LEUKOSIS DISEASES IN TERRITORIES WITH DIFFERENT LEVELS OF RADIONUCLIDE CONTAMINATION AFTER THE CHERNOBYL ACCIDENT

Haematological Scientific Centre of the Russian Academy of Medical Sciences, Moscow, Russian Federation

A.D. PROSHIN, G.I. MILUTINA
Main Department of Health in the Bryansk region, Bryansk, Russian Federation

1. INTRODUCTION

Increase in risk of leukemia is an earlier and marked stochastic effect of irradiation. Its epidemiological regularities were established mainly in studies of effects of acute irradiation as a result of A-bombing of the Nagasaki and Hiroshima population as well as radiological procedures. Occurrence of leukemia and other haemoblastosis is relatively rare: the total incidence of the diseases does not exceed 16 or 18 cases per 100,000 persons in a year. Comprehensive epidemiological information on haemoblastosis can be collected in special investigations of initial documents under special protocol. It is caused by the following reasons:
- lack of statistical registration of individual forms of haemoblastosis which are dependent on radiation exposure to variable extent;
- available information on morbidity with haemoblastosis collected in the system of cancer registration is incomplete.

2. POPULATION AND AREA UNDER STUDY

The area of Bryansk oblast is 34.9 thousand sq.km. According to the census of 01.01.1989 the population of the Oblast was 1,470,129 persons: urban population - 984,996 persons, rural population - 485,133, male - 671,376, female 978,762, children to 15 years old - 316,151 persons. 6 south-western rayons of Bryansk Oblast contaminated with radio nuclides as a result of the Chernobyl accident are: Gordeevsky, Zlynkovsky, Klimovsky, Klintsovsky, Krasnogorsky, Novozybkovsky. Cs-137 contamination density in these rayons is above 37 KBq/sq.m. The above rayons cover the study area on the protocol of Epidemiological study within frame of the Pilot project HAEMATOLOGY under IPHECA. Economic activity of 143 collective farms, 151 private farms is performed in the study area. According to the official information (1.04.92) 1,637.4 thousand hectares or 41.5% of the agricultural area is contaminated with radio nuclides, Cs-137 contamination density is above 37 KBq/sq.m.

3. METHODS OF EPIDEMIOLOGICAL FOLLOW-UP

To compile, store and analyse of epidemiological, dosimetric and demographic information specialised registry of blood diseases has been established. The following work is carried out within the frame of the registry:
- a search for and registration of epidemiological and clinical data at institutions located in study areas;
- investigation of archive documents and specimens at central specialised institutions
  Haematological Research Center, Medical Radiological Research Center, Botkin's Hospital,
  Morozov’s Children Hospital, Institute of Children Haematology, Oncological Scientific
  Center, Herzen's Research Institute of Oncology, Russian research Center of Haematology and
  Transfusion) verification of the information on fallen ill persons by inquiry hospitals, study of
  health history and diagnostic material;
- primary processing and sorting of epidemiological charts;
- study of archived laboratory materials to verify diagnosis;
- urgent and planned clinical advice of fallen ill persons by clinicians of
  Haematological Research Center;
- collecting of demographic data in study areas at Oblast, Rayon levels as well as in separate
  settlements;
- search for and recording of individual dosimetric information related to registered persons
  with haemoblastosis;
- sampling and sending of material to biodosimetry;
- inputting the following information into the database:
  a) list of settlements related to geographical co-ordinates and demographic features;
  b) level of contamination with radioactive and nonradionuclear substances;
  c) cases of disease detected among residents.

Teams of epidemiologists and haematologists have collected epidemiological information in Bryansk Oblast in field missions. Clinical expertise of validity of the diagnosis on results of laboratory and clinical examination has been performed in analysis of initial clinical information. Morphological validation of the diagnosis has been judged.

4. RESULTS

The total population of Bryansk Oblast was 1,464.1 thousand in 1991. It was 9.4 thousand persons less than in 1985. The increase in urban population +59.4 thousand, decrease in rural population -68.8 thousand persons were registered. Size of children population did not change. At the same time the number of persons of young and old age decreased, the size of the age group of 30 - 44 years old increased.

The size of urban population in study areas did not practically change in 1991, however the size of rural population decreased of 22% (-20,000 persons) in total and in individual rayons: Gordeevsky -16%; Zlynkovsky - 17%; Klimovsky - 10%; Klintsovsky - 21%; Krasnogorsky - 48%, Novozybkovsky -20%.

Epidemiological data on 3,036 patients with haemoblastosis compiled for the period from 1979 to 1993 are kept in the registry of blood diseases at Haematological Research Center.

The following abbreviates are used:
ALL- acute lymphoblastic leukemia; AnLL-acute non lymphoblastic leukemia; nsAL- non-specified acute leukemia; AAL- all acute leukemias; CLL - chronic lymphoid leukemia; CML - chronic mieloleukemia, E - erithremia; ACL- all chronic leukemias; PPHB -paraprotenemic haemoblastosis; HD - Hodgkin disease, nHD - non-Hodgkin disease (lymphomas); AHB - all haemoblastosis.

Retrospective data are not exhaustive because initial medical documents mainly health history have been lost at hospitals and archives in individual cases. For the period from 1979 to 1993 in 449 persons living in 6 study rayons haemoblastosis was first diagnosed. The annual average morbidity rate is 13.71 per 100,000. Comparison between rates of different types of haemoblastosis in 6 study rayons and in other 21 rayons of Bryansk Oblast as well as in Bryansk city has been performed. Since compared groups of the population are varied by age because of migration and other reasons rates of morbidity for the period from 1986 to
1993 have been standardised by sex and age with the use of direct method. Age structure in 21 rayons of the Oblast fixed in the census of 1989 has been used as a referent.

The standardised rates in 6 study rayons are either less or slightly differ from those in 21 rayons of the oblast for the period after the accident. Incidence of haemoblastosis in Bryansk city is markedly high than it is in the two compared areas.

From regression analysis of trends of morbidity in Bryansk Oblast for the period from 1979 to 1985 and 1986 to 1993 it is noted significant increase in incidence rate of nHD and AAL for the latter period. Comparing rate of diseases for three following periods one can see that increase in sick rate is observed in rural population of older age groups. Relative risks (RR) of a developing disease within period of 1986-1993 have been estimated for haemoblastosis in Bryansk city and 6 study rayons. Standardised expected number of cases of individual types of haemoblastosis has been estimated with the use of information on morbidity among urban and rural population of other rayons of Bryansk Oblast stratified on sex.

RR estimated for all types of haemoblastosis in Bryansk city exceed 1.0. At the same time relative risks in rayons under study do not exceed 1.0 for all haemoblastosis except ALL. The analysis of this irregularity is given below.

The comparative study of non-standardised incidence in areas of 6 rayons (1986-1993) with different level of 137 Cs contamination shows a higher (but not statistically significant) rates of ALL, HLL, HD for mostly devastated territories > 555 KBq/sq. m. The crude rates for AHB are differed significantly. This result was proven by means of standardisation and space-time analysis by method of Knox. There were no statistically significant aggregations of diseases cases in 7 years before Chernobyl accident in mostly devastated territories of Russia. In distinction from this the significant time-space aggregation of AL occurred after the accident. The critical limits of these clusters being 3 years and 25 km contradict the possible influence of rural residents migration to towns. This phenomenon needs additional investigation.

Data on cases of disease in children after the Chernobyl accident, during the period from 1986 to 1991 have been collected and analysed. 58.6 thousand children to 15 years old live in study areas. 158.6 thousand children live in referent area, 98.9 thousand children live in Bryansk city. 75 cases of ALL, 10 cases of AnLL, 3 cases of ncALL, 39 cases of nHD, 1 case of CML were registered during 8 years. Since the part of children population is relatively small, about 20%, age structure of rural and urban population of Bryansk Oblast is of regressive type. According to data of 1992, of 58,500 children 34% of them live in areas with the level radio contamination above 555 KBq/sq. m, 26% of children live in areas with radio contamination density ranged between 185 and 555 KBq/sq. m and about 39% of children live in areas with radio contamination ranged between 37 and 185 KBq/sq. m. Novozybkov town and Novozybkovsky rayon are located in the most radio contamination area, which is the most populated with children.

The annual average number of cases of acute leukemia in children is 3.48 per 100,000 persons. It is close to that registered in developed countries. The average number of cases of nHD is 2 times less, it is 1.54 per 100,000 children. This index is close to that in economically developed countries.

The following main trends of individual types of haemoblastosis are marked: asymmetric, close to log normal age distribution of ALL, with maximum at the age of 3-5 years old, incidence of AnLL reaches maximum in older groups.

Average annual sick rate for AL is the most high in Bryansk city, it is 3.79. The probability of disease developing for the first 15 years is 0.057.

Average annual rate of disease in 6 study rayons is slightly less than in Bryansk city, it is 3.41, the probability of disease developing in the first 15 years is 0.051. According to data
of cancer registry published in the issue "Cancer in 5 continents" these rates are middle. Average annual incidence of ALL in referent areas is 3.31 (the probability of disease developing is 0.049).

The marked variability of average annual rates attracts the attention. In referent areas (158,000 children) they are ranged from 1.89 to 5.04; in Bryansk city (98,900 children) - from 2.02 to 7.08, in study areas (58,600 children) - from 0 to 11.95. Increase in range of annual morbidity depending inversely on the size of population is natural for such rare events as childhood ALL. Nonetheless the incidence 11.95 estimated in areas under study in 1986 is statistically improbable (95% confidential borders are 4.9 and 24.62). When comparing there is no trend to increase in incidence rate of ALL in children in the three areas of Bryansk Oblast during 1987-1993.

The highest average annual incidence of nHD rate, 1.90, was in Bryansk city, probability of disease developing is 0.030. This was in accordance with average level of international data. At the same time the rate in referent areas and study rayons was 1.42 and 1.28 respectively, probability of disease developing is 0.021 and 0.018. For the period of the follow-up the rates of nHD developing varied within the range from 0 - 5.06 (Bryansk city); 0-1.71 (6 study rayons); 0-5.04(referent areas).

Distribution of subjects with ALL by the age at the time of diagnosis establishing is consistent with standard asymmetric distribution characteristic of this type of leukemia: from 0 to 2 years old - 1 case (7%), from 3 to 5 years old - 7 cases (50%), 6-8 years old - 2 (14%), 9-11 years old - 3 cases (22%). Two patients with nsAL were of 3 month and 12 years old. Of 6 patients with nHD was from 0-2 years old- 2 (35%) 9-11 years old- 3 (50%), 12-14 years old- 1 (17%). It was only one case of CML in girl of 14 years old. During every year of the follow-up except 1988, cases of disease among children have been registered. 4 cases annually in 1987 and 1991, 3 in 1989, 2 in 1993, 1 in 1992 and 7 cases in 1986.

Expected number of cases during 8-year period of the follow-up does not differ from empirical number relative risk is 1.08 (ALL), 0.9 (AnLL0; 0.9 (nHD). There is great difference between expected and true number of AL cases (relative risk is 6.31, p=0.007) in 1986.

During the following 5 years from 1987 to 1991 the relative risk of every haemoblastosis does not exceed 1.0. So, the excess of risk of ALL developing in children living in 6 study rayons in 1986 has been established, of 7 children with ALL in that year diagnosis was established in 2 patients before the accident, i.e. 30.03.86 and 03.04.85. Two children fell ill in June, 1986, two children - in July and 1 in August.

Three patients lived in Novozybkovsky rayon, 3 patients - in Klintsovsky rayon, 1 patient in Zlynkovsky rayon. Of 7 patients with ALL 6 were boys. This ratio differs from standard male-female ratio which is slightly varies around 1.2 in various countries.

There is no serious evidence to associate the detected excess of cases with exposure to radiation because of short latent period between the accident and time of the establishing of diagnosis . From the study of kinetics of leukemia cells population it is obvious that time is not sufficient to accumulate the pool capable to clinical manifestation of the disease.

The age of patients with ALL first diagnosed in 1986 is: 3 years old, 5 years and 2 months old, 5 years and 7 months old, 7 years and 4 months old, 7 years and 7 months old, 14 years and 3 months old, 14 years and 4 months old. It is widely distributed on age scale. More than a half of patients were of the age from 3 to 5 years old. At this age interval the maximum of standard distribution of ALL cases occurs.

Considering the possibility of build-up of ALL in study areas the incidence of the disease in adjacent area should be compared.
For this purpose we have used data of blood diseases Registry located at Haematological Research Center which were collected as a result of joint epidemiological study. Data of Belarus 6 rayons (Dobruzhsky, Vetkovsky, Kormiansky, Chechersky of Gomel Oblast, Kostyukovichsky and Krasnopolsky of Mogiliov Oblast) surrounded the study area from West and North and 3 rayons of Bryansk Oblast (Starodubsky, Surazhsky, Unechsky) located to the East of the study area have been analysed. The level of contamination in these rayons is common to that in the study rayons. All cases of diseases diagnosed in children in 1986 have been selected. 4 cases of ALL and 2 cases of nHD have been detected in children lived in 4 of 9 adjacent rayons in 1986.

Distribution of numbers of cases of haemoblastosis detected in the adjacent rayons during the first 4 years since the accident was analysed. There were no features of morbidity excess in 1986, because the cases of haemoblastosis were registered only in 4 of 9 adjacent rayons. From 6 cases of hemoblastosis 4 were AL and 2 were nHD. Tendency to excess of ALL cases in areas surrounded the study rayons was not detected.

At the same time attention is drawn to unusual male-female ratio. It was 6:1 in study rayons, and 4 patients with ALL were boys in adjacent rayons. In contrast to this acute leukemias in the period from 1986 to 1993 for Bryansk Oblast except 6 study rayons the ratio 1.18 is in consistence with commonly accepted index.

The examination of place of residence of fallen ill children demonstrated that patients lived in settlements separated 8 to 60 km. It is evident that there is no dependence of the disease distribution on a local factor.

The next step of study includes case-cohort analysis with an attempt of individual dose interval evaluation. As a first approach to this work a sample of approx. 2000 inhabitants of contaminated areas was examined. For every representative of this sample a detailed epidemiological data were collected and comprehensive medical examination was performed. As a result a strict dependence of internal radiation dose from combinations of behavioural characteristics was demonstrated. This approach could be a realistic bases for cohort under examination division into individual dose level groups. The such expensive and complex methods as tooth enamel ESR and stable chromosomal aberration analysis could be used as sample methods for limits of groups criteria correction.