

# Epidemiological studies of leukaemia in children and young adults around nuclear facilities: a critical review

## Aims and structure of the report

An epidemiological study published in late 2007 described an increased risk of leukaemia in children under 5 living within 5 kilometres of German nuclear power plants. A great deal of research has been carried out on this subject since the early 1980s. The aim of this report was to provide a synthesis and critical analysis of results related to the risk of leukaemia in children and young adults aged under 25 living close to nuclear facilities. The report is structured in three sections:

- a reminder of the main characteristics of childhood leukaemia and a description of the methods used to conduct epidemiological studies;
- the most exhaustive review possible of epidemiological studies published in the international literature describing the frequency of leukaemia close to nuclear facilities in different countries around the world. A critical analysis is made of the published results. Some results from studies not focused on nuclear facilities are also presented. The methodological limitations associated with descriptive studies are explained and discussed;
- the last section discusses the possible causes of childhood leukaemia and the main hypotheses explored to explain certain clusters of cases observed locally close to some nuclear sites.

Appendices at the end of the document provide additional explanations of the concepts and methods used in epidemiology and statistics, and of the classification of malignant haemopathies.

## Background information and methods

Leukaemia is not a common disease among children: each year in France there are around 470 new cases and 75 deaths from childhood leukaemia in a population of approximately 12 million children (aged 0-14 years). Acute lymphoblastic leukaemia accounts for nearly 80% of cases of leukaemia in children. There is a peak in the frequency of this type of leukaemia between 1 and 6 years. There are few recognised risk factors of childhood leukaemia: trisomy 21 or Fanconi anaemia, external exposure to ionising radiation at high doses or taking alkylating drugs used in chemotherapy. Other factors are suspected but their role has not been confirmed so far: exposure to low doses of ionising radiation, electromagnetic fields, pesticides, benzene, infectious agents, etc. Although many possible risk factors have been suggested, there is little information available at present to explain the causes of leukaemia and 90% of cases remain without known cause.

The method used for this synthesis is based on bibliographical research on the Scopus and PubMed databases. Additional documents have been obtained from IRSN's archives and direct contact with researchers in France and abroad. In total, several hundred documents (reports, articles in scientific journals) on the risk of leukaemia in young people aged under 25 around nuclear sites have been published. The work done has varied in nature and quality: local or multi-site cluster studies, case-control or cohort studies, radio-ecological studies, dosimetry research, etc. The review distinguishes between two types of research:

- descriptive studies, the aim of which is to estimate the frequency of leukaemia, and possibly to detect excess risk within a population;
- analytical research, the aim of which is to find the factors that could explain excess risk of leukaemia within a population.

### **Review of descriptive studies**

Descriptive studies are trying to answer the question "Is the frequency of leukaemia close to a particular site higher than elsewhere?". It is important to point out that these studies cannot find the factors likely to explain clusters of cases.

In total, descriptive results are available for 198 nuclear sites in ten different countries: the United Kingdom, Germany, France, Sweden, Spain, the United States, Canada, Japan, Switzerland and Israel. A review was conducted of all these results, distinguishing between local studies of a specific site and multi-site studies looking simultaneously at a group of sites in a country, and therefore covering a larger population. Evaluation criteria were applied in order to assess the results collected. The criteria relate to the type of data considered (morbidity/mortality), the geographical area studied (relevance of the size and boundaries of the areas considered), the power of the study (ability to reveal a low excess risk), the reproducibility of the results (excess revealed by different methods), the statistical significance of the excess, the validity of the statistical methodology, and finally the persistence of the excess over time.

At the 198 sites surveyed, three excesses met the stated evaluation criteria and can be considered confirmed clusters. These are the clusters at Seascale (near the Sellafield plant in England), Thurso (near the Dounreay plant in Scotland) and Elbmarsch (near the Kruemmel power plant in Germany). Other clusters are well documented, particularly in the United Kingdom close to the Aldermaston and Burghfield sites and in France close to the La Hague reprocessing plant, but the information currently available is not conclusive about the existence of confirmed excesses.

Among the multi-site studies surveyed (25 studies in 8 different countries), those that best meet the evaluation criteria are the recent studies carried out in the United Kingdom, Germany and France. At the level of all the sites, these studies do not show an increased risk of leukaemia in children and young adults close to the nuclear sites. The observation of an excess of leukaemia in children aged

0-4 years around German nuclear power plants is not backed up by studies carried out in other countries. Nevertheless, it should be pointed out that few studies have provided specific results for this age range.

Other studies show that localised excesses in cases of childhood leukaemia have also been detected where there is no nuclear site. Furthermore, several studies show spatial and temporal clusters of the incidence of leukaemia in children that are independent of the presence of potential sources of risk.

The discussion underlines the limitations of descriptive studies, which make interpreting the results difficult. Studies of the risks of leukaemia around nuclear sites are many and varied, so it is necessary to look at each new result in the light of the available scientific knowledge.

### **Review of research into the causes of observed localised excesses**

Following descriptive studies in which leukaemia clusters have been observed close to certain nuclear facilities, much research has been launched to identify factors that explain these excesses, in particular close to the sites at Sellafield and Dounreay, and Aldermaston and Burghfield in the United Kingdom, La Hague in France and Krüemmel in Germany. The nature of and protocols used for this research have varied: epidemiological studies (geographical case, case-control or cohort studies), measurements of doses received by the population or radio-ecological assessments. Three principal hypotheses have been put forward to try to explain a higher risk being observed close to certain nuclear facilities.

- the hypothesis of a link with environmental exposure due to radioactive or chemical discharges from the nuclear facilities;
- the hypothesis of a link with the exposure of fathers to ionising radiation before the conception of children;
- the hypothesis of the leukaemia being caused by an infection linked to population mixing associated with major construction work.

Research into a possible link with environmental exposure indicates that the doses due to discharges from the nuclear facilities are low.

The hypothesis of a link with the workplace exposure of fathers to external ionising radiation before conception now seems to have been ruled out.

The hypothesis of infection linked to population mixing around nuclear sites is backed up by several epidemiological results. According to some authors, this hypothesis could partly explain the excesses observed close to certain sites (in particular Sellafield and Dounreay). However, it has not so far been possible to identify or isolate the infectious agent(s) involved.

The implication of other environmental factors has been considered by some publications, such as electromagnetic fields due to high-voltage power lines, pesticide use in gardens or fields, the presence of other industrial sites or high exposure to radioactivity of natural origin. Nevertheless, these factors are not specific to the sites where the nuclear facilities are located and so far none of them is a recognised risk factor of childhood leukaemia.

At present, although several suggestions have been put forward, the origin of the clusters observed close to certain nuclear sites has not been established. However, it should be noted that most of these studies have methodological limitations (geographical case studies or studies of small populations), making it difficult to detect any causal link. In addition to this difficulty there is a lack of knowledge of the risk factors associated with childhood leukaemia. Carrying out large-scale analytical studies such as those under way in France, based on the national register of malignant haemopathies in children, could provide a better understanding of the causes of clusters of childhood leukaemia.

### **Conclusion**

Since the 1980s, many descriptive studies have estimated the frequency of leukaemia in young people close to nuclear facilities. These studies meet a demand for information on the part of local populations and constitute a necessary addition to the discussion on the effects of low environmental doses. The bibliographical review shows wide diversity in the approaches taken and methods used.

Localised excesses of cases of childhood leukaemia exist in the United Kingdom close to the reprocessing plants at Sellafield and Dounreay, and in Germany close to the Kruemmel nuclear power plant. Nevertheless, none of the multi-site studies currently available shows an increase in the frequency of leukaemia overall in children and young people aged 0-14 or 0-24 close to nuclear sites.

A recent epidemiological study described an excess of leukaemia in children aged 0-4 around German nuclear facilities. To date, no similar excesses have been observed in studies in other countries. The published German study offers no suggestions to explain the excess observed.

Furthermore, much research has looked for explanations for excesses of leukaemia observed around certain nuclear sites in multiple potential risk factors. Among the different areas explored, the hypothesis of infection linked to population mixing around the nuclear sites seems to be the most supported. However, the infectious agent(s) involved have not so far been found.

Determining the causes of excesses of leukaemia observed locally close to certain nuclear sites is limited by a lack of knowledge of the risk factors of childhood leukaemia. This means that it is necessary to develop analytical studies on a larger scale, at national or international level.