#### **POSTERS NEUROLOGY**

#### 1. ANTI-INFLAMMATORY EFFECTS OF COPAXONE ON THE LEVEL OF ADHESION MOLECULE EXPRESSION PATTERNS UNDER SHORT- AND LONG-TERM TREATMENT

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Introduction/Objectives: To analyse the influence of short- and long-term glatiramer acetate (GA) treatment on expression patterns of cell surface-bound adhesion molecules (AM) on peripheral blood mononuclear cells (PBMC) from patients with relapsing remitting multiple sclerosis (RRMS). BACK-GROUND: GA is baseline therapy for the treatment of RRMS. It is known to reduce relapse frequencies and to delay disease progression but the exact mechanisms of action remain elusive. Here, we investigate AM expression levels on PBMC from MS patients under short-and long-term GA therapy and from healthy controls.

Participants, Materials/Methods: Quantitative expression levels of intercellular adhesion molecules-1, and -3 (ICAM-1, -3), leukocyte function antigen-1 (LFA-1;CD11a), and very late activation antigen-4 (VLA-4; CD49d) were measured on CD3+/CD8+/CD4+ T cells, CD19+ B cells, natural killer (NK) cells, NKT, and monocytes from 23 RRMS patients and 15 healthy individuals by five-color flow cytometry (Beckman Coulter FC500). PBMC from short-term treated patients (Group 1, n=13) were analyzed at baseline (prior to GA therapy), after 1.5, 6, and 12 months. PBMC from patients receiving GA for more than two years (Group 2, n=10) were measured twice in an interval of 6 months.

Results: We found higher surface expression of ICAM-3, LFA-1, and VLA-4 on PBMC from RRMS patients than in controls. A short-term reduction in ICAM-3 on all lymphocyte subsets was observed during the first 12 months of therapy which resolved over time. Long-term GA-treated patients had with similar elevated ICAM-3 expression levels than RRMS patients at baseline. VLA-4 showed a sustained normalization in surface expression on CD4+T cells and CD19+B cells under short- and long-term GA treatment comparable to controls. Surface expression of ICAM-1, and LFA-1 remained unaffected by GA therapy.

Conclusions: The transient reduction of ICAM-3 and the sustained normalization of VLA-4 expression demonstrate anti-inflammatory effects of GA therapy on the peripheral immune cell level. Downregulation of AM expression might be of particular importance within the first year of GA treatment until additional therapeutic mechanisms like stabilization of the blood-brain barrier come into effect.

This study has been supported by Sanofi aventis Austria.

#### 2. FLOW CYTOMETRY OF NATALIZUMAB BINDING TO IMMUNE CELLS AND ITS POTENTIAL USE FOR MONITORING DISEASE ACTIVITY AND TREATMENT RESPONSE IN PATIENTS WITH MULTIPLE SCLEROSIS

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Introduction/Objectives: To examine whether natalizumab binding to peripheral blood mononuclear

cells (PBMC) from patients with relapsing remitting multiple sclerosis (RRMS) is informative on the individual treatment response. BACKGROUND: The therapeutic antibody natalizumab (TysabriTM) interferes with leukocyte transmigration into the central nervous system by blocking the alpha-4 subunit of the heterodimeric very late activation antigen (VLA)-4 integrin. In former studies we observed surface-bound natalizumab (anti-human(hu)IgG4) correlating with diminished alpha-4 expression levels on PBMC during the first 6 months of therapy.

Participants, Materials/Methods: Quantitative surface levels of alpha-4 (anti-CD49d-FITC) and natalizumab (anti-huIgG4-FITC) on T cells, B cells, natural killer (NK) cells, and NKT cells from 8 RRMS patients were determined by 5-color flow cytometry (Cytomics FC500, Beckman Coulter Vienna). Samples were collected at baseline (before start of therapy), and after 12, 24, 36, and 48 weeks before the subsequent natalizumab infusions.

Results: Analysis of mean relative fluorescence intensities (rfi) of natalizumab binding from 7 patients showed a significant and sustained increase of anti-hu-IgG4 signals in the 12, 24, 36, and 48 week measurements (p<0.007) on all lymphocyte subsets compared to baseline levels. Detailed examination of individual data sets revealed only slight variations and a decline of anti-IgG4 rfi after 24 and 36 weeks in 5 patients. Two patients showed additional peaks after 24 and 36 weeks which corresponded with clinical disease activity. Alpha-4 expression levels were diminished at all time-points. In one patient anti-huIgG4 signals did not exceed background levels until the 36 week measurement due to non-persisting neutralizing antibodies (NAB).

Conclusions: Increased binding of natalizumab to immune cells might result from variances in surface expression of VLA-4 and possibly represents an early indication of underlying disease activity. Low antinatalizumab signals provide immediate and direct evidence of NAB. Natalizumab binding to immune cells is a potential biomarker for the individual patients' treatment response.

Supported by: Biogen Idec, Austria

#### 3. ACUTE PULMONARY EDEMA CAUSED BY A MULTIPLE SCLEROSIS RELAPSE

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Introduction/Objectives: Multiple sclerosis (MS) relapses entail various clinical symptoms depending on the localization of the inflammatory lesion within the central nervous system (CNS). We present a rare initial presentation of a MS relapse with pulmonary edema caused by a left ventricular failure.

Participants, Materials/Methods: A 48-year-old MS patient presented with severe acute pulmonary edema caused by a transient cardiomyopathy. Brain MRI demonstrated an acute demyelinating lesion in the brain stem with gadolinium enhancement lesions. A significant improvement in ejection fraction of the heart and a restitution of pulmonary edema were seen after high dose cortisone treatment.

Results: The significant improvement in ejection fraction after high dose cortisone therapy confirms our theory that acute left ventricular failure caused by the active brain stem lesion. An apical ballooning syndrome (takotsubo cardiomyopathy) is the most probable explanation for transient cardiomyopathy.

Conclusions: In our case, we show a rare initial presentation of a MS relapse with pulmonary edema. Clinicians should be alert if a MS patient presents with dyspnea.

## 4. INTERLEUKIN-17 RECEPTOR IN MULTIPLE SCLEROSIS PATIENTS TREATED BY INTERFERON B-1A.

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Introduction/Objectives: Interleukin 17 / Il-17/ and its receptor Il-17 R1 produced by T-helper cells, named Th17, are involved in pathology of autoimmune diseases. Il-17 is of importance in such processes as

delayed – type hypersensitivity, including multiple sclerosis. In contrast to at least partially explained role of Il-17 in pathology of multiple sclerosis, the significance of Il-17R in MS is unclear. Therefore, we have studied the expression of Il-17R in stable phase of multiple sclerosis treated by interferon  $\beta$ -1a.

Participants, Materials/Methods: The studied material consisted of 20 MS patients with relapsing-remitting form of the disease, and fulfilling the diagnostic criteria of McDonald et al. Blood samples for immunological test were taken before treatment, after 3 months and 6 months of interferon therapy. The interleukin 17 receptor level was measured in duplicates by the ELISA immunoassay test, using RayBio human Il-17R ELISA kit / Georgia, USA/.

Results: After three months of therapy with interferon  $\beta$ 1a the level of Il-17R was significantly higher than that established at the starting point. The level of Il-17R after 6 months of therapy was insignificantly higher than that established before therapy.

Conclusions: Upregulation of IL-17R in early period of MS therapy with interferon  $\beta$  may suggest that it constitute a drug turget in MS.

## 5. TIBIAL NERVE SOMATOSENSORY EVOKED POTENTIALS IN MONITORING THE COURSE OF MULITPLE SCLEROSIS

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Introduction/Objectives: Somatosensory evoked potentials (SSEP) are a method of choice in diagnosing multiple sclerosis (MS). MS is a central nervous system (CNS) chronic demyelination disease with a constant progression tendency. The Kurtzke Expanded Disability Status Scale (EDSS) is a method of quantifying disability in multiple sclerosis and monitoring changes in the level of disability over time. SSEP are biopotentials passing through the spinal cord. SSEP of the tibial nerve are determined by evoked responses, such as neurogram, spinogram and cortical response.

The subject of our interest is the correlation between the latency of tibial nerve SSEP and the stage of neurological impairment assessed with EDSS.

Participants, Materials/Methods: The research included 49 MS patients. All patients underwent EDSS assessment. The EDSS score is based upon neurological testing and examination of eight functional systems. Those systems are: pyramidal, cerebellar, brain stem, sensory, bowel and bladder functions, visual, mental and other (to include any other neurological findings due to MS). The score ranges from 0 to 10 (0 is a normal neurological exam, 10 is a death due to MS). EDSS scores 1.0 to 4.5 refer to people with MS who are fully ambulatory, whereas EDSS scores 5.0 to 9.5 are defined by impaired ambulation. Tibial nerve SSEP studies were performed on all patients and the latency of evoked response (measured in miliseconds- ms) was determined for all, as well. SSEP of the tibial nerve was assessed by using the apparatus Medelec Synergy - Oxford Instruments.

Results: The research included a total of 49 patients, 34 females and 15 males. The mean age of patients is 34±3.1. Average duration of MS is 6.1±2.3 years. All patients had relapses, on average 12±2 relapses. EDSS score is between 2,5 and 6,5, on average 4,5. All patients had prolonged evoked response latency and extremely low amplitudes of all evoked responses. The average cortical response latency is 56.4±2.3 ms. By using Kruskal-Wallis test we analyzed the correlation between the degree of neurological impairment of MS patients (assessed by EDSS) and tibial nerve SSEP latency. The test results imply that there is a significant correlation between EDSS score and tibial nerve SSEP latency (p<0,05).

Conclusions: The degree of neurological impairment of MS patients correlates with prolonged latency of tibial nerve SSEP studies in these patients.

#### 6. PHARMACOECONOMIC MODELLING OF ALZHEIMER'S DISEASE - ASSESSMENT OF MEMANTINE IN TREATING MODERATE TO SEVERE ALZHEIMER PATIENTS

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Introduction/Objectives: In treating of moderate to severe Alzheimer patients, N-methyl D-aspartat antagonist memantine has demonstrated better results and correlations with decreased hospitalization rate, thus decreasing total health costs. Most of pharmacoeconomic studies for this disease consider societal perspective using cost effectiveness principle and QUALY parameters. This paper considers payer perspective (Croatian Department for Health Insurance) and takes into account direct cost of the disease as requested in Croatian guidelines for drugs reimbursement. Recent NICE (National Institute for Clinical Excellence) memantine coverage enabled more space for this drug's reimbursement in other countries.

The aim of the paper was to assess direct cost of illness with and without treatment with memantine, through a three year perspective.

Participants, Materials/Methods: Due to lack of (inaccurate) epidemiological data, authors have undertaken further data search: the paper demonstrates cost variables taken from Croatian real life environment of treating Alzheimer patients acquired by delphi consensus method. Markov model was created for Croatian case to assess effect of the drug on hospitalization frequency and other direct treatment costs. Model stability was tested with Monte Carlo simulations.

Results: Results demonstrate memantine domination in terms of efficiency and cost reduction. Reduced and delayed hospitalizations relate to direct costs, while less antipsychotic use, commorbidities and caregiver effort evidenced lower other costs.

Conclusions: Memantine brings substantial cost savings on annual as well as three annual time horizon. It may be concluded that memantine reimbursement may bring cost saving not only to health budget of the payer, but also to other hospital related costs.

## 7. ALZHEIMER`S DISEASE – RESOURCE PROVIDING AND ECONOMICS FOR ENSURING CARE OF PATIENTS IN PALLIATIVE MEDICINE

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Introduction/Objectives: Present health economics results demonstrate that there is a significant amount of unnecessary hospitalizations making patients spend too many days institutionalized and quite low quality and lack of palliative care, whereas the numbers from secondary data analysis indicate that hospital capacities and possibilities may provide high quality hospital palliative care.

Aim: to demonstrate possible ways of organizing and providing resources in palliative care of Alzhemier's disease patients in Croatia, using health economics and supporting centre.

Participants, Materials/Methods: Analysis of present hospital and other capacities, epidemiology, current health approaches, recommendations based on real life and secondary data. The research revealed numerous potential sources of financing and providing resources for palliative care for Alzheimer's disease patients. Such are insurance companies (basic, additional, private); philanthropy and humanitarian actions; volunteers; donations in money, services, drugs and goods; taxes (state, county and city); foundations, real estate; scientific, professional and marketing projects; sponsorships, bank loans etc. Unfortunately most of these sources are inadequately or totally unused or unrecognized.

Results: Numerous organizational and direct health costs in Alzheimer's disease palliative care come in terminal disease phase, additionally burdening life of patients and their families: facility, overhead, various services, insurance, material and drug, food, human labor (professionals and volunteers) and transport costs. All of these indicate that palliative care should be based on a non profit model.

Conclusions: It is necessary to completely redesign organizational approach in Alzheimer's disease palliative care. Such redesign should be funded from various resources, one national centre with counties'

network to organize and rearrange capacities, enabling higher quality in care with decreased number of doctors and nurses.

#### 8. EXTRACRANIAL CAROTID ARTERY DISSECTION

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Introduction/Objectives: Annual incidence of spontaneous carotid dissection has been ranging from 2,5 to 3 cases/100.000 inhabitants. It is responsible for only about 2,5% of all ischemic strokes. Spontaneous dissection of cervical arteries has been the second leading reason for ishcemic brain infarction in young people. It is evaluated that it is responsible for cerebrovascular insults in patients younger than 45 years. Extra cranial carotid artery has been affected in 75% versus 15% in extra cranial VA.

Participants, Materials/Methods: While the clinical and diagnostic criteria for CAD are well established, its pathogenesis remains include in many cases. Main predisposing factors are included trauma and preexisting disease of the arterial wall. Typical patient with CAD is presenting with unilateral headache, pain in the face, throat with HORNER syndrome. The most serious consequence of the CAD is acute ischemia in vascular territories, distally from the lesion.

Diagnosis: All available noninvasive imaging methods, including the conventional angiography as a standard criterion. Color duplex sonography, if is used early enough and often concerning the dynamics of the process of arterial dissection ,is sensitive in detection of stenosis, occlusion with or without thrombus formation.

Results: Diagnostic specific results which are met in less then 1/3 of the cases are intramural hematoma as well as a double lumen with dissected membrane. ANGIOGRAPHY: As typical findings are described the following: long irregular stenosis starting 2-3 cm from bulbi, string sign, pseudoaneurysmus (either sacular of fusiform), distal blood vessels occlusion from embolic material. Pathognomonic findings for

dissection as a double lumen are detected in less than 10%.MRI with axial section in the neck has the advantage to visualize the very intramural hematoma, as a crescend hypersignal in T1 and T2 which surrounds the narrowed lumen of the artery.

Conclusions: The prognosis has been conditioned from the severity of the initial ischaemic phenomenon and the volume of colateral circulation as well as the site of dissection. CVI which has been due to CAD is considered to have a good prognosis with data for improvement without significant sequels in 70-90% of the patients. Generally accepted initial empyrical treatment in acute CAD, especially associated with symptomatic hemodynamic stenosis beyond 70% and after excluding of the intracranial extension of dissection, is i.v. HEPARIN, followed by oral anticoagulant therapy, with a target INR 2-3 lasting 3-6 months. Surgical or endovascular therapy in CAD is indicated in refractory to drug therapy, relapsing CVI contrary to adequate anticoagulant, progressive aneurysms.

# 9. EFFECT OF THE DEEP BRAIN STIMULATION ON THE REGIONAL SEROTONIN SYNTHESIS IN PARKINSON PATIENTS: POSITRON EMISSION TOMOGRAPHY STUDY

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Introduction/Objectives: It has been proposed that the brain serotonergic system is one of the brain monoaminergic systems affected in people with Parkinson disease (PD).

Participants, Materials/Methods: Brain serotonin [5-HT] synthesis was studied in normal subjects (controls) as well as Parkinson patients scheduled for implantation of a deep brain stimulator. Inclusion criteria: Patients have advanced PD (Hoehn-Yahr, Stage II to IV), screened for dementia (e.g. Mattis dementia inventory), Psychiatric disorders (DSM IV classification, BDI and HRDS-17), Social adjustment scale (SAS), Personality changes (IOWA scale of personality changes). A subthalamic deep brain stimulator (DBS): a lead with four contacts spaced 1.5 mm was implanted stereotaxicaly. Five patients (one

female) (58.8±6.5 years) and ten normal subjects (two females) (48.9±16.6 years) had positron emission tomography (PET) scan using about 10 mCi of  $\alpha$ -[11C] methyl-L-tryptophan. Sixty minutes dynamic PET scans were taken with venous blood sampling. Patients were scheduled to have three scans; the first was scheduled before stimulator implantation and without overnight medication, the second scan was done about six months after stimulator implantation with stimulator ON, and the third scan was scheduled about one year after the first scan. Unfortunately only one patient completed all three scans, and as such no comparison was made with the third scan. Images of the brain trapping constant (K\*; µl/g/min) were colocalized with individual MRI in 3-D. 5-HT synthesis was compared to that measured in a group of normal controls of the same gender and approximately the same age. PET images were co-registered with MRI images, transformed into Talairach stereotaxic coordinates and analyzed using SPM (Statistical Parametric Mapping).

Results: The SPM comparison identified several regions in which normal subjects had higher 5-HT synthesis than Parkinson patients (BA10 bilateraly; BA11, BA22, BA40 and Insula right side, and BA41 left side), and in the right putamen. In the second scan Parkinson patients had higher 5-HT synthesis than normals in the Precuneus (BA 19), left occipital cortex, and medial globus palidus. There were also regions in which Parkinson patients had 5-HT lower than normals (BA10 bilateral, left side BA32, BA20, BA37, BA39, and insula, and the right side BA44). The stimulation several regions of difference between normals and patients were lost (e.g. BA11, BA22, BA40 and BA41), but stimulation produces some new regions (normals>patients) of significant difference (BA32, BA20, BA37, BA39, and BA44). The loss of BA11 and BA40 activations could suggest a better handle of emotional-cognitive and sensorycognitive integrations in patients after stimulation. The loss of stimulation (activation in PET study) in the right BA22 and BA41 could be related to a better fundamental role in nonverbal sound processing.

Conclusions: An inhibition of synthesis by stimulation in some limbic structures (e.g. BA32 and BA20) could be related to the patients' emotional state, while a reduction in BA37 and BA39 could be related to

a functionality of the Broca's area. Most likely other differences which are present before and after DBS represent nonspecific differences which could not be "normalized" by DBS.

## 10. COGNITIVE DISORDERS IN CHILDREN WITH HEARING LOSS CONNECTED WITH OTITIS MEDIA WITH EFFUSION

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Introduction/Objectives: In the first two years of child's life normal hearing is an important critical period for emotional and cognitive development. Cognitive processing, including e.g. auditory perception, working memory processes and long term memory require temporary integration of numerous constantly interacting areas of the brain. Temporal processing of auditory information is involved in high-level cognitive functions. Otitis media with effusion is characterized with conductive hearing loss which does not excide 35dB and can be overlooked. This entity is the most common cause of communication disorders and most frequent base for cognitive disorders in childhood. In the presence of hearing loss temporal processing is compromise which has negative consequence for processing of speech in left hemisphere .Even a mild or small hearing loss can affect a child's ability to recognize and memorize spoken language and develop auditory working memory and tectal mapping. The aim of the study is to find out if peripheral hearing deficit with particularly restrictive frequencies compromise temporal processing and thus predict cognitive disorders in childhood.

Participants, Materials/Methods: Prospective study group included 18 female (mean age 7,8 year) and 27 males (mean age 6,5 year) with hearing loss associated with otitis media with effusion. Tonal audiometry for estimation of hearing threshold and speech audiometry sound field discrimination and with earphones for each side of ears respectively performed in all study groups. All of the children undergo speech/language screening tests.

Results: Lower audiometric frequencies (500Hz, 1000Hz)have higher level of conductive hearing loss than higher frequencies (2000Hz,4000Hz)(p=0.008) for group males and females either. While testing by earphones, threshold for speech discrimination in

sound field showed no ear side effect between males and females (p=0.169). Right ears in females showed higher level of speech discrimination in sound field than right ears in males while left ears showed equal level of discrimination threshold in both groups. When tested 100% of speech discrimination, left ears in males showed higher sound level than right ears (p=0.016). However, females showed no differences between threshold for speech discrimination in sound field (p=0.891). When tested 100% of speech discrimination, there were no difference between right and left ears (p=0.799).

Conclusions: Conclusion: Children with conductive hearing loss associated to otitis media with effusion are pronounced for left hemisphere auditory processing and speech/language discrimination disturbance. Associative thinking and solving of abstract problems are more affected in females than males.

# 11. ASSOCIATION OF COGNITIVE IMPAIRMENT AND DECLINE WITH PSYCHOLOGICAL PROFILE IN PATIENTS WITH DOMINANT CAROTID ARTERY DISEASE

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Introduction/Objectives: There is unknown cause of cognitive impairment in persons who have not had stroke. Underlying vascular risk factors or atherosclerosis in general are in relationship with cognitive impairment connected with brain circulation. Internal carotid artery is the main source of brain hemisphere blood supply.

Participants, Materials/Methods: We examined dominant carotid arteries (left carotid arteries in right-handed and right carotid arteries in left-handed men and women) in 67 patients (31 male and 36 female) without history of stroke, transient ischemic attack, or carotid endartectomy. Internal carotid artery stenosis and intima-media thickness of the common carotid artery were assessed by using duplex ultrasonography. Cognitive impairment was defined with performance of the Modified Mini-Mental State, MMPI-201, PM, LB, WB-sp.

Results: Cognitive impairment and decline are associated with asymptomatic high-grade stenosis of the left internal carotid artery in 5 patients. Depression is present in 17 patients, emotional incontinence in 7 patients and speach/communication disorders is present in 3 patients.

Conclusions: The persistance of the association after adjustment for right-sided stenosis indicates that the association is not due to underlying vascular risk factors or atherosclerosis in general.

# 12. CLINICAL SPECTRUM OF NEUROLUES IN NEUROPSYCHIATRIC MORBIDITY IN BJELOVAR COUNTY, CROATIA, FROM 1931 TO 1940

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Introduction/Objectives: Lues (syphilis) is a contagious systemic disease caused by Treponema pallidum and characterized by sequential clinical stages and years of asymptomatic latency. With retrospective study we tried to estimate clinical expressions and frequency of hospitalizations of patients with neuroloues (neurosyphilis) in period from 1931 to 1940, in General Public County Hospital in Bjelovar, today Croatia.

Participants, Materials/Methods: Reviewing the Main Register of Patients of the General Public County Hospital of the Kingdom of Yugoslavia in Bjelovar, kept in the National Archives in Bjelovar, Croatia, from April 1 1931 to December 31 1936 and from January 1 1939 to December 31 1940 (with the remark that the registers of patients for the years 1937 and 1938 were unavailable and probably lost forever).

Results: In 1931 the County of Bjelovar had 73,664 residents. General Public County Hospital had three departments: dermato-venereological, surgical—gynaecological and internal department with a small unit called Lunatic Asylum. In the observed period 26,104 patients were treated in the hospital and out of these 1,488 patients were treated for neuropsychiatric morbidity and 299 of them because of neurolues.

The highest number of patients appeared in the years 1932, 1933 and 1934, representing 20% of neuropsychiatric morbidity. Almost half of the neurolues patients (134) had luetic myelopathy (tabes dorsalis) and other diagnosis in the clinical spectrum were: taboparalysis, dementia paralytica, paralysis progressiva, lues paralyticum, lues cerebri, lues III, neurolues, pachymeningitis, cephalea luetica, meningitis spinalis luetica, neurolues spinalis, lues hereditaria, arachnoiditis, apoplexio luetica, myelitis lumbalis luetica and meningomyelitis luetica.

Conclusions: A decade before the World War II lues represented a major public health issue with no adequate treatment available. Introducing the antibiotics and practical mass application of penicillin since 1943 has changed epidemiology of neurologic and psychiatric diseases with actual dominance of neuro-degenerative aetiology.

#### 13. CAMPTOCORMIA - CASE REPORT

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Introduction/Objectives: Camptocormia (Greek "kamptos" = bend and "kormos" = trunk) or "a bent spine syndrome" is abnormal posture of the trunk with involuntary thoracolumbar flexion in the upright position of the patient. It disappears lying in the supine position which is a sign excluding a fixed deformities in ankylosing spondylitis and degenerative spondylosis.

Participants, Materials/Methods: Case report: We present a 68-year-old female patient with ten years history of low back pain who gradually had began to bend forward. In age of 64 extensive spine degenerative changes, disc herniation L5S1 and spinal stenosis were found on MRI. Operative treatment was planned. The neurological examination revealed marked anteflexion of trunk, semiflexion of both legs, predominantly right tremor of hands, bradykinesia. There were no spine abnormalities while lying in a supine position. Patient was advised to delay her scheduled spine surgery and received ropinirole and levodopa / carbidopa. A few months later, in age of

65, she decided to undergo spine surgery with spondylodesis. On control examination seven month later she felt good, had minimal tremor and rigidity in both arms, wearing orthotics and maintained erect posture, but with knees semiflexion. A three months later levothyroxine therapy was introduced because of hypothyroidism. Neurological status deteriorated and she was placed on a higher dose of levodopa.

Results: Two years after surgery she felt acute pain in her back. X-ray showed breakage of osteosynthetic implant at two levels with no dislocation. Over the months the pain progressed regardless of body position. Implantation of opiod intrathecal pump was unsuccessful. Four months later, she had severe pain, VAS 9, bilateral rigidity, oedema of the left eyelid and feet, a minimal hand tremor and dysphagia. She moved arms and legs, but the trunk was fully bent and she was not able to stand up, to lye in supine position or to turn in bed. Increasing of levodopa dosage led to decrease of pain, to VAS 3, and led to ability of standing and making few steps with help of two persons. She died 6 months later.

Conclusions: Camptocormia is rare condition of multiple aetiologies. The most common are seen with parkinsonism, but also with dystonia, spine abnormalities, brain injury, stroke, neuromuscular disorders, psychogenic disorders or idiopathic. It requires a serious diagnostic evaluation before decision on ways of treatment - systemic or local therapy.

## 14. COGNITIVE AND EMOTIONAL IMPAIRMENTS IN NEUROREHABILITATION OF PATIENTS WITH MULTIPLE SCLEROSIS

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Introduction/Objectives: Multiple sclerosis (MS) is a chronic neurological disease that causes significant motor, sensory, cerebellar and cognitive disability and mood disorder. The aim of study was to explore and objective neuropsychological impairments in patients with MS. Participants, Materials/Methods: Sixty-one patients (51 women, 10 men, age 23 to 69) with MS hospitalized in medical rehabilitation hospi-

tal were included in the study. Patients were instructed to neuropsychological testing by neurologist and / or physiatrist. Neuropsychological assessment was carried out by psychologists through an individualized approach. The neuropsychological tests included: psychological interview, quantitative assessment and qualitative assessment.

**Results:** The study showed that 47.5% of patients were emotionally stable, 67.2% were dysphoric, 29.5% had mild and 3.3% moderate or severe depression, 23.0% have expressed anxiety and 11.5% were moderate to serious anxious. Patients with longer disease duration were less anxious. Attention was severely impaired in 15.0% of patients and the duration of illness showed a moderate positive correlation with attention impairment. Almost 15% of patients had serious deficits in the domain of the new learning, and 41.0% mild impairments. 29. 5% of patients showed difficulties with the retrospective memory. Impairment in formal thinking was found in 21.3% of patients. More severe deterioration in the domain of higher opinion functioning had 11.5% of patients. Almost 15, 0% of patients showed more severe dysfunction of perception, 42.6% had motor speech disorders, and 15.0% had difficulty in speech understanding. 34.5% of patients had problems in reading and 49.1% in writing. 27.9% of patients showed organic personality changes, and 26.2% personality changes due to the psychogenic factors.

Conclusions: The study pointed to a positive correlation between disease duration and impairment in perceptual functions, retrospective memory, and expression and understanding speech. Since the cognitive and emotional impairments have a significant impact on patients' everyday life, the neurorehabilitation focus should be directed to a practical training in attempt to maximize all the functions in order to reduce the deficits.

## 15. SOCIODEMOGRAPHIC CHARACTERISTICS OF NEWLY DIAGNOSED MULTIPLE SCLEROSIS PATIENTS

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Introduction/Objectives: Introduction: Multiple sclerosis is chronic inflammatory disease. Disease onset usually occurs in young adults, between 20 and 40 years old, and it is more common in females.

**Objective:** The aim of the study was to evaluate the sociodemographic characteristics of newly diagnosed multiple sclerosis patients.

Participants, Materials/Methods: We retrospectively analysed data from medical hystories of the patients treated at the Department of Neurology, Clinical Neurology Unit, Clinical Center University of Sarajevo, from January 2005 to December 2009. We collected data of newly diagnosed patients during that period, who satisfied Mc Donald criteria for MS diagnosis.

Results: During the sudy period, there were 62 newly diagnosed multiple sclerosis patients, who satisfied Mc Donald criteria for MS diagnosis. 36 (58%) patients were female, 26 (42%) were men. Mean age of the patients at the time of confirmed diagnosis was 36.30+/-10,38 years. The majority of patients were married 34 (55%). 34 (55%) patients were employed. The higher percentage of the patients 44 (71%) completed high school. The higher incidence of MS was in urban areas -54 (77%) patients. Mean EDSS score at the time of diagnosis was 2,4+/-1,63. Average time from the first symptoms to confirmed diagnosis was 47,5+/-65,74 months.

Conclusions: Gender structure, employment status, education level, marital status and living area of the patients in our study resembles those in most epidemiological MS studies. Older age of patients in our study is due to longer period of time from the first symptoms of the desease to the confirmed diagnosis.

# 16. PARTIAL SUBCLAVIAN STEAL IN A PATIENT WITH SUBCLAVIAN ARTERY ANOMALY AND VACTERL SYNDROME - CASE REPORT

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Introduction/Objectives: Subclavian steal syndrome refers to a pathological condition due to a proximal stenosis or occlusion of the subclavian artery. Most common cause of the steno-occlusive process is atherosclerosis. Others causes are unusual and include arteriopathies (Takayasu disease, temporal arteritis) and congenital lesions of the aortic arch or subclavian artery. Lusorian artery is a rare right subclavian artery anomaly with an incidence of 0.5 - 2%. It originates as the most distal aortic arch branch, and most commonly has a retroesophageal course thereby sometimes causing dysphagic difficulties (dysphagia lusoria). VACTERL syndrome is diagnosed when at least three of the following anomalies are present in a newborn: vertebral defects, anal atresia, cardiovascular anomalies (VSD being the most common one), esophageal atresia, renal anomalies, and limb defects.

Results: This report describes a 22-year old Caucasian male who presented with a headache and vertigo following sudden and temporary loss of consciousness while attended a concert four days before hospital admission. His prior medical history includes a surgical repair of esophageal atresia as a newborn and a sonographically verified ventricular septal defect. Otherwise, he is heathy and without any other medical complaints. His complete physical and neurological exam was unremarkable. During hospitalization his chest xray detected a significant scoliosis at the cervico-thoracal junction and prominent rib overlap at the cervical C5-C6 level. Magnetic resonance of the cervical spine showed following vertebral anomalies: vertebral block between the C2 and C3, C5 and C6, hemivertebra at the C5/6 level and marked osteophytosis with foraminal narrowing at the C5 level. Detailed cardiac examination was done, including an ECG and a heart ultrasound, in order to exclude an underlying heart condition. Beside otherwise known ventricular septal defect, no pathologies were detected.

Neurosonological examination revealed a reduced blood flow velocities through the right vertebral artery, with signs of retrograde flow during middle part of the cardiac cycle which corresponds to partial subclavian steal syndrome. MSCT angiography of the thoracal arteries confirmed an anomalous right subclavian artery, originating as the most distal branch of the aortic arch and coursing retroesophageally (lusorian artery).

Conclusions: Partial subclavian steal syndrome is rarely described in the literature as a consequence of an anomalous lusorian artery. What is completely unique about our patient is the concurrence of this vessel anomaly with a congenital syndrome, so-called VACTERL syndrome.

# 17. THROMBOLYSIS IN A YOUNG STROKE PATIENT WITH GORLIN GOLTZ SYNDROME AND 4G/4G HOMOZYGOTE FOR PAI-1 GENE - CASE REPORT

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Introduction/Objectives: Gorlin-Goltz or Nevoid basal cell carcinoma syndrome (NBCCS) is an autosomal dominant disorder characterized by multiple basocellular carcinomas, dysmorphic facial features due to multiple benign odontogenic keratocysts and musculoskeletal anomalies, most commonly bifid ribs. PAI-1 gene codes for the plasminogen activator inhibitor, an important antithrombolytic agent which acts by inhibiting plasminogen activators (both tissue PA and urokinase PA). Role of PAI-1 gene in vascular incidents is still debated. It has been shown that 4G/4G homozygotes have a higher transcription activity and subsequent higher PAI-1 levels. It is thought that this raises the risk for thromboembolic incidents.

Results: We present a case of a 32-year old male previously diagnosed the Gorlin-Goltz syndrome with the history of multiple basocellular carcinomas and odontogenic cysts and without known stroke risk factors, who presented with sudden-onset right-sided hemiparesis, supranuclear facioparesis and motor aphasia (NIHSS 10). Patient full-filled all inclusion criteria and was treated with intravenous thrombolysis with significant improvement (NIHSS 2). The control

brain CT scan verified small subacute ischemic lesion in the supply area of left middle cerebral artery with developmental anomaly of the interventricular septum consisting of a cavum septi and cavum vergae, as well as multiple falx and tentorial calcifications otherwise characteristic for the Gorlin Goltz syndrome. Further radiologic findings showed a bifid first rib and scoliosis. Neurosonological examination and MR angiography of neck vessels showed an occlusion of left vertebral artery and an abnormal right vertebral artery originating directly from the left side of the aortic arch. Laboratory tests initially showed an elevated aCL level, but turned out to be normal on repeated testing. Genetic typing came positive for the 4G/4G polymorphism of the PAI-1 gene.

Conclusions: Gorlin-Goltz syndrome has not yet been associated with serious neurological disorders, most notably cerebrovascular incidents. Also vertebral arteries' anomalies including the occluded left one and an aberrant right one originating on the left side of the aortic arch are additional findings, not otherwise associated with this syndrome. Finding the mutation of PAI-1 gene (4G/4G homozygote) could be important for favoring the risk for thromboembolic incidents. Additionally, we point out that thrombolytic therapy in our patient with Gorlin-Goltz syndrome was safe and successful.

#### 18.WRITING FROM UNCONSCIOUSNESS

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Introduction/Objectives: Can neurological phenomena and sypthomatology during generalized epileptic attack and symptoms of dissociative disorder provoke writing on language and letters that is initially unknown to patient and wider environment around?

Participants, Materials/Methods: Case report, 15 years old girl with periodical generalized seizures from childhood that provoke writing immediate after attack utilizing letters and language that she previously was not familiar with. Reoccurrence of attacks conformed same phenomena in a last four years. Writing skills and contents of writing became more advanced.

Results: Patient form childhood with frequent epileptic attacks and unbalanced irregular antiepileptic therapy, with permanent dizziness and borderline success at school developed writing skills that are not result of common education in her living environment. After generalized epileptic attacks and periods of unconsciousness she is regularly waking up writing on language that is not part of her wider environment in current time frame. She couldn't pronounce words but demonstrate understanding of writing contents of language that she was is not familiar with. Philological comparative study identified that language is from areas that patient cannot approach via any method of technological or transport communication available.

Conclusions: Correlation between cognition during and after epileptic attack in dissociative disorder is confirmed only with final writing outcome. It is not clear from where knowledge of forgotten language and letters is coming during generalized epileptic attacks that were provoked with unconsciousness events during attacks.

## 19. RISK FACTORS FOR CEREBROVASCULAR DISEASES COULD BE RISK FACTORS FOR ALZHEIMER DISEASE

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Introduction/Objectives: Many researches have been conducted about risk factors for Alzheimer's disease (AD). We conducted clinical study evaluating major known risk factors for cerebrovascular disease (CVD), also present in population with AD.

Participants, Materials/Methods: We used data from medical database of patients with AD at Department of Neurology Clinical hospital center Rijeka. All patients from 01.01.2001 till 31.12.2010 were taken into consideration. Diagnosis of probable AD was based upon NINCDS-ADRDA criteria and additional neuroimaging (brain CT and/or MRI) and neurophysiological (EEG) findings. Possible positive familial history was also taken into consideration. No clinical evidence of other neurological, psychiatric or systemic illness was found.

Results: We encompassed 54 patients with AD in mentioned ten year time period. Average age was 62.1±8.5 years. In four patients there was positive familial history of AD, hyperlipidemia in 38 (70,37%), arterial hypertension in 15 (27,77%), ischemic heart disease in 8 (14,81%), diabetes mellitus in 10 (18,52%), overweight and obesity in 22 (40,74%) and smoking in 23 (42,59%) patients. According to available data CVD risk factors existed three to seven years prior to cognitive changes. Interestingly, all patients had their first neurological check up in advanced stage of dementia and MMSE score range from 18/30 to 23/30. Relevant diagnostic tools (such as brain CT and/or MRI and carotid arteries color Doppler, etc.) did not disclose evidence pointing out clearly to CVD and possible vascular dementia.

Conclusions: The results of our study gained on limited sample of 54 patients, emphasize hyperlipidemia and smoking as possible risk factors for AD. Overweight, arterial hypertension and then diabetes mellitus and ischemic heart disease follow. Well known CVD risk factors in our study were significantly associated with AD appearance.

# 20. FIVE-YEAR FOLLOW-UP OF A CHINESE PATIENT WITH OPIATE DRUG PSYCHOLOGICAL DEPENDENCE AFTER TREATMENTS WITH DEEP BRAIN STIMULATION: CASE REPORT

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Introduction/Objectives: Opiate drug psychological dependence is acknowledged as a difficult problem in the world. Several studies have shown the short-term efficacy of deep brain stimulation (DBS) in reducing opiate addiction. In this case report, we report on long-term results up to five years in an opiate addiction patient.

Participants, Materials/Methods: A 24-year-old man with three-year history of opiate addiction presented with several withdraw syndromes and more than three-time failures in detoxification.

Results: The patient was treated with bilateral DBS of the nucleus accumbens (NAc) for opiate psy-

chological dependence. No relapse was found during the follow-up periods.

Conclusions: This study suggests that DBS of the NAC could be an effective treatment of patients in reducing psychological dependence with a good recovery in psychological dysfunction.

## 21. PROGNOSTIC SIGNIFICANCE OF HYPERCORTISOLEMIA IN THE STROKE PATIENTS

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Introduction/Objectives: The aim of the study was to determine morning and afternoon serum level of cortisol in patients with first acute ischemic stroke. The median time from onset of symptoms to admittance was more than 3 h.

Participants, Materials/Methods: Study group included 41 patients, 26 of them were females with mean age 78,8 and 15 were males with mean age 67,8. Serum cortisol concentrations were measured by Chemiluminescent Microparticle Immunoassay (CMIA), Abbott on ARCHITECT 2000SR Abbott.

Results: On the first measurmnet in the morning the level of serum cortisol was elevated in 34,1 % and in the afternoon was elevated in 31,7%. Hypercortisolemia was associated with older age, severity of neurological deficit and worse outcome

**Conclusions:** Prognostic significance of hypercortisolemia in the stroke patients is related to inflammatory response.

### 22. FREQUENCY OF ALEXIA, AGRAPHIA AND ACALCULIA IN ACUTE STROKE

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Introduction/Objectives: The aim of the study is to determine the frequency of alexia, agraphia and acalculia in acute stroke patients.

Participants, Materials/Methods: We analized 195 patients with acute stroke, mean age 65 ± 11.06 years, hospitalized at Department of Neurology, University Clinical Centar Tuzla from 01.04. to 01.10.2010. For clinical assessment of alexia, agraphia and acalculia we used Minessota Test for Differential Diagnosis of Aphasias. The patients were evaluated in the first week of stroke, during the acute phase of disease.

Results: Among 194 of patients (81; 41.8 % of women and 113; 58.2% of men) with acute stroke, 59 (30.40%) had alexia, agraphia and acalculia or different combinations of these disorders. Frequency of alexia, agraphia and acalculia was higer (p=0,036) among men (41; 36.3%), compared to women (18; 22.20%). The frequency of alexia, agraphia and acalculia among patients with stroke in the left (dominant) hemisphere (33; 55.9%) was significantly higher (p=0.045), compared to those with right hemisphere stroke (23; 37.7%). However, there was no significant difference (p=0.394) of frequency of alexia, agraphia and acalculia between patients with haemorrhagic (6; 42.85%) and ischemic (53; 31.17%) type of stroke.

Conclusions: Alexia, agraphia and acalculia in patients with acute stroke is very frequent (30.40%). These language disorders were more common in men, than women, and in patients with left than in right hemisphere stroke. There was no significant difference in frequency of alexia, agraphia and acalculia between hemorrhagic and ischemic stroke.

### 23. CORRELATION OF INTERNAL CAROTID STENOSIS AND LACUNAR BRAIN INFARCT

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Introduction/Objectives: Lacunar brain infarct is a type of ischemic stroke that results from perforating artery disease. Along with advanced age, arterial hypertension, diabetes mellitus, atrial fibrillation, smoking, internal carotid stenosis has also been reported as being associated to lacunar infarcts.

The aim of this study was to determine the degree of internal carotid stenosis in patients with a lacunar infarct verified on CT or MRI brain scans.

Participants, Materials/Methods: We analyzed 60 patients with a first ever lacunar brain infarct who were admitted in the Department of Neurology of University Clinical Hospital Center Rijeka during the period from January 2010 to December 2010. The degree of internal carotid stenosis was measured by duplex color ultrasound.

Results: In group of patients who had internal carotid stenosis less than 50%, lacunar infarct was confirmed in 23% of analyzed patients in homolateral and 6% in contralateral hemisphere. In patients with internal carotid stenosis from 50% to 70%, lacunar infarct was present in 16% of cases in homolateral, and in 10% in contralateral hemisphere. In a group with stenosis greater than 70% results were proven for 10% of patients in homolateral and for 6 % in contralateral hemisphere.

Conclusions: According to our results, lacunar brain infarct presented more commonly in patients with milder (<50%) degrees of internal carotid stenosis. This leads to conclusion that the degree of internal carotid stenosis is not one of main risk factors of lacunar stroke. Obtained results are compatible with those from related literature.

#### 24. PATIENT WITH CATAMENIAL EPILEPSY

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**Introduction/Objectives:** Catamenial epilepsy refers to seizure exacerbation in relation to the menstrual cycle.

Participants, Materials/Methods: This is case report of 15 years old girl with increase seizure frequency beginning three days before menstrual cycle.

Results: The diagnosis of catamenial epilepsy has been made through detail clinical examination, careful assessment of menstrual and seizures diaries, labo ratory, electroencephalographic examination and hormonal status.

**Conclusions:** Treatment with acetazolamid tablets may prove to be useful adjunctive treatment

## 25. ASSESSMENT OF DEPRESSION IN PATIENTS WITH EPILEPSY USING QUESTIONNAIRE FORM BD-II

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Introduction/Objectives: Introduction and goal: depressive states are an important comorbidity of epilepsy, but data on the prevalence, severity and treatment in our community are not sufficiently explored. The aim of this paper is to present data on the prevalence, treatment method and risk factors for the occurrence of depression in ambulatory treated patients with epilepsy.

Participants, Materials/Methods: ambulatory patients with epilepsy who came for regular check within two months. They completed the questionnaire BD-II (Beck Depression Inventory - 2nd Edition), which was designed to assess the existence and severity of symptoms of depression according to DSM-IV. With this questionnaire also was used a questionnaire with basic demographic data, data on the clinical picture and pharmacological treatment of epilepsy.

Results: we surveyed 252 patients (male 48,8%, middle age 43,6 ± 16 years, lenght of epilepsy 13,3 ± years). By a standard questionnaire scoaring our respondents were divided into 4 categories of depression: minium depression 59%, mild depression 15%, moderately 14% and severe depression 12%. Percentage of people taking antidepressants according to categories of depression was as follows: minimum 5,4%, mild 26,3%, moderately 20%, severe 54,8%. For statistical analysis in which was used hi-square test, groups with moderate and severe depression were consolidated (N=66) and compared with other subjects (N=186). Except the fact that patients with moderate and severe depression were often taking antidepressants (p<0,01), it showed also that they were in a larger number of less-educated; NSS (p<0,01), they had seizures more often (p<0,01), and most of them were older than 40 years (p<0,01). There were no statistically significant differences in relation to duration of epilepsy, number of taken antiepileptic drugs, the occurrence of generalised convulsive seizures and social categories: marital status, parenthood, employment, driving license.

Conclusions: Conclusion: the results obtained are consistent with the expected, confirming a relatively high rate of depression in patients with epilepsy and suggest the need of multidisciplinary diagnostic and therapeutic approaches in depressed patients. Some of the risk factors for the occurrence of depressive states are poor epilepsy control, age and lower education.

# 26. CASE PRESENTATION: THE COEXISTENCE OF PSYCHOLOGICAL AND SOMATIC FACTORS IN A PATIENT WITH PAROXYSMAL DYSKINESIA

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Introduction/Objectives: Paroxysmal dyskinesia (PD) represents a rare group of movement diseases, characterized by sudden attacks of involuntary movements (hyperkinesias) with different movement combinations (dystonia, chorea, athetosis, ballismus), which lasts from several seconds to several minutes (sometimes – hours) and with intact consciousness. It generally requires a normal interictal neurological

examination. The etiopathology of this disease is not completely understood (it is considered the channelopathy), therefore the evaluation of the psychogenic impact on this disease could be useful in differential diagnosis, management and treatment of PDs.

Participants, Materials/Methods: We have examined a 63-year-old patient, who had his first dyskinesic attack 30 years ago and since then has had sudden attacks of polymorphic movements (dystonic and choreoathetosic) (up to 42 attacks per day). His case corresponded to the usual description of the paroxismal kinesigenic dyskinesia (Bhatia, 1999; Jankovic and Demirkiran, 2002; van Rootselaar et al., 2009, etc.). The patient has been examined and treated in many hospitals, without any significant results. We undertook a complete clinical and neurological examination, standard laboratory tests, EEG, MRI. The patient also completed some psychological questionnaires (such as Beck Depression Inventory, Spielberger's State-Trait Anxiety Inventory, Somatoform Disease Questionnaire-20 items) and we conducted the Structured Clinical Interview for Diagnostic and Statistical Manual of Mental Disorders (SCID DSM-IV-TR).

Results: The general and neurological exams were normal, as well as the laboratory tests. Cerebral MRI detected the dilation of lateral ventricles because of the slight frontal lobe atrophy and brachidolicocephaly. There weren't observed epiphenomena on EEG during the hyperkinesic episodes, but there were some theta waves after the attacks. The patient used to consult many different doctors from different hospitals but no treatment helped him. He corresponded to the criteria of the histrionic personality of the DSM-IV-TR and also to the criteria of one of the somatoform disorders - the conversion disorder. The majority of his crises decreased after the injection of the 4ml solution NaCl 0,9% (the patient was told that it was diazepam). During the medical consilium with many neurologists, the patient suddenly had a transient spastic gait, aphonia and limb weakness, which disappeared after the injection of the placebo.

Conclusions: The PD is a very polymorphic disease and it should be differentiated from the pure conversion disorder and the mixed form, when during the disease a patient with predisposing personality treats

develops some conversion symptoms. The management of such patients should include more psychological techniques.

## 27.PREVALENCE AND CLINICAL CHARACTERISTICS OF HEADACHES IN ADOLESCENTS IN CROATIA

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Introduction/Objectives: Background: Headaches are often underdiagnosed in adolescents. The aim of this study was to examine the 1-year prevalence of primary headaches among high school children in the city of Zagreb

Participants, Materials/Methods: This was a population-based cross-sectional study, a total of 2300 questionnaires were spread among students in 7 high schools. The questionnaire consisted of demographic data, and questions regarding the presence and clinical characteristics of headaches.

Results: The mean age of students was 17.2±1.2 years, 50.2% were female. A total of 620 (30.1%) students declared that they suffer from headaches, girls more frequently, P<0.0001. The mean duration of a headache was 2.1 days. Unilateral headache was present in 31.6%, throbbing quality in 22.6% (boys 26.4%, P<0.0001), dull in 34.4% of students (girls 39.5%, P<0.0001), intensity was severe in 22.4% and moderate in 70.3%. Nausea was present in 4.0% always and in 14.7% frequently (girls 18.8%, P<0.0004), photophobia in 41.3%, phonophobia in 63.2%, osmophobia in 23.9% (NS among genders). Almost 30% of students is disabled and stays home, more frequently boys, P<0.0006. Girls (33.4%) are more likely to take drugs in every attack, P<0.0002, number per month is 3.7. Total relief declared 30%, partial 50.3% of girls, no relief 32.9% boys, P<0.0002.

Conclusions: Conclusions: The prevalence of selfreported headache among high school children in Zagreb city is relatively high. Significant gender differences in frequency and clinical characteristics were observed. Primary headaches among children and adolescents are an important public health problem and should receive more attention from school and health authorities.

### 28. SUBACUTE SPONGIFORM ENCEPHALOPATHY - A CASE REPORT

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Introduction/Objectives: Creutzfeldt- Jakob disease (CJD) is a rare, degenerative brain disorder who affects one persone in one millione people per year. In our hospital was recorded 2 sporadic cases over last 3 years. CJD appear later in life and runs rapidly with mental deterioration, myoclonus, blindness, weakness of extremities and finaly coma. It is coused by infectious form of prion protein who aggregate nad couse brain demage.

Participants, Materials/Methods: In our case report the patient age 56 year who underwent vertigo, dystaxia, transitory vision disturbance nad leftside hemiparesis was hospitalised elswhere and treated as acute stroke with normal findings of brain computed tomography (CT) and ultrasound of extracranial carotid wessels.

Results: After one monht patients condition worsend with rapidly progressive dementia, mioclonus of hands and face, trunk and extremities ataxia, motor weakness both hands and legs, lost of intelectual functions and speach ability, and blindness. All extensive inflamation test parameters where normal, except positive test on IgM B. burgdorferi. Repeated EEG pattern in different stages of disease ahowed progressively slowing of the brain rhythm and paroxysmal spike wave complex of hight voltage who started unilateral. Magnetic resonance (MR) showed generalised brain atrophy. The patient was replaced to another hospital to undergo lumbal puncture. The standard liquor tests were normal.

Conclusions: Regarding to this trial with caracteristic clinical pictures and tipical EEG pattern we conclude it was a sporadic human form of CJD.

#### 29. CEREBRAL AND SYSTEMIC ENDOTHELIAL FUNCTION IN PATIENTS WITH MIGRAINE

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Introduction/Objectives: Cerebral and systemic endothelial function in migraine patients is not well known. It is possible that cerebral endothelial function is altered, especially in the posterior cerebral circulation. Cerebrovascular reactivity (CVR) to L-arginine probably reflects the cerebral endothelium function and in migraine patients has not been determined. In addition, systemic endothelial function in migraine patients, which can be determined by flow mediated vasodilatation (FMD), is also not well known.

Participants, Materials/Methods: Forty migraine patients without comorbidities (20 migraine with (MwA), without aura (MwoA)) and 20 healthy subjects were included. By employing strict inclusion criteria we avoided the possible vascular risk factors. Mean arterial velocity in the middle cerebral artery (MCA) and the posterior cerebral artery (PCA) was measured by transcranial doppler sonography (TCD) before and after infusion of L-arginine, and CVR to L-arginine was then calculated. Systemic endothelial function was measured with FMD.

**Results:** Migraine patients without cerebrovascular risk factors, both with and without aura, had worse reactivity in PCA (p = 0.002). There was not statistically significant difference in reactivity in MCA (p = 0.29). Also we did not find statistically significant difference in FMD between migraine patients without cardiovascular risk factors and healthy subjects (p = 0.96).

Conclusions: Migraine patients without cardiovascular risk factors have worse endothelial function in the posterior cerebral circulation. It seems that migraine patients without cardiovascular risk factors do not have altered systemic endothelial function. Based on these results it is possible that migraineours have endothelial disfunction in the posterior cerebral circulation.

#### 30. APHASIA IN PATIENTS WITH ISCHEMIC STROKE

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Background and purpose: Aphasia in ischemic stroke patients is associated with increased mortality, decreased rates of functional recovery and reduced work capability. The aim was to study the frequency and characteristics of aphasia in ischemic stroke patients.

Methods: A prospective, cohort study. Total of 177 patients (94 males and 83 females) hospitalized at the Osijek neurology clinic for a first-ever ischemic stroke in 2010 were included. All patients were examined by neurologist and speech therapist to specify subtype of stroke and speech disturbance.

Results: 75 (42.4%) patients included in study had aphasia (48.2% among females, and 37.2% among males). The most frequent clinical type was expressive-receptive aphasia. Regarding subtypes of stroke, the share of small vessel stroke declines, and the share of large vessel and cardioembolic stroke increases with age. Aphasic patients were older (75 vs. 70 years), had larger share of females (53% vs. 42%), and also had nearly two times larger share of large vessel strokes (51% vs. 17%) and cardioembolic strokes (41% vs. 22%).

Conclusions: The study showed that aphasia is very frequent in patients with a first-ever ischemic stroke. Frequency of aphasia rises with age, wich is more prominent in females. Location and type of ischemic stroke strongly influence speech disorder subtypes.

#### 31. ACUTE CEREBROVASCULAR INCIDENT CAUSED BY SEPTIC EMBOLI: A CASE REPORT

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Septic emboli (SE) is a rare disorder associated with infective endocarditis, urinary tract infections, bone infections, femoral thrombophlebitis and sinusitis. We present a case of 53-year-old patient with multiple systemic embolism and cerebral infarction resulting from aortal thrombus after a surgical treatment of right fibular maleolar fracture with osteosinthetic material placement. After a surgery the patient became antisocial, with decrease in appetite and substantial weight loss.

Computerized tomography (CT scan) showed several small hypodense zones in supratentorial and periventricular region of the brain as well as bilateral pleural effusion, large infarcts of the spleen and right kidney, smaller infarcts of the lower pole of the right kidney, discontinuity of the wall of the thoraco-abdominal aorta and the thrombus present in the distal part of the abdominal aorta. The findings primarily indicate septic emboli. X-ray of right ankle showed still present postoperative fracture gap of right fibular maleola with reduced bone mineralization but no signs of bone destruction. The control MSCT of the abdomen showed large spleen abscess size 10x6 cm. Due to edema of the right ankle, the ultrasound is preformed and the thick content in the joint is found so the patient was transferred to the Surgical Clinic where splenectomy with the evacuation of perisplenical abscess together with the extraction of the osteosintetic material of the right fibular maleola was performed.

If not promptly diagnosed SE can cause devastating neurological damage. In our patient early diagnosis and intensive physical therapy facilitated almost complete regression of his neurological deficit.

# 32.ROLE OF DRUG TREATMENT AND COMBINED PHYSICAL THERAPY IN PATIENTS WITH CHRONIC PAIN IN LUMBOSACRAL REGION

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Herniation of the lower lumbar intervertebral disc is the one of the most common causes of low-back pain with sciatic radiation. Conventional treatment methods of lumbosacral radiculopathy are physical therapy or usage of oral medications such as antiepileptic drugs and antidepressants.

In our study we included 60 patients with lower back pain with radiculopathy due to intervertebal disc herniation. Patients were divided into 2 groups- first group on drug treatment+physical therapy (transcutaneal nerve stimulation-TENS, laser, therapeutic ultrasound) and second group on drug treatment. Patients were followed up for one month and outcome was calculated according to results on analogue visual scale (VAS).

At the beginning VAS was in both groups 8,0±1,5. Patients mostly have herniation at the L4L5 level, at the second place was L3L4 level and at the third place L3L3 level. Radiculopathy was evaluated by means of electromyoneurography. After 1 month of treatment VAS in the first group was lower (2,5±1,5) than in the second group (4,5±0,7);p<0,05.

We can conclude that combined treatment of patients with lower back pain is more successfull than drug treatment alone.

## 33. CORRELATION OF DRUG TREATMENT VERSUS ACUPUNCTURE IN PATIENTS WITH TRIGEMINAL NEURALGIA

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Trigeminal neuralgia (TN) is a neuropathic pain syndrome characterized by severe unilateral paroxysmal facial pain. TN pain typically remits and relapses, even when patients are on conventionally used treatments, resulting in a major source of disability and poor quality of life. Various drugs, such as carbamazepine, oxcarbazepine, phenytoin, gabapentin and baclofen, have been used to treat TN. The aim of the study was to compare drug treatment with acupuncture treatment.

Patients with TN were divided into 2 groups with equal mean VAS at the beginning of the study (8,5±1,5); 50 patients treated with drugs and 50 patients treated with acupuncture during 1 month. Success of therapy was measured by means of visual analogue scale (VAS) at the end of the study.

Drug treatment group has VAS 5,5±2,5 and acupunture grroup has VAS 4,5±1,5 (there was no statistically significant changes between the groups, both groups have shown statistically significant decline in VAS during 1 month treatment;p<0,05).

We can conclude that acupuncture is successfull tool in treatment of patients with TN, without risks of adverse events in correlation with drugs.

## 34. BLINK REFLEX AS AN ADDITIONAL CRITERIA IN DIAGNOSTICS OF MULTIPLE SCLEROSIS

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Aim. To determine differences in electrophysiological characteristics of blink reflex (BR) in multiple sclerosis (MS) and clinical isolated syndrome (CIS).

Methods. The study included 20 patients diagnosed as clinical definitive multiple sclerosis (CDMS) and 20 patients with CIS. We registered response on orbicular oculi muscle bilaterally and recordered latencies of early (R1) and late component ipsilaterally (R2) and contralaterally (R2') and irritative component (R3). We analized demographic data including sex, age and type of the disease, presence of symptoms and signs of brainstem impairment, magnetic resonance imiging (MRI) findings with special analysis of brainstem structures, presence of oligoclonal bands (OB) in cerebrospinal fluid (CSF) and visual evoked potentials (VEP).

Results. There was no difference in the distribution of symptoms and signs of brainstem. Demyelinating lesions in MRI findings, OB and changes in VEP were similarly distributed in both groups. Analysis of BR showed no difference in latencies of R1 component, as in R2 latencies on the right side. Latencies of R2 component on the left side and R2' on the right side were statistically longer in MS group. There was no difference in the appearance of R3 component.

Conclusion. BR is very sensitive and useful diagnostic tool in assessment of brainstem structure, especially because abnormalities are seen not only in CDMS but in CIS, as the first clinical manifestation of the disease. Slowing of R2 component as a result of disfunction of afferent part of reflex arc is although not very specific but highly sensitive finding.

### 35. OXIDATIVE STATUS AND SUBCLINICAL MARKERS OF VESSEL WALL DISFUNCTION

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The aim of the study was to evaluate impact of oxidative stress and concentrations of intercellular adhesion molecule-1 (ICAM-1) and oxidized LDL (oxLDL)in plasma on brain vessels- intima media thickness (IMT) and arterial stiffnes (AS) of the carotid arteries and cerebrovascular reactivity measured by means of breath holding index (BHI) in the middle cerebral artery.

We included in the study 150 volunteers (75 women and 75 men) without any atherosclerotic plaques in the brain arteries. Conventional risk factors for atherosclerosis were observed as well. Total oxidative status, ICAM-1,oxLDL were correlated with IMT,AS;BHI values after adjusting population for age and sex as well for the risk factors.

We found that increased levels of ICAM-1 and oxLDL are in positive correlation with increased IMT and AS and in negative correlation with BHI values (p<0.05). Total oxidative status was in negative correlation with IMT and AS, but in the positive correlation with BHI (p<0.05).

We can conclude that there is a good correlation between serum markers of oxidative stress and endothelial dysfunction and subclinical neuroimaging markers for atherosclerosis. E-mail: mlisak@kbsm.hr

#### 36.CYP2D6 ALLELE POLYMORPHISM: RISK FACTOR FOR PARKINSON DISEASE?

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Introduction: CYP2D6 is a candidate gene for PD because it regulates drug and toxin metabolism, but association studies have been incompatible Decreased metabolic capability of CYP2D6 protein encoded by cytochrome P450 genes could be associated with increased risk of PD morbidity and greater side effects related to antiparkinsonian medication. The CYP2D6 polymorphism has been studied comprehensively in association with Parkinson disease, but with no reliable results. Several explanations, such as differences in study design or bias in the selection of the control population, have been offered for these inconsistent results PD may be caused by genetic vulnerability to neurotoxins.

Aim: The aim of this study was determination of the incidence and comparison of non-functional alleles with the intention of detecting increased risk for PD in individuals with damaged function of enzyme CYP2D6. To assess the significance of the CYP2D6 gene in PD, we investigated non-functional alleles, CYP2D6\*3, CYP2D6\*4, CYP2D6\*6 and the wild type allele, CYP2D6\*wt, in PD patients and controls matched on age and gender.

Patients and Methods: The study included 186 subjects in total. There were 41 PD patients (19 male and 12 female), and 145 healthy controls (80 male and 65 female). An informed consent was obtained before entering the study. All PD patients underwent complete neurological examination performed by neurologist. The diagnosis and severity of PD were based on the Unified Parkinson Disease Rating Scale3 (UPDRS) and Hoehn & Yahr rating scale (H&Y). The possible exposure to toxins during lifetime was also noted.

Control group consisted of 145 healthy age- and sex-matched subjects. Inclusion criteria for control group were no previous diagnosis of PD or any form of extrapyramidal disorder. Multiplex allele-specific polymerase chain reaction (PCR) was performed in all subjects included in the study. Incidence and genotype distribution of non-functional alleles CYP2D6\*3, CYP2D6\*4, CYP2D6\*6 and CYP2D6\*wt was determined in all subjects included. All subjects were studied using standard diagnostic, genotyping, and statistical techniques. Descriptive statistics and epidemiological data are shown in Table Results: In a group of healthy volunteers the incidence of CYP2D6 alleles was: CYP2D6\*3=1.4%, CYP2D6\*4=11.0%, CYP2D6\*6=1.0%, CYP2D6-wt=86.6%. group of PD patients the incidence of CYP2D6 alleles was: CYP2D6\*3=1.2%, CYP2D6\*4=20.7%, CYP2D6\*6=1.2% and CYP2D6-wt=76.8%. Statistically significant difference was found only for allele CYP2D6\*4 (RR) = 2.10; 95% CI: 1.113-3.994). The relation of genotype distribution was \*3/wt 2.8% and 2.4%; \*4/wt 18.6% and 26.8%; \*4/\*4 1.4% and 7.3%; \*6/wt 1.4% and 2.4%; \*4/\*6 0.7% and 0.0%; wt/wt 75.2% and 61.0% in healthy volunteers and PD patients, respectively. There was no statistically significant difference between these distributions. Clinical examination of PD patients revealed a mean H&Y score of 3 (2-3) and UPDRS-III score of 16 (14-21). Epidemiological data showed 9 study PD subjects to have been exposed to one or more exotoxins (herbicides, pesticides, insecticides, heavy metals, solvents, glues and paints) during life; however, there was no statistically significant difference in H&Y score between the toxin exposed and toxin non-exposed subjects.

**Discussion:** Results of this study indicate that the allele CYP2D6\*4 could be considered as a weak risk factor for PD, which is in concordance with previous studies, although similar study should be carried out on larger sample group.

## 37. BASILAR IMPRESSION AS A POSSIBLE RARE CAUSE OF CEREBELLAR STROKE – A CASE REPORT

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We report a case of 72-year-old women who presented with severe vertigo, vomited and had a mild neck and occipital pain. She had a medical history of hypertension, angina pectoris, cholelithiasis, gastric ulcer, pyelonephritis and a history of periodical mild dizziness. Neuroimaging revealed right vertebral artery occlusion, right cerebellar stroke and basilar impression. The chosen therapeutic approach in our patient was conservative, with non steroid anti-inflammatory drugs and neck collar. Although our patient's prior risk factors for stroke support a diagnosis of vertebrobasilar stroke, it is possible that occlusion of the vertebral artery was the result of changes in the atlantoaxial anatomy and that cerebellar infarction was secondary to cranio-cervical anomaly. Although presence of vertebral artery occlusion, cerebellar stroke and basilar impression in our patient may have been coincidental, we suggest that patients with basilar impression and cranio-cervical anomalies in general may be at increased risk for vertebrobasilar vascular disease and vertebrobasilar stroke.

### 38. KLIPPEL – FEIL SYNDROME – A RARE CAUSE OF TORTICOLIS – A CASE REPORT

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Klippel-Fiel syndrome is a rare disorder characterized by congenital fusion of variable numbers of cervical

vertebrae and associated defects. Numerous associated abnormalities of other organ systems may be present. This heterogeneity requires comprehensive evaluation of all patients and treatment regimes that can vary from modification of activities to extensive spinal surgeries. Neurological simptoms may develop in 20% of patients due to hypermobility of the spine at a certain level. Occipitocervical abnormalities are the most common cause of neurological problems. Torticollis and facial asymmetry occur in 21-50% of patients. We report a case of a 38 years old patient without a history of any serious disease who first presented with torticollis with loss of extension. Clinical findings showed: a short neck, decreased cervical ROM, a low hairline, elevated scapulas, congenital strabismus and hypoplasia of both thumbs. Neuroimaging studies showed a fusion of C5-C7 vertebrae and narrowing of the lateral foramen. EMG findings showed dystonic activity in both sternocleidomastoid muscles. We found the tumorous mass in the area of suprarenal gland, implicating a pheochromocytoma. All the other anomalies were excluded. Treatment for Klippel-Feil syndrome in our patient was symptomatic and did not include neurosurgery to relieve cervical instability at the present state of the disease. Klippel-Feil is a frequent cause of torticollis in childhood but may present later in life, which was the case with our patient. The challenge to the clinician is to recognize the associated anomalies and to perform the appropriate workup of diagnosis.

# 39. BLOOD FLOW VELOCITY IN MEDIAL CEREBRAL ARTERY DURING MOTOR IMAGERY, ACTION OBSERVATION AND MIRROR VISUAL FEEDBACK OF OWN MOVEMENT: A TRANSCRANIAL DOPPLER STUDY

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The aim of this study was to monitor blood flow changes in medial cerebral artery (MCA) by means of Transcranial Doppler (TCD) in individuals during motor imagery of action observation, as well as during mirror visual feedback..

Subjects and methods: Eight young healthy volunteers (four male and four female), participated in this study. TCD recording of MCA was done during each task.. Both MCA mean blow flow velocity (MBFV) were measured while individuals seated in a confortable chair. The obtained MCA MBFV are presented as baseline values

Results: During the motor imagery of action including hand and mouth interaction, the subject is looking into a chisel while he's imagine that he is using it with his dominant hand, increase of mean blood flow velocity of contralateral MCA was observed (task 1 +1-2% than in baseline values) but not statistically significant.

In the second task, when the subject was looking in another person using the same dominant hand there was a more pronounced increase in blood flow in contralateral MCA (task2+3-4%), statistically significant (p<0.05).

Finally, when subject During mirror visual feedback of motoric hand activation, when the subject is making right hand flexions and watching it's reflexion in the mirror ,while the left hand is immobile, increase of mean blood flow velocity of contralateral right MCA was observed (task 3 +4,5% than in baseline values,p=0,017).

Conclusion: Our data showed that action observation, by activating the mirror neuron system, increase mean blood flow value in MCA of the contralateral hemisphere,. Furthermore, visual mirror feedback of own movement seems to activate premotor and parietal part of the cortexin charge for this movement. All of these results brings forward the usage of action observation and mirror visual feedback as non-expansive tools for motoric neurorehabilitation by increasing blood flow in the main source of vascularization for premotor and motor processing.

#### 40. TRANSCRANIAL SONOGRAPHY OF THE RAPHE NUCLEI IN DEMENTIA

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The current clinical criteria, as well as the histopathological classification for diagnosis of Alzheimer's Disease (AD) were focused mostly on progression of AD neurofibrillary degeneration in cortex, first hipocampal and entorhinal, then high-order cognitive neocortex.

However, recent neuropathological studies showed early involvement of brainstem, particularly the dorsal raphe nuclei in the pathogenesis of AD.

Transcranial sonography (TCS) was introduced 20 years ago for evaluation of intracerebral hemodynamics. Introduction of B-mode in the last decade provides more precise information of brain parenchyma as well. Usefulness of TCS in distinguishing some basal ganglia disorders is well documented.

Echogenicity of the midbrain line mesured by means of TCS correlate with the integrity of basal limbic system and raphe nuclei (RN)

Recent (TCS) studies showed that disruption of echogenic midbrain line might represent functional marker for the development of depression

Patients and methods: 20 subjects were included in the study: 10 patients with AD (mean age 68.,0 ±7,8) ,10 age-matched patients with MMSE higher than 26 were in the control group (mean age 65.,4 ±6,5), All of them without Major depression episode in clinical history, where studied using TCS. All the patients were treated at the University Hospital "Sestre milosrdnice" in the Department of Neurology, Zagreb, Croatia. Informed consent was obtained before entering the study. The psychiatric diagnosis of MDD and questionnaire about suicidal ideation was made according to the diagnostic criteria of DSM-IV. Severity of the disease was measured according minimental state examination (MMSE). Only patients with temporal acoustic bone windows that enabled

the identification of structures within the mesencephalic brainstem were included.

Transcranial sonography: TCS was performed freehandedly with ultrasound system (Alpha 10; Aloka, Tokyo, Japan) equipped with 2.5 MHz transducer. The measurement was done two times by two independent physicians (R.B., M.B) blinded on the results of the other and clinical data. The insonation was done throughout both temporal "bone window" on intact skull. Penetration depth was 14 cm and gain image was adopted individually. The echogenicity of the pontomesencephalic nuclei raphe was rated semiquantitatively on a three-point scale with red nucleus as a reference point: 1= RN not visible, 2=slighty echogenic/interrupted RN, 3=normal RN echogenicity (Becker et al., 1995). RN echogenicity was regarded as reduced only if the findings of both physicians agreed.

Results showed significantly lower RN echogenicity in patients with Alzheimer's Disease (mean=1,4 compare to mean score of ehogenicity in control group=2,7), without major depresive disorder (p<0,01). Reduced raphe echogenicity was found in 7 of 10 (70%) of the patients with AD but only in 3 of 10 (30%) controls

Conclusion: Our pilot study showed significantly lower RN echogenicity in patients with AD, which confirmed early involvement of the raphe nuclei in AD degenerative process.

### 41. CAROTID ARTERY STIFFNESS IN TYPE 2 DIABETES PATIENTS

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Purpose: Prevalence of type 2 diabetes mellitus (DM) is increasing. DM is a major risk factor for cerebrovascular diseases. Assessment of arterial structure and function, by non-invasive methods, can be used in early detection of vascular complications. Besides

intima-media thickness (IMT), beta stiffness index (BSI) was recently recognized as a surrogate marker of atherosclerosis. The aim of this study was to explore BSI in patients with type 2 DM.

Material & Methods: Patients with type 2 DM were examined in our Stroke prevention centre by means of ultrasound with a high-resolution echotracking system, on Aloka Prosound alpha 7 system equipped with 8MHz probe. IMT of common carotid artery was measured by high-resolution B-mode ultrasound imaging.

Results: Altogether 32 DM patients (16 female) were examined (mean age 65,9 +/- 8,7 years). Most of patients (26) were hypertensive (142 +/- 21 over 86 +/- 9 mmHg) and had increased BMI (31,1 +/- 4,8 kg/m2). Average IMT was 0,72 +/- 0,15 (right CCA) and 0,76 +/- 0,15 (left CCA). Average BSI was 11,6 +/- 5,5 (right CCA) and 11,8 +/- 3,8 (left CCA). IMT was significantly correlated with waist circumference and age, while BSI correlated with systolic blood pressure, waist circumference and heart beat rate.

**Conclusion:** Increased carotid IMT and BSI in type 2 DM patients were registered. Further studies are needed to assess the impact of these parameters on stroke risk and outcome.

### 42. DISEASES MIMICKING MULTIPLE SCLEROSIS AND ASSOCIATE DISORDERS

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Objectives: Evaluate the indexes of a faulty MS diagnosis and its association with other pathologies of the nervous system in Croatia.

Subjects: 121 MS patients, clinically definite and laboratory-supported definite MS cases (Poser's criteria). Main outcome measures: In which way and to what degree do the medical record, the most indicated and other complemental examinations contribute to the certainty of an MS diagnosis.

Results: A faulty MS diagnosis was established in 14 (16.90%) subjects. The cases of somatoform disorders (neurosis), found in three patients, showed

a highly similar clinical MS picture. Their investigation produced normal findings of CSL, MR and EMP. Coagulopathy, migraine, mitochondrial encephalomyopathy and phenylketonuria, respectively found in one patient each, displayed similarities in the clinical picture and neuroimaging findings with MS patients. Lyme disease, found in three patients, and single cases of, respectively, Leber hereditary optic neuropathy, inflammatory connective tissue disorder tissue diseases (vasculitises in SLE - systemic lupus erythematosus - and cryoglobulinemia) and central pontine myelinolysis presented the greatest difficulty in making a differential diagnosis. These patients showed similarity with MS patients in both the clinical picture and findings of the CSL analysis and MR. Two patients presented pseudotumorous MS. Association of MS with other malformations, syndromes and diseases of the neuraxis was confirmed in 15 (16.05%) MS patients, namely: hyperprolactinemia, mainly in the active stage of disease, in 8, and, respectively, aneurysm a. basilaris, myotonic dystrophy,

chronic inflammatory demyelinating polyneuropathy, sarcoidosis, Bp hypovitaminosis, syringomyelia, and antiphospholipid syndrome in one patient each. Sarcoidosis may precede MS.

Conclusions: Despite the fairly high level of development of neurology in Croatia, the percentage of faulty MS diagnosis is still rather high. Application of diagnostic criteria and common diagnostic algorithms for MS is inadequate and not yet widely accepted. The most indicated complemental examinations - EMP, CSL and MR - are still not sufficient for establishing a definite MS diagnosis. Additional laboratory and electrophysiological tests, as well as a more appropriate application of neuroimaging techniques must be directed by data collected through a detailed anamnesis. Serologic tests for Borrelia burgdorteri and inflammatory diseases of the connective tissue impose themselves as necessary and useful complement to a differential diagnosis of a relapsing-remitting MS, and analysis of coagulogram in a primary-progressive MS.