

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 11

Precaution, prevention and protection

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Atopic dysfunction (allergies)

The raised immunosurveillance in atopic individuals might protect against the development of some diseases, including brain tumours (Harding [\(2008\)](#)). Children who suffered from asthma and eczema, amongst other atopic conditions, showed a reduction in risk for medulloblastoma and PNET (Harding [\(2008\)](#)).

A history of allergies (including asthma, eczema hay fever, food or drug allergies, or hives) has been found (Petridou [1997](#), Schüz [1999](#), [2003](#), Wen [2000](#), Jourdain-Da Silva [2004](#), Rosenbaum [2005](#), Hughes [2007](#)) to have a protective effect against leukaemia, even amongst siblings (Wen [2000](#)). Heck ([2009](#)) found a link between allergies and a reduced risk of developing neuroblastoma.

A late history of asthma (Spector [2004](#)) was found to increase the risk of leukaemia. A review by Linabery ([2010](#)) of 10 case-control studies concluded that both ALL and AML were associated with atopy/allergies, and inverse associations with asthma, eczema and hay fever and ALL.

Miedema ([2012](#)) found that in children with atopic eczema, specific genotypes were found more often than in control subjects and less often in children with ALL than in control subjects, supporting the immune surveillance hypothesis.

Protective associations were observed between HL and day care attendance and repeated early common infections among non-breastfed children. Protective associations were seen between NHL and birth order 3 or more, prolonged breastfeeding, regular contact with farm animals, frequent farm visits in early life and history of asthma. The authors felt that the results partly supported the hypothesis that an abnormal maturation of the immune system might play a role in childhood HL or NHL (Rudant [2011](#)).

Birth order & multiple births

Birth order can be used as a proxy for prenatal and postnatal exposures, such as infections and in utero hormone exposure.

Von Behren ([2010](#), [2011](#)) found an inverse relationship between childhood cancer risk and birth order, specifically for CNS tumours, neuroblastoma, bilateral retinoblastoma, Wilms tumour and rhabdomyosarcoma, and a slight decrease for acute lymphoid leukaemia. Altieri ([2006](#)) found a decreased risk for Hodgkin's lymphoma for children with 5 or more older siblings.

Being one of twins may reduce the risk of leukaemia (Murphy [2008](#)). The reason for any possible risk reduction is unclear. Children who were multiples had a reduced risk of neuroblastoma (Puumala [2009](#)). The authors suggested that mechanisms other than birth weight and gestational age may influence the lower risk of neuroblastoma in multiple births.

Infante-Rivard ([2000](#)) found that having a school age sibling during the first year of life was significantly protective for those older than 4 years at the time of diagnosis. Altieri ([2006](#)) found that having many siblings increased the risk of ALL, but if they were older, the risk was significantly decreased. Westergaard ([1997](#)) found that the risk of ALL went down with increasing birth order.

Breast-feeding

There is a fairly substantial body of evidence pointing towards a protective effect against cancer of even short-term breast feeding (Smulevich [1999](#), Shu [1999a](#), Perrillat [2002](#), McNally & Parker [2006](#), Shaw [2006](#), MacArthur [2008](#), Flores-Lujano [2009](#), Greenop [2015](#)) including brain tumour and neuroblastoma (Daniels [2002](#)), and Wilms tumour (Saddlemire [2006](#)) risk. A meta-analysis reported a relative risk of 0.76 (Kwan [2004](#)). Shu ([1999a](#)), Ortega-García ([2008](#)) and Amitay ([2015](#), [2016](#)) found that the reduction in risk was stronger with a longer duration of breast-feeding, and Bener ([2001](#), [2008](#)) concluded that long-term (longer than 6 months) was protective, especially for ALL, Hodgkin's lymphoma, and non-Hodgkin's lymphoma but short-term was associated with an increased risk of all cancers. Waly ([2011](#)) did not find any link between breastfeeding and risk of leukaemia in Oman.

A study looking at the relationship of breast feeding with Hib infection (Silfverdal [1997](#)) suggested that breast feeding acts in a manner similar to vaccination, stimulating the immune system. It could therefore provide a protective effect against childhood cancer.

Complementary and alternative medicine (CAM)

Many parents use one or more CAM for their child in the context of cancer. The most used type of CAM is homeopathy, dietary supplements and aromatherapy. The most frequent goal for CAM use is to limit the side effects of conventional treatment. In a study by Philibert ([2015](#)) in 87.5% of the users the CAM was effective. However, some CAM such as herbal supplements could potentially cause interactions with cancer treatments, so more information about interactions would be useful for both parents and practitioners.

Diet

Evidence from one study suggests that there is a strong protective effect of consumption of oranges and bananas in early life (Kwan [2004](#)). Other studies (Jensen [2004](#), Petridou [2005](#), McNally & Parker [2006](#)) have suggested that consumption of fresh fruit and vegetables generally have a protective effect up to age 2 years (Kwan [2009](#)). Consumption of yellow-orange vegetables and grains during pregnancy were associated with a reduced risk of brain tumours, including cruciferous vegetables (e.g. cabbage, brussels sprouts, broccoli, cauliflower) being associated with a decreased risk of astrocytoma (Pogoda [2009](#)). The consumption of many vegetables and fruit (and protein sources Abiri [2016](#)) is associated with a decreased risk of cancer. This is at least partly due to the antioxidant elements of these foods. As some processed foods are linked to cancers, non-processed, organic (to avoid chemical contamination) vegetables and fruit should be included as main ingredients in a diet to reduce the risk of cancer. Vegetables and bean-curd were both found to be protective against acute leukaemia (Liu [2009](#)).

Petridou ([2005](#)) also found a decreased risk with maternal consumption of fish and seafood. Maternal consumption of fresh fish is associated with a decreased risk of astroglial tumours (Pogoda [2009](#)). Jensen thought that dietary carotenoids and glutathione appeared to be important.

Curcumin and turmeric have been shown to inhibit cancer (Alaikov [2007](#)) (including childhood leukaemia) at initiation, promotional and progression stages of development (Nagabhusan 2004) in different ways (Blasius [2007](#)). A mechanism for the ant-cancer effect of curcumin has been proposed by Langone ([2012](#)) who suggests that it suppresses NF-kB, inhibiting tumour-promoting proteins. A study by Banderali ([2011](#)) proposed that the inhibition of Kv11.1 activity by curcumin may lead to interference with leukaemic cell physiology and consequently the

suppression of survival and proliferation of AML cells. Curcumin is one of the ingredients of the spice turmeric.

Studies suggest carcinogens from a mother's diet can cross the placenta into an unborn baby's bloodstream, and Henshaw, says some of the carcinogens could come from processed meats and burned barbecue meats eaten by pregnant women.

Eating a healthy diet full of fruit and vegetables is important for all the family, including pregnant women and children, says Henshaw.

In addition, an Australian study found mothers who took folate and iron supplements during pregnancy had more than a 60% reduced risk of their children developing leukaemia (Irish Examiner September 2016).

Singer (2016b) found that higher maternal diet quality score was associated with reduced risk of ALL and possibly AML. No single component appeared to account for the association. The association of maternal diet quality with risk of ALL was stronger in children diagnosed under the age of 5 years and in children of women who did not report using vitamin supplements before pregnancy. These findings suggest that the joint effects of many dietary components may be important in influencing childhood leukaemia risk. Singer adds *"There were 470 cases of childhood leukaemia (0-14 years of age) in 2014. If we could prevent 20% of them, that would save 94 children from developing childhood leukaemia per year."* A previous study by Singer (2016) showed that higher maternal intake of one-carbon metabolism nutrients (folate, vitamins B12 and B6, riboflavin, and methionine) may reduce risk of childhood leukaemia.

The higher diet quality for women who are pregnant or lactating comprises 12 nutritional components: 9 'adequacy' components (total fruit, whole fruit (excluding fruit juice), total vegetables, greens and beans, whole grains, dairy products, total protein foods, seafood and plant proteins, fatty acids) and 3 'moderation' components (refined grains, Na, and empty calories).

Electromagnetic fields (EMFs)

Luukkonen (2014) found persistently elevated levels of micronuclei in the progeny of MF-exposed cells, indicating induction of genomic instability.

Ethnicity

Ma (2005) found that parentally reported ear infection during infancy was associated with a significantly reduced risk of ALL in non Hispanic white children. They highlight an important ethnic difference but it is not clear whether this may be due to cultural/environmental factors or biological characteristics.

Asian and mixed-race children were at lower risk of developing brain tumours (Chow 2010), and Hispanic and mixed-race children had a lower risk of developing neuroblastoma.

Many of the factors discussed above shed some insight, perhaps, on the sort of environmental exposures that could be avoided, in order to prevent an increased likelihood of developing cancer and the potential for relapse in children recovering after treatment. The most important factor for survival is the interval between first remission and occurrence of the first relapse (van den Berg 2011).

Infection

Children attending day care (often used as a surrogate for infectious exposure) are less likely to develop leukaemia (Perrillat [2002](#), Jourdan-Da Silva [2004](#), Gilham [2005](#), Ma [2005](#), Kamper-Jørgensen [2007](#), Urayama [2010](#)), particularly common B-cell precursor ALL (c-ALL) (Urayama [2008](#)), and neuroblastoma (Menegaux [2004](#)). Shaw ([2006](#)) found that the risk of a childhood brain tumour was reduced by day care attendance for more than a year.

It was assumed that attendance increased their exposure to infections, strengthening the immune system. In fact any social activity outside the family in the first year of life significantly reduced the risk of ALL (Gilham [2005](#)), and CNS tumours (Spix [2009](#)). Spix found this protective effect continued until the 5th year. Perrillat found that day-care without developing infections, did not offer a protective effect; neither did infections without the day-care, although Canfield ([2004](#)) did find an effect. Older siblings (Infante-Rivard [2000](#), Jourdan-Da Silva [2004](#)), or the number of infectious episodes (Neglia [2000](#), Perrillat [2002](#)) had a protective effect. However, several studies have reported no protective effect (Petridou [1997](#), Rosenbaum [2000](#), Chan [2002](#)).

The different conclusions may indicate that there are important confounders that have not been adequately considered, or we need to question whether day care attendance is a reliable proxy for infectious exposure.

Rudant ([2010](#)) found a number of factors which seemed to be protective against the risk of leukaemia that implicated early infections, as factors involved. These included birth order, attendance at a day-care centre before the age of 1, prolonged breastfeeding, repeated early common infections, regular contact with farm animals, frequent farm visits in early life, and a history of asthma or eczema.

The evidence suggests that early childhood infections in general, within the first two years of life, are protective, whereas infections in later life may not be.

Lifestyle

The results of a study by Bellizzi ([2011](#)) support the hypothesis that early-life exposure to pets, birds and particularly with chickens might be associated with a reduced risk of lymphoma.

Frequent contact with other children when 0-3 years old and ventilation during sleeping in summer were associated with a decreased risk of childhood acute leukaemia (Chen [2015](#)).

Medication use

Some medications were found to be negatively associated with infant leukaemia (Ross [2003](#)). These were prescribed for a variety of reasons and the mechanism of protection therefore is unclear. Actual medical records were used, so recall bias would have played no part in the findings, except for 'over the counter' medication.

MacArthur ([2008](#)) found that the use of immunosuppressant medication by children decreased leukaemia risk.

Meditation and Yoga

Meditation and yoga practice showed a significant decline in levels of oxidative damage to sperm DNA, the adverse effect of tobacco on the paternal genome, after 6 months (Kumar [2015](#)). This effect could be responsible for non-familial sporadic heritable retinoblastoma.

Miscarriage or still birth

A history of spontaneous abortions was negatively associated with neuroblastoma risk by Munzer ([2008](#)).

Sun protection

Children of melanoma survivors are at higher risk than other children of developing melanoma. Melanoma survivors may have a heightened awareness of the importance of their children's sun protection, but their children are not routinely protected. It is suggested that subgroups of survivors could be targeted with interventions to improve sun protection (Tripp [2016](#)).

Vaccinations

Pagaoa ([2011](#)) found that some common childhood vaccines (hepatitis B, the inactivated poliovirus vaccine) appeared to be protective against ALL at the population level. Whether this is linked to the issue of infections is unclear, but possible.

Vitamins and minerals

Maternal vitamin supplementation during pregnancy reduced the risk of brain tumours in children under the age of 5. The longer in the pregnancy the supplements were taken, the greater the degree of protection (Preston-Martin [1998](#)). This may partially make up for what is not available in the diet, but supplementation is not always as usable by the body as vitamins and minerals from natural sources. Any maternal vitamin use during the 6 months before conception through the nursing period was associated with a reduced risk of GCTs (Johnson [2009](#)).

Maternal use of vitamins, cod liver oil, folate and iron supplements have been associated (Wen [2002](#), Schüz [2007](#), Metayer [2014](#)) with a decreased risk of ALL, medulloblastoma (Bunin [2006](#)), and neuroblastoma (Olshan [2002](#), Heck [2009](#)) although children's vitamin intake was found to increase the risk of leukaemia (MacArthur [2008](#)), especially AML, if multivitamins were taken during the first year of life or for an extended period of time (Blair [2008](#)). The timing seems to be particularly critical as Ross ([2005](#)) found that vitamin use before the index pregnancy reduced risk for ALL, as did Milne ([2009](#)), but not for AML, and increased the risk of both if taken during pregnancy. It is believed that inadequate folate may cause the first 'hit' in the leukaemia pathway, or prevent the child repairing the first or subsequent hits.

Pineal calcification was detected in a quarter of patients with primary brain tumours. Adjusted for patients' ages and genders, pineal calcification was associated with a 3-fold increase in primary brain tumour (Tuntapakul [2016](#)). As the pineal gland is a major source of melatonin, the body's natural anti-cancer hormone, melatonin supplementation may be very useful in strengthening the body's immune system.

Folic acid supplementation before the 21st and 36th days of gestation resulted in significantly lower nervous system tumours (NST), especially central nervous system tumours.

Preconceptional intakes of folic acid were also lower in NST (Ortega-García [2010](#)). Folic acid supplementation during preconception may reduce the risk of childhood leukaemia (Ajrouche [2014](#)).

Folate metabolism is thought to be important in the development of leukaemia. There is some evidence to suggest that maternal folate supplementation during pregnancy may protect against childhood leukaemia (Thompson [2001](#)), though Dockerty ([2007](#)) both in the team's own New Zealand study, and in their meta analysis, including results from Australia and Canada did not find evidence to support Thompson's hypothesis. There are differences in the way that individuals metabolise folate and this may be important (Wiemels [2001](#)). Koppen ([2010](#)) concluded that "*susceptibility to (childhood) ALL is partly related to constitutional differences in folate gene polymorphisms*" (supported by Lightfoot [2010](#)) and that some polymorphisms in the MTHFR gene were associated with a decreased susceptibility to childhood ALL in non-Asian populations.

In the home

In a study by Bailey ([2015](#)) the authors concluded after pooling 12 case-control studies, that 'it would appear prudent to limit the use of home pesticides before and during pregnancy, and during childhood'. They had found links with ALL and AML.

Greenop ([2013](#)) found that preconception pesticide exposure, and possibly exposure during pregnancy, both professional pesticide treatment and paternal occupational exposure, is associated with an increased brain tumour risk, especially for low- and high-grade gliomas. The authors suggested that 'it may be advisable for both parents to avoid pesticide exposure during this time'.

Bailey ([2015](#)) found that home paint exposure shortly before conception, during pregnancy, and/or after birth appeared to increase the risk of childhood ALL. The authors suggested it may be prudent to limit exposure during these periods.