Neuromuscular disorders
Motor neurone diseases

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Biochemical markers of disease progression in sporadic amyotrophic lateral sclerosis

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The main aim of our study was monitoring of indices of antioxidant activity in SALS patients. 28 patients (13 males, 15 females; mean age 58.5±12, 3 years; mean duration 25.9±5, 5 months) were monitored during 6 months. Every month the patients were examined neurologically, ALS functional rating scale, the pulmonary dysfunction by measurement of FVC, evaluated functional disability.

The indices of antioxidant activity included the measurement of activity of Cu/Zn SOD1, GSH-peroxidase, GSH-reductase, GSH-S-transferase, catalase and levels of SH-groups in erythrocytes of SALS patients.
All SALS patients were divided into subgroups with cervical (9 persons), lumbar (4) and bulbar onset (15) of disease. Two types of progression have been identified: with rapidly progressive course (16 patients) and slow ones (12 patients).
In the whole group the decline of ALSFRS score from 29.4±8, 0 points to 20.5±7, 6 points ($p<0.001$) and the mean FVC from 80.6±23, 8% of predicted to 61.2±11, 6% ($p<0.01$) of predicted, has been seen after 6 months. The monitoring of biochemical indices revealed the decrease of GSH-peroxidase activity from 3.84±1, 11 u/g Hb to 2.98±1, 59 u/g Hb ($p<0.01$) and the protein SH-groups' levels in erythrocytes from 1.15±0, 39 μM/g Hb to 0.55±0, 17 μM/g Hb ($p<0.005$). The significant increase of catalase activity has been seen (from 3.82±2, 79 u/g Hb to 7.27±1, 64 u/g Hb, $p<0.05$). The most significant decline of antioxidant activity and SH-groups levels has been revealed in bulbar form of ALS with rapidly progressive course.
The monitoring of antioxidant activity and thiols may be specific method of evaluation of disease progression in ALS.

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Oesophageal manometry in amyotrophic lateral sclerosis patients, with dysphagia

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Background There are only few techniques currently available to assess reliably the stages of swallowing dysfunction due to ALS. The occurrence of the oropharyngeal phases of swallowing in ALS patients has been well documented. We suggest a method to detect the oesophageal disturbances due to dysphagia in ALS patients.
Objective To evaluate the use of oesophageal manometry in detecting the oesophageal phase of dysphagia in ALS patients.
Material and methods The study was carried out in 20 bulbar onset ALS patients with clinical dysphagia, fulfilling WFN criteria and 20 sex- and age- matched healthy volunteers. The standard transnasal oesophageal manometry was performed in all subjects using a flexible catheter with the solid-state transducers (Synectics, Sweden). 10 to 15 – 5 ml fluid (water) or solid piece of food (sandwich) were swallowed at 30 sec. intervals.
Results The comparison of median upper oesophageal contractile amplitude, upper oesophageal contractile duration and upper oesophageal contractile velocity during the swallowing of fluid between ALS and controls subjects were 99*58 vs. 60*22 mm Hg ($p=0.009$), 3.91*1.4 vs. 2.7*0.7 sec ($p=0.001$), 4.6*1.8 vs. 2.8*0.4 cm/sec ($p<0.001$) and during the swallowing of solid food were 96±59 vs. 44±25 mm Hg ($p<0.001$), 4.8±1.9 vs. 2.5±1.7 sec ($p<0.001$), 5.4±2.0 vs. 3.9±0.5 cm/sec ($p=0.002$).
Conclusion We conclude that ALS patients showed significant abnormalities in all parameters measured by oesophageal manometry as compared to controls. We also demonstrated the existence of disturbances in the oesophageal phase of swallowing in ALS patients with dysphagia that hasn't been carefully investigated previously.

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A9V signal sequence dimorphism of MnSOD gene and the progression rate in Russian ALS patients

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Introduction Homozygous A9V genotypes of MnSOD gene were suggested to be significant risk factors for sporadic ALS. We elucidated the role of MnSOD A9V dimorphism and its relation to oxidant stress in Russian ALS patients.
Methods Blood and CSF samples were taken from 45 sporadic ALS patients and 50 healthy individuals. The patients were assessed by Norris ALS score, each 6 months. The progression rate was determined for the period not less then a year since the onset. All samples were screened for MnSOD A9V alleles by PCR and double strand conformation polymorphism. MDA contents in serum and CSF were determined by spectrophotometry.
Results We found 23.5% and 27.5% of ALS patients homozygous for A9 and V9 alleles, respectively, 49% were heterozygous. There were no differences between frequencies of A9V alleles in patients and controls. Patients with slow, moderate and rapid progression comprised 55.6%, 26.6% and 17.8%, respectively, and lost 0–4, 5–9 and more than 10 degrees each 6 months ($r=-0.96-0.98$; $p<0.0001$). Slow progression was encountered with lower frequency in heterozygous, then in V9 ($p=0.035$), but not then in A9 homozygous patients. We found no difference between age or site of onset and MDA contents in serum or CSF in relation to A9V allelic variances in the studied cohort.
Conclusion The heterozygous genotype of A9V MnSOD may unfavourably influence ALS course not being a risk factor for the disease itself possibly due to population heterogeneity. Such conformity may be unrelated to antioxidant properties of the enzyme.

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Cognitive impairment and SPECT findings in amyotrophic lateral sclerosis

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Introduction Amyotrophic lateral sclerosis (ALS) is frequently associated to dementia. The nature of this dementia and the clinical determinants of its development remain still unclear.
Methods: Seventeen ALS pts, 15 AD pts. and 12 control subjects (CS), matched for sex, age and educational level underwent an extensive neuropsychological test battery and a brain perfusion SPET with 740 MBq of 99mTc-HMPAO. ALS patients were classified on the basis of the prevalence of motoneuron disease (first, second or both) and bulbar involvement. According to DSM IV, criteria ALS were dived in two groups: without dementia (ALS-ND n=9) and with dementia (ALS-D n=8).
Results Both ALS-D and ALS-ND showed hypo-perfusion in pons region ($p<.05$) when compared with CS. ALS-D showed a selective hypoperfusion ($p<.01$ vs. CS and ALS-ND) in fronto-temporal and bilateral basal ganglia regions similar to AD

group. AD showed a severe hypoperfusion in all associative and frontal areas but differ from ALS-D only in parietal bilateral areas. ALS-D scored worse than CS and ALS-ND in most of neuropsychological tests but they were severely impaired in verbal fluency tasks and all frontal tasks (p<. 01). A non-parametric comparison showed that dementia is more frequent among ASL pts. with second motoneuron and/or bulbar involvement.
Conclusion Our results suggest that dementia in ALS is more similar to fronto temporal dementia than to AD. The prevalence of dementia among ALS patients with second motoneuron and bulbar involvement is strictly in accordance with SPET results.

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Individual variation in amyotrophic lateral sclerosis with dementia: Clinical assessment and literature review.

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Clinical features of amyotrophic lateral sclerosis (ALS), patients with the condition of mental disturbance and dementia, seen at our hospitals between 1997 and 2001, were reviewed and compared with those in Japanese literatures. Eleven percent of ALS patients (four out of thirty-five) had this mental condition. In ALS with this condition, the mean age at onset of motor neuron signs was 59 years, and the specific initial neurological feature was bulbar palsy. Common initial mental conditions were deterioration of spontaneity and depressive state. Forced crying was seen in two. The delays to the manifestation of the mental condition since onset of motor neuron signs were varied from four months to twenty-four months (the mean, 17 months). The mean duration of neurological symptoms to fatal respiratory failure was 24 months (range, 16 to 36 months). The delays for the mental condition in our two patients (24, 24 months) were markedly prolonged compared to those in the previous reports (mean; 11 months, range; 4 to 18 months), whereas no difference was found between our patients and those in the literatures for age at onset of motor neuron signs, features of initial symptoms and characters of mental conditions. The degree of brain atrophy in MRI or CT showed no relation to the duration of neurological symptoms. The progress of radiological findings similarly had no connection with the course of the mental condition. Our results suggest that the delay to appearance of mental disturbance is widely varied individually in ALS patients with this condition.

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Sleep in amyotrophic lateral sclerosis: architecture, respiration, periodic leg movements and fasciculation

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Introduction Amyotrophic lateral sclerosis (ALS) is a progressive disease characterised by the reduction of central and peripheral motor neurons. The involvement of respiratory muscles and the partial movement disability are suggested to be the reason of sleep disturbances in ALS.
Methods Night polysomnography was performed in 18 non-selected inpatients suffering from ALS (11 men, 7 women), aged 57.9 ±SD=6.7 years, with disease duration 1.8 ±0.6 years and Norris score 67.2 ±18.0 and in 10 healthy men and 6 women (age 57.8 +6.1).
Results Total sleep time: 301.9±39.7 min (control group: 352.2±71.8). Sleep latency: 19.8±4.5 min (21.2±19.1). REM sleep latency: 123.4±83.0 min (92.8±65.4). 3+4 NREM duration: 12.9±8.3% (9.1±5.3). REM duration: 12.7±6.0% (19.1±8.6). Wake duration: 22.1±9.2% (13.6±10.8). Number of arousal 1 min. and longer: 16.1±8.7 (12.7±7.2). Number of sleep cycles: 1.8±1.2 (2.9±1.5). Apnoe/hypopnoe index (AHI): 7.9±10.5 (12.1±13.6). REM sleep AHI: 16.4 ±19.8 (12.4±14.2). Periodic leg movements in sleep were present in 50% (37.5) of subjects. The number of muscle fasciculation per 1 min counted from the superficial electrode on both tibialis anterior muscles: Wake – 2.53 (0.1), 1NREM – 2.7 (0.4), 2NREM – 3.8 (0.2), 3+4 NREM – 3.1 (0.1) and REM sleep – 3.2 (0.2).
Conclusion Sleep of patients suffering from ALS was disturbed but surprisingly most of sleep parameters didn't differ from those of the control subjects. There was no relationship between the number of muscle fasciculation and sleep stages.
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Monoclonal antibodies (CD95) in cases of lateral amyotrophic sclerosis

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Lateral amyotrophic sclerosis (LAS) is a chronic progressive disease of the nervous system with selective affection of central and peripheral motor neurons (MN). The pathology has a neurodegenerative character. However, the role of the autoimmune process in LAS pathogenesis is nowadays widely discussed. CD95 are cytotoxic lymphocytes expressing the marker of readiness for apoptosis. Development of cytokine cascade is accompanied by influx of lymphocyte cells in the zone of brain tissue lesion and expression of leukocyte adhesive complex. All this induces FAS-receptors, which are in their turn, a CD95 marker leading to hyperexpression under conditions of apoptosis of neurons. The aim of this study was to prove participation of monoclonal antibodies (CD95) in apoptosis in cases of LAS. 8 patients (5 men and 3 women) ages from 54 up to 74 were examined, mean age – 63.2 years. In all cases CD95 level in peripheral blood was determined by the immunofluorescence method. The following LAS clinical forms were discovered: progressive bulbar paralysis (1), cervical debut of pathology (8), lumbar debut (3). Irrespective of LAS clinical forms, all cases showed high CD95 level. Mean CD95 level was 16.5±1.4% while the control group had 0–1%. The difference between the main and control groups are proved to be reliable: the higher the level of MN affection, the higher CD95 concentration. Thus, the received data may be evidence of involving CD95 in brainstem and spinal cord MN apoptosis, in cases of LAS.

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Electrophysiological correlates of selective attention in patients with amyotrophic lateral sclerosis (ALS)

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There is experimental evidence for a functional contribution of the prefrontal cortex to clinical deficits caused by the neurodegenerative process in ALS. Since tasks of selective attention are subjected to the functional control of the frontal lobe, we have assessed electrophysiological and psychometric correlates specifically associated with this kind of attention.
Methods The patient group consisted of 20 subjects (15 male, 5 female; mean age 58.5 years), the control group consisted of

20 individuals (mean age 57.2 years) age- and sex-matched to the patients. Clinical and psychometric assessment included the following tests: ALS score (Caroscio), spasticity scale (Ashworth), MWTB, Beck's depression inventory (BDI), TAP, Stroop test, word-fluency, design fluency (5-point Test). Event-related potentials (ERP) were recorded in a selective attention paradigm close to Hillyard. Analysis of ERP components included: negative difference (Nd) wave, N1-component, mismatch negativity (MMN) and P3 component.

Results Concerning the Nd wave, there was a significant decrease in the patient group as compared to controls. In several patients, there was even observed a complete loss of Nd. Parietal P3 amplitude, following task-relevant stimuli (targets) was distinctly expressed within both groups, whereas P3 to rare unattended stimuli (deviants) showed a clear predominance in the patient group.

MMN amplitude was equally expressed in both groups.

Conclusion: The results indicate an impairment of selective attentional capabilities and probably even a complementary increase of automatic and controlled processing of irrelevant information in ALS patients. This may be an expression of prefrontal dysfunction within these patients.

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Ultrasonic evaluation of carotid atherosclerosis in myotonic dystrophy

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Ultrasonography provides real-time information about lumen and vessel wall irregularities of arteries. Several studies assessing carotid atherosclerosis with ultrasonography have been carried out in both healthy and diseased subjects such as cerebrovascular disease. Patients with myotonic dystrophy have various risk factors for atherosclerosis including diabetes mellitus, coagulation abnormality, obesity and insulin resistance. We, therefore, investigated the prevalence of carotid atherosclerosis and its association with risk factors in 28 myotonic dystrophy patients, without history of cerebrovascular disease. High-resolution B-mode ultrasonography was performed to determine the extent of atherosclerosis of extracranial carotid artery. The thickness of the intima-media complex (IMC) was measured as the distance between the lumen-intima interface and the media-adventitia interface. Atherosclerotic lesions were defined as plaques when the thickness of IMC was >1.0mm. Correlations between the thickness of IMC and risk factors for atherosclerosis (age, sex, smoking, hypertension, hyperlipidemia, visceral fat obesity and insulin resistance) were analysed, and then, correlations between existence of atherosclerotic lesions on ultrasonography and risk factors also studied. There was a significant positive linear correlation between the thickness of IMC and age in all patients. Patients with glucose intolerance had significant larger thickness of IMC than those without. Seven (25%) out of 28 patients had identified atherosclerotic lesions. Only age was an independent risk factor, whereas the other risk factors revealed no association with existence of lesions on ultrasonography. In conclusion, although myotonic dystrophy patients have several risk factors for atherosclerosis, age is the only predictor for the development of atherosclerotic lesion on ultrasonography.

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The spectrum of limb-girdle muscular dystrophy in Slovenia defined by molecular genetic analysis

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Objective To define the frequency of sarcoglycanopathy, dysferlinopathy and calpainopathy in Slovenia.

Methods Twenty-two out of 56 limb-girdle muscular dystrophy (LGMD) patients, with the exclusion of those with dystrophinopathy, agreed to participate. The diagnosis of LGMD was based on the distribution of muscle weakness, serum CK values, EMG, and muscle biopsy. The dystrophin, sarcoglycans, dysferlin and calpain were demonstrated immunohistochemically and/or by Western blotting. Calpain gene and dysferlin gene were investigated by molecular genetic techniques.

Results Calpain was completely absent in 9 patients (4 female and 5 male, included 2 pairs of brothers and sisters). Mutations in the calpain gene were detected in 6. In one patient, no mutation in calpain gene could be detected, while in 2 the genetic analysis is in progress. Reduction of sarcolemma immunoreactivity against alpha-, beta-, gamma- and delta-sarcoglycan was observed in another 4 patients (in one female patient and her nephew and in 2 sporadic female patients). Abnormalities of dysferlin were detected in 2 sporadic patients. The male patient with no dysferlin and 50% reduction of calpain had Miyoshi myopathy. In him, no mutation in the dysferlin gene could be detected. The female patient with 85% reduction of dysferlin had typical LGMD. Dystrophin was normal by both immunohistochemistry, as well as by its molecular weight in all 22 cases.

Conclusions Calpainopathy is a common cause of LGMD in Slovenia, comprising approximately 40% of all LGMD cases, while sarcoglycanopathies and dysferlinopathies, detected in 4 and 2 patients respectively, seem to be relatively rare.

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The glucocorticoid receptor N363S polymorphism and steroid response in Duchenne dystrophy

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Introduction Steroid administration is beneficial in Duchenne muscular dystrophy (DMD), however variable response and variable incidence and severity of side effects occur. The variables that play a role in determining steroid response in DMD have not so far been reported.

Methods Forty eight DMD patients, either prednisone or deflazacort treated, were screened by PCR/SSCP/direct sequencing of the entire glucocorticoid receptor (GRL) gene to verify if mutations in the GRL gene may be associated with a better or worse response to steroid.

Results Mutation studies revealed an heterozygous A to G mutation at GRL cDNA position 1220 in three DMD patients resulting in an asparagine to serine amino acid change at amino acid position 363 (N363S). Frequency of the N363S polymorphism was about 6% in our patient population. The N363S carriers DMD patients did not show any difference in short term evaluation of muscle strength and functional performances in comparison with the GRL non-carrier patients. However, when long-term effect of the N363S polymorphism was considered, the carriers' patients showed a trend towards a later age of loss of ambulation. In terms of steroid side effects, stomach discomfort was higher in the N363S non-carrier DMD patients than in the N363S carriers.
Conclusions Our data suggest that the N363S GRL polymorphism may be implicated in the long-term response to glucocorticoids. However, it is also evident that mechanisms other than the GRL polymorphisms are involved in clinical response to steroid in DMD.

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Short and long-term follow-up in a cohort of 48 DMD patients treated with corticosteroids.

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Introduction Steroid administration may be beneficial in Duchenne muscular dystrophy (DMD) but issues such as duration, age at starting therapy, and the extent of side effects are unclear.
Methods We analysed retrospectively the disease progression in 48 DMD patients who had been treated with prednisone or deflazacort as part of previous double-blind trials. Clinical data included functional scores, MRC score, and monitoring of side effects.
Results The mean change in functional score at 12 months was –7.4% (SD 22.3, n=48), with values ranging from –55% to +50%. Half of the patients showed improvement (negative scores). There was a significant correlation between functional score and age at onset of treatment ($r2=0.4$; $p<0.001$) with younger patients tending to improve and older patients tending to deteriorate. All treated patients showed Cushingoid appearance, increased appetite, and hirsutism during therapy but none dropped out. Fractures were not more frequent than in the untreated patients.
Conclusions Our data suggest a better response to steroid treatment when started early. Side effects should not preclude therapy.

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Long-term treatment of steroid-resistant myasthenia gravis with FK506 (Tacrolimus)

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Introduction We evaluated the efficacy and safety of long-term treatment with FK506 (Tacrolimus), an immunosuppressant, in patients with steroid-resistant myasthenia gravis (MG).
Methods We treated 12 patients (3 males and 9 females, 28–59 years old; mean, 47.3 years old) with steroid-resistant generalized MG. All patients underwent thy(mo)mectomy (4 cases of thymoma) more than 2 years (range: 2.9–27.3) before the study and had been treated with steroids (27.7+/–16.1 mg/2 days, range: 10–70). FK506 (2–4.5 mg/day) was orally administered for at least 20 months (range: 20–24). During this period, clinical signs, MG scores (max, 27 points), activities of daily living (0 to 6 ADL) and adverse effects were evaluated monthly in the first year of treatment, and every 2 months thereafter.
Results All patients completed treatment. Total MG score was significantly decreased at the end of the study (median: from 6.0 to 2.5, $p<0.05$). ADL score was improved in 6 patients. Titers of anti-AChR antibody were significantly reduced from 21.1+/–22.1 nM to 13.6+/–18.2 nM ($p<0.001$). Steroid dosage was reduced during the study in 6 of 12 patients, from 33.3+/–19.9 mg/2 days to 21.3+/–11.0 mg/2 days. One patient suffered from severe headache and eye pain, but these symptoms disappeared when the dose of FK506 was reduced. Other side effects were mild.
Conclusions FK506 would be effective and safe for long-term treatment in patients with steroid-resistant generalized MG.

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Experience on methotrexate (MTX) as an immunosuppressive drug in myasthenia gravis:

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Introduction MTX is a folate antimetabolite inhibiting dihydrofolate reductase and DNA-synthesis. Besides its implementation as a chemotherapeutic agent, it is increasingly used in autoimmune and neuromuscular autoimmune diseases. The advantage is a relatively short onset of action (1–3 months), which may reduce additional steroid treatment. The average dose for this indication is 10–20 mg/week, which also causes only few haematological side effects. Patients with restriction of pulmonary function have to be excluded.
We report 5 patients with myasthenia, benefiting from MTX medication.
Materials and methods Five patients with autoimmune myasthenia gravis were observed in our neuromuscular clinic. Electrophysiological testing, antibody testing and edrophonium testing established diagnosis. Patients received MTX between 12 month and 36 months (median 24 months), either in combination therapy or as monotherapy. MTX was given orally once a week with doses between 7.5 and 15 mg.
A complete laboratory screen and pulmonary function test was obligatory before inclusion.
Results Three of five patients with myasthenia gravis responded to MTX, steroids could be tapered or stopped. We observed no haematological side effects and no pulmonary dysfunction. However, some patients reported dizziness, nausea and fatigue after weekly ingestion of tablets.
Conclusion Our clinical observations suggest that MTX is either a treatment of choice or an interesting alternative for immunosuppression in myasthenia patients. Myasthenia patients seem to profit well with this immunosuppression. As MTX is an inexpensive drug, its implementation into immunosuppression of myasthenia patients helps to run a cost effective patient management.

P 1056

Deliveries among women affected by myasthenia gravis in Norway 1967-1998

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Introduction Myasthenia gravis (MG) affects women frequently in their childbearing years. The knowledge of the potential effect a pre-existing MG can have upon pregnancy and delivery is however yet limited.
Methods The Medical Birth Registry of Norway was established in 1967. It is based on the compulsory notification of all births after 16 weeks of gestation. We analysed data for all births in Norway from 1967–1998. The total number of deliveries was 1847493. 116 deliveries were by women diagnosed with MG.
Results In 20 (17.2%) of the 116 births, it was necessary to induce the delivery, mainly done by giving oxytocin as an infusion (9.5%). Caesarean section was performed in 20 (17.2%) births, in 13 cases after the beginning of labour. Complications during delivery were notified in 46 (39.7%) births.
Conclusion Female patients suffering from MG have reported complicated deliveries, relating this to their muscular weakness. It has also been claimed that in these cases caesarean section is often performed. Our next step will therefore be to compare the results obtained for the MG-group from The Medical Birth Registry to a normal material, to see if there is any trend. If this tends to be the case, one must discuss whether this should influence clinical practice.

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Myasthenia gravis, thymomas and associated neurological autoimmune diseases

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Background 927 myasthenia gravis (MG) patients are regis-tered in the Slovak Centre for Neuromuscular Diseases (Dec. 31, 2001).
Objectives and results Thymoma was diagnosed in 113 patients (12.3%). In 139 MG patients (l4.9%) l52 associated autoimmune diseases were diagnosed, mostly autoimmune thyroid disorders, rheumatoid arthritis, haematological disorders, and skin diseases. The autoimmune neurological diseases associated with thymoma and MG was diagnosed in 6 patients: I. Acute polymyositis (PM) combined with fulminant MG, in two cases with malign thymoma, were confirmed in 3 patients. In 2 patients, an association of MG and chronic PM were diagnosed. One patient died. II. We diagnosed LEMS in MG patient with malign thymoma, who later developed small cell lung carcinoma. III. Clinical and EMG signs of neuromyotonia, neuropathy and limbic like encephalitis developed in a patient with thymoma. Plasmapheresis, prednisone, azathioprine and thymectomy resulted in remission.
Conclusion Thymomas are associated with certain neurological autoimmune diseases with defined autoantigenes and pathogenetic relevance of autoantibodies or auto destructive T cells (myasthenia gravis in 12–30% of thymomas, other diseases are rare in thymomas: LEMS, stiff maN syndrome, neuromyotonia, peripheral neuropathy, intestinal pseudo-obstruction, limbic encephalitis). The autoantigens in PM remains unknown, however immunosuppressive combined therapy and thymectomy resulted mostly in remission, only one patient died.

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Acute polymyositis and elevated anti-acetylcholine receptor antibodies (ACHR-AB) in a patient with thymoma associated with Hashimoto's thyroiditis and suspected autoimmune myelosupression, another case of multiple autoimmune phenomena.

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Introduction Patients with thymoma tend to harbour autoimmune diseases. A case report with biopsy proven polymyositis (PM), a striking elevation of ACHR-AB and a haematological autoimmune association with anaemia, leukopenia and thrombocytopenia and Hashimoto's thyreoiditis will be presented.
Case report A 65 years old woman developed progressive generalised muscle weakness without diurnal variations over two weeks. Clinically neck flexor muscles and proximal upper extremity were predominately affected. There was no overt ocular or bulbar involvement. Laboratory investigations revealed normal serum creatine kinase (CK) values, ACHR-AB in serum were elevated (127 nmol/l); additionally she had anaemia, leucopenia and thrombocytopenia. Edrophonium test was inconclusive.
Repeated repetitive nerve stimulation did not show a decrement. EMG of several muscles was pathologic myopathic with spontaneous activity. Open muscle biopsy of the gastrognemius muscle showed a myositic pattern with inflammatory infiltrates including T-cells attacking muscle fibers and up regulation of HLA I in some muscle fiber membranes.
Due to this diagnosis, steroid treatment was initiated (25 mg prednisolone/day). Unexpectedly several days later, she aspirated and died.
Autopsy diagnosed a malignant thymoma I (Müller-Hermelink) and a Hashimoto's thyroiditis. Bone marrow revealed aplastic anaemia.
Muscle pathology in deltoid and vastus lateralis muscle confirmed polymyositis. Heart muscle showed myositic changes suggesting cardiac involvement in PM.
Discussion and conclusion Our case report describes a thymoma patient with an unexpected association of several distinct autoimmune diseases. Unusual features are the lacking elevated serum CK, cardiac involvement and association with multiple autoimmune diseases. The diagnostic relevance of elevated serum ACHR-AB remains unclear.

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The role of autoimmune lesions in mechanism of apoptosis in lateral amyotrophic sclerosis (LAS)

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Lateral amyotrophic sclerosis (LAS) is chronic progressive disease of neural system with selective affection of central and peripheral motor neurons. The presence of autoimmune compo-

nent in pathogenesis of LAS is now widely discussed. One of the ways of neuron's death is apoptosis, which results in fragmentation of DNA, creating antigen-antibody complexes. Nucleosomes, which released during apoptosis, activate immune system that causes creating of anti-DNA. SD95 – are cytotoxic lymphocytes, which express preparedness to apoptosis.
The aim of this study was to demonstrate participation of monoclonal antibodies (SD95) and anti-DNA. 12 patients (8 male and 4 female) ages from 54 up to 74 years (mean age – 63.2) were investigated. Level of anti-DNA and of SD95 was determined in blood serum. Clinically were found following patterns of LAS: Progressive bulbar paralysis with prevalence of pyramidal signs (1), cervical debut of disease (8), lumbar debut (3). All the patients showed increased level of SD95. Mean value of APO1-Fas-receptors was 16.5±1, 4%. Determining of anti-DNA level in blood showed its reliable increase ($p<0.001$) in comparison with control group (0.196±0, 01 UOD). Level of anti-DNA in investigated patients varied from 0.343±0, 02 UOD to 0.609±0, 02 UOD. Correlation between anti-DNA and SD95 was observed. The higher level of affection of motor neurons, the greater concentration of SD95 and anti-DNA (K=+0.8).
Therefore, obtained data can be evidence of involving of SD95 in apoptosis of motor neurons of brainstem in LAS. One of the causes of anti-DNA production is activation of immune system by nucleosomes revealed during cellular apoptosis.

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Interferon status of myasthenic patients

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Introduction Interferon status of myasthenic patients, in addition to the level of antibodies to acetylcholine receptors, include some other changes, for example, those of interleukin production. In medical literature, there is some information about non-identical effect of a-IFN administration.
Methods The object of the present study was investigation of interferon status of myasthenic patients. The total of 12 patients with generalized myasthenia aged 23 – 65 was studied. The indices of interferon status were measured in entire heparinized blood using S.S.Grigoryan's and some other micromethods (1988). The following interferon status indices were studied: serum IFN, titers of a-IFN, g-IFN and spontaneous IFN.
Results The results obtained revealed that the level of serum IFN in the majority of patients didn't differ from the control data (<2–8 un/ml). In 4 cases, it formed 8 and 8–16 un/ml. The level of a–IFN decreased in 92% of patients (11) and in 1 case it didn't differ from the normal values (640–1280 un/ml). The level of γ-IFN decreased in all myasthenic patients (4–64 un/ml in patients, 128–250 un/ml in the control). Spontaneous IFN in 10 patients (83%) didn't differ from the control values (<2 un/ml). In 2 cases, it formed 2–4 un/ml.
Conclusion The studied adult patients with generalized myasthenia showed a-IFN and γ-IFN deficiency.

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Antylympholin-Gt in treatment of children with myasthenia

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The **object** of the study: investigation of goat antilympholin (antilympholin-Gt) in patients with juvenile myasthenia.
Methods The total of myasthenia children observed was 14. A single preparation dose was 1.2–1.5 mg/kg of body weight. It was administered intravenously using 3–5 dropped injections. The values of humor and cellular immunity were determined.
Results Positive clinical effect was noticed in 8 of 12 cases of generalized form of disease (63%) as well as in patients with ophthalmic form of the disease. The level of both general and active lymphocytes of peripheral blood increased (mean values). Immunoglobulin level did not significantly change. Patients with immunoglobulin level decreased after treatment with antilympholin-Gt, showed complete restoration of moving activity.
Conclusion Thus, antilympholin-Gt in the dose 1.2–1.5 mg/kg of body weight may influence patients with juvenile myasthenia as both immunostimulating and immunosupressing agent. In cases with it acted as immunosupressor, the patient's demonstrated clinical improvement and even remission. In cases when it acted as immunostimulator, there was none of the clinical improvement. It is known that antilympholine-Gt acts as immunostimulator in low doses (0.5 mg/kg). Taking into account differently directed immunomodulating effect of the selected dose (1.2–1.5 mg/kg), the greater doses of antilympholin-Gt (5mg/kg) should be recommended for patients with juvenile myasthenia.

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Myasthenia gravis, pregnancy and transient neonatal myasthenia

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Background In the Slovak Republic, with a population of 5.4 million, a Myastenia Gravis Centre was established in 1978. Out of 927 registered myasthenia gravis (MG) patients, 817 were alive (most of them in remission) up to December 31, 2001, indicating the prevalence rate of 149.2 per million population. Sex – females 571, males 356 (ratio 1.6:1).
Objective and results 84 female MG patients (61 in clinical remission: no symptomatology, no therapy) delivered 109 newborns, 7 (6.4%) having signs of transient neonatal myasthenia (TNM). There was no correlation between acetylcholine receptor antibodies, the myasthenic symptoms of mothers and occurrences of TNM. Two newborns of the same mother, who was at both deliveries in clinical remission, had the most severe TNM with respiratory insufficiency. All 7 newborns had a good response to acetylcholinesterases. The transient neonatal symptoms disappeared 2–5 weeks after the birth.
Four MG females who need a long-term immunosuppressive therapy (because of MG severity and MG relapses) became gravid during immunosuppressive therapy. They refused interruption, one also prenatal investigation, and all gave birth to healthy newborns. In females with manifest MG, the symptoms worsened markedly in 10 patients, one needed artificial respiration.

These empirical observations are explainable by studies documenting the immunosuppressive effect of alpha-fetoprotein. However, we observed a manifestation of MG in the second trimester of gravidity in three women.

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Breaking of nervous realization and magnetic stimulation

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