposure (33).

## What health effects could be expected?

### Birth defects

In animal studies, dioxin exposure has been demonstrated to have effects on various homeostatic systems. In addition, it has become clear that the foetus and new-born baby are the most vulnerable subjects. Their developing systems are exposed to the dioxin concentrations of the mother during pregnancy, and postnatally by their ingestion of contaminated breast milk. The susceptibility of the foetus and new-born is the result of the many imprinting processes that take place in the perinatal period (34).

Infants born after prenatal PCB poisoning in Taiwan (Yucheng-disease) were characterised by hyperpigmentation, intra-uterine growth retardation, natal teeth, pigmented dysplasia of the nails, hirsutism, hypertelorism, conjunctivitis, clinodactyly, widely open fontanels and spotty calcifications of the skull. Mortality was high, with twenty-five percent of these hyperpigmented babies dying within four years of birth. Respiratory distress and pneumonia during the first six months of life were common (35). Follow-up revealed shorter stature and musculoskeletal changes (36).

In the discussion of what effects may be expected as a result of the background levels of PCBs and dioxins, congenital anomalies have not always had the highest priority. Animal studies have shown that the doses of toxic chemicals have to be rather high in

order to cause malformations. In Europe, this resulted in studies on this toxicological aspect being neglected, possibly wrongly so. In certain regions where exposure is high, clusters of defects can be found. In a literature search, several publications indicate congenital defects, for instance, amongst inhabitants in the neighbourhood of landfills, or after the spraying of insecticides (37;38).

After the Seveso incident - the explosion of a chemical plant in Italy, resulting in extremely high TCDD exposures - no increased incidence of congenital malformations was detected. However, many women underwent an abortion after the disaster, for fear of the consequences for their unborn baby (39).

What is striking in all the publications relating PCBs, dioxins, insecticides and herbicides with the incidence of congenital malformations, is the reported increased incidence of midline defects. This same increased incidence in midline defects is seen with maternal usage of anticonvulsant medication during pregnancy (40;41). Cleft lip and/or palate, spinal bifida, gastroschisis, heart defects, hypospadias and inguinal hernias are amongst the malformations mentioned: all are examples of midline defects (42;43). Cleft palate and hydronephrosis were seen in mice following TCDD exposure (44-46).

Presently, the incidence of hypospadias, both in Europe and the United States, is rising. Endocrine disrupting chemicals with estrogenic or anti-androgenic effects are blamed for this rise (47;48).

Another so far unexplained finding is the fact that parents with high levels of TCDD after the Seveso-incident gave birth to far more boys than girls (49). This finding,

however, was not confirmed in the offspring of subjects with Yucheng-disease (50). Pure TCDD possibly has a different effect than the mixture of PCBs and PCDFs that constituted the toxins in Yucheng-disease.

**Cleft lip**

During the years 1961 up to and including 1969 chemical combustions were conducted in the open air in Zeeburg, Amsterdam, Netherlands. A retrospective observational epidemiological study was performed, comparing the trend of the incidence of non-syndromal orofacial clefts during the sixties, for the Zeeburg maternity clinic with that of the Wilhelmina Gasthuis. Both clinics were situated in Amsterdam, but varying in distance and compass direction from the incineration works. Thereafter, the addresses of the mothers giving birth to infants with orofacial clefts were plotted on a map of Amsterdam.

Of the 8803 children born in the Zeeburg clinic during this period, 21 had a non-syndromal orofacial cleft, producing an average incidence of 2.4 per 1000 births. For the years 1963 through 1965 the incidence rose dramatically to peak at 7.1 per 1000, before plateauing at an average incidence of 1.68 per 1000 births, still 155% higher than in the Wilhelmina clinic (average incidence of 0.66 per 1000 during the years 1966 through 1969). During the ten year period the Wilhelmina clinic exhibited no such rise. The incidence of non-syndromal orofacial clefts at the Wilhelmina clinic at no time exceeded 2.3 per 1000 births during the ten year period. The addresses of the mothers of the Zeeburg clefts were grouped primarily to the northwest (and a smaller group to the west) of the incineration works, primarily downwind of the incinerations. The conclusion of a relation between the open incineration of the chemicals and a local

increased incidence of orofacial clefts was made (51). This study was referred to in the report: *Potential Human Health Effects Indaver Ringaskiddy* performed By EHA Ltd. Cork (Addendum 7.1).

**Miscarriages and premature births**

During the American war in Vietnam, huge quantities of dioxin (via contaminated 'Agent Orange'), were sprayed over large areas of central and south Vietnam. In addition to polluting the environment and causing cancers and other diseases in those directly exposed to it, dioxin has caused high rates of pregnancy loss, congenital birth defects and other health problems in their children. A pilot study was performed in 2000, among 30 Vietnamese women whose husbands and/or who themselves were exposed to Agent Orange. The women showed a high number of miscarriages and premature births. About two-thirds of their children had congenital malformations or developed disabilities within the first years of life. Most of the families were poor, aggravated by impaired health in the men, the burden of caring for disabled children, and feelings of guilt and inferiority. 60% of the children born after the contamination had congenital malformations (birth defects) (52).

**Infant deaths**

An increase in infant deaths and infant deaths with congenital disorders was seen in residents in the vicinity of a Japanese solid waste incinerator. The study was published in one of the world’s most respected medical journals in 2004. A summary of the journal abstract follows: the study investigated the association of adverse reproductive outcomes with maternal residential proximity to municipal solid waste incinerators. The

association of adverse reproductive outcomes with mothers living within 10 km from 63 municipal solid waste incinerators with high dioxin emission levels (above 80 ng international toxic equivalents TEQ/m3) in Japan was examined. The numbers of observed cases were compared with the expected numbers calculated from national rates adjusted regionally. Observed/expected ratios were tested for decline in risk or peak-decline in risk with distance up to 10 km. In the study area within 10 km from the 63 municipal solid waste incinerators in 1997-1998, 225 215 live births, 3,387 foetal deaths, and 835 infant deaths were confirmed. None of the reproductive outcomes studied here showed statistically significant excess within 2 km from the incinerators. However, a statistically significant peak-decline in risk with distance from the incinerators up to 10 km was found for infant deaths ($p=0.023$) and infant deaths with all congenital malformations combined ($p=0.047$), where a "peak" is detected around 1-2 km. The researchers concluded that a peak-decline in risk with distance from the municipal solid waste incinerators for infant deaths and infant deaths with all congenital malformations combined (53).

## Infancy and later childhood

### Haematological and immunological problems

Many studies of the thymus and T-cells have been performed, because of the striking involution of the thymus in exposed animals (46;54;55).

The Amsterdam/Zaandam group detected a lowering of blood platelet counts in relation to postnatal dioxin exposure via breast milk at 11 weeks of age (17). Lowering of blood platelet counts, as well as other health effects, was also seen in Japanese workers with

increased dioxin levels (56;57) and in two Austrian women accidentally intoxicated with high concentrations of dioxins (58).

One of the most sensitive systems affected is the immune system (59). At body burdens of only 5 ng TEQ/kg (toxic equivalency factor per kilogram) bodyweight effects on the immune-system were elicited in non-human primates (60). An extensive reduction in lymphocyte stem cells was seen in the bone marrow of the offspring of maternal rats, treated with one dose of dioxins of ten micrograms per kilogram body weight during pregnancy (61). Another study in non-human primates showed a lowering of CD4+ lymphocytes and an increase in CD8+ lymphocytes after a single dose of only ten nanograms TCDD per kilogram body weight (62).

Both Dutch dioxin groups (Amsterdam/Zaandam and Rotterdam/ Groningen) detected a significant lowering of the polynuclear leukocyte and monocyte counts shortly after birth, in the first weeks to months. Pluim detected lower concentrations of granulocytes and monocytes on the seventh day of life, in the prenatally higher dioxin-exposed babies. At eleven weeks of age the concentration of blood platelets were lower in relation to the amount of dioxin the babies ingested with their breast milk (17). In Rotterdam a similar decrease, in relation to pre- and postnatal exposure to dioxins, was detected in the concentration of granulocytes at 3 months of age, together with a lower monocyte count (63). The lowering of white blood cell and blood platelet counts is probably due to an inhibition of the bone marrow by dioxins. That in the neonatal period both thrombocytes and white blood cells were affected, possibly points in the direction of damage to stem cells (64-67).

In follow-up studies no significant differences in the number or sort of infectious diseases were detected, up to the age of about two years (28;63). Yet, in the Rotterdam study, at the age of 42 months more middle-ear infections were found in relation to the current PCB-levels of the children (68). This relation to the current PCB-levels, however, might not be related to a generally disturbed immune function, but rather could be a direct effect of PCBs on the epithelium of the Eustachian tube. It is known that PCB-metabolites preferentially accumulate in the Clara cells of the lung, possibly resulting in hypersecretion (69-71). Due to the fact that the epithelium of the lung is of the same origin as that of the Eustachian tube (which, for instance, also produces surfactant), it is logical to offer hypersecretion in the Eustachian tube as an explanation for the middle-ear infections (71). This hypersecretion could also be an explanation for the increase in respiratory diseases seen after PCB poisoning (72) as mentioned below.

These above mentioned studies were conducted amongst normal, healthy, pregnant mothers and their babies. Pathology in the mothers and babies, or complications during pregnancy, delivery, or in the neonatal period, led to the exclusion of the subjects from the particular study. This approach may be disadvantageous in that toxic effects resulting in disease during pregnancy, delivery or in the neonatal period are not detected. In other words infections, haemorrhaging and new disease entities may not be elicited, due to the exclusion of the non-optimal subjects from the studies.

There are also subtle signs that the leukocytes may be influenced through a faulty imprinting, during the critical perinatal period. Weisglas-Kuperus et al. published their

findings on background prenatal exposure to dioxins and PCBs in their Rotterdam group: this exposure may influence the development of particular immune cell populations (30;63). Eighteen month old children exhibited an increase in T-cells (CD8+, amongst others) which persisted until the age of 42 months. However, at 42 months the increase was related to the sum of maternal PCBs and not to the I-TEQ dioxin (68). Additionally, amongst the forty-two month olds, a higher incidence of chickenpox was elicited relative to the sum of the maternal PCBs, and levels of antibodies to measles were lower in relation to the sum of the PCB levels in cord blood (68).

Exposure during the sensitive perinatal period may cause permanent disturbances. Therefore, we assessed the health status and various hematologic and immunologic parameters among our longitudinal cohort. A medical history was taken and vena puncture performed in a longitudinal cohort of 27 healthy 8-year-old children who had documented perinatal dioxin exposure. Linear regression revealed a decrease in allergy in relation to prenatal ($p = 0.02$) and postnatal ($p = 0.03$) dioxin exposure. Increases in CD4+ T-helper cells ($p = 0.006$) and in CD45RA+ cells ($p = 0.02$) were seen in relation to postnatal exposure. A persistently decreased platelet count ($p = 0.04$) and increased thrombopoietin concentration ($p = 0.03$) were seen in relation to postnatal exposure. This follow-up has shown a decrease in allergy, persistently decreased thrombocytes, increased thrombopoietin, and increased CD4+ T-helper and increased CD45RA+ cell counts. This study provides indications of effects at the stem cell level of background perinatal dioxin exposure, persisting until minimally 8 years after birth (73).

**Thyroid problems**

Another aspect of imprinting is the hormonal and enzymal imprinting. Faulty imprinting caused by the introduction of certain hormones, or chemicals mimicking these hormones, during the sensitive period, can cause disturbances in the homeostasis. For instance the set point (the optimal concentration point) of the thyroid hormonal system could be set (slightly) higher or lower. The significance of such an altered set point may prove detrimental to the long-term, and possibly even the short-term, health status of the individual.

Dioxins and dibenzofurans have a similar chemical structure to that of thyroid hormones. Structurally, one of the major differences is that the chlorine atom of the former is situated in the position of the iodine atom of thyroxin. This structural similarity gave rise to the hypothesis that dioxins and furans are able to mimic the working of thyroxin. Jakobsson and colleagues demonstrated that a (T3-like) metabolite of polybromodiphenyl ethers, which they synthesised, bound remarkably to the human thyroid receptor protein. This is a clear demonstration of a man-made persistent organic pollutant binding to a human receptor (74).

During human gestation, the human foetal hypothalamic-pituitary-thyroid system is relatively quiescent and foetal thyroid hormone production is limited until a gestational age of eighteen to twenty weeks. During the second half of gestation, the functioning of the foetal thyroid gland increases, this under the influence of an increasing TSH concentration. There is also a progressive increase in the concentration ratio of free T4 to TSH, suggesting maturation of the hypothalamic-pituitary negative feedback control

system for TSH secretion (75). Chemicals mimicking thyroid hormones can disturb this process. In this light, studies on the effects of background exposure to dioxins in the Netherlands also focussed on the thyroid hormone metabolism. In both the Zaandam study of Pluim et al. and the Rotterdam study of Koopman-Esseboom et al., abnormalities in thyroid hormone metabolism were detected in relation to dioxin levels. Pluim detected a significantly higher T4 concentration during the first 11 weeks of life in the higher exposed babies, whom also exhibited a significantly higher TSH concentration at 11 weeks of age (76-79).
Koopman-Esseboom detected lower free thyroxin (FT4) and T4 concentrations shortly after birth, and also higher TSH concentrations at 2 weeks and 3 months of age, in her higher exposure group (80).

Thyroid hormones also play a part in brown adipose tissue thermogenesis. This form of heat production involves the rapid burning of the triglycerides (fats) that are packaged around the great vessels, in order to keep the baby warm. From animal studies it is known that this manner of thermogenesis, by the burning of brown adipose tissue, is jeopardised by dioxins, making survival after birth more difficult (81-83).
It seems, therefore, that current background concentrations of dioxins disturb the thyroid hormone metabolism.

**Liver problems**

The liver is the first and primary organ where dioxins and PCBs arrive. They diffuse to the liver cells after traversing the umbilical vein or after absorption by the gut. In the Zaandam study, liver size was measured by means of ultrasound. As related to the

perinatal dioxin exposure, an increase in hepatic size was expected, contrary to the trend towards a smaller size found at two weeks of age. This might be due to relative growth retardation in uteri. Between two and eleven weeks of age, the liver increased in size, more so in the higher exposed babies than the lower, resulting in similar sized livers for the two groups by eleven weeks of age (17).

Maruyama presented a model to explain dioxin and PCB behaviour after birth, in relation to breastfeeding, and she came to the conclusion that there is a sharp rise in dioxin content shortly after birth in the liver (84). At 2½ and 7-12 years of age no persistent abnormalities were found in the Zaandam cohort (28;85). In the Seveso children, exposed to dioxins following a chemical plant explosion, a similar rise in alanine aminotransferase (ALAT) was found amongst the highest exposed boys, which was decreased to normal levels after about five years (86).

**Respiratory problems**

Respiratory system effects of dioxin and PCB intoxication have regularly been documented (23). Coughing, as an immediate consequence, has been described. Of the intra-uterine exposed children of the Seveso population, 25 % died in the first four years of life due to respiratory problems. Respiratory distress and pneumonia during the first six months of life were common amongst the children born after the Yucheng incident (35).

The incidence of broncho-obstructive disease has dramatically increased over the last twenty years. While a number of hypotheses have been postulated, no conclusive

reason for this rise has been found. Hypothesising that this rise in incidence was the result of perinatal exposure to dioxins, we evaluated lung function by means of questionnaire and spirometry. Spirometry was performed in 29 healthy children (aged 7-12 years mean 8.2 years) with known perinatal dioxin exposure. The ratio of forced expiratory volume in 1 s to forced vital capacity (FEV1/FVC ratio) was determined. A complete medical history was taken. The prenatal exposure ranged from 8.74 to 88.8 (mean 34.6) ng TEQ dioxin/kg fat, measured in breast milk. The postnatal exposure ranged from 4.34 to 384.51 (mean 75.4) ng TEQ dioxin. A significant decrease in lung function in relation to both prenatal ($p = 0.045$) and postnatal ($p = 0.0002$) dioxin exposure was seen. A clinical association between chest congestion and perinatal dioxin exposure was also seen (87).

It has long been recognised that fine-particulate air pollution plays a major role in lung disease. A study published in the top scientific journal, Nature, showed a strong correlation between air pollution and death as a result of lung cancer, in Italy. The more air pollution, the higher the risk of dying from lung cancer (88). A recent study in the US found life expectancy increases with decreasing fine-particulate air pollution. The authors stated that reductions in air pollution accounted for as much as 15% of the overall increase in life expectancy in the study areas (89). Incineration produces an increase in fine-particulate air pollution. It is to be expected that the proposed Ringaskiddy incinerator will contribute to an increase in fine-particulate air pollution. The increased traffic, especially of diesel trucks, needed to transport the waste to Ringaskiddy, will further increase the fine-particulate emissions in the area. According to the US study this would mean a decrease in life expectancy, or longevity, for the exposed resident populations.

**Psychology and neurology**

Behavioural imprinting is a further example of environmental influences playing a pertinent role in the perinatal period. Appropriate reactions, such as bonding, are dependant on appropriately working hormonal systems in a baby.

In a North Carolina study, hypotonia and hyporeflexia in relation to prenatal exposure to PCBs were already detected in the neonatal period, shortly after birth (90). During infancy the higher exposed children exhibited developmental delays in gross motor function (20). In the children of mothers ingesting PCB-polluted fish from Lake Michigan a poorer visual recognition memory (Fagan Test) was associated with increasing prenatal PCB exposure. The levels of PCBs in the Michigan study were only slightly above U.S. background levels and comparable to European levels.
The Zaandam group was studied at the age of two years and seven months. Signs of enhanced neuromotor maturation were found and it was hypothesised that this may be due to the thyroxin-agonistic action of dioxins (28). Enhanced neuromotor maturation is not necessarily a favourable effect.

Prenatal exposure to PCBs and PCDFs was associated with negative behavioural effects amongst the offspring of mothers who had ingested the contaminated rice oil in Yusho, Japan. The children were apathic and uninterested (91). Monkeys exposed prenatally to PCBs exhibited hyperactive behaviour during infancy. This was followed by inactivity at four years of age (92;93). The children of mothers eating fish from Lake Michigan displayed reduced activity, with current body burdens of PCBs, at 4 years of age (94). In

another neonatal behavioural assessment study, neonates of mothers who had ingested Lake Ontario fish were tested. Results revealed significant linear relationships between the most heavily chlorinated PCBs measured in cord blood and performance impairments for the scores on the Habituation and Autonomic clusters at 25-48 hours after birth (95).

In the Dutch cities of Rotterdam and Groningen a study was performed to investigate the effects of perinatal exposure to background levels of PCBs and Dioxins on growth and development (32). The total study group consisted of 400 healthy mother-infant pairs, of which half the infants were breast-fed and half bottle-fed.
Follow-up of brain development was done at the ages of 18 and 42 months. The study detected hyperactivity and slower mean reaction times in relation to the current PCB levels in the children at 42 months of age (96). Irritability and hyperactivity are well known side effects of the use of Phenobarbital in childhood and current PCB levels might act as such. At the age of 42 months attention during free play behaviour was reduced in relation to cord and maternal PCB exposure, a persisting effect on behaviour from damage caused prenatally. These findings are similar to those seen by Jacobson (97). Prenatal PCB exposure was also adversely associated with neurological outcome at 18 months of age (98), but this was no longer seen at 42 months of age (99). A negative relation was found between cognitive functioning (from 2 to 6-8 points lower IQ) at 42 months, and the sum of the PCBs measured in maternal blood collected in the last month of pregnancy (96). Overall cognitive functioning was negatively influenced, as was the verbal comprehension score. This finding is in accordance with the study of the Jacobsons', who noted a negative effect of prenatal exposure to PCBs on cognitive

functioning, at the age of four years (97). Furthermore, at the age of eleven years, in the Jacobson study, IQ-test scores were lower in the higher exposed children. Difficulties in verbal comprehension were elicited and the ability to concentrate was reduced in the higher exposed children. The latter were more than twice as likely to be two years behind in reading skills and word comprehension (100). Similar attention and verbal IQ problems have been detected in children prenatally exposed to anticonvulsants. Negative effect on psycho-sexual development and reproductive performance were also detected in the latter group (101).

More recently, increasing prenatal PCB exposure was associated with less masculine play in boys, and more masculine play in girls. PCBs and dioxins are known as neurotoxic compounds that may modulate sex steroid hormones. Steroid hormones play a mediating role in brain development and may influence behaviours that show sex differences, such as childhood play behaviour. As part of a follow-up of the Rotterdam PCB/dioxin study the Pre-School Activity Inventory (PSAI) was used to assess play behaviour (n = 207). The PSAI assesses masculine or feminine play behaviour scored on three subscales: masculine, feminine, and composite. In boys, higher prenatal PCB levels were related with less masculinised play, assessed by the masculine scale (p(maternal) =.042; p(cord) =.001) and composite scale (p(cord) =.011), whereas in girls higher PCB levels were associated with more masculinised play, assessed by the composite scale (p(PCBmilk) =.028). Higher prenatal dioxin levels were associated with more feminised play in boys as well as girls, assessed by the feminine scale (p =.048). These effects suggest prenatal steroid hormone imbalances caused by prenatal exposure (102).

In the Rotterdam cohort at the age of 7 years fine motor performances were tested. There were more left-handed children in relation to higher prenatal PCB exposure as measured in maternal blood in the last month of pregnancy. Left-handed girls had more lateralisation between the hands, the dominant hand being better than the non-dominant hand. Left-handed boys had better co-ordination between the two hands in relation to higher prenatal PCB-exposure (103).

A recent study in Germany demonstrated the negative effects on neurodevelopment up to 42 months of age arising from prenatal, and also postnatal, exposure to PCBs. A deficit of 8 and 9 points was seen for mental and motor development respectively. At 42 months an intelligence test was performed to assess higher brain functions. Using this test postnatal exposure, as measured in blood at 42 months, was related to a significantly lower IQ (104).
Severe effects on IQ due to high in uteri exposure of a combination of PCBs and PCDFs were found in the Yucheng children (105).

During the critical prenatal and postnatal period, environmental influences like dioxin and PCB exposure, can disturb hormonal and enzymal activity set points or have direct toxic effects on developing organs. This may result in functional developmental disabilities in later life. During the first trimester of pregnancy neurons in the brain are formed. During the second and third trimesters, especially around thirty weeks' gestational age, when the growth and development of the brain takes place, brain development is characterised by the forming of dendrites, connecting the neurons, and by the start of glial myelinisation (106).

Structures in the brain necessary to process visual and auditory signals, for instance for language development, are then formed. This process continues during the first year of life, albeit somewhat slower than prenatally, and progresses thereafter at a slower pace until adolescence.

During pregnancy, the developmental process depends largely on hormones. Thyroid hormone is essential for brain development and lower levels of maternal thyroid hormone in the first trimester of pregnancy is associated with lower intelligence in children (107). Testosterone is also important, as it is necessary around the thirtieth week of pregnancy for the typical male brain development, characterised by good visio-spatial abilities. Lowering of the testosterone levels, for example as a result of an enhanced metabolism induced by medications, causes impairment of the visio-spatial abilities later in life. This is seen in the adolescent offspring of mothers using anticonvulsant medication during pregnancy (101). Dioxins and PCBs are known to be endocrine disruptors and their influence on thyroid hormone metabolism has been demonstrated in various studies (76-79). Later health effects of these influences are currently being studied by us and others (see below).

We performed Magnetoencephalography (MEG) and electro-encephalography (EEG) in the 41 healthy 7-12 year old children of the Zaandam/Amsterdam cohort. Psychological testing was performed, using standardised WISC-R, TRF and CBCL tests. Linear regression revealed an increase in social problems ($p<0.001$), thought problems ($p=0.005$) and aggressive behaviour ($p=0.001$), as reported by the teachers, seen in relation to increasing postnatal dioxin exposure. An increase in anxious/depressed feelings ($p=0.002$), as reported by the parents, was seen in relation to increasing

prenatal exposure, and an increase in social problems was seen in relation to both prenatal ($p<0.001$) and postnatal ($p=0.001$) dioxin exposure. An increase in latency and amplitude of the motion induced EEG N2b component was found. Combined statistical testing (MEG and EEG) of the first (N2a) and second (N2b) motion component yielded a significantly increased latency ($p=0.007$) and amplitude ($p=0.015$) effect, suggesting a developmental delay of several years in our group. The latency of the N200 (EEG) component elicited by a visual oddball stimulus was increased. The amplitude of the N200 component was decreased. Combined statistical testing of latency and amplitude effects of N200 ($p=0.0021$) and P3b ($p=0.011$) suggest a developmental delay. In other words, subtle but significant neurodevelopmental influences and possibly cerebral damage of cognitive and behavioral performance were seen. This is possibly due to disturbed myelinisation, and in our cohort would seem to have caused an average neurodevelopmental retardation of approximately 3 years (108).

**Dental problems**

Finnish researchers found an increased number of caries in children, in relation to postnatal dioxin exposure (via breastfeeding) (109). Dental anomalies were seen in children following the Yusho and Yucheng disasters (19;35).

**Puberty**

As part of our longitudinal study, now well into its second decade, effects of perinatal and current dioxin exposure on puberty were assessed in the Amsterdam/Zaandam cohort. Pubertal development and growth were assessed by means of physical examination and the Tanner scale. A delay in initiation of breast development was

found in girls (n=18) with higher prenatal dioxin exposure (p=0.023) and a trend towards delay with the lactational exposure (110). A Belgian study found a delay in breast development with higher current serum dioxin concentrations.

The initiation of puberty is a complex process and it is not yet clear how dioxins, which have the potential to exert anti-estrogenic effects, precisely affect this process prenatally (111).

**Malignancy**

A French study detected a cluster of patients with non-Hodgkin lymphoma around a French municipal solid waste incinerator with high dioxin emissions. 222 Incident cases of non-Hodgkin lymphoma diagnosed between 1980 and 1995 were compared with controls randomly selected from the 1990 population census, using a 10-to-1 match. Dioxin ground-level concentrations were modelled with a second-generation Gaussian-type dispersion model, yielding four dioxin exposure categories. The latter were linked to individual places of residence, using Geographic Information System technology. The risk of developing non-Hodgkin lymphoma was 2.3 times higher (95% confidence interval = 1.4-3.8) among individuals living in the area with the highest dioxin concentration than among those living in the area with the lowest dioxin concentration. Adjustment for a wide range of socioeconomic characteristics at the block group level did not alter the results. The authors concluded that although emissions from incinerators are usually not regarded as an important source of exposure to dioxins compared with other background sources, their findings support the hypothesis that environmental dioxins increase the risk of non-Hodgkin lymphoma among the population living in the vicinity of a municipal solid waste incinerator (112). An Italian

incinerator study showed the risk of developing a sarcoma is 3.3 times higher among subjects, both sexes, with the longest exposure period and the highest exposure level; a significant excess of risk was also observed in women (Odds Ratio OR = 2.41) and for cancers of the connective and other soft tissue in both sexes (OR = 3.27) (113).

**Accidents in recent years**

While it is often argued that the risk of an accident in an incineration plant is small, accidents regularly occur. The last years have witnessed numerous accidents at waste incinerators and by-product storage facilities, resulting in high local exposures. While arguably one incinerator is not the same as another, accidents have also been reported at modern facilities, facilities meeting current stringent legislation. Here follows a short selection of the many examples to be found in a media search:

1993 Explosion in vinyl chloride monomer works. This accident, involving the combustion of chlorinated materials, must have formed dangerous dioxins: the fire left ruined buildings behind it similar those left after the fire at Linda Frigera in Beroun in 1998, but no one ordered any monitoring of concentrations of this highly dangerous material either in the air or on the site. Czech Republic.

1994 Incinerator in Duiven exceeds dioxin emission norm – unclear why or how. Netherlands.

1995 An explosion occurred in an incinerator for non-industrial wastes. A large amount of aluminium included in non-industrial wastes, produced a solid lump of ash, which suspended the operation of the incinerator. It exploded when water was added. Japan.

1996 Fire in waste incinerator in Holland with high dioxin emissions

1997 Incinerator in Rotterdam exceeds dioxin emission norm. Netherlands.

1999 Increased incidence of serious diseases thought to be the result of the local incinerator. Netherlands.

2001 Toxic cloud emission from incinerator. Netherlands.

2002 Elbe floods its banks and a large storage depot for dioxins. Czech Republic.

2002 Ten employees were injured, three seriously, when an incinerator exploded at a waste disposal centre in the city of Tokai, south of Nagoya, Japan.

2004 Explosion at a hazardous waste incinerator in Campana, Argentina.

2004 Dioxin emissions following faulty filters. Netherlands.

2005 Fire at a hazardous waste incineration plant in El Dorado, Arkansas, requiring the evacuation of 1,500 people living within a few miles of the plant.

2007 Explosion in incinerator in East Liverpool, U.S.

2008 Toxic waste kept for safe disposal in Bharuch catches fire. India.

2009 Truck transporting toxic waste to U.S. Energy Department incinerator in Tennessee leaked radiation-tainted toxic waste from duct-taped hose.

"From October 2001 to March 2002, list a series of accidental releases at Bennett's existing incinerator in St. Ambroise, Quebec. In each incident, toxins were blown out into the surrounding environment through the opening of the emergency release stack. The reports contradict claims being made by the company in their draft EA submission to Ontario's Ministry of Environment." Canada.

"The Korea Atomic Energy Research Institute (KAERI) is having a hard time searching for 2.7 kilograms of uranium sent to an incinerator by accident in May. The state-run institute learned of the grave mistake on Aug. 6 and formed a task force to find the material that had drawn the attention of the International Atomic Energy Agency (IAEA). Included in the missing material are 1.9 kilograms of natural uranium and 0.8 kilograms of depleted uranium as well as 0.2 grams of enriched uranium, which is still being investigated by the IAEA." Korea.

# Conclusion

Summarising then, in the industrialised world dioxins are everywhere to be found, and we are all exposed to them. Dioxins readily pass the placenta and are found in relatively high concentrations in breast milk. Children are thus already exposed to high concentrations of these most highly toxic chemicals, prenatally and postnatally. Additionally, the dioxin and PCB intake of a toddler is more than twice that an adult, and exceeds the acceptable daily intake with a four-fold factor (114). Effects on various organ systems have been documented for children exposed to high concentrations of dioxins.

Once again, I would like to emphasise the fact that I have limited myself to the effects seen in dioxin and PCB exposures, but it must be borne in mind that particulate matter, miniscule particles escaping the chimneys, are also a major threat to children's health, having been associated with pulmonary problems, including asthma (89).

Furthermore, the cancer risk in the Cobh Urban region is already reported to be nearly 50% higher than the national average in Ireland (115). This is alarming. In other words, for every 2000 people with cancer elsewhere in Ireland, the Cobh Urban region has 3000. Monitoring negative health effects, such as mentioned in this proof of evidence, takes many years. Negative health effects are mostly only seen many years after exposure. By that stage the damage has been done and cannot be undone. According to the Environmental Impact Statement, 20% of the population at risk of exposure from the proposed Indaver site are children under the age of 14 years. One half of the population is of childbearing age (meaning an additional risk for the foetus and next generation). It is then wiser to prevent additional negative health effects by not building the proposed waste incinerator. Important questions to be posed and certainly elucidated before considering permission for the construction of a waste incinerator at Ringaskiddy include:

- Is the Ringaskiddy area a coastal area at risk for flooding? According to the World Health Organisation this would be an important reason to exclude the proposed site (116). Should flooding occur, the risk for human health effects would increase dramatically.
- How much local experience is there in monitoring environmentally related health effects in children? Probably limited, meaning that the population is extra at risk.
- What biomonitoring needs to be performed in order to have a complete picture of possible environmental exposure? In other words, sampling of a number of index (key) substances is most probably not sufficient. All possible chemical

exposures and their interactions upon each other first need to be assessed in order to have a baseline for comparison during biomonitoring.

- What outcomes of biomonitoring and health monitoring will be considered relevant? Why not others?
- What would Indaver and governmental institutions consider "acceptable" mortality and morbidity figures (117)? How many environmentally-related deaths and illnesses would be considered the threshold for cessation of activities?
- With whom does the financial responsibility for (possible) environmentally-related disease lie? Bearing in mind the generally very long period of time between exposure and negative health effects, would Indaver be compelled to set aside monies in a fund for future victims?

Dr. Callaghan, in his Statement of Evidence, replied to a query on breast milk impact concerns as follows: "The MARI model predicts only a marginal increase in dioxin intake …" (118). In other words, he accepts and reports that the dioxin intake will increase, albeit marginally. If children are already showing negative health effects at current background dioxin and PCB levels, it is certainly not wise to allow an increase in these background concentrations. Any emissions from waste incinerators, however small, whether as a result of standard operating or as a result of accidents or (human) errors, will only increase the background exposures. It is then to be expected that the negative health effects in the population at large will increase. Dr. Callaghan, in response to concerns over "acceptable" dioxin levels responded that "The EU recognises the risks associated with dioxin and has set intake limit values accordingly"

(118). What he fails to mention is that these limits have repeatedly, drastically been lowered every few years, as a result of scientific evidence of negative health effects at the then currently “acceptable” limits. At the current “acceptable” intake levels of 14 ng/kg BW/week, negative health effects are also seen. What he also fails to mention is that the intake levels are stipulated for adults, not for children and certainly not for foetuses and infants, whose daily intake far exceeds that of adults (29). In other words, he has possibly given a one-sided and incomplete picture of the risks involved for the population at large. As a professional I find it alarming that someone with no medical and no paediatric background, makes such statements, possibly placing future generations at risk. Furthermore, he states, “The key issue is not whether dioxins are released or not, it is whether the release of dioxins leads to a breach of dioxin limit values which have been designed to protect human health” (118). If I understand correctly, he therefore finds it more important to consider emissions in relation to bureaucratically (and traditionally too liberally) stipulated limits, than to consider emissions in relation to health effects. From a professional point of view this, too, is disconcerting. One would expect that the health and wellbeing of children and future generations to be infinitely more important than whether or not emissions remain below a limit, which is of course also important. Finally, it must be remembered that the background concentrations are not limited by national borders and hence any additional emissions to the environment will only add to the global burden.

It is then my opinion, as paediatrician and scientist, that it is not wise to build the proposed waste incinerator.

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