EMFs and Childhood Leukaemia

What causes 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. Acute myeloid leukaemia (AML) accounts for most of the remaining cases.

Leukaemia arises from the abnormal transformation of a single cell. Stem cells, the precursors of blood cells divide frequently, about 100,000,000,000 times 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). 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.

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.

A recent report (Buffler 2005) estimates that in 90% of the cases of childhood leukaemia, the aetiology is unclear. They believe that a wide range of factors, including environmental, sociological, lifestyle influences are implicated as well as genetic susceptibility.

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.

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 Santini (et al) in 2005. Changes in B lymphocytes can also change cellular division rates. A series of studies (Uckun et al, 1995; Dibirdik et al, 1998; Kristupaitis et al, 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.

Some animal experimentation, using chemicals to promote cancer in rats, has shown that difference 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.

Excessive exposure to chemicals, radiation and biological agents have been linked to an increased risk of developing the illness 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.

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.

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 as people get older, environmental factors play a more important role in determining whether you develop leukaemia or not.

The increase in incidence of childhood leukaemia during the 20th century suggests that 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.

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 by conventional epidemiology.

It is this situation which has really limited progress in understanding the causes of childhood leukaemia. While enormous progress has been made in understanding the biology of the disease, much research remains to be done to understand the underlying causes of the disease.

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. We need to recognise just how little we know of the underlying causes of childhood leukaemia. The term 'cause' itself would benefit from definition.

Childhood leukaemia is a collective term for a group of subtypes.

Childhood acute lymphoblastic leukaemia (ALL) is believed to be at least a two stage process, the initial damage occurring *in utero* but only 1 in 100 children going on to actually develop leukaemia, suggesting that at least a second stage (in most cases probably more than one) is required.

Non-ionising radiation

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

It is suggested that EMFs could act:

- By directly increasing the level of harmful free radicals within the body
- By decreasing the level of the protective hormone melatonin
- By affecting exposure to airborne pollutants, making them more harmful

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 premise was reviewed by Simko & Mattson (2004). They 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 intermediates in many natural processes. DNA damage could arise as a result of persistently elevated free radical concentrations, caused by long-term EMF exposure.

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 (see also Henshaw & Reiter, 2005). Vijayalaxmi (1995,1996,1999) and Badr (1999) found that melatonin protects cells from genetic damage.

A variety of bone marrow cells have been shown to produce melatonin (Tan et al 1999, Conti et al 2000, Carrillo-Vico et al 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.

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. 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

at el 1999a). The older the cable and the wetter the weather the more charged ions are emitted (Fews at al 1999b). Very small particles are particularly hazardous because of their ability to penetrate deeply into the lung and pass into the bloodstream (Seaton et al 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.

Powerfrequency (ELF) EMFs

Since the first paper by the late Nancy Wertheimer and Ed Leeper in 1979, in the USA, more than 25 epidemiological studies around the world have investigated the association between childhood leukaemia and EMF exposure.

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 recent 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 a Japanese study (Kabuto 2006). A further study, published in the BMJ (Draper 2005), 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, which may also involve electric field exposure. Other papers have found increased risk of leukaemia with proximity to high voltage powerlines (Fajard-Gutierrez 1993, Lin & Lee 1994, Li 1998). Lowenthal (2007) found that prolonged residence close to high-voltage power lines, especially early in life, may increase the risk of the development of myeloproliferative disorders (MPD) and lymphoproliferative disorders (LPD) later.

Children (especially boys aged less than 6) whose fathers were occupationally exposed to EMFs are more likely to develop leukaemia (Pearce 2007), though the strength of this association is weakened as they also looked at ionising radiation 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 2003).

Although there is disagreement as to whether this is a causal relationship or whether there is a coincidental association with some other, as yet undiscovered, factor, the relative risk is surprisingly consistent. 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 (old NRPB), the International Agency for Research on Cancer (IARC) and the World Health organisation (WHO) have all agreed that EMFs are a potential carcinogen (Class 2B) and that precaution is warranted.

There are well established means by which EMFs could cause biological effects, (DNA damage, cell alteration, tumour promotion, increase in free radical activity, reduction in anti-oxidative protection from melatonin (Lupke 2004,2006), exposure to airborne pollutants) but experiments are contradictory and inconclusive.

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.

It has also been suggested that exposure to EMFs may adversely affect the outcome of treatment for childhood leukaemia. A study (Foliart 2007) looking at this hypothesis concluded that such an exposure was not associated with factors that predicted poor survival.

Radio frequency (RF) EMFs

There have been a few studies on the increased risk of leukaemia due to living near a radio or TV transmitter (Maskarinec 1994, Hocking 1996, Dolk 1997a and b, Michelozzi 2002). They found a small increased risk in adult and childhood leukaemia, but the confidence levels were low due to the small number of cases involved.

Navarro (2003) and Santini (2002 & 2003) found evidence of ill-health as a result of living near to mobile phone masts, but they were not looking at leukaemia incidence.

Two studies on cancer incidence near masts found significant increases (Wolf & Wolf 2004, Eger 2004) and one (Wolf & Wolf) found a ten-fold increase in female cancer. Neither looked at childhood leukaemia incidence.

Although childhood leukaemia is not, we believe, 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.

References

Ahlbom A. B. et al, 2000 - *A pooled analysis of magnetic fields and childhood leukaemia* British Journal of Cancer Sep 83(5):692-8

Badr F M et al, 1999 – *Radioprotective effect of melatonin assessed by measuring chromosomal damage in mitotic and meiotic cells* Mutation Research 444: 367-372 Pubmed 10521676

Buffler PA et al, 2005 – *Environmental and genetic risk factors for childhood leukaemia: appraising the evidence* Cancer Invest 23(1): 60-75

Carrillo-Vico A et al 2004 – *Evidence of melatonin synthesis by human lymphocytes and its physiological significance: possible role as intracrine, autocrine and /or paracrine substance* FASEB J (express article), 10.1096/fj.03-0694fje. (Published online 08.01.04)

Conti A et al 2000 – *Evidence for melatonin synthesis in mouse and human bone marrow cells* J Pineal Res 28: 193-202

Dibirdik I et al 1998 – *Stimulation of Src family protein tyrosine kinases as a proximal and mandatory step for SYK kinase-dependent phospholipase C gamma 2 activation in lymphoma B cells exposed to low energy electromagnetic fields* J Biol Chem 273: 4035-4039

Dolk H et al 1997a - *Cancer incidence near radio and television transmitters in Great Britain. II. All high power transmitters.* Am J Epidemiol. 145:10–17.

Dolk H et al. 1997b - *Cancer incidence near radio and television transmitters in Great Britain. I. Sutton Coldfield transmitter.* Am J Epidemiol. 145:1–9.

Draper G. et al, 2005 - *Childhood cancer in relation to distance from high voltage power lines in England and Wales: a case-control study*, BMJ, 330(7503):1290

Eger et al 2004 – *The influence of being physically near to a cell phone transmitter mast on the incidence of cancer* Umwelt.Medizin.Gesellschaft 17,4

Fajard-Gutierrez A et al 1993 – *Residence close to high-tension electric power lines and its association with leukemia in children* Bol Med Hosp Infant Mex 50(1) : 32-8

Fews AP et al 1999a – *Corona ions from powerlines and increased exposure to pollutant aerosols* Int J Radiat Biol 75 : 1523-1531

Fews AP et al 1999b – *Increased exposure to pollutant aerosols under high voltage power lines* Int J Radiat Biol 75(12) : 1505-1521

Foliart DE et al 2007 – *Magnetic field exposure and prognostic factors in childhood leukaemia* Bioelectromagnetics 28(1):69-71

Greenland S. et al, 2000 - *A pooled analysis of magnetic fields, wire codes and childhood leukaemia*. Epidemiology, 11, 624-634

Henshaw DL and RJ Reiter 2005 - *Do magnetic fields cause increased risk of childhood leukaemia via melatonin disruption?* Bioelectromagnetics Supplement 7.

Hocking B et al 1996 - *Cancer incidence and mortality and proximity to TV towers* Med J Aust. 165:601–605

Infante-Rivard C and JE Deadman 2003 – *Maternal occupational exposure to extremely low frequency magnetic fields during pregnancy and childhood leukaemia* Epidemiology 14(4): 437-41

Juutilainen J et al 2006 - *Do extremely low frequency magnetic fields enhance the effects of environmental carcinogens? A meta-analysis of experimental studies* Int J Radiat Biol 82(1):1-12

Kabuto M et al 2006 – *Childhood leukaemia and magnetic fields in Japan: a case-control study of childhood leukaemia and residential power-frequency magnetic fields in Japan* Int J Cancer 119(3): 643-50

Kristupaitis D et al 1998 – *Electromagnetic field-induced stimulation of Bruton's tyrosine kinase* J Biol Chem 273: 12397- 12401

Li CY et al 1998 – *Risk of leukaemia in children living near high-voltage transmission lines* J Occup Environ Med 40(2): 144-7

Lightfoot TJ and Roman E 2004 – *Causes of childhood leukaemia and lymphoma* Toxicol Appl Pharmacol 199(2): 104-17

Lin RS & WC Lee 1994 – *Risk of childhood leukaemia in areas passed by high power lines* Rev Environ Health 10(2): 97-103

Lowenthal RM et al 2007 - *Residential exposure to electric power transmission lines and risk of lymphoproliferative and myeloproliferative disorders: a case-control study* Intern Med J 37(9):614-9

Lupke M et al 2004 - *Cell activating capacity of 50 Hz magnetic fields to release reactive oxygen intermediates in human umbilical cord blood-derived monocytes and in Mono Mac 6 cells* Free Radic Res 38(9):985-93

Lupke M et al 2006 - *Gene expression analysis of ELF-MF exposed human monocytes indicating the involvement of the alternative activation pathway* Biochim Biophys Acta 1763(4):402-12

Maskarinec G et al 1994 - *Investigation of increased incidence in childhood leukemia near radio towers in Hawaii: preliminary observations.* J Environ Pathol Toxicol Oncol. 13:33–37.

Michelozzi P et al 2002 - *Adult and childhood leukemia near a high-power radio station in Rome, Italy.* Am J Epidemiol. 155(12):1096–1103

Navarro EA et al 2003 - *The microwave syndrome: a preliminary study in Spain.* Electromagn Biol Med. 22:161–169.

Pearce MS et al 2007 – *Paternal occupational exposure to electro-magnetic fields as a risk factor for cancer in children and young adults: A case-control study from the North of England* Pediatr Blood Cancer 49(3):280-6

Santini R et al. 2002 - *Investigation on the health of people living near mobile telephone relay stations: I/Incidence according to distance and sex.* Pathol Biol (Paris). 50:369–373.

Santini R et al 2003 - *Symptoms experienced by people in vicinity of base stations: II/Incidences of age, duration of exposure, location of subjects in relation to the antennas and other electromagnetic factors.* Pathol Biol (Paris). 51:412–415.

Santini MT et al 2005 – *Extremely low frequency (ELF) magnetic fields and apoptosis: a review* Int J Radiat Biol 81(1): 1-11

Seaton A et al 1995 – *Particulate air pollution and acute health effects* Lancet 345: 176-178

Simko M & Mattson MO 2004 – *Extremely low frequency electromagnetic fields as effectors of cellular responses in vitro: possible immune cell activation* J Cell Biochem 93(1): 83-92

Stevens RG 1987 – *Electric power use and breast cancer: a hypothesis* American Journal of Epidemiology 125: 556-561

Tan DX et al 1999 – *Identification of highly elevated levels of melatonin bone marrow: its origin and significance* Biochim Biophys Acta 1472:206-214

Timmel CR & Henbest KB 2004 – *A study of spin chemistry in weak magnetic fields* Philos Transact A Math Phys Eng Sci 362(1825): 2573-2589

Uckun FM et al, 1995 – *Exposure of B-lineage lymphoid cells to low energy electromagnetic fields stimulates Lyn kinase* J Biol Chem 270: 27666-27670

Vijayalaxmi et al – 1995, *Marked reduction of radiation-induced micronuclei in human blood lymphocytes pre-treated with melatonin* Radiation Research 143: 102-106 Pubmed 7597136

Vijayalaxmi et al – 1996, *Melatonin and radioprotection from genetic damage: In vivo/in vitro studies with human volunteers* Mutation Research 371: 221-228 Pubmed 9008723

Vijayalaxmi et al – 1999, *Melatonin and protection from whole-body irradiation: survival studies in mice* Mutation Research 425: 21-27 Pubmed 10082913

Wartenberg D., 2001 - *Residential EMF Exposure and Childhood Leukaemia: Meta-analysis and population attributable risk*, Bioelectromagnetics, Suppl. 5 :S86-104

Wertheimer N & Leeper E, 1979 - *Electrical Wiring Configurations and Childhood Cancer,* American Journal of Epidemiology, March 109(3): 273-84

Wolf R & Wolf D, 2004 – *Increased incidence of cancer near a cell-phone transmitter station* Int J of Cancer Prevention 1(2)