Childhood Leukaemia – Electromagnetic Fields

All the references in this article identified (Name year) are listed alphabetically in "Childhood Leukaemia articles references".

Childhood leukaemia

About 500 children in the UK develop leukaemia each year and around 100 children die of it. The lifetime risk (0-15 years old) of a child developing childhood leukaemia is about 1 in 1600. Acute lymphoblastic (lymphoid) leukaemia (ALL) accounts for more than 80 per cent of all cases of childhood leukaemia and acute myeloid leukaemia (AML) accounts for about 15 per cent of cases.a

Childhood leukaemia incidence increased during the 20th century which suggests that some changes in environmental factors, including lifestyle, may be at least partly responsible. There is no single factor to which a child must be exposed if they are to develop leukaemia; and there is no single factor, exposure to which is guaranteed to result in the development of leukaemia.

With identical twins, if one develops ALL in ***infancy***, the chances are 50:50 that the other will also develop the illness. If one develops ALL in ***childhood***, the chances of the other twin developing the illness is down to 1:10. In ***adulthood***, there is only a 1:100 likelihood of the other twin developing leukaemia if one gets it. It is clear that although genetic and prenatal factors may be important in the development of childhood leukaemia, the role of environmental factors becomes more important in the development of leukaemia as you get older. These factors may also play a significant part in whether a child with an inherited pre-disposition to leukaemia goes on to develop the actual illness.

Genetics or environment?

Most of the environmental and lifestyle factors which may be implicated in the causes of childhood leukaemia are extremely difficult to investigate in an epidemiological study with a case-control design. The problems are two-fold.

- Firstly, the rarity of childhood leukaemia is such that too few cases may have a sufficiently wide range of exposures to environmental agents to allow an effect on leukaemia risk to be detected with statistical confidence.

- Secondly, many such exposures are ubiquitous, meaning that in a case-control study both cases and controls could be equally exposed and an effect on leukaemia risk would be undetectable. Air pollution and background radiation in particular fall into these categories.

The result could be that factors which may have a major bearing on childhood leukaemia risk lie undetected, even undetectable, by conventional epidemiology. It is this situation which has really limited progress in understanding the *causes* of childhood leukaemia.

Against this background of uncertainty, any description of our current understanding of the causal factors leading to childhood leukaemia needs to take account of the totality of the available laboratory and epidemiological evidence.

There have been considerable advances in understanding the biology of childhood leukaemia, for example, in the identification of gene rearrangements many of which appear to occur *in utero* and mark the first step in what is at least a two-stage process. While some aspects of the biological aetiology or the mechanics of how leukaemia develops, are known, the reasons why gene mutations occur are poorly understood.

Leukaemia arises from the abnormal transformation of a single cell. Stem cells, the precursors of blood cells, divide frequently. There are probably about 100,000,000,000 cell divisions a day in an adult and even more *in utero* when the embryo is growing rapidly. The cells that go on to become white blood cells undergo DNA rearrangement to create the large number of different types of cells needed by the immune system. This process is intrinsically prone to DNA errors – which may occur either spontaneously or as a result of exposure to external carcinogens (Lightfoot & Roman 2004).

Cells with damaged DNA usually either die or the DNA is repaired. Any unrepaired or misrepaired damage will lead to changes in chromosomes, or mutations, some of which may lead to the development of cancer. Environmental agents, which may not be genotoxic or carcinogenic themselves, can contribute to cancer by increasing the genotoxic potential of other agents, interfering with the DNA repair processes, allowing a cell with DNA damage to survive and stimulating the cell division resulting in alteration of the normal functions of the cell. Leukaemic cells show chromosome rearrangements that occur in around one per cent of newborn babies, but less than one per cent of these will go on to develop leukaemia. So, although the stage for developing the illness is set in the womb, *something else is needed* for the disease to become manifest.

Some animal experimentation using chemicals to promote cancer in rats, has shown that the differences in study outcome could be accounted for by different susceptibilities in the strain of rats used. It is recognised that 100% of the chemicals that are known to cause leukaemia in humans cause some sort of cancer when tested on rats and mice. In 73%, the chemical exposure results in leukaemia or lymphoma in rodents. It may be that humans have the same variation in susceptibility as the specially bred rats, whose sensitivities are variable enough to reduce replicability in the experiments. The fact that EMFs do have an effect in some laboratories cannot be ignored despite the problems of reproducibility.

Buffler's study (2005) estimated that the aetiology is unclear in 90% of the cases of childhood leukaemia. The authors believe that a wide range of factors, including environmental, sociological and lifestyle influences are implicated as well as genetic susceptibility.

Excessive exposure to chemicals, radiation and biological agents have been linked to an increased risk of developing leukaemia and it seems likely that no single event is responsible: rather, the causes of childhood leukaemia are multi-factorial, operating in *at least* a two-step process.

The environmental factors we are considering in this article are electromagnetic fields, both power-frequency fields, which arise out of the distribution and use of electricity, and radiofrequency fields which are generated when radio, television or telecommunications signals (primarily) are transmitted.

Electromagnetic fields (EMFs)

How could non ionising radiation, such as electromagnetic fields (EMFs), be involved in the development of leukaemia?

The evidence is mixed as to whether EMFs can be responsible for direct DNA damage. It is possible that the way EMF exposure has been measured may be responsible for the mixed results obtained experimentally.

Though experiments may be contradictory or inconclusive, nevertheless, it is suggested that EMFs could act by:

- Directly increasing the level of harmful free radicals within the body
- Affecting other cellular processes (including direct, or indirect tumour promotion), some of which may not even have been investigated as yet
- Decreasing the level of the protective hormone melatonin
- Affecting exposure to airborne pollutants, making them more harmful

Free radical effects

In body tissue free radicals are dangerous high-energy particles that damage cells and can both cause and accelerate the progression of cancer. Timmel & Henbest (2004) were the first to show that exposure to EMFs can increase the yield of free radicals by more than 60%. The theory was reviewed by Simkó & Mattson (2004), who concluded that EMFs cause a general increase in the levels of free radicals, which could explain the diverse and often inconsistent nature of observed effects of EMFs, free radicals being intermediaries in many natural processes. DNA damage could arise as a result of persistently elevated free radical concentrations, caused by long-term EMF exposure, or via the radical pair mechanism, by which magnetic fields increase the lifetime of free radicals, allowing more DNA damage to occur (Rollwitz 2004, Henshaw 2008).

Effects on other cellular processes

Binhi (2008) suggested that magnetic nanoparticles in the human body may be one of the avenues by which EMFs may be implicated in the development of childhood leukaemia. Changes in levels of cellular proteins or ions can affect cell function (such as removing unnecessary or damaged cells) and cause cancer cells to develop. Some experiments have shown that EMFs affect these functions, though they have been difficult to reproduce and therefore remain controversial. Calcium ions play a critical role in determining the rate of cell division, and the overall evidence is that magnetic fields induce changes in apoptosis (cell death), according to a review by MT Santini (2005). Changes in B lymphocytes can also change cellular division rates. A series of studies (Uckun 1995, Dibirdik 1998, Kristupaitis 1998) demonstrated EMF effects that made cells more likely to become cancerous. These findings may prove particularly important with regard to B-lineage ALL. However, the original results have not yet been replicated, perhaps pointing to the need to tighten experimental protocols.

However, cells are not autonomous units responding to damage as independent entities. Recently, there have been many reports of effects arising in non-irradiated cells as a consequence of inter-cellular communication. These non-targeted effects have been demonstrated in the descendants of irradiated cells (radiation-induced genomic instability) (Lorimore 2008) and in cells that have received signals produced by neighbouring irradiated cells (radiation-induced bystander effects) but the expression of such effects is significantly influenced by genetic factors (Wright 2008).

Evidence for indirect effects as a result of the 'bystander effect' has been shown by Wright and Mair. Mair suggested that *"EMF carcinogenesis involves the transport by macrophages of toxins (possibly including free radicals) to sites of infection or tumour localisation. This could increase mutation rates at these sites, perhaps promoting malignancy by introducing mutations, or by increasing the DNA instability of small early tumours, thereby engendering a more aggressive phenotype."* Mair also suggested that EMFs could be mutagenic on their own, or could potentiate ionizing radiation mutations.

Melatonin effects

The hormone melatonin, is thought to protect the body from cancer by (a) neutralising free radicals, (b) inhibiting the uptake of growth factors by cancer cells, (c) by increasing the likelihood of cancer cells undergoing apoptosis (cell death), and (d) by inhibiting the growth of blood vessels in tumours. Stevens (1987) proposed that the production of melatonin at night (when the majority of melatonin is produced by the body's pineal gland) was reduced significantly by light at night and magnetic fields associated with the electricity supply (Henshaw & Reiter 2005, Erren 2005). Vijayalaxmi (1995, 1996, 1999) and Badr (1999) found that melatonin protects cells from genetic damage. Lupke (2004, 2006) suggested that EMFs reduced the anti-oxidative protection from melatonin.

Melatonin has been shown to be highly protective of oxidative damage to the human haemopoietic system (Vijayalaxmi 1996) and protects from oxidative damage in animal foetus' (Wakatsuki 1999, Okatani 2001). Melatonin levels are particularly high during pregnancy (Nakamura 2001).

A variety of bone marrow cells have been shown to produce melatonin (Tan 1999, Conti 2000, Carrillo-Vico 2004). Whilst the specific function of melatonin in these cells remains unknown, its suppression could have clear implications for leukaemia initiation and / or progression. A reduction in melatonin in the leukocyte precursor cells would be expected to enhance free radical-mediated DNA damage, thereby increasing the likelihood of these cells becoming carcinogenic.

Melatonin reduces the growth of HL-60 myeloid leukaemia cells *in vitro* (Henshaw 2008).

Light at Night

Evidence suggests that increasing exposure to light at night (LAN) and the consequent disruption of circadian rhythms, especially nocturnal pineal melatonin is a significant factor in the increasing incidence of breast cancer in recent decades in industrialised countries (Blask 2005). Whether LAN features in childhood leukaemia risk is not known.

For more information, see the "Melatonin" article.

Airborne pollutant effects

Airborne pollutant particles are known to have a significant effect on health and a number of studies have reported an association between childhood leukaemia and exposure to traffic pollution (see the article on "Childhood Leukaemia" for links between childhood leukaemia and chemical exposure). The strong electric fields associated with high voltage power lines may affect the charge on the chemicals found in traffic pollution, making them more likely to be absorbed by the body. This effect can be observed up to 7 kilometres downwind of a high voltage powerline (Fews 1999a). The older the cable and the wetter the weather the more charged ions are emitted (Fews 1999b). Very small particles are particularly hazardous because of their ability to penetrate deeply into the lung and pass into the bloodstream (Seaton 1995). These small particles are in the

size range where electrical charging can significantly increase lung deposition on inhalation. The report by Draper (2005) found increased risk of leukaemia in children born within 600 metres of National Grid 400 and 275 kilovolt power lines. This distance is clearly too far away to be a direct EMF effect, but could validate the ion polarisation theory.

Power-frequency (ELF) EMFs

Since the first paper by the late Nancy Wertheimer and Ed Leeper (1979), in the USA, more than 25 epidemiological studies around the world have investigated the association between childhood leukaemia and EMF exposure. Other papers which followed this initial paper found an increased risk of childhood leukaemia with proximity to high voltage powerlines, substations or high residential magnetic fields (Coleman 1989, Olsen 1993, Fajard-Gutierrez 1993, Lin & Lee 1994, Kaatsch 1996, Thériault & Li 1997, Linet 1997, Michaelis 1997, 1998, Dockerty 1998, Li 1998, McBride 1999, UKCCS 1999, Bianchi 2000) and some as much as a 2-3 fold increase with residential proximity to powerlines (Savitz 1988, London 1991, Feychting & Ahlbom 1993). Not all studies have found an association (Verkasalo 1993, Tynes & Haldorsen 1997, Fulton 1980, Kleinerman 2000), and some of these studies used wire codes and calculated fields rather than measured fields from specific sources of EMFs. Studies by Lowenthal (2007) found that living within 300 metres of a high voltage powerlines within the first 15 years of life tripled the risk of developing a lymphoproliferative or myeloproliferative disorder in later life; and Draper (2005), in the largest single study of childhood cancer and powerlines, reported an increased risk in the children whose birth address was within 600 metres of a high voltage power line. The risk was increased 5-fold if it was in the first 5 years of life. This may be due to the air ionisation effect referred to above, which is an electric field effect. Henshaw (2008) who proposed the air ionisation effect, suggested that about 11% of childhood leukaemia cases may be linked to magnetic fields.

A review of 152 articles (Pelissari 2009) suggested that *"an association may exist between exposure to low frequency magnetic fields and acute lymphoblastic leukemia in children, but this association is weak, preventing the observation of consistency in the findings."* The authors concluded that ALL should be the focus of future studies as this seems to be the subtype with the most likely association.

Yang (2008) found genetic markers that showed that those carrying this gene variant were four times more likely to develop childhood leukaemia if they also live within 100 metres of power lines or transformers, compared to those with a fully functioning version of the gene. This groundbreaking piece of research indicates a potential for identifying individual susceptibility.

Individual studies are often limited because of the relative rarity of childhood leukaemia and the relatively low number of children exposed to high levels of EMFs.

Three reports which have pooled the data from individual studies, have found an increase in risk with exposure to magnetic fields of 0.3 – 0.4 microtesla (Ahlbom 2000, Greenland 2000, Wartenberg 2001). This level was confirmed by further studies (Kabuto 2006, Feizi & Arabi 2007).

Although there is disagreement as to whether the relationship between EMF exposure and an increased risk of childhood leukaemia is a causal one, or whether there is a coincidental association with some other, as yet undiscovered, factor, the relative risk is surprisingly consistent, even though epidemiology is a bit of a blunt instrument to detect causal factors in a multi-factorial illness. Even the Health Protection Agency – Radiological Protection Division (the former NRPB), the International Agency for Research on Cancer (IARC, 2001) and the World Health organisation (WHO) have all agreed that EMFs are a potential carcinogen (Class 2B) and that precaution is warranted.

It seems unlikely that there is a straightforward answer to whether EMFs *cause* cancer. We believe there is increasing evidence that they may play a definite role in affecting the body's ability to

cope with pre-cancerous cell damage. There almost certainly will be other factors, such as chemical and other physical exposures (Juutilainen 2006) involved in the final outcome of a diagnosis of leukaemia.

Meanwhile, there seems to be mixed opinion as to whether to recommend more precautionary limits to EMF exposure, bearing in mind that precautions are appropriate when there is uncertainty. If a relationship between the two were *proven,* then it would be the time for legislation.

An influential report (www.bioinitiative.org) by Hardell & Sage (2008) concluded that in view of the association between electromagnetic fields and childhood leukaemia, a new lower public safety limit for habitable space adjacent to all new or upgraded power lines should be applied. A new lower limit should also be used for existing habitable space for children and/or women who are pregnant.

The Stakeholder Advisory Group on ELF EMF (SAGE), the official Department of Health working group which was set up to recommend policy about powerlines to government, produced its First Interim Assessment in April 2007. They concluded that banning the building of new homes and schools within 60 metres of power lines is the best available option for reducing deaths from childhood leukaemia and possibly other diseases. The report fell short of recommending this as government policy because of fierce disagreements within the group. It said that such a policy, if implemented by the government would have a dramatic effect on property prices within power line corridors. It put the cost of restricting development at £1bn. Michael Jayne of the Royal Institution of Chartered Surveyors (RICS) called on the Government to take precautionary measures in order to ensure that the health risk is minimised by preventing the building of residential properties within specified distances of power lines.

Parental occupational exposure

Children whose mothers were occupationally exposed to low levels of powerfrequency magnetic fields during pregnancy, have a slightly increased risk of developing ALL between 0-9 years (Infante-Rivard & Deadman 2003).

In another study (Pearce 2007) the team found that paternal occupational exposure to EMFs prior to the child's conception resulted in a significant increased risk of ALL for boys aged less than 6, though the strength of this association is weakened as the research team looked at ionising radiation exposure as well.

Residential exposure

The California EMF Programme report (Neutra 2002), has been recognised as one of the more definitive documents of recent times. The authors concluded that EMFs increased the risk of childhood leukaemia. The International Agency for research on Cancer (IARC) classified magnetic fields as a "possible human carcinogen", though this was not sufficient to influence public health policy according to Kheifets (2006). The results of one Canadian study by Green (1999), based on personal measured fields rather than spot measurements found a significant increase in risk of childhood leukaemia at 0.14 microtesla (even lower than most of the published literature, which seems to show a consensus at 0.3 – 0.4 microtesla), though there was no association with living near high voltage powerlines.

For those already genetically susceptible (children with some congenital syndromes, such as Down syndrome), exposure to magnetic fields seemed to increase the risk of developing leukaemia (Mejia-Arangure 2007).

Schüz (2001) suggested that night-time levels were of particular importance, though when he made a further analysis of his findings (Schüz 2007) his conclusions were less clear. Schüz also looked at residential exposure to magnetic fields at 16.7 Hz from the electrified railway system in Germany, and found a moderate but statistically non-significant association with childhood leukaemia (Schüz 2001).

Exposure to various electrical appliances, both during pregnancy and in childhood were looked at by Hatch (1998) who found a link with childhood ALL and the use of some appliances.

Other EMF exposure

Söderberg (2002) found a slightly elevated risk for AML, but not ALL in children who had been exposed to high magnetic fields from infant incubators.

Changes in magnetic field level above 1.6 microtesla, such as can be found when travelling in electric trains, have been linked with an increased risk of miscarriage (Li 2002). It is possible that the magnetic fields may also change DNA in ways that may not be destructive enough to result in a miscarriage, but may have health implications.

Static fields

Very little has been done to identify whether exposure to static fields may be related to the risk of leukaemia. Bowman (1995) suggested that childhood leukaemia may be related to the combined effects of the earth's static magnetic fields and low levels of ELF magnetic fields resulting in various molecular ion resonances.

Effects of EMFs on survival after treatment

Exposure to magnetic fields appeared to decrease the survival time of children in remission from leukaemia, at over 0.3 microtesla (Foliart 2006), or over 0.1 microtesla (Svendsen 2007), though a further study by Foliart (2007) concluded that elevated magnetic field levels were not associated with factors that predicted poor survival.

It has also been suggested that exposure to EMFs may adversely affect the outcome of *treatment* for childhood leukaemia.

Radio frequency (RF) EMFs

Radiofrequency radiation has been part of our environment since the 1920s. It has been assumed that these signals are benign and without health consequences. However, there have been some studies that have found increases in leukaemia risk as a result of living in proximity to radio or TV transmitters *(*Maskarinec 1994, Hocking 1996, Dolk 1997a, 1997b, Michelozzi 2002*)*, that mean we cannot be complacent about the effects of RF signals. The study authors concluded that there was a small increased risk in adult and childhood leukaemia (within 2 kilometres (Ha 2007)), but the confidence levels were low due to the small number of cases involved. One study showed no such increase in risk (Merzenich 2008).

Hocking & Gordon (2003) also found an association between living near to the transmitters and decreased length of survival after leukaemia diagnosis.

Older TV and radio masts transmitted analogue signals. The situation has now changed with the arrival of digital radio and TV and the omnipresent telecommunications (mobile phone) masts. There are also other sources of digital signal transmission (WiFi, etc) that are being increasingly

situated within houses, schools, offices, leisure facilities, etc. that is increasing the general public's exposure to radiofrequency radiation significantly.

It has been suggested by many scientists that digital signals may well have a greater biological impact on living systems than analogue signals; this possible impact includes not only people, but also animals and plants. If this is so, we would expect to see increasing evidence of health problems associated with exposure, though this may not include an increase in childhood leukaemia risk.

Navarro (2003) and R Santini (2002, 2003) found evidence of ill-health as a result of living near to mobile phone masts, but they were not specifically looking at leukaemia incidence. Two studies on adult cancer incidence near masts found significant increases (Wolf & Wolf 2004, Eger 2004) and the Wolf study found a ten-fold increase in female cancer. Neither looked at childhood leukaemia incidence.

Although childhood leukaemia is unlikely, we believe, to be caused by exposure to electromagnetic fields, there seems sufficient evidence that they may have a promotional effect that we think taking a precautionary stance, minimising exposure, is the best course, whilst further research takes place.

At an International Commission for Non-Ionising Radiation Protection (ICNIRP) workshop on risk factors for childhood leukaemia, Anders Ahlbom reviewed the epidemiological data looking at childhood leukaemia and electromagnetic fields. He said "*Generally the exposure measures have been too crude, however this would tend to decrease the estimated association rather than increase it. Significant confounding is most unlikely – there would have to be a very large new factor that has not already been considered. Selection bias is possible, but unlikely to be a large effect given the number of very different pooled studies. It will not be due to chance. The evidence that ELF magnetic fields are a causal factor in the development of childhood leukaemia is stronger than that for passive smoking and lung cancer.*"