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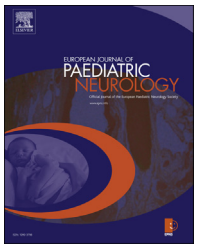

Abstracts Yekaterinburg

Diagnosis of neural crest-derived tumors in children with opsoclonus-myoclonus syndrome

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Introduction: Opsoclonus-myoclonus syndrome (OMS) is defined as the clinical syndrome with cerebellar ataxia, tremor, behavioral problems, non-epileptic myoclonus and specific eye movements – called opsoclonus. OMS is divided in 2 clinical types: paraneoplastic and idiopathic. Many researchers consider that OMS is a typical manifestation of neural crest-derived tumors in childhood. Idiopathic OMS include all the cases without tumor's detection.

Materials and methods: Since 1997 we have observed 63 patients with OMS (29 males, 34 females). They were under the care in the Russian Children's Clinical Hospital. Age of OMS onset was in average as 20,5 months (from 6 to 69 months). These patients were admitted to the Psychoneurology Department with different directive diagnoses including but not limited to encephalitis, neuroinfection's or craniocerebral injury's consequences, degenerative diseases of the nervous system, ataxia of unknown etiology, cerebral palsy. Only 3 patients have been diagnosed true running OMS before they referred to the Russian Children's Clinical Hospital. To exclude neural crest-derived tumors, we used ultrasound of abdomen, retroperitoneum and pelvis; X- Ray of thorax; CT of thorax, abdomen and pelvis; MRI of abdomen and pelvis; scintigraphy with MIBG; 24- hour urine screen for catecholamines; assay of serum tumor's markers such as neuron specific enolase, alpha-fetoprotein, lactate dehydrogenase. The most detailed study was performed for 41 patients (19 males, 22 females) due to some methods became available recently.

Results: OMS was determined as paraneoplastic etiology in 20 (7 males, 13 females) of those 41 cases. Tumors were located in the thorax (7 cases), pelvis (3 cases) and retroperitoneum (10 cases). In 3 cases tumor masses have been detected in the first month of OMS's onset. In other cases, the delay time between the onset of OMS and the tumor's detection have reached of 10.5 months in average (from 2 to 39 months). 16 patients have passed surgical intervention with extraction and further histologic detection of tumor to the present date. The following diagnoses were set after the biopsy: neuroblastoma (5 cases), ganglioneuroma (3 cases), ganglioneuroblastoma (8 cases). 4 patients with neuroblastoma took course of chemotherapy under the relevant protocols.

Conclusion: The results of our study showed that physician should pay attention to neural crest-derived tumors in relation to OMS diagnosed children. Due to this fact, in spite of neurological and immunologic tests these patients should pass the following examinations: ultrasound of retroperitoneum, abdomen and pelvis; X- ray of thorax; CT of thorax, abdomen and pelvis; MRI of abdomen and pelvis; scintigraphy with MIBG; 24- hour urine screen for catecholamines; assay of serum tumor's markers such as neuron specific enolase, alpha-fetoprotein, lactate dehydrogenase. Children with idiopathic OMS should still be observed by neurologists and oncologists jointly. These children need dynamic control examination at least once per 6 months to identify neurogenic tumors. Late diagnosis of OMS and insufficient paraneoplastic examination of children may cause dramatic consequences for patients.

The structure of sleep in children with attention deficit hyperactivity disorder

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Introduction: Studies of the structure of night sleep and ultradian rhythms in children with attention deficit hyperactivity disorder (ADHD) have significantly advanced our understanding of the syndrome pathogenesis.

Purpose: To explore the clinical features, structure and ultradian rhythms of sleep during the night. Polysomnography examination of ADHD children aged from 6 to 9 years old was carried out considering gender differences and clinical subtypes.

Materials and methods: A comprehensive unified survey of 40 children aged from 6 to 9 years old was performed. Verification of ADHD diagnosis was carried out in accordance with the ICD -10 and DSM-IV. The comparison group consisted of 20 healthy children. Polysomnography (PSG) was performed according to standard pattern during 8 hours with a hardware-software Neyronspektr - 4/VP complex. PSG scoring data analysis was carried out in accordance with A.Rechtschaffen A.Kales international standards (1968, 2002).

Results: Clinical sleep disorders analysis showed predominating insomnia disorders in patients with ADHD. Parasomnias were identified in similar proportions both in the study and control groups. Sleep macrostructure analysis revealed a significant decrease of the total sleep time (TST) up to 6.4 ± 0.06 hours in

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ADHD children, increase of latency and duration of C1 stage (the period of sleep and naps), extended C4 (delta sleep stage), an increased latent period of rapid sleep phase (REM) up to 190. 7 ±23.2 minutes compared with the control group, where the comparable figure was 116.4 ± 21.1 minutes ($p \leq 0.05$). In ADHD children REM duration was significantly reduced to 65.9 ± 5.3 minutes compared with healthy children (97.1 ± 9.2 min., $p \leq 0.05$). Wakefulness time during sleep, number of awakenings, including those of more than 3 minutes duration, were significantly reduced. The obtained indices of macrostructure of sleep changes resulted in reduced sleep efficiency index (SEI) to 81.5 ± 6.3% ($p \leq 0.05$). The cyclic sleep organization was characterized by a significant reduction in the total number of sleep cycles during night in children with ADHD to 2.7 ± 0.6 cycles, while in the control group the number of cycles per night was 4.2 ± 0.8. The first cycle of sleep in ADHD children was abnormally extended, its duration being of approximately 2.5 hours (the average rate of 1.5 hours) and took half of the total night sleep time. Share of non-REM phase (NREM) was significantly increased. As a result, in the first half of the night REM was not identified in 61 % of children. Parameters of the second cycle dynamics reflect common patterns of sleep in ADHD children as a whole. The third cycle of sleep was characterized by a significant reduction in its duration. There were no significant differences in the NREM, however, the REM duration in the final third cycle of night sleep reduced and was 26.0 ± 4.3 minutes compared with the control group, where the REM duration was 36.6 ± 6.7 minutes ($p \leq 0.05$). The most evident changes in sleep macrostructure were identified in children with the combined subtype of ADHD revealed in the form of increased REM latency with reduction of its duration. ADHD subtype with predominating hyperactivity and impulsiveness was characterized by severe violation of ultradian rhythms of sleep and reduction of the sleep cycle number to two. Sex difference in the cyclic sleep organization was expressed in its more severe deformation in boys. In that case, all three sleep cycles were impaired. The first cycle reflected general tendency in changes of PSG records, the second one was characterized by an increase in cycle time and duration of NREM and the third one by sharp reduction in the duration and sleep phases.

Conclusion: Sleep structure impairment plays an autonomous and independent role in the pathogenesis of ADHD and reflects underlying impairments formation of cerebral integrative functions including the integrative mechanisms of sleep and chronobiological processes.

Clinical and biochemical characteristics of migraine in children

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Purpose: To study clinical characteristics of children migraine, their impact on life quality and relation with calcium homeostasis and plasma nitrites.

Materials and methods: 102 children (64 boys, 38 girls) at the age of 6 to 18 years old suffering from migraine (average age 12.1±2.97). The migraine diagnosis was being established according to ICHD-2 criteria (2003). The estimation of pain intensity was conducted based on VAS, life quality – on MIDAS survey, anxiety level – based on Spilberg-Khanin test, depression.

Balashova scale. Also we conducted a survey of vegetative disorders (Vein, 2003). In 81 children activity of Ca^{2+}- according to methodology of Kazennova, Reinila et al. (1982) was analyzed; besides, we studied the level of general intracellular calcium in thrombocytes according to the methodology of M.Mayer et al. (1966; 1971) and nitrites in blood plasma (by Karpyuk et al. (2000) methodology. Control group comprised children of the same age and gender.

Results: The following characteristics of childhood migraine were shown: frequent migraine is migraine w/o aura (60.8%); combination of migraine and tension-type headache (41%), attacks with frequency rate at 2-4/month (56%), and duration did not exceed 12 hrs (66%). With age the pain intensity is rising (6.1 VAS at the age of 6-8 years till 7.4 at the age of 15-17); the attacks are accompanied by apparent associated symptomatology (nausea, vomiting – 88%, photo/phonofobia – 68%); pro- (21%) and postdromal (28%) periods occur less frequently than in adults, clinics of the periods is various. Among relief factors sleep takes the leading place (77%), at the teenage age frequency of taking painkillers is rising (71% against 48% at 11). From all the migraine characteristics frequency and intensity had more apparent effect on life quality. The duration of the migraine didn't have reliable correlations with anxiety level, depression, vegetative disorders, MIDAS scale indicators. In children suffering from migraine the level of intercellular calcium increased twice compared to healthy children of the same age (0.046±0.009/0.022±0.01 mM/ml, $p<0.001$). The changes were accompanied by an increasing of the activity Ca^{2+}ATPhase (0.38±0.09/0.33±0.07 mM/hour/mgprotein, $p=0.027$). Also in the children a reliable increase of the level of plasm nitrites (3.2±0.8/2.2±0.9 nM/ml, $p<0.001$) was shown. Higher level of the activity of Ca^{2+}ATPhase and intercellular calcium were revealed under migraine with aura and their positive correlation with seizure duration. The level of nitrites independently on the migraine type is related to the seizure frequency and reliably increased if 2 or more seizures occurred within one month.

Conclusion: At the present stage clinical implications of adults migraine were examined in terms of its impact on patients' life quality. In children's practice issues of life quality were analyzed with taking into account perinatal, social, psychological factors into consideration, but not considering characteristics of the seizure, factors of provocation, characteristics of pro- and postdromal periods. Besides the search for biochemical markers of migraine progression is being conducted. From these standpoints the relationship between level of plasm nitrites and seizures frequency may be utilized as objective criterion for decease severity and additional assessment tool of efficacy of treatment.

Features of haemostasis in children with acute arterial ischemic stroke

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Objective: To define the role of blood coagulation and procoagulant genes features in development of acute arterial ischaemic stroke in children. Materials and methods 33 children (20 male and 13 female) aged from 6 months to 17 years with acute arterial ischaemic stroke (AAIS) were observed at Neurosurgical Department of Child Hospital. All children underwent routine somatoneurological examination, neuroimaging (MRI and/or CAT), Doppler ultrasonography of cerebral blood flow. Screening of

blood clotting (activated partial thromboplastin time, prothrombin index, thrombin time, fibrinogen, International Normalized Ratio, ethanol test) was conducted in all cases and 10 genes of thrombophilia were observed in 18 cases during the acute stage of disease (1–21 days).

Results: Three children had disorders of blood clotting background: inadequate development and slow disappearance of bruises, prolonged nasal, sclerotic, gum and teeth haemorrhagies and others. Close relatives of 19 observed patients had different kinds of strokes on the maternal side, 12 – in paternal line. Infants under 1 year old had approximately upper age border-line serum platelets values, older children had median age serum platelets ones. The assessment of blood coagulation demonstrated non-significant tendency of activated partial thromboplastin time, prothrombin index and International Normalized Ratio decrease, and fibrinogen increase in peracute period (1–5 days) of AAIS. The extremal values of activated partial thromboplastin time were detected in acute period (6–21 days) of AAIS and they were significantly below than the ones in peracute period. The ratio of mutant allele in children with AAIS frequency to mutant allele in European population frequency was calculated. The comparison of thrombophilia genes' mutation frequency demonstrated that children with AAIS had significantly more often gene Prt (G20210A)(12.5:1), gene MTHR (A1298C)(5.0:1), gene FGB (G-455A)(3.05:1), genes encoding platelet receptor GPIb (2.78:1) and GPIIIa (2.59:1) than patients in European population. Mutation of factor V Leiden as a well-known cause of inherited disorder of blood clotting wasn't detected in these cases. Serum fibrinogen level showed a positive correlation with the development of secondary haemorrhage in primary ischaemic brain zones in 6–21 days of AAIS ($p = 0.0037$) and asymmetry of resistance indices measured by means of Doppler ultrasonography ($p = 0.0006$).

Conclusion: Investigation of haemostasis in children with AAIS demonstrated tendency of parameters to hypocoagulability in peracute period (the first five days) and normalization of them in acute period only. All the observed children with AAIS had gene polymorphism of thrombophilia. Mutations of genes Prt (G20210A), MTHR (A1298C), FGB (G-455A) were detected significantly more often than in European population.

Pediatric optic neuritis and risk of multiple sclerosis

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Introduction: Optic neuritis in the pediatric population is often regarded as idiopathic, but in some cases it is presented as a first symptom of multiple sclerosis. Therefore, the experience of a long-term follow-up of children with optic neuritis is highly important to assess the risk factors of transformation in multiple sclerosis.

Methods: We performed a retrospective analysis of the medical history, ophthalmoscopic data and neurological status, as well as the results of neuroimaging in children diagnosed with optic neuritis, who were treated in children's neurological and ophthalmic departments in Ekaterinburg during 1999-2011. The diagnosis of multiple sclerosis was established according to the Poser's (1983) and McDonald's (2001, 2005) criteria. Statistical analysis was performed using the "Statistica 6.0". Fisher exact test and Mann-Whitney U test were used to evaluate the association of specific parameters to multiple sclerosis outcome.

Results: Thirty-one children aged 2-17 (11.2±0.6 years) with optic neuritis were identified. Girls/boys ratio was 23/8 ($p<0.05$). All of them showed a vision loss and had a median visual acuity 0.2±0.03. 9.7% of the participants also had periorbital pain. Bilateral optic neuritis was detected in 41.9% of patients. The majority of children had monosymptomatic optic neuritis, but two of them were diagnosed with polysymptomatic optic neuritis, at least one more symptom of central nervous system damage was revealed. Magnetic Resonance Imaging (MRI) was abnormal in 48.1% of the participants and presented one or more T2-hyperintense lesions on brain MRIs. Mean follow-up duration was 3.9±0.5 years (0.5 to 9.3 years). Optic neuritis occurred mostly as a single episode of demyelination. However, 29% of children had from 2 to 5 relapses (3±0.5). According to the data, 7 (22.6%) children have been diagnosed with multiple sclerosis. In other cases, optic neuritis was considered as idiopathic. Our study demonstrated that the age, gender, unilateral or bilateral vision loss, monosymptomatic or polysymptomatic presentation, mono- or polyphase course were not associated with multiple sclerosis outcome. But we found correlation between MRI results and multiple sclerosis risk. Therefore, 46.2% of patients with an abnormal brain MRI had multiple sclerosis compared with 7.1% of patients with a normal brain MRI ($p=0.03$). Furthermore, there is a statistical significance in localization of lesions in multiple sclerosis patients, - white matter of the temporal lobes and brain stem.

Conclusion: Children with optic neuritis were found to have a 22.6% risk for developing multiple sclerosis within four years of our study. We demonstrated that the long-term prognosis of optic neuritis in children is mainly determined by the results of brain MRI at presentation. The presence of typical T2-hyperintense lesions on brain MRIs is a strong predictor of multiple sclerosis.

A case report of cerebral venous sinus thrombosis in a six-year-old child with homocystinurea

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Background: Homocystinurea is an orphan, genetic determined disease with an inherited autosomal recessive trait. The disease is associated with a mutation of the gene CBS (21q22.3). The disease is based on hereditary metabolic block in the chemical pathway of converting homocysteine to cystathionine. Homocystinurea is one of the causes of arterial and venous ischemic strokes in children.

Results: A six-year-old boy was admitted to Neurology Unit urgently complaining of intensive headache, and vomiting on the 8th day after surgery for congenital cataract. In the past history he was asked to do a rescreening test for hereditary metabolic diseases because of positive test with sodium nitroprusside. On admission he was in poor condition due to his neurological status, declined LOC, headache, repeated vomiting, loss of appetite, nuchal rigidity, photophobia, oculomotor paresis outwards and upwards, pastose

face and eyelids, tongue deviation to the left, left-sided hemiparesis of 4 points. On general examination, tall height (140 cm), overweight (40 kg) and bradycardia drew particular attention. Brain CT revealed thrombosis of the left transverse and sigmoid sinus, the superior sagittal sinus, infarction lesions were not found. Heamostasiogramme on admission showed PTI of 85%, platelets of $223*10^6$/L, fibrinogen of 2.0 g/L, APTT of 31 sec., D-dimer of 250-500ng/ml, INR of 1.22, SFMC of 0, AT III of 76%. Homocysteine level of 397 umol/L (55 fold higher than the age norm). In the most acute period the prescribed therapy included infusions, low-weight molecular heparins - fraxiparin at the dose of 100 Units/kg/day) in combination with aspirin 1 mg/kg/day. On day 7 after admission and day 9 after onset of the disease, Doppler ultrasound of the neck vessels detected thrombotic masses in the left internal carotid artery, the jugular and subclavian veins, thrombotic masses reached the mouth of the superior vena cava superior. The child was considered to be at risk for TEPA. Antithrombotic therapy was reinforced with fraxiparin 115 Units/kg/day, aspirin 2 mg/kg/day. On 15 day he had the planned change for warfarin at the titrated dose of 0.02 to 0.08 mg/kg/day to achieve target INR of 2-2.5. In the course of the disease, MRI of the brain (on 39 day) showed developing cystic and glial changes in the frontal lobes as an outcome of venous infarctions; thrombosis of the superior sagittal sinus, the left transverse and sigmoid sinus with signs of recanalization. MR angiography didn't reveal any congenital anomalies of the vascular bed. On Doppler ultrasound there was found a partial defragmentation of thrombi in the mouth of the SVC, the left subclavian vein and in the lumen of the left internal jugular vein. 42 days after the onset of the disease, no thrombi in the lumen of the left internal jugular vein, the superior vena cava and the left brachiocephalic vein were detected and he had only brisk reflexes in his left limbs. Homocysteine level changed from 397-362-338-329-312 umol/L.

A boy had a complete DNA analysis of the gene CBS in the laboratory of hereditary metabolic diseases of RAMS: a described mutation r.Gin368Term in heterozygous state (inherited from his father) and p.Thr353Met in heterozygous state (inherited from his mother) were detected in the exzone 12. Genotype of the disease p.Thr353Met/r.Gin368Term was determined. During the hospitalization, carrier state for 4 prothrombotic gene polymorphisms was detected: FGB: -455 GA, F13: 103 GT, PAI-1: -675 4G4G, MTHFR: 677 TT.

Based on phenotypical data, dislocation of the both lenses, cognitive changes, venous sinus thrombosis, changes on MRI of the brain, a positive test with sodium nitroprusside for homocysteine, very high level of serum homocysteine of 397 umol/L and molecular genetic analysis, a diagnosis of homocystinuria (B6 independent type) was made.

Conclusion: Homocystinuria is a rare/orphan disease. Severe myopia, skeletal abnormalities, cataract and borderline results of the screening tests enabled us to suspect the disease. However, the diagnosis was finally verified only after the venous sinus thrombosis. Prescribed pathogenetic therapy of

homocystinuria, including diet, high doses of pyridoxine and folic acid, resulted in lower homocysteine level by 85 umol/L, while adequate and timely therapy and secondary prevention of stroke led to minimization of the neurological outcomes and lack of life-threatening complications.

Severity of drug loads in children with burns as possible predictor of neurological complications

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Introduction: Adverse effects of medications on children nervous system, especially of narcotic type medications, has not been studied thoroughly; it is further complicated by the severity of burn injury.

Methods: Type of study: case series, 59 patients. Inclusion criteria: boys (n=39) or girls (n=20) between the age of 0 month and 4 y.o. with burn trauma. Exclusion criteria: previous neurological disease.

Results: The average age of patients was 1.3 y.o., the average size of a burned injury was 9% (varied from 1% to 60%). 30 (50.8%) patients had I-II, 29 (49.2%) patients had III-IV grade of severity. All children received pharmacological support in the form of various drugs in an amount of between 5 to 15, in average 8.4±0.24. Most often it were analgesics (n=59), sedatives (n=59), hemorheologic agents (n=24), broad spectrum antibiotics (n=31), a number of narcotic medications (n=22), and others. Children were treated with ALV (n=4), wound dressings were conducted with the help of the intravenous anesthesia and/or skin operations (n=22). Average numbers of medicines in patients with I-II grade of burn severity was 7.4±0.32 and with III-IV grade 9.5±0.42 ($p<0.05$). There were some complaints, which may be signs of neurological suffering, such as headache, sleep disorders, anxiety, seizures, tremor of extremities, decreased appetite, weakness, cognitive deficits in 14 cases (23.7%), which developed during 0-7 days after burn trauma had occurred. In most cases (71.4 %), they were observed in patients with III-IV degree of burns. A weak direct correlation between the amount of neurological complaints and the total number of medications ($\rho=0.23$) was identified. We found also a medium direct correlation between the amount of neurological complaints and the intravenous anesthesia ($\rho=0.39$), and the usage of broad spectrum antibiotics ($\rho=0.37$). Only 3 patients (all of III-IV grade severity) were examined by a neurologist. We identified clonic seizures, tremor, ataxia, nystagmus, muscular dystonia. So-called burn encephalopathy was diagnosed. One of those patients might suffer from drug resistance epilepsy in the future.

Conclusion: According to the severity of the disease, patients with burn trauma require a massive, long- term and diverse drug therapy. A part of them suffer from further neurological problems associated with burns. We consider the combination of iatrogenic factors, such as the quantity of intravenous anesthesia, antibiotics, and the quality of urgent care and so on, play an important role in this problem.

Analysis of monitoring system for the congenital anomalies of the central nervous system in the Sverdlovsk region

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Introduction: Congenital malformations are an important medical and social problem. Birth defects are the leading cause of infant mortality and contribute substantially to childhood illness and long-term disability. Among the most sensitive to prenatal defects ultrasound are the defects of neural tube (NTDs). This type of

violations refers to the early ontogeny of the nervous system during the dorsal induction phase, and is a result from the failure of the neural tube to close during the period from the third to fourth week of gestation.

Materials and methods: The present study was conducted on the basis of the Medicine genetic center in the Sverdlovsk region last year. Ultrasound examination of the fetus status was carried out on the unit Voluson E8 General Electric.

Results: During the study period in the Sverdlovsk region, according to the monitoring data the congenital anomalies and hereditary diseases were registered in 1643 cases (probands) having congenital malformations, including data on live births and stillbirths children and termination of pregnancy due to fetal anomaly following prenatal diagnosis (TOPFA). During the study period, there were 180 probands (11% from the entire database) with NTDs as isolated and outside the complex multiple birth defects. Thus, they are on the 4th place ranking in the incidence of congenital malformations after cardiovascular, musculoskeletal and urinary systems. Population frequency of the NTDs during the study period was 3.26 per 1000 (1:306). The birth defects of the CNS outcomes were as follows: live births children - 68 cases (38 %); stillborn children - 11 cases (6 %). Significant proportion of children born with NTDs was prevented and reached 56%. In these cases the defects were detected in the early stages of gestation, during prenatal ultrasound examination. Cases accounted for the largest share of isolated forms – 69.5% (n = 125). NTDs were included in the symptom of multiple congenital malformations were detected in 28.3% of cases (n = 51) and often associated with abnormalities of the cardiovascular system (33 %), of the musculoskeletal system (31%) and omphalocele (19.6%). The most common forms include spina bifida - 30% (1:1020), anencephalus – 19,4% (1:1575), hydrocephalus – 16,7% (1:1838), malformations of the corpus callosum - 15% (1:2042), holoprosencephalus – 4.4% (1:6890), encephalocele – 3.9% (1:7875). Rarely recorded microcephaly – 2.2% (1:13781), septo-optic dysplasia and iniencephalus.- by 1.1% (1:27563). The frequency of anencephaly in the Sverdlovsk region was – 6.7 per 10,000 (LB+SB + TOPFA) and higher than the average value of this indicator in Europe (EUROCAT – 0.18 – 4.83). This indicates possible lack of preconception preparation, as these neural tube defects are folate-dependent defects. In the group of eliminate fetuses NTDs was diagnosed by ultrasound at 10-14 weeks of gestation in 37 % of cases (n =37), at 16-21 weeks - in 39 % (n = 39), 22 weeks and up to 20% (n=20). In the group of live births children most cases of the CDF central nervous system (88 %, n = 2) is registered in the period more than 22 weeks of gestation.

Conclusion: Congenital malformations of the central nervous system take the 4th place ranking in the frequency of malformations. Significant proportion of children born with NTDs was prevented (56%), because defects were detected in the early stages of gestation, during prenatal ultrasound. The most common congenital malformations of the CNS include spina bifida - 30% (1:1020), anencephalus – 19.4% (1:1575), hydrocephalus – 16.7% (1:1838).

Role of polymorphisms of Gene *IL1ß* In parainfectional symptomatic temporal lobe epilepsy development

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Introduction: Repeated evidence presented in the scientific literature, suggest that genetic factors are involved in the control of immune response of the organism in the development of symptomatic temporal lobe epilepsy, that prompted us to conduct this study. Animal model studies show that the transformation of normal pattern of neuronal activity in the paroxysmal is accompanied by changes in the expression of cytokines, including IL-1ß of brain cells. Studies of Russian authors (Terskova N.V. et al., 2013) demonstrated that the highest producing mutant allelic variants of polymorphic alleles -3954*C and -511*C *IL-1ß* gene increase their pro- inflammatory effect on children with chronicle adenoiditis. Association studies of the polymorphic allelic variants may be relevant to the study of inflammation proconvulsant activity of chronic HSV- neuroinfection and help to rethink some important pathogenesis of symptomatic (para-infectious) focal epilepsy.

Purpose: To study the frequency of occurrence and prognostic role of promoter polymorphisms of *IL1β* which is associated with the highest producing regions of *-511 C>T (rs16944)* and *-3954 C>T (rs1143644)* in the development of symptomatic epilepsy in children with chronic *Herpes virus* neuroinfection.

Methods: The study included 32 children. Group 1 – control group without symptomatic focal epilepsy (16 pers.; median age - 9 ye.o.). Group 2 - children with chronic *Herpes virus* infection complicated by symptomatic focal epilepsy (16 pers.; median age – 13,5 ye.o.). Volume of research: history of the disease, epidemiological history, neurological examination, video - EEG monitoring, brain MRI, MR spectroscopy, immune status, serology, consultation of immunologist, real-time PCR.

Results: The frequency of genotypes *CC, CT, TT* gene *IL1β -3954 C>T (rs1143644)* in the first group were 44%, 38%, 19%, respectively; in the second group - 44%, 31%, 25%, respectively. Regarding the highest producing allele **C* gene *IL1β (-3954 C>T ; rs1143644)* in the first group the result was higher - 82%, p <0.05. The frequency of the genotypes *CC, CT, TT* gene *IL1β (- 511 C>T; rs16944)* in the first group are 50%, 44%, 6%, respectively; in the second group 69%, 19%, 13%, respectively. The frequency of the highest producing allele of *IL1β (-511 *C)* in the first group result was 94%, p<0.05. The frequency of homozygous carriers of alleles -3954 **C* and -511 **C* was 38% (p <0.05) in the second group. The frequency of heterozygous carrier was 63% (*CT*) in second group, p<0.05.

Conclusion: We showed the prognostic impact of possible association of heterozygous carrier of the highest producing allelic variants of polymorphic allele variants (-3954 **C* and -511 **C*) gene *IL1β* of the pro-inflammatory cytokine IL-1ß on the risk of symptomatic (para-infectious) focal epilepsy development in children with chronic herpetic neuroinfection.

Autonomic nervous system dysfunction in children with ADHD

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Introduction: Attention deficit hyperactivity disorder (ADHD) is one of the most common behavior disorder in children. Children with ADHD are in high social risk group. It is described in special literature that activation of sympathetic part of autonomic nervous system (ANS) is accompanied by high motor and psycho activity with absentmindedness, becoming easily distracted by irrelevant sights and sounds, inability to concentrate on task, quick change of thoughts. Parasympathetic part is characterized by good ability to concentrate on target, satisfactory attention, higher activity before noon. Obviously the only parasympathetic prepotency is not the best variant for children, but it is very hard to obtain "clear parasympathetic condition". The purpose of the study was investigation of ANS condition in children with ADHD and the influence of correction of ANS dysfunction with the attention parameters.
Methods: 12 girls and 56 boys aged from 6 to 11 years old (mean age was 8.53 ± 0.14); 27 (54%) children (6 girls and 21 boys) suffered from ADHD with prevalence of attention disorder, 23 (46%) children (1 girl and 22 boys) with ADHD combine type. The investigation included ANS examination (frequency of pulse and breath, respiratory sinus arrhythmia), psychological Shulte test. Correction of ANS dysfunction were performed by adaptive self regulation with pulse feedback signal (20 séances). Children were examined before and after correction.
Results: In all children with ADHD before correction the pulse increased till 91.48 ± 1.36 per minute, breath till 12.69 ± 0,31 per minute and RSA decreased till 23.16 ± 7,46; thus the tone of sympathetic ANS was high. Parasympathetic part was activated during correction of ANS: pulse became lower from 92.3 ± 10.03 to 83.8 ± 1.64 per minute ($p < 0.0001$), also the breath frequency changed from 12.7 ± 2.49 to 9.9 ± 1.97 per minute ($p < 0.0001$), RSA became higher from 23.2 ± 7.46 to 30.3 ± 6.85 per minute ($p < 0.0001$). It was followed by improvement of intellectual efficiency: attention concentration (all time test / 5 tables) from 94.9 ± 5.12 to 78.7 ± 3.98 seconds ($p < 0.0001$), steadiness of attention (the difference between minimum and maximum time for 1 table) from 39.4 ± 3.13 to 29.5 ±2.73 seconds ($p = 0.0021$) and capacity for work (all time of test doing) from 474.4 ± 25.58 to 393.2 ± 19.91 seconds ($p < 0.0001$).
Conclusion: during study an abnormal hyper sympathetic tonus of ANS in children with ADHD was detected. Increasing of parasympathetic activity of ANS during adaptive self-regulation improved attention parameters in patients. Thus, adaptive self-regulation with pulse feedback signal is an effective non- medical method for ADHD correction.

Bortezomib neurotoxicity in pediatric leukemia patients after stem cell transplantation

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Introduction: Background: proteasome inhibitor bortezomib (Velcade) together with azacitidine (Vidaza) and decitabine (Dacogen) is used in pediatric patients with hematological malignancies after bone stem cell transplantation.
Patients and Methods: The total number of children was 10 (acute lymphoblastic leukemia = 6, acute acute myeloblastic leukemia = 4), most of them had relapsed/refractory disease. The mean age was 7.1 years (range 1.6 – 14). All patients received treatment according to protocols, except for 2 patients who also had experimental chemotherapy with 2 injections of bortezomib in the dose of 1.3 mg/m2. Peripheral neuropathy 1-2 grade according NCIC-CTC scale was present in all children with lymphoblastic and 2 children with myeloblastic leukemia, including grade 1 in 6 (75%) and grade 2 in 2 patients (25 %). After transplantation, the children received monthly cycles containing azacitidine / decitabine and bortezomib in dose of 1.3-1.5 mg/m2 in day 2 and 5. Patients had from 2 to 6 cycles. The total dose ranged from 5.2 to 18.4 mg/m2 (average 9 mg/m2).
Results: Peripheral neuropathy developed in all cases. 5 patients (50%) had 1 grade, 3 (30%) had 2 grade and 2 (20%) had 2-3 grade neuropathy. None of them developed grade 4 neuropathy .The most common neurological sings were reduced or absent: ankle jerks (100%), stocks-and-gloves hypestesia (50%), gait disturbance (50%) and leg weakness (30%).
Conclusions: Bortezomib causes mild - average peripheral neuropathy in patients after transplantation. The severity of neuropathy may be linked with cumulative dose of the drug, and, perhaps, gait disturbance of perinatal origin. There were no correlation between the severity of bortezomib-induced and severity of pre-existing treatment-induced neuropathy. A more comprehensive study is needed to detect risk factors for bortezomib-induced peripheral neurotoxicity.

Single unprovoked seizures and recurrence risk factors in children

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Introduction: Seizure can be single or repeated. A lifetime risk of one seizure in population is 8-10%, a chance to get epilepsy is not more than 1%. Seizure can be provoked or unprovoked. Provoked or acute symptomatic seizure is unlikely to recur, its recurrence risk is 3- 10%. But if a first seizure is unprovoked, it recurs in 30-50% cases. Second unprovoked seizure justifies the diagnosis of epilepsy (a tendency for recurrent seizures). So, will first unprovoked seizure in children be single or repeated may be of interest in the field of childhood epileptology.
Material and methods: In a prospective study 42 patients with single unprovoked seizure and 315 with epilepsy, aged from 2 months to 18 years, were included. We analyzed characteristics of the first seizure, perinatal history, family history of seizures, neurological examination. The patients underwent EEG and neuroimaging [Computed Tomography (CT) and/or Magnetic Resonance Imaging (MRI)]. Children were followed for 3 years from the time of their first seizure.
Results: There were no single unprovoked seizure onsets at the age before 6 months of life. At the most single unprovoked seizures began at the age from one to three years old (31,0%; 13 patients). Generalized tonic-clonic and partial with secondary generalization seizures were the most common in children with single unprovoked seizures and epilepsy. But frequency of these types of seizures was more prevalent in patients with single unprovoked seizures ($\chi 2$ =13,69, $p<0,001$). There were not myoclonic, complex partial, absences and clonic single unprovoked seizures. Myoclonic seizures were in 53 (16,8%) children with epilepsy (Fisher two-tailed, $p=0,01$). Seizure recurrences were in 88,2% (315 children). Its repeated during first 24 hours in 27,0% (85) patients, during 2-6 days in 21,2% (67), 1-3 weeks in

16,5% (52), 1 month in 7,6% (24) cases, 2-6 months in 19,4% (61) children. Seizure recurrences were after 6 months and later in residuary patients (8,3%; 26). Seizure repeated in a year in 98,4% (310) patients. Seizures were single in 11,8% (42 from 357) cases. Seizure recurrences were prevalent in a term before 6 months after the first seizure in children of first year old, seizures more frequently repeated in a period from 6 months to one year after the first event in children from one year till 6 years and from 10 to 15 years old. Seizures recurrences were more frequently earlier than 3 weeks or later than one year in patients from 7 to 9 years old. Myoclonic seizures and absenses repeated during weeks, generalized clonic seizures recurrences were during month, generalized tonic-clonic, tonic and atonic seizures repeated during one year in average. We revealed the following recurrence risk factors for single unprovoked seizure: early seizure onset (before 6 month) ($p<0,001$), family history of seizures of first range relationship ($p=0,046$), neurological abnormality (including psychomotor developmental retardation) ($p=0,002$), atrophic brain change defined by neuroimaging ($\chi2=11,04$; $p<0,001$). Using general regression analyses we defined that early seizure onset ($p<0,001$) and neurological abnormality ($p<0,05$) were the only variables significantly associated with recurrence and were cumulative recurrence risk factors for single unprovoked seizure.

Conclusions: This study suggested that time of recurrence depend on type of seizure. Also early seizure onset and neurological abnormality have an important diagnostic value in the prognosis of recurrence seizure risk. These results will be useful in developing of observation protocol for children with first seizure.

The frequency of polymorphic alleles of CYP2C9 gene in Russian and Tuvan children with epilepsy

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The Krasnoyarsk region (KR) and Tuva Republic (TR) are located in the middle of Siberia. Prevalence of epilepsy in children aged from newborn to 15 y.o. is 5.04/1000, in teenagers - 5.75/1000 in KR. Prevalence of epilepsy in childhood population aged from newborn till 18 y.o. is 3.19/1000 in TR [Shnayder N.A. et al., 2011]. In the study area, ethnic polymorphic variability of gene alleles, involved in AEDs metabolism, is due to several reasons, including migration population, genetic drift, natural selection (for example, immune response genes, or skin pigmentation), the adaptation of Russian and the Tuvan population to local environmental conditions. However, the main causes of genetic drift in the pediatric population of the TR are inaccessible mountainous villages (Tuvan kozhuuns), the problem of communications between the regions (for example, only by helicopters), ethnic geographic isolates.

Purpose: The study of frequency of SNPs of CYP2C9 gene in Russian and Tuvan children with epilepsy, and assessment of the role of the SNPs as unmodified risk factors of ADRs development in case of intake of average therapeutic doses of VPA in ethnic aspect.

Methods: Methods were neurologic and somatic inspections, psychological testing, video-EEG- monitoring, laboratory techniques (clinical and biochemical blood analysis, testing of SNPs of CYP2C9 on chromosome 10q24.1-24.3: wild-type allele variant CYP2C9*1, mutant-type allele variants, including CYP2C9*2 and CYP2C9*3), MRI/CT. In this study we carried out pharmacogenetic testing in patients with epilepsy and receiving VPA drugs. Group 1 – Russian children (KR), Group 2 – Tuvan children (TR). Age of studied people varied - from 1 to 18 y.o. In total, the study included114 persons. ADRs of VPA were observed in 31% cases.

Results: We showed correlation between the genotype CYP2C9 and ADRs. The patients with homo- or heterozygous carriage of mutant SNPs (CYP2C9*2 and CYP2C9*3) had ADRs of VPA drugs, including liver damage (hepatomegaly, violation of the enzymatic function), defeat of GIT (gastropathy, dyspepsia), skin lesions (diffuse hair loss, peeling skin, acne), CNS (behavioral and cognitive disorders, learning disabilities, confusion, aggravation of epileptic seizures). Such serious ADRs of VPA drugs in patients with homozygous genotype CYP2C9*1/*1 were revealed only in 11% of cases. We showed difference frequency of the SNPs in the two ethnic groups (Russian and Tuvan). Homozygous genotype (CYP2C9*1/*1) among Russian have met in 65% of cases, which is 16.5% lower frequency of this genotype (81.5%) among the Tuvan. The frequency of heterozygous carriers of mutant SNPs (genotype CYP2C9*1/*2) in Russian (18%) exceeded those frequencies in Tuvan (6%) in 3 times. Homozygous carriers of the genotype CYP2C9*2/CYP2C9*2 and CYP2C9*2/CYP2C9*3 were found only in the Russian group of patients living in the KR. Carriers of CYP2C9*2 and CYP2C9*3 are "slow VPA metabolizers", accumulated VPA and its toxic intermediate metabolites in the body. It was the cause of serious ADRs. Selection of the dosages of VPA for these children was conducted, and personalized care with the use of slow titration of daily dosage during month was performed. We have shown that such children need lower initial daily dose of VPA (½ - 1/3 times lower than the average statistical).

Conclusion: Treatment of epilepsy must be not only effective but also safe.

Genetic predispose in the development of ischemic stroke in childhood

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Introduction: Ischemic stroke (IS) is a rare childhood disorder, have different reasons and prognosis. Over 100 risk factors for stroke have been reported and genetic predisposition to stroke had established. Thrombophilia is a one of condition or risk factor of IS.

Methods: Genetic thrombophilia testing was available on 47 patients (23 boys (48,94 %) and 24 girls (51,06 %)) to compare with healthy 44 children in the control group (28 boys (63,64%) and 16 girls (36,36%)) of Ukrainian population and included investigation of polymorphism of six genes: MTHFR C677T, MTHFR A1298C, MTRR, FV, FII, ACE I/D. All children in main group had an acute ischemic stroke, which was clinically and radiological confirmed. The study included infants and patients up to 14 years old. Results of investigation were expressed as pooled odds ratios (OD) and $\chi2$ in children of IS compared to the control. Statistical analysis of the results was calculated with $p<0.05$.

Results: In the main group 9 of the 47 patients (19.15%) had a homozygote mutation of MTHFR C677T gene, compared to the control group - 1 child (2.27%) was a homozygote ($\chi 2$ =6.62, OR= 10.18, 95% Cl 1.23-84.13; p=0.01); 26 children (55.32%) were heterozygous of this gene and 10 (22.73%) in the control group ($\chi 2$ =10.1, OR 4.21, 95% Cl 1.69-10.46; p=0.002). 8 patients (17.02%) had a homozygous mutation of MTHFR A1298C gene and 3 (6.82%) children in control ($\chi 2$ =1.37, OR 2.8, 95% Cl 0.69- 11.34; p=0.242); 22 children (46.81%) were heterozygous of this gene and 10 (22.73%) in the control ($\chi 2$=4.77, OR 2.99, 95% Cl 1.21-7.42; p=0.029). 18 patients (38.30%) had a homozygous mutation of MTRR A66G gene and 7 (15.91%) children in control ($\chi 2$ =5.72, OR 3.28, 95% Cl 1.21-8.91; p=0.017); 17 children (36.17%) were heterozygous of this gene and 7 (15.91%) in the control ($\chi 2$ =4.8, OR 3.00, 95% Cl 1.10-8.17; p=0.028). 15 patients (31.91%) had a homozygous mutation of ACE I/D gene and 2 (4.55%) children in control ($\chi 2$ =9.48, OR 9.84, 95% Cl 2.10-46.17; p=0.002)); 20 children (42.55%) were heterozygous of ACE I/D gene and 9 (20.45%) in the control ($\chi 2$ =4.14, OR 2.88, 95% Cl 1.13-7.32; p=0.042). Anybody in main and control groups had a homozygous mutation of FV and FII genes. 2 children (4.26%) were heterozygous of FV gene and 2 (4.55%) in the control ($\chi 2$ =0, OR 0.93, 95% Cl 0.13-6.93; p=0.946). 2 children (4.26%) were heterozygote of FV gene and 1 (2.27%) in the control ($\chi 2$=0.28, OR 01.91, 95% Cl 0.17-21.85; p=0.596).

Conclusions: The homozygote and/or heterozygote polymorphism of MTHFR C677T, MTRR A66G, ACE I/D genes and heterozygote polymorphism of MTHFR A1298C gene are related to an increased risk of IS in the group of Ukrainian children (p<0.05). We had not statistically information of FV and FII genes mutation in our investigation (p>0.05).

Cerebral palsy – Evidence based and alternative medicine approaches

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At the evaluation of results of therapeutic intervention we should respect many facts: Cerebral palsy is an umbrella term covering a group of non-progressive, but often changing, motor impairment syndromes secondary to lesions or anomalies of the brain arising in the early stages of its development. It is more than merely a motor disorder. There are motor problems, problems of development, perceptual-cognitive impairment, social and functional problems of daily living, emotional problems, epilepsy, and many others. We cannot «cure» all aspects of those problems. What are the potentials of the developing brain of the individual person to adapt to and to compensate for the damage we do not know? Brain function is shaped by the interaction of nature and nurture. Human brain is designed to be influenced by signals from the environment. Is it necessary to differentiate between method, technique and approach in a therapeutic perspective? There are Short-term and Long-term goals of the rehabilitation. The notion of alternative medicine has been around for 5000 years. It is a practice that is put forward as having the healing effects of medicine, but is not based on evidence gathered with the scientific method. Complementary medicine is an alternative medicine used together with conventional medical treatment in a belief, not proven by using scientific methods, that it "complements" the treatment with evidence-based medicine. Placebo response is often defined as an improvement in a subject's state and function, brought about by an inherently inert substance or intervention, purposefully used to elicit such a response through deceit. However, when so defined the response to placebo inevitably yields a large explanatory gap and an even larger ethical dilemma. Despite a wide range of accepted medical-rehabilitative interventions for neurologic abnormalities or lesions, there is often imprecise understanding of aetiology, variability in treatment and inconsistency in outcome, but it should be accepted that there is no magical cure, We have no evidence to suggest that one method of intervention is better than another. Many studies show some improvement however: (i) follow-up time is relatively short, (ii) long term follow-ups are sadly lacking, (iii) there are no studies which deal adequately with the co-morbidity issue. The only one «best» treatment for all problems of people with neurologic and/or developmental abnormalities does not exist, but there is no doubt that if we start to treat a problem early enough, we will achieve better results.

Conclusion: Treatment should be: age specific, have a holistic approach, respect quality of movement patterns and have a goal of quality of life. The goal is to help patients get the most appropriate treatment for them. After considering the evidence and the person's own values and judgment about their options, a patient and experienced doctor can come to a better decision. The best health care is not necessarily, where "everything" is done for the patient, but rather, the most appropriate. This can protect people from harmful and useless treatments.

Effect of periodic syndromes of childhood for further migraine in children

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Introduction: Childhood Periodic Syndromes (CPS) is a group of diseases characterized by timing issues that arise on a regular basis for several years in clinically healthy with other points of view of children. Some research results suggest that in patients with CPS can subsequently develop migraine. Certain periodic syndromes included in the International Classification of headaches II revision and are regarded as precursors of migraine. These include: cyclic vomiting (CV), abdominal migraine (AM), benign paroxysmal vertigo (BPV). The true incidence and prevalence of CVS, AM, BPV are unknown. The results of the limited epidemiological studies vary in the range from 0.04% to 2.3%. Currently it is unknown, what determines the formation of the predecessors of migraine, and if available, how they affect the course of the disease.

Research aim: to identify the total frequency of occurrence CPS the surveyed children with migraine and to conduct analyses of the relationship with the debut, the frequency of migraine attacks in the first year of the disease.

Materials and methods: The study included 145 children with migraines at the age from 4 to 18 years. The patients were divided into two groups. The first group of migraine without aura consisted of 92 child (53 boy, 39 girls), the average age of 10+5.9 years. The second group (comparison): migraine with aura, 53 children (26 boys, girls 27), with an average age 13+4.9 years. In all cases diagnoses corresponded to the international criteria of diagnosis of migraine. The trial design included an assessment of the occurrence of periodic syndromes childhood, the duration of their existence, the interval between termination of their debut and

migraine frequency of migraine attacks based on the diaries of a headache the first year of the disease. Quantitative indicators calculated with the help of programs Excel and Statistica-8.0. Expected arithmetic mean and standard deviation. With normal distribution, degree of reliability was determined using student's t-test. The level of statistical significance were the results ($p<0.05$).
Results: The frequency of occurrence among all surveyed (n=145) CPS was 8.96% (13 children). In group I (n=92) CPS was observed in 7 children (7.6%), while the structure is as follows: CVS 4 patients (4.3%), BPV 3 (3.26%), AM not met. In group II (n=53) CPS 6 (11.3%), while CVS 3 patients (5.6 %), AM, 3 (5.6%), BPV was not. The period of existence of CPS averaged 12+4.6 months. The interval between the last episode of the CPS and the first attack of migraine in group I of 16+5.9 months, in group II 27+10 months. The frequency of migraine attacks first year of the disease in children in history with CPS (n=13) were statistically significantly different 19+5, the children did not have them (n=132) 9+3.
Conclusion: the Presence of CVS does not give reliable possibility to predict the form of migraine, as occurs in both groups. A statistically significant difference found in the AM, which has only been observed in children with migraine with aura, and in the case of BPV registered only in children with migraine without aura. In the first year of the disease in children with familial history CPS it is possible to predict a heavy course of the frequency of attacks.

Neurodevelopmental outcomes in infants with neonatal seizures

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Neonatal seizures (NS) continue to represent a disorder with variable prognosis despite the current advances in its diagnosis and treatment. Neurodevelopmental outcome depends mostly on the underlying etiology of NS and presence of structural brain abnormalities. However, the assessment of patients in the neonatal period does not always allow an unambiguous conclusion about the prognosis. Therefore, prospective studies in infants with NS remain a key issue.
Materials and Methods: The study included 165 infants with gestational age (GA) of 22-41 weeks, birth weight 450-4040 g, Me [LQ; UQ] 1196 [900; 1570] with multiple digital-video-EEG confirmed NS were included into the study and followed for at least 12 months period. They were subdivided in four groups according to GA: (1) 84 early preterm newborns with GA 22-28 wks, (2) 52 with GA 29-32 wks, (3) 12 newborns with GA 33-36 wks. and (4) 17 term infants with GA between 37 and 41 wks. The children underwent prospective neurological assessments and examinations with Bayley Scales of Infant and Toddler Development, Third Edition (BSID-III) at the corrected age (CA) of 1 year.
Results: There was no strong correlation between the etiology of NS and unfavorable outcomes. The most common cause of NS was perinatal hypoxia (83.6%, n=133). CNS and systemic infections accounted for 12.1% (n=20) of NS. 6.7% (n=11) of NS cases were caused by the intracranial hemorrhage grade III-IV. Cerebral digenesis (1.2%, n=2), cerebral infarction and inborn errors of metabolism (0.6%, n=1 for each) were among the rare etiologies. The abnormal background EEG patterns at the CA of 36- 40 wks. were present in the majority of cases (85.7%, n=90), irrespectively of ictal EEG pattern's rate. There was no significant difference in terms of neurological outcomes between the four groups. At the CA of 1 year 35.2% (n=58) of cases have demonstrated normal psychomotor development. Cerebral palsy developed in 33.3% (n=55) of cases, psychomotor delay – in 24.2% (n=40). The mortality rate was 4.2% (n=7). Epilepsy developed in postneonatal period in 19.4% (n=32) of cases, and relative risk of epilepsy in infants with structural brain abnormalities was found 3.5 times higher compared to those without structural abnormalities. 52 infants with NS and 10 healthy term infants of the control group were assessed with BSID-III at the CA of 1 year. The composite scores for cognitive, language, motor, social-emotional and adaptive behavior scales were significantly lower in infants with NS comparing to the control group ($\chi^2(df=4)=18.49$, $p=0.001$). No significant differences were found between the groups of infants with NS of different gestational age. Of the total number of infants suffered NS the developmental delay was found in 36.5 % (n=19) for cognitive scale, 25.0 % (n=13) for language scale, 44.3 % (n=23) for motor scale, 25.0 % (n=13) for the social-emotional scale and 61.5 % (n=32) for adaptive behavior scale. The presence of structural brain abnormalities increased the risk of unfavorable neurological outcomes in our sample of infants with NS, but did not have unequivocal correlation with these unfavorable outcomes. However, high rates of neurological consequences and developmental delays in all 5 domains according to BSID-III scales emphasize the need for prospective studies in infants with NS.

The prospects of long-term use of Botulinus Neurotoxin A Type (BTA) in complex rehabilitation of children with spastic cerebral palsy

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The inevitability of appearing contractures and extremities deformations in children with cerebral palsy inevitably lead to surgical orthopedic correction. In a long-term prospect, children with cerebral palsy who undergo orthopedic operations at advanced age, have a smaller risk of recurrence compared to children in the process of active growth. To solve this, for the children with cerebral palsy it is necessary to begin and carry out anti-spastic therapy in a complex with children rehabilitation. The object of work is the analysis of efficiency of a long-term using of BTA in children with spastic forms of cerebral palsy.
Material and methods: The study included 2 groups of children: the first group consisted of 45 children with cerebral palsy, who got in a complex of rehabilitation therapy 8 consecutive injections of BTA (21 girls, 24 boys, the average age during treatment is 4.8±1.8 years). The group of comparison consisted of 41 children with cerebral palsy who had the same treatment without injections of BTA (19 girls, 22 boys, average age of 5.1±2.2 years). All researched children surely got a complex of rehabilitation actions during 1.5 months, 2 times a year. The children of the first

research group repeatedly received BTA (Disport) not earlier than in 24 weeks after the previous injection. The preparation Disport was administered into muscles in a dose from 14 to 30 PIECES/kg, on the average 26±4 PIECES/kg. The efficiency of treatment was determined by the results of complex clinical neurologic treatment of the patient, and also by application of a ball assessment on various scales and self-assessment scales.

Results and Discussion: The analysis of the level of spasticity on Ashvort's scale in a group of children receiving injections of BTA, demonstrated statistically reliable effective decrease in a muscular tone as a result of each next injection. 24 weeks later after each next injection, the muscular tone did not come back to initial indicators and differed during the first four injections. While analyzing the dynamics of motive development in children with cerebral palsy after repeated injections of BTA, it was shown that the considerable effect was reached 24 weeks later after the first two injections. The improvement on 2 and more points is noted after the first injection in 32 children (72%) and after the second injection in 29 children (64%). Next injections (the third, the fourth and the fifth) were less productive concerning these indicators. After the sixth and seventh injections the number of the children who moved to a new motive level, increased again: after the 6th injection in 25 children (55%) and after the 7th injection in 32 children (72%) with cerebral palsy, the improvements were noticed on 2 and more points. At the time of the follow- up observation of the children with cerebral palsy during the 24-months there was the tendency of reduction of a number of children who needed surgical correction of orthopedic complications after 4 repeated injections of BTA, but it was not reliable (40% against 45% in group of comparison, $p=0,883$). Observation of the children with cerebral palsy within 48 months after 8 repeated courses of botulinum therapy showed that the number of children who needed expeditious treatment, was higher in group of children without BTA injections (47% against 71% in a group of comparison, $p=0,041$).

Conclusions: The results of a research showed that a long-term injection programs of BTA considerably improve motive opportunities in children with cerebral palsy. The repeated use of BTA in children with cerebral palsy in conditions of a complex rehabilitation allows to optimize conditions for motive rehabilitation of a sick child, to slow down the rates of formation of secondary orthopedic complications and to carry out orthopedic intervention in later terms with minimizing risk of recurrence of orthopedic problems.