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THE MAIN DIRECTIONS OF PROSPECTIVE COHORT STUDY OF POPULATION LIVING AROUND THE SEMIPALATINSK NUCLEAR TEST SITE

Summary

In the paper we have presented the possibilities of prospective cohort study of health status in the radiation exposed population living around the Semipalatinsk nuclear test site. It was substantiated the necessity of international cooperation of scientists from Kazakhstan, Europe, Japan and the United States for long-term study of radiation effects for the people and the environment.

Key words: nuclear tests, cohort study, international cooperation.

As noted in the Strategic Research Agenda of Multidisciplinary European Low Dose Initiative (MELODI) platform, the overall aim of MELODI is "consolidating European initiatives on researching and better understanding the health effects of exposure to low dose ionising radiation". The MELODI platform has already integrated nearly twenty national research organisations in Europe with significant programmes in low dose risk research and now needs to extend its approach beyond the European boundaries [1. Although the European low dose radiation research platform is open to the research organisations outside Europe and there are some successful examples of collaborations between European and non-European researchers on specific research projects in the low dose radiation area, closer integration on a larger scale is still far from being optimal.

Since World War II more than 2,000 nuclear explosion tests have been conducted around the world of which the former Soviet Union conducted more than 700. The Soviet nuclear tests began in the Semipalatinsk Test Site (STS) in current Kazakhstan. The test site covers an area of 18,500 km^2 and is named after the city of Semipalatinsk, which is located approximately 150 km east of the test site. A total of 456 nuclear tests were conducted at the site during 40 years from 1949 to 1989. During 1949 to 1962 a total of 118 nuclear tests were conducted above ground and in the atmosphere, while 338 tests during 1961 to 1989 were conducted underground in boreholes and tunnels [2]. It is considered that 13 of the underground tests caused a radioactive release to the atmosphere. These releases, along with releases from the testing in 1949-1962, caused radioactive plumes that affected people and territories adjacent to the site, in particular the former Semipalatinsk oblast (region).

The health effects of exposures to fallout from Soviet nuclear weapons testing for the residents living near by the Semipalatinsk nuclear test site in Kazakhstan have not yet been investigated to their full extent. There are reports with contradicting results coming from the studies conducted on two independent cohorts. One cohort is called "historical" and the other the "new" cohort. The historical cohort was originally set up by the local research institution "Dispensary No. 4" which was later succeeded by the Research Institute for Radiation Medicine and Ecology, Kazakhstan. The historical cohort included residents from ten highly exposed and six control settlements, for comparison. The cohort's exposed group contains 9,850 permanent residents of the exposed settlements, all born before 1 June 1961. The comparison group includes 9,604 inhabitants, also born before 1 June 1961 and frequency-matched to the exposed group by age and gender. This cohort was finalized and quality assurance measures were taken within an EC funded INCO-COPERNICUS project. The most recent analysis was published in 2011 where the relationship between mortality from cardiovascular diseases and radiation exposure from the fall-out was assessed [3]. The dosimetric approach for this study was developed by the US National Cancer Institute and the whole body external dose for the cohort members ranged from 0 to 0.63 Gy. The study concluded that there was no detectable risk of radiation related mortality from cardiovascular diseases in this cohort. Nonetheless, there was weak evidence that the point estimate for the radiation related risk might increase with increasing time since exposure.

The new cohort was established as result of collaboration between Japanese and Kazakh organisations during 2001-2009. A memorandum of agreement was signed between the National Nuclear Centre of the Republic of Kazakhstan (NNC) and the Radiation Effects Association (REA) from the Japanese side in 2009 on the governance and intellectual property rights of database and utilization of outcomes of their joint survey "Study on Health Effects of Radiation on Residents near the Former Semipalatinsk Nuclear Test Site" (REA, 2010). In 2012, the Intellectual Property Rights of REA are being transferred to the National Institute for Radiological Sciences. The new cohort includes exposed inhabitants from 14 villages and control group of inhabitants from 6 villages. Overall, the cohort includes 18,204 persons, most with low to moderate whole body doses (< 0.6 Sv), but some with doses as high as 2 Sv. The study found that the mortality rate due to diseases of the circulatory system and ischemic heart disease increased significantly with increasing dose in both men and women. There was also a significant increase in mortality rate for other forms of heart disease in the high-dose group and for cerebral-vascular diseases in the moderate-dose group for both men and women. For men in the moderate-dose group, a significant increase in the mortality rate was observed for all neoplasms, malignant neo-

plasms of the oesophagus, pulmonary heart disease and disease of pulmonary circulation. Although not significant in women, tendency towards increase was also demonstrated. For cardiovascular diseases, the mortality rate was greater in men than in women and was increasing with advancing age.

These two cohorts used different control groups; numbers of residents included and dosimetric methods differed. The follow-up time was also different, with the new cohort covering the period 2001-2009 while the follow-up of the historical cohort was ended in 1999. While the "historical cohort" was a prospective study, the "new cohort" was conducted as a retrospective study. A prospective lifespan follow-up would enhance the statistical power, in particular, if full residential history and complete disease/death information could be obtained. Also, steps have to be taken to achieve a unified dosimetry system. For acute external exposures caused by the radioactive plumes, the differences are only minor. Still, the dose reconstruction needs to take into account new dosimetric methods that could give more accurate dose estimates.

Archived biological samples from Semipalatinsk residents, mainly human teeth and blood samples, can be investigated with ESR or EPR of tooth enamel and chromosomal aberration techniques, respectively. The latter includes state-of-the-art techniques like the FISH Chromosome Painting. These biodosimetric methods are suitable for more accurate retrospective dose reconstruction that can be compared to the calculated dose burdens for residents. Also urine samples exist that can be analysed by radiochemical methods for better determination of internal dose burdens.

Both cohorts have high potential to address open questions in the area of low dose radiation, especially following intake of radionuclides from the fallout. Since these two cohorts have a high probability of including the same individuals (at least partially), it is pertinent to investigate possibilities to merge the two cohorts in order to create a larger, unified cohort that could be used in prospective epidemiological research. This will avoid duplication of efforts and resources for future studies of the health effects in these populations.

The current proposal will thus investigate the feasibility of setting up a unified cohort of residents around the Semipalatinsk site. This will include preparation for prospective follow-up for various long term health effects from chronic exposure to low and moderate doses, by establishing an international multidisciplinary research team, if the feasibility is demonstrated.

The main objectives of the proposed feasibility study will include:

- developing and testing mechanisms for identification of cohort members in the two cohorts;
- identification and testing of data linkage mechanisms;
- determination of the outcomes to be studied in the future (cancer and non-cancer diseases);
- setting up and testing procedures for follow-up;
- identification of case ascertainment mechanisms and sources, depending on the outcome;
- characterization and validation of dose assessment methods used in the two cohorts (sources of exposure pathways, various dose calculation methods);
- investigation of the feasibility to collect data on confounding factors (e.g. life-style factors); and
- assessing the availability of biological samples, including characterization of archived biological samples and their potential use in the future.

The current proposal has the aim of assessing the feasibility of conducting a future prospective epidemiological study for populations residing close to the Semipalatinsk nuclear test site in Kazakhstan.

The proposed action supports preparation for a future integrated multidisciplinary study to better quantify risks for both cancer and non-cancer diseases from protracted exposures to low and moderate doses. The proposal is in line with the Strategic Research Agenda of MELODI (www.melodi-online.eu) which states that "Research on suitable human epidemiological cohorts remains a very high priority of research in forthcoming years" and "research on new prospective cohorts should be initiated". MELODI also points out the general scarcity of suitable cohorts for such prospective epidemiological studies and there is a need to extend the collaboration beyond the European countries to take advantage of the international possibilities for such research.

The Semipalatinsk cohort is very suitable for such research due to a large population exposed to a mixture of radionuclides from the fall-out. The cohort could be followed-up prospectively with regular updates and relatively good completeness of information on disease status, causes of death and migration. In particular, this cohort could be suitable for studying the risk of cardiovascular diseases due to the access to medical records, including obtaining information on confounding factors, such as lifestyle, etc. from out-patient and in-patient clinics. There are not so many populations exposed to protracted low-dose radiation worldwide suitable for studies of morbidity of cardiovascular diseases and the Semipalatinsk cohort has a potential to prove that prospective epidemiological research on association between radiation and cardiovascular diseases is feasible in this population. The dose reconstruction is challenging and has been criticised (UNSCEAR 2008) in the past for the high level of uncertainty of the doses used, in particular in the control settlements but lately significant work has been conducted by lead dosimetry experts from Russia, Kazakhstan, Japan and USA to improve these estimates and to evaluate the level of uncertainty [4, 5]. These efforts, however, lacked coordination and concentrated on the two independent rosters of residents around the nuclear test site.

The project will bring together key scientists from Kazakhstan, Europe, Japan and USA to assess the feasibility of a prospective lifelong follow-up study on health effects for residents near the Semipalatinsk test site (STS). There is a large international interest for performing research on residents near STS, and the SEMI-NUC feasibility study will assess ways to bring together existing and planned epidemiological research for a future integrated collaboration of very high quality. Reconstruction of residential history, accessibility to medical records for obtaining complete and standardised information on diagnostic criteria and confounding factors, availability of individual doses with as low uncertainty as possible are all crucial elements for high quality epidemiological research. The best way forward is to assess a possible European-international cooperation of leading experts in the area who could jointly undertake a long-term commitment for setting up and following the residents near the STS in a prospective lifelong follow-up study if the feasibility is confirmed.

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Резюме

ОСНОВНЫЕ НАПРАВЛЕНИЯ ПРОСПЕКТИВНОГО КОГОРТНОГО ИССЛЕДОВАНИЯ СОСТОЯНИЯ ЗДОРОВЬЯ НАСЕЛЕНИЯ ТЕРРИТОРИЙ, ПРИЛЕГАЮЩИХ К СЕМИПАЛАТИНСКОМУ ЯДЕРНОМУ ПОЛИГОНУ

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В статье представлены возможные направления проведения проспективного когортного исследования состояния здоровья населения Казахстана, подвергшегося радиационному воздействию вследствие ядерных испытаний.

Обоснована необходимость международного сотрудничества ученых Казахстана, Европы, Японии и США для долговременного изучения радиационных эффектов в отношении населения и окружающей среды.

Ключевые слова: ядерные испытания, когортное исследование, международное сотрудничество.

Тұжырым

СЕМЕЙ ЯДРОЛЫҚ ПОЛИГОНЫНЫҢ ТЕРРИТОРИЯСЫНДАҒЫ ТҰРҒЫНДАРДЫҢ ДЕНСАУЛЫҚ ЖАҒДАЙЫН ЗЕРТТЕУДЕГІ ПРОСПЕКТИВТІ КОГОРТТЫ ЗЕРТТЕУДІҢ НЕГІЗГІ БАҒЫТТАРЫ

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Бұл статьяда ядролық сынақтың нәтижесинде, радиация алған Қазақстан тұрғындарының денсаулық жағдайын проспективті-когортты зерттеудің бағытттары көрсетілген.

Қоршаған орта мен тұрғындардың арасындағы радиациялық эффектілерді ұзақ уақытты зерттеу үшін Қазақстан, Европа, США ғаламдарының халықаралық бірлестігінің қажеттілігі нақтыланған.

Негізгі сөздер: ядролық сынақ, когортты зерттеу, халықаралық бірлестік.