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Statement of the Commission on Radiological Protection concerning the study by Martin J. Gardner et al.

Martin J. Gardner et al.: "Results of case-control study of leukaemia and lymphoma among young people near Sellafield nuclear plant in West Cumbria", Brit. Med. Journal 300 (1990) 423 - 429,

and the supplementary work

Martin J. Gardner et al.: "Methods and basic data of case-control study of leukaemia and lymphoma among young people near Sellafield nuclear plant in West Cumbria", Brit. Med. Journal 300 (1990) 429 - 434.

Statement of the German Commission on Radiological Protection

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Stellungnahme der Strahlenschutzkommission

In the event of any doubts about the meaning, the German original as published shall prevail.

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1 Introduction

In the surroundings of two nuclear facilities in Great Britain, i.e. Dounreay and Sellafield, epidemiological studies (i.e. statistical information collected in the population) have revealed an increased incidence of leukaemia in children and adolescents (Black 1984). Leukaemia in childhood is a relatively rare, severe disease occurring in about 5 out of 10,000 children in the mean. Its causes have only partly been studied, and its incidence shows strong variations with site and time. Other investigations not connected with radiation have shown that, for reasons unknown up to now, the "relative risk" (i.e. the factor by which the probability for a child to develop disease is increased or decreased in comparison to the average), among others, depends upon the socio-economic status of the family, tending to an increased incidence in those with higher incomes (see page 5). As a result of many years of medical-statistical follow-up of the survivors from Hiroshima and Nagasaki, an increased risk of leukaemia has been established for children exposed to radiation themselves; for example, the risk of leukaemia in children of less than 10 years of age can be doubled at a whole body dose of 100 mSv. However, the offspring of radiation exposed survivors has not been found to present any sign of hereditary diseases due to radiation exposure of the parents up to now.

The present epidemiological study by M.J. Gardner and co-workers from the University of Southampton is due to a recommendation made by an independent commission of the British Health Office, chaired by Sir Douglas Black, to conduct a study of possible risk factors for the increased leukaemia rate found in children in the district of West Cumbria where the plant Sellafield is situated. Studies of this kind are performed to find out whether there are statistical correlations of the disease with suspected risk factors. For instance this included the task to prove a possibly existing correlation between increased leukaemia in children and exposure of these children to radioactive substances released into the environment.

However, this correlation was not expected to exist, since the additional radiation doses received in the surroundings of Sellafield were in the order of the natural radiation exposure, i.e. too low to explain the observed increased incidence of leukaemia (Black 1987). This statement was based on a careful investigation of all imaginable exposure pathways associated with the entire plant, including 7 nuclear reactors (of which 4 are still in operation), one fuel cell reprocessing plant, cooling ponds and a surface-near landfill for radioactive waste materials. The radiation exposure due to the fire in the oldest one of the three reactors shut down in October 1957 (Windscale plant) was also included in this study. According to Stather (1988) the expected rate of deaths from spontaneous leukaemias in the village of Seascale (3,000 inhabitants) at a distance of 3 km from Windscale, was 0.5 among 1.109 individuals born between 1952 and 1983. The reconstruction of the total radiation exposure of children and adolescents resulted in an estimated value of 0.016 additional deaths, of which about 1/9 is attributed to the fire in Windscale. It is therefore extremely improbable that the actual 4 deaths from leukaemia can be explained by releases of radioactivity from the Sellafield plant to the environment. Therefore it was essential to discover other, still unknown risk factors.

In other epidemiological studies, for example, it is investigated whether strong demographic movements, i.e. considerable short-term changes in the population figure due to an afflux to recently developed sites of industry or traffic junctions can be identified as a risk factor for leukaemia during childhood. Kinlen (1988) found this hypothesis confirmed by an increased relative risk of leukaemia within the rapidly grown housing estate Glenrothe at the bridge

over the Firth of Forth. Similar results were obtained by Cook-Mozzafari et al. (1989) who found an increased leukaemia rate at planned sites of nuclear facilities already during the planning stage. These studies on potential demographic influences, on the biological mechanisms of which only assumptions have been available up to now, are being continued at present.

2 The Gardner Study and its results

The present study is based upon 5 years of careful work, during which M.J. Gardner and co-workers registered 52 cases of leukaemia and 22 cases of Non-Hodgkin lymphoma diagnosed between the 1.1.1950 and the 31.12.1985 among individuals of less than 25 years of age who were born in the region of West-Cumbria. In order to establish the possible correlation of the diseases with the potential risk factors which must be investigated individually, every case of leukaemia or lymphoma was attributed up to eight "controls", i.e. comparative individuals according to sex, date of birth, and social factors as well as precise localization of the residence at birth[*)]. These are the instruments of a "case-control study" by means of which it is investigated whether those affected by leukaemia or lymphoma, compared to the healthy controls, were exposed more often to the risk factors for leukaemia, e.g. radiation exposure or virus infections during prenatal development. Additionally it had to be considered whether the diseased individuals were exposed more often than the healthy controls to certain plant-specific factors of which the property as a risk factor was still unknown, e.g. occupation of the parents in the plant, or proximity of the residence to Sellafield. The comparison was performed by logistic regression, determining the Odds Ratio as an approach to the relative risk (Breslow and Day 1980); this approximation is justified for rare diseases.

The investigation of possible risk factors yielded the following result:

a) Risk factors not associated with the reprocessing plant

In 7 out of 74 cases of leukaemia and lymphoma, but only in 12 out of 484 healthy controls, the mother was more than 40 years old at birth; this age of the mother thus is associated with a relative risk of 4.03 (1.41 - 11.52)[**)]. In 9 out of 66 cases of leukaemia and lymphoma, compared to 34 out of 389 non-diseased controls, the father was elder than 40 years at the time of birth; the relative risk in this case amounts to 1.58 (0.60 - 4.16). In 5 out of 28 cases of leukaemia and lymphoma, compared to 20 out of 153 non-diseased controls, the mother was subjected to abdominal X-ray examinations during pregnancy; the evaluation for this risk factor yields a relative risk of 1.34 (0.46 - 3.88). Only 4 out of 32 individuals affected by leukaemia or lymphoma later on, but 31 out of 98 non-diseased controls, had played more than once per month in the hilly country; the calculated relative risk in this case amounts to 0.36 (0.11 - 1.17). In 9 out of 64 individuals affected by leukaemia or lymphoma, compared to 25 out of 383 non-diseased individuals, the father worked for the iron and steel industry;

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*) Accordingly, the results are indicated in the following for comparison with the "local controls". Controls with a different residence at the time of birth ("area controls"), however, were registered as well due to methodological requirements. They yielded similar results of evaluation. In the present study this will be considered together with the factor of influence entitled "distance of the residence from Sellafield".

**) In parenthesis, here and in the following, the 95 %-confidence-interval is given.

the associated relative risk was 3.20 (1.23 - 8.28). In cases of the father's employment in agriculture (6 out of 64 diseased) or in the chemical industry (7 out of 64 diseased) the relative risks amounted to 2.15 (0.71 - 6.51) and 2.15 (0.80 - 5.77), respectively. With the father employed by the coal mining industry (5 out of 64 diseased), the relative risk was 0.46 (0.16 - 1.30). The influence of the socio-economic status as a risk factor is demonstrated by these strong variations of the relative risk.

b) Risk factors related to the plant

The Gardner study gave no evidence of a correlation between the leukaemia and lymphoma incidence and the release of radioactive substances to the environment by the plant Sellafield, since there were no differences between the diseased individuals and the control group neither with regard to the consumption of sea fish nor in connection with playing at the beach. However, living at a distance of more than 5 km from Sellafield was found to be associated with a relative risk ranging from 0.06 to 0.21 for each selected interval of distance, compared to the vicinity of Sellafield, where 8 out of 73 individuals affected by leukaemia or lymphoma lived, compared to 16 out of 491 non-diseased controls. Already earlier it had been noted that the 5 cases of leukaemia[*)] in the village of Seascale, which is within this radius, is beyond the expected frequency. Four of the fathers of these children had worked in Sellafield over a period of 6 to more than 13 years and had received personal doses between 97 and 188 mSv (9.7 and 18.8 rem) during the total period of work. The father's radiation exposure, therefore, was considered as a potential risk factor in the study.

In 10 out of 66 cases of leukaemia and lymphoma, compared to 46 out of 389 non-diseased controls, the father had been working in Sellafield at the time of conception of the child; this leads to a relative risk of 1.48 (0.59 - 3.75). These 10 cases include 6 cases with personal doses of the father of up to 99 mSv, which show no increase in the relative risk, compared to the controls in this lower dose range. Personal doses of the father exceeding 100 mSv were found in 4 out of 66 cases of diseased individuals and only in 3 out of 389 controls, so that this upper dose range is associated with a relative risk of 8.30 (1.36 - 50.56). If the same 10 cases are classified according to the personal dose received by the father during the last 6 months before conception of the child (accounting for the time needed for multistage development of spermia from the stem gonocytes) the relative risk is increased only in the most highly exposed group of fathers with more than 10 mSv; and in this context the relative risk amounts to a value of 5.01 (1.13 - 22.24) due to the same 4 cases, compared to the controls in this dose range. In one of these 4 cases, which are consequently in the centre of the results, the mother was more than 40 years old at the time of birth. Two of the fathers were chemical workers, one was an analytic chemist and the forth one was a journeyman plumber. More detailed data on their radiation exposure due to incorporation of radionuclides were not available at the time of the study.

The authors are, of course, aware that statistical correlations are not a proof of causes and they also express this opinion. However, hypotheses may be made as a suitable starting point of further studies. So, a prospective cohort study would be performed for instance instead of the retrospective case-control study presented here. In this sense, the authors propose the hypothesis "that the radiation exposure of the fathers previous to conception is correlated with the occurrence of leukaemia in their offspring". Considering that there was no increased

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*) of which 4 were lethal, see page 5

incidence of leukaemia in the offspring of 7,387 male atomic bomb survivors in Japan who had received an estimated mean dose of 492 mSv (Ishimaru 1981), they argue that those working in Sellafield were not subjected to short-term but protracted exposure, i.e. irradiation at a low dose rate distributed over a period of time. They also refer to an animal experimental study in mice (Nomura 1982) where increased tumour rates occurred in the first and second generation of progeny in connection with relative high doses of 360 - 5,040 mSv following x-ray exposure of the parents. Two cohort studies also conducted by Gardner (1987, 1987) in children in Seascale resulted in the finding that increased leukaemia incidence occurred only in the children born there but not in those who had moved to the village later on. It is also stated that the radiation workers in the plant of Sellafield showed no significant increase in leukaemia (Smith 1986). The authors expect further important results from similar epidemiological studies in the surroundings of the reprocessing plant of Dounreay and the nuclear weapon plant Aldermaston.

With regard to consequences for radiation protection practice, Gardner makes very careful statements. Only upon further confirmation of the hypothesis of leukaemia induction by radiation exposure of the fathers he would see an obvious necessity for sharpened protection measures.

3 Conclusions of the Commission on Radiological Protection

The Commission on Radiological Protection carefully analysed the publications by Gardner et al., since these are part of the urgently needed research activities to clarify the causes of the increased incidence of leukaemia in the vicinity of Sellafield. The Commission on Radiological Protection support Gardner's conclusion that the results, in spite of the small number of only 4 cases of diseases on which the observed correlation with radiation exposure of the fathers is based, require further verification of the hypothesis of an increased leukaemia risk in the offspring of radiation exposed fathers and refers to the importance of further results of examinations announced by Gardner.

The Commission on Radiological Protection, however, also falls in with the criticism expressed in the introductory essay by V. Beral (1990) that data on the internal exposure of the fathers concerned are still missing. Apparently it is too early to discuss dose-effect-relationships alone as a result of communicated personal doses which are characteristic of external radiation exposures. According to an estimate by Abrahamson (1990), the research director of the Radiation Effects Foundation in Hiroshima, the doses received by the fathers in Sellafield are not sufficient from a calculatory point of view to produce a genetic disposition for leukaemia, via radiation-induced mutations, in the order observed. This consideration would only be totally conclusive if the internal exposure was accounted for. The Commission on Radiological Protection concurs with V. Beral and H.J. Evans (1990) also in the opinion that the external radiation exposure of the 4 fathers recorded up to now might only be an indirect sign of influences from other causative substances or situations.

After the most recent evaluation of the data of Hiroshima and Nagasaki from 31,150 children of atomic bomb survivors there is still no basis for the assumption of an inherited disposition for tumour development after radiation exposure of the parents with a mean gonad dose of 435 mSv (Yoshimoto 1990). This applies especially also for the 250 children who were born during the first half year following radiation exposure of the parents at about 250 mGy. Gardner's assumption that protracted exposure causes a heavier hereditary burden than acute

exposure at the same dose is contradictory to the results of large-scale animal experiments known up to now with regard to radiation induced mutations. The results obtained by Yoshimoto's data collection in more than 30,000 children of atomic bomb survivors, therefore, must be judged as a strong counterargument against Gardner's hypothesis.

Should Gardner's assumption of a transmission via the blood line apply, the observed leukaemias would have to be due to dominant mutations. Geneticists (Notani 1990, Evans 1990) pointed out that in this case other dominant mutations would have to occur in the children near Sellafield. This has not been found up to now.

With a view to statistical-methodological aspects the Commission on Radiological Protection points out that not only the proportion of the fathers exposed to the highest doses of radiation in Sellafield was clearly greater than in the non-diseased controls but also the proportion of those fathers who worked for the iron and steel industry, agriculture and chemical industry and who were not subject to additional radiation exposure. A statistical investigation performed by the Commission on Radiological Protection according to the Chi-square-test in order to verify the hypothesis that the relative risk of the children of fathers employed in Sellafield did not significantly differ from that of the children of iron and steel workers, resulted in the finding that this hypothesis is in accordance with the data, viewing the broad confidence intervals of the indicated risk factors. There could exist a common cause, perhaps concerning the socio-economic situation which is responsible for the increased incidence of leukaemia and lymphoma among the children of Sellafield workers and of iron and steel employees but which is not connected with radiation.

With all attempted explanations it must be considered that the 4 cases of diseases on which Gardner's hypothesis is based, exclusively occurred in the village of Sellafield. The socio-economic structure of the former fishing village has not been changed fundamentally by the industrial settlement of Sellafield (Kinlen 1988). If a relative risk of approximately 3 is assumed in the case of the 1,109 children of the population of Seascale according to the data collected by Gardner for families of iron and steel workers or employees of the chemical industry (see page 219), then about 1.5 lethal leukaemia cases would be expected following conversion from the national average (see page 4). The 4 actual deaths from leukaemia (Stather 1988) could therefore still represent a random variation in the leukaemia rate. The Commission on Radiological Protection expects that the current epidemiological study of leukaemia cases in other regions of England and Scotland will furnish further material also with regard to this attempted explanation.

On the whole the Gardner study, due to the assumed biological importance of the results and in spite of the low case number, has the character of an indication obliging to high awareness which must be further followed within the scope of the urgent research work on the still unknown causes of leukaemia clusters. This includes primarily the absence of corresponding findings in the offspring of radiation exposed fathers in Hiroshima and Nagasaki, but also the existence of other possible explanations, e.g. by demographic or socio-economic factors. With the present state of affairs, there is no need to immediately introduce sharpened protection measures; the Commission on Radiological Protection follows the further development with the necessary high attention and supports the current research activities. An important partial result of the Gardner study is the finding that there is no correlation of the increased leukaemia risk in the surroundings of Sellafield and the release of radioactivity from this plant.

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