Chapter 6. NEUROPSYCHIATRIC EFFECTS OF CHRONIC IRRADIATION

6.1 Introduction

Problem of *chronic irradiation neuropsychiatric effects* especially under so-called *low doses* impact is the most debatable one both in the fields of radiation neuropsychiatry and radiation medicine in a whole. Stated problem complexity is defined by the following factors:

- *terminological* inaccuracies — up-to-date the common opinion is absent regarding what is the «chronic irradiation» phenomenon i.e. for how long is the radiation exposure to last to become chronic one? In what dose rates and effective equivalent dose values the neuropsychiatric effects of chronic irradiation are in general to be discussed? What is the «chronic radiation sickness» and what are its clinical and dosimetry criteria?
- *scientific-research* contradictions and difficulties i.e. the century-long discussion regarding nervous system radiosensitivity on the one hand and chronic irradiation neuropsychiatric effects extraction extreme difficulties itself — on the other. Though in monograph «Human radiation sickness» A.K. Guskova & G.D. Bajsogolov (1971) noted that ionising radiation impact on nervous system studies for the long time follow the opposite opinions. One of them overestimate the nervous system role in reactions on radiation within any dose range, whereas others — underestimate its functional reactions importance on the background of its comparative morphological radioresistance;
- *social-economical* and *political* settings involving wide spectrum of interests ranging from the so-called «atomic lobby» to the so-called «oil lobby» and «Greenpeace» that have cause impact on scientific data interpretation and lead to information concealment and radiation detriment to human health diminishing in one cases and to blunt gamble — in another ones.

Majority of authors mean the *low doses* of ionising radiation exceeding the maximal permissible values prolonged impact as the *chronic irradiation*. G.D. Bajsogolov & A.K. Guskova (1967) considered equivalent radiation dose of 1 Sv accumulation for the short term (from 1 hour to 1–3 days) as the relative border separating acute radiation injury forms from the chronic ones. In other words the radiation exposure in terms *exceeding the three days* is to be already considered the *chronic* one. However, according to the WHO definition (1978) the *impact for the 30% of life-span duration* of definite species is the chronic one. G.I. Reeves & A.J. Ainsworth (1995) referring to the work «Chronic radiation sickness cases analysis in South Ural population » by M.M. Kossenko et al. mentioned the impact duration within *not less than 3 years* as the chronic radiation sickness rise temporal criterion.

Dose values up to 1,000 R were considered as *«low doses»* in the beginning and middle of the last century [M.I. Nemenov, 1950]. U.G. Grigorjev (1963) pointed out that the two circumstances of irradiation are to be taken into account in «low radiation doses» concept defining: chronic impact of radiation and short-term impact. In *chronic* radiation impact the author considered logical to apply the ratio of discussed value to the natural radioactive background one as the criterion. He considered doses exceeding the natural background values in 10 or 100 times as low radiation doses. In case of the radiation *short-term* impact the low dose concept is considered especially indefinite. A.V. Lebedinsky & U.I. Moscalev [cited after U.G. Grigorjev] meant the dose minimally effective for any biological process as the low radiation dose. Regarding this criterion the dose values of order 0.05–5 R were considers as low ones.

V.A. Baraboj (1988) considered the *low doses* being over the natural radiation background value in 5– 10 times and at the same time approximately in 100 times lower than $LD_{50/30}$. I.e. regarding human the doses of 0.04–0.06 Gy are the low ones in cease of single irradiation. In the same work (p. 109) author presents another range for low radiation doses — from natural background values to the biological threshold of 0.25–0.5 Gy. In the next publication V.A. Baraboj (1991) specified the dose range and presented values of 0.05– 0.06 Gy.

At present time the *low doses* are considered as dose range up to 1 Gy [Rudnev M.I. et al., 1994], however the equivalent doses received in *prolonged irradiation* and not exceeding 250 mSv per year (5 maximal permissible doses) are also considered low ones [Kozlov V.F., 1987] both with values not leading to the clear non-stochastic effects rise (up to 0.5–1 Gy) [Torubarov F.S., Dahno D.V., 1990].

Regarding the «dose—effect» dependence the *dose rate less than 6 mGy·h^{-1} and acute irradiation under 0.2 Gy are used to be considered as low doses* [Bennet B.G., 1996].

Common opinion is not available up-to-date regarding the low radiation doses biological effects presence or absence themselves. Some authors consider the doses up to 1 Gy cause *unfavourable impact* at that *cumulating* in chronic exposure; others — present data regarding *stimulating favourable effects*, the rest ones insist on any effects *absence* at all.

In some authors opinion the low doses real risk calculated with non-threshold lineal model application is overestimated [Ilyin L.A., 1985; Bajenov V.A. et al., 1990; Goldman M., Filjushkin I., 1994; Kelly G.N., 1994 etc.]. Though V.A.Baraboj (1988) insisted that ionising radiation non-threshold impact concept has no proof and he stated «remaining on the fact fundament» that «ionising radiation low doses range — from natural background values up to the biological threshold of 0.25–0.5 Gy level — is of specific biological effect in particular not impacting on any numerous life indices of cell and organism, and for some physiological parameters resulting in stimulation effect on vital functions».

At the same time already N.W. Timofeeff-Ressovsky & K.G. Zimmer (1947) neglected the dose threshold itself regarding radiation negative impact on organism absence under it. M.N. Livanov (1962) considered the any impact of ionising radiation can result in *altering effect* on biological substrates leading to the threshold doses absence opinion concerning initial reactions on irradiation. However M.N. Livanov recognised the threshold relations presence in ionising radiation effects on nervous system. He also repeatedly underlined the ionising radiation low doses singular effects *cumulation* ability. Data are available about stimulating effect evolution to the exhaustion and functional insufficiency period after prolonged (over 1 month) low radiation doses impact [Kuzin A.M., 1986; Ryasnyansky I.V., 1989].

A.I. Burnazyan et al. (1983) marked that no secure threshold is present and radiation impact in the very low dose can result in injury regarding *space flights radiation safety*. Chromic exposure in 0.1–0.3 Gy doses induce non-specific, compensatory adaptation reactions adequate to extreme irritants. These dose levels exceeding with dose rates over 0.1 Gy·day^{-1} is attended with *radiation damage* rise and *pathological adaptation* elements. C. Heine & E. Vaisanen (1986) demonstrated that *space radiation* being most intensive in polar zones cause effects on cellular level and are the *somatic and physiological stress-agent of environment*.

Regarding the Chernobyl disaster the opinion was stated that low doses impact remote unfavourable consequences risk is for several orders exceeding values calculated from high dose effects extrapolation [Serkiz Y.I., 1989]. Data are presented about low intensity radiation and low doses effects are the principally new pathways of effecting on living structures, new changes in cellular metabolism. Majority of these effects are not induced by radiation but mediated by regulation systems and organism immune and anti-oxidation status deviations both with that of sensitivity to environment factors impact. The «dose—effect» dependence in low doses is of non-lineal polymodal (bimodal) character [Burlakova E.B. et al., 1996]. Worth to note that such opinions are shared by not all the radiobiologists [Yarmonenko S.P., 1996].

Consequently to this time there is no clear solution of the chronic radiation neuropsychiatric effects problem especially within so-called low radiation doses range that is one of the most actual scientific-applied problems of the Chernobyl disaster.

6.2. Chronic Radiation Sickness Neuropsychiatric Pattern in Human

6.2.1. Chronic Radiation Sickness General Issues

The *chronic radiation sickness* rise is possible in case of long-term impact of ionising radiation with doses exceeding maximal permissible [Guskova A.K. et al., 1964; Guskova A.K., Bajsogolov G.D., 1971] and/or after the acute radiation sickness surviving if the radionuclides incorporation occurred [Kurshakov N.A., 1963; Gorizontov P.D., 1974]. The term «CRS» and its first clinical description belongs to N.A. Kurshakov, I.S. Glazunov, A.V. Kozlova et al. and the CRS main diagnostic principles were presented by A.K. Guskova (1961). CRS is the *general disease* of organism. At the same time the local radiation injuries dominate in case of radionuclides impact with sharp organic tropism or under external local irradiation.

A.K. Guskova & G.D. Bajsogolov (1971) considered that physiological shifts in some systems registration in doses under 0.01 Sv integrally will become available along with events occurring in organism precise detection possibilities rise. However the integral effect in their opinion will be mainly of adaptation mode. Integral doses range of 0.01–0.1 Sv in its any dimensional position (local or general exposure) is transitional to the next one (0.1–1 Sv) with specific radiation injuries taking place in the most affected by radiation tissues. In case of dose close to 1 Sv within terms of years on months the slowly forming not severe CRS ran rise. General exposure doses exceeding 1 Sv are presumably striking ones.

CRS in battlefield conditions is peculiar regarding clinical progress and first of all — with relatively more severity. That is due to the organism general reactivity alteration and its resistance decrease towards ionising radiation impact in war situation various conditions. Because of these circumstances the CRS of the 1st severity degree rise is rather probable in wartime conditions (both as in extreme situations) under impact less than 1 Gy (0.6–0.9 Gy) that as a rule is not available in peace time [Molchanov N., 1960].

Chronic radiation effects regarding the *space flights* medical-biological providing aspects were presented by A.I. Burnazyan et al. (1983) as following:

0.015–0.1 Gy range. Genetic and remote consequences are of stochastic mode. Physiological systems reactivity elevation, arterial pressure decrease, heart rhythm slow-down, lymphocyte count lowering, capillary permeability initial alterations.

0.15–0.3 Gy range. Remote and genetic consequences linear dependence, cellular and physiological systems functional strain state, reserved structure-functional units mobilisation, threshold doses for organism majority physiological systems reaction.

0.35–0.45 Gy range. Exceeds substantially the genetic consequences and some viscera tumours outcome doubling dose. Pronounced radiation injury effects in dose rates 0.1–1 Gy·day^{-1}. Threshold doses for atrophy and hypoplastic processes genesis. Injured systems compensation hyperfunction, compensatory mechanisms «disintegration» under extreme irritants additional impact.

0.5–1 Gy range. Remote somatic and genetic consequences incidence increase. Organism functions central and peripheral regulation mechanisms alteration threshold doses. Cellular renovation acceleration, cell compensatory

hyperfunction, threshold doses for destructive, dystrophy and sclerotic alterations in several organs. Neurocirculatory dystonia. CRS can form depending on dose rate values.

1.5–4 Gy range. Death risk pronounced increase due to irradiation stochastic consequences. Organism functions regulation level depression, nervous, endocrine, cardiovascular, haemopoietic and other organism systems functional failure. Cellular renovation processes alteration, in high dose rates — destructive processes domination over the reparation ones. Undamaged cellular and tissue units hyperfunction. Various severity degree CRS cases number rise.

According to the actual estimations [Dolgikh A.P. et al., 1993] the *non-stochastic effects hazard* precise enough quantitative estimation is at present unavailable however their *clinical presentations* genesis risk estimation is possible. In authors opinion the general risk criterion application is possible under homogeneous irradiation both with that of estimations conduction on the basis of *effective dose (ED) of radiation* value unambiguously defining clinical effects:

1. Symptoms absence (ED less than 23 mSv, dose rate 4 mSv·year^{-1}).

2. Deviations from norm absence in clinical-laboratory parameters, however the compensation-restoration processes strain. Deviations available in various non-radiation factors combined impact (ED — 20–90 mSv).

3. Transient not pronounced *leukopenia* (down to $4 \cdot 10^9 \cdot L^{-1}$), *immunity* indices alterations from norm lower limit to the 1.5 standard deviation scale from average values in some indices, *neuroendocrine system* biochemical parameters bias (ED — 80–300 mSv, dose rate 10–50 mSv·year^{-1}).

4. *Leukopenia* (less than $4 \cdot 10^9 \cdot L^{-1}$) in 30% of exposed persons, all *immunity* indices alterations for 1.5–2 standard deviation scale from average values, *neuroendocrine system* biochemical parameters pronounced alterations (ED — 0.3–0.6 Sv, dose rate 50–110 mSv·year^{-1}).

5. *CRS genesis* threat, *immune deficiency states* (ED — 0.6–1.1 Sv, dose rate 100–200 mSv·year^{-1}).

Neuroendocrine system functional state alterations can be observed already in 50–100 mSv doses and *immune system* transient non-stochastic effects — in doses 100–200 mSv for 10 years that are substantially lower the permissible values constituting 500 mSv for 10 years. Authors concluded that immune and neuroendocrine systems are rather enough radiosensitive.

Some *deterministic radiation effects* thresholds are shown in table 6.1

Table 6.1

DETERMINISTIC RADIATION EFFECTS THRESHOLDS ESTIMATION (from Publication 41(ICRP, 1984), Publication 60 (ICRP, 1990) et al.)

Tissue and effect	Threshold		
	Integral equivalent dose in single exposure, Sv	**Integral equivalent dose received after prolongation or long-term exposure, Sv**	**Integral equivalent dose received after prolongation or long-term exposure during numerous years, Sv·year^{-1}**
Gonads			
Temporal sterility	0.15	—	0.4
Permanent sterility	3.5–6	—	2
Ovaries			
Sterility	2.5–6	6	>0.2
Eyes			
Fixed turbidities	0.5–2	5	>0.1
Cataract	5	>8	>0.15
Bone marrow			
Haemopoiesis decline	0.5	—	>0.4

N.A. Kurshakov (1963) insisted on the CRS recognition as the *separate nosologic form*. He underlined at that the injury character is defined both with radiation effects and radioactive substances *chemical toxicity*. Local and generalised *infection* rise is the CRS regular complication stipulated by immunobiologically weakened organism resistance decrease.

A.K. Guskova et al. (1964) considered principally rightful the chain of consecutive non-specific but rather characteristic alterations integration rising under long-term impact of ionising radiation relative low doses in *the single nosology position — CRS*. These authors regarded to the *CRS characteristic peculiarities*:

1. *Majority of organs and systems injury*, where anatomical and functional disorders severity and terms of rise are defined in general by total or mainly local irradiation, integral dose value, exposure type and intensity both with one or another organs structure and physiological peculiarities.

2. *Prolonged mode and undulating progress* reflecting the growing injury effects combination with reparation and adaptation reactions. The expression rate of the last ones depends upon the accumulated in time dose value both with organism and its separate systems individual peculiarities. The most important among them are: age, preceding inferiority of one or another organ or system, additional deteriorating physiological and pathological impacts presence (pregnancy, childbirth, chronic general somatic diseases).

According to the definition by N.A. Kurshakov, I.S. Glazunov & P. Kireyev (1969), N.A. Kurshakov (1963) & P.D. Gorizontov (1974) the CRS is either pathological process stipulated by permanent continuous/repeated impact of radiation factors in low doses or such impacts aftermath that already are over but have injured the organism physiological state. Authors underlined that *CRS can be the ARS consequence* especially in case of incorporated radioactive substances accumulation. If the reparation processes in ARS not resulted in complete recovery, the restoration defects remain in organism or some its systems and disease obtain chronic progress as the acute pathology aftermath. In cases of acute injury with long half-life period radionuclides incorporation not only the terminated radiation impact consequences are present but the remaining internal irradiation.

N.A. Kurshakov & I.S. Glazunov (1960) considered as CRS in this term more narrow and precise meaning the *periodically repeated internal and external low dose irradiation result where each irradiation episode itself can not be the radiation sickness cause but the total effect is summarised or cumulated.* At that the irradiation effects summation is occurring on the background of survivor organism reactivity changes in time. N.A. Kurshakov (1963) noted that after the radiation impact actual termination the biological processes go through the pathological conditions. Ionising radiation impact consequences remain in organism both as central nervous system functional state disorders and direct injuries in organs and systems. At that the radiation alterations are so pronounced that their reversibility can occur being *limited* to the rather extent and compensatory adjustments — *insufficient*.

A.K. Guskova et al. (1964), A.K. Guskova & G.D. Bajsogolov (1971) did not share the opinion regarding the ARS transformation into CRS possibility and considered CRS as *clinical syndrome risen under prolonged recurrent ionising radiation impact in relatively low but still exceeding maximal permissible doses.* Authors worked out the *radiation sickness classification*. Recognition of time and three-dimension absorbed dose forming factors determining role in all peculiar biological effects of various ionising radiation types impact was the stated classification general theoretical principle.

A.K. Guskova & G.D. Bajsogolov (1971) divided:

1. *Full-scale clinical forms*, which genesis is mainly stipulated by total external irradiation (γ-, roentgen, neutron) or rather rapidly and homogeneously distributing in organs and tissues ^{3}H, ^{24}Na, ^{137}Cs isotopes incorporation;
2. Forms with slowly progressing clinical syndrome of *separate organs and systems predominant injury*.

A.K. Guskova et al. (1964) divided the following CRS *periods* under relatively homogeneous irradiation:

1. Disease *forming* period.
2. *Restoration* period.
3. *Remote consequences and outcomes* period (with a lot of similarities to the ARS consequences).

Real reparation processes are available in systems with high physiological regeneration capacity (hemopoiesis, spermatogenesis, skin and mucous epithelial cover regeneration). Systems having no or limited in regeneration capacity (*nervous*, cardiovascular, endocrine) respond on the chronic radiation impact with functional-dynamical disorders complex for the long time masking the injuries amount elevation in organs structure; real reparation processes are presented there to the less extent.

In remote terms after radiation impact termination or radiation impact intensity substantial lowering down to levels surely not exceeding the permissible ones it is more proper to mean the *outcomes* or *consequences* of disease been in the past [Guskova A.K. et al., 1964]. *Radiation injury remote consequences* can rise both after ionising radiation single exposure and radionuclides or low radiation doses chronic impact [Jzuravlev V.F., 1990]. Worth no mark that remote consequences selection to the separate group is to some extent artificial as in many cases they are in close relation to the radiation sickness chronic form. That is difficult to differentiate what symptoms are related to the radiation sickness with chronic progress and what ones — to its remote consequences [Litvinov N., Ponomarkov V., 1960].

V.F. Jzuravlev (1990) concluded that remote radiation effects can be stipulated by disorders and injuries combination in connective tissue, blood vessels and parenchyma organs. *Atrophy or dystrophy, degeneration and sclerotic processes* are of particular importance in neuropsychiatry as they can rise in nervous tissue and circulation system in remote radiation period, *dyshormonal disorders* are also important here.

Sclerotic states develop after the ionising radiation direct impact on parenchymal cells and organs and tissues various structures. Direct dose dependence is observed in these effects rise with dose threshold presence being within 1–5 Gy range [Streltsova V.N., Moscalev U.I., 1964].

Dis-hormonal disorders present no direct dose dependence and have low threshold dose value 0.01–0.1 Gy. Endocrine disorders appear as the mediated and indirect effecting mechanisms result. Triggering point is the initial radiation-induced depression, structure and function damage of gonads, thyroid and adrenals. Alterations are registered in all endocrine glands [Jzuravlev V.F., 1990].

Memory deterioration, quick fatiguability, dizziness, cortex main processes instability and weakening, neuralgia are described among radiation remote consequences [Litvinov N., Ponomarkov V., 1960].

Foreign authors [Behrens Ch., 1951; Cronkite E.P., 1962, 1967] regarded to CRS some injuries evolved in chronic progress after repeated or fractionated irradiation both with irradiation severe remote aftermath in form of radiation necrosis, bone sarcoma, radiation-induced skin cancer and leukaemia (including those risen after the single exposure).

Chronic radiation syndrome of CRS as the *separate* clinical form according to G.I. Reeves & E.J. Ainsworth (1995) is divided only in Russia and other former Soviet Republics. Among the explanations here is that only in the former USSR the so long-term human exposure to ionising radiation substantial values was available.

M.M. Kossenko (1990) presented data about *chronic radiation sickness* diagnostic in 935 cases after radiation accidents in South Ural. At that she pointed out that radioactive iodine, caesium, strontium and plutonium were the

most biologically important. Author paid especial attention to the mentioned radionuclides *radiochemical* mechanism of action.

CRS constituted more than 80% of radiation injuries from external total γ-irradiation on IC «Mayak» and was fixed in 1,596 victims [Okladnikova N.D., et al., 1991, 1994]. Integral radiation doses reached 10 Gy in year maximal doses of 2–3 Gy per year. For 40 years the 333 persons total died from the CRS. However the integral mortality index among CRS patients according to data by V.N. Doshenko (1991) was lower than that in silicosis patients (control) [Ilyin L.A., 1994]. CRS was observed in persons received the highest radiation doses both with post-radiation disorders in haemopoietic, nervous, immune systems and osteoalgetic syndrome [Akleyev A.V. et al., 1994, 1995].

L.A. Buldakov (1996) in materials summary from International Symposium «Chronic Radiation Impact: Remote Effects Risk» (Chelyabinsk, 9–13 January, 1995) presented data from report by A.F. Lyzov et al. regarding the CRS incidence in IC «Mayak» personnel in first years after launch. Year dose average values from only external γ-radiation constituted in reactor, radiochemical and plutonium productions respectively 0.5, 1.03 and 0.4 Gy in males and 0.2, 0.7 and 0.4 Gy respectively in females. CRS incidence in three industry types constituted respectively 5, 23 and 12%. A.K. Guskova (1996) in Symposium Proceedings review paid attention on the clear dependence presence of CRS on dose value. At that the CRS diagnostic was conducted in total irradiation integral doses being several Greys of order and irradiation intensity exceeding 0.25–0.5 $Gy \cdot year^{-1}$.

6.2.2. Chronic Radiation Sickness Neuropsychiatric Effects Conditioned by Local Exposure to Radiation

CRS stipulated mainly by *local irradiation* is the historically most early described form of radiation disease. Radiologists already in the previous century beginning noted the rising injuries in radiation therapy application on definite organs and structures. For the first time they were considered common for the radiation sickness in general. However in 50th W. Bloom (1948), Ch. Behrens (1951) and other radiobiologists started to separate the *general and local radiation* effects.

CRS clinical pattern can progress with some peculiarities depending on impact character and radioactive substance nature. Under external irradiation long-term impact in low doses the early alterations in *blood* and *vegetative-vascular disorders* are observed. In incorporated radionuclides presence in organism the *asthenic* symptomatic is on the foreground in disease pattern, further the *central nervous system organic alterations* rise. *Osteoalgetic syndrome* is especially peculiar for the CRS induced by radioactive substances deposition in bone tissue [Kurshakov N.A. et al., 1960].

A.K. Guskova & G.D. Bajsogolov (1971) disagree with several researchers regarding the somewhat *radiation sickness common amorphous form* after radioactive substances incorporation, but consider total and local irradiation biological effects separately. These authors consider the radiotoxicological conception of *«critical organ»* as one of progressive and practically important ones. Stated conception not denies the importance of secondary or primary but to the less extent expressed alterations in other organs and tissues. Here under the pronounced irregularity or local irradiation the separate organs and structures are divided being responsible for injury outcome due to the radiation dose primary accumulation there. Critical organs especial role is defined by the dose value being enough for structure and function substantial disorders origin at that the distinct alteration in other tissues are not yet risen.

Geometry of *external irradiation* from various sources and *dose distribution in body volume* importance for clinical effects peculiarities was demonstrated in works by V.P. Bond, E.P. Cronkite, C.L. Dunham (1960), H.P. Jammet et al. (1966), N.A. Kurshakov et al. (1966), G.D. Bajsogolov & A.K. Guskova (1967), U.G. Grigorjev et al. (1967), A.K. Guskova & G.D. Bajsogolov (1971).

CRS clinical pattern specificity was fixed depending on the *incorporated radioactive substances chemical toxicity*. V.F. Jzuravlev (1990) pointed out to that radionuclides toxicity is estimated with tissue dose absorbed in organism and cumulated for the time of presence there. That defines the incorporated radionuclides biological effect. However in spite of radioactive substances toxicity degree «integralisation» — by means of the absorbed tissue dose introduction, the *specific peculiarities of organism chronic radiation injury* from one or another radioactive substance were fixed. That specificity is defined by radionuclide tropism to ones or another tissues, emission spectrum, decay and clearance half-life, solubility, ability to enter various chemical reactions etc. In some cases the stated specificity of radionuclides biological impact can serve the valuable differential-diagnostic criterion enabling the radioactive substance stipulating injury supposition or even identifying.

Not numerous suggestions regarding the incorporated radionuclides neuropsychiatric effects are available in literature [Lazarev N.V., 1951; Bajenov V.A. et al., 1990; Jzuravlev V.F., 1990]. Table 6.2 shows some described neuropsychiatric effects of several radionuclides after incorporation.

Table 6.2

NEUROPSYCHIATRIC EFFECTS OF INCORPORATED RADIONUCLIDES
[by Lazarev N.V., 1951; Bajenov V.A. et al., 1990; Jzuravlev V.F., 1990 et al.]

Radionuclide	Described neuropsychiatric effects

Zinc (^{65}Zn) β- and γ- emitter $T_{1/2}$=57 min	Accumulated in muscles, skeleton, skin, liver, hypophysis, pancreas, and gonads. Among other symptoms the *brain bioelectrical activity* disorders were described.
Strontium (^{89}Sr) β- and γ- emitter $T_{1/2}$ = 50.5 days (^{90}Sr) β-emitter $T_{1/2}$=29.12 years	Selectively deposited in skeleton (mainly in bone growth zone) especially in pregnancy and lactation; enters f0etus through placenta; enters breast milk. Less than 1% is accumulated in soft tissue. Among other symptoms the *asthenic-vegetative and osteoalgetic syndromes* are described *with central nervous system organic damage outcome.*
Iodine (^{131}I) β- and γ- emitter $T_{1/2}$=8.04 days (^{133}I) β- and γ- emitter $T_{1/2}$ = 20.8 hours etc.	*Thyroid, hypophysis and kidneys* are the critical organs [Dedov V.I. et al., 1993] especially in children; is also deposited in placenta and fetus. Can induce *thyroid*, parathyroid and breast tumours, polyglandular endocrine pathology etc. *Regional polyneurites* were described [Ulitovsky D.A., 1962], peculiar *neck disesthesia and neuralgia, Gorner's syndrome*, *migraine* attacks, voice hoarseness [Gusev E.I. et al., 1988]. Radioactive iodine impact can lead to *hypothyroidism rise in fetus, newborns and children* and finally — *to cretinism* [Ilyin L.A., 1994] and other psychoneurological disorders.
Caesium (^{134}Cs) β- and γ- emitter $T_{1/2}$=2.062 years (^{137}Cs) γ- emitter $T_{1/2}$=30 years etc.	Relatively homogeneously distributed in organism. Accumulated in muscles, liver, kidneys, lungs, skeleton, enters foetus through placenta, enters breast milk. Data are available about caesium accumulation in *brain* [Myrgorodskij O.A. et al., 1993]. Both with other manifestations of caesium incorporation the *asthenic-vegetative and depressive syndromes with outcome in central nervous system organic damage with vegetative polyneuritis* are known.

Table 6.2 (continuation)

Radionuclide	Described neuropsychiatric effects
Gold (^{198}Au) β- and γ- emitter $T_{1/2}$=2.696 days	Selectively accumulated in reticular-endothelial system tissues. Express tropism to the *nervous tissue especially in spinal cord* [Guskova A.K., Bajsogolov G.D., 1971]. *Regional polyneuritis* and *multiple pareses* are described besides the other poisoning symptomatic [Ulitovskij D.A., 1962].
Mercury (^{203}Hg) β- and γ- emitter $T_{1/2}$=46.6 days	Tropism to the kidneys, also accumulated in thyroid, hypophysis, *brain*. Under intoxication the combined injury is possible with ionising radiation and stable mercury salts.
Thallium (^{204}Tl) β- and γ- emitter $T_{1/2}$=3.779 years	Is accumulated in muscles, skeleton, parenchymal viscera. In the *skin* is mainly deposited in hair follicle growth zone and resulting from the creatine synthesis alteration in hair bulbs the *alopecia* can be observed.
Lead (^{210}Pb) β- and γ- emitter $T_{1/2}$=22.3 years	Pronounced *osteotropism*. However accumulates also almost in all viscera and tissue. Is one of the most biologically dangerous radionuclides leading in particular to the *nervous system injury* (polyneuropathy, encephalopathy etc.).
Radium (^{226}Ra) α-, β- and γ-emitter $T_{1/2}$=1600 years	*Deposited in bone tissue*, kidneys, salivary glands. Radium intoxication is characterised with bone tissue destruction, radiation osteitis rise leading to increased brittleness and bone pathological fractures. *Asthenic-vegetative disorders, specific osteoalgetic syndrome* (pain in hand and leg bones, sternum, ribs, sometimes — spine), *central nervous system organic injury, radiation cataract* are known both with other radium injuries.
Thorium (^{228}Th) α-, β- and γ-emitter $T_{1/2}$=1.9131 years	*Osteotropic. Pronounced neurological symptomatic* is described on the haemopoiesis relatively mild reaction.
Uranium (^{238}U) α-, β- and γ-emitter $T_{1/2}$=4.468·10^{9} years	Extremely strong protoplasmic poison. *Bones are the critical organ.* Is also accumulated in parenchymal organs. Uranium intoxication is peculiar with polytropism where in particular the *asthenic-vegetative syndrome and vegetative dysfunction, central nervous system organic damage and paralyses* are characteristic.

Note: nuclear-physical properties of radioactive isotopes are presented according to Bajenov et al. (1990).

In radionuclides incorporation the extent and localisation of blood vessels injury is defined by *radioactive substances selective distribution in organs and tissues*. Vessels damage can lead to sclerotic alterations rise in viscera after chronic irradiation [Moscalev U.I., 1989]. Pathological changes occur mainly in the *most actively functioning vessels* at the time of exposure [Alexandrov S.N., 1978]. A.K. Guskova & G.D. Bajsogolov (1971) connected the *osteoalgetic syndrome* forming with blood circulation regional disorders.

Works demonstrating the *radiation cataract* genesis availability *after internal irradiation* are of particular interest. A.V. Lebedinsky & Z.N. Nahilnitskaya (1960) presented data regarding cataract rise under ^{89}Sr, ^{90}Sr and ^{210}Po introduction to organism. The *strontium cataract* authors describe with the following. Needless to say that Sr in organism actually shares the life of Ca, being distributed and fixed like it in viscera and tissues. In normal lens Ca amount reaches 10 mg%. Iris contains much more quantities — 39 mg% and especially high content is found in tunica choroidea — 63 mg%. In cataract genesis the Ca content in lens can rise more than in five times i.e. reaching 50 mg%. The same ratios are peculiar to the *radioactive strontium* too. After ^{90}Sr incorporation the radionuclide in constantly rising amounts is deposited and solidly fixed in lens. Lens injury occurs due to its targeting for β-particles from iris and ciliary processes. Alterations primary localization in lens front part is the *polonium cataract* peculiarity, that is explained by the α-emitter polonium main fixation with corpus ciliare reticuloendothelium [Volkova K.V., 1957].

H. Spiess et al (1978) & E.E. Adams et al. (1981) reported about the *cataract* cases incidence rise in patients who received Peteostra injections containing ^{224}Ra for ankylosing spondylitis or tuberculosis management. Cataract genesis probability constituted 1–4.5% 7–26 years after the radium radiotherapy. In radium concentration in iris pigment cells the α-radiation can alter the lens cell fission that is considered cataract rise reason. No differences presence was revealed up-to-date regarding cataract genesis from internal and external irradiation [Taylor G.M., 1983].

Radium deposition in eye pigment tissues (corpus ciliare, tunica choroidea and iris) can lead to lens epithelium germinal zone α-irradiation where sensitive cells are located being capable for fission. These cells produce the lens fibers. After irradiation the derived cells degenerate and result in cataract genesis in lens back pole [Griffith T.P. et al., 1985]. Similar effect is possible in α-irradiation form incorporated plutonium isotopes both with ^{224}Ra & ^{226}Ra decay producing radon and toron (^{222}Rn & ^{220}Rn) capable for diffusion in lens epithelium. In case of constant values of ^{224}Ra, ^{226}Ra and ^{239}Pu incorporation for 50 years the *tissue doses on eye pigment cells* can constitute 1.7–8.7, 12–62 and less than 0.1 Gy respectively [Thorne M.C., 1985; Moscalev U.I., 1989]. In osteotropic radioactive substances chronic incorporation the *central nervous system* irradiation occurs from the skeleton. At that the highest tissue doses are received by *hypophysis* [Sarapultsev I.A. et al., 1972]. The more frequent than in control *pituitary tumors* genesis is revealed in remote terms after ^{131}I, ^{211}At, ^{90}Sr, ^{144}Ce, ^{147}Pm, ^{106}Ru, ^{95}Nb, ^{241}Am, ^{252}Cf, ^{239}Pu,

^{238}Pu radionuclides incorporation [Streltsova V.N., Moscalev U.I., 1964]. Data regarding the *hypothalamus-hypophysis-gonads* system reaction on internal irradiation are limited to the few number of experimental studies devoted to the gonads functional state evaluation [Moscalev U.I., 1989].

Radionuclide distribution in organism can change depending on *the central nervous system initial state*. Radioactive substances content in viscera is elevated after the central nervous system agitation with cardiozolum. Central nervous system depression with luminal results in some radionuclides content decrease in parenchymal organs with bone deposition value elevation [Burnazyan A.I., 1968; Jzuravlev V.F., 1990].

The radioactive substances *neurotropism* data almost complete absence in available literature is noticeable. In fundamental monograph «Incorporated radionuclides radiobiology» by U.I.Moscalev the chapter devoted to the nervous system is absent. Not enough attention to nervous system radionuclides deposition problem is provided in reference edition «Harmful chemical substances. Radioactive substances» commonly edited by L.A. Ilyin & V.A. Filov (1990) and in «Radioactive substances toxicology» monograph by V.F. Jzuravlev (1990).

Only isolated data are present regarding *mercury, gold and led* radioactive isotopes accumulation possibility in nervous system. V.A. Lebedinsky & Z.N. Nahilnitskaya (1960) presented data about the ^{24}Na, ^{32}P, ^{131}I, ^{210}Po radioactive isotopes so-called indicator amounts introduction in organism results in EEG distinct alteration through primary electrical activity elevation changed further with its depression. ^{90}Sr induced the electroretinogram alterations both with that of skin and oral mucosa nervous terminations and receptors sensitivity. Skin nerves injury was observed in ^{32}P intraperitoneal injection.

Works devoted to the *neuromediator systems* state study after radionuclides incorporation are also extremely rare and results presented there are rather contradictory. Though N.A. Zapolskaya & A.V. Fedorova (1965) reported about the cholinesterase activity depression under the low dose impact from ^{24}Na and ^{32}P. A.V. Fedorova (1965) on the contrary revealed the cholinesterase activity elevation under low dose irradiation by incorporated ^{137}Cs and ^{90}Sr. V.V. Borisova et al. (1988) demonstrated that ^{137}Cs in chronic incorporation with integral absorbed doses of 0.1–0.2 Gy result in *acetylcholine and histamine* neuromediators synthesis and metabolism somewhat *stimulation*. At that the synthesis intensity clearly exceeds the decay rate and leads to mediators accumulation in organs and tissues. At 1.6–2 Gy doses approach the named mediators disintegrating enzymes activity depression was observed. Thus for the first time the mediators synthesis activation is observed, and further the hypoenzymemia occurs in spite of tissue and viscera mediator content elevation. Actually identical effects at the same doses were observed in ^{90}Sr and ^{45}Ca chronic uptake. Authors concluded that incorporated radionuclides effects on metabolism in separate viscera and tissues can be direct and indirect i.e. mediated through metabolic processes.

Preconditions for some radioactive substances *neurotropism* are present: *radioactive carbon, sodium, potassium, phosphorus* can take part in chemical reactions as the respective stable isotopes, *caesium* — like potassium, *strontium* is identical to its metabolic homologue — *calcium* etc. And however the *biological membranes resistance for radioactive ions transport* phenomenon is recognises as fixed one, it is remained unclear up-to-date why the stated ion membrane transport selectivity is not realised in all cases (for instance in bone tissue basal membrane) [Durakovich A., 1987].

Data are published regarding the ^{137}Cs accumulation rate in brain in particular is in 2.5–3-fold over that for potassium [Dubrovina Z.A. et al., 1972]. At that authors demonstrated the K^+ and Cs^+ antagonism absence in organism i.e. potassium and caesium metabolism are independent. O.A. Mirgorodsky et al. (1993) marked the ^{137}Cs activity in brain elevation for 25% within 3-month-long feeding (620 Bq·day^{-1}) compared to the one month term. Authors received data about 0.2–0.5% of total ^{137}Cs organism content being accumulated in rat brain. The ^{85}Sr accumulation (1,200 Bq·day^{-1}) in rat brain was not high that authors explain with ^{85}Sr short half-life period ($T_{1/2}$=64.8 days). Researchers concluded the *brain ability for radionuclide accumulation* and ^{137}Cs in particular.

No convincing data about *blood-brain barrier non-permeability for radioactive substances* were found in available literature. Obviously the named barrier permeability is defined by radioactive substances ability to form ones or another chemical compounds with respective capability for barrier transition. However F.S. Torubarov in private discussion referring to the long-term experience in the field of radiation neurology excluded the radioactive substances capability to overcome the blood-brain barrier except the cases of the named barrier damage that is observed only under rather high radiation doses (2–10 Gy according to R.N. Hawkins & L.G. Cockerham (1987)).

Incorporated radionuclides *radiation effects* modification with their *chemical neurotoxicity* itself i.e. their *radiochemical impact* can result in specific psychoneurological disorders. Real reparation absence in nervous system can condition those disorders stability and extreme therapeutic resistance.

Obvious lack of works devoted to *radioactive substances neurotropism problem* restricts our opinions regarding nervous system radiation injuries rise pathogenetic mechanisms under internal irradiation. Stated field studies conduction is considered extremely actual.

6.2.3. Neuropsychiatric Effects in the full-scale Chronic Radiation Sickness

Completely sharing opinions of A.K. Guskova & G.D. Bajsogolov (1971) that *«...already before the disease outlined syndrome forming the separate peculiar to radiation impact disorders appearance is present. These disorders under data presence regarding the maximal radiation values indubitable exceeding ... are to be estimated as pathological process forming symptoms and named with term* ***«chronic radiation sickness before clinical stage»*** (P. 359–360), we present in this part the analytical review of works reflecting neuropsychiatric effects both in CRS and general chronic irradiation in a whole. We considered them within *CRS before-clinical stage* structure in case of general chronic exposure under presence of

enough well-reasoned cause-consequence connection between neuropsychiatric manifestations and ionising radiation chronic impact (if no indications were present about the outlined CRS diagnostic).

Three or *four degrees of CRS severity* are divided according to the clinical pattern expression and severity criteria. The very mild stages of radiation exposure not result yet in morbid process genesis with its dynamic regularities but stipulate functional disorders in the most radiosensitive viscera and systems: hemopoietic and nervous ones. These disorders mainly correspond the vegetative-endocrine manifestations, are reversible and according to opinion of N.A. Kurshakov (1963) are to be considered as not the CRS lightest form but as *organism reaction on irradiation*. CRS in early stages is characterised with first of all with organism various systems *nervous regulation* alteration. Early disease presentations are reduced to unstable, reversible and capable for treatment disorders. In disease further genesis the organism general asthenisation symptoms are rising and progressing, metabolic processes alterations and various neurotrophic injuries occur. *Neurotrophic disorders* rise *and haemopoietic system function depression* leads to organism resistance weakening and various infectious complications rise [Kurshakov N.A. et al., 1960].

Threshold values of n*ervous system reaction* on single or repeated irradiation are very low and are within dose range of 0.1–10 mGy. They considered the supreme parts of central nervous system being highly radiosensitive and relatively low radioaffectable [Grigorjev U.G., 1963; Tsypin A.B., 1964]. According to the data of A.K. Guskova & G.D. Bajsogolov (1971) those reactions can be revealed in adequate methods application within *all dose range of occupational loading*. However in their opinion problem is in these reactions interpretation i.e. border definition between reaction physiological character and pathophysiological manifestations. In ionising radiation general impact the so-called functional shifts in nervous system activity are one of the *most sensitive indicators of overexposure* [A.K.Guskova et al., 1964].

The low doses chronic irradiation unfavourable effects *cumulation* possibility was surely demonstrated in many authors' works. Though N.N. Livshits in «Organism radiation injury» monograph edited by I.G. Akojev (1976) marked that nervous system and supreme nervous function alterations in repeated irradiation firstly are easily compensated and than the exhaustion period occurs. Works by T. Vasculescu & V. Papilian (1970), T. Vasculescu et al. (1973) are approvals here as 0.5 Gy acute irradiation resulted in less spread and intensive *structural* brain disorders than the fractioned to ten-time 0.05 Gy each exposure.

Regulation shifts complex is gradually rising in nervous system under ionising radiation long-term impact first of all effecting the *vegetative-visceral innervation* sphere. A.K. Guskova et al. (1964) noted that various *neurovisceral* and first of all *neurovascular regulation* disorders are the main clinical syndrome in early terms. These disorders are presented with various unstable general and focal neurological symptoms, stipulated by intracerebral blood and liquor circulation alterations. Other authors [Glazunov I.S., Kirejev P.M., 1959; Smirnova N.P., 1969; Barabanova A.V. et al., 1969; Kantarovich L.L., Zakharov G.G., 1971; Soldatova V.A. et al., 1971 etc.] to describe the similar events applied terms *«vegetative dysfunction or dystonia», «neuro-circulation dystonia of hypotonic type»* and also *«vaso-vegetative dystonia»* [Golodets R.G., 1993].

Gradual evolution of neuroregulational circulation and heart function disorders to the more clinically pronounced *vascularisation chronic insufficiency* (headaches, pain in extremities — more often in legs, stable arterial hypotension, vessels reactivity perversion and weakening, etc.) were considered characteristic for the *cardiovascular system* state in CRS [Guskova A.K., Bajsogolov G.D., 1971].

A.V. Barabanova et al. (1969) divided the *neurocirculation dystonia as CRS part* in 0.7–1.5 Sv doses; non-specific close enough to somatogenic ones *asthenic syndrome* in 1.5–4 Sv doses; in doses of 2–4 Gy — the *central nervous system organic damage* similar to the indistinct forms of *diffuse demyelinating encephalomyelosis and brain circulation dynamic disorders*. According to these authors data the chronic irradiation in doses up to 0.3 Sv results in no any nervous system alterations distinguished from control. In 0.5–0.7 Gy doses the *regulation disorders* are registered confidentially more often but not exceeding the adaptation systems reactivity borders physiological widening. In 37% of persons exposed to 0.7–1.5 Sv the *neurocirculation dystonia of hypotonic type* is revealed with arterial-venous branches spastic-atonic state, skin temperature decrease more often in distant parts. That in combination with pain, numbing, arm and leg skin paresthesias and hyperesthesias form the *extremities peripheral circulation* alteration syndrome. Authors consider that in such cases the brain blood supply is not altered substantially and the brain and muscles bioelectrical activity is normal excluding the α-activity stable amplification in EEG with evoked potentials expression elevation. According to opinion of A.V. Barabanova (1969) the ionising radiation only in 1.5–4 Sv doses are important in *asthenisation* genesis. In doses exceeding 4 Gy the *microorganic symptomatic* is registered reminding mild forms of *diffuse demyelynating encephalomyelosis*.

A.K. Guskova & A.V. Barabanova (1968), A.K. Guskova & G.D. Bajsogolov (1971) divided the three consequently rising *CRS neurological syndromes* depending on integral dose values and irradiation intensity.

1. Neuroviscearal regulation disorders syndrome.
2. Asthenic syndrome.
3. Central nervous system organic injury syndrome.

Syndromes clinical-physiological characterisation we will present here in details. As *neurovisceral regulation disorders syndrome* clinical peculiarities the authors stated above regarded the following. Complaints on fatiguability, headaches, pain in extremities, dizziness, unpleasant sensations rise in physical loading, body position change and overheating. These complaints are objectivised with skin vasomotor reactions lability and other signs of regional circulation instability (sweatiness, stable spread dermographism, physiological termotopographia disorders, capillary circulation disorders, skin vessels reactivity on pharmacological medications alteration). Asymmetric increased tendonal and depressed skin reflexes both with transient vestibular, oculo-vestibular oculo-static disorders are

marked in neurological state. No signs of nuclear structures irritation usually were observed: post-rotation post-caloric nystagmus can be even weakened and shortened in time in spite of vestibular reflex vegetative component sharp expression.

According to the data of A.K. Guskova & G.D. Bajsogolov (1971) no typical neurosomatic signs of process primary localisation in *diencephalic region* were usually revealed. However some features of autonomous nervous system pathology were similar to mesencephalic centers dysfunction symptoms. At that F.M. Sosnovskaya (1968) & G.I. Kirsanova (1968) reported about the normal *brain cortex bioelectrical activity*. A.K. Guskova & A.V. Barabanova (1968) marked the vagotonia tendency presence. *Electromyography (EMG) studies* results reflected unstable and multidirectional disorders of muscle bioelectrical activity through activity elevation in relaxed and tonic strain states, activity unstable decrease in contraction. *Neurocirculation shifts* and *discirculation manifestations* are noted in various organs and viscera function and are of labile mode.

In ionising radiation continued impact the nervous system next stage is risen described by A.K. Guskova & G.D. Bajsogolov (1971) as the *asthenic syndrome* (after its radiation or combined aetiology statement in diagnosis). V.A. Soldatova et al. (1971) considered the asthenic syndrome characteristic for CRS of the 2nd severity degree. According to opinion of A.K. Guskova & G.D. Bajsogolov (1971) the asthenic syndrome under ionising radiation impact is most close to somatogenic asthenia pathology group. Nervous system functional activity and internal organs function distinct depression is marked. Asthenic syndrome in irradiation is peculiar with extreme stability. Elevated physical and to the less extent psychical exhaustibility regarding the earlier perfectly executed loading is characteristic. Self-feeling (state of health) of patients becomes worse to the working week or year end, under tasks settling requiring prolonged energies and strain application. Further especially with unfavourable psychotraumatising issues application or age involution the personality alterations are formed that according to opinion of A.K. Guskova & G.D. Bajsogolov (1971) are hardly differed from purely neurotic ones. Supreme nervous function alteration objective signs and psychophysiological disorders are joined than.

Muscular hypotonia, hypomimia, muscular tone physiological distribution disorders with amplified locomotive reflex reactions registration, reflexes magnitude and asymmetry algebraic sign changes in body position change, reflexes equalisation from hands flexors and extensors, mild static-coordination disorders, skin reflexes relatively stable depression both with vegetative reflexes depression were observed in *neurological state* on asthenic syndrome stage after radiation impact. Multiform and often registered however not clearly formed skin sensitivity disorders are characteristic through threshold values and adaptation to irritant alterations, various dysesthesia, generalised locomotive reactions on spontaneous pain and pain irritation introduced from outside [Guskova A.K., Barabanova A.V., 1968; Guskova A.K., Bajsogolov G.D., 1971].

The *EMG-studies* revealed widening and pronounced expression of close and remote synergic reactions in various muscular groups; muscle complete physiological relaxation absence presented with spontaneous bioelectrical activity presence in muscle not taking part in locomotion, alteration in muscles-antagonists reciprocal interactions and risen in more pronounced cases muscle bioelectrical activity amplitude gradual decrease with elevated irregular exhaustibility in random movements. Though alteration of central effects on motoneuron and its exhaustion signs were registered [Guskova A.K., Barabanova A.V., 1968]. Centre of gravity deviations amplification compared to control correlating with cerebellum mild insufficiency were marked *in stabilographic study* [Barabanova A.V., 1969]. Alterations of reflex correct interrelation with irritant intensity and this parameter instability were revealed by A.K. Guskova through the *equitonometric study* results. *Muscular tone study* with sclerometer (i.e. device registering muscular density in respective units) indicated the muscular tone physiological distribution alteration in relaxed state and tone elevation weakening in random strain. Locomotive sphere disorders clinical-physiological manifestations were testified with several *biochemical alterations*: activation of enzymes related to motoneuron (aldolase, alanine aminotransferase, aspartate aminotransferase); creatinine serum content decrease and creatinine excretion with urine intensification.

Polyeffector electrophysiological study (EEG, EMG, ECG, skin-galvanic reaction) revealed in asthenic syndrome the 7-fold errors amount elevation in task execution, locomotive responses latent periods sharp elevation and instability. Muscular tonic strain was registered in relaxed state, expressed vegetative components and reactions rose accompanying the purposeful locomotive task execution. The so-called «false alarms» rise was marked according to the EMG-study data (muscles bioelectrical activation in pauses between irritant application) [Glazunov I.S., Blagoveshanskaya V.V., 1971]. A.K.Guskova & G.D.Bajsogolov (1971) underlined these alterations non-specific nature and in-fact their «hidden character» i.e. the stated shifts revelation under locomotive sphere disorders clinically pronounced signs absence.

Analysers function alterations in asthenic syndrome was presented with thresholds elevation and instability, disorders of physiological adaptation to irritant, various analyser systems interaction widening and perversion. Functional lability of thermal, visual and hearing analysers was somewhat decreased with signs of inertness and elevated fatiguability and more rapid exhaustibility. However according to data of A.K. Guskova & G.D. Bajsogolov (1971) no substantial difference between persons suffering asthenic syndrome depending on exposure to ionising radiation absence or presence were revealed.

In occupational chronic irradiation with integral exposure dose elevation A.C. Yefimova (1968) marked the *skin and optic analysers* distinct disorders. Under ionising radiation impact with 0.05–1.5 Gy doses no substantial alterations in these analysers sensitivity thresholds were revealed by the author. However, in low dose range impact the skin chronaxy elevation was surveyed and in doses over 1.5 Gy — that of optical chronaxy.

I.S. Glasunov & V.V. Blagoveshenskaya (1971) observed the *analysers* thresholds elevation, paresthesia, supreme nervous function disorders both with agitation process weakening and analysers fatiguability in persons exposed for 5–15 years to radiation integral doses of 150–700 mSv.

E.A. Drogishina et al. (1958) [cited from V.A. Soldatova et al., 1971] described the chronic radiation *skin injuries* — alteration in nervous-receptor apparatus, peripheral capillary circulation and pain sensation disorders. V.M. Mastrukova (1958) paid substantial attention to radiation damages of *sensitive nervous terminations and afferent innervation* in organism general radiation reaction genesis. V.M. Orlov (1968) demonstrated the epidermal dystrophy, derma collagen alterations, fibres degeneration, hair follicles and sebaceous glands atrophy with the sweat ones preservation in the seemed being undamaged skin under occupational exposure.

N.S. Delytsina (1969) and U.G. Grigorjev (1979) noted the *skin analyser functional state* clear alterations presence after irradiation depending on dose value. Single exposure to 0.3–5 Gy dose repeated 8–12 times induced the tactile sensation decrease. EEG reaction on tactile irritants amplification was marked.

E.V. Yermakov (1960) studying the *EEG alterations* in CRS revealed in 42% of patients the dysrhythmia and α-activity amplitude decrease both with slow pathological δ-waves, in 40% of patients — sharply depressed reaction on irritant. Author concluded that the definite parallelism exists between the CRS clinical presentations degree and EEG pattern alterations.

Autonomous nervous system disorders pathogenesis in ionising radiation long-term impact was analysed by E.V. Yermakov & B.F. Murashov (1971). Authors noted that *hypophysis-adrenal cortex system* functional capacity is decreasing, at that decrease degree is directly proportional to the radiation injury severity. According to EEG data the substantial more deviations were revealed than in norm, and in CRS clear presentation there were much more of them compared to disease initial period. These alterations were: the α-activity amplitude decrease and slow (2–3 and 6–7 Hz) low amplitude (30–50 μV) activity rise. Brain bioelectrical activity alterations clearly diffuse character in chronic irradiation in authors opinion pointed out to the *subcortex structures* dysfunction and namely *brain stem (frontal or rostral part) reticular formation activating effect decrease*. Central nervous system primary disorders in ionising radiation long-term impact are expressed in reticular formation and hypothalamus predominant damage with pituitary-adrenal system further involvement in pathological process.

V.K. Seltser & A.I. Stepanov (1971) studied the *central regulation state neurophysiological parameters* in remote terms after radiation impact (hundreds of mGy). Brain bioelectrical activity was peculiar with synchronisation level elevation. Authors registered diffuse α-rhythm spread in frontal parts. No α-rhythm amplitude amplification was observed after hyperventilation. Besides that the synchronous slow waves series appeared. According to rheoencaphalography data the pulse blood perfusion value decrease and peripheral vascular resistance elevation were marked. Authors pointed out that in case of damage corresponding to the level of *hypothalamus and reticular formation* being radiosensitive structures the other hazards besides the radiation are to be taken into account. At the same time low radiation doses impact as general irritant can modify the organism reactivity making it more sensitive to the further impacts.

Other researchers reported about the no substantial changes of brain background bioelectrical activity in chronic general exposure with integral doses up to 1.5 Gy. In doses 1.5–4 Gy the *quick* (β-) and *slow* (rare α- and θ-) *rhythmic* with clear depression on the response to the light. In hyperventilation and sometimes in rhythmic photo-phonostimulation the synchronised in pulse and breath activity was marked. Reactions on irritants often remained for the long time however being formed not always clearly. Deep and stable *activity depression* was marked in response to the settled tasks. The induced by light flash long-term not fading and non-specific evoked cortex potential rise was very characteristic both with on the contrary — the α-waves group flash comparative rarity in pauses between irritant application. That in authors' opinion indicates the agitation processes perfect concentration in brain cortex. In correcting test execution the typical for asthenia errors number rise was marked without their clear domination in work various stages execution. In repeated tests instead of «working-in» phenomenon the errors number elevated, common vegetative reactions appeared following the fatigue and later — unpleasant subjective sensations. All the mentioned shifts in analysers activity and EEG were expressed in persons suffering asthenic syndrome combined with circulation disorders clinical signs especially with venous haemostasia or arterial spasm type [Sosnovskaja F.M., 1968; Gyskova A.K., Bajsogolov G.D., 1971].

In the next work F.M.S osnovskaya (1971) presented somewhat another results of *brain bioelectrical activity* examination after chronic irradiation. Author marked the α-activity depression, however no amplitude or α-rhythm regional or frequency characteristics reliable shifts were revealed. The α-activity indices not depended upon irradiation dose. The α-activity shift to the high frequencies side was observed in patients suffering CRS. Tendency of curves number with β-activity was noticed along with irradiation dose elevation. Author regarded the *quick oscillations amplification to ionising radiation impact*. At the same time the low-amplitude diffuse θ-oscillations presence in exposed persons actually not differed them from healthy ones. However, *the dependence of pathological slow activity dependence upon integral irradiation dose was determined*. That pathological activity was presented with high sporadic slow oscillations of diffuse character or more often — with α- and θ-waves. The EEG patterns with slow activity pathological forms were found two-fold more often in persons exposed to 1.5–4 Sv doses for 5–20 years compared to those with 0.5–0.7 Sv doses for the same time period. In persons with diagnosed radiation sickness such EEG-patterns were registered in 42% of cases. Diffuse pointed oscillations of various expression rate more often of not high amplitude were observed in 30% of patients under 1.5–4 Sv exposure doses. Reaction on rhythmic

photostimulation was absent or feebly marked. Paroxysmal hypersynchronic α-, θ- and δ-waves were registered after hyperventilation. F.M. Sosnovskaya (1971) concluded that central nervous system rough functional alterations in majority of cases are absent in persons exposed to ionising radiation occupational impact. At the same time author noted the unidirectional mode with clear tendency of EEG-alterations elevation depending on ionising radiation integral dose.

Study of parallels between *cerebral circulation* disorders *and brain bioelectrical activity* was presented in work of G.I. Kirsanova & F.M. Sosnovskaya (1971) regarding neurocirculation dystonia in persons exposed to occupational iradiation. Authors concluded the pronounced cerebral circulation disorders absence under exposure to 0.5–4.5 Sv doses. Only the neurocirculation dystonia of hypotonic type slight prevalence with cerebral vessels reactivity decrease was marked especially in high doses and CRS. Authors underlined in their opinion the functional nature of these disorders. The EEG functional shifts in authors opinion testified the brain blood supply rate pronounced alterations absence. It is marked that fast oscillations relative increase qualitatively differs that from other hypotonic states.

It is interesting in out opinion to compare the brain bioelectrical activity alterations in ionising radiation and *microwave electromagnetic field* chronic impact [Shandala M.G. et al., 1977; Takashima S. et al., 1979]. The EEG-patterns in persons who experienced the contact with microwave radiation for 2–14 years was peculiar with high-amplitude α-rhythm with regional differences smoothing and β-index growth. The α-index abrupt decrease, β-activity elevation both with frequency and amplitude asymmetries were observed in more long-term (14–20 years) microwave radiation impact [Suvorov N.B. & Kukhtina G.V., 1984]. Presented data though indicate the EEG actual identity both in ionising and non-ionising (microwave) radiation impacts that in both cases reflect human brain *limbic-reticular structures dysfunction*.

Nervous system organic alterations according to data of A.K. Guskova et al. (1964) are surveyed in total irradiation with doses of 2.0–3.0 Gy. Diffuse muscular hypotonia, mild locomotive disorders, static ataxia, tendon reflexes asymmetric elevation with reflexogenic zones widening and muscles-antagonists reciprocal interrelations perversion, skin reflexes depression, sensitivity disorders — often of conductive-segment type were marked there. Later A.K. Guskova & G.D. Bajsogolov (1971) noted that *nervous system anatomic radiation injuries* genesis possibility is peculiar to high doses range i.e over 4 Gy of total and 10–50 Gy local irradiation. Total irradiation minimal dose leading to the stable alterations rise in nervous system most radiosensitive structures (myelinconducting tracts, autonomous nervous system ganglions) is 2–4 Gy. Respective terms of genesis are 1–3 years. V.A.Soldatova et al. (1971) marked that *nervous system organic damage* is possible in remote terms after contact to ionising radiation with threshold dose value exceeding 1.5 Gy.

A.K. Guskova & G.D. Bajsogolov (1971) insisted on the own proposed diagnosis *«encephalomyelosis» syndrome* and refused terminology of other authors (encephalopathy, encephalitis) as being far from essential content of pathology process rising in nervous system in prolonged general exposure. In such cases the signs of very mild pyramid and later — cerebellar insufficiency with some sensation types alterations (vibration and further — pain ones) appear first. Though the process is somewhat spreading among spinal cord and medulla diameter from the front-lateral to their back parts. Conductive structures of spinal-stem level are injuries to the higher extent. Nuclear and cortex structures in general participate mainly in clinical pattern functional branch genesis. A.K. Guskova & G.D. Bajsogolov (1971) named the alterations in physiological over-segment effects on peripheral motoneuron as leading pathogenetic pathway that is proved with synergies widening and neck-tonic reactions elements. Process in nervous system is of diffuse character with small diffuse micronecrotic focuses forming localised mainly in myelin structures in combination with moderately expressed ganglionic cells alterations (more in mesencephalon, cerebellum cortex and the cortex 3rd layer small cells) and spread neuroglia-vascular reactions. Certain cycle character is observed in these alterations forming that enables to suppose the secondary demyelination waves allergic nature.

I.S. Glazunov et al. (1971) described in details the clinical-physiological pattern of *radiation demyelinating encephalomyelosis* observed in 43 patients survived the radiation sickness (total irradiation integral doses 3–5 Gy) or roentgentherapy (local irradiation with doses exceeding 150 Gy).

Organic neurological symptomatic was characterised with clinical manifestations mildness and diffuse nature both with high similarity with initial and unclear forms of diffuse sclerosis or diffuse encephalomyelitis. Patients complained on general weakness, dull headache, weakness and unpleasant sensations in arms and legs, instability and dizziness in body position change. *Objectively* the nervus trigeminus branches outlet points painness (15%), convergence weakening (19%), nystagmus and nystagmoid (31%), muscular hypotonia (53%), a bit positive Romberg's sign (19%), skin reflexes values changes (resuscitation — 34%, depression — 13%) with asymmetry, abdomen reflexes decrease (29%) pain sensation alteration with peripheral type and especially vibration sensation disorders were revealed. No rough organic signs i.e. pareses or pyramid pathological symptoms were observed in any examined patient. The *radiation genesis* was testified by nervous system any organic damage signs absence before exposure and nearly absent — in lower doses.

I.S. Glasunov et al. (1971) regarded the neurological symptomatic instability and reverse progress possibility, organic microsymptomatic rise on the background of already formed CRS background or in recovery/remote period after ARS to the radiation demyelinating encephalomyelosis *clinical peculiarities*. In authors opinion the *pro-gradient character absence* both with *softness and delicateness,* «microorganic» type of organic symptoms was the difference from diffuse sclerosis. Attention was paid to the *dissociation* presence between injury objective and subjective signs. So in cerebellum symptoms (muscular hypotonia, nystagmus, instability in walk and Romberg's test) the co-ordination trials were executed in a good way. Tendon reflexes resuscitation with their asymmetry was combined with muscular

hypotonia with its degree being higher on elevated reflexes side. Frequent complaints on numbness, pains in extremities etc. Not always combined with objectively revealed sensation disorders. At the same time patients with no subjective disorders the superficial, vibration or discriminative sensitivity alterations were revealed objectively.

EMG-studies revealed muscles electrical activity elevation in remote and close synergies as agitation *transmission alteration* and its amplified irradiation. Potentials amplitude decrease under enough or a bit lowered oscillations frequency was observed in muscles random contractions. The *EMG-pattern of aftereffect* constituted in potentials no critical breakdown after signal to the movement termination (as in healthy persons) but continuation for 0.8–1.4 sec producing oscillations volleys or reaction close to *myasthenic*. *Extension speed slow-down* was determined in *chronoreflexometry* on spinal level both with reflex sound- and visual-locomotive reactions time elevation up to 300–460 msec.

Myelin coatings are extremely sensitive in brain tissue function alterations due to metabolism disorders after radiation sickness. I.S. Glazunov et al. (1971) explained the *demyelination* in radiation impact by the following:

1. Direct effect on myelin (under massive local external irradiation).
2. Microcirculation disorders.
3. Sensitized tissue immune reactions.
4. Metabolic disorders where any injury of any enzymatic reactions branch can lead to myelin destruction was meant.

I.S. Glazunov et al. (1971) considered that organic symptomatic presence in remote period after irradiation is to substantial extent explained by *demyelination* processes.

Pathophysiological manifestations of nervous system organic damage under irradiation according to the data of A.K. Guskova & A.V. Barabanov (1968) consisted in the following. *EMG-pattern* was characterised with separate reposing muscles electrical activity rough alterations, synergic reactions spread sometimes exceeding in extent the working muscle activity, physiological reciprocal interrelations alterations in random movements. Not only amplitude but also frequency characteristics of muscles are changing. Creatine-creatinine metabolism is altered (serum creatinine decrease with urine excretion elevation). *EEG-patterns* are peculiar with slow and quick rhythmic amplification (diffuse or in separate zones) with α-activity reduction.

According to opinion of A.K. Guskova & G.D. Bajsogolov (1971) the convincing proofs of lethal exits in CRS as the result of nervous system damage are absent. Neurological syndromes observed in persons died from hypoplastic anaemia and leukaemia in CRS outcome both with haemorrhage in brain tissue under radiation sickness complicated with infection processes and haemorrhage syndrome were of no any specificity.

Genuine reparation processes in adult human nervous system anatomical alterations rise are extremely unlikely. Slowly progressing diffuse degeneration-dystrophy process being in the *radiation encephalomyelosis* basis can be accompanied mainly with neuroglia-vascular proliferative reactions complex both with nervous activity functional reorganisation but not the neuronal structures genuine restoration.

R.G. Golodetz (1962–1993) summarising the many-years *psychiatric work experience* in occupational diseases clinic noted that in radiation sickness initial stages the asthenic complains are combined with vaso-vegetative dystonia manifestations. In case of disease rise where the two stages are surveyed — *functional alterations stage* and *gradually forming organic alterations one* the asthenic symptomatic becomes of high stability. Elevated fatiguability, emotional lability with disposition to tearing and resentment reactions, headaches, dizziness, sleep disorders in form of its rhythm perversion or sleepiness with nightmares timely changed by stable insomnia — all are related to the chronic radiation disease most early symptoms. Their forming occurs gradually and in initial stages is of no substantial differences from the same states of another origin. Along with CRS progress the asthenic group presentations are noticeably deteriorated with their somatogenic nature being more and more clearly presented. Fatiguability, irritability, vaso-vegetative disorders are elevated; more profound sensitive reactions are formed with interests exhaustion, general mood background decrease, mnestic-intellectual weakness is revealed; complaints on viscera and endocrine system function disorders became more and more pronounced; laboratory analysis results deviations appear particularly in haematological and biochemical ones.

Vaso-vegetative disorders became higher pronouncement being presented with multiform *senestopathy, paresthesia and algias*. Patients complain on extremely burdensome and hardly enduring feeling of burning, pricking, numbing and pulsation; loud sounds, bright light, smells and other irritants intolerance. *Optic-vestibular and psycho-sensory disorders, crisis states* appear. The last ones are characterised with sudden rise and are progressed with vegetative «storm» type accompanied with extreme weakness, multiform senestopathy and pains especially in head, heart and gastrointestinal tract zones. Crisis states duration is different; in more severe cases they last for several hours/days and after attack termination patients only gradually experience relief of weakness and «broken-down» feelings. In single cases the short-term consciousness loss sometimes with generalised tonic convulsion is surveyed on the crisis supreme point — pattern being close to the *diencephalic epilepsy*. Often the *perception disorders* on the stated manifestations background are observed in the form of elemental hypnagogic hearing, visual and tactile hallucinations. Sometimes the *delirious mood* is marked *with relation ideas* (i.e. patients are a burden on everybody, colleagues changes attitude to them, even relatives and friends are not glad, «sick with them» and «are tired bothering)», especially on the depressed general mood background. In some patients the earlier not appropriate to them *psychoasthenic features* are revealed with diffidence, fears, anxious apprehensions, obsessive manifestations, sometimes — hypochondriac fixation and «retire into» or «leave for» disease.

R.G. Golodetz (1993) selected the following variants of *asthenic syndromes:*

1. Asthenic-neurotic.

2. Asthenic.
3. Asthenic depressive with anxious apprehensions and obsessions.
4. Asthenic-hypochondriac.
5. Asthenic with productive psychopathological symptomatic.
6. Asthenic-organic:
    a) asthenic-adynamic;
    b) asthenic with pronounced vascular disorders;
    c) asthenic with diencephalic crises.

Asthenic syndrome divided variants reflect the CRS progress periods. In early stages the functional and neurodynamic disorders prevail presenting sometimes similarities with *neurotic* ones. Further the *organic* components are revealed with elevating clearness presented both in psychopathological and neurological patterns. The exhaustibility signs elevation occurs, mnestic functions difficulties become more clear with intellectual activity slow-down and exhaustion; emotional lability is changed by affective reactions stagnation and inertness with hypochondria forming on this background and in some cases — the stable productive symptomatic too. Distinct neurological symptoms appear being reflected in EEG data (pathological activity, brain bioelectrical activity depression with curves flattening, asymmetries and focuses rise, profound brain structures irritation events). Subcortex structures involvement in process being especially radiosensitive ones is presented not only in multiform somatic-vegetative disorders with expressed senesto-algetic symptoms but also in more pronounced affective alterations with anxious apprehension, fears and other mental disorders forming both with the disease itself undulating progress. According to the *experimental-psychological studies* data the cognitive activity disorders are revealed in all cases of CRS clinic with memory and attention weakening, psychic processes elevated fatiguability and inertness that along with radiation injury progress obtain the especial expression.

In CRS mental disorders *differential diagnostic* according to opinion of R.G. Golodetz (1993) the following issues are to be taken into account. Vascular disorders expression with weakling phenomenon and mnestic functions weakness, general anxious background in mood are to be differentiated from cerebro-vascular pathology. Affective tone decrease, circle of interests narrowing and paranoiac mood — from endogenous disease respectively.

R.G. Golodetz (1993) paid attention that *asthenic states* formed in CRS patients are peculiar with extreme severity. Already in disease early stages they are combined with multiform somatic-neurological, vaso-vegetative, endocrine, metabolic-trophyc and hematological alterations providing *vital character* to the *asthenia. Vascular disorders* presentation is also typical including the vaso-vegetative crises. Forming *hyperpathetic background* with elevated sensitivity to external irritants is peculiar phenomenon especially regarding smells and sounds (by hyperosmia and hyperacusis types) both with *senesto-algetic manifestations* expression. Asthenic syndrome progress dynamic is also of definite peculiarities i.e. progradient nature (even after ionising radiation contact termination) with tendency to prolonged undulating progress [Golodetz R.G., 1993].

I.S. Glazunov & A.A. Vyshnevsky (1972) and A.A. Vyshnevsky (1973) marked that *asthenic syndrome* in CRS patients is peculiar with psychopathological symptomatic pronounced polymorphism. Authors revealed the so-called «asthenic» crises with headaches, general weakness and apathy intensification in 39% of cases in disease structure. Stormy affective manifestations were prevailing in such cases among extraverted persons.

Work by R.G. Golodetz *«To the issue of schizophrenia clinical peculiarities being complicated by some occupational factors impact»* (1962) is in our opinion of particular interest being up-to-date the single in its kind (among the available literature). Author presented the dynamic survey results in 12 schizophrenia patients exposed to occupational chronic (for 7–10 years) ionising radiation impact. Schizophrenia arose in them not long before or during work period. Patients were young men (25–30 years) with substantially deteriorated heredity and reticence, senzitivity and mistrustfulness features presence in anamnesis of 5 cases from 12 ones and abortive psychotic episodes experiences in adolescent age.

Schizophrenia process dynamic was peculiar with substantial originality: slow gradually progress quasi growing out from *asthenic syndrome* occupying for the definite time central place in clinical pattern. Changed attitude to surrounding and expressed paranoid symptomatic was revealed with disposition to symbolic and interpretative delirium. Productive psychopathological symptomatic was characterised with higher brightness of presentation, their extremely sensitive colouring and substantial polymorphism. Most often the *paranoid syndrome* was present *with pronounced hypochondriac formations*. Not rare the circulation inclusions were observed too with depressive and hypomaniac components changes. Author regarded to the atypical manifestations also the relative accessibility even in the psychosis supreme point being observed in 10 from 12 patients.

Asthenic background not rare is being the prodrome preceding schizophrenia typical manifestations rise. However, in patients exposed to chronic irradiation the asthenic symptomatic *was peculiar* with its massive character, somatic-vegetative and endocrine disorders clear presentation which genesis was related by R.G. Golodetz (1962) to the ionising radiation impact. Hy*pochondriac symptomatic* rose particularly easily on pronounced asthenic signs background in disease initial stages. Among patients characteristic complaints the indications on poor memory, headaches frequent attacks and extreme affective instability were in the first rank. Pronounced asthenia and untypical for schizophrenia patients accessibility and behaviour adequacy were drawing attention. Author underlined that asthenic background, somatic-vegetative and endocrine disorders for definite time conceal the disease real nature.

In schizophrenia more remote stages the productive symptomatic was full of *senestopathy wit bright sensible coluoring*. Process progress undulation was marked. In remission period and defective states patients presented complaints with expressed somatic shade.

R.G. Goldetz (1962) concluded that schizophrenia process genesis was taking place with no dependence upon ionising radiation impact. However the schizophrenia genesis and clinical progress peculiarities author connected to the irradiation.

Thus R.G. Goldetz (1963) actually described the *schizophrenia radiation pathomorphosis*. I.K. Syzin (1955) marked noticeable elecrophysiological and clinical changes in epilepsy progress under the patients consumption of 20–100 μ Ci (740–3,700 kBq) ^{24}Na, ^{32}P and ^{131}I radioactive isotopes.

However, A.K. Guskova & G.D. Bajsogolov (1971) not agreed both with psychotic disorders rise possibility under irradiation and fact of ionising radiation effect on endogenous psychic diseases progress. In their opinion R.G. Goldetz (1962) underestimated the other pathogenic factors role.

As it was in details presented in Chapter 3, Y. Nakane & Y. Ohta (1986) revealed the extremely high schizophrenia prevalence (6%) in Nagasaki A-bombing survivors whereas the respective value in Japanese population constitutes only 0.2–0.8%. J. Amimkhanov (1995) reported about oligophrenia, schizophrenia and epilepsy specific weight elevation in persons resident close to Semipalatinsk nuclear test-site. So the available data testify the ionising radiation effect on mental diseases both structure and prevalence.

W.M. Court-Brown (1966) reported that under exposure doses of 1.5–2 Gy the fatiguability, apathy, sleepiness, dizziness, headaches rise that in authors opinion leads to *depression*. D.F. Khritinin (1989) demonstrated that in CRS the *apathetic-abulic and asthenic-abulic syndromes*, attention concentration and stability with memorizing alterations, intellectual inability, emotional weakness, asthenic-depressive states are moved to the first ground.

Neurones injury in *normal ageing, Alzheimer's disease and ionising radiation impact* according to opinion of J.A. Joseph (1992) combines the corpus striatum dopamine- and cholinergic systems depression as the result of neurone membranes free-radical damage.

N.Ya. Tereschenko (1968), A.K. Guskova & G.D. Bajsogolov (1971) noted that *nervous system radiation injury in children* clinical peculiarities are the cortex insufficiency expression and more complex associative links main damage, slow-down of functions physiological forming and neuro-psychical activity gradual complication appropriate to the growing organism. These clinical peculiarities both with proved nervous tissue higher general injurability in children are explained with originality of developing brain reaction on radiation. Such peculiarities pathophysiological pathways are related to the radiobiology general regularity of developing structures predominant injury. Brain cortex in child continues its differentiation and progress after birth. The most complicated association complexes and behaviour reactions are also formed in childhood. Thereby stated structures and functions became «critical» under kid irradiation. Stated structures injury with *underdevelopment or retarded morpho-functional forming type* is the main clinical syndrome in ionising radiation impact on immature brain.

I.S. Glazunov & N.Ya. Tereschenko (1974) after frontal and frontal-temporal zones irradiation with 1–2 Gy doses in children observed *cerebrasthenia and encephalopathy* genesis. In their clinical presentation the complaints on headaches, dizziness, memory deterioration, quick fatigue in physical or mental loading, effective sphere disorders were marked.

B. Modan et al. (1977), E. Ron et al. (1982) & I. Yaar et al. (1982) reported that threshold of 1 Gy is present regarding *IQ decrease and mental diseases risk elevation* in children.

In *CRS pre-clinical stage* the nervous function alterations are mainly of reflex character and are accompanied with endocrine and cardiovascular system reactions. *Polyaetiologic asthenic and neurotic syndromes* were marked after irradiation to 0.7–1.5 Sv doses that were in opinion of A.A. Losev (1968) stipulated by non-specific reactions on radiation summation with impact of other more appreciably asthenisating exo- and endogenous factors (overfatigue, psychic traumatising, age involution).

According to the data by A.K. Guskova & G.D. Bajsogolov (1971) in thorough clinical-physiological population study of persons never contacted to ionising radiation or any other unfavourable occupational factors the nervous regulation lability was revealed in 15–30% of cases. At that the full-scale syndrome of *neuro-circulation dystonia* was revealed in 9–11% of cases. However after long-term irradiation with doses 0.7–1 Sv the named syndrome was observed in 50% of examined persons. A.K. Guskova & A.V. Barabanova (1971) reported that after integral dose attainment of 0.7–1.5 Sv the neurological syndrome of neurovisceral regulation alteration (neurocirculation dystonia of hypotonic type) and asthenic syndrome are observed in 37% of cases. Under exposure to the doses of 1.5–4 Sv the mentioned disorders were met in 70% of cases.

Below we present the *CRS clinical pattern* statement (mainly of neuropsychiatric components) based on its classical description by N.A. Kurshakov (1963).

The first (mild) degree of CRS starts gradually. Sometimes exposed persons consider themselves completely healthy and the disease is revealed accidentally in planned clinical examination. At that the blood alterations or *neurological symptoms* are the most characteristic being the *earliest signs* of rising pathology. *Neurovisceral regulation* alteration is the nervous system reaction earliest form. Complaints on headaches in cranium various parts appear — most often in frontal one. They rise and increase in strain and emotional experiences. Sometimes headache became of migraine type. Dizziness, nausea, darkening in eyes in position change are observed. Patient became more and more irritable, quickly becomes tired, working capacity is noticeably decreased. Patient is troubled with sleeping disorders. *Asthenic syndrome* is revealed objectively with emotional instability, marked memory decrease and elevated fatiguability.

Autonomous nervous system dysfunction symptoms are of dominating role in disease initial period: unpleasant sensations in heart region, rushes of blood with skin rapid turning red in separate parts, face skin reddening or turning pale, heat sensation, cyanosis, extremities marmorated skin. Vasomotor disorders are accompanied by elevated sweating, tendon and periosteal reflexes amplification, eyelids and stretched arms fingers pronounced tremor. Pyloromotoric reaction and dermographism alterations are observed both with arterial blood pressure instability with tendency to decrease. Appointments on numerous and various pain sensations are prevailed in patients complaints [Kurshakov N.A. et al., 1960].

Pains in bones, joints and muscles are characteristic. *Osteoalgetic syndrome* is especially pronounced in case of osteotropic radionuclides deposition. Pains are more intensive in warmth and in repose relieving in movements. Vibration sensitivity is usually depressed whereas superficial sensitivity types are damaged slightly. According to *neurophysiological studies* data the EEG alterations, sensitivity thresholds elevation, perception perversions, latent periods extension are registered. Such neurophysiological manifestations reflect the *cortex neurodynamic* alterations and *cortex-subcortex interrelations* disorders.

Endocrine shifts and *metabolic* disorders stipulate *asthenic state* along with neurodynamic alterations. Metabolic reactions are labile: both elevated and decreased serum cholesterol and sugar levels are revealed being connected to the both nervous regulation disorders and liver and state of other viscera taking part in metabolism. Glycogen content alterations, protein metabolism disorders and microelements content deviations are marked. Irritable weakness signs characteristic for neurasthenia, psychoasthenic events etc. are the typical symptoms here. Working capacity of patients decreases.

Various regulation disorders are present *in all* organism systems. Pressure decrease in retina central artery was described. *Sexual function* disorders can be revealed: impotence in males and ovarian-menstrual cycle alteration in follicular hormones lack in females. *Trophic disorders* are characteristic here with central and peripheral agents important role in genesis. General appearance of patients testifies the gradually rising *premature tissue wasting away*: face colour deterioration, tissue turgor decrease, skin becomes more flabby, peeling and pigmented. Skin chaps poor healing takes place both with hair loss intensification. In general, the nervous system damage is characterised with *asthenic-vegetative syndrome*.

Blood pattern is unstable and labile: both moderate leukocytosis and leukopenia can be observed however with leukopenia prevail ($3.5–4.5 \cdot 10^9 \cdot L^{-1}$) and somewhat left-side shift and lymphocytosis 40–50%. Leukocytes qualitative alterations are marked with nuclei partial pyknosis being early sign. Platelet number is also unstable, often decreased down to $160,000–180,000 \cdot L^{-1}$. Erythrocyte content is also variable with reticulocytosis and anisocytosis rise. Some irritation signs with elements maturation and differentiation alterations are present in bone marrow material. Blood coagulation depression is marked. Small vessel walls became more brittle with increased permeability, however no haemorrhage events are observed.

The second (moderate) degree of CRS is peculiar with symptomatic widening and intensification. The more extended organ injuries are revealed with more severe alteration degree. At that pathological changes reversibility becomes less and less pronounced. As in CRS mild degree the patients complaints also not in whole completeness correspond to objective signs. One among other most frequent and resistant complaints is the headache poorly subject to curative arrangements. Exhaustion, breakdown are observed with appetite and sleep disorders in form of both sleepiness and insomnia. Dizziness, sensation of gravity or emptiness in head, feeling of inability for mental strain are characteristic. Substantial memory decrease, excessive irritable weakness and nervous system quick fatiguability are revealed leading to disablement.

Cerebroasthenic events not rare are revealed after long-term exposure to radiation in *low doses*. In such cases brain bioelectrical activity are revealed in form of cortex rhythmic activity amplification and high-amplitude α-activity diffuse spread with needle-shaped sharp and slow waves rise in pulse rhythm especially in brain frontal parts. Cortex reactivity and irritability thresholds are often decreased.

Nervous system injury is of progressing character and in case of CRS of the 2nd degree corresponds to the *diencephalic syndrome*. Autonomous nervous system is affected in all levels i.e. segment and over-segment ones. Paroxysmal tachycardia attacks, chill, fever, cold extremities, subfebrile body temperature that can not be related to internal organs state, sleepiness or insomnia are observed. Skin-vascular reactions are clearly expressed. Water, carbohydrate and other types of metabolism disorders, hair loss, losing flesh or on the contrary — obesity occurs. Diencephalic syndrome progress is peculiar with cycle nature i.e. the deterioration periods are changed by improvement episodes. However if the etiologic factor continues to impact, the diencephalic disorders deterioration leads patient to the next more severe disease degree and complete disability. In incorporated radionuclides deposition in bones the pain in bones rise is characteristic especially in legs (*osteoalgetic syndrome*). Pains are usually intensified in warmth and repose. Pain in bones are accompanied with muscular and nervous truncus painfulness. Objectively the pain sensitivity alterations are defined of *radix* or *polyneuritic types*.

Endocrine system pathological changes are of phase pattern and following the organ hyperfunction the hypofunction occurs. Pituitary disorders in diencephalic syndrome structure are constituted in metabolism alteration. Pronounced adrenal disorders especially of their cortex layer are presented with vascular hypotonia, asthenia, salt and carbohydrate metabolism alteration. Expressed Addison's syndrome with pigmentation is met. Libido is depressed in both gender patients. Impotency is met in males and dysmenorrhea and amenorrhea with pregnancy course disorders.

Skin trophic alterations are expressed in some cases as dermatoses with skin itch, peeling, sometimes hypertrophy and becoming callous. Nails are thinned, covered with longitudinal or transverse streaking, become brittle, hair loss is intensified.

Blepharoconjunctivitis, *visual organ* refracting mediums alterations are registered. Radiation cataract is risen relatively late and progressing slowly [Vishnevsky N.A., 1958, 1964]. The pathologic process onset from lens back capsule with all lens gradual involvement is peculiar for *radiation cataract*. Latent period before initial sins rise is from 2 to 7 years. In radiation cataract genesis both the ionising radiation direct impact on lens fibres regeneration and eye refracting mediums alteration due to vascular trophic and permeability disorders are supposed. General metabolic disorders impact is also supposed here. *Retina angiopathy*, visual organ accelerated involution signs to the higher extent reflect the ionising radiation general impact and CRS itself manifestations genesis.

Vascular alterations are usually more pronounced than heart disorders. Cardiovascular hypotonia with blood pressure moderate decrease is typical. Small vessels elevated brittleness is revealed. No convincing data regarding coronary heart insufficiency (disease) character for radiation sickness were obtained.

Atrophy and sclerotic processes rise in *digestive* and *respiration systems*. At the same time N.A. Kurshakov (1963) paid especial attention to that parenchyma organs alterations not rare found in experimental CRS in clinic are possible but *not characteristic*.

Haemopoietic system injury is the characteristic sign of stable CRS. Leukocyte content decreases down to $2.0 \cdot 10^9 \cdot L^{-1}$ and lower with left-side shift prevalence in neutrophil formula. Pronounced and stable reticulocytopenia is marked sometimes accompanying the anaemia. Bone marrow samplings study reveal the cell elements in myelocyte stage (more often — young one) content decrease. Monocyte percent is elevated. The right shift is observed in red branch with erythroblasts mature forms elevation and erythropoiesis alteration through megaloblast type. Megakaryocytes content is decreased. Reticular elements number is usually elevated.

In *the third (severe) degree of CRS* the pathological symptomatic furthermore spread and deepening is observed. In this form the striking discrepancy can take place between satisfactory self-feeling and threatening objective signs. Symptomatic corresponds to the described above but is peculiar with higher expression.

Central nervous system organic damage is characteristic here. Neurological disorders are mainly of diffuse pattern. Alterations are peculiar with pathological symptoms stability. In rare cases the pathological events partial regress can be observed but in majority of cases the *steadfast progressing* to deterioration is observed. Sometimes the process undulating course is marked with remissions and exacerbations.

Central nervous system diffuse injury is rising through the *demyelinating encephalomyelitis (diffuse encephalomyelosis)* or *toxic encephalitis* type with preemptive involvement of mesencephalon and diencephalon. *Funicular myelosis* signs are observed. Reflex, locomotive and sensation spheres disorders are revealed objectively. Deviations are found from the cranial nerves side. Tendon reflexes are altered to the side of both elevation and depression, especially the knee and Achilles ones. Tendon and periostal reflexes anisoreflexia is observed with decrease or complete drop-out of abdomen ones on the side of dominant pyramid insufficiency. In stable pyramid insufficiency the pathological signs and clonuses can be revealed. Muscular tone alteration of pyramid type occurs. Static disorders (ataxia in Romberg's test), oculo-vestibular alterations and nystagmus are typical. Fine changes in analysers peripheral parts progressing through the neurodystrophic ones are marked. In osteotropic radionuclides incorporation the pain in bones is characteristic both independent one and risen under percussion. Most often this pain is felt in shin bones and sternum. Usually it intensifies in warmth and repose, especially at night. Rough sensation alterations are rare with the exception of severe injuries from radioactive substances incorporated in bones resulting in *radiculoneuritic syndrome*. The especially severe depression of vibration sensation is described in such cases. Besides that painful sensations appear in body various parts especially in arms and legs distal parts.

N.A. Kurshakov et al. (1960) described in CRS of the 3rd degree clinical pattern the *encephalopathy* expressed by severely progressing *vascular disorders* of original vasopathy type with periodical crises. In fine functional study the alterations in *analysers* state (visual, olfactory, gustatory, hearing, vestibular and skin) are revealed.

Hypothalamic zone injury in CRS of the 3rd degree are presented with rough alterations in cardiovascular, digestive and neuroendocrine systems function. All types metabolic disorders, tissue trophic and haemopoietic organs function alterations are registered.

N.A. Kurshakov (1963) considered that symptoms stipulated by *cerebral ataxia* takes important place in CRS clinical presentation. They are combined with vegetative functions disorders, hyperthermia, arterial hypotonia and spinal liquid pressure deviations. *Cortex and diencephalic* disorders combination defines further progress of functional and structure alterations in nervous system. That results in all organs and systems neural regulation disorders.

Vascular alterations with tine fall-down and permeability elevation lead to *subarachnoid hemorrhages and haemorrhages in brain tissue. Bleeding* in CRS of the 3rd degree is presented rather more often and to the greater extent than in milder CRS degrees.

Rather more expressed *impotency* in men is observed both with *menstrual cycle* disorders and *pregnancy* progress in women because of hypotrophic disorders in genital system.

Blood alterations are expressed sharply and are peculiar with stability. Granulopoiesis sharp depression ($1.0–1.2 \cdot 10^9 \cdot L^{-1}$), thrombocytopenia, erythrocyte content decrease, reticulocytopenia, hyperchromia and pronounced anisocytosis are marked. Myeloid elements maturation is expressed in bone marrow with erythropoiesis perversion through megaloblastic type. However no complete devastation of bone marrow can take place, the haemopoiesis regeneration is not occurring and treatment is extremely complicated and even unavailing. Prognosis is extremely unfavourable.

CRS of the 3rd degree under provoking unfavourable circumstances impact (intercurrent infection, environment conditions deterioration etc.) can present the hazardous turn to the terminal period that was considered by N.A. Kurshakov (1963) as the *CRS fourth — final degree*. In this terminal stage the disease with accelerating rate is progressing to the lethal exit. Self-feeling in patients exacerbates, complaints severity rises. Apathy and general weakness rise. Sleep and appetite are deteriorated, dyspeptic disorders appear, head aches and pain in bones become more intensive. In some cases adynamia is so pronounced that patients in all ways long for having rest with any external irritants elimination. Neurological symptomatic described above is exacerbated. *Infection diseases* are joined defining disease prognosis. *Expressed disorders of dystrophic type* are revealed in organs and systems. Heart function and vascular tone weakening signs are found. Adrenal failure stipulated adynamia and hypotonia rise in patients.

Small vessel brittleness is increased with their walls permeability elevation leading to the tissue swelling. *Vascular disorders* are the main factor of *haemorrhagic diathesis* rise being stipulated by blood system alterations. Haemorrhages appear on body surface (small petechia and larger ecchymoses), mucosa and internal viscera tissues. Haemorrhages are accompanied by trophic bedsores rise and infection-septic focuses. *Subarachnoid haemorrhages* can take place and more rare — haemorrhages in brain tissue.

Blood indices are especially characteristic here. Bone marrow haemopoiesis sharp depression takes place. Lymphopoiesis is also greatly depressed however usually to the less extent. Leukocyte content can reach down to $0.01–0.1 \cdot 10^9 \cdot L^{-1}$. In severest cases only the single cells are found in smears. Thrombocytopenia is sharply expressed: platelet content goes down to several thousand and even less. Erythropoiesis is altered to the less extent — 1.5 - 2.0· 10^9 RBC·L^{-1}. Reticulocytosis can still remain. ESR (erythrocyte sedimentation rate) is elevated substantially. Blood coagulation, RBC osmotic resistance in terminal period are lowered. Bone marrow pattern is characterised by its «devastation». *Death* can occur in haemopoiesis catastrophic collapse and sepsis rise.

CRS diagnostic is of substantial difficulty especially in the diseases onset. Asthenic-vegetative disorders rise often can be explained by several completely outsider non-radiation causes. Every of these symptoms is of diagnostic value only in combination with other ones and only in case of long-term contact presence to radioactive materials in doses exceeding the maximum permissible. At that the precise *dosimetry data* are required with other toxic and unfavourably effecting factors possible impact exclusion. Especial attention is to be drawn to the *individual radiosensitivity*. Symptoms rise and ionising radiation impact connection identification is important. *Nervous regulation of internal organs alterations especially of vascular system are to be considered the CRS earliest manifestations.*

As early as 60th it was noticed that visual, hearing, vestibular, olfactory, gustatory and skin *analysers* functional state studies both with *electroencephalogram* registration are of particular importance in CRS early diagnostic [Kurshakov N.A. et al., 1960].

A.K. Guskova et al. (1964), A.K. Guskova & G.D. Bajsogolov (1971) etc. marked the *clinical-physiological examination methods* information value (EEG, EMG, chronaxymetry, various analysers irritation thresholds evaluation, vegetative-vascular reflexes search etc.) for asthenic syndrome in CRS objectivisation and quantitative estimation. *Brain bioelectrical activity* is most justified under various functional loading both with separate analyser systems interaction thresholds determination. Authors underlined that especial attention is to be paid to the clinical-physiological studies of not sharply expressed pyramid and later — cerebellum insufficiency (muscular tone electromyography and mechanography registration, reflexes and interaction in locomotive analyser system examination both with brain bioelectrical activity) in the period of *nervous system organic post-radiation alterations* forming.

N.A. Kurshakov (1963) marked that CRS clinical pattern has no any specific pathognomonic signs except cases accompanied with incorporated radionuclide release. Observed symptoms can be met in other pathology too. But still the symptomatic is very characteristic for this disease and *these characteristic features combination both with anamnesis data usually provides enough groundwork for CRS diagnostic*. In less severe cases with meagre and not full-scale symptomatic the disease identification is more difficult. Hematological symptomatic, *nervous and endocrine systems* with digestive organs alterations degree and character, disease process progress dynamic are of particular importance.

Other authors [Barabanova A.V. et al., 1969] underlined the nervous system alterations polyetiological nature under radiation and marked that nervous system disorders can not be determining ones in CRS diagnostic. In their opinion the neurological and all the more rare and poorly expressed personality alterations can be leading in clinical presentation under ionising radiation doses exceeding 10 Gy.

A.K. Guskova et al. (1964) & A.A. Letavet et al. (1964) expounded *the general principles* for valid *CRS diagnostic*:

1. Patient *anamnesis* complete study and his *«professional route»*. At that the contact possibility to the unfavorable exogenous factors combination is to be born in mind. The named contact duration both with survived earlier occupational and non-occupational diseases are to be taken into account.

2. Information from the place of employment regarding the examined persons *working conditions in contact to radiation*. General and individual *radiometry and dosimetry control* data: single-moment, for working day or integral for the definite term (week, month, year) dose values. Term of daily stay in exposure zone. Value of occupational environment and residence place radioactive contamination. Protective facilities and devices presence and efficiency, ventilation efficacy, local protection devices application. In this part the anamnesis data reported by the patient are to be rather enough *objectively estimated and documented* otherwise the disease occupational (radiation) aetiology issue identification in majority of cases will be impossible.

3. Present complaints and objective *alterations arise terms and sequence* (before or after the works in contact with ionising radiation start and what term after i.e. months, years), impact of intermissions on alterations dynamic.

4. Symptoms severity degree *dependence* upon *irradiation levels and work duration* under ionising radiation impact conditions.

5. Certain *symptoms complex* presence *characterising CRS* (leukopenia, blood cells qualitative disorders, thrombocytopenia, *nervous system functional or organic alterations*, endocrine organs, respiratory organs, liver function disorders, blood biochemical shifts).

6. Pathological process *progress dynamic* with remote consequences in particular.

7. *Biosubstrates* study results *for radioactivity*, skin and overalls radioactive contamination in works with open-type radioactive materials.

8. *Single-type and diseases*presence in persons group working in similar conditions can be the diagnosis confirmation.

9. As the clinical presentation strict specificity is absent, the CRS every specific case interpretation reliability requires the thorough *differential diagnostic* execution regarding similar with clinical symptomatic diseases of other, non-radiation aetiology and under unfavourable radiation-hygienic conditions.

M.M. Kosenko et al. in work *«Chronic radiation sickness cases analysis in Southern Ural population»* [cited from G.I. Reeves & E.J. Ainsworth (1995)] presented the CRS following diagnostic criteria, on the basis of which the disease was formally identified in 940 survivors of South Ural radiation accidents:

1. Ionising radiation impact duration not less than 3 years with not less than 1 Gy individual bone marrow dose accumulation verification.

2. Medical confirmation presence in long-term survey of clinical manifestations proposed by A.K. Guskova & G.D. Bajsogolov as the CRS criteria.

3. Other diseases absence with similar symptomatic.

More than 10-year-long experience of health state study in Chernobyl accident survivors various groups enables to *estimate among them the CRS genesis possibility*. A.K. Guskova (1997) considers at present there is no enough scientific-clinical basis for CRS diagnostic in survivors. At the same time data are presented regarding the *CRS genesis* risk being marked in effective doses of 0.6–1.1 Sv [Dolgih A.P. et al., 1993]. Thereto A.K. Guskova & G.D. Bajsogolov (1971) pointed out that some alterations revealed in 0.1–1 Sv doses can be described in brief as *radiation sickness respective forms pre-clinical stage*. At that single typical for radiation impact alterations can rise yet before the clear radiation syndrome formation. Those alterations in opinion of A.K. Guskova & G.D. Bajsogolov (1971) are to be estimated as pathological process forming symptoms and designated with term *«chronic radiation sickness pre-clinical stage»* in case of data presence regarding maximum exposure levels indubitable excess.

In health state integral estimation of so-called «self-settlers» to the Chernobyl exclusion zone i.e. persons with unauthorised residence in the 30-km zone of Chernobyl NPP («returnees»), we revealed the osteoarthralgetic syndromes and cerebrovascular pathology domination; mental health deterioration due to the both borderline psychic and schizophrenia spectrum psychotic disorders; brain electrical activity diffuse organic alterations with diencephalic-limbic-reticular complex dysfunction; ageing process atypia; chronic thyroiditis incidence elevation where autoimmune processes role can not be excluded; oxidation homeostasis alterations; lymphocytosis incidence elevation; pronounced qualitative and quantitative hemopoiesis alterations; oxidation/reduction potential intensity and specific immunity decrease; *radiation impact specific cytogenetic markers* elevation [Nyagy A.I. et al., 1995, 1996, 2001].

Integral individual radiation doses reconstruction with 1986 year period dose contribution taking into account was conducted in 200 «self-settlers» in various settlements of exclusion zone (GP «RADEK»: U.P .Ivanov, A.K. Suhoruchkin, V.I. Marchenko). Clinical pattern, cytogenetic study results both with dosimetry data enabled us to suppose the *CRS clinical stage* forming in examined persons resident in villages Novije Shepelichi (2 persons, effective dose — 2.07 Sv), Lubyanka (average effective dose — 0.53±0.19 Sv), Chernobyl city (0.5±0.16 Sv) and *CRS pre-clinical stage* — in examined residents of villages Opachichi (0.26±0.07 Sv), Kupovatoje (0.16±0.05 Sv), Rudnya-Ilyinetskaja (0.14±0.02), Paryshev (0.13±0.02 Sv). According to these dosimetry estimations the internal irradiation was the main contributor to the integral dose.

Other *dosimetry estimates* are available regarding the exclusion zone population. So according to the data of M.N. Savkin (1993) the year effective doses for people resident in 30-km zone were less than 5 mSv·year^{-1} in 1989–1991 period. At that the estimate is not taking account of dose received in 1986.

V.S. Repin (1996) conducted the external and internal irradiation doses retrospective reconstruction in the 30-km exclusion zone evacuees. *External γ-irradiation* doses according to the author's data were within range 2–660 mGy, at that median of Pripyat city residents doses was 12 mSv and that of other settlements of 30-km zone — 14 mSv. Doses exceeding 250 mSv were received by 0.1% (approximately 100 persons) and over 500 mSv — 0.03% (about 10 ones) of the exclusion zone population. Theoretical possibility for the 30-km zone residents to receive the irradiation dose on the value of *ARS genesis* was found being $7 \cdot 10^{-5}$. According to the data of V.S. Repin (1996) the radiation risk main quota for the 30-km zone adult population is connected to external γ-irradiation whereas radionuclides inhalation uptake allotment not exceeds 11%, other radiation factors — 0.6–4%.

I.P. Los in National Report of the Ukraine (1996) presented the following dosimetry estimate of exclusion zone «self-settlers» according to the *direct measurements results*. External irradiation doses with thermo-luminescent dosimetry data in 1989 constituted from 1.4 (Razjezjeje village) to 14 mSv·year^{-1} (Lubyanka village). Internal exposure doses (through radioactive cesium body content assay results) were from 0.5 (Ostashev village) up to 3.9 mSv·year^{-1} (Gorodische village). At that the *integral radiation doses* are marked for the stated territories residents being within dose range peculiar for other contaminated territories population.

More that 10-years-long monitoring of the ChNPP accident consequences cleaning-up participants (liquidators) health state enables to conclude that somatic-neurological and neuropsychiatric disorders in liquidators (especially of 1986–1987 period) are practically identical to the CRS clinical pattern described above. Liquidators doses are within very wide range with upper limit of 1–3 Sv [Chumak V.V. et al., 1995]. Somati-neurological and neuropsychiatric disorders in liquidators, that since 1986–1987 for 3–5 years worked or continue working on exclusion zone various units, are to the most extent corresponding to CRS diagnostic criteria [Guskova A.K. et al., 1964; Letavet A.A. et al., 1964]. Liquidators health state characteristic alterations risen as the emergency repair works result under 0.5–1.0 Gy and over external irradiation short-term dose accumulation with further exposure to low doses and/or radioactive materials incorporation conditions are obviously to be considered as the *radiation sickness progress subacute form*.

Health state integral estimation in people exposed to chronic irradiation enabled to identify the *dysadaptation state* forming threshold dose — TD_{50}=120 mSv [Plachinda U.I., 1994–1996]. Received results entirely correspond to the data of A.K. Guskova & G.D. Bajsogolov (1971) regarding the some effects revealed in 0.1–1 Sv exposure doses are characterised as the *radiation sickness appropriate forms pre-clinical stages*. Characteristic somatic-neurological and neuropsychiatric manifestations both with *radiation sickness pre-clinical forms* classification in persons exposed to ionising radiation impact within stated dose range enables to optimise the diagnostic and curative-prophylactic aid to survivors.