Cancer in Children and Young People

The Cancer in Children and Young People set of articles is separated into 12 sections, each of which can be individually downloaded. It is a 'work in progress' incorporating new information whenever time permits.

Section 6

Other possible contributory factors

- 1. Childhood cancer incidence and types of cancer
- 2. Genetics and parental exposure
- 3. Ionising radiation
- 4. Non-ionising radiation electromagnetic fields (EMFs)
- 5. Chemical and infections
- 6. Other possible contributory factors
- 7. Types of childhood cancer Astrocytoma to kidney cancer
- 8. Types of childhood cancer Leukaemia to thyroid cancer
- 9. Challenges affecting survivors of childhood cancer

10. The needs of parents, family, GPs of childhood cancer survivors and things which may help

- 11. Precaution, prevention and protection
- 12. References

Childhood Cancer 6. Other possible contributory factors and ones which have been largely discounted

We include in this first section other factors that have been linked to the development of childhood cancer in general, or more than one type of cancer. When *specific* cancers are associated with a particular factor, this is included in Sections 7 'Astro to Kidney' and 8 'Leuk to Thyroid cancer'. We include, in this article, factors which were thought to be implicated in increasing the risk for developing childhood cancer, but increasing research has, by and large, excluded them. At the end we include factors which are thought to decrease the risk of childhood cancer.

Smulevich (1999) found significantly higher risk for children who have cancer in close relatives, with maternal pathology associated with pregnancy, including threatened miscarriage, toxaemia and hormone treatment during pregnancy. Pre-term births were significantly associated with brain-cancer risk. They also found links to low birth weight equal to, or less than, 2500 g in children born from full-term pregnancy, for all cancers combined and for leukaemias specifically. There was a slightly higher risk for those whose birth weight equalled or exceeded 4000 g. Risk of nephroblastoma was also significantly related to this factor. A medical history of dermatitis or viral hepatitis in the child increased the risk.

Malnutrition was observed in approximately one-third of children with cancer (Srivastava 2015). It was not clear whether this may have been to do with cause or effect. Malnutrition is associated with solid tumours and those coming from rural community.

Younger maternal age, maternal smoking, delivery by caesarean section and low Apgar score at 5 minutes were independently associated with increased risk of childhood cancer (Bhattacharya 2014).

Maternal factors

Contreras (2016) estimated elevated risks of several childhood cancers in the offspring of mothers who had diabetes (ALL, Wilms' tumour) and were overweight prior to pregnancy (leukaemia), as well as mothers who gained insufficient (AML) or excessive weight (astrocytomas).

Maternal age

Slight increases in risk for leukaemia, lymphoma, central nervous system tumours, neuroblastoma, Wilms tumour, bone tumours and soft tissue sarcomas were found with increased *maternal* age (Johnson 2009).

Maternal health

Maternal diabetes may be a risk factor for childhood cancer (Westbom 2002).

Birth

Some birth characteristics including older parental age and low gestational age may be related to childhood carcinoma aetiology (Johnson 2011). Hopman (2016) showed that individuals who had had a childhood cancer had significantly greater facial asymmetry than the controls.

Birthmarks & birth defects

Mertens (1998) found a higher reported frequency of birthmarks in both those with acute lymphoblastic leukaemia (ALL) and those with acute myeloid leukaemia (AML), or childhood cancer in general (Johnson 2007). Children with cancer, especially germ cell tumours, retinoblastomas, soft-tissue sarcomas and leukaemias (Carozza 2012), were more likely to have birth defects. Children with chromosomal birth defects were 30 times more likely to develop leukaemia; children with nonchromosomal birth defects were one and a half times more likely to develop childhood cancer, particularly brain tumours, lymphomas, neuroblastoma and germ cell tumours (Fisher 2012).

Children with neonatal tumours were more often associated with congenital malformations than other paediatric cancers (Berbel Tornero 2008). Y Sun (2016) reported that cancer and birth defects cluster in families more often than expected by chance. Children who had a full sibling with a congenital malformation (CM) had no increased risk of cancer except for those who had a full sibling with a CM in the nervous system or in the eye, ear, face or neck. Children with a half-sibling with a CM tended to have an increased cancer risk in early adulthood.

An association has been found with rib anomalies and childhood cancer, specifically AML, renal tumours and hepatoblastoma (Zierhut 2011).

Birth weight

Skalkidou (2002) suggested that elevations of insulin-like growth factor (IGF-I) in early life might explain the increased risk of cancer in individuals born with a higher birth weight.

A study that looked at children aged 0-14 years newly diagnosed between 1991-1996, found that children with cancer were, on average, 30g heavier at birth than controls. Children with hepatic tumours weighed on average 500g *less* than controls at birth and those with leukaemia were 50g heavier. Girls had a higher risk of ALL with birth weights over 4,000g (A Smith 2009).

In an international study of 40,000 cases of childhood cancer by O'Neill (2015), risk associations were found between birthweight and several childhood cancers. Risk was strongest for leukaemia, tumours of the central nervous system, renal tumours and soft tissue sarcomas. In contrast, increasing birthweight decreased the risk of hepatic tumours (see Smith above). Associations were also observed between high birthweight and risk of neuroblastoma, lymphomas, germ cell tumours and malignant melanomas.

The estimated risk for all cancers has been found to be statistically and significantly higher in children with a birth weight of more than 4,000g (Rangel 2010); specifically leukaemia, non-Hodgkin lymphoma and Wilms tumour. A moderate increased risk of both leukaemia and non-Hodgkin lymphoma was also associated with birth weight between 3,000 and 3,999 g. High birth weight was associated with all cancers also when adjusted by gestational age, length at birth, and gender. An increase in hazard rate with a 1 kg increase in birth weight was found for leukaemia, CNS cancers and other cancer diagnoses (Samuelsen 2009, Paltiel 2015). Papadopoulou (2012) says "Current evidence suggests that birth weight might be a too crude indicator to reveal a genuine association of fetal growth with specific lymphoma categories; hence, there is an emerging need for use of more elaborate proxies, at least those accounting for gestational week."

Birth and diagnosis month

Basta (2010) found that there was a birth peak in March for ALL aged 1-6; in September for boys aged 0-14 for acute non-lymphocytic leukaemia; October for astrocytoma. A diagnostic peak was

found in March for lymphomas in girls; January for Hodgkin lymphoma; and October for boys with osteosarcoma. The authors suggest that their results are consistent with a role for environmental factors in the aetiology of these diagnostic groups.

Birth order

A decreasing risk with increasing birth order was seen in the central nervous system tumours, neuroblastoma, bilateral retinoblastoma, Wilms tumour and rhabdomyosarcoma. We observed increased risks with increasing birth order for acute myeloid leukaemia but a slight decrease in risk for acute lymphoid leukaemia (Von Behren <u>2010</u>).

Ethnicity

The incidence of Hodgkin and non-Hodgkin lymphoma and lymphoid leukaemia were higher in Florida's Hispanic children compared with whites and the incidence in black and mixed-race children was significantly lower than whites. The incidence of lymphoma in Florida's Hispanic children (primarily Cuban and Central American origin) differed from similar reports from Texas and California, where Hispanics are primarily of Mexican origin (Wilkinson 2001).

Socioeconomic status

In Korea there was found to be an inverse relationship between childhood cancer mortality and parental socioeconomic position (Son <u>2010</u>), as in parts of Brazil (de Camargo <u>2011</u>).

Childhood environment

Childhood cancer is a complex illness and is likely to be due to more than one factor acting together in the developing child's biological systems. If the child has already developed a susceptibility due to genetic changes of some sort, then their homes and lifestyles will bring them into contact with many experiences that may result in a changed cell developing into a cancer.

Crohn's disease

The relative risk of cancer in childhood-onset CD as well as the risk of death seem to have increased (Duricova <u>2017</u>).

Diet

We have seen in section 5, that childhood cancer risk is increased by pesticide exposure. Many pesticide residues have been measured on vegetables and fruit, the most contaminated being apples, lettuce, potatoes, grapes and some carrots, many containing the residue of more than one pesticide. One lettuce sample was found to contain inorganic bromide at a level 22 times above that considered safe for children. It may be worth thinking about ensuring a supply of organic food for your child, especially if there are concerns about his or her health.

Wheat grains contaminated by groundwater arsenic

In a study by Sharma (2016) groundwater contamination by arsenic in India was measured to be higher than the USEPA safety limits for both adults and children indicating a high risk of cancer and other health disorders. Consumption of Arsenic (As) contaminated wheat grains was found to pose a higher risk of cancer and non-cancer health disorders and children were found to be

more prone to cancer and other heath disorders due to As exposure via wheat grains and groundwater as compared to adults.

Heavy metals in soil

Potential ecological risk from metal elements in an area studied in Pahang, Malaysia were evident for cadmium, arsenic, lead, and copper, with copper being consistently greater in the abandoned mining area. Greater potential health risk was found among children (Diami 2016).

Geopathic stress

Geopathic stress may be a factor in undermining biological systems within the body (Saunders 2003). Sleeping on lines of geopathic (earth) stress is recognised in many countries as being a significant factor in the development of cancer. Geopathic stress lines are not recognised by most main-stream scientists, as it has not been determined what physical attributes they have. They are usually detected by dowsing. However, peer-reviewed papers are available that show that good dowsers are better at finding drinkable water than scientists using the latest geophysical surveying tools, although it is not known why this is so.

Residential status

There was a statistically significant increase in the rate of leukaemia and brain / CNS tumours reported in South and North east Florida (Amin 2010). The authors concluded *"This evidence is suggestive of the presence of possible predisposing factors in these cluster regions."*

Sunlight

Musselman & Spector (2011) found a link between sunlight exposure and risk of childhood cancer, possibly due to the role of vitamin D as a regulator of cell growth and differentiation.

Eight out of 10 primary and secondary schoolchildren in Switzerland knew about the risk of skin cancer and recognized the most susceptible phototype. Knowledge increased significantly with age. Girls, older children, fair-skinned participants and those who preferred a tanned skin obtained the highest knowledge score (Vuadens 2017). However, the high awareness of the risk of skin cancer among Swiss schoolchildren does not translate into appropriate attitudes. Community-wide intervention programmes involving parents, teachers, peers and primary care clinicians could be considered for Swiss prevention campaigns to improve children's sun behaviour and change their current pro-tan attitude.

Factors which have been largely discounted as causes of childhood cancer. These include the following:-

Human Growth Hormone (GH)

After more than 20 years since an association was first suggested, the link between leukaemia, and GH, has not been confirmed (Bell <u>2010</u>).

Ultrasound scans

Concerns arose in the early 1980s about potential links between ultrasound scans in pregnancy and an increased risk of childhood leukaemia.

There has been little evidence that in *utero* diagnostic ultrasound tests are linked with an increased risk of childhood leukaemia (Naumburg 2000, Shu XO 2002), although Naumburg found a small increase in risk for ultrasound scans carried out in the second trimester of pregnancy. Dr Razum in Germany did a re-analysis of the Naumburg results and suggested that her data was consistent with the probability that a small proportion of cases of childhood leukaemia might be attributable to prenatal ultrasound exposure. It is also possible that ultrasound was used selectively, when abnormal pregnancies were suspected, or being investigated.

Some studies have shown an association between ultrasound exposure and left-handedness in boys (Kieler <u>1998</u>, Salvesen <u>1999</u>, <u>2002</u>), which could show that foetal development can be affected, possibly in ways that have not been looked at.

Although the risk levels are small and contested, ultrasound scans as a form of "baby TV" should not be routine, but should be used for diagnostic or therapeutic use only. There is concerning evidence of links between ultrasound scans and autism. The Health Protection Agency (HPA) states that there have been some reports suggesting possible neurological effects on the unborn child. The concern is that with souvenir scans the beam of ultrasound stays static over the baby's head for longer in order to get a sharp mug shot.

Ziskin & Morrissey (2011) comment that some higher power Doppler ultrasound devices under some conditions are capable of raising foetal temperature several degrees and their use in examinations of the foetus should be minimised.

Vitamin K injections

Since the 1960's vitamin K has been used widely in the UK, throughout Europe and the US, being given as a single injection just after birth. This is a cheap and effective way of avoiding vitamin K deficiency, a rare but serious condition, with no recorded treatment failures, even in babies with liver disease, who are at most risk.

Research carried out by Parker (<u>1998</u>) found a very slight increase in risk for children developing ALL with intra-muscular vitamin K injections.

A review by Roman (2002) found no evidence to support these findings, and a joint UK Medicines Control Agency, Committee on the Safety of Medicines and Department of Health expert group has concluded that overall, the available data do not support an increased risk of cancer, including leukaemia, caused by vitamin K.