CHERNOBYL DISASTER - PROMOTION OF FOLLOW-UP STUDIES

Anatoly Romanenko, Vladimir Bebeshko [1]

Research Centre of Radiation Medicine (Kiev, Ukraine)

Problem of clinically observed effects of irradiation and other damaging agents of Chernobyl accident is analysed in connection with the previous data. Several international and national scientific programs were performed during the 10 years after the accident Obtained data are extremely useful for the elaboration of the system of radiation emergency medical preparedness and assistance network in Europe Difficulties in diagnostic, therapeutic and statistical evaluation measures were characteristic for the first years after the accident. Future perspectives must include scientific investigation and practical help for the main groups of irradiated population on the international basis with the wide access to obtained data for the international community.

The analysis of the materials and the circumstances under which they have been received are the basis for determining the following stages in learning the factors of the CPPA influence upon the health conditions of the exposed population: stage 1: 1986 - 1990; stage 2: 1991 - 1992;stage 3 1993 - 1997

During 1986 - 1990 the investigations were carried out under the circumstances of the USSR within the framework of the Union programmes while special medical centres of the Union subordination, located in Moscow, took part in them. The major part of these investigations had been classified till 1989. To organise and conduct a long-term personal monitoring of people exposed to irradiation as a result of the CPPA the development of All-Union Distributed Registry (AUDR) of the People Exposed to the Irradiation Effect as a Result of the CPPA Disaster was being carried out. It was supposed to include 600 thousand of those suffered.

As a result of the studies of early and middle-term effects some scientific knowledge was obtained:

1. The observation of the health effects of ARS survivors showed the relative effectiveness of medical rehabilitation measures as well as the presence of postponed uncompensated disorders in different systems, mainly in kind of malfunctions of vegetative nervous system, diencephalic syndrome, changes in cellular immunity, digestive diseases, initial signs of myocardial dystrophy and bronchial mucous membranes atrophy

2 Presence of the reactions of disadaptation on the level of nervous, immune and endocrine system was found in population with radiation doses above 0 2 Gy These reactions were accompanied by the clinical signs of asthenic and asthenovegetative syndromes.

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1 Contributing co-authors D Bazyka A Kovalenko, L.Lyashenko, D. Belyi, I Homaziuk, N Bilko

In 1991-1992 the research was carried out under conditions of the USSR disintegration, development of national Ukrainian programs of investigations of the medical consequences of the CPPA First international scientific teams also contributed their efforts. It was revealed that:

1.ARS patients prospective follow-up showed regulatory disorders, as well as antioxydative defence, lipid exchange, haemopoietic and immune systems changes with the prevalence of blood system and gastroduodenal ulcerous and erosive processes.

2 In population exposed to the negative factors of CPPA a period of pathologic disturbancies frequency increase was begun with body's various organs and systems dysregulation .

3. General somatic pathology increase of inflammatory and dysmetabolic origin was shown .

4. The investigations of the specific features of liquidators' diseases conducted in the ICR RCRM showed chronic progredient course with the frequent psychoneurologic disorders.

5. Morbidity and mortality changes were shown in different regions contaminated as a result of CPPA. Most of the data obtained in regional hospitals were not supported by dosimetry.

During 1993 - 1995 the most of scientific research was conducted in accordance with the state programs such as National Program of Elimination the CPPA Effects and other . It was also formed by international scientific programs together with some international organisations (WHO, CEC and others).

1. Stochastic effects were shown in Ukrainian and Belorussian population (thyroid cancer)

2. A concept was established of late non-stochastic effects formation

Acute radiation syndrome (ARS) convalescents represented the most severely damaged group of the Chernobyl accident victims. 95 patients with ARS (40 %) in anamnesis exhibited haematologic disorders such as transient and stable leukopenia and leukocytosis Prevalence of chronic pathology was detected in the somatic status especially the tendency to increase of digestive tract diseases and stable increased respiratory pathology frequency Increased incidence of cardiovascular diseases was accompanied by the decrease of physical work capacity that was more typical in group of patients after ARS II-III. The decrease of physical and mental working capacity and concrete pathology of different organs and systems caused growth the number of disabled patients Almost all patients after ARS have the certificates of disablement

Psychoneurological disorders such as syndrome of vegetative dysfunction, asthenic, psychoasthenic and cerebropathic conditions have the tendency to decrease in comparison to 1986 level. Transformation to organic neurovascular pathology (arterial hypertension, discirculatory encephalopathy, psychoorganic syndrome with change of personality) was characteristic for the late effects. Mental capacity measured on sensomotor and abstract-logical activity models decreased with the degree of radiation damage.

Local radiogenic effects included 39 patients with radiation skin injuries and 17 cases of radiation cataracts. The frequency correlated with ARS stage and was equal to 100% in ARS-III. Other findings included vascular pathology of fundus and macular dystrophy are still under our observation.

Hypothyroidism was registered in 6 patients Steady and increasing blood cortisol and ACTH levels were changed by the sharp decrease. A stable hypotestosteronemia and low level of luteinizing hormone were revealed as well as a constant increase of prolactine which could promote a development of atherosclerosis In most of the patients a polyanime (spermidine and putrescine) blood concentration was increased . It could point on probable tumour promotion but up-to-date none of the cancer cases in persons with verified ARS diagnosis were shown

The changes of activity of enzymes of antioxidant defence, activation the processes of peroxide oxidation of lipids, weakening the mechanism of antiradical defence, increase of membranes damage by lizosomal enzymes were revealed in erythrocytes Hyperenzymemia is the evidence of destructive components on the cellular and tissue levels and is the prognostic negative sign that characterises the severity of pathological state. In 1991-1992 the essential decrease of haemoluminiscence indices were determined that could characterise the fall of level of peroxide system energetic abilities and could serve as the definition of long-term sequences.

Initial stage of pancytopenic immunodefficiency was substituted in one third of followed-up patients by quantitative and qualitative changes of immunity, including T-suppressor cell decrease and serum IgG and IgM discrepancies. At the remote period after the irradiation ARS convalescents could be divided in three different subgroups. The first consisted of persons with normalisation of immune system parameters. Second subgroup formed persons with constant lymphocytosis, monocytosis and dysimmunoglobulinemia. In the third subgroup of patients variable cellular immunity changes were associated with mixed immunoglobuline deficiencies.

It's assumed now that late effects in persons who were exposed in the dose limits under 1 Gy have to be divided into stochastic and non-stochastic. Correlation of stochastic effects with irradiation

could be revealed only statistically.

Due to the previous results obtained on hibakushi cohorts efforts were made to find the access of stochastic effects leukemia and thyroid cancer in exposed territories of Ukraine, Russia and Belorusssia on the base of published information . Obtained data led us to the suggestion that a significant changes in the health of the population exposed to a multi-factorial influence of Chernobyl accident had occurred during last decades. Today we know that the persistent functional destabilisation along with the individual reparative and compensatory insufficiency on the various levels of integration in irradiated patients with dystress and xenobiotic exposure etc. could lead to a total desintegration regulatory syndrome i e the primary formation of the functional and preclinical changes on the different levels with the subsequent evolution to distinct clinical pathology.

We are standing on the previously established position that the increase of functional consequences is originated at least in 0,25- 1 Gy dose limit from the primary initialising defects of regulation predominantly in central and vegetative nervous systems, hormonal-humoral regulation and immune systems interaction.

Psychoneurologic consequences are at present the important problem. Addition of the stressogenic factors of post-extremal situation in now a days supports the development and stabilisation of neurotic and anxious phobic reactions with the exit to the distinct psychosomatic pathology like somatic depressions, vegetative dysfunctions and stress diseases. The evolution of central and vegetative nervous systems consequences demonstrated a wavy type of clinical symptomatology. Intensive annual oscillations were characteristic for the patients with cardiovascular pathology. Similar tendencies were detected in broncho-pulmonary and gastrointestinal tract. The analysis of 119344 clean-uppers carrying in national register showed the increasing of the morbidity rates Pathomorphological studies also showed vascular disorders, the distrophycal, atrophycal, sclerotic and dyscirculatory disorders of parenchymatous organs.

There is a significant increase of mild mental retardation and borderline emotional and behavioural disorders prevalence in the prenatal irradiated children as well as their parents' mental health deterioration in comparison with the control.

The chronology of thyroid gland changes included: the initial reaction (1986), the period of "thyroid calm"(1987-1989), 1990-1992 - beginning of realisation of oncogenic effects (1990-1992)and the stage of prominent disorders- autoimmune thyroiditis, hypothyreosis and thyroid cancer (from 1992).

Haemopoietic and immune systems are traditionally considered to be highly sensitive to irradiation, especially in childhood. Haematological survey of Pripyat-town children and those who lived at contaminated territories of Ukraine during the primary iodine period revealed no features of haematological disorders characteristic to acute radiation syndrome Equivalent doses were in the interval of 1 2 to 12 cGy. Various changes of mononuclear cells, granulocytes and platelets, their membranes and organells in some patients with irradiation reactions were related, to our opinion,

not only to irradiation but to the whole complex of Chernobyl factors The certain part of interest should be here given to the lead as a factor of the discoordination of heme synthesis but at present detected lead concentrations in blood samples of Ukrainian, Belorussian and Russian children are under the admitted limits as revealed by Soviet and international experts (IAEA,1990)

Ten years follow-up studies didn't reveal any specific radiogenic influences on a haemopoietic cells, the increased metabolic activities were the most persistent findings during all the period. High compensatory abilities of haemopoietic tissue could be demonstrated. A distinct decrease of qualitative alterations could be seen in granulocytes, lymphocytes and platelets of children irradiated in the first days of the accident

Data of investigations showed to our mind the high valuability of detection of the early aberrations of structural elements of osteon - bone hydroxyapatite - the main source of macroergic substances and the microelements needed for the normal haemopoietic function in irradiated individuals.

Our experience of studying the Infra-Red spectra of bone tissue at the early stages of leukemia and in irradiation showed the necessity of extending the investigations in this sphere. Wide screening of urine pyrophosphates which are predominantly of boneorigin could allow us to determine the development of leukemia and osteosarkoma.

Immunologic studies demonstrated an increased frequency of some gene complexes associated with HLA antigens A, B, C, the decrease of helper/inducer and mitogen response related antigens and the increased expression of pan-B and B-blast antigens The significant signs of immune system overtension were the presence of premature CD1+, CD4+8+, CD10+ cells, intensified enzymatic activities and decreased phagocytosis accompanied by the consequences in CD25 and CD71 receptors.

The key point in the described late irradiation health effects is the involvement of the informational and regulatory control systems. The consequencies at that level, to our mind, initiate the alterations of the vegetative effector systems and main physiological processes The possible explanation lies in the balance of alteration and compensation, regulation rates Molecular and cell reparation in the tissues with the higher rates is out of the control of damaged highly differentiated postmitotic nervous and endocrine cells where the reparation and compensation rates are much slower at the cell level and may be found only at the system level. In the case when the alteration effect doesn't predominate upon the reparative activities the total radiogenic defect liquidation was the result. In the case of low level simultaneous irradiation the stimulation of reparative activities can lead to the hypercompensation or so called radiation hormesis To our mind, the attitude to the mentioned effect must be very careful in clinical studies because of the absence of the data about the distinct positive health effects in long-term investigations concerning the contamination with the not divided radionuclide compositions for example in Chelyabinsk, Semipalatinsk, Windscale etc.

In many cases the real circumstances were the opposite The exposure with the alteration effect can be higher than a threshold determined as revealed by our data by three major phenomena (a) genetic and phenotypic predisposition, (b)the influence of risk factors of non- radiation origin,

(c)accompanying pathological and pre-morbid disorders. Synergism of Chernobyl accident negative factors including dystress is the characteristic feature in our clinical practice In these patients the rehabilitation wasn't obtained with the radiation defect repair. Regulatory links can't return to the old level of organisation. In the other words, a dysregulatory and desintegration defect is retained with various degrees of expression It could be the excellent soil for the functional premorbide or distinct somatic pathology, prolonged and aggravated course of diseases.

New medical technologies, data collection systems, soft and hardware were elaborated for revealing of low-dose radiation exposure in various fields of general and laboratory medicine (psycho-neurology, cardiology, broncho-pulmonary diseases, haematology, immunology, clinical chemistry etc) Special attempts are made to enable the health effects screening in exposed population on the regional level at the special regional hospitals and sophisticated studies of non-stochastic and stochastic effects in the Institute of Clinical Radiology RCRM etc.

Complex investigation of the specific markers for the diagnosis of radiation induced stochastic and non-stochastic disorders is of extremely value and the research in the field of radiosensitivity to low doses in our Centre could be extended, and the problem of professional selection for work in the irradiation zone and they could be the basis of the radiation induced onco-haematologic pathology. A leading place there could be given to immunologic phenotypic and genotypic features estimation assays, cytogenetic studies of stable and non-stable lymphocyte and spermatozoid aberrations, EPR and NMR-studies etc These studies also are the background for the radiation emergency medical aid and preparedness system which must include three stages:

1. emergency aid with the help of first line medical efforts, local medical preparedness is also essential at this stage;
2 early and mid-term effects evaluation and counterstanding with the aid of up-to-date medical tech nologies,
3 longitudinal follow-up studies by the qualified institutions and medical staff.

Our post-Chernobyl experience showed the effectiveness of such a system in Kramatorsk and Chernobyl NPP incidents.