Chapter 5. NEUROPSYCHIATRIC EFFECTS OF ACUTE IRRADIATION

5.1. Introduction

Following chapter is devoted to the modern opinions regarding human nervous system injury after ionising radiation acute impact on the present «radioecological» stage of radiation medicine progress. The intention to title the chapter as «*High radiation doses* neuropsychiatric effects» however there is no clear definition of the «high» (both as the «low») radiation doses in literature up-to-date.

According to the accepted terminology in the field of radiation security and dosimetry, the *low doses* are considered as received in *long-term* exposure and not exceeding 250 mSv per year (5 maximum permissible doses). Regarding the «dose-effect» dependence dose rates less than 6 mGy·hour^{-1} are considered as low ones both with that of acute irradiation doses not exceeding 0.2 Gy [Bennet B.G., 1996]. The *high radiation doses* are considered capable of resulting in acute radiation sickness (ARS) and directly hazardous to the life of affected person. Usually these doses are considered exceeding 1 Gy [Burnazyan A.I. et al., 1975; Ilyin L.A. et al., 1985; Kozlov V.F., 1987]. At the same time data are presented regarding radiation sickness genesis possibility in combat circumstances with doses less than 1 Gy (0.6–0.9 Gy) [Hempelman L.H. et al., 1952; Molchanov N., 1960]. A.K. Guskova et al. (1988) on the background of Chernobyl nuclear power plant accident experience concluded that total irradiation dose of ~0.7 Gy may be qualified as the minimal value resulting in blood content alterations peculiar to the ARS of 1st degree. U.G. Grigorjev (1963) regarded the 6– 10 Gy values to the «high radiation doses». However the concepts of «high» or «big» doses in the foreign literature are as a rule regarded to the dozens of Gray levels [Kimeldorf D., Hunt E., 1965; Gilbert H., Kagan A., 1980; Coggle J., 1983; Mettler F.A., Moseley R.D., 1985; Gutin P.H. et al., 1991; Mettler F.A., Upton A.C., 1995]. In our opinion the terms «high», «medium» and «low doses are to be regarded as scientific slang that on the one hand reflects their high practicality and on the other — their application introduces terminological mess.

Mature nervous cells according to G.W. Casarett (1980) are the fixed post-mitotic cells and therefore according to the radiobiology law of J.A. Bergonie & L. Tribondeau are to be radioresistant. However in the known monographs published in late 50th–60th about ionising radiation effects on nervous tissue the named high radiosensitivity was demonstrated [Grigorjev U.G., 1958, 1963; Livshits N.N., 1956, 1961; Lebedinsky A.V., Nahilnitskaya Z.N., 1960; Livanov M.N., 1962; Kimeldorf D., Hunt E., 1969]. Finally the conception was proposed about nervous system high radiosensitivity under its low radio susceptibility. This conception also regards the contradictory attitude [Grigorjev A.U., 1991].

Objections also could not be avoided in the report of United Nations Scientific Committee on Atomic Radiation Effects — UNSCARE (1982). So the reversible functional disorders and behaviour alterations were marked taking place in animals under radiation doses exceeding 0.5 Gy. In some cases the ionising radiation can cause effects in doses of several dozens μGy *but no any testifying is available of irreversible alterations rise in such doses*. From the point of view of irreversible damage the central nervous system of adult is less sensitive than other viscera and tissues according to the report authors. UNSCARE experts underlined that in the further years no any new data substantially changed these opinions. New information was received in the field of vascular system role in pathogenesis of neurological syndromes induced by radiation [Reinhold H.S., 1980] however its real role remains unclear because the vascular alterations were registered later than in 1 year after exposure. Neurophysiological methods enabling the ionising radiation impact on brain registration [Livshits W.N., 1960; Minamisawa T. et al., 1972, 1977] indicated that it is radiosensitive within some aspects. However in general the UN SCARE experts concluded that *the brain is considered rather radioresistant one*. Doses ever the 20 Gy are required to receive morphological disorders [Zeeman W., 1961].

The same UNSCARE report (1982) stated that continuously elevating amount of data testified concept regarding possibility of neurones structure damage by relatively low radiation doses. Thus data were presented about brain cortex degeneration under 1–6 Gy doses of ionising radiation impact. Such degenerative alterations increased with the survey period after irradiation [Vasculescu T. et al., 1973], pointing out that *nervous tissue is not to be considered simply radioresistant*. In the Report 2nd volume on page 382 the UNSCARE experts were ought to recognise that *in spite of the nervous system earlier was regarded to radioresistant tissues, it can be considered radiosensitive one.*

Nervous system radiation injuries are regarded to the *non-stochastic effects* of radiation exposure i.e. «effects, severity of which changes proportionally to the dose value and therefore the threshold can appear». Besides the integral irradiation dose the nervous system three-dimensional position, time parameters and brain maturation degree at the time of irradiation are of substantial importance in its injuring effects realisation. The nervous system reaction types on radiation impact are stated: *functional or reflex response* in form of the non-specific orientation reaction on exposure as the irritant, and *nervous system tissue direct damage* under high radiation doses impact [Guskova A.K., Shakirova I.N., 1989; Torubarov F.S., 1989]. At that the clear dose dependence is considered regarding the *early somatic effects* manifestation satisfactory presented with sigma-shaped curve with definite minimal dose value presence marked as the threshold [Ilyin L.A., 1985].

Some of these seemed generally acceptable and stable positions rise objections. So it is not acceptable to agree that nervous system injuries are presented with exclusively non-stochastic effects, as the *stochastic* ones exist also (tumour forms of irradiation remote consequences [Moscalev U.I., 1991] and, probably, genetic effects).

Besides that the statement «nervous system traditionally is considered radioresistant in spite of functional reactions ability under low radiation doses» [Guskova A.K., Shakirova I.N., 1989] is unacceptable. That means the nervous system is highly radiosensitive (meaning «functional» alterations in response to the radiation impact) and at the same time — the radioresistant too (regarding «organic» radiation damage). Such argumentation are based upon the scientifically not substantiated opinion regarding «functional diseases» or «purely functional alterations not accompanied by organic, structural damage» existence possibility [Sarkisov D.S., 1994].

Obviously the diseases selection into «functional» and «organic» ones was based upon the insufficient knowledge value concerning disease pathogenesis — all the diseases with unclear genesis mechanisms were regarded to the «functional». Here, for example, up to the end of nineteenth century the epilepsy, tetanus, catalepsy etc. were regarded to the neuroses (as the «functional disorders» classical examples) as at that time considered them having no pathologic anatomy basis [Ushakov G.K., 19878]. However F.Raymond (1907) as early as in the XX century beginning pointed out that anatomical alterations in neuroses are absent not absolutely but only the available for detection with «modern study methods» [Cited from G.K. Ushakov, 1987]. Consequently the diagnostic technology progress implacable will lead to the so-called functional diseases circle narrowing. The recognition of such «purely functional» disease as schizophrenia as brain organic disease due to computer EEG, neuropsychiatric research and MRI-tomography application results is the indisputable proof here [Fuller Tory A., 1996].

One cannot agree with the «functional pathology» identifying with organs and tissues alterations reversibility. As truly marked D.S. Sarkisov (1994) the reversible alterations always are accompanied by respective morphological injuries and thereby are not functional but structure-functional ones, and moreover even the severe alterations (liver cirrhosis, expressed liver hypertrophy etc.) in case of inducing reason elimination can undergo complete or nearly complete reversed genesis.

On the background of stated above the statement of nervous system «functional radiosensitivity» and at the same time «organic radioresistance» inconsistency becomes obvious. Any nervous system function alterations induced by ionising radiation have in its basis the organic (biochemical, ultrastructural etc.) neuron alterations i.e. actually are the structure-functional symptoms. Psychologically that is understandable the intention of radiologists to consider the nervous system radioresistant (or at least «morphologically radioresistant») as otherwise the main radiobiology dogma will be not executed — the Bergonie—Tribondeau law stating the fissile cells being radiosensitive only. However the permanently increasing amount of experimental and clinical data testify the named law limited nature.

In this chapter we intended to make stress on both the «dose—effect» dependence review in wide dose range and the threshold dose values determination regarding radiocerebral effects providing especial attention to the neuro- and psychological aspects.

Some psychoneurological disorders and health problems connected to the ionising radiation impact according to the International Diseases Classification of 10th review (1992) are shown in Table 5.1.

5.2. Nervous System Radiation Damage under the Local Exposure

Local exposure from external ionising radiation sources leads to the characteristic clinical syndromes forming. Head irradiation in definite doses can induce the skin and mucosa injury, lens alteration, and in high doses — other eye structures and *brain* damage. Neck irradiation results in *conductive alterations with expressed vegetative-vascular disorders*, including head vessels regional circulation disorders and thyroid gland hypo- and dysfunction. Lung fibrosis, heart muscle and *spinal organic damage* rise after mediastinum zone and chest irradiation in oesophagus cancer, lung or mediasinum tumours. After abdomen and pelvis minor zones exposure the *regional vegetative-vascular disorders occur* with pronounced lymphopenia. In case of extremities irradiation the skin, vessels local alterations prevail both with secondary ones in muscular and bone tissues trophic [Guskova A.K., Bajsogolov G.D., 1971].

Table 5.1

SOME DISORDERS RELATED TO THE IONISING RADIATION IMPACT THROUGH THE DISEASES INTERNATIONAL CLASSIFICATION 10th REVISION (GENEVA, WHO, 1992)

VI. NERVOUS SYSTEM DISEASES
G62.2 Other identified polyneuropathy Radiation-induced polyneuropathy
G93.8 Other identified brain diseases Post-radiation encephalopathy
G95.8 Other identified spinal cord diseases Myelopathy: Radiation-induced
XV. PREGNANCY, CHILDBIRTH AND AFTERBIRTH PERIOD
O35 Maternal care regarding known or foetal suspected anomalies or injuries *Including* foetus state being reason for examinations, hospitalisations or pregnancy termination
O35.6 Maternal care regarding (suspected) foetus radiation injury
XVI. CERTAIN STATES OCCURRING IN PRENATAL PERIOD
P00.5 Fetus and new-born injury owing to the injury of mother Fetus and new-born injury owing to the injury of mother classified in S00–T79 (*including* T66 Radiation sickness)
XIX. INJURIES, POISONINGS AND OTHER IDENTIFIED CONSEQUENCES OF EXOGENOUS CAUSES
T66 Unidentified radiation effects Radiation sickness
XX. EXOGENOUS CAUSES OF MORBIDITY AND MORTALITY
W88 Radiation impact *Including* radioactive isotopes X-rays
X58»X59 Accidental impact of other and non-identified factors
Y35»Y36 Legal interventions and military operations
Y36.5 Military operations with nuclear weapons application Radiation impact from nuclear weapons Other direct and secondary effects of nuclear weapons
Y70»Y82 Medical procedures side effects in diagnostics and treatment
Y78 Radiology procedures application side effects
Y85»Y89 Consequences of morbidity and mortality exogenous causes
Y86 Other accidents consequences
Y89 Other exogenous causes consequences
XXI. FACTORS EFFECTING HEALTH STATE AND CONNECTED TO HEALTH PROTECTION SERVICES
Z00»Z13 Persons faced health protection services for examinations and treatment
Z01.6 Radiological examination
Z40»Z54 Persons faced health protection services for specific procedures and health protection
Z51 Radiotherapy
Z54.1 Recovery after radiotherapy
Z55-Z65 Persons with potential health detriment due to social-economical and psychosocial circumstances
Z57 Occupational impact of risk factors
Z57.1 Occupational radiation impact
Z58 Problems connected to the environmental physical factors
Z58.4 Radiation impact
Z80-Z99 Persons with potential health detriment due to family, personality anamnesis and definite conditions impacting health
Z92.3 Personal radiation history Therapeutic irradiation (*excluding* Z57.1 Occupational radiation impact Z58.4 Radiation impact)

B. Rajewsky (1959) presented the dose of 10–40 Gy as the threshold value for *nervous tissue initial injury* and the 30–60 Gy for *severe damage*. Dose of 50–300 Gy several authors consider the approximate value for *brain tissue direct early necrosis* induction without separate brain structures clear selectivity in damage. At that the brain damage signs appear already in first days or even hours after irradiation. Their clinical content is the *convulsive or hyperkinetic syndrome*, brain swelling signs with *general brain and meningeal symptoms* and *paralyses* rise. Lethal exit occurs within first 1–5 days [Brunner H., 1920; Eldred E., Trowbridge W.V., 1952; Grigirjev U.G., 1963; Guskova A.K., Bajsogolov G.D., 1971, etc.].

Brain local exposure with 15–30 Gy doses also leads to the central nervous system necrotic alterations however with some selectivity i.e. the *gray substance, ganglionic elements, autonomous nervous system and sensitive nuclei* damage

dominate. Necrosis focus relation to the altered vascularisation zones is noted as the result of sharply expressed injuries in vessels where endothelium in damaged in doses of 12–16 Gy. According to A.K. Guskova & G.D. Bajsogolov (1971) the *vascular disorders* under the doses of 8–12 Gy stipulate in high extent the more remote narrow-localised brain necrotic alterations rise (more often in brain white substance). The relatively long-term period of symptoms gradual elevation through the central vessels thrombosis type or their «shimmering» because of brain ischemia for the first time of transient nature precedes expressed focal pathology clinical manifestations. Symptomatic is formed within several months or years.

Brain damage selectivity is elevated under 4–6 Gy doses impact. Necroses rise terms are prolonged. Demyelination focuses are located mainly in brain stem and spinal cord white substance; sections of altered ganglionic cells are alternated with relatively safe elements. Astrocyte neuroglia reactions are mainly of proliferative character. Cloudy swelling and sometimes — degeneration are observed in olygodendroglia element [Bebekova A.F., 1961; Portugalov V.V., 1956, 1962]. Soft, disseminated slowly progressing clinical symptomatic presents itself some kind of dissociation between its mild expression and gradually forming sharp pathohistological pattern. Vascular disorders in this dose range are moved to the backside or appear later compared to the advance in time functional shifts in neurones activity.

Mainly reversible deviations in some neurones and more clear prevalence of general disseminated non-sharp alterations over focal drop-out symptoms are typical for the again lower dose range according to A.K. Guskova & G.D. Bajsogolov (1971). In their opinion the brain general discirculation disorders role under local irradiation in high doses is not enough significant. However their importance is appreciably rising in lowest dose range where they can become primary ones in several neurological disorders pathogenesis.

Spinal cord focal post-radiation necroses clinical presentation is of much common with myelitis subacute forms, and alterations in conducting tracts myeline — with such slowly progressing demyelination processes as funicular myelosis or disseminated sclerosis spinal form [Kurshakov N.A. et al., 1962].

Peripheral nervous system is the least opened to injury. Regional polyneuritis is described in case of dozens of Grays exposure on receptors and peripheral nerves. A.K.Guskova & G.D.Baisogolov (1971) noted the so-called *toxic-ischemic neuritis* accompanying extremities severe local radiation trauma. Neurological symptomatic in such cases is more close to the ascending *vegetative ganglioneuritis* presentation but with its severity and pain type is similar to the real *causalgia*.

As it was noted above, at present they consider that single fractional irradiation in doses less than 2 Gy is the *tolerant (non-injuring)* for the central nervous system [Van der Kogel A.J., 1986, 1991; Fike J.R. et al., 1988; Asai A et al., 1989]. Tolerant dose of 55 Gy for 5.5 weeks for head exposure and 65 Gy — for small zones irradiation during 6.5 weeks are considered experimentally and clinically determined. Radiation damage probability is elevated with fraction value rise and integral dose absorption for short period. Spinal cord neck and lumbar part exposure tolerant doses vary between 35 Gy for 4 weeks and 50 Gy for 5 weeks, that for thorax part — up to 45 Gy for 4.5 weeks [Badmajev K.N., Smirnova R.V., 1982; Guskova A.K., Shakirova I.N., 1989; Griem M.L., 1989; Moskalev U.I., 1991; Schultheiss T.E. et al., 1995].

At the same time A.L. Karpovsky (1985) after single irradiation with doses of 1–6 Gy selected the separate disease — *central nervous system slowly progressing disease* [Cited from Moscalev U.I., 1991], and A.J. van der Kogel (1991) demonstrated the *central nervous system chronic progressing injury* rise probability in remote period after irradiation with relatively low doses.

Eyes are considered as one of the most radiosensitive organs. U.I. Moscalev (1989) noted that however any eye part can be injured by ionising radiation, but *lens* is the most radiosensitive for remote consequences. B. Rajevsky (1959) regarded lens epithelium to the tissue type with moderate radiosensitivity. According to U.I. Moscalev (1989) the *minimal cataract-inducing dose* is 3–5 Gy. A.K. Guskova et al. (1964) presented the value of 2 Gy. The IAEA experts (1992) consider 0.5 Sv as threshold equivalent dose for radiation cataract in human under single exposure; for new-borns — single irradiation with equivalent dose on lens of 0.1 Sv and 0.2 Gy in a child (the absorbed dose of 1 Gy corresponds to the 1 Sv equivalent dose for eye β- & γ-irradiation; for neutrons, protons and other particles the absorbed dose value calculation into the equivalent is to be conducted with weight coefficients application).

Eye vessels and hemodynamic disorders were registered under total irradiation integral doses of 0.5–1.0 Sv through regional hypotension and eye vessels permeability elevation. Eye vessels morphological injuries were registered in doses of 1.5–4.0 Sv total and especially 30–50 Gy local irradiation [Lvovskaja A.N., 1969].

Eye retina and optical nerve according to A.K. Guskova & G.D. Bajsogolov (1971) both with all ectoderm neuronal elements are to be regarded to the high radiosensitive structures through the functional reactions criterion both with substantial morphological radioresistance. As stated above the *retina electric potential* alterations *and phosphene rise* observed already in 1 mGy dose both with dark adaptation disorders are the most radiosensitive phenomenon. *Retina circulation transient disorders* were registered in total and local irradiation with 1.5–10 Gy doses. Extremely stable and almost irreversible *retina structural alterations* were observed in doses of 30–50 Gy. Eye vessels structure injuries and *secondary glaucoma genesis* as the anterior parts stricture-dystrophic alterations aftermath were found in remote terms after exposure to highest doses. Glaucoma acute attacks were observed after eye zone irradiation with 60–100 Gy doses with preceding iridocyclitis, uveitis, anterior camera haemorrhages and anterior camera corner obliteration. Usually glaucoma rises in 2–15 months after irradiation and was of malignant clinical pattern. Miotic medications and surgery against glaucoma not decreased the pressure, blindness, extremely intensive pain were risen that ought to conduct the eye enucleation. Uveal tract vessels alterations especially that in iris and corpus ciliare were the

glaucoma rise cause leading to the blood circulation disorders, exudation and hemorrhages [Dolfus M.A., 1950; Jones J.J., Reege A.B., 1953; Starichkov M.S., 1959 — cited from Guskova A.K. & Bajsogolov G.D., 1971].

Majority of data regarding nervous system injury after radiotherapy were received from *neoplasm* therapy experience however the ionising radiation were applied for non-oncology diseases management. Scholz applied the brain irradiation with 43 Gy for 3 days in *schizophrenia* treatment. However the brain damage was revealed 20 months later. Bailey et al. considered the wire made from ^{60}Co application for *lobotomy* conduction [Cited from F.A. Mettler, Jr. & R.D. Morsley, Jr., 1985]. V.B. Dutov et al. (1989) and Smirnov V.K. et al. (1991) reported the positive therapeutic effect of impulse roentgen irradiation application for *schizophrenia* management with mainly deficient and apathetic-abulic symptomatic. Stimulating effect of impulse X-ray exposure remained for 5–6 days. However no any data are available regarding radiotherapy application remote consequences.

In 50–60th nearly 20,000 Israel children were exposed to X-ray irradiation on head for *ringworm management*. Average doses on brain constituted 1.3 Gy. E. Ron et al. (1982) the 20 years later revealed clear trend to the *central nervous system damage* signs growth among irradiated in childhood compared to the non-exposed. More low school progress, IQ and some psychological tests indices decrease, graduating less number of school forms, some mental disorders genesis risk elevation, mental retardation incidence moderate elevation were noted. Authors concluded that *ionising radiation impact on the developing brain can result in the central nervous system injury*. I. Yaar et al. (1979, 1980, 1982) studied the brain spontaneous and evoked electric activity in those patients. EEG visual analysis enabled to reveal only slight deviations in electrical cerebral activity among examined persons. At the same time the spectrum analysis revealed the β-range spectrum power substantial increase that was estimated as the radiation impact «trace». On the background of EEG spectrum and brain visual evoked potentials analysis authors testified the possibility of *brain remote radiation damage* rise.

E. Ron & B. Modan (1984) demonstrated excessive amount of *brain malignant tumour* cases in children irradiated for the *ringworm management*. The relative risk elevation parallel with age growth at the time of exposure was registered after 1.21–1.39 Gy doses applied on the brain outer layer and 0.95–1.21 Gy — on the depth of 2.5 cm. R.E. Shore et al. (1976) on the epidemiological study basis estimated the *brain tumours genesis* risk value within range 1.3–6.3 cases per 1 million people/year that were exposed to 10 mGy dose. *Brain tumours* incidence elevation in 8 times with average latent period of 22 years was revealed in children exposed to radiotherapy for head and neck tumours. U.I. Moscalev (1991) presented precise review of ionising radiation blastogenic effect on nervous system.

Pathophysiology of remote *intellect alterations* after cranial radiotherapy remains unclear [Mulhern R. et al., 1991]. Authors selected abstract thinking and ability to ponder on, ability for knowledge reception, ability for problems solving, adaptation to environment, creativeness, general knowledge, linguistic and mathematical abilities (giftedness), memory and speed of thinking among various definitions of intellect. Neuropathological findings after cranial radiotherapy that can potentially correlate with neuropsychological alterations include focal or diffuse zones of *white substance demyelination, mineralized microangiopathy* both with *non-specific cerebral atrophy*. Clinic-histologic syndrome *«leukoencephalopathy»* was revealed both in children and adults. This pronounced encephalopathy is characterised with lethargy, progressing attacks and pareses. Roentgen computer tomogrammes usually present the white substance density decrease with calcification and spots of white substance coagulation necrosis. However the cranial radiotherapy effect on IQ analysis both in children with brain tumours and acute lymphoblastic leukaemia is the extremely complicated task because of many other factors presence resulting in the intellectual alterations. Authors concluded that the IQ isolated alteration in adults is the less sensitive indicator of cognitive function disorders than in adults. In any case according to the authors' opinion, patients are guaranteed the daily duties execution, work, social and personality adaptation both with life satisfaction after cranial radiotherapy.

P.F. Pradat et al. (1994) pay attention to that *peripheral nerves* commonly are considered radioresistant on the contrary to the central nervous system. However experimental and clinical observations present proofs of peripheral nerves injury after radiation therapy. Pathophysiology of this phenomenon in authors' opinion remains unclear. Vascular disorders probably are of important role here. The axons and Schwann cells direct injuries are marked both with nerved hardening in focuses of radiation fibrosis. Clinically the *brachial (shoulder) plexopathy* is the radiation therapy well-known complication but the radiation injury can be observed in all the *peripheral nervous system* structures — nervi craniales, radices, plexus and nervous stems. Early and reversible plexopathy syndrome differs from classical progressing form with unfavourable outcome. Radiation-induced tumours of peripheral nerves are rare.

D.D. Roman & P.W. Sperduto (1995) underline that ionising radiation is the invaluable therapeutic facility in cancer management. After patient survival providing by means of radiotherapy the concern is to be focused upon the remote side-effects management. One of such effects — *the neuropsychological injury* remains incompletely understandable. The so-called low radiation doses on the whole brain (18–24 Gy) induce in children the *mild remote IQ decrease*. In this population group the high level of studying inability is observed with academic progress decrease that can be stipulated more obviously by *attention and memory disorders* than the intellectual level decrease. Children exposed to the high radiation doses for brain tumours radiotherapy were peculiar with more pronounced *cognitive decrease*. Authors consider that some cognitive functions including the memory also, can be more subject to the damage than other ones.

T.E. Schulthesis et al. (1995) note that in spite of central nervous system radiation injury pathognomonic characteristics absence the *demyelination and malacia* are the permanently dominating morphology signs of *radiation myelopathy*. *Cerebral atrophy* was observed most often in patients suffering neurological deficiency after chemo- and radiotherapy with *neurocognitive deficiency* being connected to the *white substance* diffuse injuries. In authors opinion the *radiation myelopathy* genesis is possible in 57–61 Gy doses on spinal cord in chemotherapy absence. *Brain necrosis* in

adults is observed under doses exceeding 50 Gy. The *neurocognitive effect* however was noted in lower doses too especially in children. The radiation effects expression for brain is considered higher compared to that for spinal cord. White substance diffuse damage can be stipulated by ionising radiation impact and induce neurological deficiency, but the *leukoencephalopathy* was rare observed in chemotherapy absence.

The MRI-studies high informative capacity was demonstrated in the last years works regarding the radiation injury consequences and their high coincidence with histological data. This non-invasive diagnostic technology application is considered as capable for the *tolerant doses more precise identification* for the central nervous system [Kennedy A.S. et al., 1955]. E. Laramore (1991) demonstrated that ionising radiation with high linear energy transfer rate i.e. neutrons, π-mesons and heavy ions effectively destroy the malignant neoplasm and the side-effects in brain normal tissues are almost absent.

5.3. Acute Radiation Sickness Neuropsychiatric Characterisation in Human

5.3.1. Problem State at Present

Acute radiation sickness (ARS) is the general generalised disease induced by the short-term impact of ionising radiation (from several hours to 1–3 days) both from external or internal exposure in effective doses exceeding 1 Sv [Kurshakov N.A., 1963; Guskova A.K. et al., 1964; Guskova A.K., Bajsogolov G.D., 1971].

L.A. Ilyin (1994) presented data that about 500 persons suffered the ARS before Chernobyl disaster in the former USSR after radiation accidents, radiation norms violation in some facilities, research institutes engaged in atomic programs (mainly in the atomic industry maintenance period) and in the institutions of military profile (including accidents on the nuclear submarines).

A.K. Guskova & G.D. Baisogolov (1971) marked that *physiological* deviations registration in several systems (including nervous one) under 0.01–0.1 Sv integral doses and even less than 0.01 Sv will become available with diagnostic technologies improvement. Some *specific* alteration of physiologic regeneration in tissues most subject to radiation injury both with chromosome apparatus alteration are registered within dose range 0.1–1 Sv. The clear syndrome of *radiation disease* can be observed in this dose range under general relatively uniform irradiation. In one-moment and short-term exposure to the doses around 1 Sv the unclear form of ARS is induced. In case of the same doses absorption for years or months the slowly forming clinical syndrome of not severe chronic radiation disease can rise. Dose values of 1–10 Sv are to be regarded to the *indubitably injuring* category. Through the further dose evelation (10–100 Sv) the *bowels, blood circulation and nervous systems* injuries obtain leading positions in patho- and tanatogenesis. Conditions when the lethal exit occurs within hours or even minutes after irradiation (death «under beam») in authors opinion is successfully described with the *radiation trauma* term proposed by P.D. Horizontov & A.A. Vyshnevsky.

On the thirteenth of August 1986 the USSR Ministry of Public Health by the order No1082 sanctioned medical documentation Form No133/U being Annex No2 to the Central Military-Medical Board (CMMB) of the USSR Defence Ministry (DM) directive NoDM-21 (1986) *«Registration Form for Person Exposed to Radiation Impact in NPP Accident»*. According to this document the military-medical institutions were to settle the following diagnoses: 1) healthy; 2) somatic disease without clinic-haematological indices; 3) radiation reaction with haematological indices instability; 4) radiation reaction with asthenic-vegetative syndrome; 5) radiation reaction with neurocirculation dystonia; 6) radiation reaction with stomach and bowels functional disorder; 7) radiation reaction with skin and mucosa isolated β-injury; 8) ARS. Obviously the autonomous nervous system (vegetative) regulation disorders were regarded as ionising radiation impact presentation or radiation sickness pre-clinical form. However academician L.A. Ilyin on the IAEA International Conference «Ten Years after Chernobyl: Summarising Accident Consequences» April 8–12, 1996 (Vienna) in discussion stated that vegetative-vascular dystonia diagnostics in clinics among «practically healthy» ChNPP accident survivors was conducted according to the authorities directive aiming the Trade Unions funding their hospitalisation. As the result many of those persons are sure they survived the ARS.

In the USSR the accidental normative for professional irradiation was not more than 0.25 Sv whereas that for troops in case of nuclear assault constituted 0.5 Sv [Ilyin L.A., 1994].

American military radiologists presented the *pathophysiology effects* dependence *upon irradiation doses* as following (Table 5.2):

Table 5.2

DOSE RANGES AND RESPECTIVE PATHOPHYSIOLOGY MANIFESTATIONS (by R.W.Young, 1987)

Doses Range (Gy)	Pathophysiology manifestations		
	Prodromal effects	Disease manifestation period effects	Survival
0.5–1	Mild	Blood cellular content mild decrease	Actually undoubted
1–2	From mild to moderate	Bone marrow injury initial symptoms	Highly probable (>90%)
2–3.5	Moderate	from moderate to severe injury of bone marrow	Probable. Mortality rate from 5 to 50%

3.5–5.5	Severe	Bone marrow severe injury	Mortality rate from 50 to 99% within 3.5–6 weeks
5.5–7.5	Severe	Bone marrow pancytopenia and bowels moderate injury	Death within 2–3 weeks
7.5–10	Severe	Combined gastrointestinal and bone marrow injuries; hypotension	Death within 1–2.5 weeks
10–20	Severe gastrointestinal injuries; early transient battle–unworthiness; gastrointestinal death		Death within 5–12 days
20–30	Gastrointestinal and cardiovascular injuries		Death within 2–5 days

A bit different is the opinion of Nagasaki Association Working Group for Hibakusha Medical Care (1996) regarding biological effects dependence upon single general irradiation dose that is shown in Table 5.3.

Table 5.3

IONISING RADIATION SINGLE DOSE AND IMPACT ON HUMAN ORGANISM (According to the Nagasaki Association for Hibakusha Medical Care (NASHIM) data, 1996)

Dose	Effects
Less than 0.25 Sv	No impact presented
0.5 Sv	Temporary decrease in leukocyte content
1 Sv	Nausea, vomiting
1.5 Sv	Radiation «hang-over» (state like alcohol «hang-over») occurs in 50% of persons
2 Sv	5% of people die
4 Sv	50% of persons die within 30 days (half-lethal dose)
7 Sv	100% of persons die

At present the *half-lethal dose* LD_{50} is about 2.8 Gy for Hiroshima and Nagasaki victims and probably 3 Gy — for the Chernobyl accident victims [Wagemaker G. et al., 1996].

A.K. Guskova & G.D. Bajsogolov (1971) precisely worked out classification of the radiation sickness and ARS in particular. *Cerebral form* of ARS occurs under doses exceeding 100 Sv, *toxemic* — in case of 50–100 Sv, *intestinal* — 10–50 Sv and *typical (bone marrow)* — 1–10 Sv. The last form is divided in the three severity degrees corresponding the average dose ranges: *1st (mild)* — 1–2.5 Sv, *2nd (moderate)* — 2.5–4 Sv and *3rd* — 4–10 Sv.

However, not all the researchers agree with opinion of A.K. Guskova & G.D. Bajsogolov (1971) regarding the ARD selection in several forms depending on the leading syndrome. N.A. Kurshakov & I.S. Glazunov (1960) considered that not only organs and tissues «critical» within stated doses range are injured in acute radiation sickness but other organs and systems of organism. These authors especially disagreed with concept that exclusively haemopoietic system state defines disease outcome in doses up to 10 Gy. In their opinion the *nervous*, cardiovascular, digestive and other system disorders are to be taken into account. But according to the opinions of A.K. Guskova & G.D. Baisogolov (1971) those disorders on the contrary to the haemopoiesis alteratiins are not so pronounced to impact substantially on organism state. However as it was stated above, A.L. Karpovsky (1985) selected the separate disease — *the central nervous system slowly progressing radiation sickness* after single radiation exposure to 1–6 Gy doses [Cited from Moscalev U.I., 1991], and A.J. van der Kogel (1991) demonstrated the *central nervous system chronic progressing injury* genesis possibility in remote period after irradiation with relatively low doses.

F.S. Torubarov (1989, 1993) divide the following neurological syndromes in the structure of typical ARS of extremely severe degree (average doses on whole body 4–6 Gy): *acute radiation encephalopathy, toxic encephalopathy* and central nervous system *haemorrhage syndrome.*

In typical (bone marrow) form of ARS the disease genesis goes through the phase of *initial general reaction* (I phase); phase of *supposed clinical welfare* or *latent* one (II phase); phase of *disease expressed manifestations* or *disease height* (III phase) and *recovery* (IV phase). Depending on ARS severity degree and reparation-adaptation reactions state the *ARS outcomes and consequences* are: complete recovery, recovery with defect, stabilisation of previous alterations, deterioration with clinical manifestations progressing. At that authors disagree with opinion of N.A. Kurshakov (1954-56) and P.D. Horizontov (1955, 1958) regarding the ARS evolution into the chronic radiation sickness (CRS) arguing that with formal resemblance of CRS symptoms and ARS consequences. A.K. Guskova & G.D. Bajsogolov (1971) insist on the CRS pathogenesis and ARS outcomes principal discrepancy: in first case the alterations are stipulated by tissue destruction and necrobiosis permanently rising processes due to the on-going dose accumulation, and in the second — by incomplete repair of defect caused by acute injury. At the same time N.A. Kurshakov himself (1963) underlined the necessity of «ARS consequences» and «CRS» concepts separation, noting that *«...chronic radiation sickness can be the consequence of acute radiation sickness if the active substances deposition took place in organism...».* Some authors refuted in a whole the possibility of complete recovery after ARS explaining that with genetically anomalous cell clones rise [Court Brown W.M., 1966].

N.A. Kurshakov (1963) presenting no dose range borders selected the following degrees of ARS: *most mild* (transient subjective and functional reactions), *mild* (phase-type evolution of disease however without wholly presented clinical symptomatic), *moderate* (expressed bright symptomatic with consequences forming) *and severe* (complete amount of symptomatic with lethal exit possibility). Author presented the ARS neuropsychiatric manifestations clinical description marking absence of symptomatic adequacy completeness regarding injury degree. Soon after the irradiation in the *initial reaction phase* the exposed persons experienced peculiar state similar to the alcohol intoxication or stunning, that on the analogy of the roentgen rays impact was named *«Rontgenkater»* i.e. *roentgen «hang-over»*. Patients could be anxious or on the contrary — sluggish and sleepy. In some cases the headache, dizziness, nausea and sometimes vomiting were observed at that. According to EEG data the central nervous system supreme parts irritability and reactivity alterations were registered with rise of acute waves, tachyarrhythmia and peripheral irritations threshold decrease. Appetite alterations and taste feelings distortion, dryness and elevated thirstiness occurred. Sleep disorders rose with otherwise insomnia or frightening dreams. Sometimes the sensation organs functions deterioration occurred. Superficial skin sensitivity decreased, bone-joint sensation with vibration sensitivity was overirritated. In severe cases the breathlessness and temporary consciousness could be observed and sometimes — complete prostration, shock-type state and even convulsions. Autonomous nervous system disorders were presented with cold sweat, vascular reactions with reddening, and in severe cases — pale skin. Usually the white dermographism was present. Brady- or tachycardia appeared, sometimes — the heart rhythm disorders. For the short time arterial blood pressure could rise up that rapidly turning down due to cardiovascular system hypotonia. Nasal bleeding and small haemorrhages could appear in hyperemic mucosa. Hyperemia, cyanosis, veins dilatation, retina swelling increasing around the visual nerve papilla and macula lutea appeared since first hours on the eyegrounds. Meningism events could occur in some cases i.e. slightly expressed Kernig's symptom, mild occiput strain. Muscular tone and tendons reflexes increase was observed with quickly-transient unstable pathologic reflexes in some cases. Remarkably those symptoms could be absent in mild cases. Thereby according to N.A. Kurshakov's opinion (1963) the organs and systems physiological activities *hyperirritation functional reactions* dominate in ARS first period. *Organic consequences* of radiation trauma are expressed to the less extent. P.S.Kupalov (1959) insisted on radiation sickness initial neurological symptoms existence both with nervous system substantial radiosensitivity.

The nausea and vomiting are of most important diagnostic and prognostic value within *primary general reaction phase* [Hempelman L.H. et al., 1952; Oughterson A.W., Warren S., 1956; Guskova A.K., Bajsogolov G.D., 1971; Anno G.H. et al., 1989]. Neuroregulation and vascular disorders are of substantial role here both with neutrophilic leukocytosis. According to opinion of A.K. Guskova & G.D. Bajsogolov (1971) the vegetative-vascular and psycho-emotional lability to the higher extent are related to the situation in a whole but not proper to the irradiation. Possibility of non-specific adaptation reactions rise through Selye's stress-reaction type was pointed out. Nervous system function alterations signs with brain generalised and rarely — focal neurologic symptoms stipulated by pronounced haemo/liquorodynamic disorders and separate neuron groups activity early alterations authors regarded to the ionising radiation direct injury signs.

General weakness, fatigue, apathy, apathy, dizziness, headache, paresthesias, neurological symptoms, nausea, vomiting, diarrhea, rarely — sleepiness, depression, piteousness, anxiety, fear, conscious paroxysmal disorders, psychosensory disorders are regarded to the *early psychoneurological manifestations* of human acute irradiation [Portnov A.A., Fedotov D.D., 1971; Davidov B.I., Ushakov I.B., 1991].

In further after 1–4 days of initial period the *second phase of «apparent welfare»* or *latent period*. N.A. Kurshakov (1963) connected it to the adaptation genesis both with central nervous system over-irritation processes termination that resulted in its soothing and depression processes domination. According to EEG data the cortex bioelectrical activity and its irritability decrease was observed in this period. Self-estimation of patients health improved with the named period coming: nervous agitation smoothened, «radiation hang-over» passed, normal sleep restored, headaches decreased or disappeared, nausea and vomiting relieved, body temperature normalised, vegetative reactions stabilised. However the «welfare» occurred only apparent as the pathology process continued to develop.

After exposure to radiation doses less than 1 Gy the ARS clinical syndromes are not developed and second phase can directly evolved into recovery phase [Hempelman L.H. et al., 1952; Guskova A.K., Bajsogolov G.D., 1971]. In cases when exposure doses was equal or exceeded the epilation value (3 Gy) the named phenomenon was revealed and progressed in patients since 12–17th day. The separate *focal neurological symptoms* were registered or became clearer in patients on this stage that indicated mainly the brain blood and liquor circulation regulation instability both with nervous centres activity functional alterations. Pronounced static ataxia was revealed and in some cases — co-ordination disorders, nystagmus, convergence limitations, mild pyramid insufficiency symptoms were revealed. Tendon and periostal reflexes as a rule were a bit elevated, however in disease substantial severity they were decreased. Transient but clear reflexes asymmetries rose, neck-tonus reflexes were marked. According to I.S. Glasunov et al. (1955, 1971, 1973) the hyperesthesia elements and some sensation disorders hyperapathetic shades observed in first phase completely disappear in these terms yielding to the perception thresholds elevation and various analyser systems lability decrease. Disorders clinic-neurological dynamics was testified with *physiological studies* results through cortex reactivity alterations, flexors/extensors chronaxy coefficients decrease, synergic reactions widening etc. A.K. Guskova & G.D. Bajsogolov (1971) consider the EEG slow waves rise and their synchronisation with pulse rhythm characteristic for this disease period. Authors concluded that in this phase of ARS the some smoothening of general *nervous-regulation disorders* stipulated by ionising radiation impact as the irritant takes place. However at the same time the *ionising radiation injuring effects* signs elevation takes place.

According to N.A. Kurshakov (1963) with further pathology development the «hidden» disease course with whenever rapid or slow symptomatic progress now evolves into the clinically presented one and the *third phase of expressed clinical events* is initiated. The general state deterioration was noted with headaches, dizziness, sleep disorders (insomnia or anxious sleep), appetite and digestive process disorders. Particular attention N.A. Kurshakov (1963) paid on tissue trophic alterations forming as they are on the one hand the ionising radiation initial impact aftermath and on the other — are to be considered as neurotrophic ones resulted from *neuro-humoral mechanisms* indirect impacts. *Neurological symptoms* in the ARS most expressed clinical presentation become of particular importance. Headaches intensified and sometimes were terrible. Sometimes vomiting, dizziness, hyperacousia, photophobia, sleeping disorders occurred. Meningeal symptoms were revealed again. Cerebellum, brain nerves and brain stem injury sharp signs rose only in late disease stages. Tendon reflexes elevation and irregularities, pathologic reflexes and nystagmus were revealed. All these symptoms are non-specific, but their combination and rise sequence are peculiar to the ARS. Serious alterations of nervous system can rise within 4 weeks after irradiation. Autonomous nervous system supreme centres regulating metabolic processes both with viscera state and function stipulate the *nervous component* role in somatic disorders symptomatic. Supreme nervous function reactions instability was noted both with its main processes dissociation with depression reactions prevalence. Various dystrophic processes in parenchymatous viscera and pituitary, adrenals, thyroid, sexual sphere failure symptoms were revealed.

Neurological symptomatic in ARS severe cases according to A.K. Guskova & G.D. Bajsogolov (1971) is non-specific, being the result of generalised infection, intoxication and anemia. Consciousness of patients sometimes was a bit dimmed. Clear meningeal symptoms of various intensity were appearing. trigeminus and occipital points were sharply painful. General sluggishness and adynamia were increasing. Muscular tone regularly substantially decreased. Tendon and periostal reflexes were as a rule high with irregular asymmetry presence. Pathological reflexes could be observed. No induction of reflexes was possible in some the most severe patients within terminal period. *Psychics disorders* if appeared were typical for infection or toxic delirium. Sometimes the *sharp focal neurological symptoms* (up to the total ophthalmoplegia etc.) were available to detect on the pronounced generally-cerebral manifestations background without conscious loss or other distinct stroke signs. Authors explained that with gradually elevating signs of brain and maters swelling on the background of what the haemorrhages occurred not due to the vessel rupture but through diapedesis or plasmorrhage type per altered vessel wall. The vessel thrombosis with surrounding area ischemia also could take place. At the same time A.K. Guskova & G.D. Baisogolov (1971) marked only the scanty neurological symptomatic through asthenic complaints elevation and tendon, periostal, skin reflexes and muscular tone decrease when the III phase manifestations were expressed not sharply. Physiological examinations revealed nervous system several functions severe disorders. The neurological symptomatic role is considered leading one in exposure doses exceeding 50–80 Gy [Guskova A.K., Shakirova I.N., 1989].

The *psychopathological pattern* of ARS was presented by A.A. Portnoj & D.D. Fedotov (1971). Initial reaction on irradiation is characterised with typical *dysphoria syndrome* or its maniac variant (the last one is most often observed on the 2nd stage after exposure — the apparent welfare) i.e. the state of euphoric agitation long since known as *«roentgen hang-over»*. Weakness, sluggishness, apathy, quick fatigue, fears, abrupt headaches, insomnia, nausea and vomiting are revealed in 3rd stage (of disease pronounced symptoms). In extremely severe cases after the short period of apparent welfare the weakness and apathy symptoms rapidly are elevated both with general somatic state deterioration, that is followed by stunned state and various in extent delirium, soporose state and coma. In disease 4th stage in case of relative mild injury the somatogeneous asthenia is observed whereas in case of severe radiation damage — amnestic syndrome, rough psychosensoric disorders and polyneuritis. The peculiar *encephalopathy* forms with *hypothalamic-pituitary zone* expressed injury accent are described as ARS remote consequences. Besides signs common for all encephalopathy types, the relatively stable asthenia is observed here with cataplexia, disphoria transient attacks and vegetative disorders, adaptation capacities failure (hot, cold, atmospheric pressure deviations intolerance etc.).

Substantial attention in works of numerous foreign authors specially in the field of *military radiobiology* is devoted to the *post-radiation neurovascular dysfunction* under the substantial radiation doses impact [Doyle T.F. et al., 1974; Bruner A., 1977; Hawkins R.N. et al., 1983; Cockerham L.G. et al., 1984; Yawkins R.N., Cockerham L.G., 1987].

Irradiation with high doses result in hemodynamic disorders and *post-radiation hypotension* with arterial pressure collapse down to 50% of normal value. Post-radiation hypotension can induce *cerebral circulation decrease* in spite of autoregulation mechanisms present in central nervous system capable of adequate cerebral blood perfusion maintenance in case of arterial blood pressure decrease [Chapman P.H., Young R.J., 1968; Farrar J.K. et al., 1981].

Post-radiation hypotension can stipulate the *regional cerebral blood flow decrease* in *hypothalamus, hippocampus, visual cortex and post-central brain convolution*. Neurological symptoms, cortex and hippocampus neurones spontaneous activity alterations can be observed as the result of rising cerebral ischemia and cytotoxic swelling [Suzuki R. Et al., 1983].

The *blood-brain barrier* opening is another one complication of post-radiation cerebral ischemia that can be related to the brain vasogeneous-swelling rise. The last research results testify the blood-brain barrier damage possibility in doses from 2 to 10 Gy [Ashani Y. et al. — Cited from Yawkins R.N., Cockerham L.G., 1987].

In patients survived expressed clinical events phase lasting for 2–4 weeks the evolution into the disease fourth — *recovery* phase. Gradually the ARS symptomatic smoothening was marked in various sequences. The supreme nervous function main processes ratio restored, however the asthenisation, reactions instability and their quick exhausting remained for long time. Cortex and subcortex interaction combinations normalised. Tendency of diencephalic functions normalisation led to metabolic disorders decrease. Sometimes the obesity or unhealthy

thinness tendency was observed [Kurshakov N.A., 1963; Guskova A.K. et al., 1964; Guskova A.K., Bajsogolov G.D., 1971].

Numerous studies indicated that the *cerebrovascular disorders* hold leading place in ARS consequences clinical presentation. Circulation alterations mainly consist in vessels resilient-elastic state deterioration, blood flow volume and intensity lowering there, cranium cavity venous outflow deterioration. Brain hypoxia being the blood circulation failure aftermath that both with ionising radiation direct injuring impact on tissues redoubles neurotrophic and dysmetabolic disorders, therefore leads to cortex neurones functional activity depression [Guskova A.K. et al., 1977; Torubarov F.S. et al., 1983].

Capillaries are considered the most sensitive part of blood vessels system. The blood vessels inner wall-layer injury is restored through endothelium regeneration. As the *endothelium* is more often subject to regeneration especially in vessels damage zones, these cells become more radiosensitive within wounds active regeneration. Large arteries irradiation induce *atherosclerosis* progressive genesis. The same injuries are revealed in moderate and large size veins however to the less extent [Casarett C., 1980].

Process regional localisation is peculiar for radiation vascular injuries. Pathological changes occur not in all the vessels but in the most *actively functioning* at the time of irradiation. At the same time in elderly the ionising radiation impact results in vessels diffuse damage [Alexandrov S.N., 1978].

A.K. Guskova & G.D. Bajsogolov (1971) associated the *osteoalgetic syndrome* forming with blood circulation disorders. In their opinion the tendency for hypotension with arteries and veins tone lowering, blood flow decrease in separate vascular basins are peculiar for vascular reaction on radiation.

Among the ARS *proximate* (weeks - months) psychoneurological consequences the *autonomous nervous system dysfunction* and *general asthenisation*, transient *myelo- or encephalopathias* are described presenting in its turn similarities with diffuse sclerosis and cerabro-vascular pathology [Gorban N.G., Torubarov F.S., 1990; Guskova A.K. et al., 1964, 1988; Guskova A.K., Bajsogolov G.D., 1971; Guskova A.K., Shakirova I.N., 1989; Kurshakov N.A., 1963; Torubarov F.S. et al., 1989].

In ARS remote period under 3–5 Gy doses impact the *radiation demyelinating encephalomyelosis* is described [Glazunov I.S. et al., 1971]. A.K. Guskova & G.D. Bajsogolov (1971) characterising the ARS possible remote consequences under doses pronounced level formulated the following:

1. Neurological syndromes of diffuse micro-organic process with conducting structures main alterations (myelin).
2. Regional and mainly intracerebral circulation insufficiency syndromes being more real in case of doses distribution pronounced irregularity in body volume (head, neck sinocarotid zone etc. exposure in high doses).
3. Multiform functional disorders with vegetative-vascular dysfunction or general asthenisation features prevalence.

At that in authors opinion the functional disorders presentations in ARS outcome are of no any specificity and are by origin the undoubtedly polyetiological syndromes that not allows to consider their pathogenesis only starting from radiation impact point. These disorders obviously are connected to the central nervous system defective functional compensation stipulated by neurones biochemical and histochemical alterations that are defined by I.S. Glazunov et al. (1971) as *dysadaptation syndrome*. Stated neurological pattern is not specific only for reaction on irradiation. It is rather similar to psychoneurological syndromes in other general somatic diseases. Central nervous system structural damage clinical manifestations are registered extremely rarely and in patients survived the ARS of severe and extremely severe degree. They are presented with pyramid insufficiency signs, mild static-coordination disorders, nystagmus and other symptoms most of all resembling mild forms of *diffuse demyelinating process* (of *encephalomyelosis*-type) [Guskova A.K., Shakirova I.N., 1989].

Not-rough *intellectual-mnestic disorders, hypothalamic-pituitary dysfunction,* rarely — *progressing myelopathy and brain necrosis* were observed among the ARS remote aftermath [Guskova A.K., Shakirova I.N., 1989; Torubarov F.S., 1991].

E.I. Gusev et al. (1988) introduced the following *central nervous system radiation injury classification* (Nervous Diseases Textbook for medical schools students):

A) General irradiation:

- *Radiation asthenia* presenting similarities with neurosis in spite of physical factor impact and brain microstructure alterations presence in its origin. Corresponds to the radiation sickness 1st (mild) stage of severity degree.
- *Vegetative-vascular dystonia* where combinations are possible with asthenic events through asthenic-vegetative or asthenic-depressive syndromes. Vegetative paroxysms are also peculiar.
- *Meningeal syndrome* in radiation sickness of 2nd–3rd degree.
- *Radiation encephalomyelopathy* resembling meningoencephalitis however being the degenerative-destructive injury with brain direct alterations and massive reflectorial and humoral events in its basis. Corresponds to the radiation sickness 3rd severity degree.
- *Coma-type form* in radiation sickness extremely severe (4th) degree.

B) Local irradiation:

- *Radiation neuralgia* peculiar with paresthesias, focal sensitivity disorders, trophic alterations both with spontaneous and reactive pains. In osteotropic radionuclides incorporation the *osteoagletic syndrome* rises, after iodine isotopes absorption by thyroid — the peculiar neck dyzesthesia or neuralgia.

- *Radiation polyneuropathy* with brightly expressed hardly-knocking-over pain syndrome, sensory and vegetative-trophic disorders both with peripheral (sluggish) paresis or paralysis.
- *Focal encephalo- and myelopathy* with cortex injury syndromes, cerebellum syndrome or subcortex structures and brain stem various levels damage symptomocomplex, lower spastic paraparesis, conductive sensitivity disorders, pelvic organs functions alterations, Brown—Secar syndrome.
- *Brain focal necrosis*, presented with general and local cerebral symptoms combination.

According to the IDC-10 the *radiation sickness* is issued in Section XIX. INJURIES, POISONINGS AND OTHER IDENTIFIED CONSEQUENCES OF EXOGENOUS CAUSES under rubric *T66 Unidentified Effects of Radiation*. In modern literature the ARS is mainly named as «*Acute Radiation Syndrome*», at that the chronic form of radiation sickness is not separately outlined [Conclin J.J., Walker R.I., 1987; Young R.W., 1987; Wagemaker G., Bebeshko V.G., 1996, etc.]. However, the «Acute Radiation Sickness» (ARS) can be met also [Wagemeker G. Et al., 1996].

5.3.2. Psychoneurological disorders in acute radiation sickness survivors after Chernobyl disaster

On April 26, 1986 (1–24 a.m.) the accident at the Unit 4 of the Chernobyl NPP took place during the planned test of one of the safety systems. According to the International Scale of the Assessment of Events the Chernobyl accident is classified as the accident of the 7th (highest) level [National Report of Ukraine, 2001]. The Chernobyl accident was the most severe ever to have occurred in the nuclear industry. The impact of the accident on the workers and local residents has indeed been both serious and enormous. The Chernobyl accident occurred during a low-power engineering test of the Unit 4 reactor. Safety systems had been switched off, and improper, unstable operation of the reactor allowed an uncontrollable power surge to occur, resulting in successive steam explosions that severely damaged the reactor building and completely destroyed the reactor [UNSCEAR 2000 Report to the General Assembly. Annex J].

Approximately 300 MCi ($11 \cdot 10^{18}$ Bq) of radioactive materials exploded into the environment from the destroyed reactor [National Report of Ukraine, 1996]. During the first days and weeks after the accident the radiation situation was determined with nuclear decay of short-lived radionuclides, mainly of iodine isotopes — ^{131,132,133,135}I. Further radiation doses were formed mainly with long-lived radionuclides, particularly, ^{90}Sr and ^{137}Cs, as well as together with transuranium elements in the Chernobyl exclusion zone [National Report of Ukraine, 2001].

The radiation exposures resulting from the Chernobyl accident were due initially to ^{131}I and short-lived radionuclides and subsequently to radiocaesiums (^{134}Cs and ^{137}Cs) from both external exposure and the consumption of foods contaminated with these radionuclides. From the radiological point of view, ^{131}I and ^{137}Cs are the most important radionuclides to consider, because they are responsible for most of the radiation exposure received by the general population [UNSCEAR 2000 Report to the General Assembly. Annex J].

The non-sufficient level of the culture of nuclear safety in the former USSR was recognised the main cause of the Chernobyl accident. As a result, the units with serious failures of the construction of the reactor, its management system and security were acknowledged to the usage. This together with non-adequate actions of the personnel were the direct causes of the Chernobyl accident [National Report of Ukraine, 2001].

The accident caused the deaths within a few days or weeks of 30 power plant employees and firemen (including 28 deaths that were due to radiation exposure), brought about the evacuation of about 116,000 people from areas surrounding the reactor during 1986, and the relocation, after 1986, of about 220,000 people from Belarus, the Russian Federation, and Ukraine. About 240,000 workers («liquidators») were called upon in 1986 and 1987 to take part in major mitigation activities at the reactor and within the 30-km zone surrounding the reactor; residual mitigation activities continued until 1990. All together, about 600,000 persons received the special status of «liquidator» [UNSCEAR 2000 Report to the General Assembly. Annex J].

The highest doses were received by the approximately 600 emergency workers who were on the site of the Chernobyl power plant during the night of the accident. The most important exposures were due to external irradiation, as the intake of radionuclides through inhalation was relatively small in most cases. Acute radiation sickness (ARS) was confirmed for 134 of those emergency workers. Forty-one of these patients received whole-body doses from external irradiation of less than 2.1 Gy. Ninety-three patients received higher doses and had more severe ARS: 50 persons with doses between 2.2 and 4.1 Gy, 22 between 4.2 and 6.4 Gy, and 21 between 6.5 and 16 Gy [UNSCEAR 2000 Report to the General Assembly. Annex J].

A total number of hospitalised patients with suspected diagnosis of ARS due to the Chernobyl accident included 499 persons [Sergeev G.V., 1988]. In 237 cases of them diagnosis was confirmed clinically. After subsequent re-estimation of clinical and haematological data diagnosis was validated in 145 patients and later — in 134 of them [Guskova A.K. et al., 1987; Ilyin L.A., 1994; Souchkevitch G.N., Tsyb A.F. (Eds)., 1996]. Two patients died at the place of the accident. For 7–96 days after the accident 28 injured patients died. For the subsequent years 15 patients died due to different causes [Kovalenko A.N. (Ed), 1998].

The first descriptions of neurological and mental disorders of the ARS-patients as a result of the Chernobyl accident were performed by F.S. Torubarov et al. (1989). Autonomic [vegetative] vascular dystonia (VVD) and neurotic disorders were observed in the clinical picture of mild ARS [or ARS of the 1st severity degree] (0.8–2.1 Gy); moderate ARS [or ARS of the 2nd severity degree] (2.0–4.0 Gy) — VVD; severe ARS [or ARS of the 3rd severity degree] (4.2–6.3 Gy) – acute radiation and radiation-toxic encephalopathy, acute psychosis with visual and acoustical

hallucinations, brain oedema; very severe to lethal ARS [or ARS of the 4th severity degree] (6.0–16.0 Gy) — acute radiation and radiation-toxic encephalopathy, subarachnoidal-parenchimatous haemorrhage, acute brain oedema and swelling [Torubarov F.S. et al., 1989].

Diagnosis, descriptions of clinical pattern and treatment of ARS-patients in the acute phase of the disease in survivors of the Chernobyl accident were performed by A.K. Guskova et al (1987, 1989). Overexposed persons in the acute phase were diagnosed and treated at the specialised medical institutions in Moscow and Kiev — the 6th Clinical Hospital of Institute of Biophysics (Moscow), Kiev Roentgen-Radiological and Oncological Institute, and Kiev Research Institute for Haematology and Haemotransfusion [Kovalenko A.N. (Ed.), 1998].

Survivors with verified ARS were exposed to general external γ-irradiation with doses 1 – 13 Gy, whereas β- & γ-radiation exposure dose of skin in some of them reached up to several thousand rads. At once after victims admission to the 6th Clinical Hospital of Institute of Biophysics (Moscow) the neutron radiation estimates were conducted through activated ^{24}Na assay in blood. Activated radionuclide was not found in liquidators suffering ARS that in particular led to conclusion regarding chain nuclear reaction absence in destroyed reactor. Extensive local radiation injuries occurred being the main cause of death in 17 from 28 lethal exits [Iljyn L.A., 1994].

Cariological data retrospective analysis in persons exposed to uniform general β- & γ-radiation impact after the ChNPP accident indicated that total radiation dose of 0.7 Gy can be estimated as minimal for ARS onset of the 1st severity degree [Guskova A.K. et al., 1988].

A.K. Guslova & I.A. Gusev (1996) marked out that survivors with diagnosed ARS were exposed to external γ-radiation with doses 0.7–13 Gy. Radiation doses on skin due to β-particles was 10–20 times higher. Internal radiation dose on lungs was <0.8 Gy; on thyroid in 8 patients — over 4 Gy, including two persons with respective values within range 11–13 Gy. According to the authors' data the recovery occurred almost in all survivors with exposure doses up to 4 Gy, in two thirds of cases with 4–6 Gy and 2 patients from 21 exposed to 6–13 Gy of radiation. Following clinical peculiarities were regarded to the ARS after Chernobyl disaster:

- various viscera and skin combined injuries high prevalence limiting curative arrangements application effectiveness for post-radiation myelosuppression relief (bone marrow transplantation etc.);
- substantial extent of skin injuries;
- severe injuries combination with wide-mass people involved in accident events leading in its turn to the respective social resonance.

The recent reports present data about the ARS diagnosis confirmation only in 134 cases from 237 initially established [Wagemaker G. et al., 1996; Guskova A.K., 1997]. Among them 41 patient had the ARS of 1st (mild) degree at that one more person is subject to continuous discussion regarding ARS presence. All these patients survived the acute phase (1986). Fifty patients had the ARS of 2nd degree with one lethal exit among them. Seven from twenty-two patients suffering ARS of 3rd degree died. All but one patient from the most severely injured with ARS of 4th degree died in spite of applied intensive management. In total the 209 persons survived the acute phase (1986) and 28 people died. Within 10 further years the 9 patients died with confirmed ARS diagnosis and 5 victims — with unconfirmed one. Their deaths are considered not related to the survived ARS severity degree and in majority of cases were not directly stipulated by radiation impact [Wagemeker G. et al., 1996].

A.Ye. Romanenko et al. (1995) and L.P.Kindzelsky (1995) presented data that 29 persons from 237 those with ARS diagnosed in 1986 died from radiation causes in terms from 7 to 96 days. The 27 patients with ARS of 3rd—4th degree and one female patient with 2nd degree died in the 6th Clinical Hospital of Institute of Biophysics (Moscow). One patient with estimated general radiation dose about 20 Gy died on the 7th day in one of Kiev city clinics. Clinical progress, forming and recovery periods of 3rd—4th degree ARS were narrowing the previously accepted opinions however the bone-marrow syndrome and blood cytopenia rise was somewhat delayed due to incorporated radionuclides additional injuring effect.

The ARS took place mainly among the Unit 4 operators, shift and service personnel of turbine hall, firemen and several citizens not relevant to the accident cleaning-up but been present on various reasons close to the power plant. No individual dosimetry data were available. According to cytogenetic estimate (chromosome aberrations calculation in bone marrow smears and peripheral blood lymphocyte cultures) the absorbed dose value was within 1–13.8 Gy range and corresponded the ARS severity from mild bone-marrow to the intestinal form clinical manifestations. Main impact factors were: 1) external relatively uniform γ- and β-irradiation; 2) active γ- and β-nuclides skin application and 3) those nuclides incorporation [Kindzelsky L.P. et al., 1995].

At present time the 180 liquidators of the ChNPP accident consequences with «ARS» diagnosis established in 1986 live in Ukraine. They are surveyed mainly in Research Centre for Radiation Medicine [Bebeshko V.G. et al., 1996]. All patients in Ukraine with ARS diagnosed in 1986 have equal medical and social prerogatives [Romanenko A.Ye. et al., 1995]. Those patients with unconfirmed «ARS» diagnosis (so-called «ARS-0» subgroup) are considered the ARS subclinical form survivors [Halavka I.G., 1996]. At the same time A.K. Guskova (1997) insists that retrospective «ARS» diagnosis is verified only in 134 persons from ChNPP personnel and firemen (with doses 0.7–13 Gy). In her opinion no reliable data are present for ARS and chronic radiation sickness genesis among other contingents. The ARS diagnostic in Kiev among other persons (besides those 134 mentioned above victims with verified diagnosis) A.K. Guskova (1997) explained by «social motivation» without proper scientific-clinical arguments.

F.S. Torubarov et al. (1989) presented the neurological pattern analysis results from ARS of the 1st—4th degree victims exposed to relatively uniform γ- and β-irradiation after Chernobyl disaster. The ARS was diagnosed on clinical-laboratory criteria ground. Results are shown in Table 5.4.

Some authors stated opinion that radiation reactions under general radiation exposure doses under 1 Gy are as a rule not followed by neurological manifestations but the *neuro-visceral regulation* disorders and *general asthenisation* are revealed in doses 1–4 Gy [Guskova A.K., Shakirova I.N., 1989; Torubarov F.S., 1991]. *Asthenic manifestations* correlated through incidence and extent with the survived ARS degree (66%, 50% and 33% of patients with ARS of the 3rd, 2nd & 1st degree respectively) and according to several authors remark were dependent upon social-professional factors, job placement adequacy and premorbid personality features in ChNPP survivors [Guskova A.K. et al., 1988].

Vegetative-vascular dystonia and neurotic disorders were observed in ARS of the 1st severity degree (0.8–2.1 Gy) and *vegetative-vascular dystonia* — in ARS of the 2nd degree (2.0–4.0 Gy) [Torubarov F.S. et al., 1989]. The *brain tissue microdestruction* signs according to the neuro-immunological tests results were revealed under general irradiation with doses 2.0 Gy and over [Guskova A.K. et al., 1988].

The *general-brain and brain-shell symptoms* both with *autonomous nervous system disorders* were described under 4.0–6.0 Gy exposure. The small-focal and diffuse cerebral microsymptoms along with coordination disorders were found more rare however with elevation tendency along with dose value rise. In such a cases the *acute radiation and radiation-toxic encephalopathy, acute psychosis* with visual and hearing hallucinations, *brain swelling* were surveyed in ChNPP accident survivors suffering ARS of the 3rd degree (4.2–6.3 Gy). *Acute radiation and radiation-toxic encephalopathy, subarachnoid-parenchymal hemorrhages, pronounced brain oedema and swelling* were observed in the 4th degree of ARS (6.0 – 16.0 Gy) [Guskova A.K., Shakirova I.N., 1989; Torubarov F.S., 1991].

F.S. Torubarov (1989, 1993) selected the following neurological syndromes in *ARS remote period*: asthenic-vegetative, diencephalic, nervous system organic damage syndrome (*radiation, discirculation or combined encephalopathy*) and asthenic-dystrophy one.

Six month and 1.5 years after survived ARS the nervous system functional disorders were registered most often by way of *neuro-circulation dystonia with asthenic-neurotic syndrome, vegetative-vascular dystonia and diencephalic crises* both with *polyneuropathy* manifestations [Bebesko V.G. et al., 1988]. According to the data by B.P. Prevarsky et al. (1991) the nervous system alterations were observed most often in 1986 in the form of vegetative-vascular dystonia combined to arterial hypertension. No nervous system organic damage signs were observed at that time.

N.G. Gorban (1989) studied the *cerebral hemodynamic* state in ARS through *rheoencephalography* application within latent period terms and recovery period (2–4 months and 1–3 years). Author received data regarding pulse volume characteristics reliable decrease, peripheral resistance and venal tone elevation tendency both with cerebral dystonia rise being most expressed in ARS of the 2nd & 3rd degree patients within recovery period. N.G. Gorban (1989) concluded that cerebral hemodynamic alteration can be considered as one among neurological disorders underlying condition in ARS patients.

Table 5.4

INITIAL REACTION SYMPTOMS AND NEUROLOGICAL DISORDERS IN ACUTE RADIATION SICKNESS PATIENTS OF VARIOUS SEVERITY DEGREE (by F.S. Torubarov et al., 1989)

Symptoms	Severity degree							
	IV (6-16 Gy) n= 20		III (4.2-6.3 Gy) n= 21		II (2-4 Gy) n= 43		I (0.8-2.1 Gy) n= 29	
	abs.	%	abs.	%	abs.	%	abs.	%
Vomiting	20	100	20	95	39	86.5	16	59.3
Nausea	20	100	20	95	41	91	21	77.7
Headache	15	75	18	85.8	24	53.3	13	48
Dizziness	8	40	5	23.8	4	8.88	4	14.8
General weakness	15	75	16	66.2	23	51.1	18	66.6
Hyperthermia	10	50	14	66.6	11	24.4	2	7.4
Mouth dry	15	75	1	4.76	11	24.4	1	3.7
Skin hyperemia	20	100	5	23.8	2	4.44	0	0
Diarrhea	9	45	6	28.3	9	20	4	14.8
Parotid glands swelling	15	75	3	14.3	1	2.2	0	0
Eye gripe	0	0	1	4.76	0	0	3	11.1
Skin burning	0	0	2	9.52	0	0	0	0
Stomachache	0	0	0	0	2	4.44	3	11.1
Mouth after-taste	0	0	0	0	4	8.88	1	3.7
Shivering	0	0	0	0	3	6.66	2	7.4
Limpness	7	35	3	14.3	1	2.3	0	0
Hinderedness	2	10	1	4.8	0	0	0	0
Euphoria	2	10	1	4.8	0	0	0	0
Kernig's symptom	1	5	0	0	0	0	0	0
Nystagmus	10	50	7	33.3	4	9.3	4	13.8
Eye hyporotation aside	3	15	2	9.52	0	0	0	0
Convergence disorders	2	10	1	4.76	4	9.3	3	10.3
Nose-lip wrinkle flattening	7	35	6	28.6	7	16.3	6	20.7
Tongue deviation	3	15	1	4.8	1	2.3	0	0
Muscular hypotony	2	10	2	9.5	0	0	0	0
Anisoreflexia	10	50	2	9.5	5	11.6	0	0
Hyporeflexia	10	50	8	38.1	9	20.9	5	17.2
Feet clonus	0	0	1	4.8	0	0	0	0
Babinsky's symptom	1	5	1	4.8	0	0	0	0
Rossolimo's symptom	1	5	1	4.8	0	0	0	0
Marinesku—Radovichi's symptom	1	5	4	19	1	2.32	0	0
Hyperesthesia	1	5	0	0	0	0	0	0
Instability in Roemberg's test	2	10	2	9.5	0	0	0	0
Hand and feet hyperhydrosis	0	0	0	0	4	9.3	5	17.2
Stable red dermographism	0	0	0	0	6	13.9	1	3.45
Stable white dermographism	4	20	1	4.7	0	0	0	0
Hand fingers tremor	4	20	3	14.3	3	6.98	3	10.3

U.P. Petrov et al. (1989) revealed the *background EEG* alterations though α-range spectrum power depression and EEG spectrum low components (θ-range) contribution elevation that set patients apart from healthy persons. In *modeling operator activity* execution the brain functional state alterations occurred. Patients survived ARS of the 1st degree were peculiar with synchronisation decrease and desynchronisation within first minute of rest due to θ- & β-ranges contribution somewhat rise with following partial restoration to the fifth minute of rest that in authors' opinion indicated the central nervous system functional state strain. Alpha-activity decrease was also peculiar for 2nd degree — ARS survivors along with slow-wave activity amplification on second and fifth minutes. EEG alterations in the 2nd degree ARS-patients in aftereffect period were of stable pathological nature (θ-range dominance) without restoration to background level tendency.

A.M. Kogan & P.V. Chesalin (1989) registered the slow- and medium-latent *evoked auditorial potentials* (EAP) and *evoked visual potentials* (EVP) on chess-pattern application in various terms of ARS recovery period. In 1986 the EAP alteration extent was distinctly rising along with radiation diseases severity elevation that was presented through

both slow- and medium-latent altered components number increase and also alterations appear almost in all request components that could mean functional shifts presence for all stem length. In ARS patients of severe degree the alterations were observed along the whole hearing tract length i.e. from acoustic nerve effecting potential up to thalamic-cortical projections. Authors marked out the latent periods elongation and amplitude decrease among ARS patients of moderate and heavy severity degree explaining that with *impulse conduction slow-down, afferentation hampering and brain stem structures functional activity level decrease*. In ARS patients of mild degree conversely the two waves amplitude elevation was observed i.e. stem conducting systems activity amplification and irritation signs. A.M. Kogan & P.V. Chesalin (1989) supposed the radiation effects phase mode presence i.e. the *stem structures* non-sharp *irritation* signs in mild disease degree changed by *functional activity* elevating *depression* in *moderates and severe degree of ARS*. In EAP registration in 1986 A.M. Kogan & P.V. Chesalin (1989) revealed the statistically significant decrease of all visual responses components amplitude in ARS survivors without clear dependence on radiation sickness severity. Those alterations reflected both specific and non-specific brain structures *functional activity decrease* with sensory information complex intra-cortex processing alteration. One – one and a half year after irradiation the revealed sensory responses alterations were still present however authors marked out the respective indices tendency to normalisation at that with somewhat more pronounces extent in patients survived ARS of severe degree.

Psychic state and working capacity in patients within ARS recovery period and immediate consequences were characterised by F.S. Torubarov & O.V. Chinkina (1989). Authors concluded that psychic state and mental working capacity both with present alterations structure and extent in *early terms* of ARS recovery i.e. 4 – 6 months after irradiation are closely connected in victims to the survived ARS severity degree and premorbid personality features, competency extent and activity/behaviour orientation basis adequacy along with social issues solution degree. In more *remote terms* of recovery period i.e. 12–18 months after accident the professional belonging, rational job placement and survivors' personality peculiarities in opinion of F.S. Torubarov & O.V. Chinkina (1989) became the leading role in mental health disorders genesis, workability limitation and social disadaptation forming. In terms of *immediate consequences* within 2.5–3 years after the exposure authors marked the mental disorders with pronounced exhaustion extent were found more often in patients who survived ARS of more severe degree and in more elder persons. Authors consider the rational job placement of survivors remains important role in their recovery completeness.

Psychological studies of ARS survivors (1st — 3rd degree) held in remote period indicated severe anxiety, depression, mental workability deterioration presence both with *specific alterations in personality semantic structure* [Chinkina O.V., 1989; Torubarov F.S. et al., 1989; Chinkina O.V., Torubarov F.S., 1991].

F.S. Torubarov & O.V. Chinkina (1995) in subsequent works presented the results of complex *clinical-psychological* examination during 9 years of 75 persons who participated in Chernobyl NPP accident cleaning-up and survived of the 1st — 3rd degree ARS. Authors' analysis indicated that *psychological disorders* became the highest prevalence and severity during the restoration period i.e. up to 1.5 years and within ARS nearest consequences — 1.5–5 years since the overexposure moment. In all survey stages the person's various activity efficacy (mainly requiring high requirements to basic attention and operative memory characteristics), psychic processes run stability both with unfavourable mental states incidence and pronouncement dependence upon *the ARS severity degree* were marked. Revealed memory, attention and various types sensory-motive activity alterations represent in authors opinion the same phenomenon manifestation: the extremely rapidly occurring *exhaustion* pattern. Gradual progressing of exhaustion pattern in combination with health state and activity decreased self-estimation reflects in all cases the *reserve capacities decrease* in patients due to the over-irradiation. That is more pronounced in patients suffering more severe injury. Concomitant deterioration of decreased mood background with expressed anxiety incidence as stable condition, readiness for high anxiety response on any really anticipated life events followed by regulation alteration in emotional sphere indicate the *anxious-depressive disorders* genesis. Authors noted also the psychological signs of *personality neurotic development* incidence elevation. In all patients surviving ARS F.S. Torubarov & O.V. Chinkina (1995) observed tendency towards functional capabilities improve 3 years after the irradiation however the negative tendency recommenced 5–6 years later.

Sympathetic-adrenal system disorders in persons survived ARS were revealed by L.P. Imshenetskaja & I.I. Gorpinchenko (1993). Both hormonal and mediator branch activity depression of sympathetic-adrenal system was fixed compared to the healthy non-irradiated humans. Catecholamines metabolism is altered. DOPA content substantial decrease is found i.e. of the main biochemical precursor of epinephrine, norepinephrine and dopamine. Authors concluded that sympathetic-adrenal system depression is resulted from hypothalamic structures involvement in pathological process including the sexual hormones axis. All that points out to the general resistance sharp decline in male organism exposed to ionizing radiation impact.

Cytogenetic studies by M.A. Pilinskaja et al. (1993-1995) ascertained that even 9 years after survived ARS the remaining elevated value of radiation impact unstable markers both with stable ones incidence elevation compared to spontaneous level are observed. Induced cytogenetic effect expression degree is positively correlated to the supposed radiation dose reconstructed through the initial radiation damage severity estimation.

According to the data by V.G. Bebeshko, A.N. Kovalenko & D.A. Belyj (1996) the haemopoietic system alterations as transient or *stable leukopenia and leukocytosis* were registered in 40% of ARS patients. *Immunity* indices quantitative and qualitative alterations with phase-type evolution were observed in 1/3 of patients. Anti-oxidation protective system enzymes changes, lipids peroxidation activation, anti-radical protection mechanism weakening, membrane structures damage growth and lysosomal enzymes (hydrolases) elevation were registered in *erythrocytes*. *Cortisol* basal level stable elevation in blood plasma with *corticotropin* concentration substantial decrease was marked.

Prolonged hypotestosteronemia was accompanied by pituitary low *gonadotropic activity* and hyperprolactinemia. Atherogenic alteration in *lipids* were revealed in a half of examined persons. *Polyamines* (spermidine and putrescine that are of some importance in tumour processes diagnostic) blood level substantial elevation was present 5–6 years after the irradiation. *Somatic status* was characterised with respective diseases evolution into chronic clinical forms. Tendency towards digestive organs morbidity elevation was defined along with respiratory system diseases incidence elevation followed by its further decrease. Distinct transformation of psycho-vegetative disorders into *organic neuro-vascular pathology* (hypertensive disease, discirculatory encephalopathy, psycho-organic syndrome) was marked. *Mental workability* studied with sensory and abstractive-logical activity models application was decreased along with radiation injury degree. Circulatory system diseases incidence rise and *physical working capacity* implacable decrease were revealed especially in patients survived the ARS of the degree 2nd — 3rd. Seven cases of *radiation cataract* were registered both with six cases of *hypothyroidism*. No solid tumors were found among patients with verified ARS diagnosis. At that time the *disability* rate among ARS survivors reached 90% whereas according to the data by G.V. Sergejev (1988) no more than 16 persons (≈8%) from all those ones were not working in first years after the accident.

D. Belyi, O. Gergel & A. Kovalenko (1996) demonstrated the *cardiovascular pathology* progressing elevation in persons who survived the ARS. Number of patients with pathological changes in electrocardiogram elevated from 4.8% in 1987 up to 11.3% in 1994, those suffering myocardial hypertrophy — from 1.2% up to 22.6% respectively. Number of cases with ischemic heart disease increased for 17.2%, with essential hypertension — for 15.5%. Physical working capacity decreased for 50-60% from healthy human value. Two patients suffered the acute myocardial infarction. Thirteen persons died between 1987 and 1994, four from them — from acute heart failure. However the named pathology genesis presented no connection to radiation dose value as cardiovascular diseases were found more rare in ARS patients of degree II – III than in those survived degree I. Authors supposed three factors of stated pathology pathogenesis: 1) neuro-humoral regulation alterations after ARS presented with vegetative-vascular dystonia transformed further into ischemic heart disease or hypertensive disease; 2) vascular endothelium radiation damage; 3) high incidence of atherogenic type dyslipoproteinemia.

However A.K. Guskova (1995) in «Radiation and Human Brain» affirmed that neurological syndromes in persons survived ARS (0.7–9.0 Gy) are coupled with somatogenic asthenisation, psychological stress, functional reserves inadequate utilisation within job placement and are limited to *vegetative regulation functional shifts and somewhat decrease of adaptation to the loads*. In further publication A.K. Guskova & I.A. Gusev (1996) characterising the Chernobyl accident survivors exposed to 0.7–13 Gy of external γ-radiation do disregard any kind of neuropsychiatric effects except distress and unfavorable social-psychological resonance. At the same time A. Guskova & A. Barabanov (1996) pointed out to the extremely severe pain syndrome within structure of combined radiation injuries and neurological disorders in *endogenous intoxication* syndrome structure. A.K. Guskova (1997) concluded the defining role of the *non-radiation factors* (i.e. premorbid personality, social motivation, job placement adequacy) in psychological and personal disorders in patients — ARS survivors.

Estimate of remote psychoneurological consequences of irradiation and ARS in particular remain thereby contradictory. *Neuropsychiatric and neuro-psychophysiological characterisation* of ARS survivors is issued in the present part of monograph with post-radiation encephalopathy diagnostic criteria development on its basis. The neuropsychiatric consequences of ARS-patients has been monitored up to present on the base of one per year in-patient medical examinations in RCRM, Kiev. All ARS-patients are instituionalised in the Radiation Pathology Department of the Institute for Clinical Radiology, RCRM. Routine clinical neuopsychiatric examinations together with electroencephalography and rheoencephalography are available every year.

110 ARS-patients were enrolled in the study. The 105 (95%) of them were males. Age of involved in the study was 20–75 years old with average 37.0±1.05 years. Retrospective clinical and karyological analysis enabled to adjust the ARS severity degree and demonstrated the typical bone-marrow form of ARS presence only in 73 of patients. The last point became basis of three sub-groups selection among the main study group: ARS-0 — 37 patients with not confirmed ARS diagnosis (average dose of general relatively uniform γ- and β-radiation 0.2±0.05 Gy); ARS-1 — 38 patients survived the 1st degree ARS (1.07±0.12 Gy); ARS-2 — 35 patients survived the 2nd and 3rd degree ARS (2.69±0.20 Gy). All examined persons from main study group were managed in Radiation Pathology Department of Institute for Clinical Radiology of RCRM, AMS of Ukraine. Neuropsychiatric and neuro-psychophysiological examinations to ARS survivors (all involved ones were the right-handed persons) were applied in 1987–1996 in Neurology Department of Institute for Clinical Radiology of RCRM, AMS of Ukraine.

Neuropsychiatric symptomatology dynamics within period 1987–1995 is shown in table 5.5, where the progressive pattern of psycho-neurological, oto-neurological and ophthalmologic disorders among the ARS survivors is obvious.

Table 5.5

NEUROPSYCHIATRIC SYMPTOMATOLOGY DYNAMICS IN PERSONS SURVIVED THE ACUTE RADIATION SICKNESS

Symptom	Study period (number of persons involved)					
	1987–1988 (n= 110)		1990–1991 (n= 110)		1993–1995 (n= 110)	
	abs.	%	abs.	%	abs.	%

Convergence weakness	7	**6.4**	38	**34.5**	48	**43.6**
Nystagmus	4	**3.6**	9	**8.18**	17	**15.5**
Hearing decrease	2	**1.8**	9	**8**	23	**21**
Vestibulopathy	4	**3.6**	19	**17**	44	**40**
Pyramid disorders	8	**7.3**	18	**16.4**	32	**29.1**
Extrapyramidal disorders	7	**6.4**	10	**9.09**	18	**16.4**
Peripheral nervous system disorders	26	**24**	38	**34.5**	49	**44.5**
Sensing disorders	25	**23**	35	**31.8**	65	**59.1**
Co-ordination disorders	10	**9.1**	16	**14.5**	52	**47.3**
Vegetative disorders	105	**95**	108	**98.2**	108	**98.2**
Perception disorders	30	**27**	62	**56.4**	79	**71.8**
Attention disorders	26	**24**	68	**61.8**	83	**75.5**
Memory disorders	22	**20**	63	**57.3**	80	**72.7**
Thinking disorders	4	**3.6**	14	**12.7**	50	**45.5**
Emotional-volitional sphere disorders	98	**89**	106	**96.4**	106	**96.4**
Decrease of intellect	0	**0**	2	**1.82**	22	**20**
Intellectual working capacity decrease	25	**23**	63	**57.3**	78	**70.9**
Eyeground pathology	17	**15**	48	**44**	70	**64**
Eye lens alterations	18	**16**	44	**40**	58	**53**
Acuity of vision decrease	13	**12**	34	**31**	46	**42**

The main neuropsychiatric pathology in the delayed period is *brain organic damage* that was firstly classified as «dyscirculatory encephalopathy» and further (since 1996–1997) as «postradiation encephalopathy» and/or «postradiation dyscirculatory encephalopathy». The dynamic of brain organic damage in ARS-patients for 1987–2001 is presented in figure 5.1.

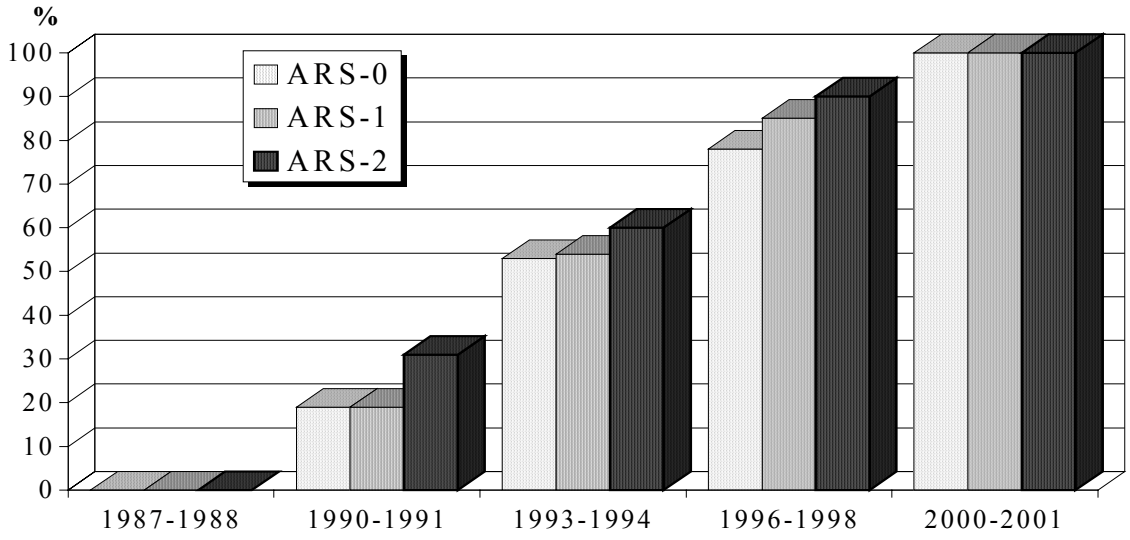

Figure 5.1. The dynamic of brain organic damage in ARS-patients for 1987x2001.
ARS–0 — no confirmed or pre-clinical ARS; ARS–1 — mild ARS or ARS of the 1st severity degree; ARS–2 — moderate to severe ARS or ARS of the 2nd and 3rd severity degree.

The elaborated unified methodology for neuropsychiatric assessment was used since 1996 [Nyagu A.I. et al., 1999] that included neurological and psychiatric examination, neuro- and psychophysiological investigations and pathopsychological testing in the Department of Neurology of the Institute for Clinical Radiology, RCRM.

The characterisation of the ARS-patients and comparison groups examined in 1996–1998 according to the unfied neuropsychiatric methodology are presented in table 5.6.

Table 5.6

CHARACTERISATION OF THE EXAMINED ARS-PATIENTS AND COMPARISON GROUPS

Group	n	Age at the time of examination, years (M3M)	Dose, Gy, M3m
I group (ARS)	70	47.2±1.2	1.78±0.2
ARS–0 (pre-clinical ARS)	20	45.4±2.5	0.58±0.17
ARS–1 (mild ARS)	30	47.0±2.2	1.45±0.3
ARS–2 (moderate to severe ARS)	20	55.2±7.5	3.4±0.4
II group (liquidators of 1986–1987)	80	47.3±0.97	0.54±0.05
subgroup IIA (liquidators who have been working in the Chernobyl exclusion zone in 1986–1987 for a short-time period (less 3 months)	37	46.0±1.13	0.57±0.06
subgroup IIB (liquidators who have been working in the Chernobyl exclusion zone in 1986–1987 for a long-time period (3–5 and more years)	43	50±1.77	0.47±0.05
Control group A (healthy)	15	44.1±3.86	—
Control group B (patients with dyscirculatory encephalopathy)	15	53.1±2.98	—
Control group C (veterans with PTSD)	20	43.4±1.83	—

Clinical neurological examination was classically carried out. Psychiatric examination was performed on the base of the typical psychiatric interview and using of the scales, pathopsychological and psychometric tests as follows:

- Brief Psychiatric Rating Scale, BPRS [Overall J.E., Gorham D.R., 1962];
- Scale for the Assessment of Negative Symptoms, SANS (WHO Coordinated multi-center study on the course and outcome of schizophrenia, 2/93 ©Andreasen N.C., 1984);
- Screening Schedule, WHO 5368.1 MNH (11/78) (WHO Collaborative study on determinants of outcome of severe mental disorders, 1978);
- PTSD Scales: Impact of Events Scale (IES) (©Horowitz M.J. et al., 1979) and Arousal Scale of PTSD (IDA) (©Snaith et al., 1978);
- Unmasking Depression. Self-rating Depression Scale (SDS) (©Zung W.W.K., 1974);
- General Health Questionnaire, GHQ-28;
- Adapted and validate MMPI version;
- Working capacity diagnostic method (test of A. Landolt);
- Wechsler Adults Intelligence Scale (WAIS)

Neuro- and psychophysiological investigations included:

- *computerised EEG* (cEEG)
- *somatosensoric evoked potentials (SSEP)*
- *checkerboard reversible pattern visual evoked potentials* (VEP)
- *brainstem auditory evoked potentials* (BAEP)
- *assessment of vestibular function*
- *sympathetic skin response* (SSR)
- *autonomous nervous system tests*
- *distant thermography*
- *rheoencephalography*
- *ultrasonic dopplerography*

Neurological characterisation. The main subjective symptoms frequency in the ARS-patients are shown in table 5.7.

Table 5.7

SUBJECTIVE SYMPTOMS IN THE ARS-PATIENTS

Subjective symptom	ARS-patients (n= 70)
Headache	58(83%)
Memory deterioration	54(77%)
Limb pain	52(74%)

Fatigue	46(69%)
Limb sweating	41(58%)
General weakness	40(57%)
Vertigo	37(53%)
Co-ordination disorders	35(50%)
Odd skin sensations	33(47%)
Irritability	29(41%)
Depressive mood	22(31%)
Sleepy	22(31%)

Almost the all ARS-patients complain of recurrent or persistent headache, limb pain and odd skin sensations, fatigue, vertigo, memory and working capacity deterioration, irritability.

The objective neurological symptoms are shown in table 5.8. According to the neurological examination the severe focal symptoms were absent. At the same time the microfocal abnormalities as convergence weakness, mild face muscles asymmetry, vestibular dysfunction, delicate pyramidal and extrapyramidal insufficiency, signs of oral automatism (subcortical signs), mild asymmetry of the tendal and periostal reflexes, coordination disorders were revealed.

Paroxysmal states were characteristic for a majority of the ARS-patients. Overwhelming majority of this paroxysmal states are autonomic-vascular paroxysms or Pefield's «diencephalic autonomic epilepsy» with the paroxysmal activity focus at the hypothalamus. However, an increase of frequency of epileptic syndromes with complex partial seizures was also observed. The sensoric-algetic and autonomic disorders were diagnosed in almost the all ARS-patients (table 5.8).

Table 5.8

NEUROLOGICAL SYMPTOMS IN THE ARS-PATIENTS

Neurological symptom	ARS-patients (n= 70)
Acuity of vision deterioration	29(41%)
Convergence weakness	34(49%)
Nystagmus	17(24%)
Hearing deterioration	24(34%)
Vestibular disorders	44(63%)
Pyramidal signs	25(36%)
Extrapyramidal signs	22(31%)
Sensory disorders	42(60%)
Coordination disorders	35(50%)
Paroxysmal states	46(66%)
Sensoric-algetic disorders	65(93%)
Autonomic disorders	67(96%)
Diffusive microfocal neurological signs	45(64%)
Blood pressure increase	22(31%)

The onset of the neuropsychiatric disorders in the liquidators of 1986–1987 as well as in a majority of the ARS-patients was as dysautonomia (autonomic-vascular dysfunction), which fast (during 2–5 years) developed towards encephalopathy. The acute radiation and radiation dyscirculatory encephalopathy were diagnosed in the patients who had ARS of the grave severity degree (more 4 Gy) [Torubarov F.S. et al., 1989].

Consequently, the sensoric-algetic, autonomic, vestibular-ataxic and epileptic syndromes together with mild pyramidal and extrapyramidal insufficiency are the neurological signs of organic brain damage (encephalopathy) at the remote period of irradiation. Frequency of these symptoms increased following irradiation by 0.5 Gy and more. It should be noted the direct correlation between the frequency and severity of encephalopathy and the ARS severity degree. Moreover, in a number of cases there was no correlation between the encephalopathy severity and the degree of cardio-vascular system damage, lipid metabolism, blood pressure. It testifies to the peculiarities of the encephalopathy in the overirradiated persons when atherosclerosis or arterial hypertension was absent [Nyagu A.I. et al., 1997–1999].

Psychiatric and pathopsychological characterisation. In 1987–1988 psychopathological manifestations appeared to be variants of *asthenic syndrome* with pronounced vegetative dysfunction almost in all ARS-patients. Some patients were recorded with dysphoria, and in some cases — agitating and explosiveness at that phase.

By 1990–1991 *cerebrasthenic syndrome* and some types of neurotic states were prevailed in the majority of the patients. At this stage it is first to diagnose clear symptoms of *brain organic damage*, at that against a background of senesto- and/or paranoial-hypochondriac manifestations it was observed mild to moderate intellectual-mnestic

decrease with the signs of endoformism of some symptoms (psychic activity decrease by the type of apathetic phenomena, autistic behavioural elements, thinking inconsistency, inadequate emotional reactions).

In 7–8 years after ARS the deterioration of mental state was recorded. The *organic brain damage* was diagnosed in 56% of the patients, the frequency of which depended on ARS severity degree as well as for the disorders of psychopathic type. Senestopathies were complicated and supplemented with psychosensory disorders. The mentioned symptoms in many respects made for growing decrease in volitional motives, autisation, psychosocial disadaptation as the result of apatho-abulic disorders. Depressive and anxiety symptoms were also caharacteristic.

In 1996–1998 *organic mental disorders* predominated that were diagnosed in 84% of the ARS-patients. The patients were registered with pains of various localisation, paresthesia and senestopathies. Last ones were as distressing, painful and perverted sensations, which caused hyperbolic treatment, were accompanied by the pronounced emotional reaction and essential drawing in thinking up to overvalue ideas and obsessions. Quite often paroxysmal psychosensory disorders as metamorphopsia and autometamorphopsia were observed. Depressive symptoms increased and became more «anergic». It was typical decrease in memorisation, storage and reproduction of new information (dysmnesia) was typical for memory disorders, though it was also observed fallout of early gained knowledge and everyday skills. The decrease in attention stability, switching and concentration were revealed. Cognitive dysfunction were presented through suspicious or paranoid thinking and/or excessive anxiety for a solitary, often abstract question (religion, «justice» and «injustice»), and also hypochondriac formations — quite often of supervaluable type. It was exhibited changes of speech tempo and flow as circumstantialities and viscosity. Besides it was revealed decreased ability to perseverance and persistence as for goal-oriented activity, especially at long and supposing delayed compensation, poor contact with environmental with outsider tendencies as well as apathy and abulia.

In 2000–2001 *organic mental disorders* were diagnosed in 100% of the ARS-patients. *Negative psychopathologic symptomatology* and *«anergic» depression* are the characteristic psychopathology 15 years after ARS. Negative psychopathologic symptomatology like an affective flattening (sometimes reaching the degree of apathy), abulic manifestations, anhedonia, tendency to being alone, social withdrawal right up to autism – all these are of dominant importance for psychopathological picture in the ARS remote period.

Mental state of the ARS-patients and liquidators of 1986–1987 is greatly distinguished from the control groups. Somatic concern, blunted or inappropriate affect, emotional withdrawal, as well as suspiciousness and unusual thought content dominated in the irradiated patients according to the BPRS (table 5.9). Thereby, at the remote period after irradiation the negative psychopathological symptoms are of particular importance.

Table 5.9

INDICES OF THE BRIEF PSYCHIATRIC RATING SCALE (BPRS) IN THE MAIN AND CONTROL GROUPS

Index	I group (n= 70)	II group (n= 80)	Group A (n= 15)	Group B (n= 15)	Group C (n= 20)
Somatic concern	4.2±0.2**	4.1±0.2**	1.8±0.1	3.8±0.4*	3.3±0.3*
Anxiety	2.4±0.1*	3±0.2*	1.1±0.1	3.3±0.2*	4.1±0.3**
Emotional withdrawal	3.5±0.2**	2.2±0.2**	0.5±0.1	1.3±0.1*	1.9±0.3*
Conceptual disorganisation	0.7±0.1	0.6±0.2	0	0.5±0.2	0.5±0.1
Guilt feelings	1.7±0.2*	1.3±0.2*	0	0.7±0.2	2.5±0.2**
Tension	1.1±0.2	1.6±0.3*	0	1.7±0.1*	2.8±0.3**
Mannerisms and posturing	0.5±0.1	0.4±0.1	0	0.5±0.2	0.8±0.1
Grandiosity	0	0.2±0.1	0	0	0
Depressive mood	2.5±0.2*	3.6±0.2**	1.2±0.2	3.1±0.3**	3.8±0.4**
Hostility	0.4±0.1	0.5±0.2	0	0	1.8±0.2*
Suspiciousness	3±0.2**	2.1±0.2*	0.3±0.1	1.9±0.2*	1.1±0.2
Hallucinatory behaviour	0.3±0.1	0.2±0.1	0	0	0
Motor retardation	2.1±0.1*	1.9±0.2*	0	1.9±0.2*	0
Uncooperativeness	1.5±0.1*	2.4±0.2*	0	0	2.1±0.1*
Unusual thought contents	2.9±0.2**	2.1±0.2*	0.5±0.1	1.3±0.2	1.5±0.2
Blunted or inappropriate affect	3.6±0.2*	2.2±0.2*	0	1.1±0.2*	0.6±0.1
Sum 1–16	30.4±0.4**	28.4±0.5**	5.4±0.2	21.1±0.4**	26.8±0.5**

Notes: * — probability $p<0.05$ relatively to the control group A

** — probability $p<0.01$ relatively to the control group A

A reduction of remembering, saving and reproduction of new information was characteristic for memory deterioration. Sometimes fallout of long ago obtained knowledge and everyday skills were also observed. The acoustic-speech memory was particularly often disordered. A reduction of attention stability, switching and

concentrations was revealed. As a whole, mental capacity to work was reduced according to the criteria of efficiency, endurance, accuracy and reliability, moreover mainly to the account of weak quantitative and qualitative results of work.

Total *intelligence quotient* (IQ) in the ARS-patients in 2000-2001 was 102.2±14.5 (M±SD), verbal IQ — 103.2±17.3 and performance IQ — 100.9±9.0. The IQ discrepancies with the performance IQ decrement testifies to brain organic damage in adults. Moreover, in spite of averaged IQ of ARS-patients corresponds to «mean» intelligence, the majority of the ARS-patients are quite high-qualified specialists with high level of education. Consequently, their IQ should be higher than that registered.

The cognitive disorders included a worsening of planning, long-term goals forming, abilities to mobilise a facility of the personality for these goals achievement, a possibility to foresee of obvious consequences in the future, abilities to development and realisation of the alternative problem-deciding strategies, as well as simultaneous execution of several tasks. Besides, suspicious or paranoid thinking and/or overweening worry by the abstract problem (East religions, «recovery systems» and «correct life-way», «fairness and unfairness»), circumstantiality and viscosity of thinking and speech were revealed.

The affective disorders included mainly affect flattening, up to apathy sometimes, with a narrowing of a circle of interests and contacts with environment, social withdrawing and autism. Depressive disorders were mainly observed in combination with languor, adynamia, hypobulia, lack of initiative. Anxiety-depressive disorders, feeling of despair and an impossibility to influence or change the future were also revealed. Obsessive-phobic and dysphoric states were diagnosed comparatively less.

The negative psychopathological symptoms were studied with the SANS (table 5.10). A majority of the negative symptoms included unchanging facial expressions, paucity of expressive gestures, poor eye contact, affective nonresponsiveness, lack of vocal inflections, poverty of content of speech, increased latency of response, physical anergia, a reduction of recreational interest and activities, a reduction of sexual interest and activity, trends to be alone, social withdrawal.

Table 5.10

INDICES OF THE SCALE FOR THE ASSESSMENT OF NEGATIVE SYMPTOMS (SANS) IN THE MAIN AND CONTROL GROUPS

Index	I group (n=70)	II group (n=80)	Group A (n=15)	Group B (n=15)	Group C (n=20)
Affective flattening or blunting	2.4±0.1**	2.1±0.2**	0	0.4±0.1	0.7±0.1
Alogia	2.2±0.1**	1.9±0.2*	0	1.3±0.3*	0.4±0.1
Avolition—apathy	2.6±0.1**	2.5±0.2**	0	0.9±0.1*	0.6±0.1*
Anhedonia—asociality	2.7±0.1**	2.6±0.2**	0	0.5±0.2	1.5±0.2*
Attention	2.7±0.2**	2.3±0.2**	0	2.1±0.2**	0.5±0.2

Notes: * — probability $p<0.05$ relatively to the control group A

** — probability $p<0.01$ relatively to the control group A

A majority (62%) of the examined irradiated patients has increased risk of development of severe mental disorders according to the Screening Schedule. The results of this schedule have also confirmed a prevalence ($p<0.01$) of the negative symptoms comparatively with the positive.

The PTSD study with related scales has shown that the all examined survivors were exposed to psychoemotional stress concerning the Chernobyl disaster: average score on the Impact of Events Scale (IES) in the group I — 23.5±1.4 and in the group II — 27.4±1.2. Memory about the disaster and associated arousal take a leading place in psychopathology of the 8(11%) ARS-patients and the 22(27%) liquidators of 1986–1987. It concerns predominantly those who had not been prepared to emergency and took a part in the accident consequences cleaning up works involuntary. Among another patients PTSD had no dominant clinical value.

According to the Unmasking Depression Self-rating Depression Scale (SDS) the minimal to mild and the moderate to marked depression were revealed in the 41(58%) ARS-patients and in 45(56%) liquidators of 1986–1987, the severe to extreme depression — in 7(10%) and 17(21%) patients correspondingly. Moreover, according to the General Health Questionnaire GHQ-28 the all examined survivors self-estimated their mental and physical health is significantly worse than usually.

In 5–10 years after ARS there was the characteristic «floating» abnormal averaged MMPI-profile with simultaneous raising of both «neurotic» and «psychotic» scales. At that, the MMPI-profiles of the irradiated persons differ significantly from the profiles in the control groups (figures 5.2 and 5.3).

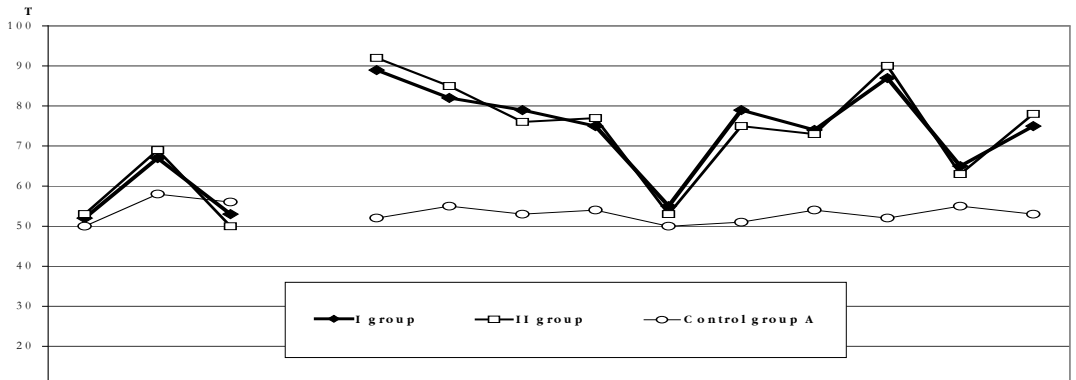

Figure 5.2. Averaged MMPI-profiles of the ARS-patients (I group) and liquidators (II group) comparatively with the norm (control group A)

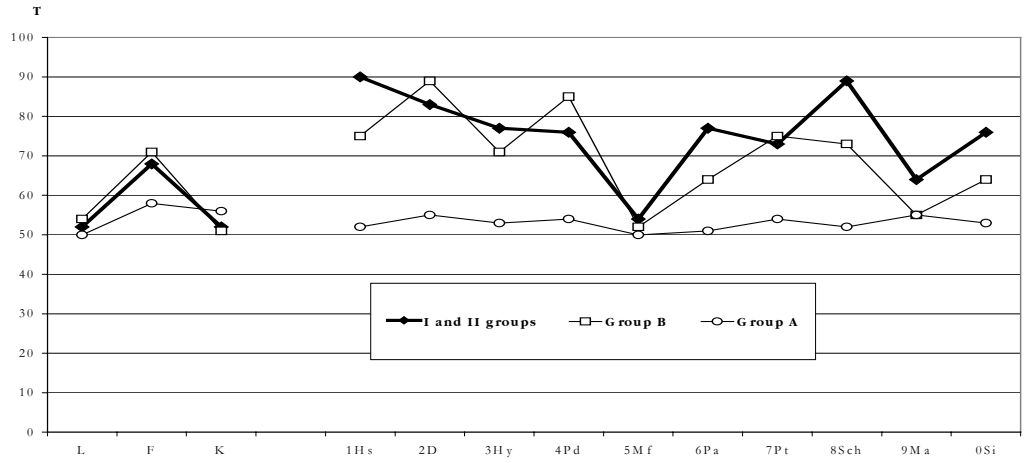

Figure 5.3. Averaged MMPI-profiles of the irradiated persons (I and II groups) comparatively with the norm (control group A) and PTSD (control group B)

The patients of the I and II groups distinguished with strongly pronounced stress and personality disadaptation associated with the signs of the disintegration of the intellectual and emotional spheres. There is the psychosomatic predisposition — hypochondriac and depressive symptoms were associated with inert thought, dogmatism as well as caution and even hostility in the interpersonal contacts. Chronic feelings of mental discomfort and diffidence, a reduction of general productivity, guilt and inferiority complexes were complicated with apathetic signs and somatic concern.

Thus, the MMPI-profile of the irradiated persons testifies to the asthenic type of reactions together with depressive experience complicated with hypochondriac and paranoiac symptoms. Moreover, a significant increase ($p<0.01$) of the schizophrenia, hypochondria, paranoia, epilepsy and odd sensoric perception MMPI-scales together with a decrease of the personality «nucleus» power and intelligence quotient scales were revealed. These MMPI-scales deviations correlated feebly with the value of irradiation dose ($r=0.12–0.25$, $p<0.05$) at the force of factor (dose of irradiation) influence $\eta^2=0.19–0.34$, $p<0.01$.

In 13–15 years after ARS there was still the characteristic «floating» abnormal averaged MMPI-profile with simultaneous raising of both «neurotic» and «psychotic» scales. At the same time the depression and schizophrenia scales dominated.

The results of correlation analysis between the age, absorbed dose and mental health are shown in table 5.11. The neurotic symptoms have no significant correlation with the dose and age. Some symptoms (e.g. aggression), on the contrary, were decreased proportionally to an increase of the dose. At the same time such symptoms as lack of interests and initiative, alogia and, particularly, inattentiveness correlated with both the age and dose. Social and emotional withdrawal, affective flattening, anhedonia—asociality, suspiciousness, motor retardation, unusual thought content, as well as the summarised BPRS-score correlated with the absorbed dose stronger ($r=0.3–0.5$) than with the age ($r=0.14–0.34$).

The schizophrenia-like psychopathology (unchanging facial expression, paucity of expressive gestures, poor eye contact, affective nonresponsiveness, lack of vocal inflections, poverty of content of speech, increased latency of response, physical anergia, a reduction of recreational interest and activities, a decrease of sexual interest and activity, a tendency to be alone, social withdrawal) dominate ($p<0.05$) following irradiation at the dose 0.3–0.5 Gy and more. At the same time the affective and somatoform symptoms (anxiety, depression, irritability, somatic concern) prevail ($p<0.05$) in the liquidators irradiated at the dose less 0.3 Gy. Thus, at the ARS remote period and in the liquidators of 1986–1987 the brain organic damage has been forming. At that the apathetic-abulic endoformous brain organic syndrome prevails among the liquidators (including the ARS-patients) irradiated at the doses 0.3–0.5 Gy and more while cerebrasthenic syndrome or cerebrasthenic and dysthymic variants of brain organic syndrome predominate among the liquidators irradiated at the doses less 0.3 Gy. [Loganovsky K.N., 1995, 1999–2001; Loganovsky K.N., Loganovskaja, 2001].

Table 5.11

LINEAR CORRELATION COEFFICIENTS BETWEEN THE AGE, ABSORBED DOSE OF IRRADIATION AND PSYCHOPATHOLOGICAL SYMPTOMS

Symptom	Age	p	Absorbed dose	p

Lack of interest and initiative	0.22	<0.05	0.23	<0.05
Social withdrawal	–0.12	>0.05	0.26	<0.05
Aggression	0.09	>0.05	–0.26	<0.05
Affective flattening	0.21	<0.05	0.36	<0.01
Alogia	0.46	<0.01	0.51	<0.01
Avolution—apathy	0.22	<0.05	0.12	>0.05
Anhedonia—asociality	0.34	<0.01	0.46	<0.01
Inattentiveness	0.56	<0.01	0.43	<0.01
Somatic concern	–0.23	<0.05	–0.31	<0.01
Anxiety	–0.20	<0.05	–0.29	<0.05
Emotional withdrawal	0.21	<0.05	0.46	<0.01
Tension	–0.06	>0.05	0.03	>0.05
Suspiciousness	0.05	>0.05	0.26	<0.05
Motor retardation	0.19	<0.05	0.32	<0.01
Unusual thought content	0.08	>0.05	0.22	<0.05
Blunted or inappropriate affect	0.16	<0.05	0.41	<0.01
Excitement	–0.07	>0.05	–0.18	<0.05
Summarised BPRS-score	0.14	<0.05	0.40	<0.01
Depression (SDS)	0.17	<0.05	0.06	>0.05
Impact of Events Scale (IES) (PTSD)	–0.10	>0.05	0.16	<0.05
Arousal Scale of PTSD (IDA)	–0.08	>0.05	–0.21	<0.05
GHQ-28	0.02	>0.05	0.05	>0.05

Mental and behaviour disorders according to the ICD-10 criteria in the ARS-patients are presented in table 5.12.

Table 5.12

MENTAL AND BEHAVIOUR DISORDERS ACCORDING O THE ICD-10 CRITERIA IN THE ARS-PATIENTS

Mental and behaviour disorders	ICD-10 code	ARS-patients (n= 70)
ORGANIC, INCLUDING SYMPTOMATIC, MENTAL DISORDERS:	F00–F09	62(88%)
• With cerebrasthenia dominance	F06.6	8(11%)
• With brain organic syndrome dominance:	F07;F06	54(77%)
Cerebrasthenic type	F06.7	11(16%)
Dysthymic type	F06.3	9(13%)
Apathetic-abulic type	F07.0	21(30%)
Paranoid type	F06.2	6(9%)
Explosive type	F07.8	2(3%)
Dementia type	F02.8	5(7%)
SCHIZOTYPAL DISORDER	F21	9(13%)
ENDURING PERSONALITY CHANGE AFTER CATASTROPHIC EXPERIENCE	F62.0	8(11%)
SOMATOFORM DISORDERS	F45	9(13%)
DYSTHYMIA	F34.1	7(10%)

Note. Total rate of mental disorders is more 100% because of sometimes a patient was diagnosed with more one disorder (comorbidity).

Psycho- and neurophysiological investigations. As a result of the visual and computerised EEG analyses we revealed the following patterns of brain electrical activity (table 5.13). The EEG-patterns with interhemispheric asymmetry and paroxysmal activity as discharges of acute and slow waves and «spike—wave» and «polyspike—wave» complexes were characteristic for the irradiated persons.

Table 5.13

EEG-PATTERNS AMONG THE EXAMINED PERSONS

EEG-pattern	I group (n= 70)	II group (n= 80)	Group A (n= 15)	Group B (n= 15)	Group C (n= 20)
Organised with α–activity dominance	0	22(27%)*	12(80%)*	6(40%)*	12(60)*
Hypersynchronic	7(10%)	7(9%)	3(20%)	2(13%)	4(20%)
Flat polymorphous	58(83%)	55(69%)	0*	5(33%)*	2(10%)*
Disorganised with α–activity dominance	2(3%)	10(12%)	0	1(7%)	2(10%)
Disorganised with δ–activity dominance	3(4%)	8(10%)	0	1(7%)	0
Laterality of abnormal activity:					
– bilateral	14(20%)	6(7%)	3(20%)	4(27%)	3(15%)
– lefthemicpheric	40(57%)	25(31%)*	—	1(6%)*	2(10%)*
– righthemispheric	16(23%)	27(35%)	—	4(27%)	3(15%)

Note. * — probability $p<0.001$ relatively to the I group according to the χ^2 criterion.

The EEG-patterns of irradiated patients distinguished significantly from the control groups. The normal EEG-patterns were absent in the ARS-patients. The EEG-patterns with interhemispheric asymmetry, particularly the lefthemispheric EEG-patterns with lateralisation of abnormal activity towards the left brain hemisphere predominated in the patients of the I and II groups [Loganovsky K.N., 1999–2001; Loganovsky K.N., Loganovskaja, 2001].

The flat polymorphous EEG-pattern with diffusive δ- and β-power predominantly in the fronto-temporal areas lateralised to the left, dominating, hemisphere together with paroxysmal activity against a background of low-voltage (10–25 μV) EEG was characteristic for the irradiated patients. In addition to the flat EEG the disorganised EEG-patterns were also typical for the irradiated persons. The disorganised EEG-pattern with α-activity distinguished with disorganised high-voltage α-activity dominating throughout the brain increased amplitude of β-activity, diffusive θ- and δ-activity of quite high amplitude together with bilateral paroxysmal activity. The disorganised EEG-pattern with θ- and δ-activity characterised with decreased α-activity against a background of high- or middle-amplitude dysrhythmic EEG. These EEG-patterns testify to organic brain changes and sometimes increased seizure readiness of the brain.

The degree of brain bioelectrical activity disturbances is directly proportional to the value of absorbed dose ($r=0.41$; $p<0.05$) and the age of a patient at the time of examination ($r=0.2$; $p<0.05$). Thus, brain electrical activity disturbances in the ARS-patients and liquidators of 1986–1987 caused sufficiently by the aftermath of radiation exposure.

Spectral analysis of brain electrical activity gave the characteristic EEG-pattern for the irradiated patients: a simultaneous increase of δ-(1–4 Hz) and β-(>12–32 Hz)-power together with a decrease of (>4–7 Hz) and α-(>7–12 Hz)-power (figure 5.4). This EEG-pattern was characteristic for both the ARS-patients and the liquidators of 1986–1987 who had not been diagnosed with ARS. However, the EEG-patterns of the patients of the I group differ from those on the II group with increased δ-power, particularly in the left fronto-temporal region, and more depressed of θ-power. This EEG-pattern of the irradiated patients testifies to structural and functional changes of the brain predominantly in the fronto-temporal cortex (particularly in the left, dominating, hemisphere) and the limbic-reticular-diencephalic complex.

The dose–effect relationship for the EEG-parameters was observed in the liquidators of 1986–1987 (figures 5.5 and 5.6). Irradiation at the dose more 0.3 Gy caused an increase ($p<0.001$) of δ-power and a decrease of α-power. The duration of irradiation (work at the exclusion zone) did not influence on these EEG-parameters.

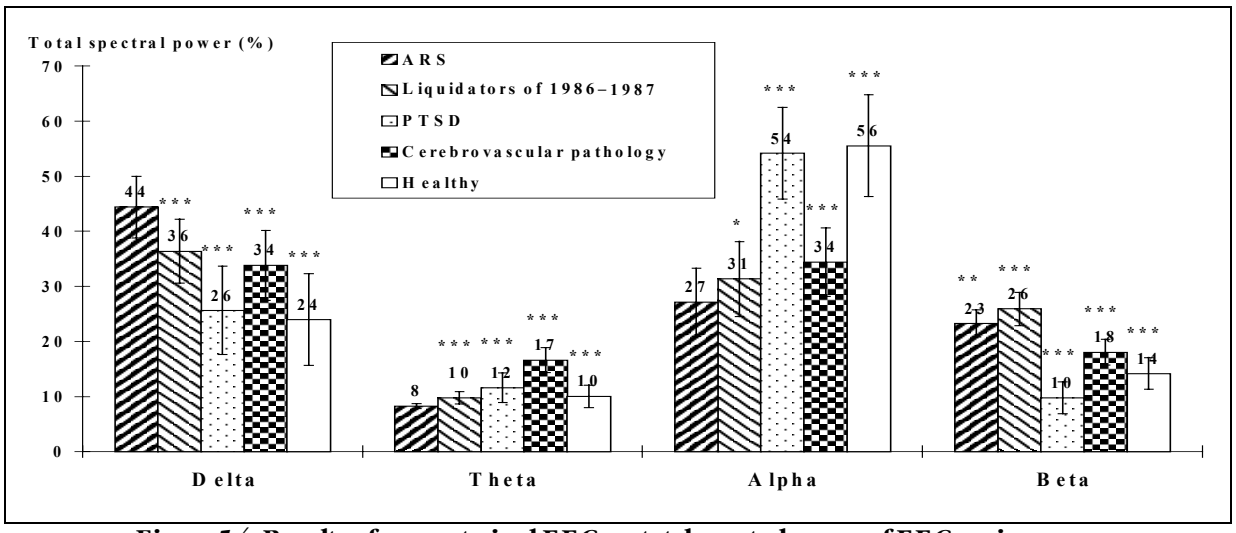

Figure 5.4. Results of computerised EEG з total spectral power of EEG main ranges

Notes: probabilities comparatively with the I group: * — P<0.05, ** — P<0.01, *** — P<0.001.

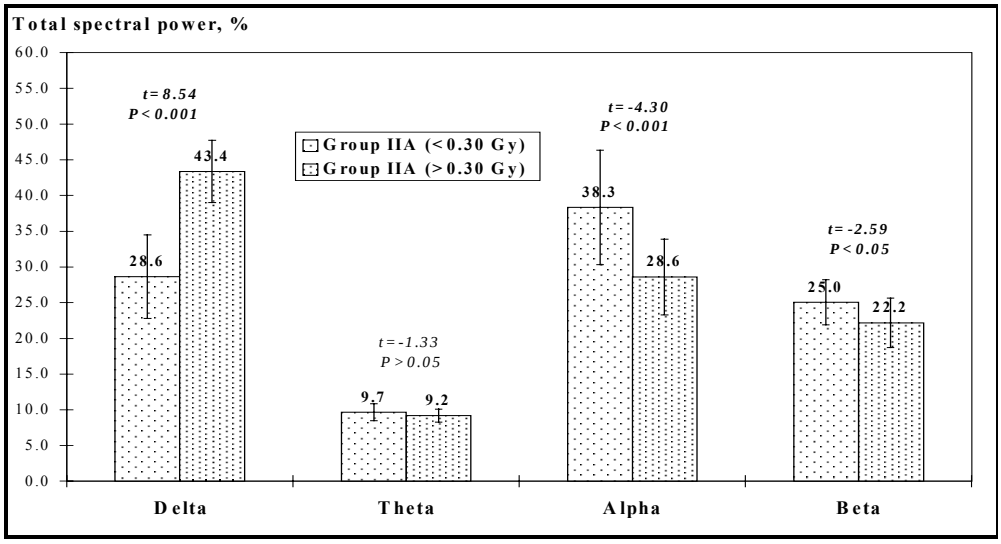

Figure 5.5. Total spectral power of EEG main ranges in the liquidators of 1986x1987 who have been working at the Exclusion zone for a short-term period depending on the dose

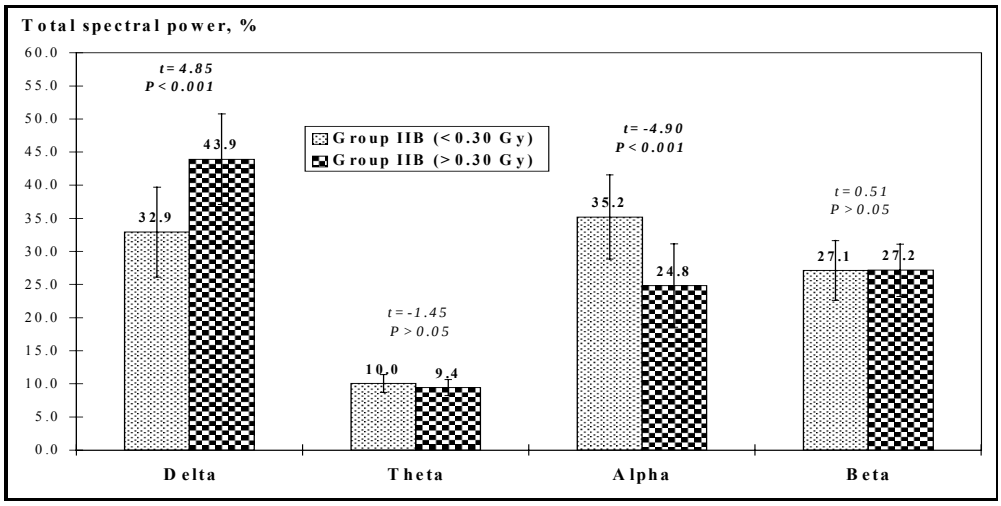

Figure 5.6. Total spectral power of EEG main ranges in the liquidators of 1986x1987 who have been working at the Exclusion zone for a long-term period depending on the dose

Long-term work (3–5 and more years) at the exclusion zone at irradiation at the doses less 0.3 Gy increased ($P<0.05$) δ-power (figure 5.7), and at the doses more 0.3 Gy increased ($P<0.05$) β-power (figure 5.8).

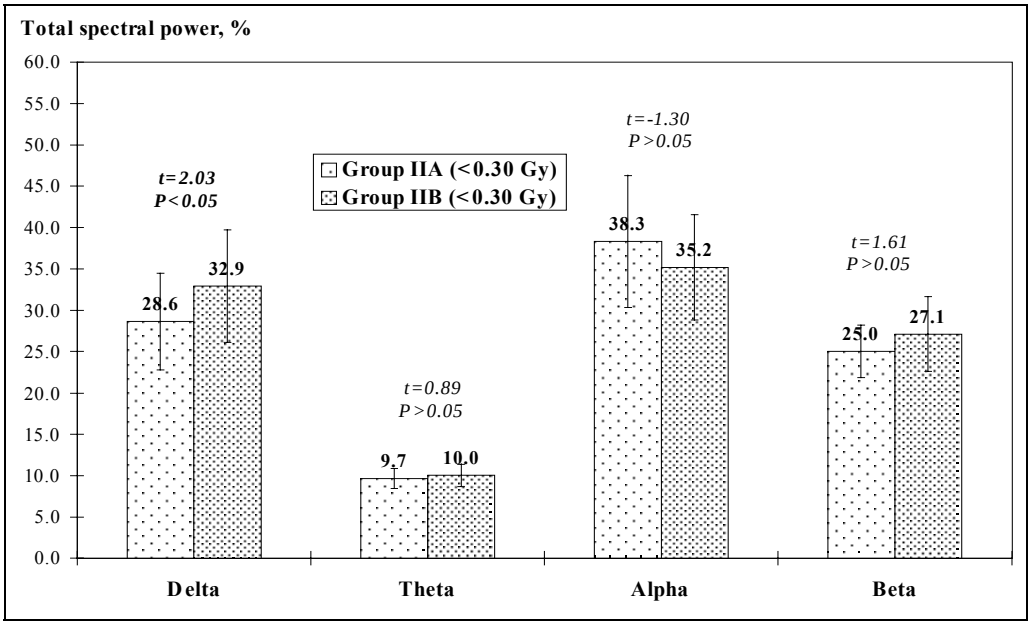

Figure 5.7. Total spectral power of EEG main ranges in the liquidators of 1986-1987 irradiated in doses less 0.30 Gy depending on the work duration at the Exclusion zone

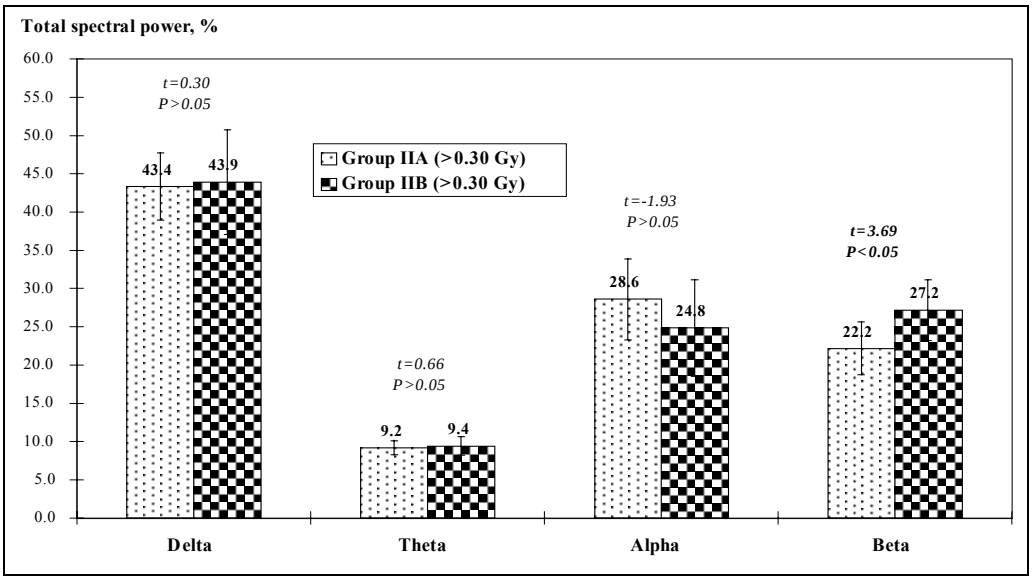

Figure 5.8. Total spectral power of EEG main ranges in the liquidators of 1986-1987 irradiated in doses more 0.30 Gy depending on the work duration at the Exclusion zone

The linear dose—effect relationship was established for δ-power in the left temporal region T_3 (figure 5.9).

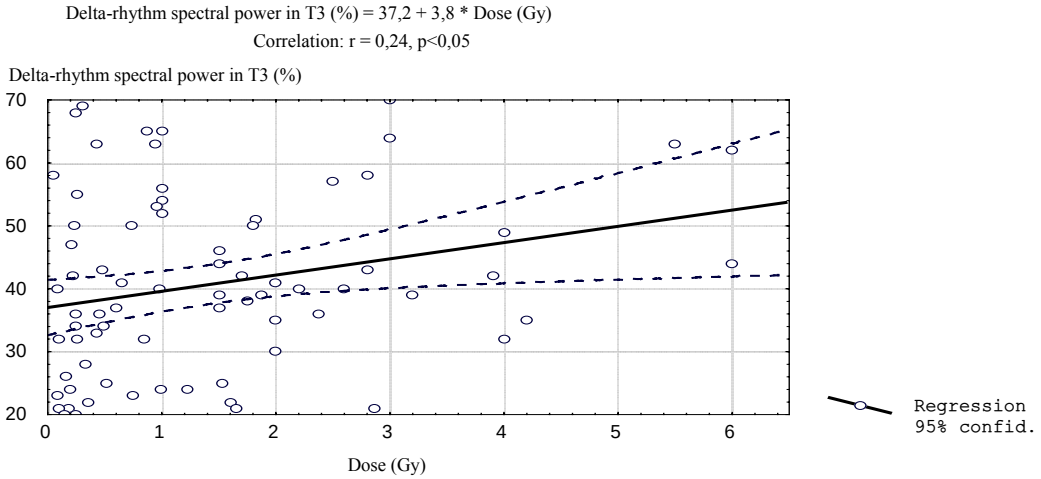

Figure 5.9. Linear dose3 effect relationship for δ-power in the left temporal region (T_3) depending on the absorbed dose value

Technology of brain bioelectrical activity analysis by help of deflection factors clear demonstrated significant differences between irradiation aftermath and well-known neuropsychiatric pathology (figure 10). After irradiation δ- and β-power dramatically increased, significantly more than at chronic cerebrovascular pathology (DEP) and PTSD consequences. At the same time θ-power deflection from the mean norm in the irradiated persons was diametrically opposite comparatively with both DEP and PTSD. A development of cerebrovascular pathology and PTSD is associated with an increase of θ-power (which is generated in hippocampus), however irradiation provoked a depression of this EEG-range that also confirms a pathology of limbic system as the characteristic sign of the postradiation brain damage.

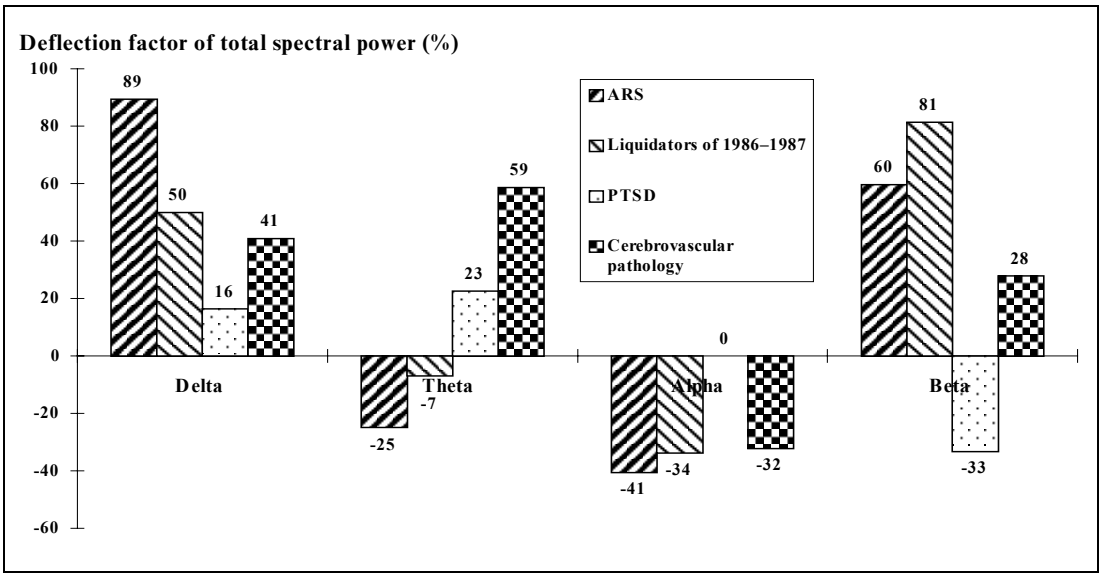

Figure 5.10. Deflection factors values (%) of total spectral power of EEG main ranges

Note. The deflection factor was used for detection of the degree and direction of the psychophysiological parameter deviation from the norm. It was calculated according to the formula as follows:

$Df = (A_1 — A_k) \cdot 100\ \% \div A_k$,

where Df — the deflection factor, A_1 — the value of the index to be studied, A_k — the mean normal value of this index. The deflection factor is positive if the parameter was increased in a patient comparatively to the norm, and it is negative when the parameter was decreased.

Latent period (LP) values of *somatosensoric evoked potentials* (SSEP) early components N_{20} & P_{25} in projective hemispheres zone, intermediate N_{140} and late P_{300} & N_{400} both in projective and associative zones were fixed in ARS-patients being higher ($p<0.05$) than in control whereas amplitude values of early (N_{20} & P_{25}) and late (P_{300} & N_{400}) SSEP components in projective zone (C_3) — somewhat lower than in control ($p>0.05$). Revealed peculiarities indicate the perception and somatic-sensory information processing alteration presence on somatic-sensory afferent

system all levels with afferentation central pathways alteration prevalence under somatic-sensory afferent system non-specific (extralemniscus) part pathological activation and respectively specific (lemniscus) part depression in ARS remote period [Loganovsky K.N., 1993, 2000].

Somatic-sensory afferentation specific manifestations were revealed in survivors through SSEP topographic mapping application. Amplitude reduction and LP elevation of SSEP early (N_{20} & P_{25}) and late (P_{300} & N_{400}) components in projective zone (left central lead C_3 under right medial nerve stimulation) was fixed. Correlation analysis revealed the confidential ($p<0.01$) and moderately pronounced relation presence between SSEP revealed asymmetry and absorbed radiation dose ($r=0.4$). Neither description of stated SSEP asymmetry was found in available literature nor among examined persons from various control groups [Loganovsky K.N., 1992, 1993, 2000] that enable to consider it as characteristic for radiation exposure aftermath where along with somatic-sensory afferent system extralemniscus part irritation the signs are revealed of primary and secondary somatic-sensory cortex pathology both with that of tertiary parietal associative zone (left dominating hemisphere angular and supramarginal convolutions zone) where tactile, kinesthetic, vestibular, visual and hearing information is integrated. Namely the tertiary parietal associative zone is considered at present the material substrate of the human perception and cognition most complex forms [Lurija A.R., 1969; Duus P., 1996] which disorders clinical manifestations are to such extent presented in patients who survived ARS.

Checkerboard reversible pattern VEP and their parameters topographic distribution in the irradiation patients distinguished significantly from the norm. P_{100} amplitude was increased and its latency was decreased; N_{145} and P_{200} latencies were delayed mainly as a result of deformation of the latest VEP components (table 5.14).

TABLE 5.14

AMPLITUDES AND LATENCIES OF VISUAL EVOKED POTENTIALS

Index	I group (n= 70)	II group (n= 80)	Group A (n= 15)	Group B (n= 15)	Group C (n= 20)
VEP, latency, ms					
P_{100} O_2	82.0±1.1	89.2±1.1**	96.8±1**	102.6±1.2**	88.8±1.5*
N_{145} O_2	128.1±1.5	138.2±1.5**	147.0±1.6**	158.0±1.4**	140.0±1.3**
P_{200} O_2	237.3±1.7	221.4±1.7**	208.0±1.6**	221.0±1.4**	187.0±1.6**
VEP, amplitude, μV					
P_{100} O_2					
N_{145} O_2	4.2±0.1	3.2±0.2**	2.6±0.1**	3.6±0.1*	3.6±0.2*
P_{200} O_2	7.6±0.1	5.6±0.3*	4.2±0.1**	5.2±0.2*	4.2±0.2*
	5.9±0.2	4.9±0.3*	5.6±0.3	4.6±0.3*	5.5±0.4

Notes: probabilities comparatively with the I group: * — $P<0.05$, ** — $P<0.01$.

VEP deformation could testify to organic changes of the brain. VEP acceleration and an increase of their amplitude testify to an increased readiness of the brain for paroxysmal states. Taking into account an absent of visual nerve damage it is possible to suppose that this VEP-pattern associated with an irritation of the diencephalic-limbic-reticular structures together with disorders of sophisticated cortical-subcortical processes of sensoric information processing.

Specific peculiarities of the *brainstem auditory evoked potentials* (BAEP) in ARS remote period are late (III, IV, V) components BAEP deformation, expressed asymmetry of basic components and interpeak intervals as well as V component and III-V interpeak interval latencies increase; V component amplitude decrease; VI (thalamic) component amplitude increase. More over in 6% of the persons who had ARS, it is revealed a significant lengthening of III-V interpeak interval with sharp deformation of BAEP latest components, that can testify to demyelinisation at brain stem level. In ARS remote period the oppression of bottom stem regions structures is predominant. And with it, in some cases irritability phenomena in stem structures, to a greater extent, in thalamus are registered, that intensify due to irradiation dose grow [Yuryev K.L., 1998, 2000].

The most expressed abnormalities of *vestibular function* were observed in the nearest terms after ARS. Further it was registered the reducing of vestibular dysfunction. But in 8–10 observation years a deterioration of vestibular function is registered, that can be explained through organic neurovascular pathology development. There is a direct correlation between vestibular abnormalities severity and the ARS severity degree and, hence, the absorbed irradiation dose.

The type of vestibular reactions also changed in post-accidental year dynamics. If at the first stage (1986–1987) the phenomena of vestibular dysfunction were characterised with expressed statokinetic balance disorders, at the last stage (1996–1998 and later) a spontaneous symptomatology was in the foreground: it was revealed the increase of quantity of persons with spontaneous nystagmus almost twice. The changes of separate parameters of experimental nystagmus, evoked as thermal/caloric as rotary stimulations were also registered. In 9–10 years after ARS the experimental nystagmus assumed a tonic character. These changes in the whole indicate progressing central regulatory mechanisms disturbances of vestibular analyser.

At functional stimulation of the signs of disturbances of experimental nystagmus central regulatory mechanism are registered: dysrythmia, presence of additional nystagmus peaks, deformation of its separate peaks, «dumb» field, reverse phenomenon. During realisation of loading stimulation it was observed expressed touch and

vegetative reaction, that testifies to significant decrease of adaptation-compensation regulatory mechanisms in central (cortical) departments of vestibular analyser.

In dynamics it was registered an increase in spontaneous vestibular symptomatology: occurrence or strengthening of spontaneous or position nystagmus, increase in tone experimental nystagmus, decrease in frequency and increase in the average angular speed of slow nystagmus phase. These data testify to progressing phenomena in the central regions of vestibular analyser and agreeing with an increase in organic CNS and vascular system pathology.

Thus, the registration of spontaneous and evoked bioelectrical brain activity of a head in ARS remote period testifies to *pathology of diencephalo-limbico-reticular structures and associative frontal regions, mainly dominant left hemisphere with expressed abnormalities of central mechanisms of afferentation.*

The abnormalities of autonomic nervous system functional state were performed first of all through change of *sympathetic skin response* (SSR). It was typical for the ARS patients sharp amplitude decrease of SSR hands (156±153 μV on the right and 176±177 μV at the left) and feet (45±35 μV on the right and 45±32 μV on the left), significant (an average more, than 1,5 times more) increase of potential duration and, for the most of examined persons, change of its phase structure. At the same time the values of latent periods SSR did not really differ from the values in control. In research dynamics the gradual fading (SSR amplitude decreased on hands and feet) was registered, and in some cases even the disappearance of SSR, which more often was on feet. The above described clinical data and revealed changes of the SSR peculiarities (dramatic amplitude decrease, phase duration increase and change of phase response structure) testify to a mainly central nature of sympathetic nervous system abnormalities (mainly, in hypothalamus), to decrease in tone and reflex activity of sympathetic vasoconsrictors and sudomotoric skin fibres, which provide with peripheral vascular resistance, thermoregulation and vegetative-trophic influences [Vashchenko E.A. et al., 1997].

Vagotonic symptoms are predominant at rest for the ARS patients. Cardio-vascular system vegetative regulation abnormalities were revealed in the majority of the patients, who had parasympathetic directness more frequent, but in ARS-1 subgroup the abnormalities of sympathetic type were predominant. (including the mixed type). Moreover, it is established, that the number of cases with vertigo while performing orthostetic test depended on ARS severity degree. Hypertensive reaction for isometric test was the most frequent in the patients of ARS-0 subgroup. So cardio-vascular system vegetative regulation abnormalities were registered in ARS remote period as due to floating nerve tone fall of vegetative nervous system sympathetic area, accompanied with vasoconstrictal functional deterioration, especially in the cases, when it is necessary the urgent adaptation of cardio-vascular system to physical loading. Vegetative abnormalities appeared to be more significant in the ARS patients with less severity degree. This fact reflects multifactor etiopathogenesis of these abnormalities, in origination of which exposure to ionising radiation is one of pathogenetic factors. These abnormalities are one of pathophysiological mechanisms, that determine complex development of various (sensory-algetic muscle-tone and vegeto-tropho-vascular) displays of *progressing vegetative insufficiency syndrome.*

In more than 3/4 of the ARS patients the thermographic image of hands, forearms, shins and feet was characterised with hypothermia – «thermo-amputation» limb symptom. In addition, it was quite often registered the asymmetry of integument temperature on hips and trunk as well as paroxysmal-distant proportion changes.

Hypertonic and dystonic-hypertonic types of RhEG-curves are *predominant* in ARS remote period. However the most great number of cases of hypertonic type curves was revealed in ARS-2 subgroup patients, that testified to morphological vascular changes of vessels. *Sphygmic blood filling* was also more decreased in the ARS-patients with more severity degree. The frequency of sphygmic blood filling interhemespheric asymmetry and cerebral venous circulation disorders was also expected to increase depending on ARS severity degree and exceeded ($p<0.05$) the frequency in control group. The increase in fine brain vessel tone and brain vessel resistance was true more often in the ARS-patients, but dependence on a severity degree was not revealed. Using USDG of main neck vessels it was revealed the interhemispheric asymmetry of circulation disorders with predominant disorders in the left hemisphere, mainly in vessel basins left of internal carotid and supratrochlear arteries. It is established, that sphygmic blood filling interhemispheric asymmetries are connected to pronounced *blood flow linear speed changes* in them in 37.5% of ARS-0 subgroup patients, and in 62.5% — with initial changes; in ARS-1 and ARS-2 subgroups patients — in 45% of cases with initial, and 27.5% — with the pronounced changes of main neck vessels. At that the changes at terminal vessel level were revealed in 48% of the patients with intracranial blood flow disorders. At the same time in 75% of cases of the control group only initial changes of main neck vessels were revealed.

The changes of brain vascularity certainly depends on ARS severity degree, and the number of stable morphological brain vascular disorders predominates in ARS-2 subgroup. Vascular changes also correlate with lipid metabolism, arterial pressure level, eye-ground changes. At the same time it is necessary to mention, that there is no direct correlation between vascular changes and the displays of such neurological syndromes as cerebrasthenic, brain organic, statocoordinative and sensory-algetic in some cases. Thus, we can assert, that in these cases the encephalopathy is conditioned not only by dyscirculation mechanism, but, perhaps, direct or indirect exposure to ionising radiation to brain tissue, i.e. the matter is in encephalopathy of another genesis, with vascular factor as of great, but not main importance – in postradiation encephalopathy.

Relative risks (RR) of neurophysiological abnormalities analysis has shown that ARS increases in 5 times a risk of development of brain functional organisation, work at the exclusion zone in 1986–1987 — in 3.65 (the long-term work — almost in 4 times), whereas chronic cerebrovascular pathology and PTSD — in 3 and 2 times correspondingly (figure 5.11) [Nyagu A.I. et al., 1999].

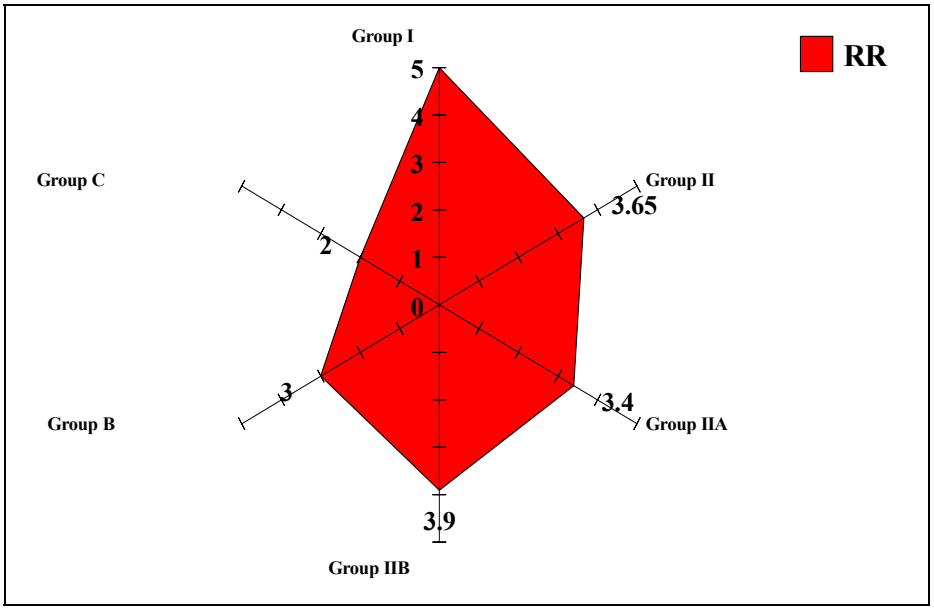

Figure 5.11. Relative Risks (RR) of neurophysiological abnormalities

Contribution analysis allows to calculate a contribution of the main factors influencing on the brain electrical activity after irradiation. The force of influence of the irradiation dose on an increase of δ- and β-power of EEG is 48% ($F=25.2$; $F_{05}=4.0$; $p<0.05$) and 22% ($F=6.5$; $F_{05}=4.0$; $p<0.05$) correspondingly, and upon an decrease of θ- and α-power — 44% ($F=21.3$; $F_{05}=4.0$; $p<0.05$) and 26% ($F=9.5$; $F_{05}=4.0$; $p<0.05$) correspondingly. The force of influence of the duration of work at the exclusion zone on an increase of β-power is 22% ($F=10.1$; $F_{05}=4.0$; $p<0.05$).

At the same time the force of influence of the age on an increase of δ- and β-power is 13% ($F=5.5$; $F_{05}=4.0$; $p<0.05$) and 25% ($F=11.9$; $F_{05}=4.0$; $p<0.05$) correspondingly, and upon a decrease of θ- and α-power — 22% ($F=10.1$; $F_{05}=4.0$; $p<0.05$) and 24% ($F=11.5$; $F_{05}=4.0$; $p<0.05$) correspondingly. It should be stressed the atypical age-related EEG changes in the irradiated patients. In contrast to physiological ageing which accompanied with «slowing» of EEG as an increase of θ-power and a decrease of β-power, the age-related EEG-changes are associated with a decrease of θ-power and an increase of β-power.

Psychological stress (PTSD) dose not influence on both δ- and θ-power. At the same time an increase of stress associated with an increase of α-power (the force of influence — 20%; $F=9.3$; $F_{05}=4.0$; $p<0.05$) and a decrease of β-power (the force of influence — 21%; $F=9.9$; $F_{05}=4.0$; $p<0.05$). That is to say psychological stress provoked diametrically opposite effects on brain electrical activity in comparison with exposure to ionising radiation.

Cerebrovascular pathology (arterial hypertension and cerebral atherosclerosis) does not influence on spectral power of δ-range of EEG in the irradiated persons. The force of influence of arterial hypertension on an increase of θ- and β-power is 24% ($F=11.2$; $F_{05}=4.0$; $p<0.05$) and 30% ($F=15.4$; $F_{05}=4.0$; $p<0.05$) correspondingly. The force of influence of cerebral atherosclerosis on a decrease of θ- and β-power is 23% ($F=10.6$; $F_{05}=4.0$; $p<0.05$) and 35% ($F=19.3$; $F_{05}=4.0$; $p<0.05$) correspondingly, and on an increase of α-power — 32% ($F=16.9$; $F_{05}=4.0$; $p<0.05$).

Comorbidity of physical diseases in the irradiated patients does not influence significantly on the changes of spectral parameters of brain electrical activity.

Thus, psychophysiological disorders in the ARS-patients and liquidators of 1986–1987 are polyetiological: the age of a patient, psychological stress, cerebrovascular pathology, the duration of work at the exclusion zone have influenced in their genesis. However, the value of absorbed dose has provided a major contribution in the revealed psychophysiological disorders. Accordingly the characteristic psychophysiological pattern of the ARS-patients and liquidators of 1986–1987 should be considered as the deterministic effect of ionising radiation [Nyagu A.I. et al., 1997–1999].

Principles and methods of treatment. More than 90% of the ARS-patients are recognised to be disabled. Mental health protection is one of the leading problem, even may be the priority one for the survivors in the result of the Chernobyl disaster. The extreme urgency of the problem is determined with progressing disturbances at all three main mental activity organisational levels: social, personal and cerebral [Nyagu A.I. et al., 1998, 1999].

Social rehabilitation. Now, perhaps, the only more or less reliable social guarantee is an acknowledgement of working disability, i.e. an invalid status. The patients' desire to get an invalid status is in many respects caused by necessity to find social protection and, first of all, in its material aspect. It is more advantageous to be an invalid than healthy in current circumstances. The harm from this situation (caused by imperfection of legislative base) is

obvious: along with growing social burden for this country it is taking place an aggravation of psychosomatic pathology as well as forming a passive personality and straightening «the complex of a victim».

Social measures system should cover the following basic directions:

- medical guarantee;
- employment with possible
- retraining and training for a new profession;
- social facility and privileges for those who works;
- material support;
- involving to civil activity

Correction of personality abnormalities. Disorders of a personal level are closely connected to social and cerebral level states. With expressed changes of the two levels personal disorders correction is utterly difficult. In any case, the main personal disorders correction method is *psychotherapy*. The psychopharmacology should be used only at decompensation of personality disorders.

The correction of cerebral disorders in the survivors is carried out by principles as follows: complexity, stability and succession between stages (clinical, ambulatory-policlinic, ambulatory and sanatorium treatment). Neuropharmacology should include vasoactive and nootropic drugs, neuroprotectors, antidepressants (predominantly, selective serotonin reuptake inhibitors — SSRIs) and atipic antipsychotic (if necessary).

The correction of *mental disorders* is carried out at syndromological level. When giving particular mental help to the survivors, it is used the whole arsenal of pharmaceutical, psychotherapeutic and other remedies. It is worth mentioning the importance of *out-patient methods of treatment and rehabilitation* of irradiated persons with psychoneurological pathology. The maintaining therapy under ambulatory conditions means to prescribe the remedies increasing organism resistance. Moreover, psychological and psychotherapeutic maintenance as well as general hygienic measures [Nyagu A.I. et al., 1998, 1999].

Neuropsychiatric aftermath of ARS and overexposure to ionising radiation should be of a prior attention in the remote period of irradiation. In the Conclusions of the 3rd International Conference «HEALTH EFFECTS OF THE CHERNOBYL ACCIDENT: RESULTS OF 15-YEAR FOLLOW-UP STUDIES» Kiev (Ukraine), 4 to 8 June 2001 it was noted, that various somatic disorders, including delayed neuropsychiatric complications and radiation skin damage, have been observed in survivors of bone marrow syndrome. At 15 years after the accident other types of health effects seem to have emerged. These are primarily neuropsychiatric and cardiovascular diseases.

Among the recommendations of the Conference there was that attention should be focused on the groups that were significantly exposed to radiation due to the Chernobyl accident. These groups include workers who manifested clinical symptoms of acute radiation syndrome, recovery operation workers (in particular from 1986 to 1987) and some others categories.

Organic mental disorders in ARS-patients in the remote period we propose to classify as *postradiation syndrome (encephalopathy)* which includes significant personality changes, impairment of cognitive and thought functions, impairment of memory, difficulty in concentration and performing mental tasks, apathy, abulia, social estrangement, anhedonia, fatigue, headache, dizziness. We propose to include this syndrome as **F07.3 Postradiation syndrome (encephalopathy)** in the Chapter F00–F09 Organic, including symptomatic, mental disorders of the ICD-10.

Follow-up (1987-2001) neuropsychiatric and neuropsychophysiological investigations testify to the fact that ARS-patients survived after the Chernobyl disaster have progressive structural-functional brain damage – *postradiation encephalopathy*. The pathophysiological basis for post-radiation encephalopathy is a pathology of diencephalo-limbico-reticular structures and associative frontal regions mainly predominant left hemisphere with expressed disorders of central afferentation mechanisms.

According to the current ICD-10 criteria post-radiation encephalopathy can be performed as: T66 — unspecified irradiation effects: radiation sickness + G 93.8 — other specified brain diseases: post-radiation encephalopathy + F00-F09 — organic, including symptomatological mental disorders. According to ICD-9 postradiation encephalopathy can be coded in the following way: 990 — radiation sickness + 348 — other brain sickly states (encephalopathy) + 310 — specific non-psychotic mental disorders on ground of brain organic damage (or 293 – transient psychotic states caused by organic diseases; 294 — others psychotic states (chronic) as the result of organic diseases; 300.9 — neurosis of exogenous aetiology; 301.9 — psychopathic disorders of exogenous aetiology.

However, we propose to include this syndrome as **F07.3 Postradiation syndrome (encephalopathy)** in the Chapter F00–F09 Organic, including symptomatic, mental disorders of the ICD-10.

Diagnostic criteria of postradiation encephalopathy are [Nyagu A.I. et al., 1997,1999]

1. Verified radiation sickness.

2. Fast progressive course type of neuromental disorders with expressed psychovegetative syndrome predominance in 1–2 year after ARS period, which is developing into brain organic syndrome in 3–5 years.

3. Postradiation encephalopathy signs like:

a) endoformous brain organic syndrome with predominance of senesto- and paranoic-hypohondriac symptomatology in combination with apatho-abulic disorders;

b) microfocal neurological symptomatology, mainly of diencephalo-stem level with sensory-algetic, muscle-tonic, vestibular-ataxic syndromes and soft pyramidal and extrapyramidal symptoms;

c) progressing vegetative/autonomic insufficiency (the decrease of SSR hands and especially feet amplitude; its value asymmetry; increase of occurrence threshold, and quite often - absence of SSR; decrease of limbic infra-red

emission («thermoamputation») and its trunk asymmetry; cardiovascular system regulation disturbances as parasympatheticotonia);

d) flat or disorganised EEG type with paroxysmal activity, interhemispheric asymmetry with δ- and βpower spectral power predominance;

e) deformation and asymmetry of SSEP main components at increasing of latent periods and decreasing of early and late components amplitude;

f) deformation, decrease of the latent periods and increase of VEP main components amplitude;

g) BAEP late (III, IV, V) components deformation, increase of the latent period of V component and III-V of an interpeak interval, decrease of V component amplitude;

h) the signs of cerebral circulation disorders at absence of its stable disturbances.

4. Absence of neuropsychiatric pathology of other genesis.

The diagnosis with postradiation encephalopathy is founded, if the 1st and the 2nd criteria and not less than three signs of the 3rd criterion are present. In cases, when against a background of ARS the cerebrovascular pathology was developing (arterial hypertension, atherosclerosis) at steady cerebral hemodynamic disorders the brain organic damage should be classified as *postradiation dyscirculatory encephalopathy*.

15-year experience in studies of medical consequences of the Chernobyl disaster testifies to a priority importance of the problem concerning mental health protection in the survivors as a result of overcoming unfavourable consequences of the accident.

Therapeutic resistance of mental health abnormalities is determined by a composite influence of unfavourable factors of the Chernobyl accident consequences, where radioactive and psychogene ones are of the greatest importance, the influence of which is becoming stronger because of social-economic problems in the post-soviet period. As a result it is forming extremely complicated and multimorphic clinical pictures of mental and, in particular, psychosomatic disorders, which are very difficult to be corrected. Moreover, last time problems of mental health protection in the survivors as a result of another extreme situations (wars, acts of terrorism, catastrophes, natural disasters, etc.) are becoming actual more than usual [Nyagu A.I. et al., 1998,1999].

The current Ukrainian system of rendering treatment-prophylactic help in a sphere of mental health protection in the survivors as a result of extreme situations, in particular the Chernobyl accident, is not effective enough, by mainly of organisational reasons:

- there is no *psychiatric service of extreme situations* in this country
- there is no *united co-ordinative centre for mental health protection* in the survivors as a result of extreme situations.
- there is no multiple-discipline treatment-prophylactic institutions giving medical help to the survivors as a result of the Chernobyl disaster, *specialised psychiatric and narcological beds and/or departments* in the structure of multiple-discipline treatment-prophylactic institutions. As a consequence, practically any problem of mental health abnormalities of the survivors appears to be unsolvable at existing multiple-discipline treatment-prophylactic institutions giving them medical care. As a result, an adequate medical care is not frequently given to this significant contingent of the patients.
- the absence of succession in treatment of mental disorders of the survivors as a result of the Chernobyl accident between specialised psychiatric (narcological) and somato-neurological stationers.

Hence, to establish *National Service for mental health protection in survivors as a result of extreme situations* is an actual problem. The effective protection of mental health is possible only at simultaneous correction of neuropsychiatric, personal, somatic and social spheres of the survivors that combines with optimisation of potentials of an organism.