LEUKEMIA FOLLOWING THE CHERNOBYL ACCIDENT

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Abstract—**The accident at the Chernobyl Nuclear Power Plant in Ukraine in 1986 led to a substantial increase of thyroid cancer among those exposed as children. The other cancer that is the most sensitive to the effects of ionizing radiation is leukemia, and this paper evaluates the evidence relating exposure to Chernobyl radioactivity and leukemia risk. Two types of objectives are identified, namely, scientific evidence and public health, and two approaches to addressing such objectives are discussed. Empirical studies in affected populations are summarized, and it is concluded that, possibly apart from Russian cleanup workers, no meaningful evidence of any statistical association between exposure and leukemia risk as yet exists. However, it is important to carry on with such studies to satisfy various public health objectives.**
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INTRODUCTION

THE ACCIDENT at the Chernobyl Nuclear Power Plant in April 1986 released large amounts of radioactive compounds that contaminated substantial areas, particularly in Belarus, the western areas of Russia, and Ukraine, which at the time of the accident were part of the former Soviet Union. However, many other countries, particularly those in Western Europe, were also contaminated to a lesser degree. The accident was the largest nuclear accident in history, and it is clearly of major importance to identify the health consequences arising from that accident.

Within the three most affected countries, there are several identifiable groups of individuals who were exposed to radioactive contamination, namely cleanup workers, evacuees and residents of contaminated territories. The approximate numbers and mean effective doses for these groups are shown in Table 1.

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Since the accident, a large number of studies have been reported regarding the health consequences of the accident. These studies include those of thyroid cancer (particularly among those exposed as children), leukemia, breast cancer, autoimmune thyroiditis, cardiovascular disease, and cataracts. The relationship between Chernobyl exposure and thyroid cancer risk in those exposed as children has clearly been demonstrated, and there is little doubt as to the causality of this association as Ron (2007) has described. This paper examines the epidemiologic evidence relating to some of the other health consequences of the Chernobyl accident, and in particular focuses on leukemia. It should be noted that the evidence concerning Russian cleanup workers, and in particular their subsequent risk of leukemia, has already been covered by Ivanov (2007) in his accompanying paper and is not further addressed in the present paper.

OBJECTIVES OF STUDIES

Before examining the empirical evidence and reaching conclusions from that evidence, it is first necessary to consider the objectives in studying associations between Chernobyl exposure and diseases, and the types of studies used to examine those associations. It is necessary to distinguish between two types of objectives namely scientific and public health. The scientific objective for a radiation epidemiologic study can be defined as adding knowledge to the existence and quantification of the corresponding dose-response relationship—knowledge that can be applicable in other situations. For example, this is the prime objective of the study of atomic-bomb survivors (NAS/NRC 2005). However, in the case of Chernobyl studies, with the exception of thyroid cancer, doses were generally too low and the corresponding risk estimates too imprecise to allow scientific objectives to be fulfilled.

On the other hand, public health objectives would seem to be valid objectives in the case of Chernobyl exposures. Such objectives include:

- estimating the resources which would be required to deal with the health consequences of the accident;

Table 1. Estimates of mean effective doses (mSv) for population groups of interest.

Population	Approximate size of population	Mean effective dose (mSv)
Liquidators (1986–1987, 30-km zone)	240,000	100
Evacuees of 1986	116,000	33
Persons living in contaminated areas:		
● Deposition density of ^{137}Cs >37 kBq m^{-2}	5,200,000	10
● Deposition density of ^{137}Cs >555 kBq m^{-2}	270,000	50

- providing reassurance to those exposed to the effects of Chernobyl as to the likelihood of any health consequences; and
- obtaining direct confirmation as far as possible of the consequences because this was the largest nuclear accident in history.

It should be noted, however, that to achieve a public health objective it is equally important as for a scientific objective to follow conventional scientific principles to achieve that objective.

POSSIBLE APPROACHES

There are two possible approaches to carrying out studies with public health objectives. The first of these is the so-called risk projection method in which risks derived from studies of individuals exposed at much higher doses than Chernobyl populations are applied to the doses experienced by the Chernobyl population in order to project risks. The other method is to carry out empirical studies in the affected populations themselves. The advantage of the first approach, and correspondingly the disadvantage of the second approach, is the issue of statistical power. Higher-dose studies will provide more precise risk estimates than low-dose studies. On the other hand, the first approach involves extrapolating the results in populations who may have very different types of exposure (e.g., high doses and high-dose rates) and in a different population than the affected population. Such extrapolation is, of course, unnecessary for empirical studies conducted directly on the affected population.

In order to illustrate the risk projection approach for leukemia, Table 2 shows projected numbers of leukemias expected to occur by 2005 and 2065 from Chernobyl exposure for various affected countries (Cardis et al. 2006). It must be emphasized that there is a good deal of uncertainty in such predictions. These estimates are based on applying the statistical models provided by the BEIR VII Committee (NAS/NRC 2005) (derived from the atomic-bomb survivors study) to Chernobyl doses. This approach would then satisfy any of the public health objectives listed above, but it is, of course, limited by the transferability of the risk model from the Japanese population exposed at high doses and high-dose rates to a European population exposed at low doses and low-dose rates (apart from the thyroid gland). Nevertheless, the technique is of use particularly when extrapolating to future dates as, of course, such projections cannot be made directly from empirical studies of low statistical power.

Table 2. Predicted number of leukemia cases in Europe following the Chernobyl accident.

Country group	Average whole-body dose (mSv) 1986–2005	Leukemia due to radiation[a]	
		Up to 2005	Up to 2065
1	0.1	80	200
2	0.3	200	500
3	0.7	160	400
4	1.8	300	800
5	6.1	200	500
Total		940	2,400

[a] Numbers depend on dose and size of population at risk.

EMPIRICAL STUDIES OF LEUKEMIA

The remainder of this paper will be concerned with the epidemiologic evidence that has been provided from empirical studies conducted in Chernobyl-affected populations. In general, with the possible exception of cleanup worker studies, these studies of leukemia have the following limitation:

- as mentioned above, lack of statistical power;
- they are often of an ecologic design which introduces the well-known "ecologic fallacy;"
- they often involve comparison between an exposed population who may be monitored more intensively (e.g., cleanup workers) and the general population of a country; with differential monitoring this factor will generally introduce a bias in favor of an association; and
- often, individual doses are not available.

Bearing these limitations in mind, the evidence that has been accumulated from such studies is now considered. Studies of high-dose populations such as the atomic-bomb survivors have shown that the dose-response relationship of leukemia is linear-quadratic and that the magnitude of risk varies considerably with age at exposure, with those exposed at younger ages having higher risks on the relative risk scale than those exposed at older ages. Therefore, studies are grouped according to age at exposure.

Exposure in utero

Several ecologic studies have been reported of leukemia occurring among those exposed in utero (Petridou et al. 1996; Ivanov et al. 1998; Steiner et al. 1998; Noshchenko et al. 2001). None of these studies provide evidence for an association with leukemia with the possible exception of the Greek study (Petridou et al. 1996), but in view of the ecologic nature of the studies and the generally small number of cases available for analysis, it cannot be said that this provides substantive evidence for a lack of association. Rather, these studies must be considered as uninformative.

Exposure in childhood

Again, several ecologic studies have been reported on leukemia occurring among those exposed as children (Ivanov et al. 1993; Parkin et al. 1993; Gapanovich et al. 2001; Ivanov and Tsyb 2002; Ivanov et al. 2003). None of these studies provide evidence of a positive association, but, again, as with the in utero exposure studies, these studies are limited because of their ecologic nature and the small number of cases available. Two case-control studies have been reported (Noshchenko et al. 2002; Davis et al. 2005). The first (carried out in Ukraine) is a subset of the second (carried out in Belarus, the Russian Federation, and Ukraine). The former study reports an association with leukemia in males, but is subject to a design flaw in that controls were chosen from areas other than those that provided the cases and the risk estimates appear far too high to be realistic. The latter study reports mixed results with, again, the study in Ukraine showing a significant association with leukemia and the other components of the study not showing a significant association. Therefore, at this time, one cannot conclude meaningfully if those exposed in childhood are showing some evidence of an association with leukemia.

Exposure in adulthood

These studies may be further subdivided into two groups: mainly studies in the general population and studies in cleanup workers.

Studies in the general population are again all of the ecologic type and overall show no evidence of any meaningful association (Prisyazhniuk et al. 1995; Bebeshko et al. 1997; Ivanov et al. 1997).

With regard to cleanup workers, an early study in Estonia only yielded one case of leukemia (Inskip et al. 1997). A number of studies of Russian cleanup workers have appeared as already discussed by Ivanov (2007). A study of cleanup workers in Ukraine (Buzunov et al. 1996) found that workers who first worked at Chernobyl in 1986 had increased risk of leukemia relative to those who first worked in a later year.

Many of these cleanup worker studies make use of the doses recorded in Chernobyl State Registries and generally had follow-up based on the same Registries. Potentially this creates several limitations for these studies, although it is not possible to quantify the bias that might have been introduced.

In order to overcome these problems, two studies are currently being conducted of cleanup workers in Belarus and Russia, and the Baltic countries and Ukraine (UN Chernobyl Forum 2005). These are based on cohorts assembled from Chernobyl State Registries and monitored by means independent of those Registries. Nested case-control studies within the cohort are being carried out for leukemia cases detected within the cohorts. Interviews are carried out with cases and controls and a dose estimation technique ("RADRUE") is then used to estimate individual doses from a combination of routes within the 30-km zone identified from questionnaires and measurements of dose fields in the same area at the appropriate time. Results of these two studies have not yet appeared, but it is anticipated that they should be available shortly and will shed an interesting light on the detectability of leukemia induced by Chernobyl exposure among cleanup workers.

CONCLUSION

With respect to leukemia induced by Chernobyl, risk projection approaches suggest that 940 cases are expected to have developed by 2005 and 2,400 cases are expected to develop by 2065. However, these estimates have considerable uncertainty (Cardis et al. 2006).

In a number of studies carried out in Chernobyl-affected populations, as yet no meaningful evidence for excess leukemia incidence has been accumulated for those exposed in utero, as children, or adults as members of the general population. This is hardly surprising given the very limited power of such studies and other limitations.

Amongst cleanup workers, some evidence of an association with leukemia has emerged for Russian cleanup workers, but, as yet, evidence from the other most affected countries has been inconclusive.

For various public health reasons, it will be important to continue monitoring for these associations in the future by appropriately-designed, conducted, and analyzed scientific studies on those directly exposed to Chernobyl fallout.

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