

EPILEPTIC AND EPILEPTIFORM  
ENCEPHALOPATHIES

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The term *epileptic encephalopathies* is used to describe a group of epilepsies or epileptic syndromes characterized by the following symptoms:

1. early beginning – often in the first year of life;
2. resistance to medication therapy;
3. bad prognosis regarding the individual development.

The etiology of epileptic encephalopathies is a multifactor one and some antenatal, perinatal and postnatal reasons for their arising were being discussed. The antenatal cases arise from anomalies in development, phacomatoses, intrauterine infections and circulation disorders; the perinatal – more frequently from hypoxic-ischemic encephalopathia and the postnatal ones – from trauma, meningo-encephalitis, metabolic disorders (mitochondriopathias), vascular diseases and infections, among them Rasmussen syndrome. The etiology in more of the epileptic encephalopathies remains unclear.

Unlike the epileptic encephalopathies, where there exists clinically manifested fits, the epileptiform encephalopathies are associated with diseases having epileptiform activity in the EEG, but lacking clinically manifested epileptic fits in part of the patients. The epileptiform activity indicates cortical irritability, but that does not mean that the patient suffers from epilepsy.

The treatment of the epileptic and the epileptiform encephalopathies proves difficult having in mind the medication control as well as the necessity of coordinated efforts of neurologists, pediatrics and psychologists.

**Key words:** epileptic encephalopathies, epileptiform encephalopathies, EEG.

## SUMMARY

Many reports concerning potential immunomodulatory effects of one outstanding class of drugs – statins, have been published recently. Statins are widely used as lipid-lowering agents, that inhibit 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase. Statins may also have therapeutic potential for a variety of immune-mediated disorders such as MS, rheumatoid arthritis, type I diabetes mellitus, and graft rejection in organ transplantation.

Studies of immunomodulatory effects of statins in patients with RRMS, treated with and without interferon beta showed that statins inhibit proliferation of in vitro stimulated T-cells. The most potent effect showed simvastatin, followed by lovastatin, and mevastatin in a dose-dependant manner. Observed were also some proinflammatory properties.

Oral atorvastatin prevented or reversed chronic and relapsing paralysis of the mice in EAE model of MS. Secretion of proinflammatory Th1 cytokines - IL-2, IL-12, interferon- and TNF-alpha was suppressed by atorvastatin. On the other hand, atorvastatin promoted differentiation of Th0 cells into Th2 cells.

Currently, a pilot clinical trial is evaluating the role of simvastatin (Zocor) in 30 patients with RRMS. The results demonstrated significant decrease in the number (44%) and volume (41%) of new gadolinium-enhanced lesions, compared to baseline values.

A clinical randomized double-blind, placebo-controlled phase II trial was planned for evaluation of the efficacy and safety of atorvastatin in patients with clinically isolated syndrome (CIS) at risk to develop MS.

Data that up to now have been obtained from experiments with animals, in vitro studies with human immuno-competent

cells and from open-label clinical trials suggest that statins are hopeful therapeutic candidates for MS. Nevertheless, the results from larger clinical randomized, double-blind, placebo-controlled trials are awaited.

**Key words:** statins, multiple sclerosis, treatment.

## SUMMARY

DIAGNOSTIC RESPIRATORY POLYGRAPHY AND  
CPAP-THERAPY IN OBSTRUCTIVE SLEEP APNEA  
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Obstructive sleep apnea syndrome (OSAS) is characterized by repeated episodes of upper respiratory way obstruction during sleep leading to oxygen desaturations and EEG-arousals. The treatment of choice in OSAS is nasal continuous positive airway pressure (CPAP). The chronic compliance with CPAP still remains poor.

**Patients and methods:** 75 patients (middle age of  $48.2 \pm 10.5$ ) were investigated at the Sleep laboratory of the University Hospital "Queen Joanna" in order to characterize their sleep disordered breathing and CPAP-therapy. Using limited respiratory polygraphy (Stardust - Respirationics®). A diagnostic night was performed and the following parameters were registered: Apnea index (AI) as the number of apneas (obstructive and mixed) per hour; Apnea/Hypopnea index (AHI) as the number of apneas and hypopneas per hour; Hypopnea index (HI) as the number of hypopneas per hour. OSAS was diagnosed when  $AHI \geq 15$  was scored and in case of  $AHI \geq 30$  the OSAS was considered as severe. In all patients with OSAS a titration night with CPAP was tried and the percentage of patients who accepted CPAP and were compliant with therapy over the time was calculated.

**Results:** In 68 (91%) from 75 patients OSAS was diagnosed and in 49 (65%) the sleep disturbance was assessed as severe. The 15 women studied had significantly higher age and fewer severe OSAS. On hospital discharge 34 patients (50%) were considered as patients on CPAP-therapy. The patients on CPAP had significantly worse respiratory parameters – higher AHI, AI, HI and more time spent with oxygen saturation below 90%. In the long term follow-up only 20 (58% from the CPAP group, 29% from the patients with OSAS) patients from the 34 initially on CPAP were still on individual CPAP. Neither of the adverse events in the beginning were chronically persistent and considered responsible for CPAP failure and the subjective assessment of CPAP was very good.

**Conclusion:** OSAS is a very frequent and severe disturbance of breathing during sleep and is associated with higher risk and mortality from cardiovascular diseases. The treatment of OSAS with CPAP normalizes blood pressure and left ventricular function and leads to better quality of sleep and daytime performance and to a reduction of health care costs. In contrast the chronic compliance with CPAP remains poor also in our group and the main reasons for that are financial and family problems.

**Key words:** Obstructive sleep apnea syndrome, CPAP-treatment, CPAP-compliance.

## SUMMARY

COGNITIVE DISTURBANCES AND LEARNING  
DISABILITY IN PATIENTS WITH EPILEPSY*M. Rasheva, M. Radeva, M. Milanova*

Many patients with epilepsy suffer from different cognitive disturbances and learning problems. Also in patients with cognitive disturbances and learning problems epileptic syndromes are seen with high prevalence. The aim of this study is to assume the art, frequency and characteristics of cognitive disturbances and learning disability in patients with epilepsy and to point out their medical treatment and prognosis.

**Patients and methods:** 138 patients (80 men and 58 women) in the age between 3 and 28 (mean 16.4 years) were studied and divided in three groups depending from the epileptic syndrome:

1. Patients with malignant epileptic syndromes;
2. Patients with refractory partial epilepsies;
3. Patients with idiopathic generalized epilepsy with absences. As a fourth control group patients with leading diagnosis learning disability in whom epilepsy was secondarily diagnosed were assessed (29 patients). In all patient somatic and neurological status, EEG, CT and/or MRI and neuropsychological tests were performed.

**Results:** In the group with malignant, specific epileptic syndromes with frequent polymorph seizures (12 patients) the prognosis concerning epilepsy and intellectual deficiency was bad. In the second group of 79 patients with refractory, partial epilepsies with long duration and high mean seizure frequency, medication with more than two antiepileptic drugs couldn't control the epileptic seizures. The reduction of seizures is below 50% and the cognitive deficiency persists. In hippocampal sclerosis surgical treatment shows good efficacy concerning both cognitive impairment and course of epilepsy. In the third group of children with new idiopathic absence epilepsy learning difficulties are seen in 10 from 18 patients (55.6%). The treatment with valproates is very effective for both clinical and electrophysiological symptoms. In the children with specific learning difficulties, in whom partial epileptic seizures were diagnosed, the prognosis is relatively good and the therapy with valproates alone or in combination with lamotrigine is effective.

The frequency of learning problems and cognitive disturbances in epilepsy is high. Quality of life in patients with epilepsy depends on frequency, art and severity of epileptic seizures and also on conservation of cognitive function.

**Key words:** epilepsy, learning disability, specific epilepsy syndromes, EEG, cognitive disturbances.

## SUMMARY

DIAGNOSIS OF ALCOHOLIC POLYNEUROPATHIES  
BY RESIDUAL LATENCY PARAMETER*A. Alexandrov, M. Daskalov, L. Christova,  
N. Samardjieva, D. Kosarov, B.A. Ishpekova*

The aim of the study is a quantitative valuation of residual latency (RL) - fixed EMG parameter for diagnosis in patients with alcoholic polyneuropathy (APNP). RL on motor fibre is calculated by the formula:  $RL = DL - (DD/CV)$ , where DL is distal latency, DD - distal distance and CV - conduction velocity. RL determines conduct of impulse on terminal branching of motor fibre. Quantity delay of CV at extremely nerve branching may be determined only by parameter RL. CV and DL are measured at median, ulnar, peroneal, and tibial nerves. Motor conduction studies were performed using standard techniques with surface electrode stimulation and

recording at skin. The investigation was carried out in 40 patients with alcoholic polyneuropathy: 3 women with an age range of 50 to 57 years (mean age  $46.5 \pm 2$ ) and 37 men with an age range of 29 to 66 years (mean age  $46.5 \pm 1.5$ ). The results received at alcoholic polyneuropathy show remarkable decrease of CV while DL becomes longer at motor fibers of lower limbs {n. fibularis:  $CV = 39.77 \pm 0.71$  (m/s) and  $DL = 6.48 \pm 0.19$  (ms); n. tibialis:  $CV = 39.54 \pm 0.68$  (m/s) and  $DL = 5.85 \pm 0.33$  (ms)}. By upper limbs {n. ulnaris:  $CV = 48.25 \pm 1.13$  (m/s) and  $DL = 4.02 \pm 0.15$  (ms); n. medianus:  $CV = 49.47 \pm 1.32$  (m/s) and  $DL = 4.85 \pm 0.22$  (ms)} is not observed decrease of CV and increase of DL. Calculation values of RL for investigated nerves at APNP in comparison with control group are as follows: n. fibularis:  $RL = 4.67 \pm 0.18$  (ms), healthy subjects:  $RL = 3.11 \pm 0.09$  (ms); n. tibialis:  $RL = 4.07 \pm 0.32$  (ms), healthy subjects:  $RL = 3.23 \pm 0.05$  (ms); n. ulnaris:  $RL = 2.63 \pm 0.15$  (ms), healthy subjects:  $RL = 1.59 \pm 0.03$  (ms); n. medianus:  $RL = 3.43 \pm 0.19$  (ms), healthy subjects:  $RL = 1.67 \pm 0.03$  (ms). The method is easily realizable and is important for the diagnosis of alcoholic polyneuropathy, which permits correct therapy of patients.

**Key words:** alcoholic polyneuropathy, residual latency, EMG.

## SUMMARY

CENTRAL DEMYELINATION IN PATIENTS WITH  
CHRONIC INFLAMMATORY DEMYELINATING  
POLYNEUROPATHY – CLINICAL, ELECTROPHYSIO-  
LOGICAL AND MRI STUDY*Iv. Petrov, K. Kostov, R. Ikonov, Iv. Ivanova*

Chronic inflammatory demyelinating polyneuropathy (CIDP) is an acquired demyelinating disease of the PNS characterized by a slow course of progressing or relapsing proximal-distal sensory-motor polyneuropathic syndrome. The exact pathogenetic mechanism of peripheral demyelination at CIDP is yet unclear but it is considered as mediated by cellular and humoral immune factors with peripheral myelin being the target structure. In some cases CNS involvement in the demyelination process is evidenced.

The work presents 14 patients (10 men and 4 women), mean age 47.1 years (in the range 28 – 64 years), complying with the clinical, electrophysiological and biopsy criteria for CIDP with present clinical, electrophysiological and/or MRI data for parallel CNS engagement. Clinically, in the presented patients, on the background of expressed, chronically progressive or relapsing polyneuropathic syndrome, are found discreet pyramidal signs. Neither of the patients has clinical data for MS, preceding or following the onset of CIDP. Nine patients at somatosensory evoked potentials showed delayed speed of conduction by the central somatosensory routes (prolonged inter-peak latencies N13 – N20 after stimulation of n. medianus and N22-P38 after stimulation of n. tibialis), 5 patients presented data for trunk dysfunction at auditory evoked potentials. Four patients subjected to MRI showed rounded hyperintense T2 zones and TIRM-images with different localization similar to those at MS. Although at this stage there is no morphological evidence for CNS lesions, the observed changes in AEP, SEP and MRI show doubtless demyelination of central structures with subclinical course in some of the patients with CIDP.

**Key words:** chronic inflammatory demyelinating polyneuropathy, central demyelination, pyramidal signs, MRI, AEP, SEP.

## SUMMARY

## CHRONIC INFLAMMATORY DEMYELINATING POLYNEUROPATHY – CLINICAL, ELECTROPHYSIOLOGICAL AND MORPHOLOGICAL STUDY

*I. Petrov, R. Ikonov, K. Kostov, I. Ivanova, S. Gabrovski, G. Kondarev*

Chronic inflammatory demyelinating polyneuropathy (CIDP) is an acquired demyelinating disease of the peripheral nervous system with nosological uncertainty and clinical heterogeneity. The present work aimed at studying the clinical, laboratory, electrophysiological and biopsy characteristics of CIDP. The studied group consisted of 58 patients (45 men and 13 women) aged 17 – 72 years (average age 52.1) complying with the diagnostic criteria of the American Academy of Neurology (1991). The patients were subjected to clinical examinations, liquor tests, neuroelectrophysiological test and biopsy examination (n. suralis and muscle). The results showed that CIDP was most often evidenced as mainly distal sensorimotor polyneuropathy affecting more the lower limbs. In 10.3% the clinical features were mainly proximal. The onset of the disease was most often in the 4th and 5th life decade. A certain relationship was evidenced between the clinical course and the onset of the disease, with chronic relapsing forms occurring significantly earlier than the chronic progressive ones. Pyramidal signs were observed in 24.1% of the studied individuals. Ataxia was found in 13.8% and injury of the cranial nerves was established in 15.5% of the patients. The liquor tests most often revealed immunoreactive liquor syndrome while the electrophysiological tests provided data for demyelinating polyneuropathy. The biopsy examination of n. suralis reported changes of demyelination/remyelination type, axonal degeneration, onion bulbs, accumulation of regeneration fibers, and the muscle biopsy depicted denervation atrophy. The study showed that CIDP manifested significant clinical and laboratory heterogeneity. The reliable diagnosis requires a complex clinical, laboratory, electrophysiological and, if necessary, biopsy examinations. The timely exact diagnosing is important for the successful treatment of the disease.

**Key words:** chronic inflammatory demyelinating polyneuropathy, clinical features, biopsy of n. suralis, muscle biopsy, electroneurography, diagnosis.

## SUMMARY

## MOSAIC FSHD ALLELE WITH SEEMINGLY NONPATHOGENIC ALLELE ALREADY SHOWS DOSAGE EFFECT.

*B. Buzhov, I. Tournev, G. Padberg, B. Ishpekova, R. Lemmers, S. van der Maarel*

Facioscapulohumeral muscular dystrophy (FSHD1A) is inherited in AD way and characterizes with descendant skeletal muscle involvement. It is caused by D4Z4 repeat contraction at 4q35. In the patients the deleted fragments contain between 1 and 10 repeats and all the alleles related with the disease seem to be “A” type. Nonpenetrant alleles in the pathological range are described. A dosage effect in the compound heterozygous patients is already shown. Still no data for a possible dosage effect of a mosaic allele and a nonpenetrant allele in the pathologic range leading to a severe FSHD phenotype existed so far.

**Key words:** Facioscapulohumeral muscular dystrophy, AD type of inheritance, mosaic allele, nonpenetrant allele.

## SUMMARY

## ABNORMALLY SEVERE FSHD PHENOTYPE IN A FAMILY WITHOUT 4Q35 DELETION

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**Abstract:** Facioscapulohumeral muscular dystrophy (FSHD1A, OMIM 158900) is an autosomal dominant myopathy with settled diagnostic criteria. The gene responsible for the disease is mapped on the long arm of chromosome 4. In most of the cases the disorder is associated with deletion of an integral number of 3,3 kb tandemly repeated units (D4Z4), with dimensions of the pathological alleles  $\leq$  38 kb. Genotype-phenotype correlations are found, but for the borderline sized fragments they are excluded. In about 5% of the patients, FSHD does not present with contraction at 4qter and is thought to be caused by other unidentified loci. These genetically heterogeneous patients show pronounced hypomethylation of CpG's, strongly supporting the key role of D4Z4 hypomethylation in the cascade of epigenetic events causing FSHD1. Here we describe a family with an unusually severe affected proband with FSHD1 clinical picture and lack of 4qter deletion and emphasize on the key role of the clinical examination in establishment of the diagnosis in genetically excluded cases.

**Key words:** Facioscapulohumeral muscular dystrophy, AD type of inheritance, mosaic allele, nonpenetrant allele.

## SUMMARY

## ISCHAEMIC STROKE IN PAROXYSMAL NOCTURNAL HEMOGLOBINURIA: REPORT OF A CASE

*P. Atanassova, J. Grudeva-Popova, T. Vassileva, I. Hristova*

Paroxysmal nocturnal hemoglobinuria (PNH) is an acquired haemopoietic stem cell disorder associated with periodic hemolytic events. It is a rare condition, which usually occurs in younger people. Recurrent venous and, less commonly, arterial strokes are the most prevalent neurological manifestation in patients with PNH, often with unfavorable outcome. Only a few cases with isolated cerebral arterial thrombosis have been reported.

We report the case of a 26-year-old woman, who developed ischaemic cerebral infarction as the initial thrombotic complication of previously undiagnosed PNH. We present this case to draw attention to this rare cause of haemolytic anaemia, which should be considered in any patient, of any age, who has signs of chronic haemolysis.

**Key words:** paroxysmal nocturnal hemoglobinuria, ischaemic stroke

## SUMMARY

## ALZHEIMER'S DISEASE

*N. Toteva*

Alzheimer's disease (AD) is the most important cause of dementia. It has also become a major health problem because of the burgeoning numbers of aged individuals, the long duration of AD, and its high cost of care. Although advances over the past decade have increased our understanding of the molecular pathology of AD, its diagnosis remains largely clinical. Several criteria have been devel-

oped for the diagnosis of AD. No single element of the clinical picture is unique to AD. Currently no laboratory test can confirm AD during life or permit identification of individuals at risk for the disease. Cholinesterase inhibitors remain the mainstay of AD treatment, but do not appear to alter the progression of disease.

**Key words:** dementia, decline of cognitive function, impairment of memory, cholinesterase inhibitors