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Chapter 4. BRAIN IRRADIATION IN PRENATAL PERIOD

4.1. Introduction

In 1920–1940 the prenatal irradiation ability to result in heavy mental disorders was revealed. The first radioneuroembryological studies concerned the pregnant women receiving radiotherapy for myoma or cancer of uterus. *Among effects of the prenatal irradiation* the severest forms of central nervous system radiation damage were described such as microcephaly, microphthalmia, hydrocephaly and mental defects [Zappert J., 1926; Robinson M.R., 1927; Goldstein L., Murphy D.P., 1929a, 1929b; Shall L., 1933; Stocckel W., 1933; Murphy D.P. et al., 1942]. In further years the fact of brain malformations elevation (i.e. anencephaly, hydrocephaly, microcephaly) under prenatal radiation exposure after roentgen-diagnostic procedures was also confirmed [Grantoth G., 1979].

In radiation biology the mitotic active cells are considered axiomatic as more subject to injuring action of ionising radiation than more differentiated ones, that are not dividing or dividing seldom. Whereas the radiosensitivity of mature nervous system is a subject of sharp discussion during already almost the century, the high sensitivity of developing nervous system to ionising radiation impact is of no doubt [Bergonie J., Tribondeau L., 1906, 1959; Mole R.H., 1986; Michel C., 1989; Davidov B.I., Ushakov I.B., 1987; Holahan E.H. Jr., 1987; Davidov B.I. et al., 1991; Moskalyov Yu.I., 1991].

Brain damage *in utero* as a result of irradiation is attributed to the so-called *embryotoxic effects* of ionising radiation. These effects — *the development malformations* — take an intermediate place between somatic and genetic radiation damages [Bazhenov V.A. et al., 1990]. *Teratogenic radiation effects* (congenital abnormalities) to which brain damage *in utero* is attributed frequently is the wider concept itself, as assumes the abnormalities and malformations formed as a result of embryo development process alterations due to both irradiation *in utero* and genetic impact of ionising radiation. It is unavailable to agree with the statement of D. Gofman (1994) that consequences of irradiation *in utero* are presented completely with non-stochastic effect of ionising radiation: it is known that irradiation *in utero* with diagnostic purposes increases frequency of brain tumors for 30% [Moskalev Yu.I., 1991]. Therefore, in case of prenatal irradiation the *stochastic (probabilistic) effects* (cancer-genesis and probably genetic effects) are observed both with *non-stochastic (deterministic) consequences* (mental retardation, microcephaly etc.).

During the period of prenatal development the neurones of human brain are formed with speed of more than 250,000 ones per minute. That allows to conclude that nervous tissue is the critical one regarding the irradiation in period of prenatal development. The eight consecutive stages are distinguished in brain genesis:

1) induction of a nervous plate,
2) local division of the cells in different zones,
3) migration of cells from zone in which they have arisen to places of final location,
4) cells aggregation resulting in brain identified zones forming,
5) immature neurones differentiation,
6) formation of connections between neurones,
7) selective death of some cells and
8) elimination of some earlier generated connections and stabilisation of the other ones.

The strong determinancy of the neuroblasts mitotic activity termination terms is fixed, at that these periods are considered as the most critical in life of all the neurons [Dobbing J. & Sands J., 1973; Rakic P., 1975, 1978; Cowen O., 1984; Edelman G.M., 1985].

First 8 weeks of prenatal development correspond to embryonic period or stage of organogenesis. The fetal period proceeds from the 8th week till birth. Japanese and American neuroembryologists follow the 4-stages scheme of the nervous system prenatal development dividing in periods. The 1st stage (0–7 weeks after fertilisation) corresponds to the neurones and neuroglia predecessors formation and also to their mitotic activity. In the 2nd period (8–15 weeks) the increase of neurones number, migration of them to constant places and loss of mitotic activity take place. On the 3rd stage (16–25 weeks) the cellular differentiation undergoes intensification, synapse genesis (beginning on the 8th week) increases and cytoarchitecture of brain is outlined. In the 4th period (26 weeks and more) the continuation and amplification of cellular differentiation both with formation of cytoarchitecture and synapse genesis takes place [Mole R.H., 1982, 1986; Shull W,. Otake M., 1986, 1991; Michel C., 1989; Otake M., 1994].

During the 8–15th weeks after fertilisation — the most critical period of cerebral cortex formation — the developing brain is of maximum radiosensitivity. Some researchers are inclined to opinion that the radiosensitive phase of the developing human brain is corresponded to the 10th week of pregnancy when the neuroblasts number exponential increase takes place. According to the remark of B.I Davidov & I.B. Ushakov (1987) applying the neuroblasts proliferation activity as a criterion of radiosensitivity, it must be recognised that developing cerebellum is to be the most radiosensitive at the last 3-months period of pregnancy when «small» neuroblasts of cerebellum cortex are under the quick fission.

J. Dobbing & J. Sands (1973) and P. Rakic (1975, 1978) presented data indicating that proliferation of neurons practically terminates by 16th week after fertilisation. The two peaks of nervous cells migration from

proliferation zones are known in cerebral cortex prenatal development: the first one occurs on 7–10th weeks, and the second one — on the 13–15th weeks after fertilisation [Winick M., 1976; Rozovski S.J., Winick M., 1979].

The non-differentiated nervous cells migration process from periventricular zones, where proliferation of cortical neurones takes place, to loci of their final arrangement is an active temporal phenomenon which is mainly defined by cells surfaces interaction. Any damages of cellular membranes (even transient ones) can alter the time of migration. Although, according to the opinion of M. Otake et al. (1989), there are no yet direct indications about the ionising radiation low doses impact on neuronal membranes or radial neuroglia cells serving as the migrating neurones directing mechanism, the very low doses of ionising radiation, within the 0.01 Gy limits, can and practically cause changes in cellular thymidine-kinase and plasmatic membrane of the migrating haemopoietic stem cells [Feinendegen et al., 1982,1984]. In spite of mentioned effects transient nature (as lasting 10-14 hours), in such punctual process which the neuronal migration is, any delay can be resulted in future dysfunction because of the neurones occupation infringements of their natural functional places. Besides that, under the chemical damage of developing brain in rodents the quantitative changes are observed in protein participating in «recognising» of radial neuroglia cells and neuroglia fibrillar acido-protein [Brock T.O. & O'Callaghan J.P., 1987], that obviously can also occur under the radiation damage.

Although there are some differences in terms and duration of specific processes of brain prenatal development, the cerebral cortical histogenesis in human is similar in a whole with that in other mammals concerning their morphological characteristics and stages of development. As M. Otake et al. (1989) mark, the terms of the highest radiosensitivity comparability represent the significant histological interest with the human cerebral cortex neuroembryological infringements revealed at those terms. That was found out by epidemiological researches of the people irradiated in prenatal period as a result of the nuclear bombings and by experimental finds of irradiated rodents [Kameyama Y. Et al., 1978, 1985-1989; Hoshino K., Kameyama Y., 1988].

Experimental research results indicate that embryo cells within the early development stage are the most vulnerable and sensitive to irradiation among the all cells in mammalians. On the other hand the *nervous tissue* is the most radiosensitive one from all embryo cells. Thus the mica embryo exposure to 0.05 Gy half-a-day after conception induced morphological and cytological alterations in nervous tissue. Rugh R. (1962) concluded the availability of the central nervous system anomalies rise after irradiation in low doses within nearest terms after the conception.

S.J. Kaplan (1962) after rat prenatal irradiation with doses of 0.1–2.0 Gy observed the behaviour disorders and brain organic pathology signs.

D.M. Schlesinger & R.L. Brendt (1978) revealed that radiation exposure in pre-implantation period leads to the high incidence of zygote death but the survived cells are of normal morphology and growth potential.

B. MacMahon (1985) demonstrated that irradiation *in utero* with diagnostic purposes elevated the *brain tumors* incidence for 30%.

C. Michel & H. Fritz–Niggli (1986) revealed the eye and brain anomalies incidence elevation ($p<0.05$) compared to control in posterity of 8-day pregnant mice after exposure to roentgen radiation with 0.125–0.25 Gy doses. However irradiation to the doses exceeding 0.5 Gy resulted in no any further elevation of eye and brain malformations incidence.

R.P. Jensh et al. (1995) studied the *histological and neurophysiological postnatal effects* of rats roentgen irradiation with 2.0 Gy dose on the gestation 17th day. Following radiation effects were registered in prenetally irradiated posterity in mature age: growth retardation, brain morphological alterations as microcephaly, cerebellum cortex cells pathological changes, hippocampus cytoarchitecture injuries, reflexes formation deterioration, hyperactivity. Authors concluded that prenatal irradiation induce *behaviour and morphological alterations* that are remained during the whole life.

Structural and functional defect of brain in case of intrauterinal irradiation can be both the result of the of ionising radiation direct action on neuroblasts and the consequence of cellular genes function disorders that is necessary for normal brain function. A.E. Borovitskaya et al. (1989) performed the rats irradiation in doses 0.5 Gy on 18th day of prenatal development to elucidate the nervous cells opportunity of maintenance of structural genes normal expression level in postnatal period. The authors revealed that cells of the prenatally irradiated brain are not capable to support the high level genes expression for a long time and, thus, to compensate the developing structural and functional disturbances.

It is considered to be proved that irradiation in doses over 0.5 Gy represents the significant risk for developing nervous system and the ionising radiation impact on child in high doses (4–5 Gy) during neonatal period can lead to mental retardation. The risk of anatomic abnormalities (hydrocephaly, anencephaly, encephalocele and spina bifida) is high in case of irradiation within doses 0.5–1.5 Gy in pregnancy 18–30th days period. Up to 30–50th days of gestation the anatomic malformation risk is somewhat reduced. However, from 60th to 130th days the embryo again becomes sensitive to irradiation, with microcephaly and mental retardation rise risk [Dekaban A.S., 1968; Mole R.H., 1982].

In opinion of a number of researchers, all the periods of pregnancy can present pathologic effects owing to irradiation in utero. Although these effects are various, R.L. Brent et al. (1986) concluded, that there is no any period of pregnancy, in which embryo not suffers from radiation in doses over 0.5 Gy. Threshold dose is about 0.2 Gy. All the radiation embryological effects in opinion of these authors are multi-cellular and probably *non-stochastic*. Proceeding from the available experimental and clinical data, maximum permissible irradiation dose for women of reproductive age is considered 0.005 $Gy \cdot year^{-1}$ and irradiation from X-ray-diagnostic procedures only up to 0.05 Gy enable not to interrupt the pregnancy [Brent R.L. et al., 1986; Kriegel H. et al., 1986].

At the same time the points of view are present concerning the human developing nervous system radiosensitivity doubtfulness especially within so-called low radiation doses range. In particular M.B. Meyer, J.A. Tonascia, T. Merz (1976) revealed no any cases of severe mental retardation in study of the 1,455 children received low radiation doses after diagnostic procedures applied to their mothers pelvis region. K. Neumeister (1976) also revealed no severe mental retardation in 19 children irradiated in prenatal period with 0.015–0.1 Gy doses. Later K. Neumeister & S. Wasser (1988) after the 221 child study in remote period (20 years) after prenatal irradiation due to roentgen-diagnostic procedures conduction concluded that radiation exposure *in utero* with doses less than 0.1 Gy *nor requires* pregnancy termination.

M.M. Kosenko et al. (1992) registered no both fertility and birth-rate decrease among population exposed to irradiation after radioactive wastes release into Techa river (Southern Ural) with average dose on gonads of 0.16 Sv. In International Symposium «Chronic Radiation Impact: Delayed Effects Risk» (Chelyabinsk, January, 9–13, 1995) Proceedings L.A. Budlakoff (1966) presented the data report by S.A. Shalaginoff concerning no revelation of antenatal irradiation direct connection to the *oligophrenia* incidence; the last one according to the author's data depended upon the population ethnic origin and lifestyle. Among the descendants irradiated prenatally the mental retardation frequency not exceeded the control values.

Both with that the data are available concerning even the elevated natural radiation background pathogenic impact; data are based upon the 70,000 China residents health state study where the chromosome aberrations incidence elevation was revealed [Tao Z., Wei L., 1986]. However D. Chen & S.A. Mednic (1990) revealed no intellectual progress disorders and even fixed verbal intellect more high values compared to control in children examination 10–11 years old among China regions with high natural radiation background levels.

At the same time N. Butorina & E. Malinina (1995,1996) after the 219 children study within age of 6–8 years having problems in school progress and resident on radioactively contaminated territories of Ural revealed the mental health significant disorders. Authors concluded that chronic irradiation in both prenatal period and all the postnatal life may lead to the *cerebral asthenic symptom complex* the most completely corresponding to the *organic psychosyndrome* (F07.8). In case of the non-specific EEG-deviations the cerebroasthenia was combined with the *school problems* (F81.3), *hyperkinetic* (F90.0 & 90.1), *emotional and somatoformal* (F45.1) *disorders*. The EEG paroxysmal type was correspondent to the *epileptiformal syndrome*. The further survey revealed the border-line disorders polymorphism, their specific peculiarities and paroxysmal character that enabled authors to suppose the development of *border-line type of epilepsy*.

Mental retardation risk as a result of foetal irradiation, especially during the 8–15th weeks of pregnancy, can exceed the traditionally regarded risks of cancerogenesis and genetic consequences: from the dose of 0.01 Gy on foetus the 200 cases of mental retardation per 10^5 persons are induced that is 0.2% [Hoel D.G., 1987]. According to the data of R.D. Saunders (1989) and O. Vos (1989) the risk of oligophrenia is estimated as 43–48% per 1 Gy or 0.4–0.5% per 0.01 Gy under the radiation exposure during the 8–15th weeks of pregnancy.

Epidemiological study by Y. Rodvall et al. (1989) on twins cohort in Sweden whose mothers were exposed to the X-ray examinations during pregnancy demonstrated that *central nervous system tumours* genesis risk in these children in 1.5 (for leukaemia — 1.7). Received data in authors opinion testify that foetus may be subjected to *cancerogenesis risk* in it is roentgenological examination. At that nervous system tumours genesis risk is one of the most high among all the oncology diseases group.

G. Coscia & A. Pilot (1994) consider that risks related to routine diagnostic procedures in pregnancy not exceed the permissible values, whereas such method as CT scan can be more dangerous. In any case the authors underline that unwarranted irradiation in pregnancy is to be avoided.

According to *«International Basic Safety Standards for Protection from Ionising Radiation and Safety of Sources of Radiation»* [Gonzalez A., 1995] the consequences of embryo irradiation appear after irradiation at any stage of the embryo development and include the posterity death, malformations, mental retardation and cancerogenesis. The intellectual abilities (IQ) decrease is revealed after the acute irradiation in higher doses, mainly during the 8–15th weeks after conception. For low doses of irradiation these potential consequences for embryo are not found among new-borns.

The risks of embryo irradiation effects in period from 8th till 15th week after conception are:

- IQ decrease by 30 numbers per 1 Sv;
- dose required for the IQ decrease from normal level to that of severe mental retardation is 1 Sv and over;
- dose required for the IQ decreasing from mild level to that of severe mental retardation is several hundred of mSv [Gonzalez A., 1995].

In our belief in prenatal irradiation cerebral effects interpretation the opinion should be considered of the experts in this field — Masanori Otake & William J. Schull who have devoted all their life to research of radioneuroembryological effects in nuclear bombings survivors: «...*Till now, however, neither experimental nor epidemiological data have not given the sufficient basis for the confirmation of existence or absence of a threshold in dependence «dose—effect» that represents a subject of extreme importance from the point of view of the radiologic protection ...»*

4.2. Prenatal Irradiation Consequences in Hiroshima and Nagasaki Atomic Bombing Victims

Study of consequences of prenatal irradiation of a brain as a result of A-bombing in Hiroshima and Nagasaki began in 1948 when the children were 2 years old and proceeds till now. To the persons irradiated *in utero* the children born between the 6th (for Hiroshima) or 9th (for Nagasaki) of August 1945 till May 31, 1946 were referred. The *gestation age (Y)* in opinion of the Japanese colleagues is the most important factor in the determination of ionising radiation damaging action character:

Gestation age (Y) = [280 — (date of birth — 6 or 9.08.1945)] (1)

In the majority of cases (83%) the gestation age was determined on the basis of an estimation of number of days of pregnancy on a moment of nuclear bombings from mothers words during interview with taking into account the date of child birth. In the other cases the gestation age was calculated on the basis of registered birth date in so-called *koseki*-records. The gestation weeks (G) after ovulation (conception) were calculated by the formula:

Gestation weeks G = (Y — 14 days) / 7 days (2)

at that G was accepted for a zero in a case $G < 0$.

The initial quantitative estimations of influence of ionising radiation as a result of atomic bombing in Hiroshima and Nagasaki were based on the distance from hypocentre of explosion where an exposed person was placed. Till now in Japanese and American literature the terms *«proxymally»* and *«distantly»* irradiated are remained, where under first one as a rule persons been on distance up to 2,000 ì from hypocentre, and under second as a rule — on distance exceeding 2,000 m are understood.

The Japanese and American researches of intrauterinal irradiation consequences of brain are mainly limited by study of severe intellectual retardation, IQ, school progress, attacks, micricephaly, growth and development.

All the cases of *severe mental retardation* were diagnosed clinically among prenatally irradiated children up to 17th years of age. The Japanese and American colleagues guided the following diagnostic criteria of severe mental retardation:

1. Inability to carry out simple calculations;
2. Inability to support simple conversation;
3. Inability to self-service or complete uncontrolness;
4. Stay in specialised medical and/or educational institutions.

The *intelligence tests* were showed (presented) in 1955–1956 among clinical institutions of Hiroshima and Nagasaki, when the prenatally irradiated children were in the age of 10–11 years. The improved version of the test Koga, test Tanaka B, Japanese version of the test Stanford—Binet were applied.

The *school progress* was estimated on the basis of school marks study in children from 1st to 4th forms in 44 primary Hiroshima schools in 1956, when the children were 10–11 years old.

Term *«attacks»* used by the Japanese and American researchers to prevent mess included all cases of attacks, epilepsy and spasms.

Microcephaly was diagnosed in case of head circumference appeared less than $M—2\sigma$ in researches among A-bombings prenatally irradiated survivors 9–19th years of age.

Dosymetric providing was based upon a trial estimation of doses on models, presented in scientific reports T65DR, 1965 and DS86, 1965.

The studies held by the Atomic Bombing Casualty Commission (ABCC) in Hiroshima and Nagasaki during 50–60th indicated the *mental retardation* prevalence increase in persons irradiated prenatally in places close enough to A-bombing hypocentres. The group of 169 children from Hiroshima was examined in 1954 as the group of all the kids irradiated prenatally and born in pregnant women been not far than 2,200 meters from hypocentre. The extraordinary high concentration of *oligophrenia (and microcephalia*) was marked in children with gestational age of 7–15 weeks at the time of A-bombings and distance up to 1,200 meters from hypocentre [Plummer G., 1952; Yamazaki J.N. et al. 1954; Miller R.W., Mulvihill J.H., 1956; Yokota S. et al., 1963].

R.W. Miller (1956, 1965) pointed out to the *intrauterinal irradiation* as the only reason of mental retardation and microcephaly in atomic bombing survivors. Among 169 children irradiated *in utero* in Hiroshima the 33 cases of microcephaly were present (head dimensions less than $M—2\sigma$) with mental retardation in 15 cases and mentally healthy in 18 ones respectively. The 13 cases of pronounced microcephaly were registered too (head dimensions less than $M—3\sigma$) all of whom were irradiated in early terms of pregnancy between 7th and 15th weeks (8 cases within distance less than 1,200 meters from hypocentre, 4 ones — within 1,201 to 1,500 meters and 1 case — within 1,501 to 2,000 meters respectively). and the only 4 children from described above ones with pronounced microcephaly were mentally healthy. Among the disorders accompanying microcephaly in Hiroshima R.W. Miller (1956, 1965) mentioned the substantial growth retardation, 2 cases of mongolism, 2 cases of hip joint dislocation, 3 cases of strabismus and 1 fatal case of primary liver carcinoma in proximally children irradiated in utero. Both with microcephalia the 5th finger medium phalanx shortening, congenital agenesia of several phalanxes, congenital nanism, hepatitis, pyelonephritis, lipidosis, brain psammoma, myopia, sacral meningocele, hypospadias.

G.N. Burrow, H.B. Hamilton & Z. Hrubec (1964, 1965) examined the children irradiated prenatally within age of 13–14 years old in Nagasaki and reported the *mental retardation and congenital malformations* increase in boys exposed to radiation within 1.999 meters from hypocentre. These authors marked also the average head

circumference minimal values among group born in mothers with the highest absorbed ionising radiation doses, exceeding 0.5 Gy, who were irradiated within 1,500 meters from hypocentre and presented the symptoms of Acute Radiation Syndrome. Besides that the acuity of vision decrease, growth and physical development retardation signs were present in girls irradiated during pregnancy first trimester in mothers with symptoms of the Acute radiation syndrome. But no leukaemia or malignancy rises were registered. According to the some authors opinion, as per study results of the arterial pulse, blood pressure and urological examination no signs of ionising radiation impact were present.

S. Kawamoto (1966) presented data that among 102 children irradiated *in utero* in Nagasaki within 1,999 meters from hypocentre the *microcephaly* (less than M—2σ; boys — less than 52.0 cm, girls — less than 50.0 cm) was revealed in 7 (6,9%) cases and among the 173 prenatally irradiated within 2.000 to 2.999 meters from hypocentre — only the 5 (2.9%) ones suffered the microcephaly (3 persons with mental retardation). As one of the probable reasons of microcephaly cases higher number among survivors irradiated *in utero* within 2.000 meters from hypocentre in Nagasaki compared to that in Hiroshima, the author presupposed the A-bombing γ-irradiation higher intensity both with absorbed irradiation doses higher values within same distances in Nagasaki than that in Hiroshima. In author's opinion the foetal, neonatal and infantile mortality could be very high among proximally irradiated, that was going with relatively low level of microcephaly (compared to that in Hiroshima), whereas the microcephaly incidence elevated in children irradiated within 2,500 meters distance from hypocentre. S. Kawamoto (1966) also reported about some cases of microcephaly combination with mental disorders, strabismus, myopia, nystagmus, chronic gastroenteritis, possible Recklinhgausen's disease, medium otitis and tonsils hypertrophy.

S. Kawamoto, T. Fujino, H. Fujisawa (1965) examined in 1961 the 218 kids irradiated prenatally in Nagasaki regarding *ophthalmologic pathology*. They reported about the numerous cases of small heterochromous spots or pigmentary nevi on the iris and pupil membrane, lens turbidity. The attention was focused on lens subcapsular turbidity higher registration in prenatally irradiated children within distance of 1,400 meters from A-bombing hypocentre.

J.W. Wood, K.G. Johnson, Y. Omori (1967a, 1967b, 1967c) examined in dynamics from since 1954 the 183 irradiated *in utero* Hiroshima kids. In the 33 cases the *microcephaly* (less than M—2σ) was present and in 14 persons — the pronounced microcephaly (less than M—3σ). Among the 15 cases of *microcephaly and oligophrenia* combination the 10 cases of pronounced microcephaly, 13 cases of exposure to radiation within 1,500 meters from hypocentre, 11 cases of irradiation on 7—15 gestation weeks, 2 cases of premature birth and 2 cases of mongolism were marked. The average age of mothers during microcephalic children birth was 28.7 years, while that for microcephaly without mental retardation consisted 27.0 years and for 15 cases of microcephaly with mental retardation — 30.8 years respectively. Among 10 cases with pronounced microcephaly (less than M—2σ) with oligophrenia at least the 9 ones were with growth retardation (less than M—2σ). Besides that in these 15 cases of microcephaly and oligophrenia combination the strabismus was revealed in 4 cases, severe myopia with microcornea — in 1 case, hip joint congenital dislocation — in 1 case. Among these 15 children the 4 ones died from the following reasons: drowning (signs of mongolism were present), acute poliomyelitis, tubercular peritonitis and primary hepatocarcinoma. At the same time among the 18 children with microcephaly without mental retardation the 2 ceases of renal pathology were revealed, 3 cases of myopia, hepatitis, cobblers (funnel-shaped) chest, hip joint congenital dislocation, congenital agenesis of several phalanges on the right hand. Besides that under the 150 children examination with no microcephaly signs the hemiparesis due to the cerebral psammoma, juvenile cirrhosis (hepatosplenomegaly with leucocytosis), hypospadias, congenital glaucoma, congenital syphilis (3 cases), liver tuberculosis and nephritis were revealed. From these 150 children the 3 ones died because of fever and convulsions, meningocele and pyelonephritis, and because of suicides. J.W. Wood et al. concluded that children with microcephaly but without mental retardation have no high prevalence of non-infective diseases or growth and development retardation, whereas the children with microcephaly and oligophrenia are characteristic with growth & development substantial retardation, higher diseases and deaths incidence.

Professor Tabuchi et al. (1967) from the Hiroshima University in 1963–1966 conducted the dynamical survey of children irradiated prenatally in Hiroshima. Among the 545 children irradiated prenatally within 3.000 meters from hypocentre the *microcephalia* was revealed in 45 (8.3%) of them with pronounced degree (more than M–3σ) in 12 (2.2%) cases respectively, that was confidentially more frequent than in 13 (2.7%) cases of microcephaly among the 473 of non-irradiated children (control). Among the 152 children irradiated *in utero* during first three months of pregnancy there were 26 (17.1%) cases of microcephaly and 10 (6.6%) of pronounced one, whereas among 211 children irradiated during the 4–7th months of pregnancy the microcephaly was fixed in 15 (7.1%) of children, and the severe microcephaly — in 2 (0.9%) respectively. Among the 12 proximally irradiated (range less than 999 meters) *in utero* children the 6 ones (50%) presented microcephaly of pronounced degree in all the cases, among the 108 children irradiated within 1,000–1,499 meters from hypocerntre the 24 (22.2%) persons had microcephaly with pronounced degree in 6 (5.6%) of cases. The authors concluded that microcephaly frequency is the most high in children irradiated prenatally in early pregnancy terms. Further up to the end of year 1965 the 44 patients with microcephaly were confirmed in diagnosis and remained alive. The microcephaly was complicated with *degeneration signs* on face and head, skin pigmentation marked disorders, extremities degenerative alterations including brachydactilia, hematologic diseases both with *epileptiformal convulsions* rise high risk.

R.J. Connor, S. Kawamoto, Y. Omori (1971) examined the 1,608 children irradiated *in utero* in Hiroshima and Nagasaki. In those children whose mothers were exposed to irradiation doses exceeding 1.0 Gy, the *head dimensions*

and height at the age of 10–17 years old were lower than norm. The authors revealed no any differences in development and growth rate between all the children irradiated *in utero* within 2,000 meters from hypocentre. Head dimensions decrease as the radiation effect was the leading one among the irradiated during first gestational trimester.

W. Blott & R.W. Miller (1972) examined the cohort of 1,613 persons irradiated *in utero* in Hiroshima and Nagasaki A-bombing. Authors searched for correlation between *mental retardation* prevalence at the age of 17 years old and the mother *absorbed radiation doses*. The oligophrenia prevalence value confidential elevation was registered under doses exceeding 0.5 Gy in Hiroshima and 2.0 Gy in Nagasaki, with the mental retardation risk growing proportional to the radiation absorbed dose. From the authors' point of view the lower dose threshold for oligophrenia in Hiroshima compared to that in Nagasaki is explained with the neutrons contribution in doses forming that in its turn actually was absent in Nagasaki.

So the study in 50–70th of prenatal irradiation consequences after Hiroshima and Nagasaki A-bombing revealed in several cases the *microcephaly, oligophrenia, physical development retardation, dysembryogenic stigmas*. But the casual nature of the studied cohorts and the dosimetry supplementation insufficiency required the re-evaluation of the early surveys results of A-bombings survivors irradiated in utero. As the result of absorbed doses revision the neutrons dose contribution (with one of the highest relative biologic effectiveness) was determined as the substantially higher one in Hiroshima than in Nagasaki.

The further studies of the prenatal brain irradiation consequences are held in RERF, Hiroshima under the supervision of *W.J. Shull & M. Otake*. For many years the Atomic Bombing Casualty Commission (ABCC) and than its successor — RERF composed the several crossing each other models of the intrauterinal irradiation consequences after Hiroshima and Nagasaki A-bombings.

First one was the initiated in 1959 study of the *severe mental retardation* as the Hiroshima and Nagasaki prenatal irradiation consequences clinical example. According to the DS86 dosimetry estimation the prenatal brain irradiation clinical cases constitute 1,544 persons (96.6%) from the 1,598 clinical cases (including 509 non-irradiated ones) with available irradiation dose values according to preliminary estimation T65DR. All the 30 cases (including 5 ones among the non-irradiated persons) of the diagnosed severe mental retardation are included there [Otake M. et al., 1987]. The thirty cases of oligophrenia were diagnosed within age of 17 years in ABCC clinical divisions on the only clinical impressions background without the intellectual test application.

The second study model applied the *IQ psychometric evaluation*. The works were initiated in 1953 in Hiroshima and in 1955 — in Nagasaki. The prenatally irradiated persons identification was based upon the births registration and pregnancy case histories also applied in ABCC genetic project in 1948–1954. The Intellectual Quotient (IQ) was evaluated in Hiroshima and Nagasaki clinical institutions with Koga, Tanaka B Tests application both with Stanford—Binnet Test (Japanese version). Initially the research subject constituted 1,768 cases. Further reduction to 1,673 (595 of them were non-irradiated ones) was made, including 9 cases with uncertain irradiation dose values and 86 of them without intellectual testing because of refuses, illnesses and outer migration before the psychometric studies launch. The eight kids from this cohort within age 10–11 years old suffered the severe mental retardation; six of them were among the 470 children irradiated prenatally with absorbed doses values of 0.01 Gy and over; two of them were among the 595 non-irradiated children. The IQ in all eight cases constituted 56–64 points. No one case of severe mental retardation was revealed among the 608 children present in both cities at the time of A-bombings but irradiated with doses less than 0.01 Gy. The DS86 dosimetric estimation was held among 1,202 (71.8%) of the prenatally irradiated hibakusha from those 1,673 persons with present IQ estimations and irradiation doses values determination results according to T65DR, including 8 cases of severe mental retardation [Schull W.J. et al., 1991].

The third study model was bases upon the *school progress* estimation results among pupils of 1–4 years of education in the 44 Hiroshima primary schools. The described data were collected in August—September 1956 [Otake M. et al., 1988]. Similarly as in the IQ estimations the children were within age of 10–11 years and majority of them graduated the 4th form. The school files included the attendance estimations, progress with the seven subjects (language, civil law basis, arithmetic, natural sciences, music, drawing and gymnastics), general behaviour and health status. The marks were put within the 5-rank system: «+2» (excellent, over 5%), «+1» (a bit over the average level, percentille 94–75), «0» (average, percentille 74–25), «–1» (a bit worse than average level, percentille 24–5) and «–2» (poor, less than 5%). Those teachers estimations were converted into the ordinary 5-rank system — «5», «4», «3», «2» and «1» respectively. This study model included the 1,090 from 1,126 pupils of primary schools in Hiroshima. Pupils with non-estimated dose values, not irradiated *in utero* and refusing to co-operate were not included. The fourteen children from this model were diagnosed as the severely mentally retarded ones. On the background of DS86 dosimetric estimation the school progress model constituted 929 (85.2%) of cases from 1,090 persons with revealed irradiation doses via T65DR, including 14 cases of severe mental retardation. No school progress data were collected in Nagasaki.

The last one, fourth model — *the attacks study* — included the 2,083 non-irradiated and exposed to radiation *in utero* children. The children were first examined in 1948 and than surveyed in dynamics up to 1964. The attacks here included all the clinical appointments to the fits properly, epilepsy or convulsions. To avoid misunderstanding the unified term «attacks» was applied. On the dosimetric estimation DS86 background the paroxysms study model included 1,183 (56.8%) cases from 2,083 persons with estimated irradiation dose values via T65DR, including 22 cases of severe mental retardation [Dunn K. et al., 1990]. The majority (98%) of those 900 persons with no data via DS86 had the defined doses via T65DR with values less than 0.1 Gy, i.e. corresponding to the low doses within

DS86. Consequently according to the opinion of M. Otake et al. (1989) the assumption is available that those studied persons exclusion could make no substantial impact on the obtained dependence «dose—effect».

The irradiation doses reconstruction with models presented in T65DR and DS86 scientific reports were of substantial difference. According to T65DR the foetal absorbed doses were estimated only basing on the shaded maternal kerma (*kerma — kinetis energy released in material*), increased with averaged correction parameters. In DS86 model the absorbed dose values were calculated individually without averaged correction parameters application, that enabled to estimate the dispersed radiation energy. At present the foetal absorbed doses via DS86 estimation are not determined yet and the Japanese and American authors in recent works use actually the maternal uterine absorbed dose values. The foetal doses are recognised as equivalent to those on uterus. Taking into account that estimated with DS86 dose in the air from neutrons constituted approximately 0.04 Gy within distance 2,000 meters from hypocentre in Hiroshima and was actually equivalent to zero in Nagasaki, the integrated absorbed dose values were applied in prenatal brain irradiation problem research results re-evaluation. The neutron relative biological effectiveness was accepted as equal to 1 [Otake M. et al., 1989].

In DS86 dosimetric estimation application the highest risk of mental development retardation was observed in case of irradiation in terms of 8–15 weeks after conception. Within this critical period the incidence of *mental retardation development is linearly depending on irradiation dose*. No radiation-induced intellectual disorders were revealed in prenatally irradiated at terms less than 8 weeks of gestation.

The lowest values of intellect were revealed in the groups of children irradiated within 8–15 weeks of gestation and to the less extent — within 16–25 weeks. The possibility of unrecognised mental retardation cases was assumed. Among the most sensitive group of children irradiated within 8–15 weeks after conception the Intellectual Quotient (IQ) regression from the irradiation dose is described with *linear–squared model* where 1 Gy is corresponding to IQ decrease for 21–27 points or approximately 0.25 points per 0.01 Gy.

The school progress research in Hiroshima children revealed the substantial decrease for all the subjects in groups irradiated within 8–15 and 16–25 weeks of pregnancy. Remarkably that the major decrease was in the fields of *arithmetic, exact and analytical sciences*, and a bit less pronounced — in social subjects, music, drawing and gymnastics. Some decrease in school progress was revealed also in group irradiated within 0–7 weeks of pregnancy. Both with the described disorders the *neurologic deficiency* manifestations were registered in mode of fits, photofobia, diplopia, other vision disorders and the hearing acuity deterioration.

Attacks are the frequent consequences of brain development disorders. So K. Dunn et al. (1990) conducted the re-evaluation of paroxysms study results in prenatally irradiated children launched already in 1948. In persons irradiated with doses less than 0.1 Gy within 0–7 weeks after conception no paroxysms were registered. The paroxysms incidence was the highest under the irradiation within 8–15 weeks with doses exceeding 0.1 Gy and was of linear dependence on the foetal irradiation dose. No paroxysms incidence increase was registered in persons with more late terms of irradiation during pregnancy.

The *alternative non-traditional explanations* of the revealed psychoneurologic disorders among irradiated A-bombing survivors were assumed: genetic variations, nutrition disorders, bacterial or viral infections during pregnancy, embryonic hypoxia etc. However in spite of that any of the alternative factors can contribute to the psychoneurologic deficiency forming, the fact remains inexplicable: why does the *mentally retarded children number increase with irradiation dose growth.*

The epidemiological data are rather contradictory and the «dose—effect» dependence character estimation is embarrassing especially regarding the determination or refutation of the exact fact of injury threshold existence. Both with that the dosymetric data indicate the *dose threshold* existence within 0.12–0.23 Gy doses towards mental retardation rise after intrauterinal irradiation in terms of 8–15 weeks, and probably 0.23–0.70 Gy — in terms of 16–25 weeks respectively. The presented data were received on the basis of the 1,566 persons (1,242 in Hiroshima and 324 in Nagasaki) irradiated prenatally and survived after the A-bombing survey results revaluation [Schull W., Otake M. 1986, 1991; Yamazaki J., Schull W.J., 1990; Otake M. et al., 1987, 1989, 1991, 1993; Otake M., Schull W. et al., 1988; Schull W., 1993].

W. Schull et al. (1991) conducted the *brain MRI-study* in five persons with mental retardation irradiated within 8–15 weeks after fertilisation. In two children irradiated during 8–9 weeks of gestation the heterotopic large grey parts of brain were registered that according to the authors' opinion presents direct evidence of the *altered neuronal migration* to the final functional places. The two patients irradiated at the terms of 12–13th weeks presented no clear signs of grey heterotopia, but the macrogyria was revealed reflecting the cortical zone development disorders. Besides that the brain ventricles enlargement was marked. In one patient irradiated in term of 15th week of prenatal development in spite of brain lower dimensions its architectonics seemed to be normal. Authors concluded that the revealed brain morphological disorders are the consequences of *neuroembryogenic disorders after brain prenatal irradiation.*

On May 28, 1995 in Kiev on the symposium *"Brain damage in prenatal irradiation"* of the International Conference «Mental Health Consequences of the Chernobyl Disaster: Current State and Future Prospects» Y. Imamura, Y. Nakane, H. Kondo, M. Kishikawa, A. Nikawa, Y. Ohta (Nagasaki University) presented the report «*Lifetime prevalence of schizophrenia of people prenatally exposed to A-bomb radiation in Nagasaki*». The authors marked that now the neuroembryologic alterations role is described in schizophrenia genesis. The prenatal irradiation consequences studies in Hiroshima and Nagasaki indicate the mental retardation and microcephaly growth. At the same time the schizophrenia risk is known being in the three times higher in persons with mental retardation than in the whole population and the suggestions of mental retardation and schizophrenia interconnections are found in clinic. Also the data were received concerning neuroembryologic disorders presence in brain of mentally retarded

persons irradiated within 8–15th weeks of pregnancy after the atomic bombing. Probably the ionising radiation impact in middle period of pregnancy (period of neurones migration) could occur to be the anatomic and functional disorders reason. Thus, the Japanese researchers assumed that *ionising irradiation prenatal impact as the result of atomic bombing increase the risk of schizophrenia.*

The Neuropsychiatric Department of Nagasaki University founded the Register for 4,586 persons resident in Nagasaki among whom the schizophrenia was diagnosed since 1960 according to criteria of International Diseases Classification (9th revision). Among those Y. Imamura et al. selected persons born within August 9, 1945 and May 31, 1946, i.e. who could be irradiated in utero. Such persons occurred to be 80 ones (47 males and 33 females).

At the same time the Centre for Scientific Information of atomic bombing consequences (Nagasaki University) identified the 1,926 persons irradiated prenatally after the atomic bomb explosion in Nagasaki.

Y. Imamura et al. compared names and birth dates of the 80 patients with schizophrenia born within period from August 9, 1945 to May 31, 1946 with Data Base of prenatally irradiated persons in Nagasaki. As the result, in 21 patients with schizophrenia (12 men and 9 women) the prenatal irradiation episode was confirmed. The schizophrenia cases in gender and pregnancy trimesters distributions at the moment of A-bombing is presented in Table 4.1.

Table 1

SCHIZOPHRENIA CASES IN PRENATALLY IRRADIATED PERSONS AFTER NAGASAKI ATOMIC BOMBING
(According to the Data Report by Y. Imamura et al., Kiev, 1995)

	Men			Women			Total		
	Schizo-phrenia cases	*Irra-diated in utero*	*%*	***Schizo-phrenia cases***	*Irra-diated in utero*	*%*	***Schizo-phrenia cases***	*Irra-diated in utero*	*%*
1st trimester 0–13 weeks *(06.02.46–31.05.46)*	6	336	1.8	2	326	0.6	8	662	1.2
2nd trimester 14–27 weeks *(07.11.45–05.02.46*	5	326	1.5	6	336	1.8	11	662	1.7
3rd trimester 28–40 weeks *(09.08.45–06.11.45)*	1	284	0.3	1	318	0.3	2	602	0.3
Total	**12**	**946**	**1.3**	**9**	**980**	**0.9**	**21**	**1926**	**1.1**

Japanese colleagues consider the revealed value of schizophrenia incidence (≈1.1%) actually is the schizophrenia prevalence value among prenatally irradiated survivors in Nagasaki (10.9 per 1,000). They remark here that schizophrenia prevalence in Japan varies from 2.2 to 8.8 per 1,000. Thus authors concluded that the *schizophrenia prevalence in irradiated prenatally Nagasaki population is significantly higher than among population.* The schizophrenia was registered substantially more often in persons irradiated prenatally after the atomic bomb explosion in middle terms of pregnancy than that in later ones. Y. Imamura et al. (1995) concluded that their studies confirmed the hypothesis concerning *some cases of schizophrenia being the result of radiation neuroembryonal disorders.*

The described work is of indubitable interest. Firstly, the official data of RERF (Hiroshima) indicate that after the Hiroshima and Nagasaki A-bombings in 1945, the 2,800 intrauterinal deaths and 1,600 clinical cases were registered. After the revision and verification according to the DS86 only the 1,566 cases of prenatal irradiation were fixed: 1,242 in Hiroshima and 324 — in Nagasaki [Otake M. et al., 1989, 1991, 1993; Dunn K., 1990; Schull W.J. & Otake M., 1991; Otake M. & Schull W.J., 1993]. At the same time Y. Imamura et al. (1995) report about the Register for prenatally irradiated persons after Nagasaki A-bombing. Register content is the 1,940 (1,926 in Report) clinical cases. Consequently the 50 years-long joint Japanese-American studies of prenatal irradiation on brain were fulfilled over only the 16.7% of cohort.

Secondly, Y. Imamura et al. (1995) presented in Report the schizophrenia prevalence values among Nagasaki atomic bombing prenatally irradiated survivors constituting ≈ 1.1%, and in Conference Proceedings — only ≈ 0.7%, that probably reflects the received results preliminary nature. Thus the schizophrenia risk problem (both with other endogenous mental diseases) after the prenatal irradiation is extremely actual. The settled problem significance is confirmed by works substantiating the schizophrenia ethiopathogenesis with neuroembriologic disorders, in particular with influenza viruses effects in prenatal period [Mednick S.A. et al., 1988; Adams W. et al., 1993].

According to summarised results of ionising irradiation remote consequences on human health ABCC/RERF epidemiological studies of I. Shigematsu (1994) and Y. Hasigawa presented on 5th Co-ordinating Meeting of the WHO Co-operating Centres, Paris, December 5–8, 1994, the *strong connection of the ionising irradiation*

impact in survivors irradiated in utero after atomic explosion is fixed towards microcephaly, mental development retardation, low IQ and poor school progress; the *weak connection* — towards the chromosomal aberrations in lymphocytes; *connection absence* — towards the non-cancer mortality. Other neuropsychiatric consequences of intrauterinal irradiation were not presented.

4.3 Neuropsychiatric effects in children exposed in prenatal period after the Chernobyl disaster

In the light of described above the psychoneurological circle study in kids exposed to radiation in prenatal period is of exclusive theoretical and applicable value. Available data regarding this contingent are incomplete and contradictory.

In USSR the permissible thyroid dose in children for the accident period was 300 mGy. The *secret* report to IAEA in August 1986 stated that number of persons with thyroid doses exceeding 300 mGy was more than 150,000. The *secret* letter by L.A. Ilyin from 09.23.86 B-2613 to S.P. Burenkov (USSR Public Health Minister) drew attention to that *radioactive iodine* negative impact can lead to *hypothyroidism in foetus, newborns and children*, and finally — to cretinism [Ilyin L.A., 1994].

At the same period in 1986 E.J. Sternglass assumed that low dose irradiation after Chernobyl disaster can lead to the *stable cognitive deficiency* in kids exposed in prenatal period. However the experts in Report of International Advisory Committee for International Chernobyl Project (IAEA, Vienna, 1992) concluded that outside the 30-km zone doses received by foetus are substantially lower than 0.1 Gy therefore foetal radiation consequences are improbable. IAEA international experts panel concluded there are no enough reasons to suppose hereditary or congenital diseases elevation both with oligophrenia or Dawn's syndrome under ionising radiation prenatal impact. Unfavourable consequences can occur however due to life conditions alteration or nutrition deterioration. Hereditary health detriment from radiation was estimated as 7% per 1 Sv or 70 persons per 10,000 population resident in locations with average radiation doses 0.1 Sv.

Opinions of IAEA international experts were shared both by several native researchers. For some received results the radiation doses received by 136 pregnant women and in 1.5-2 – fold exceeding permissible values made no unfavorable impact on fetus and newborn in early neonatal period [Gerasimovich G.I. et al., 1988].

Opposite results were received [Zakrevskij A.A. et al., 1993] within study of 345 new-borns in 338 pregnant women exposed to ionising radiation impact after Chernobyl accident compared to 100 new-born kids delivered before April 26, 1986. The *multi-foetal pregnancies* 3-fold incidence increase was fixed in exposed women; in every one from two cases newborn asphyxia was found; initial body mass decrease ($p<0.05$) was revealed (3407.0 g vs. 3588.0 g in control), «dysadaptation syndrome» high incidence was surveyed (respiratory disorders, muscular tone lowering, reflexes instability, swelling-haemorrhage syndrome etc.) with platelet and fibrinogen high content and immune globulin content decrease within early neonatal period dynamics. Authors concluded the ionising radiation impact in pregnancy on new-born early neonatal adaptation.

M.V. Fedotova et al. (1992), Moscow province Institute for Obstetrics and Gynecology selected 3 main pathways of low radiation doses possible impact on foetus and new-born:

1. Mother's organism alterations before and within pregnancy
2. Placenta structure and function disorders
3. Direct radiation impact on foetus and new-born

Study of 370 kids exposed in prenatal period after Chernobyl disaster revealed no excess of microcephaly, central nervous system malformations and brain dysgenesia cases in age of 3.5–5 year sold. However *psycholocomotive progress partial retardation* was fixed (14–23%) both with *speech progress terms delay for 0.5–1.5 years*. *Brain bioelectrical activity maturation alterations*, more often with its acceleration (27.4%); *convulsive threshold decrease*, somewhat more often in early cerebrogenesis critical group of children (8–15 weeks) than in group of late cerbro- and corticogenesis (16–24 weeks) — 12.4% and 8.2% respectively (in control groups — 3.5–5.7% respectively) and *myelination processes delay* correlated with fine psychomotor formation retardation were also revealed [Tereschenko N.Ya. et al., 1992]. N.Ya.Tereschenko et al. (1991) revealed the pituitary-thyroid and hypothalamic-pituitary hormonogenesis alterations observed more often than i other age groups.

Staff of Institute for Biophysics (Moscow) A.M. Lyaginskaja, N.Ya. Tereschenko and I.Ya. Vasilenko (1992) noted that *thyroid irradiation* with radioactive iodine isotopes in children sometimes exceeding 1 Gy is the ChNPP accident most dangerous aftermath. Foetal thyroid is extremely radiosensitive. Iodine thyroid uptake is elevated in pregnant women especially within second half of pregnancy period. Radioactive iodine enters foetus through placenta. Transition values depend upon pregnancy terms. First iodine is diffusely distributed through embryo body and since thyroid function onset is selectively accumulated there. Thyroid gland accumulates about 50–60% of all foetal iodine. Foetal thyroid absorbed doses are 2–3-fold over than that in mother. Thyroid radiation damage is the initial link of other endocrine glands involvement in pathological process through the *thyroid-pituitary-hypothalamus* system. Endocrine status disorders in authors opinion can present itself through mental and physical progress alteration in prenatally irradiated children especially in those with thyroid radiation doses 1 Gy and over.

V.I. Dedov, I.I. Dedov and V.F. Stepanenko (1993) reported about novel interesting phenomenon i.e. exogenous iodine accumulation increase in hypophysis for 10 and more times over the other organs without thyroid. Authors concluded that along with thyroid, *the pituitary is also critical organ* in exposure to iodine radioactive isotopes.

Stated fact can be of undoubted role in mental and physical progress alterations forming among kids irradiated in prenatal period.

Authors (A.I. Nyagu et al., 1993) conducted in 1990–1992 the complex analysis of *psychosomatic health* state in 147 kids exposed to radiation in utero from Pripyat city compared to 101 child of the equal age — native residents of Kiev city. Dosimetry supply included individual dose on foetus reconstruction with Monte-Carlo method. Individual doses on thyroid in kids exposed within second and third pregnancy trimesters varied within range 0.1–1.2 Sv, average values of external γ-radiation were 7 mSv and not exceeded 13 mSv. Thyroid function alterations were revealed in prenatally irradiated kids both with immune state disorders, larynx-ear-nose system and gastrointestinal tract diseases, psychoneurological disorders. The last ones were mainly presented with emotion-volitional disorders in asthenic symptoms complex, both with mental progress retardation of various severity degree. The lowest mental progress indices were found in children irradiated within first three months of prenatal period. That enabled us to connect the described findings with prenatal irradiation under other disaster factors possible combined impact.

Signs of *mental progress retardation* were met in 77% of kids from Pripyat city exposed in utero within first pregnancy trimester, in 69% of those exposed in second trimester and in 45% — in third one. Among kids resident in Kiev city the percent of persons with decreased mental development value was substantially lower ($p<0.05$). In 25.5% of cases in Pripyat group the *brain organic pathology* signs were revealed. Brain circulation disorders according to the rheoencephalography data were observed a bit more often in children from Pripyat city exposed to radiation within first pregnancy trimester.

Fibrosis and sclerotic changes in thyroid were found in 26 kids exposed in utero with simultaneously no such alterations in control. In hormonal indices analysis depending on individual thyroid doses the direct dependence was surveyed of hypothyroidism risk degree upon thyroid radiation dose with threshold values 0.3 Gy.

T-cells and T-helpers function decrease with immune globulin A low serum content high incidence were marked in Pripyat city study group. These alterations not correlated with thyroid radiation doses and terms of prenatal exposure. Revealed disorders could maintain low resistance to infection diseases.

Thereby the conducted study provided ground to conclude that psychosomatic health in kids born in women pregnant at the time of ChNPP accident is unsatisfactory both in Pripyat city evacuees and Kiev residents. Number of disabled children in 1992 among those irradiated in utero was in 4 times over the average population value [Nyagu A.I. et al., 1993, 1995]. Worth to note that described above studies were conducted without unified and standardised methodology application for children mental health estimation. Therefore we are to acknowledge that received results regarding mental health of children exposed in prenatal period were preliminary. Methodological restrictions were overpassed within framework of World Health Organisation (WHO) Pilot Project «Brain Damage In Utero» that will be presented in detail below.

Y.I. Stepanova et al. (1993) examined the kids irradiated in prenatal period after the ChNPP accident. The 340 of them were born in mothers evacuated from Pripyat city, 169 — from mothers resident in territories of amplified radioecological control. Foetal thyroid doses were within range 0.035–1.8 Sv. Authors revealed that physical progress indices (including head circumference) was not different from control in «ecologically clean» region. At the same time about half of examined children were peculiar with pronounced deviations in mental progress qualified as *dysontogenic forms of borderline intellectual deficiency*. The affective lability, locomotive excitation, memory and attention disorders and working capacity were observed. Children occurred unable for tasks requiring volitional exertion and attention. Their intellectual activity was found concret, torpid, poorly switchable and with less expressed ability for help utilisation. Besides that the *autonomous nervous system dysfunction* signs were revealed in 73.3% of kids born in female evacuees from Pripyat city pregnant at the time of accident.

Biogenic amines study in prenatally irradiated children was held by Y.I. Stepanova et al. (1995). Three groups of children were examined: 1) kids born in women pregnant at the time of accident and evacuated from Pripyat city (n=89); 2) kids born in females pregnant at the time of accident and remained resident in territories of strict radiological control (n=84); 3) kids born in 1986 and resident till now in «radioecologically clean» region (n=67). Foetal thyroid doses in both groups were within range 0.001–3.058 Gy. Total radiation doses in children of 1st study group constituted from 5 to 376 mGy; in 2nd group — from 0.3 to 33 mGy. Epinephrine excretion elevation and norepinephrine excretion decrease with epinephrine/norepinephrine ratio increase was revealed in children exposed to radiation in prenatal period. Found disorders indicated the sympathetic-adrenal system hormonal branch dominance over the mediator one in prenatally irradiated kids and therefore autonomous nervous system parasympathetic part activity prevalence over sympathetic one. At the same time norepinephrine/dopamine ratio was substantially higher in 1st study group that indicated sympathetic nervous system functional capacity exhaustion in kids born from female evacuees from Pripyat city pregnant at the time of accident. Catecholamines precursor metabolism disbalancement was revealed stipulated by 3,4-dioxyphenylalanine (DOPA) conversion to dopamine alteration that was pointed out by excessive DOPA excretion with sharp decrease in dopamine release.

In the next publication Y.I. Stepanova (1996) reported about study in dynamic of 1,144 children: born from pregnant evacuees from Pripyat city (1st study group); born from strict radiation control territories pregnant female residents at the time of accident (2nd study group) and those born in 1986 in «radioecologically clean» territories (3rd study group). Foetal absorbed thyroid doses ranged within 0–3.34 Gy. Total foetal radiation doses in 1st study group constituted 5–380 mSv, in 2nd — 1–33 mSv. Autonomous nervous system dysfunction was revealed in 73.3% of children in 1st group and in 53.4% — in 2nd. Characteristic symptoms there were: headache, dizziness, locomotive disorders, fatigue, pain in lower extremities. Neurological microsymptomatic was observed with emotional

unstableness, locomotive excitation. In that work Y.I. Stepanova (1996) reported that number of kids with intermediate intellectual level was identical in all three study groups. Author also revealed no any differences in number of children with intellectual deficit among these study groups. However tendency towards number of kids with high IQ lowering and with low IQ case number elevation in 1st and 2nd study groups compared to control. Author concluded that multifactor impact of Chernobyl disaster unfavourable factors defined health deterioration in children irradiated in prenatal period shortening amount of practically healthy kids down to 5%. Substantial impact on health state deterioration in these children was made by average absorbed radiation dose value is residence region.

Some *lowering of psychic processes general development level* (operative memory, attention, speech), awareness level, formation degree of thought operations appropriate to respective age were marked in 140 kids born in females been pregnant at the time of the ChNPP accident and then evacuated from Pripyat and Chernobyl cities. In 30.5% of cases among kids irradiated in prenatal period the mental progress retardation was surveyed whereas in control — in 15%. No difference in neurotic and psychopathetic disorders incidence was revealed between prenatally exposed children and control [Bugajov V.N. et al., 1993]. In another report V.N. Bugajov et al. (1993) presented data regarding *speech sensory disorders* revealed in 18% of kids. Autonomous nervous system dystonia was observed in an all cases here. Genealogical analysis revealed that family sensory aphasia mainly of acoustic-mnestic type was present only in 2% of probands relatives. The rest 16% authors qualified as *mediobasal frontal syndrome*. In control dyslalia was revealed only in 8% of cases. Authors made preliminary conclusion regarding connection (r=0.7) between irradiation in early and late gestation age and speech sensory disorders in 4 - 5 years because of brain minimal dysfunction in medial-basal parts.

Examination of 30 kids age 5–6 years irradiated in prenatal period in Pripyat city at the time of ChNPP accident and since permanently resident in Kiev revealed *deviations in mental progress* in half of cases [Chuprikov A.P. et al., 1992; Chuprikov A.P., Pasechnik L.I., 1993; Chuprikov A.P. et al., 1995].

Ye.G. Chuprikova and V.M. Danilov (1996) conducted *the EEG-study* of 220 children and adolescents age 3 – 16 years resident in radionuclide contaminated territories or resident there at the time of accident. Probably the kids exposed to radiation in prenatal period were among them. Without dosimetry data application authors interpret the revealed organic mental disorders as *postradiation encephalopathy* and the epileptic & epileptiform manifestations — as - *postradiation epilepsy*. Expressed presentations of organic dysontogenesis with brain structures maturation retardation and medial-stem brain parts dysfunction; diencephalic brain parts, temporal zones and left hemisphere extreme vulnerability neurodynamic disorders with thalamo-hypothalamic structures and limbic-reticular complex irritation; hypertension syndrome; brain vessels tone pronounces disorders; EEG-patterns polymorphism and multifocality; predisposition for epiactivity rapid generalisation with its multifocality under marked out by post-radiation epilepsy authors EEG-pattern complication, Ye.G. Chuprikova and V.M. Danilov (1996) attributed to the studied children electrophysiological peculiarities.

A.P. Chuprikov et al. (1995) mark the *epileptic and epileptiform states* in kids survived after the ChNPP accident. Epileptiform phenomenon of *paroxysmal depression* was marked out by A.P. Chuprikov et al (1996) in children evacuated from Pripyat city and resident now in Slavutich with its origin explained through corticofugal interrelations paroxysmal alteration with depression processes prevalence of stem origin.

Catamnestic study of 33 Byelorussian children resident in territories with soil contamination value exceeding 15 $Ci \cdot km^{-2}$ (555 $kBq \cdot m^{-2}$), that at the time of accident were on terms of 8–15 weeks of prenatal development, indicated the reliable predominance of *asthenic states* (60.61% vs 20.0% in control from «ecologically clean» regions), *autonomous nervous system dystonia* (75.76% and 23.33% respectively) and *mental progress retardation* (39.39% and 3.33% respectively) in 58.3% of cases combined with *brain bioelectrical activity maturation slowdown* incidence [Igumnov S.A., 1993].

F.M. Gaiduk, S.A. Igumnov and V.B. Shalkevich (1994) presented results of catamnestic study of 154 children age 6–7 years been on prenatal development stage at the moment of Chernobyl disaster and exposed to radiation impact on territories with soil contamination density for ^{137}Cs over 15 $Ci \cdot km^{-2}$ (555 $kBq \cdot m^{-2}$). Authors revealed high incidence of *asthenic syndrome, autonomous nervous system dystonia, neurotic disorders, central nervous system residual organic pathology, mental progress retardation (IQ=70–79)*, followed by *EEG pathological types i.e. hypersynchronous and slow ones*. Authors concluded that along with exogenous-organic factors (including ionising radiation) the social factors are also of important value in mental progress genesis among kids exposed to radiation impact in prenatal period. In the next publication (1995) authors marked that exogenous-organic factors negative impact in mental progress retardation origin is redoubled by unfavorable psycho-social factors i.e. «psychological deprivation» as the result of forced resettlement or residence under «psychosocial isolation» conditions in contaminated regions [Igumnov S., 1995].

S.A. Igumnov et al. (1996) presented *clinical-dosimetry analysis* of Byelarus children irradiated in prenatal period. Mental disorders in those kids were diagnosed according to *IDC-10* diagnostic criteria with Wechsler test application. In kids 7–9 years old exposed to prenatal irradiation researchers found compared to control group of non-exposed children reliable excess of the following behavioural disorders: *speech specific disorders — F80* (18.8% and 7.8% respectively); *specific disorder of motor function development — F82* (12.3% and 4.4%); *hyperkinetic disorders — F90* (8.4% and 2.2%); *emotional disorders with onset specific for paediatric age — F93* (20.1% and 6.7%) both with total number of children with mental and behavioural disorders including *combined forms* (40.9% and 21.1%). Thyroid prenatal radiation doses in kids varied within range 0.05–2.15 Gy. Authors received data indicating reliable incidence elevation of *borderline intellectual deficit* (IQ=70–79) depending upon prenatal radiation dose.

S.V. Bazylchik and I.V. Lobach (1995) from Radiation Medicine Institute (Minsk) conducted study of intellectual progress with Wechsler test among 52 children irradiated in prenatal period and 78 kids exposed to radiation during first year of life. Authors marked in both groups the *intellectual progress lower values* compared to control, at that intellectual progress in exposed within first year of life occurred being worse than in irradiated in utero.

In Russia within framework of State Program «Children of Chernobyl» the staff of Moscow Institute for Psychiatry conducted in 1992 the pre-school children population in one of the regions of Tula province with ^{137}Cs soil contamination density from 5 to 15 Ci·km^{-2} (from 185 to 555 kBq·m^{-2}). The 1,041 children age from 2 months up to 7 years old were examined. Average absorbed doses of external radiation since accident till study moment constituted 10±0.31 mSv, of internal radiation — 4.3±0.22 mSv, on thyroid — 0.18±0.002 Sv respectively. There were 28.5% healthy kids among studied ones, 29.8% — with subclinical disorders and 41.7% — with nervous-psychical pathology. The most prevalent forms of revealed neuropsychiatric pathology were *residual-organic mental disorders, general mental progress delay and perinatal encephalopathy*. Oligophrenia, neuroses, personality anomalies, paediatric cerebral palsy and schizophrenia were registered rather more rare. Among syndromal variants the *neurotic and neurosis-like states, cerebrasthenic syndromes and mental retardation syndromes* were found most often. *Autonomous nervous system-vascular dystonia, hypertension-hydrocephalic syndrome and muscular dystonia syndrome* were the most characteristic neurological disorders. Authors intended to present the multidimensional statistical analysis results in further publications [Yermolina L.A., et al., 1994].

In the next publication L.A. Yermolina and N.K. Suhotina (1995) presented the comparative analysis of neuropsychiatric pathology in paediatric population of exposed to radiation prenatally in post-natal period. Authors marked the neurotic and neurosis-like disorders incidence mainly of subclinical level among kids irradiated within first year of life. Children exposed to radiation in prenatal period substantially more often presented the *general and partial mental underdevelopment* signs both with border-line manifestations of etiologically unidentified forms of *central nervous system exogenous-organic damage*. Among conceived, carried and born in post-accident period children exposed to external and internal radiation authors revealed elevation of exogenous-organic pathology borderline forms stipulated by detriments of pre- and perinatal periods both with mild forms of mental progress retardation. At that L.A. Yermolina and N.K. Suhotina consider the ionising radiation impact as leading one in mental retardation and borderline exogenous-organic neuropsychiatric disorders growth genesis.

However population cytogenetic studies in children resident in zones with various degree of radioactive contamination revealed no elevation in cell number with aberrations and unstable aberrations of chromosome type 6 years after the ChNPP accident. Individual cytogenetic examination of kids with thyroid radiation doses 2.0–3.6 Gy from ^{131}I revealed no increase in chromosome-type metathetical aberrations [Bochkov N.P. et al., 1994].

At the same time O.S. Uljanova et al. (1995) from Institute for Radiation Hygiene (Saint-Petersburg) consider that psychological strain and stress related to accident could have rather more biological aftermath than radioactive contamination. Authors received no convincing differences in *psychomotor progress* between prenatally irradiated children and kids born before accident. However psychomotor indices deterioration tendency was marked in children within 8 – 25 weeks of gestation at exposure. Factor analysis revealed the gender, number of children in family, peculiarities of mother behaviour in 1986 i.e. food products consumption from own farms and iodine prophylaxis execution after accident were of substantial impact on psychomotor development in children.

Chernobyl disaster impact on mental progress is studies all among the world. *Down's syndrome* incidence elevation is reported being registered in Sweden among kids whose mothers in pregnancy lived within zones of the most intensive radioactive fallout. That can be the ionising radiation impact aftermath [Ericson A., Kallen B., 1994]. At the same time other authors consider *cancer, mental development disorders and genetic abnormalities* prevalence changes in relation to Chernobyl disaster improbable ever found in Sweden [Moderg L., Reizenstein P., 1993].

Several German researchers concluded that *21st chromosome trisomy* prevalence elevation in Western Berlin in January 1987 was casually connected to the ionising radiation short-term impact after Chernobyl disaster [Sperling K. Et al., 1994].

Down's syndrome study in Lothian (Scotland) in 1978–1989 revealed statistically relevant case number elevation in 1987 not explained by demographic changes. Time relation was marked between Down's syndrome cases incidence rise and Chernobyl disaster. However they notify there are no scientific explanation to connection between these two events at the present level of knowledge [Ramsay C.N. et al., 1991].

Ukrainian Institute for Neurosurgery received data regarding application rate elevation with *congenital malformations* for the 5 years after Chernobyl disaster. *Brain dropsy* provided increase in 19.6%, brain and spinal hernias — in 8.5%. *Medulloblastomas* were characterised with increase in 59.6%. Yu.A. Orlov (1993) assumed that medulloblastoma incidence elevation was related to the named tumors origin from cells formed in terms of foetal prenatal development and ionising radiation impact after the Chernobyl disaster could induce the medulloblastoma growth.

I.Z. Holovonsky (1993) marked out that territories with population of 2.5 million children age up to 5 years old were exposed to radioactive contamination after the Chernobyl disaster and pointed out those kids having high risk of *mental retardation*.

M. Hoshi et al. (1994) within «Chernobyl—Sasakawa» Project framework studied in 1991–1992 the ^{137}Cs content in organism of 10,062 children age 5–16 years resident in Mogolyov and Gomel provinces of Byelarus. Average ^{137}Cs content in children organism was 21–48 Bq·kg^{-1} in Mogilov province and 28–126 Bq·kg^{-1} in Gomel

one. Respective effective doses were under 1 mSv·year^{-1}, however revealed ^{137}Cs activity values according to authors' data were substantially over the reported in the past in former Soviet Union (2.3 Bq·kg^{-1}).

N.K. Suhotina et al. (1993) revealed elevation of *etiologically unclear asthenic-vegetative disorders* in kids resident in radioactively contaminated regions of Russia compared to control. Those disorders were observed mainly among children suffering mild residual organic cerebral deficit. Authors not excluded psychogenic factors impact.

V.S. Podkorytov et al. (1994) explored the *psychoneurological sphere* state in comparative epidemiological study among 910 *schoolboys/schoolgirls* age 6–7 & 11–12 years old from whom 470 were resident in Zhitomyr province on territories with radioactive contamination and 440 — in «radioecologically clean» Kharkov province. Authors received data that 74–79% of kids suffer psychic, neurological and speech disorders of borderline level. At that kids from «radioecologically clean» regions had more serious disorders that in authors' opinion indicate another ecological hazards role in revealed neuropsychiatric pathology genesis. V.S. Podkorytov et al. (1994) assumed that exposed to radiation kids received more adequate medical aid that provided positive impact on their health state.

Though prenatal impact of Chernobyl disaster can alter children function both through developing brain organic damage and psychosocial problems surrounding child at birth and development. Prenatal brain damage problem was defined by the World Health Organisation (WHO) as prior one among health consequences of Chernobyl disaster that was reflected in Pilot Project «Brain Damage In Utero» being one of four WHO initiatives within framework of *International Program for Health Effects study of Chernobyl Accident (IPHECA).* «Brain Damage In Utero» Project aim was to reveal mental progress retardation and other brain dysfunction cases in children exposed to prenatal radiation after the Chernobyl NPP accident among radioactively contaminated territories of Ukraine, Byelarus and Russia. WHO expert panel elaborated and proposed research methodological approaches taking into account the Japanese work experience in stated field [Prilipko L., 1993; Yule W., 1996].

Group of Ukrainian researchers revealed 1,021 child (main study group) born between April 26, 1986 and February 26, 1987 in mothers resident at the time of accident within radiation contaminated territories (Narodichi, Ovruch & Korosten regions of Zhytomyr province and Polesskoje & Ivankov regions of Kiev province) or otherwise evacuated from estrangement zone.

The 544 of them were examined (including 115 (21%) kids and mothers evacuated from Pripyat and Chernobyl cities, 234 (43%) — Narodichi, Ovruch & Korosten regions of Zhytomyr province residents both with 195 persons (36%) — Polesskoje & Ivankov regions of Kiev province inhabitants) — the «experimental group» and 759 children, mothers and teachers resident in «clean» regions (Kharkov city and Kharkov province) where soil contamination density was less than 1 Ci·km^{-2} (37 kBq·m^{-2}) — control group. In total the 1,303 kids, mothers and teachers were examined.

Studied contingent revelation was held through Data Bank of National Register of Ukraine and studied regions medical institutions registration records. Revelation and examination of less prenatally exposed children number than intended (1,400 kids) was stipulated first of all be high migration level at that respective information regarding migrants was absent. Besides that some part of kids was due to social-economical reasons presented as exposed in prenatal period however in documents adjustment their mothers were found not been present in pregnancy within territories subjected to radioactive contamination.

Besides that the problematic nature of initial intention to study the cohort of kids exposed to prenatal radiation in Ukraine (n=1,400) together with their mothers and teachers is proved by fact that within 50 years only 324 persons from Nagasaki atomic bombing prenatal survivors (at least 1,940 ones) were studied with joint American-Japanese efforts i.e. only 16.7% of cohort [Schull W.J., Otake M., 1986; Otake M. Et al., 1987, 1989, 1991; Yamazaki J., Schull W.J., 1990; Schull W.J. et al., 1989; Otake M., Schull W.J., 1993; Imamura Y. et al., 1995].

Representative «experimental» region (Polesskoje region Kiev province) epidemiological and demography data analysis enabled to reveal that only 20% of all prenatally irradiated children in region were examined. Taking into account the casual in general mode of children selection for the study one can consider with definite assumption that the prenatally irradiated kids representative sampling was studied [Bendat J.S., Piersol A.G., 1971].

All studied children attended public schools and pre-school institutions. No any formally established psychiatric diagnoses including that of schizophrenia were present among all studied kids irradiated in prenatal period. Marked out fact is contradictory to the Health Ministry of Ukraine formal statistical data, that state mental disorders prevalence among Ukrainian children in 1985–1990 varied from 230 up to 262 cases per 10,000 paediatric population. That is on the ground of «zero» hypothesis one could expect detection by local paediatric psychiatric service the 12–15 mental disease cases per 544 kids irradiated in prenatal period. We can not exclude that psychiatric diagnoses absence is medical documentation is explained with mental disorders criteria narrowing in out country for the last time on the one hand and socially conditioned avoidance of psychic diseases diagnostic — on the other. No data regarding the dead children in stated group were found.

No significant difference was found between main study and control groups through gender and prenatal development terms at the time of the ChNPP accident that provided availability of selected groups application for study purpose accomplishing.

Ionising radiation impact estimation regarding named contingent was held on ground of ^{137}Cs territory contamination density formal data. For 48 examined kids evacuated from Pripyat city the foetal individual external γ-radiation doses were reconstructed with Monte-Carlo method application in Dosimetry Department USCRM of MH & AMS of Ukraine (G.M. Gulko & V.V. Chumak). Average individual foetal doses constituted 0.007±0.002 Sv and not exceeded 0.013 Sv whereas individual thyroid doses in kids exposed in second and third pregnancy trimesters

were within range 0.1–1.2 Sv. Thyroid functional state was studied in these 48 children including serum thyroid hormones assay.

Children born in mothers evacuated from estrangement zone was exposed to the highest radiation impact risk in cerebrogenesis period. At present those children are at maximum in couple resident in Kiev and Slavutich cities.

Child non-verbal intellect estimation was held with «Draw-a-Man» «Raven Coloured Matrices» tests application. «Draw-a-man» is the psychometric methodology enabling child non-verbal (performance) intellect quantitative assessment. Worth to note that stated test is not enough objective for non-verbal IQ definition and to the major extent serves the teacher as singular index of child readiness for school education [Harris D., 1963]. «Raven Coloured Matrices» test serves for constructive praxis quantitative estimation as the part of kid non-verbal intellect [Raven J., 1986].

Verbal intellect in children is estimated with «British Picture Vocabulary Scale» — BPVS. It enables the verbal intellect quantitative estimation [Dunn L.M., Dunn L.M., 1982].

According to IDC-10 index IQ=70 is the threshold between low norm and mental retardation mild degree.

All named methods are fulfilled by children.

Emotional-behavioural disorders estimation was conducted by means of Ratter Scale (A2) filled in by parents. Besides that Ratter Scale (B2) was applied filled in by the teacher and including the same positions as previous one amplifying therefore the respective data reliability [McGee F. et al., 1985; Venables P. et al., 1983].

General Health Questionnaire (GHQ-28) was applied for mothers mental health estimation. Questionnaire reflects psychic adaptation value, anxiety and depression values, somatised disorders and social dysfunctions. Test for parents verbal intellect estimation (vocabulary sub-test by Wechsler) was applied to reveal to what extent mother understands definite words which meaning she further will be able to explain the child.

Demographic map presented to the parents was also applied both with Data Card of Examined Person (DCEP).

Worth to note that work with kids was conducted in field conditions not always been equal and not always corresponding the standard parameters.

In spite of standards absence for native population we applied available British and German standardised indices for psychological testing results analysis. Native standards absence, undoubtedly decrease the individual estimate accuracy. Foreign standards application however enables substantial error avoidance in kids intellectual progress estimation without gender and age taking into account. It also makes possible group compare with differences registration.

Data Base creation for the examined children was held according to the WHO requirements in Microsoft Windows medium with PC software Microsoft Access & Microsoft Excel application.

Besides that we conducted original statistical analysis within Data Base structure in *dbf*-format by means of standard applied statistical programmes of SYSTAT type. Statistical processing was held through hierarchic sequence according to the solving task complexity. First differences with solitary indices between main study and control groups were estimated with parametric and non-parametric criteria. Non-parametrical χ^2 criterion was applied for qualitative (clinical) indices. Differences reliability between groups was estimated by means of Fisher Tables application. Quantitative indices differences estimation was held with variation analysis. Arithmetic mean values were calculated in groups with mean square and linear deviations and mean errors of arithmetic means. Differences reliability was defined with Student criterion and probability integral [Gubler Ye.V., 1978; Martin J.M. et al., 1980; Hays W.L., 1981; Kuzma J.W., 1984].

Indices with reliable differences between main study and control groups were subjected to correlation and regression analyses with factors impacting mental health in children (individual foetal and thyroid radiation dose, radioactive contamination degree of residence territory, prenatal term on April 26, 1986, mother's educational level etc.). Finally data regarding links character and closeness between mental health indices in children and Chernobyl disaster main pathogenic effects were received [Misuk N.S. et al., 1975].

Brain functional state estimation was conducted by means of computerised electroencephalography (CEEG) with brain biopotentials 19-channel analyser «Rista» manufactured by ECB «Rhythm» (Taganrog City, Russia) and BERG-FOURIE Analyser manufactured by OTE Biomedica Company (Italy) application.

The BERG-FOURIE Analyser application for prenatally irradiated kids examination was defined by its technical capabilities for brain electrical activity fast spectrum section precise analysis [Zenkov L.R., Ronkin M.A., 1991; Sciaretta G., Erculiani P., 1977]. Four electrodes were bipolarly positioned on frontal-parietal zones (F_3—P_3 & F_4—P_4). Analysis epochs (periods) constituted 8 sec and 60 sec in BERG mode. Spectrum power pseudo-three-dimensional graphs and spectrum histograms were analysed with frequency range 0.5–32.0 Hz.

Brain biopotentials 19-channel cartographer «Rista» application enabled to conduct visual, spectral and periodometrical EEG-analysis. Brain spontaneous electrical activity registration was held in unipolar way with reference electrodes placed on ear lobes. Scalp electrodes were positioned according to the International system. «10–20».

Neurophysiological studies were held in Neurology Department Laboratory of Research Centre for Radiation Medicine AMS of Ukraine in 1995. CEEG was registered in child passive awaken state with closed or opened eyes, and also under 3-minutes-long hyperventilation with closed eyes. The 50 kids of «experimental» group were studied whose mothers were evacuated from the estrangement zone and 50 clinically healthy children of similar age resident in Kiev City (control group). All studied children were right-handed persons.

Brain spontaneous electrical activity estimation and interpretation was held according to algorithm by Ye.A. Zyrmunskaja (1991) both with classical manuals for paediatric EEG [Faber D.A., Alferova V.V., 1972; Niedermeyer E., Lopes da Silva F., 1982].

Following CEEG indices were subjected to math processing: spectrum power and dominant frequency of main EEG ranges in all channels, power index and main frequency ranges amplitude in hemispheres both with asymmetry indices.

Intergroup differences were studied on variation analysis basis. Difference reliability was estimated with Student criterion. Within analysis process the differences for gender and cerebrogenesis period on April 26, 1986 were studied. Neurophysiological parallels of pathopsychological parameters were explored with correlation analysis. Statistical processing was held with electronic tables Microsoft Excel 4.0 application in Microsoft Windows 3.11 medium.

Screening clinical analysis indicate the psychoneurological and somatic pathology presence in 2/3 of kids in «experimental» group. Digestive system and upper respiratory ways disorders, minimal cerebral dysfunction, neurosis-type states, autonomous nervous system dystonia both with thyroid function alterations prevail here.

No cases of pronounced mental retardation were found among studied children exposed to ionising radiation in prenatal period. At the same time neurosis-type states were diagnosed in majority of them with leading asthenic-vegetative syndrome on the background of both minimal cerebral dysfunction and somatic pathology.

Neurosis-type states were more often (63%) met among evacuated children. Thyroid functional state alterations role was surveyed in their forming. Emotion-volitional disorders in form of affective instability, social alienation and aggressiveness were the characteristic psychopathological manifestations of neurosis-type states in kids exposed in utero. This triad of symptoms is considered among schizophrenia elevated risk criteria however not always being obligate for it [H. Van Angeland, 1992]. Besides that there were revealed three cases of paediatric autism.

Summarised psychological study results in «experimental» and control groups are shown in Table 4.2.

Verbal intelligence estimate. The average standardised IQ values were received in «experimental» and control groups as the result of held verbal intellect studies with screening-method «British Picture Vocabulary Scale» application. Received values occurred being practically identical: 92±2.0 & 93±2.1 respectively. Distribution examination revealed that in 61 (11.34%) of kids in «experimental» group and in 66 (8.87%) in control one the IQ occurred being lower than 70. In spite of children with verbal IQ<70 incidence was somewhat higher in «experimental» group than in control, these differences were only approaching ones to the statistical reliability ($p>0.05$).

Non-verbal intelligence estimate. Non-verbal intellect study was held by means of «Draw-a-Man» test application and revealed that average standardised values in «experimental» group were reliably lower than in control — 105±2.6 & 114±2.2 respectively ($p<0.05$). Besides that IQ<70 was found in 11 (2.01%) of kids of «experimental» group whereas in control one — only in 8 (1.06%) children i.e. the two-fold difference is present however occurred statistically unreliable with χ^2 criterion.

Non-verbal intellect in children was estimated also by means of screening-methodology «Raven Coloured Matrices». Average percentile values for Raven coloured progressive matrices in kids from «experimental» and control groups were almost equal: 47.3±2.9 and 48.9±3.1 respectively. However distribution assay revealed that in 59 (10.95%) of children in «experimental» and 92 (12.12%) — in control groups the IQ was <70 i.e. kids exposed to prenatal irradiation had less cases number of non-verbal intellect retardation however those differences occurred statistically unreliable.

Distribution IQ scores according to the «Draw-a-Man», «Raven Coloured Matrices» and «British Picture Vocabulary Scale (BPVS)» of prenatally exposed and non-exposed control children are presented on figure 4.1.

It is revealed in «experimental» group in comparison with control one statistically significant increase of children with reduced intellectual abilities (IQ=70–90) as well as significant decrease of children with high intellectual abilities (IQ=110–140) and intellectually gifted children (IQ>140) according to all three intelligence tests.

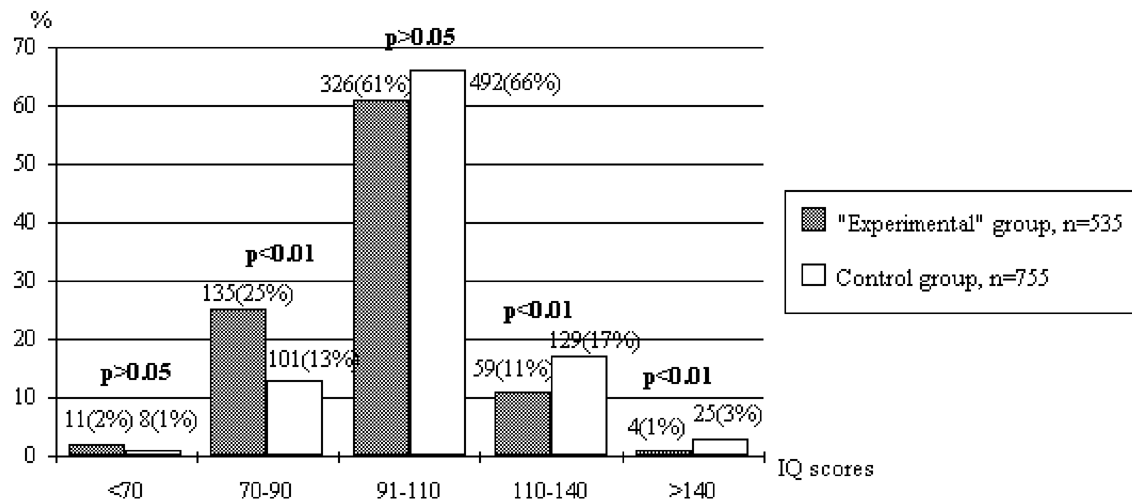
Table 4.2

INDICES CHARACTERISING MENTAL HEALTH IN CHILDREN EXPOSED TO RADIATION IN PRENATAL PERIOD AND THEIR MOTHERS

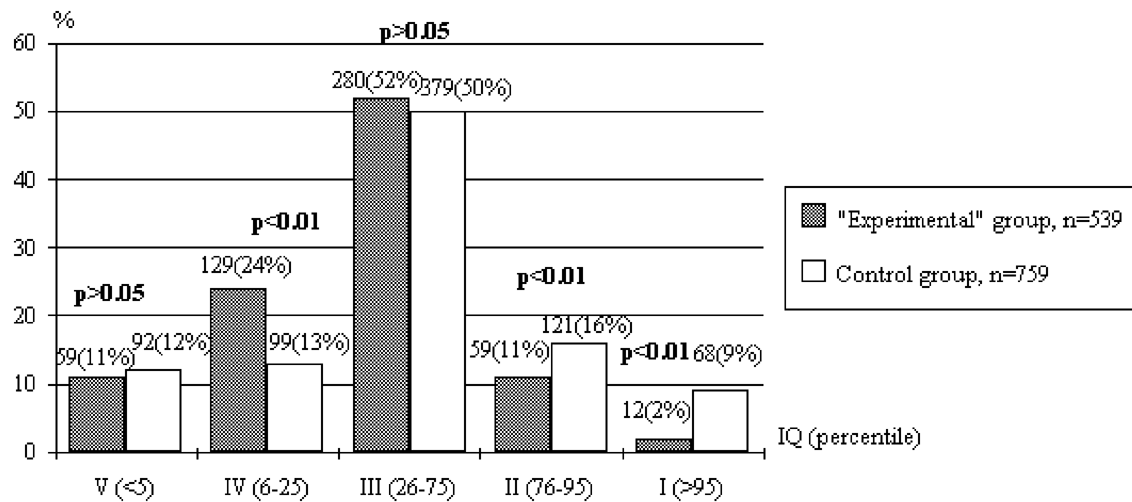
Groups	Number of children with revealed **mental retardation** **IQ<70**					Number of kids with **emotional, behavioural and non-differentiated disorders**		Indices characterising degree of **mental health in mothers**	
	Non-verbal intellect (**Draw-a-Man**)	Verbal intellect (**BPVS**)	Non-verbal intellect (**Raven Coloured Matrices**)	**General intellect lowering (A)***	**General intellect lowering (B)****	**Ratter** scale **б(2)**	**Ratter** scale **ы(2)**	General Health Question-naire **GHQ-28**	**IQ**
«Experimental», n=544	11 (2.06 %) n=535	61 (11.34 %) n=538	59 (10.95 %) n=539	19 (3.49 %) n=544	23 (4.34 %) n=544	152 (41.76 %) n=364	137 (34.86 %) n=393	24.26±0,4 n=382	33.6±0,6 n=377
P For χ^2 or Student's criteria	>0.05	>0.05	>0.05	<0.05	<0.05	<0.01	>0.05	<0.01	<0.05
Control, N=759	8 (1.06 %) n=755	66 (8.87 %) n=744	92 (12.12 %) n=759	8 (1.05 %) n =759	16 (2.10 %) n=759	214 (28.69 %) n=746	269 (38.93 %) n=691	20.73±0,5 n=639	43.6±0,5 n=750

Note: (A)* - IQ<70 through Raven Coloured Matrices and BPVS
(B)** - IQ<70 through any two intellectual tests

Non-verbal intelligence (‘Draw-a-Man’ test)



Non-verbal intelligence (‘Raven Coloured Matrices’)



Verbal intelligence (‘British Picture Vocabulary Scale’)

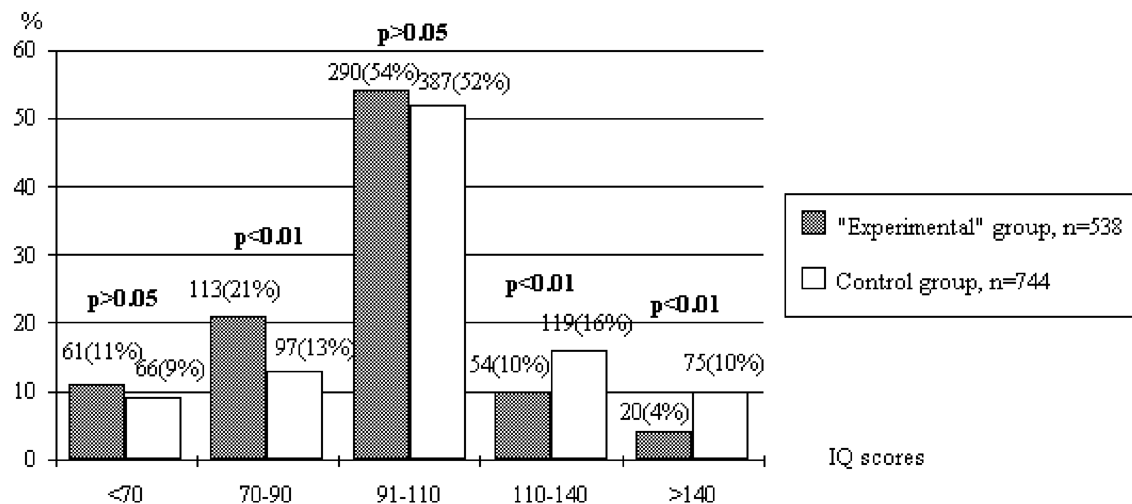


Figure 4.1. Distribution of IQ scores in the prenatally irradiated children (‘Experimental’ group) and non-exposed control children

IQ integral decrease calculations held through two algorithms:

A) Simultaneous IQ lowering under 70 through Raven test and British Picture Vocabulary Scale;

B) Simultaneous IQ lowering under 70 through any two tests:

1) Raven test and British Picture Vocabulary Scale;
2) Raven test and «Draw-a-Man» test;
3) British Picture Vocabulary Scale and «Draw-a-Man» test.

On the ground of algorithm «A» the IQ<70 was revealed in 19 (3.49%) of children in «experimental» group and in 8 (1.05%) of them — in control. The same for algorithm «B» — in 23 (4.34%) and 16 (2.1%) respectively. For both algorithms the differences between «experimental» and control groups were found statistically relevant ($p<0.05$) i.e. the IQ<70 cases are met among prenatally irradiated children reliably more often than in control.

Such indices of intellectual coefficient are characterised according to ICD-10 as mental retardation mild degree with two-fold incidence prevalence in «experimental» group compared to control. At that if the nonverbal intellect lowering is predominant in control group, the verbal one decrease is present in «experimental» cohort. That can reflect the left hemisphere dysfunction domination in prenatally irradiated children.

It's remarkable that average values of mental retardation prevalence in Kharkov province paediatric population according to Ukrainian Ministry of Public Health in 1986–1993 constituted 0.6% (53.3–62.4 per 10,000 paediatric population) but for all the Ukraine — 0.65% (58.8–70.1 per 10,000 kids) that is substantially lower that we have revealed. That can indicate on the one hand the applied diagnostic methods high sensitivity and on the other — low registration rate of psychosomatic disorders and mental retardation in particular.

Emotional and behaviour disorders estimation in children. Ratter's methods for parental and teacher's estimation of psychic state estimation in children were applied within study. As the result of study conduction with Ratter's parental scale A(2) application the emotional or behaviour disorders were surveyed in 152 (41.76%) from 364 kids exposed to radiation in prenatal period and 214 (28.69%) from 746 children resident in ecologically «clean» zones.

From those 152 (41.76%) kids in «experimental» group the predominantly emotional disorders were revealed in 61 (40.13%), behavioural ones — in 57 (37.5%) and non-differentiated emotional-behavioural disorders — in 34 (22.37%).

Among 214 children resident in ecologically «clean» territories in 66 (30.84%) of them the mainly emotional disorders were revealed, in 96 persons (44.86%) — behavioural and in 52 kids (24.3%) — non-differentiated emotional-behavioural ones.

According to Ratter's scale B(2) study data among 393 children irradiated in prenatal period the emotional, behavioural or non-differentiated disorders were found in 137 (34.86%) cases. From those 137 kids in 43 of them (31.39%) mainly the emotional disorders were revealed, in 75 (54.74%) — behavioural and in 19 kids (13.87%) — non-differentiated emotional-behavioural ones.

Examination of 691 children in ecologically «clean» zones indicated that in 269 (38.93%) cases the emotional-behaviour or non-differentiated disorders were found, in 96 (35.69%) mainly the emotional disorders were defined, in 127 (47.21%) — the behavioural ones and in 46 (17.1%) — non-differentiated emotional-behavioural disorders.

Thereby number of children in «experimental» group suffering emotional-behavioural disorders according to the parental estimates occurred higher than for teachers' estimates, whereas in control group — in teachers' evaluation the number of children with emotional-behavioural disorders was vice-versa higher that in parental opinion.

Intellectual level estimate in mother. Verbal sub-test of Wechsler test application indicated that parental intellectual development in «experimental» group was lower than in control: 33.6±0.6 and 43.6±0.5 «raw» scores respectively ($p<0.05$). Probably the shorter education terms in mothers of «experimental» group (12.3±0.3 years) compared to mothers in control (13.3±0.3 years) was important here. The named sub-test application was most doubtful and questionable in all examination procedure because of motivation absence in parents both with their attention high exhaustion capability.

Mental health estimate in mother. According to the results received through General Health Questionnaire GHQ-28 application the mental health in parents from «experimental» group was substantially worse ($p<0.01$) than in control: 24.26±0.4 and 20.73±0.5 points respectively (according to scale 0–1–2–3 estimate criteria). Neurosis-type and affective disorders were prevalent in parental psychopathological manifestations among first group. At the same time mainly asthenic and neurotic disorders were revealed in parents resident in ecologically «clean» territories.

Data Card of Examined Person (DCEP) and Demographic Questionnaire. Clinical analysis of DCEP indicates the more pronounced and often registered psychoneurological pathology in children from «experimental» group compared to control. No reliable differences for anthropometry indices (new-born body weight and length) were found between study groups. Tendency towards lower body weight and length ($p>0.05$) was marked out in new-borns among «experimental» group. Higher number ($p<0.05$) of complications at deliveries and older parental age were surveyed there compared to control.

In *correlation relations analysis* of prenatally irradiated children mental health indices the following results were established (Figure 4.2). IQ according to the «Draw-a-Man» test was closely connected to IQ value according to the British Picture Vocabulary Scale (correlation ratio $\eta=0.8$) and the child's verbal intellect in it's turn — to the mother's education level ($\eta=0.765$) & IQ through Raven Coloured Matrices application ($\eta=0.684$). Intellectual and

emotional-behavioural disorders connection to delivery complications and mother mental health deterioration was fixed ($p<0.01$) in kids exposed to radiation in prenatal period. Reliable relation of intellectual development worsening was determined to ionising radiation impact with territory ^{137}Cs-radioactive contamination criterion. Radiation factor contribution constitutes 29%.

Dependence with correlation relation coefficient value $\eta=0.85$ was revealed between foetal development period at the time of Chernobyl accident and «Draw-a-Man» standard estimation conducted within age 7–8 years old. The higher was pregnancy term on April 26, 1986 the higher drawing quality was. Dependency was of parabolic mode with approximation error value 7.9%. Explanation through ionising radiation pathological impact in early gestation terms can not be excluded here.

Hypothyroidism, nodular goiter, fibrosis and sclerotic processes were revealed in thyroid of kids born in pregnant women evacuated from Pripyat city. In hormonal indices analysis depending on individual internal radiation doses on thyroid the reliable ($p<0.01$) moderately pronounced ($r=0.5–0.6$) unidirectional connection «dose—effect» was fixed: along with thyroid dose growth with 0.3 Gy threshold the thyrotropin serum content is elevated (Figure 4.3). Taking into account free thyroxin normal serum content the received data stipulate assumption about hypothyroidism genesis risk degree direct dependence upon thyroid prenatal radiation dose with 0.3 Gy threshold.

Correlation interrelations analysis indicated that along with thyroid prenatal radiation dose rise the emotional-behavioural disorders revealed with Ratter scale A(2) are elevated too. Revealed connection is in a good way approximated through parabolic dependence ($p<0.05$). Besides that the non-verbal intellect estimated through «Draw-a-Man» test application in worse ($p<0.05$) in children with prenatal thyroid radiation doses exceeding 0.3 Gy than in kids with respective values under 0.3 Gy.

Under thyroid abnormalities as known the mental disorders are observed with mental retardation in particular [Hetzel B.S. 1994; Xue-Yi C. et al., 1994]. Therefore here comes possibility to connect the intellectual and emotional disorders to thyroid radiation pathology in kids exposed to irradiation in prenatal period.

On *EEG visual analysis* background children from «experimental» group were different from control (and norm from literature data) with epileptiform activity presence — in 8 cases (26.7%) through «peak—wave» or «polypeak—wave» complexes in anterior-temporal zones of usually left hemisphere and/or through paroxysmal rhythmic bilateral oscillations in sharp δ-waves form; δ- & β_1-activity dominance with α- & θ-rhythmic decrease both with high amount of inter-hemisphere asymmetries combined with paroxysmal activity.

Computer EEG results in prenatally irradiated children compared to control group of clinically healthy kids are shown in Figure 4.4. According to *EEG spectrum analysis* as the figure shows the children from «experimental» group are peculiar with diffusely higher spectrum power of δ-range with lower one of θ-range especially in left parietal-temporal zone, diffusely lower α-range spectrum power and higher one in β_1-range especially in the left frontal-temporal zone. At that θ-range lower frequency is registered in the named children especially in left temporal zone under α- & β_1-ranges increased frequency in posterior brain parts.

According to *EEG periodometry analysis* the kids irradiated in prenatal period are peculiar with δ- & β_1-ranges higher indices in left hemisphere under α-activity much lower index and amplitude. At that θ-range index and amplitude in right hemisphere among this group occurred been lower and β_1-range ones — higher than in control.

Data analysis indicated that children exposed to radiation in prenatal period and been on April 26, 1986 within the most critical period of cerebrogenesis (8–15 gestation weeks) have higher spectrum power of δ-range especially in left hemisphere central registration electrode C_3; α-range somewhat higher power in posterior brain zones along with β_1-range diffusely elevated power and index compared to both all other kids from «experimental» group and control.

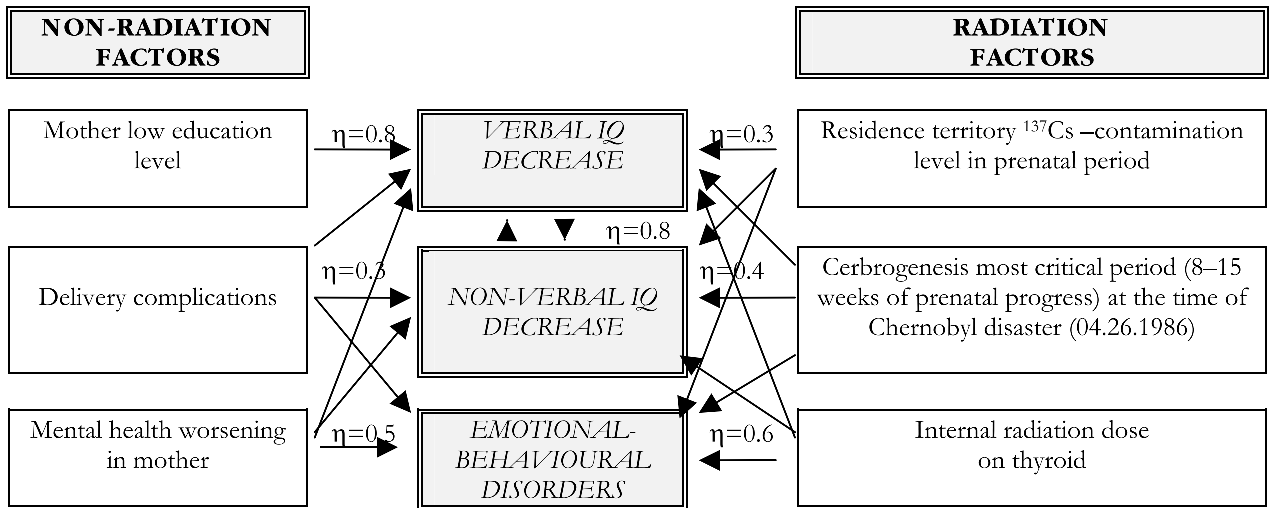


Figure 4.2. Factors making impact on mental health in children exposed to radiation in prenatal period

η — correlation interrelations coefficient.

⟶ — reliable effect ($p<0.05$) of the factor.

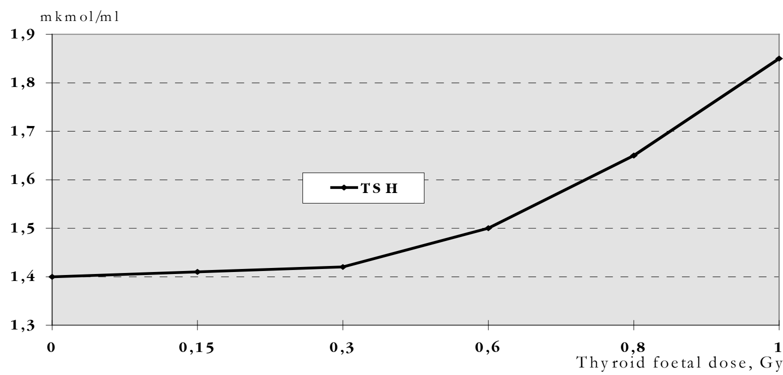


Figure 4.3. Dependence between serum thyrotropin (TSH) content and thyroid foetal dose

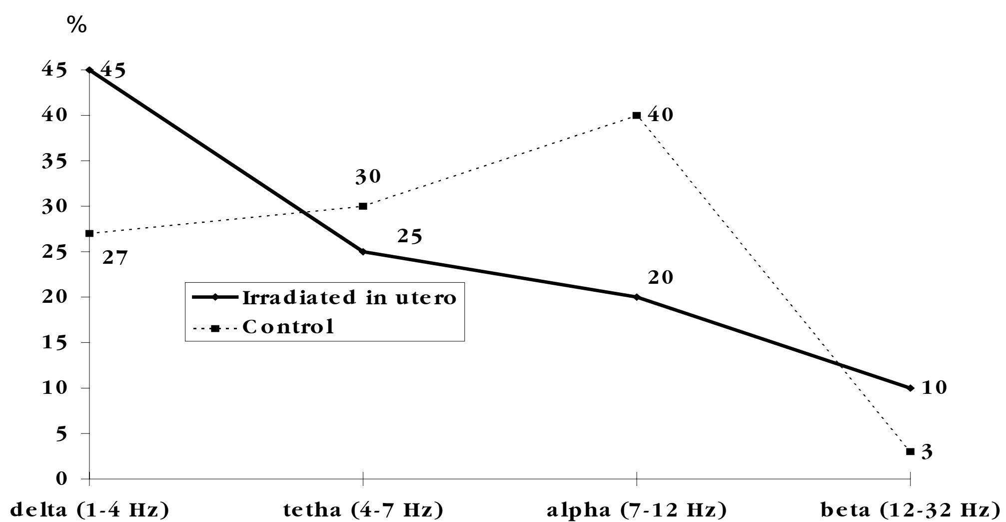


Figure 4.4. EEG spectrum power (%) in Эexperimental Ю (n= 50) and control (n= 50) groups

Besides that delivery complication impact on brain neurophysiological parameters in children 7–8 years later. Pathology of delivery occurred leading to slow rhythmic spectrum power amplification in right hemisphere (r=0.23–0.47) and α-range depression (r=–0.49–[–0.57]) in right hemisphere posterior zones. At the same time the left hemisphere but not right one alterations were most characteristic for kids irradiated in prenatal period.

Correlation analysis indicated that non-verbal intellect estimated through Raven Coloured Matrices and «Draw-a-Man» test application was inversely proportional to δ-range spectrum power (r=–0.49) in central-posterior brain zones and directly proportional to spectrum power values of θ- (r=0.32), α- (r=0.23) and β_1 ranges (r=0.35) in right hemisphere posterior parts. At the same time the verbal intellect estimated by means of Picture Vocabulary Scale was inversely proportional to central-posterior brain parts δ-range spectrum power (r=–0.37) and directly proportional to the θ- spectrum power (r=0.34) of left hemisphere posterior parts. Therefore there is possibility to connect the revealed verbal intellect decrease predominance in prenatally irradiated children suffering left-hemisphere dysfunction.

The following characteristic EEG-patterns were classified on the held research background for kids exposed to radiation in prenatal period (Table 4.3).

Table 4.3

Brain bioelectrical activity patterns in prenatally irradiated children compared to the norm

EEG-pattern	Children exposed to radiation in prenatal period n=50	p χ^2	Children from control group n=50
Age norm:			
Dysorganised with α-activity predominance	8 (16.0 %)	<0.05	24 (48.0 %)
Hypersynchronous	5 (10.0 %)	>0.05	16 (32.0 %)
Pathological:			
Dysorganised slow	23 (46.0 %)	<0.05	8 (16.0 %)
Dysorganised with paroxysmal activity	14 (28.0 %)	<0.05	2 (4.0 %)
Laterality:			
Left-hemisphere	20 (40.0 %)	<0.05	6 (12.0 %)
Cross-type	10 (20.0 %)	>0.05	2 (4.0 %)
Right-hemisphere	13 (26.0 %)	>0.05	10 (20.0 %)
Symmetry	7 (14.0 %)	<0.01	32 (64.0 %)

Normal variants of brain bioelectrical activity in children from «experimental» group were found much rare than in control.

Slow dysorganised pattern (with δ-activity predominance) was characterised by low- or high-amplitude dysorganised activity with slow-type activity dominance mainly of δ-range or irregular α-activity. Reaction on eyes opening was decreased or absent, hyperventilation induced bilateral paroxysmal activity rise. Medullar reticular formation, posterior hypothalamus, thalamus and non-specific nuclei and nucleus caudatus activity decrease is basic in physiology of this pattern. At that the ascending biases on cortex from anterior hypothalamus are dominating which activity is amplified due to its liberation from other non-specific system parts depressing effects.

Dysorganised pattern **with paroxysmal activity** is in general similar with one described above however is peculiar with «peak—wave-» or «polypeak—wave» complex high-amplitude oscillations, sharp θ- and δ-waves. Reaction on eyes opening is decreased or absent, hyperventilation induces bilateral paroxysmal activity rise. Stated syndrome forming pathway is consistent in both specific and associative thalamus nuclei irritation, medullar reticular formation and posterior hypothalamus activity depression, at that anterior hypothalamus and nucleus caudatus are is steady state. In this pattern the brain convulsive capability is increased [Zhyrmunskaja Ye.A., 1991].

The two described EEG-types are registered reliably more often in kids exposed to radiation in prenatal period than in control group that is obviously reflecting the developing brain function-structural organisation alterations in these children.

The BERG-FOURIE analysis application enabled the more precise examination of inter-hemisphere asymmetries in children. Those studies revealed the β-activity spectrum power reliable prevalence with 20–23 Hz

dominating frequencies and left-hemisphere lateralisation in kids exposed to radiation in prenatal period compared to the healthy ones in control group.

We have selected the four types of brain biopotentials inter-hemisphere distribution (Table 4.3). *Symmetrical pattern* was characterised with α-activity somewhat depression over the left i.e. dominating hemisphere in combination with δ-rhythmic slight prevalence in the left frontal zone. At that asymmetry index not exceeded 5%. Such pattern characteristic for the normally progressing kids is reliably more rare observed in children exposed to radiation in prenatal period (all examined kids were right-handed persons).

Right-hemisphere dysfunction was consistent in slow and/or epileptiform rhythmic lateralisation to the right frontal-parietal-temporal zone. Although this type of inter-hemisphere asymmetry was observed more often in «experimental» group, the differences were not reliable.

Selected *cross-type variant of asymmetry* was consistent in the slow rhythmic displacement to frontal-temporal zone of one hemisphere and parietal-temporal zone — of another one. Differences between study groups for the present asymmetry type were also nit reliable.

Left-hemisphere-type of disorders was characterised with slow, rapid and/or epileptiform rhythmic displacement to the left frontal-temporal zone along with α-activity marked depression in left hemisphere. This type being reliably more often registered in kids exposed to ionising radiation in prenatal period reflects the limbic-reticular complex dysfunction and left hemisphere hyperactivation. The left-hemisphere EEG-pattern is reputed reflecting brain dysfunction that is basic for schizophrenia-spectrum disorders and is considered by some authors as schizophrenia biological markers. At the same time left-hemisphere dysfunction is characteristic for affective disorders [Flor-Henry P., 1969, 1973, 1983, 1989; Gruzelier J.H., Hammond N., 1976; Gur R.C. et al., 1978, 1982]. Left-hemisphere disorders predominance revealed in prenatally irradiated children is conformed to the earlier published data regarding left-hemisphere dysfunction prevalence in persons exposed to ionising radiation impact after the Chernobyl disaster [Loganovsky K.N., 1995].

Received in Ukraine data analysis demonstrated the mild degree mental retardation and border-line emotional-behavioural disorders prevalence elevation among prenatally irradiated kids both with their parents' mental health deterioration in contaminated regions compared to control ones.

Both non-radiation factors and radiation effects indirect impact through thyroid pathology was surveyed in mental disorders pathogenesis among children exposed to radiation in prenatal period after the Chernobyl disaster. Received results indicate the intellectual and emotional-behavioural disorders connection in prenatally irradiated kids to the radiation-induced thyroid pathology with 0.3 Gy threshold of prenatal thyroid exposure. Radiation factor contribution to the child's intellectual progress deterioration estimated though elaborated criterions application constituted 29%.

Dysorganised slow and dysorganised with paroxysmal patterns brain bioelectrical activity patterns predominance was fixed in kids exposed to radiation in prenatal period. Both specific and associative thalamus nuclei irritation with medullar and posterior hypothalamus activity depression is basic for those patterns reflecting brain convulsive capacity elevation.

Spectrum analysis, BERG-FOURIE and periodometrical analyses of brain bioelectrical activity revealed slow, rapid and/or epileptiform rhythmic lateralisation to the left frontal-temporal zone under α-activity marked depression in left hemisphere among 40% of children exposed to radiation in prenatal period. This type reliably more often registered in prenatally irradiated kids reflects the limbic-reticular complex dysfunction and left hemisphere hyperactivation considered as biological marker of schizophrenia spectrum disorders. Correlation analysis enables the revealed verbal intellect decrease connection to the left-hemisphere dysfunction in prenatally irradiated children.

Children prenatally exposed to radiation in terms of cerebrogenesis most critical period (8 – 15 weeks of gestation on April 26, 1986) have more pronounced brain functional state disorders compared to the both other kids from «experimantal» group and control one.

Neurophysiological studies indicate the limbic-reticular structures dysfunction presence mainly in the left i.e. dominating hemisphere in prenatally irradiated children. Revealed alterations reflect brain functional-structure development and are stipulated by the Chernobyl disaster factors complex prenatal and post-natal impact where ionising radiation effect on developing brain can not be excluded.

Revealed mental retardation and emotional-behavioural disorders prevalence elevation tendency in children exposed to radiation in prenatal period is probably connected to post-accident situation factors complex: radiation impact on foetus, pregnant females life-style and nutrition mode alteration, perinatal pathology, economic situation deterioration etc.

The following positions were marked out in WHO Publication «Health Consequences of Chernobyl Accident» (1996) on the ground of 4,210 children examination in Ukraine, Belarus and Russia:

- *mild degree mental retardation* incidence in main study group (irradiated in utero) is higher compared to control group;
- tendency of *behavioural reactions* and *emotional sphere* alterations cases number increase in kids from main study group was revealed;
- *borderline neuro-mental disorders* incidence *in parents* from main study group was reliably over the control.

Studies held by three states indicate the explored problem actuality and long-term survey organising necessity for all cases of prenatally irradiated children under profound psychological, clinical, neurophysiological and other

examinations conduction with individual foetal doses reconstruction [Prilipko L.L. et al., 1995; Kozlova I.A. et al., 1995; Nyagu A.I. et al., 1995; Kozlova I.A. et al., 1995].

Worth to note that kids born from pregnant evacuees from estrangement zone are the most critical persons for prenatal irradiation especially from ^{131}I. Evidently namely this group of children is the most adequate one for prenatal brain damage aftermath study and compare to Japanese researchers data. Further study conduction in this field is of particular theoretical and scientific-practical importance. Endogenous psychic diseases and especially schizophrenia genesis risk study among children irradiated in prenatal period after the Chernobyl disaster is of particular scientific interest. International co-operation organising is considered perspective in this field.

Neuropsychiatric Effects of Acute Prenatal Exposure. During the recent years our studies of neuropsychiatric effects of prenatal irradiation were continued. The dosimetric support of this study was provided by Prof. V.S. Repin and Dr. S.Yu. Nechaev (Department of Dosimetry and Radiation Hygiene, Institute for Epidemiology and Prophylaxis of Radiation Injures, Research Centre for Radiation Medicine of Academy of Medical Sciences of Ukraine, WHO Collaborative Centre, Kiev).

Considerable strides have been made in the recent past in the knowledge and understanding of the effects of ionising radiation on the developing brain. A dose of 10 mSv is postulated to cause a reduction in IQ (intellectual quotient) of 0.3 [Corbett R., 1998]. The developing human brain is substantially more susceptible to teratogenic insults than most other embryonic and foetal structures [ICRP Publication 49, 1986].

The brain develops in 4 overlapping stages. The main developmental event of the first stage (0–7 weeks after fertilisation) is the commencement of neuronal mitosis during which the brain produces two to three times the full adult complement of neurones [Teicher M.H. et al., 1997]. Impaired cell division presumably gives rise to fewer neurones and may result in dysraphic abnormalities (at 3–4 weeks), cerebellar agenesis (at 4–10 weeks) and small head size (at 3–12 weeks) [ICRP Publication 49, 1986].

The second stage (8–15 weeks) is the first critical period of cerebrogenesis and corresponds to the most rapid proliferation of neuronal elements and substantial migration of neurones to the neocortex from their proliferative zones near the cerebral ventricles [Rakic P., 1978,1994; Sidman R.L., Rakic P., 1982]. Disturbances in cell migration may result in ectopic grey matter and dysplasia [ICRP Publication 49, 1986]. Learning disorders and some form of mental retardation may arise from abnormal migration [Teicher M.H. et al., 1997].

The third stage (16–25 weeks) is the second critical period of cerebrogenesis and corresponds to the progress of neuronal differentiation and synaptogenesis and the beginning of the formation of brain architecture [ICRP Publication 49, 1986]. The most striking neurobiological event at this stage is programmed cell death or apoptosis, when more than 50% of migrated neurones are eliminated prior to birth [Teicher M.H. et al., 1997]. The recently proposed neurodevelopmental theory of the genesis of schizophrenia shows that the second trimester of pregnancy is critical, and disturbed neuronal apoptosis is considered as a key neurobiological abnormality leading to schizophrenia [Saugstad L.F., 1998]. Programmed cell death, essential to the development of the normal brain and its adnexa, could be accelerated or otherwise altered by ionising radiation [ICRP Publication 49, 1986].

The fourth stage (26+ weeks) indicates cell differentiation, progressive growth of dendrites and axons, further formation of synapses and cerebral cytoarchitecture [ICRP Publication 49, 1986; UNSCEAR, 1993]. Synaptic development is also characterised by distinct waves of overproduction and elimination [Teicher M.H. et al., 1997]. Possible damage of thalamocortical innervation (at 24–33 weeks) is indicated by abnormal cortical differentiation, and by involution of subpial granular layer (at 24–38 weeks) — so-called marginal heterotopias [ICRP Publication 49, 1986].

Over the years, the Atomic Bomb Causalty Commission (ABCC) and its successor, the Radiation Effects Research Foundation (RERF), have established several overlapping samples of individuals prenatally exposed to the atomic bombing of Hiroshima and Nagasaki. According to the DS86 system of dosimetry there are 1,544 clinical samples of prenatally exposed survivors from a sample of 1,599 (including 509 nonexposed persons) derived from the T65DR system of dosimetry. Severe mental retardation has been clinically diagnosed in 30 (5 in nonexposed) children [Otake M., Schull W.J., 1984; ICRP Publication 49, 1986]. Analysis of the Koga intelligence test scores obtained in 1955 on the prenatally exposed survivors has revealed a progressive shift downwards in the distribution of these scores with increasing exposure. There is an apparent dose-related reduction in mean IQ for the groups irradiated in the periods 8–15 weeks and 16–25 weeks after fertilisation. This effect is still apparent when the seriously retarded are excluded from the analysed population [Shull W.J., Otake M., 1985].

Data on the incidence of severe mental retardation as well as variation in intelligence quotient (IQ) and school performance show significant effects on those survivors exposed 8–15 and 16–25 weeks after ovulation. Studies of seizures also exhibit a radiation effect in survivors exposed 8–15 weeks after ovulation. Magnetic resonance imaging of the brains of some mentally retarded survivors has revealed a large region of abnormally situated grey matter, suggesting an abnormality in neuronal migration. Radiation-related small head size is related to a generalised growth retardation [Otake M., Schull W.J., 1998]. A recent reanalysis of the dosimetry data indicated that the dose threshold for the development of mental retardation after intrauterine irradiation at gestation terms of 8–15 weeks is 0.06–0.21 Gy. At gestation term of 16–25 weeks, it is 0.25–0.87 Gy [Otake M. et al., 1996].

The question of the increased lifetime prevalence of schizophrenia in survivors prenatally exposed to atomic bomb radiation is still open to discussion [Imamura Y. et al., 1995]. Among 1,867 prenatally exposed individuals, 18 subjects (0.96%) had developed schizophrenia later in life. The prevalence was significantly higher in people exposed in the second trimester of pregnancy than in those exposed in the third trimester. The closer they had been to the

hypocentre, the higher was the prevalence. No statistically significant linear relationship was found [Imamura Y. et al., 1999].

Brain damage due to prenatal exposure was recognised by World Health Organisation (WHO) as a priority area in the assessment of the health consequences of the Chernobyl accident. Such acknowledgement led to the establishment of the WHO Pilot Project «Brain Damage in Utero» of the International Programme on the Health Effects of the Chernobyl Accident (IPHECA). Analysis of the results in the three countries (Belarus, Russian and Ukraine) has shown the following:

a) incidence of mild mental retardation in prenatally irradiated children is higher when compared with the control group;

b) an upward trend was detected in cases of behavioural disorders and in changes in the emotional problems in children exposed *in utero*;

c) incidence of borderline nervous and psychological disorders in the parents of prenatally irradiated children is higher than that of controls.

On the basis of the investigations it was impossible to arrive at a final conclusion on the relationship between an increase in the number of mentally retarded children and exposure to ionising radiation due to the Chernobyl accident because of an absence of dosimetric support of the studies [Souchkevitch G.N., Tsyb A.F. (Eds.) 1996; Nyagu A.I. et al., 1996; Kozlova I.A. et al., 1999].

Recently some related studies have been published. Children irradiated *in utero*, living on the radioactively contaminated areas in Russian Federation (Tula Region, ^{137}Cs deposition density 185–555 kBq·m^{2}), at the age of 1–7 years had the highest indices of mental morbidity and were more likely to display borderline intelligence and mental retardation. This morbidity was linked by the authors to radiation [Ermolina L.A. et al., 1996].

In Belarussian prenatally irradiated children, especially those exposed in 8–15 weeks, there were revealed more functional and organic disorders of central nervous system (CNS), borderline intelligence quotients (IQ) and abnormal EEG that were firstly linked to both radiation and psychosocial factors [Gayduk F.M. et al., 1994]. However, further these mental disorders among Belarussian children irradiated *in utero* were recognised as a result of sociodemographic and socio-cultural factors only [Igumnov S.A., 1996]. Among these children there were revealed an increased prevalence of specific developmental speech-language and emotional disorders, as well as a lower mean full scale IQ and more cases of borderline IQ, which did not show the existence of a dose-effect relationships. No statistically significant distinctions in average IQ were found between the different subgroups of children in relation to the gestational age at the time of the Chernobyl accident. The authors attributed these disorders exclusively to unfavourable social-psychological and social-cultural factors [Kolominsky Y. et al., 1999]. At the same time, the same authors concerning the same children recently reported that average IQ for the subgroup of highly exposed children (thyroid doses more than 1 Gy) was lower in comparison with average IQ for the whole exposed group (85.7±6.4 vs 89.6±10.2 at the age of 6–7 years, P=0.014; 89.1±7.1 vs 94.3±10.4 at age 10–12 years, P=0.003) [Igumnov S., Drozdovitch V., 2000).

In contrast to the results of the WHO Pilot Project «Brain Damage in Utero» and another relevant studies, there are three recently published papers [Bromet E.J. et al., 1998,2000; Litcher L. et al., 2000] where the authors concluded that 1) the mental and physical health of evacuee and non-evacuee children is similar and quite normal [Bromet E.J. et al., 1998]; 2) the evacuee children (including irradiated *in utero*) were not different from their classmates based on data derived from objective and on the majority of the subjective measures used to assess attention, memory, intelligence and school performance [Litcher L. et al., 2000]; 3) more evacuee mothers subjectively reported memory problems [Litcher L. et al., 2000] and somatic symptoms [Bromet E.J. et al., 1998,2000] in their children than classmates' mothers; 4) greater Chernobyl-focused anxiety is associated with slightly poorer performance on measures of attention [Litcher L. et al., 2000]; 5) the most important risk factors were maternal somatization and Chernobyl-related stress symptoms [Bromet E.J. et al., 2000]. However, as noted the authors, no dosimetric data were available, and there were no normative data in Ukraine for the measures used in the study [symptoms [Bromet E.J. et al., 2000; Litcher L. et al., 2000].

In the frame of the WHO Pilot Project «Brain Damage in Utero» we have previously revealed a significant increase of borderline and low range IQ, emotional and behavioural disorders, a decrease in high (IQ>110), as well as statistically significant higher prevalence of mental retardation (IQ<70) in Ukrainian prenatally irradiated children compared to controls: 21 (3.9%) vs. 12 (1.6%) correspondingly (χ^2=6.27; df=1; P<0.05) [Nyagu A.I. et al., 1996,1998]. Besides, we found that the thyroid-stimulating hormone (TSH) level grows with foetal thyroid dose increase with the 0.3 Gy threshold [Nyagu A.I. et al., 1993]. The radiation-induced malfunction of the thyroid-pituitary system was proposed as one important biological mechanism in the genesis of mental disorders in prenatally irradiated children [Nyagu A.I. et al., 1996,1998]. It was hypothesised that the cerebral basis of mental disorders in the prenatally irradiated children is the malfunction of the left hemisphere limbic-reticular structures, particularly in those exposed at the 16–25 weeks of gestation that obviously reflect developmental abnormalities of brain structure and function as a result of interaction of prenatal and post-natal factors where it is possible to assume radiation effects on the developing brain. It was also proposed that the left hemisphere is more vulnerable to prenatal irradiation than the right [Loganovskaja T.K., Loganovsky K.N., 1999].

Thus, in the majority of studies an increased prevalence of cognitive, emotional and behavioural impairments have been revealed in prenatally children exposed as a result of the Chernobyl accident. An at issue point remains the contribution of prenatal irradiation of a foetus and, especially, of the foetal thyroid gland to the genesis of brain damage in these children.

The objectives of our recent study was the psychometric, neurophysiological and neuropsychiatric (according to the International Classification of Disease, 10th Revision (ICD-10) criteria) characterisation of acutely prenatally irradiated children. This study involves acutely prenatally exposed children — born between April 26th, 1986 and February 26th 1987 from pregnant women at the time of the accident who had been evacuated from the 30-kilometer zone surrounding the Chernobyl NPP to Kiev — and their classmates. This sample seems to be optimal for examination of possible distinguished effects of exposure in different periods of cerebrogenesis.

Design and Sample. The design was a cross-sectional assessment of children who were in utero (born between April 26th, 1986 and February 26th, 1987) at the time of the Chernobyl accident (April 26th, 1986) and their mothers have been evacuated to Kiev. This group was acutely prenatally exposed to both radiation and non-radiation factors at the time of explosion, being at the Chernobyl exclusion zone, and evacuation route. Inhabitants of the town of Pripyat (n=49,360) and railway station Yanov (n=254) were evacuated on April 27th, 1986, residents of the 10-kilometre zone surrounding of the Chernoby NPP (n≈10,000) — on May 2nd — 3rd, 1986, since May 4th, 1986 stepwise evacuation of population of the 30-kilometre zone surrounding of the Chernobyl NPP was began. To the middle of August, 1986 there were evacuated 90,784 people from 81 settlements of Ukraine [National Report of Ukraine, 1996].

Obviously, that acutely prenatally exposed children-evacuees from Pripyat towards Kiev are the most adequate subcohort for comparison with the Japanese prenatally exposed to atomic bomb in Hiroshima and Nagasaki cohort in view of 1) acute prenatal exposure, and 2) as much as possible urbanised sample.

The WHO Pilot Project «Brain Damage in Utero» International Advisory Board estimated the number of births to be identified in the interval April 26th, 1986 to February 26th, 1987 in the Ukrainian radioactively contaminated areas (including the Chernobyl exclusion zone — 30-kilometer zone surrounding the Chernobyl NPP) as 1,400. However, in 1993–1994 we could indeed identify 1,021 (73%) of these children only, 272 (27%) of them evacuees from the Chernobyl exclusion zone. The reduced group of the identified prenatally irradiated children could be explained by both medical and spontaneous abortions (miscarriages) and migration. As a result of the WHO Pilot Project «Brain Damage in Utero» in Ukraine we have examined 544 (53%) prenatally irradiated children only, 115 (21%) of them were evacuees from the Chernobyl exclusion zone. The reduced number of the examined children irradiated *in utero* could be explained by: 1) migration and «dispersion» across Ukraine and other countries, 2) incorrect registration as prenatally irradiated children, 3) local organisational problems, and 4) refuses to be examined.

In 1997–1998 according to the database of the National Register of Ukraine we identified the official cohort of prenatally irradiated children in Ukraine consisted of 733 children including 278 (38%) children born from mothers who had been evacuated from the Chernobyl exclusion zone in 1986. 145 (52%) of them live in Kiev, 133 (48%) — in 26 regions of Ukraine (3–10 children per region). Besides, we have identified additional 69 prenatally irradiated children-evacuees living in Kiev according to the data of the Specialised Clinical and Epidemiological Register (SCER) of the Research Centre for Radiation Medicine (RCRM) of Academy of Medical Sciences (AMS) of Ukraine. Thus, we have identified 347 prenatally irradiated children-evacuees including 214 (62%) living in Kiev. Among the latest there is the subcohort consisted of 182 (85%) children-evacuees from the town of Pripyat.

From the subcohort of 182 prenatally irradiated children-evacuees from the town of Pripyat living in Kiev we randomly selected 100 (55%) children for the study (acutely exposed group). The comparison group consisted of 100 gender- and age-matched children selected from the same classrooms as the children of acutely exposed group. Children of both group were officially included to the SCER of the RCRM of AMS of Ukraine and were profoundly medically examined by general paediatrist, paediatrist-psychoneurologist, paediatrist-endocrinologist, paediatrist-Ear-Nose-Throat (ENT), paediatrist-ophtalmologist, paediatrist-cardiologist, paediatrist-haematologists, paediatrist-pulmonologists, paediatrist-gastroenterologists, paediatrist-surgeon, paediatrist-gynecologist (for girls), and genetics using general and biochemical blood tests, immunological tests, urine tests, coprogram, thyroid and visceral ultrasonography, electrocardiogram (ECG), electroencephalogram (EEG), rheoencephalogram (RhEG) as well as fibrogastoscopy, cardiac ultrasonography, and magnetoresonance imaging (MRI) for diagnostic reasons. These examinations have been carried out at the Children Department of the Out-Patients' Clinic of the Radiation Register of the RCRM of AMS of Ukraine.

It should be emphasised that neuropsychiatric assessments presented here are based on neurological and psychiatric examinations, psychometry of both children and their mothers, and conventional and computerised EEG, which have been carried out by us and associates at the Neurology Department of the RCRM of AMS of Ukraine.

The assessments took place in 1997–1999 when the children were 10–12 years old.

Estimation of Prenatal Age at Exposure. The most important single factor in determining the nature of the insult to the developing brain from ionising radiation exposure is gestational age. There are possible errors in the estimation of prenatal age at exposure. Postovulatory age is usually estimated from the onset of the last menstrual period, and adjustment is then made for the differences between that date and the probable date of fertilisation (usually taken to be 2 weeks later). Women with irregular menstrual cycles or who miss a menstrual period could erroneously identify the onset of their last cycle [ICRP Publication 49].

In order to avoid the aforementioned uncertainties concerning the estimation of prenatal age at the time of the Chernobyl accident we used the adapted formulas offered for estimation of prenatal age at atomic bombing in Hiroshima and Nagasaki [Otake M. et al., 1991]:

Days of pregnancy (Y) = 280 — (date of birth — April 26th, 1986),

where the day of birth having been obtained by interview with the mothers of the children and the mean duration of pregnancy is taken to be 280 days.

Gestational weeks after fertilisation at the time of the accident were calculated by the following equation:

Gestational weeks (G) = (Y — 14 days) / 7 days,

where G was taken to be zero if G<0.

Dosimetry. Individual reconstruction of foetal doses, foetal thyroid doses and foetal doses on the brain has been carried out in the Department of Dosimetry and Radiation Hygiene (Chief — Prof. I.A. Likhtariev) of the RCRM of AMS of Ukraine. It should be stressed that individual reconstruction has been carried out for the all children of the both acutely exposed group and comparison group due to the Kievers were also exposed to the Chernobyl accident fall-outs although significantly less than evacuees.

The main sources of irradiation of pregnant women were as follows: 1) external γ-irradiation of the whole body; 2) irradiation of thyroid by radioactive iodine isotopes; 3) internal irradiation by inhaled radionuclides; 4) internal irradiation by radioactively contaminated food. The dose depended on the settlement, the route of evacuation, and the places of intermediate and final evacuation. The estimation of individual doses was carried out by the methods of retrospective dosimetry that were elaborated on the base of measurements of the dynamic of exposure dose rate (EDR) at the settlements, analysis of 30,000 «route sheets» (information on clear address at the settlement, the date ant the time of evacuation, the route of evacuation, the place of intermediate and final evacuation), direct measurements of radioactive iodine content in 10,000 evacuees, ^{137}Cs deposition density at the place of intermediate evacuation [Likhtarev I.A. et al., 1994; Repin V.S., 1996].

Reconstruction of foetal doses was based on reconstruction of doses of pregnant women and further estimation of foetal doses. At estimation of foetal dose due to external irradiation the screening properties of mother's body were taking into account, and at estimation of thyroid foetal dose — mother's thyroid dose. Shield factor of buildings in towns was taken to be 10, in rural settlements — 3. Behavioural factor for pregnant women was taken to be 0.4.

Summarised dose on the whole foetus was taken to be equal to the dose of pregnant woman. The tissue-equivalent human phantom was exposed to real Chernobyl fall-outs in order to calculate the dose on the foetal human brain. At the places of foetal organs in the phantom LiF detectors with sensitivity 0.01 mSv were disposed. The transfer coefficient from EDR to equivalent dose on the foetal brain (K_{dbrain} = 0.57 $\cdot 10^{-2}$ mSv per 1 mR $\cdot h^{-1}$) was obtained, which does not depend on the prenatal age due to screening of foetal head by mother's pelvic bones [Repin V.S., 1996]. Finally, the dose on the foetal brain was calculated as the summarised dose of mother's external irradiation multiplied by K_{dbrain}.

In the earliest period after the Chernobyl accident (April 26th — May, 1986) internal irradiation by radioactive iodine had the most impact on the absorbed dose forming in population. Radioiodine from pregnant woman transfers to foetus quite rapidly. The rate of transfer increases in hundreds times in proportion to the term of pregnancy. Foetal thyroid begins its functioning at about the 8–12 weeks when it absorbed 50–70% of the whole radioiodine transferred to foetus. Radioiodine concentration is maximal at about the 20–25 weeks [Instruction of Ministry of Public Health of the USSR, 1986]. Consequently, foetal thyroid doses were reconstructed since the 8th week after fertilisation.

Foetal thyroid doses were calculated on the base of direct measurements of radioiodine contents in mothers' thyroid taking into account age and correction factors, ratio of radioactive iodine isotopes release from the reactor, wind speed and direction. The mean standardised thyroid dose of the adult population of Pripyat was taken to be 0.605 Gy (standard error 7%). Protective effect of stable iodine was taken to be 0.75. At present there are no officially adapted model for calculation of foetal thyroid dose that can be from 1 to 10 of mother's thyroid dose (*31, 32*). Taking into account that the coefficient of transplacentar transfer of iodine is 1 and iodine concentrations in maternal and foetal structures are equal maternal and foetal thyroid doses were taken to be equal and not depending on the prenatal age.

Intelligence assessment. The intellectual ability of children was assessed by the adapted and normalised version for the Ukrainian children of the WISC [Wechsler D., 1992], which was carried out by Prof. Yu.Z. Gilbukh and colleagues (1992) from the Research Institute of Psychology of Academy of Pedagogic Sciences of Ukraine. The child's performance was summarised in three composite scores, the verbal, performance and full scale IQs, which provide estimates of the individual's intellectual abilities.

Testing procedures were performed at standard conditions at the Neurology Department of the SCRM of AMS of Ukraine in a quite, adequately lit, well-ventilated room without an accompanying adult, seating and materials arrangement corresponded to recommendations by [Wechsler D., 1992; Gilbukh Yu.Z. (Ed.), 1992] together with co-operative relationships between the child and the examiner. The entire test was administered in a single session.

Following subtests of the WISC were used: verbal scale — information, vocabulary, similarities, and digit span; performance scale — picture completion, block design, object assembly, and coding. We used eight subtests only of the WISC, as manuals permit it, to predict a possible fatigue of children due to following testing and examinations. The sum of subtest scaled scores on the affected scale was prorated to obtain the verbal and performance score that was used to derive the IQ score. To prorate the child's score on four verbal and four performance subtests we multiplied the sum of the four scaled scores by 1.25. The sums of verbal and performance subtest scaled scores were prorated separately and the resulting verbal and performance scores were summed to yield the full scale IQ score.

Scaled score equivalents of raw scores, standardised to age, and IQ equivalents of sums of scaled scores for verbal, performance, and full scales were obtained from the norms and conversion tables for Ukrainian children [Gilbukh Yu.Z. (Ed.), 1992]

Cerebral electrical activity assessment. Quantitative electroencephalography (QEEG) is a set of non-invasive tools that are capable of quantitatively assessing activity of the brain with sensitivity and temporal resolution superior to those of any other imaging methods. The EEG power spectrum is quite stable and characteristic for healthy human beings. At the same time many brain dysfunctions, including environmentally induced, can be distinguished by QEEG with specificity of about 95% and sensitivity of 60–95% [Hughes J.R., John E.R., 1999]. The level of sensitivity and specificity

of QEEG for brain injury (which is possible to expect in acutely prenatally irradiated children) meets the standards of sensitivity and specificity maintained for MRI, sonograms, blood analysis, and other common clinical diagnostic measures [Hoffman D.A. et al., 1999]. Thus, QEEG is one of the most adequate diagnostic technologies for assessment of radiation effects on the brain.

Neurophysiological investigations were carried out in the neurophysiological laboratory of the Department of Neurology, RCRM of AMS of Ukraine in the first half of the day during the passive awake state of a child. The children were nonmedicated for 3 and more days.

Brain electrical activity was recorded monopolarly using the International 10–20 System on 19 channels, referenced to linked ears on an brain potential analyser «Brain Surveyor», SAICO, Italy. EEG were registered at 1) passive awakeness, eyes closed — 1 min, 2) passive awakeness, eyes open — 30 s, 3) hyperventilation, eyes closed — 3 min, and 4) passive awakeness after hyperventilation, eyes closed — 1 min. Spectral analysis of brain electrical activity was conducted. Epochs of analysis consisted of 60 seconds, and analysed frequencies were in the 1–32 Hz range. Estimation and interpretation of conventional and QEEG activity were performed according to E.A. Zhirmunskaya's algorithm (1991) together with paediatric EEG classic manuals [Farber D.A., Alferova V.V., 1972; Zenkov L.R., Ronkin M.A., 1991; Niedermeyer E., DaSilva F.L. (Eds.), 1993].

Additional measurements. This report focuses on intelligence and EEG assessment as well as clinical psychiatric and neurological diagnostic in the children. At the same time the children were also measured by a number of psychological tests, analysis of which we hope to present further. For this paper these measures were used for verification of clinical diagnosis.

Aiming to follow up the children who had been examined before, parents were asked to complete a Russian translation of the Rutter A (2) Behaviour Rating Scale which was used in the WHO Pilot Project «Brain Damage in Utero» in 1993–1994. Parental rating assesses problems associated with health, hyperactivity, and behavioural and emotional disorders [Rutter M.A., 1967]. Russian translation of Achenbach's Child Behaviour Checklist (CBCL), the questionnaires for the children and the parents, was also used [Achenbach T.M., 1991; Carter A.S. et al., 1995]. Moreover, the Children Questionnaire of Neurosis (CQN) by V.V. Sednev (1998), validated and standardised for Ukrainian children, was applied for revealing of depression, asthenia, behavioural disorders, autonomic nervous system dysfunction, sleep disorders, anxiety, and sincerity.

Following the WHO Pilot Project «Brain Damage in Utero», mothers were also asked to complete the General Health Questionnaire (GHQ-28), reflecting the level of her mental adaptation, the level of anxiety and depression, and also social functions [Goldberg D., Bridges K., 1987; Goldberg D., Williams P., 1988]. The vocabulary subtest of the Wechsler Adult Intelligence Scales (WAIS) was used to estimate the verbal intelligence of the mother. Moreover, posttraumatic stress disorders (PTSD) in mothers were assessed by the Impact of Events Scale and Arousal Scale of PTSD [Horowitz M.J., 1976], as well as mother's unmasking depression — by the Self-rating Depression Scale [Zung W.W.K., Wonnacott T.H., 1970].

Finally, mothers were asked for demographic background, family history, educational level of the family, social and economical status as well as they completed a standardised questionnaire on radiation history. On the base of the Diagnostic and Statistical Manual of Mental Disorders, 4th Edition (DSM-IV) Scale of Stress-Factors we elaborated a standardised questionnaire on stress-factors related to the Chernobyl accident that reflects a severity of *real* stress events (but not affective symptoms or Chernobyl-focused anxiety) following the Chernobyl accident to the birth of the child. For instance, separation with the husband and family during evacuation; absence information about the husband, participated in emergency work at the Chernobyl NPP, and family; consumer problems at the places of evacuation; low level of medical care, etc.

Clinical Psychiatric and Neurological Assessment. The children of the both acutely prenatally exposed and comparison groups were examined by standardised clinical psychiatric interview and standardised clinical neurological examination at the Department of Neurology, RCRM of AMS of Ukraine. The mental disorders and the diseases of the nervous system were assessed according to the diagnostic criteria of ICD-10 (Chapter V: Mental and Behavioural Disorders & Chapter VI: Diseases of the Nervous System). ICD-10 diagnostic was made on the base of clinical psychatric and neurological examinations, psychometry, conventional and QEEG taking into account the results of the profound clinical, laboratory, and instrumental examination at the Children Department of the Out-Patients' Clinic of the Radiation Register of the RCRM of AMS of Ukraine, including MRI of the brain for diagnostic reasons.

Statistical Analysis. Statistical processing included descriptive statistics, *t* test, Chi-square tests, relative risk (RR) assessment, correlation and multiply regression analyses [Kuzma J.W., 1984]. The paired *t* test was used to analyse data when a pair of measurements was obtained on each individual [Montgomery D.C., 1976]. The Bonferroni correction was used when multiple statistical test were performed [Kirk R.E., 1982]. Statistical analysis was performed using STATISTICA 5.0 and MS EXCEL 97 software.

Descriptive Characteristic. The age (M±SD) was 11.3±0.4 years for the children from acutely exposed group and 11.48±0.82 for classmates; 54% of the evacuee children and 56% of the comparison groups were male.

Distribution of children by prenatal age at the time of the Chernobyl accident is shown in figure 4.5.

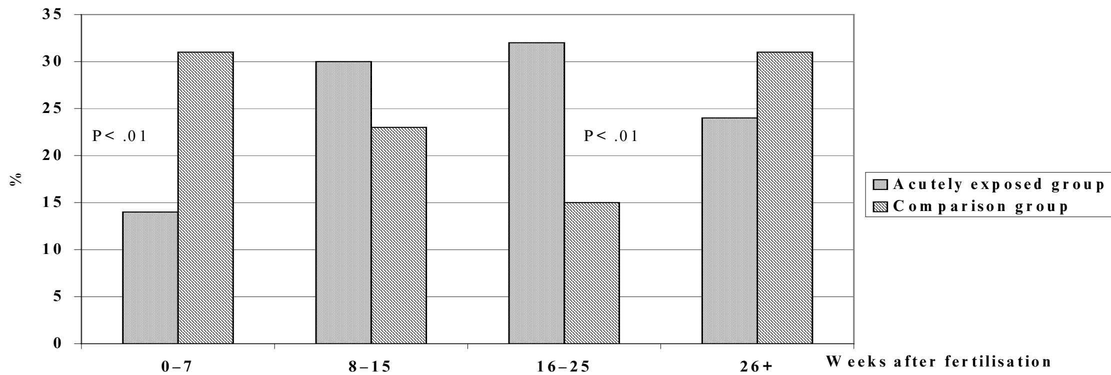


Figure 4.5. Distribution of children by prenatal age at the time of explosion (April 26th, 1986)

Taking into account a randomised procedure of the children selection, a significant reduction of number of the children irradiated at 0–7 weeks after fertilisation in acutely exposed group in comparison with classmates (14% vs. 31%; χ^2=8.29; P<0.01) could be explained as the result of abortions and/or miscarriages among pregnant women-evacuees. However, it is difficult to explain why there is also a significant reduction of the number of children from Kiev at 16–25 weeks after fertilisation in comparison with acutely exposed group (32% vs. 15%; χ^2=8.04; P<0.01).

Mean, standard deviation, and range of the individual foetal doses (summarised foetal dose of external irradiation, mSv; equivalent dose on the foetal brain, mSv; cumulated thyroid foetal dose (since the 8th weeks after fertilisation), Gy) for the two groups of children are presented in table 4.4. It is clear that the children of the two group correspond to the Japanese sample [ICRP Publication 49, 1986]: prenatally exposed to atomic bomb radiation survivors of the foetal dose category less than 0.01 Gy (n=1,201) — to the Ukrainian comparison group, and those of the dose category 0.01–0.09 Gy (n=322) — to the Ukrainian acutely exposed group.

Table 4.4

INDIVIDUAL FOETAL DOSES

Dose	Value	Acutely exposed group	*t*-test	P	Comparison group
Summarised foetal dose of external irradiation, mSv	M±SD Range	31.9±14.4 (10.74 – 92.52)	21.31	<0.001	1.2±0.5 (0 – 2.67)
Equivalent dose on the foetal brain, mSv	M±SD Range	20.7±9.43 (6.98 – 60.12)	21.14	<0.001	0.8±0.5 (0 – 2.52)
Cumulated thyroid foetal dose (since the 8th weeks after fertilisation), Gy	M±SD Range	0.66±0.32 (0.22 – 2.04)	17.52	<0.001	0.04±0 (0.041)

Distribution of summarised foetal dose of external irradiation, equivalent dose on the foetal brain, mSv, and cumulated thyroid foetal dose (since the 8th weeks after fertilisation) among the children of the acutely exposed group are shown in figures 4.6, 4.7, and 4.8 correspondingly. These foetal doses did not differ depending on the prenatal age at the time of the accident.

As seen in figure 4.8, radiation exposure to foetal thyroid was quite significant: the permissible dose limit of 0.3 Gy on the thyroid [Ilyin L.A., 1994] was exceeded in 97% of the children of the acutely exposed group, moreover, the foetal thyroid of 17% of them was exposed to 1 Gy and more.

Among the acutely exposed group there were 5% disabled children and their disability was officially recognised to be caused by the consequences of the Chernobyl accident. Except one child with haemophilia, the four another children had neuromental disorders: moderate mental retardation (1), epilepsy (1), and encephalopathy (2). The child with haemophilia attended the school programme at home, the child with moderate mental retardation was institutionalised into the special boarding school. Moreover, 7% of the children-evacuee systematically missed the school and attended the school programme at home due to different medical reasons except flu (epilepsy, paroxysmal states, behavioural problems, fatigue, headache, lack of concentration, exhaustion, etc). The other children attended the public schools.

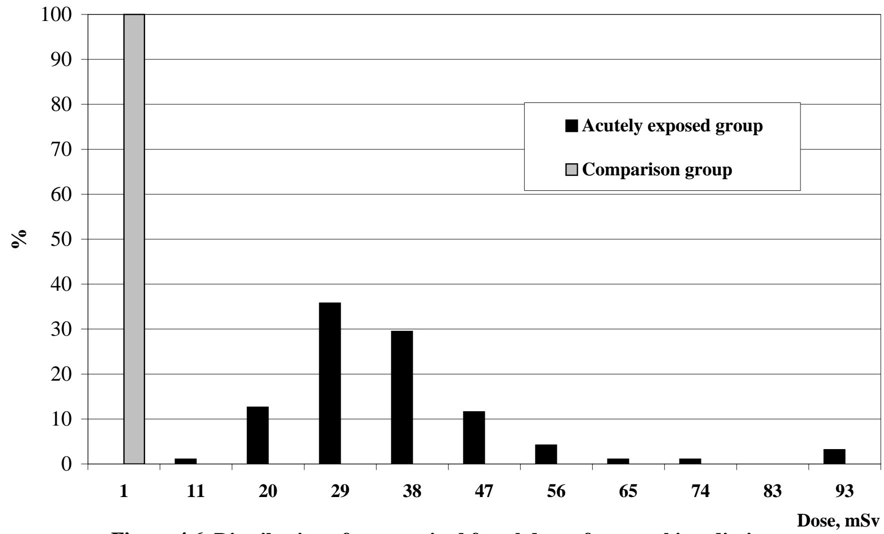


Figure 4.6. Distribution of summarised foetal dose of external irradiation

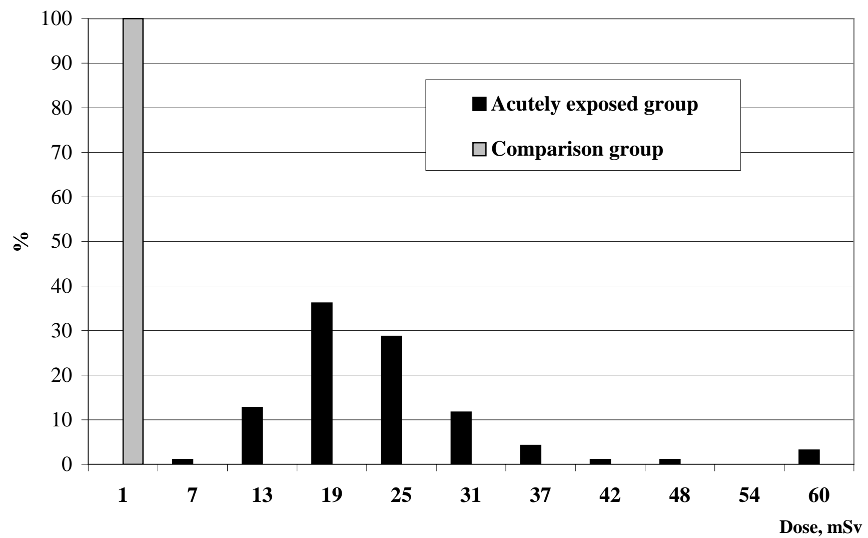


Figure 4.7. Distribution of equivalent doses on the foetal brain

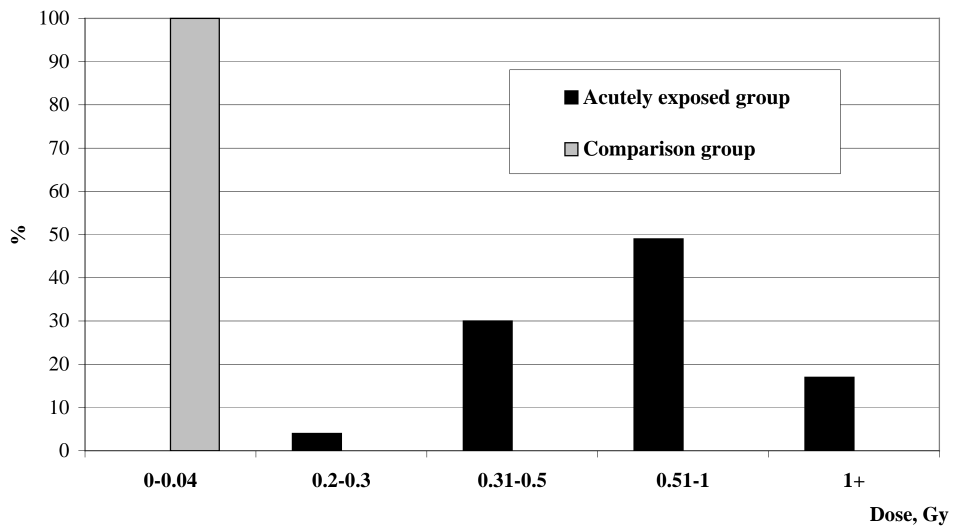


Figure 4.8. Distribution of foetal thyroid doses

General health of children in the countries of the former U.S.S.R. is assessed according to the five «health groups»: the 1st health group includes absolutely healthy children; the 2nd — practically healthy children (no complaints, but there are some subclinical symptoms revealed by profound clinical, laboratory and instrumental examination only); the 3rd — children with chronic disease(s) in remission; the 4th — handicapped children with chronic disease(s) in exacerbation demanding active therapeutical intervention and/or institutialisation; the 5th — handicapped children with severe chronic disease(s) in decompensation stage demanding hospitalisation with absence of learning and self-service. As seen in figure 4.9, among the children-evacuees there were significantly less practically healthy children (the 2nd health group) (10% vs. 36%; χ^2=19.09; P<0.001) and significantly more children with chronic diseases in remission than in classmates (87% vs. 64%; χ^2=14.3; P<0.001) (the 3rd health group). The 3rd health group in the both groups was predominantly comprised by chronic decompensated tonsillitis and adenoids of the 2nd–3rd severity degree; cardiomyopathy; chronic inflammatory diseases of stomach and intestine at the stage of exacerbation; diffusive thyroid hyperplasia of the 3rd degree, euthrosis (normal thyroid functions); moderate to severe disorders of refraction (hypermetropia, myopia, astigmatism). The conclusion about the health groups is given by experts of the Children Department of the Out-Patient's Clinic of the Radiation Register of the RCRM of AMS of Ukraine. No single child from the both groups was recognised as absolutely healthy.

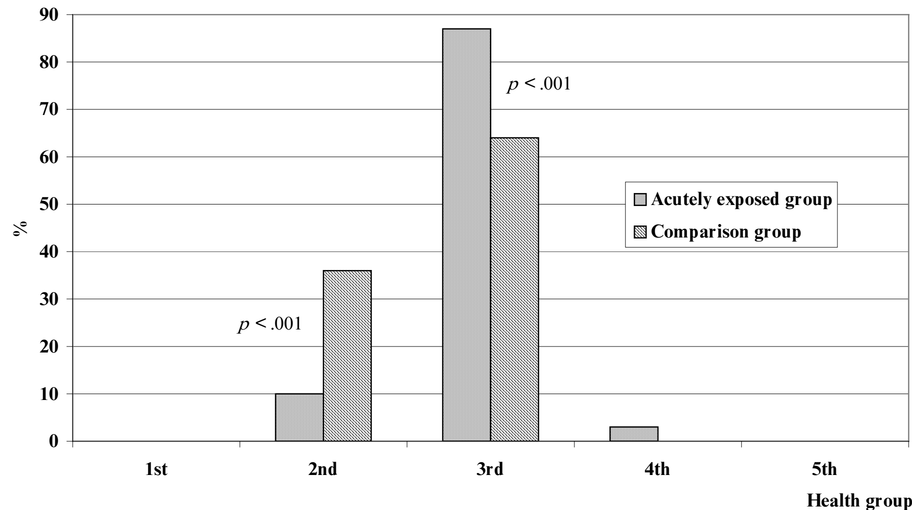


Figure 4.9. Distribution of children by the health groups

The acutely exposed children in comparison with the classmates had more often moderate complications of postnatal period, paroxysmal states, including epileptical, enuresis/encopresis at the age more than 4 years. The evacuated mothers had more often moderate abnormalities and toxicosis of pregnancy (63% vs. 32% correspondingly, χ^2=19.27; P<0.001).

In the families of the acutely exposed children in comparison with the classmates living conditions were better; 2 and upwards children were more often; 85% of the fathers took part in the Chernobyl accident consequences clean up; 8% of the mothers were disabled and their disability was officially recognised to be caused by the consequences of the Chernobyl accident; the fathers took more alcoholic drinks and tobacco; less number of the parents graduated a university and more — had specialised secondary education.

According to our questionnaire on stress-factors related to the Chernobyl accident, a severity of *real* stress events was dramatically more pronounced in the mothers-evacuees than in the classmate's mothers: 14.9±6.1 vs. 3±5.3, t =10.56, P<0.001. In spite of the mothers-Kyievers had not been apparently exposed to *real* Chernobyl-related stress-events (extreme situations) as evacuation, family separation etc., in contrast to the mothers-evacuees, the mothers of the both groups have quite significant symptoms of Chernobyl-related PTSD, which were more pronounced in the mothers-evacuees. Mean score of the Impact of Events Scale and Arousal Scale of PTSD in the mothers-evacuees was 18.8±10.6 and the mothers-Kyievers — 14.8±9.9, t = 2.02, P<0.05.

Mother's unmasking depression estimated by the Self-rating Depression Scale was higher in the mothers-evacuees than in the classmate's mothers: 56.3±10.4 vs. 42±12.5, t=5.22, P<0.001.

The mothers-evacuees had also worse than the classmate's mothers mental adaptation and social functions as well as more symptoms of anxiety and depression estimated by the GHQ-28: 9.6±9.6 vs. 4.8±4.9, t=3.71, P<0.001.

The verbal intelligence of the mother measured by the vocabulary subtest of the WAIS was lower in the mothers-evacuees than in the mothers-Kyievers: 43.2±10.9 vs. 52.4±8.4, t = –5.09, P<0.001.

Intellectual ability of children. Distribution of verbal IQ, performance IQ and full scale IQ among the children of the both groups is presented in table 4.5. Among the children of acutely exposed group in comparison with classmates there were significantly more children with an average verbal IQ of 91–110) (53% vs. 22%; χ^2=20.5; P<0.001) as well as significantly less of children with an high-advanced verbal IQ of 121–> (9% vs. 45%; χ^2=32.88; P<0.001) and an high-advanced full scale IQ of 121–> (27% vs. 55%; χ^2=16.21; P<0.001).

Table 4.5

DISTRIBUTION OF VERBAL IQ, PERFORMANCE IQ AND FULL SCALE IQ

IQ range	Acutely exposed group	χ^2	P	Comparison group
Verbal IQ <70–80	3	3.05	>0.05	0
81–90	9	3.19	>0.05	3
91–110	53	20.50	<0.001	22
111–120	26	0.04	>0.05	30
121–>	9	32.88	<0.001	45
Performance IQ <70–80	3	3.05	>0.05	0
81–90	3	3.05	>0.05	0
91–110	20	0.03	>0.05	19
111–120	27	0.6	>0.05	32
121–>	47	0.08	>0.05	49
Full scale IQ <70–80	3	3.05	>0.05	0
81–90	3	3.05	>0.05	0
91–110	33	3.03	>0.05	22
111–120	34	2.97	>0.05	23
121–>	27	16.21	<0.001	55

Mean values of all verbal subtests and performance subtest — picture completion of the WISC were significantly lower in the acutely exposed children in comparison with classmates (table 4.6). Although the mean verbal IQ, performance IQ, and full scale IQ in children of the both groups were in high range, acutely exposed group has a significantly lower mean verbal IQ (105.3±13.1 vs. 118.1±13; *t*=–6.94; P<0.001) and mean full scale IQ (112.1±15.4 vs. 120.9±11.5; *t*=–4.58; P<0.001). The mean performance IQ is not significantly different, however (117.3±18 vs. 119.2±10.2; *t*=–.92; P>0.05).

Table 4.6

WISC SUBTESTS, VERBAL IQ, PERFORMANCE IQ AND FULL SCALE IQ

Measure	Acutely exposed group (M3SD)	*t*-test	P	Comparison group (M3SD)
Verbal scale				
Information	9.8±2.5	–4.53	<0.001	11.4±2.5
Vocabulary	12.3±3.4	–6.84	<0.001	15.4±3
Similarities	11,4±2.5	–4.89	<0.001	13.2±2.7
Digit span	9.7±2.6	–3.6	<0.001	11±2.5
Performance scale				
Picture completion	14.8±3.4	–3.46	<0.001	16.2±2.2
Block design	12.5±3.5	–1.61	>0.05	13.2±2.6
Object assembly	10.9±3.3	–.72	>0.05	11.2±2.5
Coding	11.7±3.2	2.55	<0.05	10.6±2.9
Verbal IQ	105.3±13.1	–6.94	<0.001	118.1±13
Performance IQ	117.3±18	–0.92	>0.05	119.2±10.2
Full scale IQ	112.1±15.4	–4.58	<0.001	120.9±11.5

Note: Bonferroni corrected α-level of <0.004 was used to assess statistical significance (0.05 divided by 11 comparisons within measures of intelligence)

Taking into account a similar performance IQ in the both groups, significant WISC performance/verbal discrepancies ($IQ_{P–V}$ = performance IQ – verbal IQ), with verbal decrements, were revealed in acutely exposed group in comparison with classmates: 12.1±13.8 (*paired t* = 8.7, P<0.001) vs. 1.2±11.8 (*paired t* = 1, P>0.05); *t*=6; P<0.001.

WISC performance/verbal discrepancies take on clinical significance at the magnitude more than 25 points [Rutter M., Hersov L., 1985]. According to this criterion ($IQ_{P–V}$>25), among the acutely exposed group there are

significantly more children with disharmoniously developed intelligence due to verbal decrements than in the comparison group (17% vs. 4%; $\chi^2 = 8.99$; $P<.01$), especially among those irradiated at 16–25 weeks after fertilisation. Among the children irradiated at 16–25 weeks after fertilisation (from acutely exposed group) there were 9 children of all 17 (more than $^1/_2$) with $IQ_{P-V}>25$.

In table 4.7 intellectual development of children of both groups corresponding to different periods of cerebrogenesis at exposure is presented. There is a tendency towards a deterioration of full scale IQ and verbal IQ, as well as an increasing of intellectual disharmony (IQ_{P-V}) in children of acutely exposed group who were exposed at 16–25 weeks after fertilisation. Among those irradiated at 16–25 weeks the full scale IQ and verbal IQ are the lowest in acutely exposed group and intellectual disharmony is one of the lowest.

Table 4.7

INTELLECTUAL DEVELOPMENT OF CHILDREN CORRESPONDING TO DIFFERENT PERIODS OF CEREBROGENESIS AT EXPOSURE

Age in weeks after fertilisation	Acutely exposed group	*t*-test	P	Comparison group
Total Subjects	100			100
Full IQ (M±SD)	112.3±15.4	–4.58	<0.001	120.9±11.5
Verbal IQ (M±SD)	105.3±13.1	–6.94	<0.001	118.1±13
Preformance IQ (M±SD)	117.3±18	–0.92	>0.05	119.2±10.2
Intellectual disharmony IQ_{P-V} (M±SD)	12.1±13.8	6	<0.001	1.2±11.8
paired t	*8.7*			*1*
P	<0.001			>0.05
0–7 Subjects	14			31
Full IQ (M±SD)	110±14.7	–2.73	<0.01	122.2±11.9
Verbal IQ (M±SD)	103.9±15.3	–3.26	<0.01	119.4±13.5
Preformance IQ (M±SD)	115±14.6	–1.47	>0.05	121.4±10.7
Intellectual disharmony IQ_{P-V} (M±SD)	11.1±12.8	2.28	<0.05	2±11.4
paired t	*3.3*			*1*
P	<0.001			>0.05
8–15 Subjects	30			26
Full IQ (M±SD)	113.1±10.9	–1.37	>0.05	117.6±12.5
Verbal IQ (M±SD)	106.3±10.5	–2.59	<0.01	114.9±13
Preformance IQ (M±SD)	117.9±12	.74	>0.05	115.6±10.5
Intellectual disharmony IQ_{P-V} (M±SD)	11.6±10.9	3.29	<0.001	0.8±12.5
paired t	*5.8*			*0.3*
P	<0.001			>0.05
16–25 Subjects	32			15
Full IQ (M±SD)	109.2±20	–2.28	<0.05	120.5±13.5
Verbal IQ (M±SD)	102.7±15.5	–2.88	<0.01	117.1±16.2
Preformance IQ (M±SD)	114.7±23.3	–0.75	>0.05	118.3±9.7
Intellectual disharmony IQ_{P-V} (M±SD)	12±14	2.62	<0.01	1.3±12.6
paired t	*4.8*			*0.4*
P	<0.001			>0.05
26–term Subjects	24			31
Full IQ (M±SD)	116±13.1	–2.01	>0.05	122.3±9.1
Verbal IQ (M±SD)	108.3±11.2	–3.78	<0.001	119.6±10.7
Preformance IQ (M±SD)	121.4±18	0.3	>0.05	120.2±9.4
Intellectual disharmony IQ_{P-V} (M±SD)	13.1±17.6	3	<0.01	0.6±11.8
paired t	*3.7*			*0.3*
P	<0.001			>0.05

There were 157 children (85 in acutely exposed group and 72 in classmates) who were at the 8th and more weeks after fertilisation at the time of the accident. For 154 (98%) of these children the foetal thyroid dose was reconstructured. IQs of the children in proportion to the foetal thyroid dose is presented in table 4.8 and figure 4.10. All classmates and 4 children from acutely exposed group had the prenatal thyroid dose in the range of 0.04–0.3 Gy. It should be noted that the dose of 0.3 Gy on the thyroid was the dose limit for the children at the time of the Chernobyl accident [Ilyin L.A., 1994]. As it is shown in table 4.8 and figure 4.10, full scale IA and, especially verbal IQ, were reduced in dependece to the foetal thyroid dose. Performance IQ is slightly reduced after the foetal thyroid dose of >1 Gy only.

Table 4.8

FULL SCALE IQ, VERBAL IQ AND PERFORMANCE IQ AT PRENATAL EXPOSURE TO DIFFERENT THYROID DOSE

Thyroid doetal dose, Gy	Full scale IQ, M3SD	Verbal scale IQ, M3SD	Performance scale IQ, M3SD
0.04–0.3 (n=76)	119.6±10.8	116.6±12.3	118.0±9.5
0.31–0.6 (n=31)	113.3±15.2	106.9±12.1	118.0±17.9
0.61–1.0 (n=33)	113.2±14.9	105.5±12.7	119.3±19.2
1.0+ (n=14)	108.4±18.9	102.3±15.2	112.9±20.7

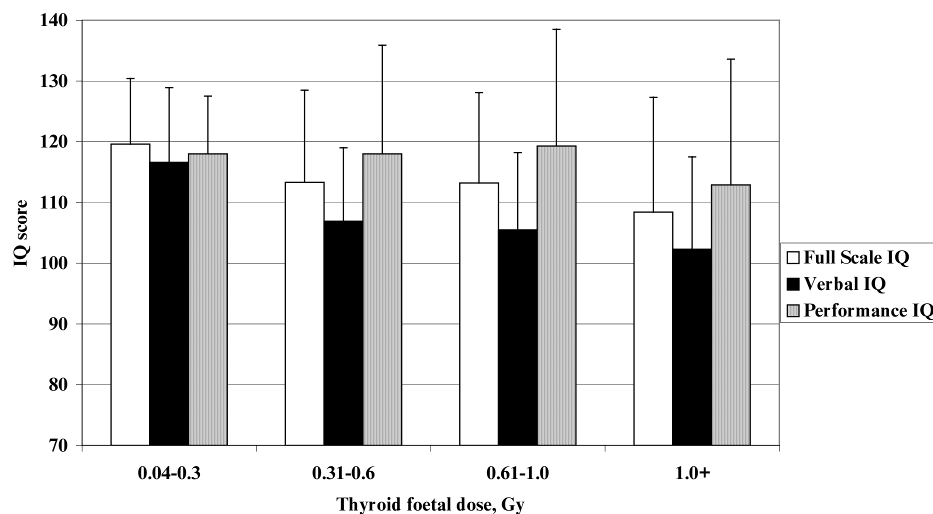


Figure 4.10. Children intelligence in proportion to the thyroid foetal dose

According to the results of regression analysis the children's intelligence is etiologically heterogeneous (table 4.9). Higher educational, intellectual, and economical levels of a family, as well as older parents at the time of childbirth (at the examined age ranges 18–35 years for the mothers and 19–42 — for the fathers) are the contributors towards a higher child intelligence. Higher doses of prenatal irradiation, especially foetal thyroid dose, more severe stressogenic events and additional mother's hazards in the prenatal period, worse a mother's mental health, as well as childbirth problems are the contributors towards a lower child intelligence.

Foetal thyroid dose seems to be the main predictor of verbal intelligence deterioration (regression coefficient = 0–.34–(–0.39); P<0.001) and WISC performance/verbal discrepancies, with verbal decrements (regression coefficient = –0.31; P<0.001) (table 4.9), especially among the children irradiated at 16–25 weeks after fertilisation (figure 4.11).

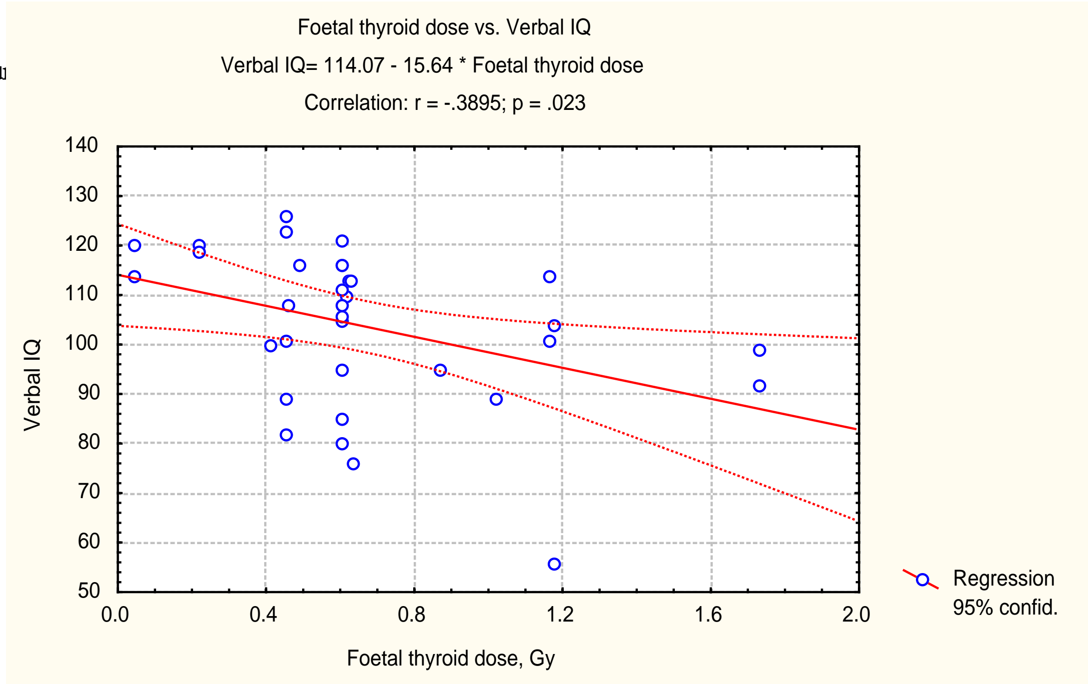
Table 4.9

REGRESSION ANALYSIS OF THE PREDICTORS OF THE CHILDREN'S INTELLECTUAL DEVELOPMENT

Predictor	Regression coefficient	$F_{(df1, df2)}$	P
Information subtest of WISC			
Mother's intelligence (vocabulary subtest of WAIS)	0.21	$9.2002_{(1,198)}$	0.003
Father's age	0.20	$8.1679_{(1, 198)}$	0.005
Father's educational level	0.18	$6.6469_{(1, 198)}$	0.01
Mother's age	0.18	$6.3917_{(1, 198)}$	0.01
Mother's educational level	0.14	$4.0504_{(1, 198)}$	0.04
Vocabulary subtest of WISC			
Thyroid foetal dose	–0.39	$25.7159_{(1,152)}$	0.000001
Mother's intelligence (vocabulary subtest of WAIS)	0.36	$28.9968_{(1,198)}$	0.000000
Foetal dose	–0.29	$18.3566_{(1, 198)}$	0.00003
Dose on the foetal brain	–0.29	$17.6903_{(1, 198)}$	0.00004
Stress-events after the accident during pregnancy	–0.15	$4.6808_{(1, 198)}$	0.03
Similarities subtest of WISC			
Thyroid foetal dose	–0.24	$8.4675_{(1,152)}$	0.004
Mother's intelligence (vocabulary subtest of WAIS)	0.22	$9.7155_{(1,198)}$	0.002
Dose on the foetal brain	–0.21	$9.0083_{(1, 198)}$	0.003
Foetal dose	–0.20	$8.5392_{(1, 198)}$	0.004
Stress-events after the accident during pregnancy	–0.16	$5.1838_{(1, 198)}$	0.02
Economic level of family	0.16	$5.0957_{(1, 198)}$	0.02
Mother's GHQ-28	–0.15	$4.6937_{(1, 198)}$	0.03
Digit Span subtest of WISC			
Thyroid foetal dose	–0.26	$10.5202_{(1,152)}$	0.001
Mother's intelligence (vocabulary subtest of WAIS)	0.24	$11.8890_{(1,198)}$	0.0007
Dose on the foetal brain	–0.24	$11.5737_{(1, 198)}$	0.0008
Foetal dose	–0.23	$11.0999_{(1, 198)}$	0.001
Mother's additional hazards during pregnancy	–0.15	$4.8516_{(1, 198)}$	0.03
Mother's Self-rating Depression Scale (Zung)	–0.15	$4.3983_{(1, 198)}$	0.04
Father's educational level	0.14	$4.2379_{(1, 198)}$	0.04
Verbal IQ			
Thyroid foetal dose	–0.34	$18.7662_{(1,152)}$	0.00003
Mother's intelligence (vocabulary subtest of WAIS)	0.33	$24.6009_{(1,198)}$	0.000002
Dose on the foetal brain	–0.28	$17.2540_{(1, 198)}$	0.00005
Foetal dose	–0.28	$17.1946_{(1, 198)}$	0.00005
Father's educational level	0.16	$4.8868_{(1, 198)}$	0.03
Economic level of family	0.15	$4.5543_{(1, 198)}$	0.03
Stress-events after the accident during pregnancy	–0.14	$3.9069_{(1, 198)}$	0.049
Mother's educational level	0.14	$3.9227_{(1, 198)}$	0.049
Picture completion subtest of WISC			
Economic level of family	0.26	$14.2983_{(1, 198)}$	0.0002
Mother's intelligence (vocabulary subtest of WAIS)	0.22	$10.0078_{(1,198)}$	0.002
Dose on the foetal brain	–0.19	$7.1427_{(1, 198)}$	0.008
Foetal dose	–0.18	$6.4733_{(1, 198)}$	0.01
Father's age	0.17	$6.2598_{(1, 198)}$	0.01
Father's educational level	0.16	$5.0650_{(1, 198)}$	0.02
Mother's GHQ-28	–0.16	$5.1748_{(1, 198)}$	0.02
Mother's educational level	0.15	$4.7358_{(1, 198)}$	0.03
Childbirth abnormalities	–0.15	$4.3178_{(1, 198)}$	0.04

Table 4.9 (continuation)

Predictor	**Regression coefficient**	$\mathbf{F}_{(df1, df2)}$	**P**
Block design subtest of WISC			
Mother's educational level	0.18	$6.9333_{(1, 198)}$	0.009
Economic level of family	0.17	$6.0673_{(1, 198)}$	0.01
Mother's PTSD	–0.14	$4.1347_{(1,198)}$	0.04
Object assembly subtest of WISC			
Father's educational level	0.18	$6.5096_{(1, 198)}$	0.01
Economic level of family	0.17	$6.1768_{(1, 198)}$	0.01
Mother's intelligence (vocabulary subtest of WAIS)	0.14	$4.0587_{(1,198)}$	0.04
Coding subtest of WISC			
Economic level of family	0.28	$17.1997_{(1, 198)}$	0.00005
Father's educational level	0.16	$5.3818_{(1, 198)}$	0.02
Mother's GHQ-28	–0.14	$4.0682_{(1, 198)}$	0.04
Performance IQ			
Economic level of family	0.32	$22.9500_{(1, 198)}$	0.000003
Mother's intelligence (vocabulary subtest of WAIS)	0.23	$10.6177_{(1,198)}$	0.001
Father's educational level	0.21	$8.7027_{(1, 198)}$	0.004
Mother's educational level	0.17	$5.8003_{(1, 198)}$	0.02
Disharmony of intellectual development $IQ_{P>V}$			
Thyroid foetal dose	0.31	$15.8215_{(1,152)}$	0.0001
Foetal dose	0.23	$11.5167_{(1, 198)}$	0.0008
Dose on the foetal brain	0.22	$10.5278_{(1, 198)}$	0.001
Economic level of family	0.19	$7.1229_{(1, 198)}$	0.008
Mother's Self-rating Depression Scale (Zung)	0.16	$4.9322_{(1, 198)}$	0.03
Full scale IQ			
Mother's intelligence (vocabulary subtest of WAIS)	0.32	$22.3837_{(1,198)}$	0.000004
Economic level of family	0.26	$14.4738_{(1, 198)}$	0.0002
Dose on the foetal brain	–0.20	$8.0329_{(1, 198)}$	0.005
Thyroid foetal dose	–0.20	$5.8691_{(1,152)}$	0.02
Father's educational level	0.20	$7.9749_{(1, 198)}$	0.005
Foetal dose	–0.19	$7.5897_{(1, 198)}$	0.006
Mother's educational level	0.15	$4.6695_{(1, 198)}$	0.03
Verbal IQ *(children exposed at 16–25 weeks after fertilisation, n=47)*			
Thyroid foetal dose	-0.39	$5.7221_{(1,45)}$	0.022
Mother's intelligence (vocabulary subtest of WAIS)	0.42	$5.8961_{(1,45)}$	0.022
Vocabulary sutest of WISC *(children exposed at 16–25 weeks after fertilisation, n=47)*			
Thyroid foetal dose	-0.51	$11.0984_{(1,45)}$	0.002
Mother's intelligence (vocabulary subtest of WAIS)	0.42	$6.0628_{(1,45)}$	0.02



Foetal thyroid dose vs. Verbal IQ
Verbal IQ= 114.07 - 15.64 * Foetal thyroid dose
Correlation: r = -.3895; p = .023
Verbal IQ
140
130
120
110
100
90
80
70
60
50
0.0
0.4
0.8
1.2
1.6
2.0
Foetal thyroid dose, Gy
Regression
95% confid.

Brain electrical activity of children. The children of acutely exposed group had significantly less age normal patterns of brain electrical activity in comparison with the classmates (16% vs. 54%, χ^2 = 31.74, P<0.001) (table 4.10). There were four abnormal EEG-patterns in prenatally irradiated children as follows. (1) *Low-voltage EEG* (20–25 μV) with excess of slow (δ) and fast (β) activity together with depression of α- and θ-activity with paroxysmal activity shifted to the left fronto-temporal region was the one of the most distinguished conventional EEG-pattern in the children of acutely exposed group (31% vs. 8%, χ^2=16.85, P<0.001). (2) *Disorganised slow EEG-pattern* with δ-activity domination characterised by disorganised activity of moderate (40–55 μV) or high (70–80 μV) amplitude with a mainly δ-range slow activity domination and non-regular α-activity where hyperventilation led to bilateral paroxysmal activity discharges, as well as 3) *disorganised EEG-pattern with paroxysmal activity*, similar in general to the one described above, but characterised by generalised paroxysmal discharges and bursts of acute, θ- and δ-waves of high amplitude where the hyperventilation led to the bilateral paroxysmal activity increase, were found equally in the both groups. (4) *Epileptiformal EEG* with «spike» or «polyspike—wave» complexes in the fronto-temporal region, mainly of the left hemisphere, and bilateral paroxysmal activity in the form of δ-waves of very high amplitude (higher than 100 μV) was the another of the most distinguished conventional EEG-pattern among the children of the acutely exposed group (17% vs. 1%, χ^2=15.63, P<0.001).

Table 4.10

CONVENTIONAL EEG-PATTERNS

EEG-pattern	Acutely exposed group	χ^2	P	Comparison group
Age norm	16	31.74	<0.001	54
Organised	0	4.08	<0.05	4
Disorganised with predominance of α-activity	10	5.36	<0.05	22
Hypersynchronous	6	17.15	<0.001	28
Abnormal	84	31.74	<0.001	46
Low-voltage	31	16.85	<0.001	8
Disorganised slow	16	.16	>0.05	14
Disorganised with paroxysmal activity	20	.27	>0.05	23
Epileptiformal	17	15.63	<0.001	1
Interhemispheric asymmetry	73	24.8	<0.001	38
Left hemisphere lateralised dysfunction	37	15.36	<0.001	13
Right hemisphere lateralised dysfunction	15	.87	>0.05	20
Cross-hemispherical dysfunction	21	11.32	>0.001	5

Interhemispheric asymmetry of the EEG was revealed significantly more often in acutely exposed children compared with the classmates (73% vs. 38%, χ^2=24.8, P<.001) according to an asymmetry index >5%. An increase of the abnormal or/and a decrease of the normal EEG-signs in one hemisphere in comparison with another were the criteria adopted for the lateralised dysfunction detection (table 4.10). Three types of interhemispheric asymmetry were found in the children of the both groups. A *left hemisphere lateralised dysfunction* was characterised by slow and/or epileptiformal activity in the fronto-temporal region together with α-activity depression in the left hemisphere. The left-hemispherical type of EEG-laterality was found more often among acutely exposed children in comparison with classmates (37% vs. 13%, χ^2=15.36, P<0.001). A *right hemisphere lateralised dysfunction* characterised by abnormal activity in the right fronto-temporal region did not differentiate the acutely exposed children from classmates (15% vs. 20%, χ^2=0.87, P>0.05). We described a so-called *cross-hemispherical dysfunction, which* consisted of abnormal activity simultaneously in the fronto-temporal region of one hemisphere and in the parieto-temporal region of another hemisphere. This was found in 21% of the children from acutely exposed group and 5% of the children from comparison group (χ^2=11.32, P<0.001).

According to the spectral EEG-analysis a significant difference was found between acutely exposed and comparison groups (table 4.11). The acutely prenatally irradiated children dramatically distinguished from the classmates by an increase (P<.001) of δ- and β-power and a decrease (P<0.001) of θ- and α-power. However, the pattern of summarised EEG spectral power in the children of the both groups exposed at 0–7 and 26+ weeks after fertilisation was statistically equal (except more δ-power among those acutely exposed at 26+ weeks). The children prenatally acutely exposed at 16–25 weeks of gestation have the most distinguished pattern of summarised EEG spectral power (increased δ- and β- and decreased θ- and α-power), as well as those exposed at 8–15 weeks (increased δ- and decreased θ-power) in comparison with classmates.

Table 4.11

EEG SPECTRAL ANALYSIS

Age in weeks after fertilsation	Acutely exposed group	*t*	P	Comparison group
Summarised δ (1–4 Hz)-power (%)				
All	47.65±12.54	8.65	<0.001	33.59±10.34
0–7	44.99±10.71	3.2	=0.001	33.36±12.51
8–15	48.53±15.03	4.25	<0.001	32.98±12.34
16–25	49.81±13.10	5.46	<0.001	34.05±8.17
26–term	45.05±8.41	4.01	<0.001	33.99±10.12
Summarised θ (4–7) –power (%)				
All	15.96±5.61	–8.9	<0.001	23.32±6.07
0–7	16.75±6.08	–3.05	<0.01	23.12±7.27
8–15	17.76±7.04	–4.99	<0.001	26.35±5.84
16–25	14.01±4.05	–8.47	<0.001	23±3.79
26–term	15.89±4.68	–3.12	<0.01	21.09±6.42
Summarised α (7–12) –power (%)				
All	26.62±10.24	–5.5	<0.001	33.50±7.17
0–7	29.79±12.77	–1.07	>0.05	33.7±8.28
8–15	24.55±7.88	–3.12	<0.01	30.93±7.39
16–25	25.25±11.63	–3.36	<0.001	33.74±6.95
26–term	29.31±8.37	–2.55	<0.01	35.42±7.85
Summarised β (12–32) –power (%)				
All	16.49±6.42	4.28	<0.001	13.33±3.63
0–7	15.86±7.13	1	>0.05	13.94±2.75
8–15	14.97±7.72	1.48	>0.05	12.75±2.59
16–25	17.76±5.8	3.7	<0.001	13.2±3.1
26–term	17.09±7.06	2.27	<0.01	13.92±4.63

Note: Bonferroni corrected α-level of <0.001 was used to assess statistical significance

Obviously, children's pattern of cerebral electrical activity is, like intelligence, etiologically heterogeneous. According to correlation and regression analyses we found that the children's EEG-pattern is associated with age, current neuropsychiatric disorder, perinatal pathology, mother's mental health, as well as exposure to disaster — both to stress and radiation. Foetal dose was the predictor for an increase of summarised δ-power (regression coefficient =0.46; P<0.001) and β- power (regression coefficient =0.22; P=0.002), and for a decrease of θ- power (regression coefficient =–0.48; P<0.001) and α-power (regression coefficient =–0.35; P<0.001) (table 4.12). This dose—effect relationship was the most pronounced in the children exposed at 8–25 weeks, especially at 16–25 weeks, after fertilisation. Thyroid foetal dose was the predictor for an increase of summarised δ-power (regression coefficient =0.49; P<0.001) and for a decrease of θ- power (regression coefficient =–0.5; P<0.001) and α-power (regression coefficient =–0.32; P<0.001). This dose—effect relationship was the most pronounced in the children exposed at 16–25 weeks after fertilisation (figure 4.12).

The correlations between intelligence and spectral power of EEG were revealed as follows. Full scale IQ deterioration was associated with an increase of δ-power (r=0.25–0.35; P<0.001), especially at the left frontal region (r=0.31–0.35; P<0.001), a decrease of α-power (r=0.27–0.36; P<0.001), especially at the left parieto-occipital region (r=0.33–0.36; P<0.001), as well as a lateralisation of β-power to the left fronto-temporal region (r=0.2; P=0.02). Verbal IQ deterioration was associated with an increase of δ-power (r=0.25–0.41; P<0.001), mainly in the left hemisphere, especially at the left frontal region (r=0.38–0.41; P<0.001), a decrease of α-power (r=0.22–0.38; P<0.001), also mainly in the left hemisphere, especially at the left frontal region (r=0.34–0.38; P<0.001), as well as an increase of β-power (r=0.27; P<0.001). Performance IQ deterioration was associated with an increase of δ-power (r=0.15–0.28; P<0.001), mainly in the right hemisphere, especially at the right parietal region (r=0.21–0.28; P<0.001), a decrease of α-power (r=0.17–0.26; P<0.001), also especially at the right parietal region (r=0.23–0.26; P<0.001), as well as an increase of β-power (r=0.21–0.27; P<0.001) at the right temporal region. WISC performance/verbal discrepancies, with verbal decrements were associated with lateralisation of δ-power towards the left parietal region (r=0.24; P=0.04), a decrease of θ-power in the left fronto-temporal region (r=0.27–0.31; P<0.001), as well as an increase of β-power (r=0.2–0.27; P<0.001).

Table 4.12

RELATIONSHIPS BETWEEN EEG AND DOSES OF PRENATAL IRRADIATION

Age in weeks after fertilsation	Dose	Regression coefficient	$F_{(df1, df2)}$	*p*
Summarised δ (1–4 Hz)-power (%)				
All	Thyroid foetal	0.49	$61.2214_{(1,152)}$	0.000000
	Foetal	0.46	$54.5663_{(1,198)}$	0.000000
0–7	Foetal	0.45	$12.7301_{(1, 43)}$	0.0008
8–15	Thyroid foetal	0.43	$11.3462_{(1,54)}$	0.001
	Foetal	0.42	$10.7512_{(1,54)}$	0.002
16–25	Thyroid foetal	0.49	$15.6218_{(1,45)}$	0.0002
	Foetal	0.46	$13.3483_{(1,45)}$	0.0006
26–term	Thyroid foetal	0.54	$18.6339_{(1,53)}$	0.00009
	Foetal dose	0.49	$13.91842_{(1,53)}$	0.0005
Summarised θ (4–7) –power (%)				
All	Thyroid foetal	–0.5	$64.3190_{(1,152)}$	0.000000
	Foetal	–0.48	$60.3387_{(1,198)}$	0.000000
0–7	Foetal	–0.34	$6.9570_{(1, 43)}$	0.01
8–15	Thyroid foetal	–0.51	$17.2614_{(1,54)}$	0.0001
	Foetal	–0.53	$19.1616_{(1,54)}$	0.00006
16–25	Thyroid foetal	–0.63	$32.0500_{(1,45)}$	0.000001
	Foetal	–0.59	$26.8140_{(1,45)}$	0.000004
26–term	Thyroid foetal	–0.43	$10.2321_{(1,53)}$	0.002
	Foetal dose	–0.44	$11.0047_{(1,53)}$	0.002
Summarised α (7–12) –power (%)				
All	Thyroid foetal	–0.32	$22.9415_{(1,152)}$	0.000003
	Foetal	–0.35	$27.0970_{(1,198)}$	0.000000
0–7	Foetal	–0.26	$3.6292_{(1, 43)}$	0.06
8–15	Thyroid foetal	–0.26	$3.5650_{(1,54)}$	0.06
	Foetal	–0.31	$5.3726_{(1,54)}$	0.02
16–25	Thyroid foetal	–0.35	$6.7276_{(1,45)}$	0.01
	Foetal	–0.39	$8.6232_{(1,45)}$	0.005
26–term	Thyroid foetal	–0.39	$8.2347_{(1,53)}$	0.006
	Foetal dose	–0.3	$4.4584_{(1,53)}$	0.04
Summarised β (12–32) –power (%)				
All	Thyroid foetal	0.14	$3.7750_{(1,152)}$	0.05
	Foetal	0.22	$9.9334_{(1,198)}$	0.002
0–7	Foetal	0.09	$0.4783_{(1, 43)}$	0.5
8–15	Thyroid foetal	0.11	$0.6035_{(1,54)}$	0.4
	Foetal	0.23	$2.8587_{(1,54)}$	0.1
16–25	Thyroid foetal	0.14	$0.944_{(1,45)}$	0.3
	Foetal	0.44	$6.6197_{(1,45)}$	0.01
26–term	Thyroid foetal	0.17	$1.3397_{(1,53)}$	0.2
	Foetal dose	0.11	$0.5989_{(1,53)}$	0.4

Figure 4.12. Relationships between summarised δ (1ж4 Hz)-power (%) and summarised θ (4ж7) ж power (%) vs. foetal thyroid dose, in children of the both groups (n=47) exposed at 16ж25 weeks after fertilisation

Inspite of intelligence is an integrative function of the human brain, full scale IQ and, especially, verbal IQ is closer associated with the left hemisphere functions, whereas performance IQ — with the right hemisphere ones. According to the data obtained a possible cerebral basis of full scale IQ and verbal IQ deterioration as well as WISC performance/verbal discrepancies, with verbal decrements, in prenatally irradiated children is dysfunction of the left frontal, temporal and parietal lobes. This dysfunction apparently involves the cortico-limbic system, prefrontal cortex (frontal associative area), the secondary cortical receptor fields (temporal associative area), and the tertiary parietal associative area at the left, dominating, hemisphere [Joseph R., 1996; Duus P., 1996].

It seems to be possible to attribute this central nervous system dysfunction to prenatal exposure to ionising radiation, especially at the second critical period of cerebrogenesis (16–25 weeks after fertilisation) — the time of the most sophisticated events of brain creation, as well as limbic system, brain asymmetry and hemisphere dominating forming [Cowan W.M. et al., 1984; England M.A., 1996; Zecevic N., 1998]. Moreover, radiation-induced malfunction of the foetal thyroid-pituitary system cannot be excluded.

ICD-10 diagnosis. According to the ICD-10 clinical descriptions and diagnostic guidelines neurological disorders were revealed in 65 of the children of the acutely exposed group and in 25 of the classmates (χ^2=27.85; P<0.001) (table 4.13). The overwhelming majority of this pathology were episodic and paroxysmal disorders, which were revealed significantly more often in acutely exposed group than in comparison group (61% vs. 29%; χ^2=20.69; P<0.001). The children-evacuee had significantly more epilepsy (G40), and migraine (G43) than classmates. Epilepsy and other paroxysmal disorders were verified by clinical EEG, when clinical pattern of episodic or paroxysmal disorder corresponded to paroxysmal brain electrical activity (spikes, spike-waves, acute and slow waves of high amplitude >100 mkV).

Table 4.13

DISEASES OF THE NERVOUS SYSTEM, MENTAL AND BEHAVIOURAL DISORDERS ACCORDING TO THE ICD-10 CRITERIA

ICD-10 code	Acutely exposed group	χ^2	P	Compa-rison group
Diseases of the nervous system (G00—G99)				
Without neuropathology	38	27.85	<0.001	75
Episodic and paroxysmal disorders (G40—G47):	61	20.69	<0.001	29
G40 Epilepsy	8	5.7	<0.05	1
G43 Migraine	8	8.33	<0.05	0
G44 Other headache syndromes	36	3.43	>0.05	24
G47 Sleep disorders	9	2.06	>0.05	4
G90.8 Other disorders of autonomic nervous system	5	5.13	<0.05	0
Mental and behavioural disorders (F00—F99)				
Without psychopathology	10	35.07	<0.001	48
Organic, including symptomatic, mental disorders (F00–F09):	25	13.78	<0.001	6
F06 Other mental disorders due to brain damage and dysfunction and to physical disease	20	8.66	<0.01	6
F07 Personality and behavioural disorders due to brain disease, damage and dysfunction	5	5.13	<0.05	0
F12 Mental and behavioural disorders due to use of cannabinoids	1	1.01	>0.05	0
Neurotic, stress-related and somatoform disorders (F40–F48):	36	0.56	>0.05	31
F45.3 Somatoform autonomic dysfunction	23	10.04	<0.01	7
F48.0 Neurasthenia	13	4.01	<0.05	24
F51 Nonorganic sleep disorders	6	2.08	>0.05	2
Mental retardation (F70—F79):	2	2.02	>0.05	0
F70 Mild mental retardation	1	1.01	>0.05	0
F71 Moderate mental retardation	1	1.01	>0.05	0
Disorders of psychological development (F80–F89)	12	12.77	<0.001	0
Behavioural and emotional disorders with onset usually occurring in childhood and adolescence (F90–F98)	33	4.34	<0.05	20
Mental comorbidity	24	11.03	<0.001	7

Mental and behavioural disorders according to the ICD-10 criteria were revealed in 90 of the children of the acutely exposed group and in 52 of the classmates (χ^2=35.97; P<0.001) (table 4.13). Organic, including symptomatic, mental disorders (F06, F07), somatoform autonomic dysfunction (F45.3), disorders of psychological development (F80–F89), and behavioural and emotional disorders with onset usually occurring in childhood and adolescence (F90–F98) were diagnosed significantly more often in acutely exposed group than in comparison group. Mental comorbidity was 24% in acutely exposed group and 7% in comparison group (χ^2=11.03; P<0.001).

Organic mental disorders were verified by Brain Mapping of QEEG and Visual Evoked Potentials (VEP) and in a number of cases by MRI and CT. Two cases of F07 (Personality and behavioural disorders due to brain disease, damage and dysfunction) 6 of F06 (Other mental disorders due to brain damage and dysfunction and to physical disease) from acutely exposed group and 1 of F06 from comparison group were due to epilepsy (G40). Two cases of F07 from acutely exposed group were linked to mental retardation (F70 and F71). One case of F07 and 14 cases of F06 from acutely exposed group, as well as 5 cases of F06 from comparison group were attributed to the evidences of perinatal, predominantly pre- and intrenatal, pathology, i.e. pathology during *in utero* period and delivery, as follows: moderate to severe toxicosis of pregnancy, uterine haemorrhage during pregnancy, risk of miscarriage, waterless period during delivery, too short- or too long-time period of delivery, hypoxia of foetus and asphyxia of newborn.

The more severe neuropsychiatric disorders — mental retardation, epilepsy, and organic mental disorders — were diagnosed in 25 acutely exposed children and in 6 classmates (χ^2=13.78; P<0.001). The majority (16) of the acutely exposed children with these disorders (including 2 cases of mental retardation) were irradiated at 8–15 and 16–25 weeks after fertilisation. Thyroid foetal dose of these children with severe neuropsychiatric disorders was significantly higher than in other children of the acutely exposed group (0.78±0.31 vs. 0.59±0.28, t = 2.79, P<0.01).

It is clear that the children's neuromental disorders are etiologically heterogeneous. Higher economical level of a family, better somatic health of a child, better mental health of parents are the contributors towards a better children's neuromental health. Higher doses of prenatal irradiation, especially foetal thyroid dose, more severe stress events, and additional mother's hazards in the prenatal period, worse a mother's mental health, as well as problems of the perinatal period are the contributors towards children's neurological and mental health deterioration.

Discussion and Conclusions. The UNSCEAR Report-2000, Annex J: Exposure and Effects of the Chernobyl Accident touched the problem of the psychological development of the children who were exposed to radiation from the Chernobyl accident in utero basing on a one publication only [Kolominsky Y. et al., 1999] where cognitive, emotional and behavioural disorders in prenatally irradiated children were attributed exclusively to unfavourable social-psychological and social-cultural factors.

The WHO Pilot Project «Brain Damage in Utero» International Advisory Board assumes that prenatal exposure to the Chernobyl disaster can give rise to a dysfunctional child, either because of organic damage to the developing brain or because of the disturbed psychosocial milieu. Indeed, intelligence peculiarities, neurophysiological abnormalities, and neuromental health deterioration in the children acutely prenatally exposed to both radiation and stress are etiologically multifactorial. In spite of the children were affected by multiple exposure including prenatal stress and current social, economical, and medical problems in their families, the «dose—effects» relationships concerning both intelligence and EEG-parameters, which are the most marked at the critical periods of cerebrogenesis, testify to significant contribution of prenatal irradiation into the brain damage.

This study confirms and develops the results of the WHO Pilot Project «Brain Damage in Utero» [Souchkevitch G.N., Tsyb A.F. (Eds.), 1996; Kozlova I.A. et al., 1999] and relevant studies [Ermolina L.A. et al., 1996; Gayduk F.M. et al., 1994; Igumnov S.A., 1996; Kolominsky Y. et al., 1999; Igumnov S., Drozdovitch V., 2000] concerning mental health and intelligence deterioration in children exposed *in utero* as a result of the Chernobyl disaster. Unlike to the study [Kolominsky Y. et al., 1999] where the authors did not find evidences of the contribution of prenatal irradiation on the children's intelligence deterioration, we have done it. The differences between the results of the study [Kolominsky Y. et al., 1999] and ours we can explain by follows: 1) different sample: we examined acutely exposed in 1986 children, but they — those resettled in 5–7 years after the disaster, and 2) different measures: they analysed full scale IQ only, but we — verbal IQ (including subtests), performance IQ (including subtests), WISC performance/verbal discrepancies, and full scale IQ. Exactly deterioration of verbal IQ and WISC performance/verbal discrepancies, with verbal decrements, were in proportion to the foetal thyroid dose.

Our data do not confirm the results of the studies [Bromet E.J. et al., 1998,2000; Litcher L. et al., 2000] concerning similarity and normality of mental and physical health, intelligence similarity of acutely prenatally exposed children in the Chernobyl exclusion zone evacuated to Kiev and children-classmates living in Kiev, as well as that the most important risk factors were maternal somatization and Chernobyl-related stress. A possible explanation of the differences between the results of the studies [Bromet E.J. et al., 1998,2000; Litcher L. et al., 2000] and ours study seems to be as follows: 1) Restricted neuropsychological battery for children's intelligence assessment allowed them [Litcher L. et al., 2000] to measure spatial intelligence only, which indeed looks likely to be intact; 2) An absence of clinical neuropsychiatric examination by ICD-10 or DSM-IV criteria and screening-like physical examination in the works [Bromet E.J. et al., 1998,2000] resulted their conclusion concerning evacuee children's mental and physical welfare to be the point at issue. 3) Inadequate using of gestation months for analysis, but not periods of cerebrogenesis (0–7, 8–15, 16–25, and 26+ weeks after fertilisation), and possible uncertainties in the gestation term estimation did not enable in the studies [Bromet E.J. et al., 1998,2000; Litcher L. et al., 2000] to estimate the most important single factor in

determining the nature of the insult to the developing brain from ionising radiation [ICRP Publication 49, 1986] — exposure in critical and «non-critical» periods of prenatal development. 4) An absence of dosimetrical data for both children-evacuee and non-evacuee did not enable them [Bromet E.J. et al., 1998,2000; Litcher L. et al., 2000] to study a possible dose—effect relationship and to estimate the contribution of ionising radiation towards intelligence and psychological development of the children. However, the most important reason of the differences between their and our studies seems to be the different paradigms of the researches: psychosocial model of the studies [Bromet E.J. et al., 1998,2000; Litcher L. et al., 2000], and neuropsychiatric or neurobilogical — in us.

It should be noted the limitations and uncertainties of this study. First of all, there is the problem of a representativeness of the sample taking into account a possible bias towards «improving selection», where some disabled children due to neuropsychiatric problems could be dropped out from the study. Ideally, the all parentally exposed children, or at least all those who had been evacuated from the Chernobyl exclusion zone, should be involved in the study. The sample — evacuee in Kiev and non-evacuee classmates living in Kiev — looks quite good from the point of view of similarity of informational and urban saturation environment, providing as much as possible in Ukraine and similar for the all examined children opportunity for intellectual development. On the other hand, classmates from Kiev are not exactly «non-irradiated» group. Moreover, again they should be randomised from population sample in order to predict the bias due to both the noted above «improving selection», and «deteriorating selection» when, for instance infants prodigy attending special advanced schools, are also out of the sample. It should be also stressed the uncertainties of individual doses estimation due to an absence at present of generally accepted agreement concerning model of foetal dose assessment. Probably, like in Japan, there will be further new dosimetrical systems and reassessment of psychometrical, neurophysiological and other data.

As it was mentioned above, our sample corresponds to the Japanese sample [ICRP Publication 49, 1986]: prenatally exposed to atomic bomb radiation survivors of the foetal dose category less than 0.01 Gy (n=1,201) — to the Ukrainian comparison group, and those of the dose category 0.01–0.09 Gy (n=322) — to the Ukrainian acutely exposed group. However, there is an extremely important radiological difference between the Japanese and Ukrainian samples — prenatal exposure to radioactive isotopes of iodine. The prenatally exposed to atomic bomb had not been irradiated by radioiodine, but the prenatally exposed children as a result of the Chernobyl disaster received quite significant foetal thyroid doses. This fact makes to be difficult to extrapolate the all data (risks, thresholds of the effects, etc.) from the Japanese sample on the Chernobyl one. It seems, that the acutely prenatally exposed children at the Chernobyl exclusion zone is an unique sample that should be used for reassessment of risks of prenatal irradiation at radiation accidents on nuclear reactors.

The results of this study agree with the Japanese studies concerning 1) dose related full scale IQ reduction [Shull W.J., Otake M., 1985], 2) an increase of paroxysmal disorders [Shull W.J., Otake M., 1999], 3) critical periods of cerebrogenesis — 8–15 and, especially, 16–25 weeks after fertilisation [Shull W.J., Otake M., 1985]. The most vulnerability of the brain under exposure at 16–25, but not 8–15 weeks after fertilisation, as in the Japanese sample, we can explain by 1) maximal radioiodine concentration in foetal thyroid at about the 20–25 weeks [Instruction of Ministry of Public Health of the USSR, 1986], 2) more «delicate» than in atomic bomb survivors intelligence disturbances that corresponds exactly to the events of the brain creation at 16–25 weeks after fertilisation (neuronal differentiation, limbic system and brain asymmetry forming, apoptosis beginning etc. [Cowan W.M. et al., 1984; England M.A., 1996; Zecevic N., 1998]. An absence of dramatical increase of mental retardation, especially its severe form, as well as microcephalia obviously can be explained by significantly lower than that in atomic bomb survivors foetal doses of irradiation.

Following recommendation of W.J. Shull & M. Otake (1991) concerning future studies of the prenatally exposed survivors and the WHO Pilot Project «Brain Damage in Utero» International Advisory Board for the second phase of the project, we used QEEG and WISC. This resulted in interesting findings of verbal IQ reduction and WISC performance/verbal discrepancies, with verbal decrements, which were in proportion to the foetal thyroid dose, especially among those children exposed at 16–25 weeks after fertilisation. Previously we reported [Nyagu A.I. et al., 1993,1996,1998] about TSH level grows with foetal thyroid dose increase with a 0.3 Gy threshold. Probably, these children had been affected by intrauterine hypothyroidism resulted in intelligence disturbances during the life. Obviously, an international psychoendocrine study should be organise for exploration of functions of the pituitary-thyroid system as a possible biological basis of mental health problem in children irradiated in utero as a result of the Chernobyl disaster.

The prenatally acutely exposed children have quite distinguished pattern of summarised EEG spectral power (increased δ- and β- and decreased θ- and α-power), in comparison with both the classmates and literature normative data [Rutter M. , Hersov L., 1985; Niedermeyer E., DaSilva F.L. (Eds.), 1993]. Foetal dose and thyroid foetal dose were the predictors of this QEEG-pattern, especially among children irradiated at 16–25 weeks after fertilisation.

Neurophysiological abnormalities together with intelligence disturbances, both dose-related, especially at 16–25 weeks after fertilisation, as well as a «concentration» of the most severe neuropsychiatric disorders among the children exposed at the critical periods of cerebrogenesis, can testify to the developing brain abnormalities due to multiple factors with effects of prenatal irradiation.

Verbal IQ deterioration together with lateralisation of abnormal electrical activity to the left hemisphere support our previous report about the predominance of the left hemisphere dysfunction in prenatally irradiated children [Loganovskaja T.K., Loganovsky K.N., 1999]. Association of verbal IQ and left hemisphere is well-known [Flor-Henry P., 1983], full scale IQ is closer related to the left than to the right hemisphere [Joseph R., 1996]. It seems that the left hemisphere is more vulnerable to exogenous impacts including ionising radiation, than the right hemisphere, probably due to dominating of the left brain and, consequently, its more functional activity.

A possible cerebral basis of intelligence disturbances in prenatally irradiated children is dysfunction of the left frontal, temporal and parietal lobes, involving the cortico-limbic system, prefrontal cortex, temporal associative area, and the tertiary parietal associative area at the left, dominating, hemisphere [Duus P., 1996; Joseph R., 1996]. However, the predominance of the left hemisphere dysfunction is leading towards higher risk of schizophrenia spectrum disorders in prenatally irradiated children, that is why the long-term follow up study of this cohort is of great importance for clinical medicine and neuroscience.

Thus, the neuromental health of the acutely prenatally irradiated children at the Chernobyl exclusion zone is deteriorated in comparison with the non-evacuee classmates living in Kiev due to more frequency of episodic and paroxysmal disorders, organic, including symptomatic, mental disorders, somatoform autonomic dysfunction, disorders of psychological development, and behavioural and emotional disorders with onset usually occurring in childhood and adolescence. Obviously, their neuromental health disorders are etiologically heterogeneous including psycho-social and economic factors, medical problems in their families, however an effect of real stress events (but not only their perception) during pregnancy together with prenatal irradiation cannot be excluded.

Intelligence of the acutely prenatally irradiated children is deteriorated due to reduction of full scale and verbal IQ, as well as WISC performance/verbal discrepancies, with verbal decrements. In spite of the children's intelligence is multifactorial, the contribution of prenatal irradiation was revealed.

Characteristic neurophysiological changes of the acutely prenatally irradiated children are also etiologically heterogeneous, but the dose—effect relationship, especially at critical periods of cerebrogenesis, can testify the impact of prenatal irradiation.

This study suggests that prenatal exposure to ionising radiation at thyroid foetal dose 0.2–2 Gy and foetal dose 11–92 mSv can result in detectable brain damage.

The data obtained reflect great importance, interdisciplinarity, and complexity of such problem as brain damage *in utero* following radioecological disaster and a necessity to integrate international efforts to its solving.