Risk of Childhood Leukaemia in the Vicinity of Nuclear Installations

Findings and Recent Controversies

Dominique Laurier, Bernd Grosche and Per Hall

From the Institute for Protection and Nuclear Safety, Fontenay-aux-Roses, France (D. Laurier), the Federal Office for Radiation Protection, Institute for Radiation Hygiene, Oberschleissheim, Germany (B. Grosche) and the Department of Medical Epidemiology, Karolinska Institutet, Stockholm, Sweden (P. Hall)

Correspondence to: Dominique Laurier, Institute for Protection and Nuclear Safety, IPSN, DPHD/SEGR/LEADS, B.P.6, FR-92265 Fontenay-aux-Roses, Cedex, France. Fax: +33 146 570 386. E-mail: dominique.laurier@ipsn.fr

Acta Oncologica Vol. 41, No. 1, pp. 14–24, 2002

The identification of a local excess of cancer cases, possibly associated with ionizing radiation, always receives substantial media coverage and communication about clusters is difficult. We reviewed studies that examined the risk of leukaemia among young people near nuclear installations. An excess of leukaemia exists near some nuclear installations, at least for the reprocessing plants at Sellafield and Dounreay and the nuclear power plant Krümmel. Nonetheless, the results of multi-site studies invalidate the hypothesis of an increased risk of leukaemia related to nuclear discharge. Up until now, analytic studies have not found an explanation for the leukaemia clusters observed near certain nuclear installations. The hypothesis of an infectious aetiology associated with population mixing has been proposed, but needs to be investigated further. The review illustrates two recent examples in France (La Hague reprocessing plant) and in Germany (Krümmel power plant), where controversies developed after reports of increased leukaemia risks. These examples show the importance of recalling the current epidemiological knowledge and of using systematic recording of cases to replace the alleged excesses in a more general framework. Some elements should also be suggested from the recent French and German experiences to reinforce credibility in the results.

Received 3 May 2001
Accepted 21 September 2001

In 1983, a local TV station announced a cluster of childhood leukaemia in Seascale, Great Britain, a few kilometres from Sellafield nuclear fuel reprocessing plant in West Cumbria. Even before that time, many scientists set out to analyse the risk of leukaemia near nuclear installations. Today, after nearly 18 years of accumulated results, the existence of an increased risk of leukaemia among young people living near a nuclear installation still remains highly controversial.

Childhood leukaemia, i.e. among people aged 0–14 years at diagnosis, is a rare disease, with incidence rates between 1.5 and 5.0 per 100000 per year (1). Nearly 80% of cases are acute leukaemia, for which the complete remission rate is almost 75% (2). The aetiology of childhood leukaemia is poorly understood but congenital malformations, such as Down's syndrome, are known to be associated with an elevated risk of leukaemia (3, 4). Epidemiological studies, in particular those dealing with the Hiroshima and Nagasaki survivors, have shown that leukaemia is induced by ionizing radiation, especially among young people. The risk in relation to time after exposure seems to have a wave-like appearance, starting 2–3 years after exposure, peaking after 7–8 years, and thereafter declining (5–7). Other causative factors have been suggested, such as exposure to pesticides (8) or to benzene (9, 10). An infectious aetiology has also been hypothesized (11–13).

For many years, the topic of a possible tendency of childhood leukaemia to be detected in clusters has been discussed (14), and the occurrence of a leukaemia cluster near the Sellafield site had an impact in two directions: clustering and radiation. This review is restricted to the problem of clustering near nuclear installations.

STUDIES OF LEUKAEMIA CLUSTERS

So-called 'cluster studies' are performed to estimate the frequency of leukaemia in a given geographical area, e.g. around nuclear installations, and eventually to test for an abnormally high aggregation of cases. The methodology of these cluster studies is generally very simple. It consists in dividing the study area into zones according to the distance to the nuclear installations. In each zone, the number of observed cases during a given period is compared with the number of expected cases during the same period. The expected cases are normally based on the calculation of person-years, which are multiplied by the national or regional incidence rates. The relative risk is generally estimated by the ratio of the observed number of cases divided by the expected number of cases.

Local studies

A large number of local cluster studies, focusing on one specific area, have been published since 1984, but the data are conflicting (15).

In England, three clusters have been identified between 1983 and 1987, and have been extensively discussed in the literature. The first cluster of leukaemia cases was reported near the Sellafield reprocessing plant, and relied on 5 cases observed between 1950 and 1983 in the village of Seascale (16). The persistence of an excess over time has been confirmed (17). The second cluster was reported in 1986 in Scotland, near the nuclear reprocessing plant of Dounreay (18). The persistence of this cluster has also been confirmed, although the relative risk has tended to decrease with time (19). The third cluster was observed in 1987 near the nuclear weapon plants of Aldermaston and Burghfield (20). The excess persisted when different periods and geographical limits were studied, but the risk was found to be lower (21). Other clusters have been suggested since then, but were not confirmed thereafter (22).

Neither incidence nor mortality studies conducted in California or around the sites at Rocky Flats (Colorado), Hanford (Washington State) or Oak Ridge (Tennessee) showed an excess of leukaemia cases (23–25). Between 1982 and 1984 an excess number of leukaemia cases was noted around the Pilgrim plant, Massachusetts (26), but was counterbalanced by a deficit of cases between 1985 and 1986 (27). The incidence of leukaemia among children (0–14 years of age, during 1975–1985) increased with reconstructed doses in the region of the Three Mile Island plant, Pennsylvania, but the study involved 4 cases and was not statistically significant (28, 29).

Other studies performed in Israel near the Dimona nuclear power plant (30) or in France near the Marcoule nuclear site (31) show no excess of childhood leukaemia.

Multi-site studies

Multi-site studies consider the risk of leukaemia around several nuclear installations simultaneously. The effort is to identify elevated rates rather than single localized excesses. The methodology is the same as that for cluster studies, but multi-site studies involve larger numbers of cases, making it possible to generalize the results.

Most of the multi-site studies were performed in England and Wales and the largest study, so far, included 4100 leukaemia cases among children aged 0–14 years around 29 nuclear installations in England and Wales (21, 32, 33). Other multi-sites studies were conducted in Scotland (19), the United States (34), Ontario, Canada (35), France (36, 37), Germany (38, 39), Japan (40), Sweden (41) and Spain (42). As can be seen in Table 1, with the exception of one study, the leukaemia rates near the

Table 1

Incidence and mortality of childhood leukaemia around nuclear installations: multi-site studies, in chronological order

Source	Study subject	Age, years	Sites	Study period	Result O/E;RR [1]
Baron 1984 (43)	Mortality	≤14	6, England and Wales	1963–1970	1.60
				1972–1979	1.42
Cook-Mozaffari et al. 1987 (110)	Mortality	≤24	All, England and Wales	1959–1980	1.15 [2]
Jablon et al. 1990 (111)	Mortality	≤9	All 62 commercial sites, USA	1950–1984	1.03
		10–19	All 62 commercial sites, USA	1950–1984	0.94
Clarke et al. 1991 (112)	Incidence	≤14	6, Ontario, Canada	1964–1986	1.06
Hill & Laplanche 1992 (36)	Mortality	≤24	6, France	1968–1987	0.86
Keller et al. 1992 (113)	Incidence	≤14	All, former West Germany	1980–1991	1.06
Möhner & Stabenow 1992 (114)	Incidence	≤14	3, former East Germany	1961–1988	1.26
Bithell et al. 1994 (21)	Incidence	≤14	All, England and Wales	1966–1987	0.99
Hattchouel et al. 1995 (37)	Mortality	≤24	13, France	1968–1989	0.80
Iwasaki et al. 1995 (40)	Mortality	≤24	All, Japan	1973–1987	1.06
Sharp et al. 1996 (19)	Incidence	≤14	7, Scotland	1968–1993	0.97
Kaletsch et al. 1997 (109)	Incidence	≤14	All, former West Germany	1991–1995	1.05
				1980–1995	1.00
			3, former East Germany	1991–1995	0.92
Lopez-Abente et al. 1999 (42)	Mortality	≤24	7, Spain	1975–1993	1.21

[1] O/E = Observed/Expected leukaemia cases; RR = Relative risk.
[2] $p\text{-value} < 0.05$.

Table 2

Incidence and mortality of childhood leukaemia around nuclear installations: multi-site studies, focusing on the youngest age category and closest proximity to the plant

Source	Study subject	Age, years	Site, distance from nuclear installation	Study period	Result O/E;RR [1]
Cook-Mozaffari et al. 1987 (110)	Mortality	≤9	All, England and Wales within 6 miles Operation started before 1955	1959–1980	3.95 [2]
Keller et al. 1992 (113)	Incidence	≤4	All, former West Germany within 5 km	1980–1991	3.01 [2]
			All, former West Germany within 5 km Operation started before 1970	1980–1991	7.09 [2]
Kaletsch et al. 1997 (109)	Incidence	≤4	All, former West Germany within 5 km	1991–1995	2.00
			All, former West Germany within 5 km Operation started before 1970	1991–1995	0.49
			All, former West Germany within 5 km	1980–1995	2.87 [2]
			3, former East Germany within 5 km	1991–1995	1.37 [2]

[1] O/E = observed/expected leukaemia cases, RR = relative risk.
[2] p-value < 0.05.

nuclear installations did not differ from what was expected (32).

However, an elevated risk was found in the youngest age groups at the closest distance to the nuclear facilities (Table 2). It is notable that some studies have observed the same mortality rates for leukaemia before and after start-up of the nuclear installations (43, 44).

Studies near non-nuclear installations

Studies were also conducted among populations living near 'potential' sites, i.e. sites envisaged for construction of a nuclear installation (21, 38, 45), or non-nuclear power plants (43). In these studies, the risk of childhood leukaemia around potential sites was similar to that observed around active nuclear installations (Table 3), and again elevated rates have been observed in the youngest age group at the closest vicinity of the 'plants' (Table 4).

Statistically significant excesses in leukaemia incidence among children have also been observed in areas where there were no nuclear installations and no specific source was suggested, for example in Cambuslang, Scotland (46), or in the village of Sittensen, Germany (47).

Studies of leukaemia spatial distribution

Numerous studies have dealt with the distribution of leukaemia cases over time and geographical areas, independently of the location of nuclear reactors (48–53). These studies generally take into account large areas and thus consider large numbers of cases with sophisticated spatial statistical methods. A recent international study (EuroClus) included more than 13000 cases of childhood leukaemia in Europe (54). In most of these studies the conclusion reached was that there is a tendency towards spatial clustering of childhood leukaemia cases but the reasons remain to be discovered.

Discussion

None of the studies mentioned rely on individual data, but are based on aggregated data, i.e. number of cases in a certain geographical area. They are therefore subject to important limitations. In particular, migration of subjects is not controlled, which means that this approach does not distinguish between a patient who has lived in the area since birth and a patient who has been resident for a few months. It has been shown that even using aggregated data

Table 3

Incidence and mortality of childhood leukaemia around potential nuclear installations, in chronological order

Source	Study subject	Age, years	Potential sites	Study period	Result O/E;RR [1]
Cook-Mozaffari et al. 1989 (45)	Mortality	≤24	England and Wales	1959–1980	1.14
Keller et al. 1992 (113)	Incidence	≤14	Former West Germany	1980–1991	1.42 [2]
Bithell et al. 1994 (21)	Incidence	≤14	England and Wales	1966–1987	1.02
Kaletsch et al. 1997 (109)	Incidence	≤14	Former West Germany	1991–1995	1.35
				1980–1995	1.05

[1] O/E = observed/expected leukaemia cases, RR = relative risk.
[2] p-value < 0.05.

Table 4

Incidence and mortality of childhood leukaemia around potential nuclear installations, focusing on the youngest age category and closest proximity to the site

Source	Study subject	Age, years	Potential site–radius	Study period	Result O/E;RR [1]
Keller et al. 1992 (113)	Incidence	≤4	Former West Germany within 5 km	1980–1991	4.16 [2]
Kaletsch et al. 1997 (109)	Incidence	≤4	Former West Germany within 5 km	1991–1995	1.52
				1980–1995	3.82 [2]

[1] O/E = observed/expected leukaemia cases, RR = relative risk.
[2] p-value < 0.05.

on migration has an influence on the regional distribution of childhood leukaemia (55). These types of studies do not take temporal pattern, i.e. time between a potential causal exposure and the occurrence of the disease, into account. They could therefore not be used for hypothesis testing and should be considered descriptive.

Local cluster studies consider small areas, with small numbers of observed cases. The results are therefore very sensitive to random fluctuations in the spatial and temporal distribution of observed cases and is highly dependent on time period and size of area under study (56).

The expected number of cases is difficult to calculate since the source population from which the cases were recruited is difficult to identify. This difficulty also introduces problems when trying to choose the actual incidence rates and to take into account the fluctuations in the background rates.

With the exception of the very low number of cases, the multi-site studies share the same limitations as those indicated for cluster studies (aggregated data, no control of migration, no information about potential exposures). For example, some authors noticed that the observation of an excess risk in the youngest age group at the closest vicinity to some sites could be due to a markedly low incidence in the control regions and these results need to be confirmed in future studies (32, 38).

It is important to differentiate between studies of anecdotally reported clusters and hypothesis-driven analyses. The former were performed specifically in response to an announcement of excess incidence (the Seascale cluster, for example). They therefore have as their goal the verification of the existence of this excess, and not the evaluation of the probability of rejecting the null hypothesis (no excess of cases near the sites studied). The latter, where some relate to single sites and (local studies) and others to a number of sites (multi-site studies), do allow the testing of a hypothesis (increased number of cases in certain areas).

All these limits bring the value of cluster studies into question (57, 58). In response, some authors and organizations have drafted recommendations and procedural guidelines for performing and interpreting cluster studies (59). A first suggestion is that monitoring around a site should be continued after any cluster is observed, to verify the persistence of the excess. A second suggestion is to adopt new methods to reduce some of the defects of these studies (60, 61).

The methods described above have also been used when studying the spatial distribution of cancers near non-nuclear installations, such as industrial facilities (62), radio transmitters (63), and power lines (64). The increased use of this type of analysis has even led to the establishment of the Small Area Health Statistics Unit in Great Britain (65).

Even so, it has to be pointed out that these descriptive (or ecological) studies can show nothing more than the simultaneous occurrence of two or more phenomena. Based on their results, it cannot be concluded that a nuclear installation has an influence on the observed risk (given the rates were elevated), nor can it be ruled out that the installation has no influence (given the rates were not elevated). For conclusions like these, it is necessary to conduct analytical studies.

HYPOTHESES TO EXPLAIN LEUKAEMIA CLUSTERS

Since 1984, studies have been launched to search for factors that might explain the observed excess in incidences of leukaemia. These analytic studies are mainly case-control studies, but radioecological studies and geographical studies have also been conducted to bring some insight into specific hypotheses. Essentially, three hypotheses have been explored: environmental exposure to ionizing radiation, paternal pre-conception exposure and infectious agents.

Environmental exposure to ionizing radiation

Prompted by the reports from Seascale and Dounreay, radioecological studies have been performed, mainly in Great Britain (66–68). A thorough dose reconstruction was carried out in 1995 for individuals less than 25 years of age who lived in the village of Seascale (17, 69). All routes of contamination as well as possible sources of exposure were taken into account. The estimated bone marrow doses were attributable to 80% from natural radioactivity, 5% from medical exposure, 6% from other sources such as Chernobyl and weapons fallout and roughly 9% from releases from the Sellafield plant (routine discharges and accidental releases).

The calculated numbers of cases attributable to radiation exposure were 0.46 and 0.04 for all sources of exposure and for releases from the Sellafield plant, respectively (compared with the 12 cases actually recorded in Seascale between 1955 and 1992) (17). Comparable analyses were done for the population of young people living in Thurso, near the Dounreay reprocessing plant. The contributions of various sources of radiation exposure to the risk of radiation-induced leukaemia before age 25 were as follows: natural sources 79%, Sellafield discharges 0.3%, Dounreay discharges 1.2%, weapons fallout 12%, medical exposure 7.5% (67, 70).

It should be stressed that these radioecological studies are risk assessment processes. The dose estimations are reliant on several assumptions with uncertainties that are difficult to quantify. Furthermore, the applicability of risk models to such low levels of chronic exposure is challenged. Nevertheless, the results appear coherent and the available information indicates that the hypothesis of a causal role of environmental exposure to radioactivity cannot explain leukaemia clusters among young people near nuclear installations (21, 71).

Several case-control studies have examined factors that might lead to increased radiation exposure or contamination (72–75). Among the large number of factors studied, a few, such as recreational use of beaches (73, 75) and consumption of local fish and seafood (75), were found significantly to increase the risk of leukaemia. However, these factors could only be considered vaguely linked to environmental exposure to radioisotopes or to other toxic substances. Any conclusion that a causal relation exists between the risk of leukaemia and environmental contamination calls for considerable caution, since radiation doses ascribed to these activities have not been measured.

Paternal pre-conception exposure

In 1990, Gardner et al. (72) proposed the hypothesis of a genetically transmitted disease to explain the Seascale cluster. In this case-control study it was observed that the risk of leukaemia among children of fathers having cumulated a gonadal dose above 100 mSv before conception was eight times higher than among other children. Several attempts have been made to verify the existence of such a relation, but the overall results invalidate the hypothesis (76, 77).

Infectious agent

The hypothesis of an infectious aetiology of childhood leukaemia was proposed a long time ago (13). Viral transmission favoured by high rates of population mixing has also been suggested to explain the occurrence of clusters of childhood leukaemia cases near some nuclear installations (78). An alternative hypothesis supposes that acute lymphoid leukaemia might be a rare response to common infection among subjects with immature immune systems (79). A tendency for leukaemia cases to cluster in time and space (53, 80, 81) or a suggested seasonality in the occurrence of leukaemia indirectly supports this hypothesis (82).

An increased leukaemia incidence among children younger than 15 years of age associated with the construction of industrial sites in rural regions of Great Britain have been seen as an explanation to the leukaemia clusters observed near the Sellafield and Dounreay reprocessing plants (83, 84). A study performed in Cumbria, UK, confirmed an association between population mixing and the risk of leukaemia before the age of 15, on the basis of both geographical and individual data (85). The model derived by the author predicted more than half of the number of leukaemia cases actually recorded in the village of Seascale during the same period. These new results led Sir Richard Doll to state that '…time may now have come when Kinlen's hypothesis of population mixing as a cause of childhood lymphatic leukaemia can be regarded as established' (86).

Discussion

The studies performed to investigate possible explanations to the observed clusters of leukaemia cases around nuclear installations have important potential limitations. One main limitation of studies conducted locally is their small size, which dramatically limits the interpretation of the results. Most of the case-controls studies were based on low numbers of subjects. Since parents to cases and controls could remember past behaviour and consumption habits differently, there is a problem of recall bias. This problem was solved in a few studies by including tumour controls.

Most studies supporting the infectious hypothesis were geographical studies and associated with well-documented biases. To date, however, no laboratory experimental support has appeared and the underlying agent or mechanism still remains unidentified. But some results, e.g. elevated leukaemia risk with less vaccination in childhood or later or no kindergarten attendance, seem to point in the same direction.

Up until now, analytical studies have found neither the explanation for the leukaemia clusters observed near certain nuclear installations, nor the explanation for the elevated numbers observed among very young children around numerous sites. The understanding of the causes of leukaemia clusters should rely more on large-scale studies, such as the case-control studies being launched in the US, the UK and in Germany (87–89).

THE CLUSTER OF LEUKAEMIA CASES IN NORD-COTENTIN, FRANCE

In an attempt to describe the problems involved in estimating the likelihood of childhood leukaemia being associated with radioactive releases from nuclear installations, two examples are given.

Table 5

Descriptive studies of leukaemia frequency among young people living near the La Hague reprocessing plant, Nord-Cotentin, France, in chronological order

Source	Study subject	Age, years	Study period	Radius, km	Histological type	Observed cases	Expected cases	Obs./Exp.	95% CI
Dousset 1989 (90)	Mortality	≤24	1970–1982	10	Leukaemia	0	0.4	0.0	0.0–8.9
Viel & Richardson 1990 (91)	Mortality	≤24	1968–1986	35	Leukaemia	21	23.6	0.9	0.6–1.4
				10		1	1.1	0.9	0.0–4.9
Hill & Laplanche 1992 (36)	Mortality	≤24	1968–1987	21	Leukaemia	12	14.9	0.8	0.4–1.4
				10		1	0.8	1.2	0.0–7.0
Viel et al. 1993 (115)	Incidence	≤24	1978–1990	35	Leukaemia	23	19.6	1.2	0.7–1.8
				10		3	1.2	2.5	0.5–7.3
Hattchouel et al. 1995 (37)	Mortality	≤24	1968–1989	16	Leukaemia	2	5.4	0.4	0.1–7.3
Viel et al. 1995 (92)	Incidence	≤24	1978–1992	35	Leukaemia	25	22.8	1.1	0.7–1.6
				10		4	1.4	2.8	0.8–7.3
Guizard et al. 1997 (98)	Incidence	≤24	1993–1996	35	Leukaemia	8	7.1	1.1	0.5–2.2
				10		0	0.7	0.0	0.0–5.5
Guizard et al. 2001 (116)	Incidence	≤24	1978–1998	10	Leukaemia	5	2.3	2.2	0.7–5.7
		1–6		10	ALL	4	1.0	4.2	1.1–10.7

Abbreviations: CI = confidence interval; ALL = acute lymphoblastic leukaemia.

Nord-Cotentin is a region in the north-west of France, where four nuclear facilities are located, including the La Hague nuclear fuel reprocessing plant.

Several descriptive studies conducted between 1989 and 1995 did not show any excess risk of leukaemia near the reprocessing plant (36, 37, 90, 91) (Table 5). In 1995, a new cluster study observed an elevated incidence of leukaemia in the 10-km zone (92). Based on four cases, the risk almost reached borderline significance (Table 5).

In 1997, the results of a case-control study of leukaemia risk factors including 27 cases of leukaemia and 192 controls in Nord-Cotentin showed several factors to be associated with the risk of leukaemia (75). Among those factors was the recreational use of local beaches by the children ($p < 0.01$) and/or by their mothers during pregnancy ($p < 0.01$) and an increased consumption of local fish and shellfish ($p < 0.01$). The authors concluded that they had found '… some convincing evidence in childhood leukaemia of a causal role for environmental radiation exposure from recreational activity on beaches'. The study was criticized because of the limitations of such as small sample size, potential bias, and the discrepancy between the actual results and the conclusions drawn by the authors (93–95). A controversy developed, echoed by large media coverage on a regional and national scale.

The French Ministries of Environment and Health decided to commission 'a new epidemiological study in the Nord-Cotentin region', but the Committee disintegrated in July 1997 because of internal conflicts (96). As a consequence, the French government initiated two new missions.

The first mission was to analyse the epidemiological evidence in more detail, and to make proposals regarding the surveillance of adverse effects of exposure to ionizing radiation in France (97). The first task was to extend the monitoring of leukaemia incidence among young people in Nord-Cotentin. Based on the newly created local registry, no new case of childhood leukaemia was reported between 1993 and 1996 within the 10-km zone around the La Hague reprocessing plant (98) (Table 5). The authors concluded that there was no significant increase of leukaemia incidence among young people in the Nord-Cotentin (97). Very recently, a new study was published, with a follow-up extended to 1998. The authors still observed a borderline elevated incidence in the 10-km zone around the plant, due mainly to cases of acute lymphoblastic leukaemia in the age range 1–6 years old (Table 5).

The purpose of the second mission, conducted by the Nord-Cotentin Radioecology Group (GRNC), was to estimate doses from ionizing radiation and deduce the associated risk of leukaemia. GRNC brought together more than 50 experts from diverse organizations and a critical review of discharges from nuclear facilities and environmental radioactivity measurements was conducted. The exposure reconstruction was as complete and realistic as possible, considering all sources of radiation for all possible exposure pathways. The contributions to the risk of radiation-induced leukaemia before the age of 25 were estimated as follows: natural sources 74.1%, weapons fall-out and the Chernobyl accident 1.4%, medical exposure 24.3%, and releases from the local nuclear installations

0.2% (99). The final report concluded that the exposure attributable to local nuclear facilities was unlikely to be involved to any salient degree in the elevated incidence of leukaemia observed among young people near the La Hague reprocessing plant, and could not explain the associations observed in the case-control study (100–102). All members of GRNC agreed on the methodology, but several participants expressed reservations about the interpretation of the results, mainly because the uncertainties concerning the measurements had not been evaluated. The operating rules of GRNC including members of non-governmental organizations, unrestricted diffusion of documents outside the group, and free interpretation of the results by all members increased the public confidence in the results.

Discussion

The existence of an excess of leukaemia cases among young people in the vicinity of the La Hague reprocessing plant associated with ionizing radiation has not been confirmed. The radioecological study showed that the low doses received by the local population as a result of releases from local nuclear installations could not account for the elevated incidence of leukaemia. One important element of the report was to put these results in perspective with current epidemiological knowledge. The inclusion of experts from environmental organizations in GRNC has been an important element in the credibility of the final results.

Several investigations are ongoing in Nord-Cotentin. The leukaemia incidence follow-up is now performed prospectively by the cancer registry of La Manche. A study has been launched to evaluate the hypothesis of a link between population mixing and the risk of leukaemia. The French government has commissioned GRNC to continue the work. The goal is to quantify the uncertainty associated with the results of the radioecological study, to assess the impact of chemical discharges from nuclear installations in the environment and on the health status of the residents in Nord-Cotentin.

THE CLUSTER OF LEUKAEMIA CASES IN ELBMARSCH, GERMANY

The Krümmel power plant, located in the Bundesland Schleswig-Holstein, is a boiling water reactor of unique design with a relatively high amount of airborne tritium releases. Next to the power plant is the nuclear research facility GKSS situated.

Between December 1989 and May 1991, seven cases of haematological disorders occurred in individuals under 25 years of age at diagnosis in the community of Elbmarsch, located on the banks of the Elbe River opposite the plant (Bundesland Lower Saxony). Owing to the fact that the increase occurred six years after the start-up of the plant, radioactive discharges were suspected to have a causative association with the disorders. One case of aplastic anaemia, 1 case of second primary malignancy (in a young man previously treated with chemotherapy), and 5 cases of childhood leukaemia were identified. These 5 cases occurred between 1990 and 1991 in Elbmarsch, while 0.12 cases were expected based on the national rates, which resulted in a 41.5-fold increase. From 1990 to 1996, nine cases of childhood leukaemia were observed within a 10-km radius of the plant, based on data from the German Childhood Cancer Registry. The number of children living within this area was approximately 9000, giving 2.77 expected cases and an approximately 3.25-fold significant increased risk (103–105). The most important studies are listed in Table 6.

At the time of the occurrence of the Krümmel cluster, the Ministry of Social Affairs of Lower Saxony established a committee to investigate another cluster in Sittensen. This cluster of childhood leukaemia occurred prior to the Elbmarsch cluster and was not thought to be related to ionizing radiation released from a nuclear power plant. A case-control study was initiated to investigate possible risk factors for childhood leukaemia (106). In 1991, the Sittensen committee started to investigate the Krümmel cluster as well. Additional intensive interviewing of the parents was done. In 1991, another committee was established by the Schleswig-Holstein government and an inter-governmental working group was set up. A group of non-governmental activists joined the various meetings of the committees. Later, a joint working group, named 'Exposure Indicators', was established by the governments in Schleswig-Holstein and Lower Saxony and entitled to search for those indicators, in various directions.

A large number of possible environmental materials, which could contain carcinogenic substances, were analysed (105). Blood samples were drawn from supposedly exposed individuals and an early study indicated an elevated number of chromosomal aberrations in the Elbmarsch population (103). Subsequent and larger studies revealed no indication of an elevated rate of dicentric aberrations, either in children (107) or in women (unpublished data).

Discussion

To date, there is no plausible explanation for the German clusters. No agent under study has been shown to have a relationship with childhood leukaemia. However, the discussion on a causal relationship between radioactive discharges and haematological disorders lingers on. The possible pathways and involved radionuclides under discussion vary over time.

The Bundeslaender Schleswig-Holstein and Niedersachsen have supported a case-control study on adult

Table 6

Studies of leukaemia frequency among the population living near the Krümmel nuclear power plant, Germany, in chronological order

Source	Study subject	Age, years	Study period	Radius, km	Histological type	Observed cases	Expected cases	Obs./ Exp.	95% CI
Dieckmann 1992 (117)	Incidence	≤24	1990–1991	1 community	Blood disorders	7	<1		
Schmitz-Feuerhake et al. 1993 (103)	CA								
Hoffmann & Greiser 1993 (108)	Incidence	All	1984–1993	5	Leukaemia, all	58	47.1	1.2	p = 0.14 *
		All, male				36	24.3	1.5	p = 0.02 *
		All, female				22	22.8	1.0	p = 0.94 *
		All			CML	12	6.3	1.8	p = 0.06 *
		All, male				8	3.5	2.4	p = 0.02 *
		All, female				3	2.8	1.1	p = 0.92 *
Schmitz-Feuerhake et al. 1997 (118)	CA								
Hoffmann et al. 1997 (104)	Incidence	≤14	1990–1995	5	Leukaemia	6	1.3	4.6	2.1–10.3
			1990–1991	5		5	0.4	11.8	4.9–28.3
Grosche et al. 1999 (105)	Incidence	≤14	1990–1991	1 community	Leukaemia	5	0.1	41.5	15–92
			1990–1996	10		9	2.8	3.3	1.6–6.0
Bruske-Hohlfeld et al. 2001 (107)	CA	≤14							

Abbreviations: CI = confidence interval; CA = chromosomal aberrations; CML = chronic myeloid leukaemia.
* No CI given, only p-values.

leukaemia. The results of this study are expected around the middle of 2001. The study is based on a report that there might not only be an elevated number of childhood leukaemia cases, but also of adult leukaemia (108).

CONCLUSIONS

Since 1984, a large number of cluster studies to evaluate the risk of childhood leukaemia have been conducted near nuclear installations. These studies have generally been small, including only a few cases, and most of them show no excess of leukaemia among the young people living in the vicinity of these installations. An excess incidence of leukaemia exists near some nuclear installations, at least for the reprocessing plants at Sellafield and Dounreay and the nuclear power plant at Krümmel. Nonetheless, excesses of leukaemia have also been identified far away from any nuclear installations, and the results of the multi-site studies invalidate the hypothesis of an increased risk of leukaemia related to radioactive discharge.

Some investigators in England and Germany observed an elevated risk among the youngest children living near nuclear plants or potential nuclear plants. These findings are intriguing and still seek an explanation (88, 109). The hypothesis of an infectious aetiology associated with population mixing needs to be investigated further.

The identification of a local excess of cancer cases, possibly associated with ionizing radiation, always receives substantial media coverage, and communication about clusters is difficult. To communicate cancer risks associated with ionizing radiation is complicated since the risk perception of the general public is hampered by an opinion that ionizing radiation causes immediate and harmful effects regardless of dose. Few individuals realize that the excess mortality from solid cancers among A-bomb survivors in Hiroshima and Nagasaki is 400–500 cases. Recent examples show the importance of recalling the current epidemiological knowledge and of using systematic recording of cases to replace the alleged excesses in a more general framework. Some elements should also be suggested from the recent French and German experiences in order to reinforce credibility in the results. In particular, a plural composition for commissions, including operators, governmental and non-governmental experts, should be proposed to facilitate direct communication with the general population.

REFERENCES

1. Parkin DM, Kramarova E, Draper GJ, et al. International incidence of childhood cancer, IARC scientific publication no. 144, vol. II. Lyon: International Agency for Research on Cancer, 1998.
2. Liesner RJ, Goldstone AH. ABC of clinical haematology: the acute leukaemias. Br Med J 1997; 314: 733–6.
3. Robison LL. Down syndrome and leukemia. Leukemia 1992; 6: 5–7.

4. Ross JA, Davies SM, Potter JD, Robison LL. Epidemiology of childhood leukemia, with a focus on infants. Epidemiol Rev 1994; 16: 243–72.
5. United Nations Scientific Committee on the Effects of Atomic Radiation. Sources and effects of ionizing radiation. UNSCEAR 2000. Report to the General Assembly, with scientific annexes. New York: United Nations, 2000.
6. United Nations Scientific Committee on the Effects of Atomic Radiation. Sources and effects of ionizing radiation. UNSCEAR 1994 Report to the General Assembly, with scientific annexes. New York: United Nations, 1994.
7. Doll R, Wakeford R. Risk of childhood cancer from fetal irradiation. Br J Radiol 1997; 70: 130–9.
8. Meinert R, Schuz J, Kaletsch U, Kaatsch P, Michaelis J. Leukemia and non-Hodgkin's lymphoma in childhood and exposure to pesticides: results of a register-based case-control study in Germany. Am J Epidemiol 2000; 151: 639–46.
9. Finkelstein MM. Leukemia after exposure to benzene: temporal trends and implications for standards. Am J Ind Med 2000; 38: 1–7.
10. Pearson RL, Wachtel H, Ebi KL. Distance-weighted traffic density in proximity to a home is a risk factor for leukemia and other childhood cancers. J Air Waste Manag Assoc 2000; 50: 175–80.
11. Greaves MF. Speculations on the cause of childhood acute lymphoblastic leukemia. Leukemia 1988; 2: 120–5.
12. Kinlen L. Leukaemia. In: Doll R, Muir CS, Fraumeni JF, eds. Trends in cancer incidence and mortality. Plainview, NY: Cold Spring Harbor Laboratory Press, 1994: 475–91.
13. Mueller N. Overview: viral agents and cancer. Environ Health Perspect 1995; 103: 259–61.
14. Heath CW Jr. Epidemiologic implications of feline leukemia virus. Review. J Am Vet Med Assoc 1971; 158 (Suppl 2): 1119 + .
15. Laurier D, Bard D. Epidemiologic studies of leukemia among persons under 25 years of age living near nuclear sites. Epidemiol Rev 1999; 21: 188–206.
16. Black D. Investigation of the possible increased incidences of cancer in West Cumbria. London: HMSO, 1984.
17. Committee on Medical Aspects of Radiation in the Environment. The incidence of cancer and leukaemia in young people in the vicinity of the Sellafield site, West Cumbria: Further studies and an update of the situation since the publication of the report of the Black Advisory Group in 1984. London, UK: Department of Health, 1996.
18. Heasman MA, Kemp IW, Urquhart JD, Black R. Childhood leukaemia in northern Scotland. Lancet 1986; 1: 266.
19. Sharp L, Black RJ, Harkness EF, McKinney PA. Incidence of childhood leukaemia and non-Hodgkin's lymphoma in the vicinity of nuclear sites in Scotland, 1968–93. Occup Environ Med 1996; 53: 823–31.
20. Roman E, Beral V, Carpenter L, et al. Childhood leukaemia in the West Berkshire and Basingstoke and North Hampshire District Health Authorities in relation to nuclear establishments in the vicinity. Br Med J 1987; 294: 597–602.
21. Bithell JF, Dutton SJ, Draper GJ, Neary NM. Distribution of childhood leukaemias and non-Hodgkin's lymphomas near nuclear installations in England and Wales. Br Med J 1994; 309: 501–5.
22. Ewings PD, Bowie C, Phillips MJ, Johnson SA. Incidence of leukaemia in young people in the vicinity of Hinkley Point nuclear power station, 1959–86. Br Med J 1989; 299: 289–93.
23. Enstrom JE. Cancer near a California nuclear power plant. Letter. Lancet 1985; 2: 1249.
24. Crump KS, Ng TH, Cuddihy RG. Cancer incidence patterns in the Denver metropolitan area in relation to the Rocky Flats plant. Am J Epidemiol 1987; 126: 127–35.
25. Goldsmith JR. Childhood leukaemia mortality before 1970 among populations near two US nuclear installations. Lancet 1989; 1: 793.
26. Clapp RW, Cobb S, Chan, Walker B Jr. Leukaemia near Massachusetts nuclear power plant. Lancet 1987; 2: 1324–5.
27. Poole C, Rothman KJ, Dreyer NA. Leukaemia near Pilgrim nuclear power plant, Massachusetts. Lancet 1988; 2: 1308.
28. Hatch MC, Beyea J, Nieves JW, Susser M. Cancer near the Three Mile Island nuclear plant: radiation emissions. Am J Epidemiol 1990; 132: 397–412.
29. Wing S, Richardson D, Armstrong D, Crawford-Brown D. A re-evaluation of cancer incidence near the Three Mile Island nuclear plant: the collision of evidence and assumptions. Environ Health Perspect 1997; 105: 52–7.
30. Sofer T, Goldsmith JR, Nusselder I, Katz L. Geographical and temporal trends of childhood leukemia in relation to the nuclear plant in the Negev, Israel, 1960–1985. Public Health Rev 1991; 19: 191–8.
31. Bouges S, Daures J, Hebrard M. Incidence des leucémies aiguës, lymphomes et cancers thyroïdiens chez les enfants de moins de 15 ans vivant autour du site nucléaire de Marcoule de 1985 à 1995. Rev Epidémiol Santé Publ 1999; 47: 205–17.
32. Cook-Mozaffari PJ, Darby SC, Doll R, et al. Geographical variation in mortality from leukaemia and other cancers in England and Wales in relation to proximity to nuclear installations, 1969–78. Br J Cancer 1989; 59: 476–85.
33. Goldsmith JR. Nuclear installations and childhood cancer in the UK: mortality and incidence for 0–9-year-old children, 1971–1980. Sci Total Environ 1992; 127: 13–35.
34. Jablon S, Hrubec Z, Boice JD Jr. Cancer in populations living near nuclear facilities. A survey of mortality nationwide and incidence in two states. JAMA 1991; 265: 1403–8.
35. McLaughlin JR, Clarke EA, Nishri ED, Anderson TW. Childhood leukemia in the vicinity of Canadian nuclear facilities. Cancer Causes Control 1993; 4: 51–8.
36. Hill C, Laplanche A. Mortalité par cancer autour d'installations nucléaires françaises entre 0 et 24 ans. France, Paris: INSERM/Douin, 1992.
37. Hattchouel JM, Laplanche A, Hill C. Leukaemia mortality around French nuclear sites. Br J Cancer 1995; 71: 651–3.
38. Michaelis J, Keller B, Haaf G, Kaatsch P. Incidence of childhood malignancies in the vicinity of west German nuclear power plants. Cancer Causes Control 1992; 3: 255–63.
39. Michaelis J. Recent epidemiological studies on ionizing radiation and childhood cancer in Germany. Int J Radiat Biol 1998; 73: 377–81.
40. Iwasaki T, Nishizawa K, Murata M. Leukaemia and lymphoma mortality in the vicinity of nuclear power stations in Japan, 1973–1987. J Radiol Protect 1995; 15: 271–88.
41. Waller LA, Turnbull BW, Gustafsson G, Hjalmars U, Andersson B. Detection and assessment of clusters of disease: an application to nuclear power plant facilities and childhood leukaemia in Sweden. Stat Med 1995; 14: 3–16.
42. Lopez-Abente G, Aragones N, Pollan M, Ruiz M, Gandarillas A. Leukemia, lymphomas, and myeloma mortality in the vicinity of nuclear power plants and nuclear fuel facilities in Spain. Cancer Epidemiol Biomarkers Prev 1999; 8: 925–34.
43. Baron JA. Cancer mortality in small areas around nuclear facilities in England and Wales. Br J Cancer 1984; 50: 815–24.
44. Jablon S, Hrubec Z, Boice JD, Jr, Stone BJ. Cancer in populations living near nuclear facilities. Vol 2—individual facilities: cancer before and after start-up. Washington: National Cancer Institute, 1990.

45. Cook-Mozaffari P, Darby S, Doll R. Cancer near potential sites of nuclear installations. Lancet 1989; 2: 1145–7.
46. Hole DJ, Lamont DW, Brogan RT, Gibson BE, Gray MM, Gillis CR. Concurrent childhood and adult excesses of leukaemia in geographical areas. Lancet 1994; 343: 1439–40.
47. Grosche B. Leucémies infantiles dans le voisinage des centrales nucléaires en Allemagne. Symposium sur les agrégats de leucémie. Ottawa, Canada: Atomic Energy Control Board, 1992.
48. Ederer F, Myers MH, Mantel N. A statistical problem in space and time: do leukemia cases come in clusters? Biometrics 1964; 20: 626–38.
49. Openshaw S, Craft AW, Charlton M, Birch JM. Investigation of leukaemia clusters by use of a geographical analysis machine. Lancet 1988; 1: 272–3.
50. Draper GJ. The geographical epidemiology of childhood leukaemia and non-Hodgkin lymphomas in Great Britain 1966–83. Studies on medical and population subjects N° 53 OPCS. London: HMSO, 1991.
51. Knox EG, Gilman E. Leukaemia clusters in Great Britain. 2. Geographical concentrations. J Epidemiol Community Health 1992; 46: 573–6.
52. Westermeier T, Michaelis J. Applicability of the Poisson distribution to model the data of the German Children's Cancer Registry. Radiat Environ Biophys 1995; 34: 7–11.
53. Petridou E, Revinthi K, Alexander FE, et al. Space-time clustering of childhood leukaemia in Greece: evidence supporting a viral aetiology. Br J Cancer 1996; 73: 1278–83.
54. Alexander FE, Boyle P, Carli PM, et al. Spatial clustering of childhood leukaemia: summary results from the EUROCLUS project. Br J Cancer 1998; 77: 818–24.
55. Grosche B, Hinz G, Tsavachidis C. Leukemia morbidity and mortality in Bavaria. In: Health effects of low dose ionizing radiation—recent advances and their implications. Proceedings. London: BNES, 1988: 139–44.
56. Valenty M, Laurier D. Distribution géographique de la mortalité par leucémie chez les 0-24 ans en France. Rev Epidémiol Santé Publ 1997; 45: 527–30.
57. Wartenberg D. Should we boost or bust cluster investigations? Epidemiology 1995; 6: 575–6.
58. Urquhart JD. Studies of disease clustering: problems of interpretation. In: Elliot P, Cuzick J, English D, Stern R, eds. Geographical and environmental epidemiology: methods for small-area studies. Oxford: Oxford University Press, 1996: 278–85.
59. Center for Disease Control. Guidelines for investigating clusters of health events. MMWR 1990; 39: 1–23.
60. Elliott P, Cuzick J, English D, Stern R. Geographical and environmental epidemiology: methods for small-area studies. Oxford, UK: Oxford University Press, 1996.
61. Richardson S. Current developments in biostatistics. Rev Epidémiol Santé Publ 1996; 44: 482–93.
62. Wilkinson P, Thakrar B, Walls P, et al. Lymphohaematopoietic malignancy around all industrial complexes that include major oil refineries in Great Britain. Occup Environ Med 1999; 56: 577–80.
63. Dolk H, Elliott P, Shaddick G, Walls P, Thakrar B. Cancer incidence near radio and television transmitters in Great Britain. II. All high power transmitters. Am J Epidemiol 1997; 145: 10–7.
64. Feychting M, Ahlbom A. Magnetic fields and cancer in children residing near Swedish high-voltage power lines. Am J Epidemiol 1993; 138: 467–81.
65. Elliott P, Westlake AJ, Hills M, et al. The Small Area Health Statistics Unit: a national facility for investigating health around point sources of environmental pollution in the United Kingdom. J Epidemiol Community Health 1992; 46: 345–9.
66. Stather JW, Wrixon AD, Simmonds JR. The risks of leukemia and other cancers in Seascale from radiation exposure. National Radiological Protection Board, NRPB-R177. London: HMSO, 1984.
67. Dionan J, Muirhead CR, Wan SL, Wrixon AD. The risks of leukemia and other cancers in Thurso from radiation exposure. National Radiological Protection Board, NRPB-R196. London: HMSO, 1986.
68. Dionan J, Wan SL, Wrixon AD. Radiation doses to members of the public around AWRE, Aldermaston, ROF, Burghfield and AERE, Harwell. National Radiological Protection Board, NRPB-R202. London: HMSO, 1987.
69. Simmonds JR, Robinson CA, Philipps AW, Muirhead CR, Fry F. Risks of leukemia and other cancers in Seascale from all sources of ionising radiation exposure. National Radiological Protection Board, NRPB-R276. Chilton, UK: HMSO, 1995.
70. Committee on Medical Aspects of Radiation in the Environment. Investigation of the possible increased incidence of childhood cancer in young persons near the Dounreay nuclear establishment, Caithness, Scotland. United Kingdom, London: HMSO, 1988.
71. Doll R. Epidemiological evidence of effects of small doses of ionising radiation with a note on the causation of clusters of childhood leukaemia. J Radiol Protect 1993; 13: 233–41.
72. Gardner MJ, Snee MP, Hall AJ, Powell CA, Downes S, Terrell JD. Results of a case-control study of leukaemia and lymphoma among young people near Sellafield nuclear plant in West Cumbria. Br Med J 1990; 300: 423–9.
73. Urquhart JD, Black RJ, Muirhead MJ, et al. Case-control study of leukaemia and non-Hodgkin's lymphoma in children in Caithness near the Dounreay nuclear installation. Br Med J 1991; 302: 687–92.
74. Roman E, Watson A, Beral V, et al. Case-control study of leukaemia and non-Hodgkin's lymphoma among children aged 0–4 years living in west Berkshire and north Hampshire health districts. Br Med J 1993; 306: 615–21.
75. Pobel D, Viel JF. Case-control study of leukaemia among young people near La Hague nuclear reprocessing plant: the environmental hypothesis revisited. Br Med J 1997; 314: 101–6.
76. Doll R, Evans HJ, Darby SC. Paternal exposure not to blame. Nature 1994; 367: 678–80.
77. Little MP, Charles MW, Wakeford R. A review of the risks of leukemia in relation to parental pre-conception exposure to radiation. Health Phys 1995; 68: 299–310.
78. Kinlen LJ. Epidemiological evidence for an infective basis in childhood leukaemia. Br J Cancer 1995; 71: 1–5.
79. Greaves MF. Aetiology of acute leukaemia. Lancet 1997; 349: 344–9.
80. Alexander FE, Boyle P, Carli PM, et al. Spatial temporal patterns in childhood leukaemia: further evidence for an infectious origin. EUROCLUS project. Br J Cancer 1998; 77: 812–7.
81. Birch JM, Alexander FE, Blair V, Eden OB, Taylor GM, McNally RJ. Space-time clustering patterns in childhood leukaemia support a role for infection. Br J Cancer 2000; 82: 1571–6.
82. Gilman EA, Sorahan T, Lancashire RJ, Lawrence GM, Cheng KK. Seasonality in the presentation of acute lymphoid leukaemia. Br J Cancer 1998; 77: 677–8.
83. Kinlen LJ, O'Brien F, Clarke K, Balkwill A, Matthews F. Rural population mixing and childhood leukaemia: effects of the North Sea oil industry in Scotland, including the area near Dounreay nuclear site. Br Med J 1993; 306: 743–8.

84. Kinlen LJ, Dickson M, Stiller CA. Childhood leukaemia and non-Hodgkin's lymphoma near large rural construction sites, with a comparison with Sellafield nuclear site. Br Med J 1995; 310: 763–8.
85. Dickinson HO, Parker L. Quantifying the effect of population mixing on childhood leukaemia risk: the Seascale cluster. Br J Cancer 1999; 81: 144–51.
86. Doll R. The Seascale cluster: a probable explanation. Br J Cancer 1999; 81: 3–5.
87. Robison LL, Buckley JD, Bunin G. Assessment of environmental and genetic factors in the etiology of childhood cancers: the Children's Cancer Group epidemiology program. Environ Health Perspect 1995; 103: 111–6.
88. Meinert R, Kaletsch U, Kaatsch P, Schuz J, Michaelis J. Associations between childhood cancer and ionizing radiation: results of a population-based case-control study in Germany. Cancer Epidemiol Biomarkers Prev 1999; 8: 793–9.
89. UK Childhood Cancer Study Investigators. The United Kingdom Childhood Cancer Study: objectives, materials and methods. Br J Cancer 2000; 82: 1073–102.
90. Dousset M. Cancer mortality around La Hague nuclear facilities. Health Phys 1989; 56: 875–84.
91. Viel JF, Richardson ST. Childhood leukaemia around the La Hague nuclear waste reprocessing plant. Br Med J 1990; 300: 580–1.
92. Viel JF, Pobel D, Carre A. Incidence of leukaemia in young people around the La Hague nuclear waste reprocessing plant: a sensitivity analysis. Stat Med 1995; 14: 2459–72.
93. Clavel J, Hemon D. Leukaemia near La Hague nuclear plant. Bias could have been introduced into study. Br Med J 1997; 314: 1553.
94. Law G, Roman E. Leukaemia near La Hague nuclear plant. Study design is questionable. Br Med J 1997; 314: 1553.
95. Wakeford R. Leukaemia near La Hague nuclear plant. Scientific context is needed. Br Med J 1997; 314: 1553–4.
96. Comité scientifique pour une nouvelle étude épidémiologique dans le Nord Cotentin. Rapport final du Comité scientifique: volets épidémiologique et radioécologique. Paris: 1997.
97. Spira A, Boutou O. Rayonnements ionisants et santé: mesure des expositions à la radioactivité et surveillance des effets sur la santé. Collection des rapports officiels. Rapport aux Ministres de l'Environnement et de la Santé. Paris: La Documentation Française, 1999.
98. Guizard AV, Spira A, Troussard X, Collignon A. Incidence des leucémies de 0 à 24 ans dans le Nord Cotentin. Rev Epidémiol Santé Publ 1997; 45: 530–5.
99. Nord-Cotentin Radioecology Group. Estimation of exposure levels to ionizing radiation and associated risks of leukemia for populations in the Nord-Cotentin: Synthesis. Fontenay-aux-Roses: Institut de Protection et de Sûreté Nucléaire, 2000.
100. Groupe Radioécologie Nord-Cotentin. Estimation des doses et des risques de leucémies associés. Volume 4. Fontenay-aux-Roses: Institut de Protection et de Sûreté Nucléaire, 1999.
101. Laurier D, Rommens C, Drombry-Ringeard C, Merle-Szeremeta A, Degrange JP. Evaluation du risque de leucémie radio-induite à proximité d'installations nucléaires: l'étude radio-écologique Nord-Cotentin. Rev Epidémiol Santé Publ 2000; 48: 2S24–36.
102. Rommens C, Laurier D, Sugier A. Methodology and results of the Nord-Cotentin radioecological study. J Radiat Protect 2000; 20: 361–80.
103. Schmitz-Feuerhake I, Schroder H, Dannheim B, et al. Leukaemia near water nuclear reactor. Lancet 1993; 342: 1484.
104. Hoffmann W, Dieckmann H, Schmitz-Feuerhake I. A cluster of childhood leukemia near a nuclear reactor in northern Germany. Arch Environ Health 1997; 52: 275–80.
105. Grosche B, Lackland D, Mohr L, et al. Leukaemia in the vicinity of two tritium-releasing nuclear facilities: a comparison of the Kruemmel Site, Germany, and the Savannah River Site, South Carolina, USA. J Radiol Protect 1999; 19: 243–52.
106. Kaatsch P, Kaletsch U, Krummenauer F, et al. Case control study on childhood leukemia in Lower Saxony, Germany. Basic considerations, methodology, and summary of results. Klin Paediatr 1996; 208: 179–85.
107. Bruske-Hohlfeld I, Scherb H, Bauchinger M, et al. A cluster of childhood leukaemias near two neighbouring nuclear installations in Northern Germany: prevalence of chromosomal aberrations in peripheral blood lymphocytes. Int J Radiat Biol 2001; 77: 111–6.
108. Hoffmann W, Greiser E. Retrospektive Inzidenzstudie Elbmarsch. Inzidenz von Leukämien, malignen Lymphomen, multiplen Myelomen und von verwandten Erkrankungen in den Landkreisen Herzogtum Lauenburg, Harburg und Lüneburg, 1984–1993.. Bremen: Bremer Institut für Prävention und Sozialmedizin, 1994.
109. Kaletsch U, Meinert R, Miesner A, Hoisl M, Kaatsch P, Michaelis J. Epidemiologische Studien zum Auftreten von Leukämieerkrankungen bei Kindern in Deutschland. Bonn: BMU, 1997.
110. Cook-Mozaffari P, Ashwood FL, Vincent T, Forman D, Alderson M. Cancer incidence and mortality in the vicinity of nuclear installations. England and Wales 1959-80. London: HMSO, 1987.
111. Jablon S, Hrubec Z, Boice JD, Jr., Stone BJ. Cancer in populations living near nuclear facilities. Vol 1—Report and summary. Washington: National Cancer Institute, 1990.
112. Clarke EA, McLaughlin J, Anderson TW. Childhood leukaemia around Canadian nuclear facilities—Phase I. Ottawa, Canada: AECB, 1991.
113. Keller B, Haaf G, Kaatsch P, Michaelis J. Untersuchung der Häufigkeit von Krebserkrankungen im Kindesalter in der Umge-bung westdeutscher kerntechnischer Anlagen. Bonn: BMU, 1992.
114. Möhner M, Stabenow R. Childhood malignancies around nuclear installations in the former GDR. In: J. Michaelis, ed. Epidemiology of childhood leukaemia. Symposum der Akademie der Wissenschaften und der Literatur. Mainz: Gustav Fischer, 1992.
115. Viel JF, Richardson S, Danel P, et al. Childhood leukemia incidence in the vicinity of La Hague nuclear-waste reprocessing facility (France). Cancer Causes Control 1993; 4: 341–3.
116. Guizard AV, Boutou O, Pottier D, et al. The incidence of childhood leukaemia around the La Hague nuclear waste reprocessing plant (France): a survey for the years 1978–1998. J Epidemiol Community Health 2001; 55: 469–74.
117. Dieckmann H. Incidence of leukemia in the Elbmarsch area. Gesundheitswesen 1992; 54: 592–6.
118. Schmitz-Feuerhake I, Dannheim B, Heimers A, Oberheitmann B, Schroder H, Ziggel H. Leukemia in the proximity of a German boiling-water nuclear reactor: evidence of population exposure by chromosome studies and environmental radioactivity. Environ Health Perspect 1997; 105 (Suppl 6): 1499–504.