

## **Factsheet: What causes childhood leukaemia?**

Despite a wealth of research, much uncertainty remains over the causes of childhood leukaemia. A wide variety of factors have been linked with development of the disease and these are set out below. This brief overview does not attempt to provide an exhaustive list of evidence.

### **1. Factors which may increase the risk of childhood leukaemia**

#### **Ionising radiation**

Ionising radiation occurs as either electromagnetic rays (such as x-rays) or particles (such as alpha and beta particles). It occurs naturally (e.g. from the decay of natural radioactive substances) but can also be produced artificially. Everyone receives some exposure to natural background radiation.

The link between exposure to high dose radiation and the development of childhood leukaemia is well-established. Epidemiological evidence for this comes from studies of *in utero* irradiation of the foetus through obstetric x-rays and studies of Japanese atomic bomb survivors.

It is estimated that exposure to background ionising radiation is implicated in around 25% of cases of childhood leukaemia, with exposure both *in utero* and early in life being important. See Wakeford (2004<sup>1</sup>) for a review. There is some evidence that paternal pre-conceptual exposure may be important (Gardner *et al*, 1990<sup>2</sup>).

#### **Non-ionising radiation**

Non-ionising radiation includes the low-frequency electric and magnetic fields generated by electrical supply equipment and electrical appliances, the fields generated by telecommunications systems, and also optical radiation such as sunlight and artificial light sources.

- **Electric and magnetic fields (EMF)**

Since the first study reporting an association between childhood cancer and electrical wiring was published by Wertheimer and Leeper in 1979<sup>3</sup>, more than 25 further studies have been published including two major pooled analyses (Greenland *et al*, 2000<sup>4</sup>; Ahlbom *et al*, 2000<sup>5</sup>) both of which were supportive of a link. The largest study to date (Draper *et al*, 2005<sup>6</sup>) reported a significantly increased risk of leukaemia in children in England and Wales living within 600 metres of a high voltage overhead power line. CHILDREN with LEUKAEMIA has carried out an in-depth review of the evidence linking EMF and childhood leukaemia. [Click here to download a copy of this review.](#)

- **Light at night**

There is a suggestion that children's increasing exposure to light at night may be increasing their risk of leukaemia through disruption of

their circadian rhythm and suppression of the hormone melatonin (Henshaw & Reiter, 2005<sup>7</sup>).

## **Chemical exposure**

- **Air pollution**

The risk from air pollution is difficult to detect in epidemiological studies as a result of the ubiquitous exposure in developed countries. Knox (2005<sup>8,9</sup>) found an increased risk of childhood cancer for birth addresses within 1 km of hot spots for various air pollutants.

- **Parental smoking**

Epidemiological evidence to support a link with childhood leukaemia is inconsistent, however at least one study has found increased chromosomal abnormalities in amniocyte cells of foetuses of smoking mothers (De la Chica *et al*, 2005<sup>10</sup>).

- **Pesticides**

Associations have been reported between childhood leukaemia and either parental or child exposure to pesticides (e.g. Infante-Rivard, 1999<sup>11</sup>).

- **Prescription drugs (pre-natal exposure)**

One study has reported an association between childhood ALL and maternal use of antihistamines and allergy remedies (Wen *et al*, 2002<sup>12</sup>). Robison *et al* (1989<sup>13</sup>) reported a link between maternal use of anti-emetic medication and AML.

- **Parental alcohol consumption**

There is weak evidence for a possible link between maternal alcohol consumption during pregnancy and AML but no evidence for a link with ALL<sup>14</sup>.

- **Recreational drugs (pre-natal and pre-conceptual exposure)**

Maternal use of marijuana has been reported to increase the risk of both childhood ALL (Wen *et al*, 2002) and AML (Robison *et al*, 1989<sup>Error! Bookmark not defined.</sup>). There is evidence that the risk may be higher when both parents use the drug.

- **DNA topoisomerase inhibitors**

This includes some drugs used in chemotherapy, benzene metabolites (from air pollution and cigarette smoke), certain fruits, tea, coffee, wine, soy and cocoa and many other substances. Topoisomerase inhibitors inhibit DNA repair and are strongly associated with one of the chromosome rearrangements common in infant leukaemia.<sup>15,16,17</sup>

- **Diet**

N-nitroso compounds (found in cured meats and hot dogs) have been linked with childhood leukaemia in at least one study (Peters, 1994<sup>18</sup>).

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## **Infectious exposure**

There is evidence of an excess of cases of childhood leukaemia in locations with an unusual type of population mixing. It has been proposed that this is due to an, as yet unidentified, infectious agent and that leukaemia is a rare consequence of exposure to this agent. In isolated communities a higher proportion of the population would have been previously unexposed to such an infection and a rapid influx of newcomers into such a community would lead to an increased level of contact between the infected newcomers and the susceptible original residents (Kinlen, 1995<sup>19</sup>).

- **Flu**

Recent studies have suggested a link between influenza infection and childhood leukaemia (Kroll, Draper et al. 2006<sup>20</sup>) (Kwan, Metayer et al. 2007<sup>21</sup>)

## **2. Factors which may reduce the risk of childhood leukaemia**

### **Diet**

Evidence from one study suggests that there is a strong protective effect of consumption of oranges and bananas in early life (Kwan *et al*, 2004a<sup>22</sup>).

### **Folate and folate metabolism**

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 *et al*, 2001<sup>23</sup>). There are also differences in the way that individuals metabolise folate and this may be important (Wiemels *et al*, 2001<sup>24</sup>).

### **Infectious exposure**

Lack of exposure to infections in early life results in an immature immune system and this may increase risk of childhood leukaemia (Greaves, 1997<sup>25</sup>). For example, a recent study found that children attending day care from young age (and therefore assumed to be exposed to more infections) are less likely to develop leukaemia. (Gilham *et al*, 2005<sup>26</sup>).

### **Vaccination**

A number of studies have suggested that early vaccination can be protective against childhood leukaemia (Ma, Does et al. 2005<sup>27</sup>)

### **Breast feeding**

There is a fairly substantial body of evidence pointing towards a protective effect of breast-feeding. A recent meta-analysis reported a relative risk of 0.76 (0.68 – 0.84) (Kwan *et al*, 2004b<sup>28</sup>).

### **3. Other factors associated with childhood leukaemia**

#### **Maternal age >35years**

Most studies have observed an increased risk for childhood leukaemia with advanced maternal age (e.g. Reynolds, 2002<sup>29</sup>) although one study has reported a risk association in ALL with young maternal age (Shu, 2002<sup>30</sup>).

#### **Miscarriage history**

Maternal history of previous miscarriages is a frequently reported risk factor for development of ALL – and in some cases AML - in a subsequent child (e.g. Perrillat, 2002<sup>31</sup>) (Dorak, Pearce et al. 2007<sup>32</sup>).

#### **Birth order**

Being the first born child has been associated with increased risk in some studies (e.g. Dockerty, 2001<sup>33</sup>) although the opposite has also been reported (e.g. Shu, 2002<sup>30</sup>). One study identified being the only child as a risk factor (van Steensel-Moll, 1986<sup>34</sup>).

#### **Socioeconomic status**

Incidence of ALL is higher in areas of high social class (e.g. Alexander 1991<sup>35</sup>, Stiller & Parkin, 1996<sup>36</sup>). Evidence from developing countries suggests that incidence of ALL in children aged 1-4 years is rising with improved socio-economic conditions (Hrusak, 2002<sup>37</sup>).

#### **Birth weight**

Higher birth weight is associated with increased risk of childhood leukaemia (Hjalgrim, 2003<sup>38</sup>) particularly in boys (Dorak, Pearce et al. 2007<sup>39</sup>).

#### **Congenital disorders**

Children with Down's Syndrome and certain other genetic syndromes are much more susceptible to leukaemia (Reynolds, 2002<sup>Error! Bookmark not defined.</sup>).

#### **Gender**

The gender effect in incidence of ALL is well-established, with boys being approximately 20% more likely to develop ALL than girls (e.g. Pearce & Parker, 2001<sup>40</sup>). Males also have a worse prognosis (Eden, 2000<sup>41</sup>).

#### **Ethnicity**

Incidence of ALL is significantly lower among black children in the US (Reynolds, 2002<sup>29</sup>). This may be a social class effect.

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