

## Neuroepidemiology Neurogenetics

P 1176

### **“Direct” molecular diagnosis of spinal muscular atrophy in Moldova**

V. C. Sacara, S. A. Groppa

*Scientific Research Institute of Mother and Child Health Service, Chisinau, REPUBLIC OF MOLDOVA*

**Objective** SMA is one of the most common and severe autosomal-recessive diseases of children. The pathology involves dysfunction and loss of anterior horn cells, leading to muscle atrophy and weakness. Three forms of SMA are recognized. All forms are caused by mutations in a single gene. In 95–98% a homozygous deletion of exon 7 and (or) 8 exon of the telomeric copy of the survival motor neurone gene (SMN1), which maps to chromosome 5q13, can be demonstrated by PCR.

**Materials and methods** 20 families with risk of SMA passed clinic-neurological, electromyography investigations and molecular study. DNA preparations were made from peripheral blood samples by routine methods, from chorionic villus samples and used for PCR. The EcoRV digestion necessary to distinguish the PCR product of exons 7(150bp) of SMN (8ex/BseNI (183bp) and its copy gene.

**Results** Molecular studies at the SMN1 locus were performed in 65 individuals. The results of direct DNA diagnosis of SMA in admitted to the clinic for suspected SMA are: in 18 out of 20 families (90%) The diagnosis of SMA was confirmed at the molecular level by revealing homozygous deletion of exons 7 and (or) 8 of the SMN1 at the probands. In 4 cases, we performed prenatal diagnosis (PD) SMA. In 2 out of 4 fetuses, we detected heterozygous deletion of the exons.

**Conclusions** Deletion detection and carrier testing is a decisive step in elaborating a reliable strategy of prenatal diagnosis in families at a high risk of SMA.

P 1177

### **Genetic and clinical analysis of spinocerebellar ataxia type 8 (SCA8) repeat expansion in Serbia**

I. Topisirovic, N. Dragasevic, D. Savic, A. Ristic, M. Keckarevic, I. Petrovic, D. Keckarevic, B. Culjkovic, S. Romac, V. S. Kostic

*Institute of Neurology CCS, Belgrade, YUGOSLAVIA*

**Introduction** Spinocerebellar ataxia type 8 (SCA8) is the first form of slowly progressive ataxia causally associated with untranslated CTG repeat expansion on chromosome 13q21.

However, the role of the CTG repeat in SCA8 pathology is not yet well understood.

**Patients and methods** We investigated the occurrence of the SCA8 triplet expansion (CTA/CTG repeats; CRs) in a sample of 115 patients with ataxia [including 63 patients with dominant pattern of inheritance (ADCA), 28 patients with apparently recessive cerebellar ataxia (ARCA), and 24 apparently sporadic patients], 125 healthy controls, 64 unrelated individuals with non-triplet neuromuscular diseases, and 70 unrelated patients with schizophrenia.

**Results** All the studied individuals were negative for CTG expansions, except one male patient (18/100 CRs), aged 43, from the group of apparently sporadic patients. Beside ataxia with brisk tendon reflexes, he had infrequent incontinence, not explained by other causes, and abnormal visual and auditory evoked potentials. Asymptomatic father (28/140 CRs) and son (24/92 CRs) were explained by the low penetrance of the disease. In healthy Serbian population (378 total chromosomes) these alleles were in the range between 14 and 34 CRs.

**Comment** Our findings support the notion that allelic variants of the expansion mutation at the SCA8 locus can predispose ataxia.

#### P 1178

##### **Clinic-genealogical features of hereditary neuropathies with pressure palsies, in Novokuznetsk population**

*O. V. Rudenkova, I. R. Schmidt, M. A. Peganova  
Institute of Postgraduate Training, Novokuznetsk, RUSSIAN  
FEDERATION*

**Aim** Our study was to make a clinico-genealogical analysis of families with hereditary neuropathies (HNs) with liability to pressure palsies.

**Methods** Neurological, clinico-genealogical; gene segregation analysis, and electromyographic studies.

**Materials** Fifty kinships with the obtained data of 232 relatives have been studied. There were 187 first-line relatives: 81 parents, 75 siblings, 31 children and 45 second-line relatives. Segregation analysis was conducted in 56 nucleus families: parents and their children.

**Results** Characteristic features of HNs with liability to pressure palsies were identified in 65.8±3.5% relatives of the first-line. The difference was found to be statistically significant ( $P < 0.01$ ) when  $t=5.1$  and  $x^2=128.7$ ,  $P \times 2 < 0.0001$  compared to the population rate sample. Correlation coefficient was  $r = +0.33$ . Segregation analysis carried out according to Vainberg's proband method has demonstrated that HNs with liability to pressure palsies in our studied patients were inherited through autosomal-dominant type with incomplete penetrance and variable gene expression found out in the families and probands. Autosomal dominant mode of transmission has been confirmed by detectable changes of impulse conduction velocity through peripheral nerves and by increased residual latency identified in clinically healthy relatives of first-line. This fact provides evidence that some family members are most likely to be at high risk for developing pressure palsies. Marked changes of residual latency may help to identify the most vulnerable nerve for inadequate compression.

**Conclusion** HNs with liability to pressure palsies in our population are characterized by a typical clinical polymorphism and autosomal-dominant mode of transmission with incomplete penetrance.

#### P 1179

##### **Parkin proven disease: common founders but divergent phenotypes**

*J. A. Wiley<sup>1</sup>, S. Lincoln<sup>2</sup>, T. Lynch<sup>1</sup>, W. J. Langston<sup>3</sup>, R. Chen<sup>3</sup>, A. Lang<sup>4</sup>, E. Rogaeva<sup>4</sup>, J. Harris<sup>5</sup>, K. Marder<sup>6</sup>, C. Klein<sup>7</sup>, G. Bisceglia<sup>2</sup>, J. Hussey<sup>2</sup>, W. Andrew<sup>2</sup>, J. Hardy<sup>8</sup>, M. Farrer<sup>2</sup>  
<sup>1</sup>Mater Misericordiae Hospital, Dublin, IRELAND, <sup>2</sup>Mayo Clinic, Jacksonville, FL, USA, <sup>3</sup>The Parkinson's Institute, Sunnyvale, CA, USA, <sup>4</sup>University of Toronto, Toronto, ON, CANADA, <sup>5</sup>Columbia University, New York, NY, USA, <sup>6</sup>Taub Institute, New York, NY, USA, <sup>7</sup>Medical University of Luebeck, Luebeck, GERMANY, <sup>8</sup>NIH, Bethesda, MD, USA*

**Objective** To describe six probands with Parkinson's from six families each having inherited a common parkin exon 3, 438 to 477bp deletion (exon 3 40bp del).

**Background** Farrer and colleagues previously reported 2 families in which a parkin exon 3 40bp deletion segregated with disease. We now report the clinical phenotype in four additional probands with homozygous or compound heterozygous parkin exon 3 40bp deletion.

**Methods** Semi-quantitative multiplex PCR was performed for exon deletion/duplication. In addition, all exons and intron-exon boundaries were sequenced. Haplotype analysis was performed by genotyping fluorescently labelled markers about the parkin gene.

**Results** Four of six were compound heterozygotes, one was novel with an exon 3 40bp deletion and an exon 3 duplication, whereas three probands had an exon 3 40bp deletion and an exon 7 924 bp C>T (R275W) mutation. Of the remaining probands, one was homozygous for the exon 3 40bp deletion and one had early-onset parkinsonism and only a single exon 3 40bp deletion and a normal parkin allele. Haplotype analysis suggests that the exon 3 40 bp deletion originates from a common Irish founder.

**Conclusion** Parkin proven disease can have common founders but divergent phenotypes. Disease has a variable clinical presentation and mode of inheritance although haplotype analysis revealed the common exon 3 40bp deletion originated from an Irish founder. These patients now provide a powerful resource to examine the effect of environment/genetic background on the clinical pathology of genetically defined Parkinsonism.

#### P 1180

##### **Subtle mutations in Polish SMA patients**

*M. Jędrzejowska<sup>1</sup>, W. Wiszniewski<sup>2</sup>,  
I. Hausmanowa-Petrusewicz<sup>1</sup>  
<sup>1</sup>Polish Academy of Science, Neuromuscular Unit, Warsaw,  
POLAND, <sup>2</sup>National Research Centre of Mother and Child,  
Department of Medical Genetics, Warsaw, POLAND*

Autosomal recessive proximal spinal muscular atrophy (SMA) is the neuromuscular disorder caused by the mutation (deletion, conversion or subtle mutation) of the telomeric copy of the survival motor neuron gene (SMN1). The loss of the nearly identical centromeric copy does not cause SMA. About 95% of SMA patients show homozygous absence (deletion or gene conversion) of at least exon 7 telomeric copy of SMN gene, the rest present a compound heterozygosity with a subtle mutation on one allele and a deletion or gene conversion on the other.

In our study, we searched for small intragenic mutation among twelve non-deleted SMA patients. There are 25 different subtle intragenic mutations in 58 patients described up to date, which include missense, nonsense, frame shift mutations, inversions,

deletions and splice site mutations. All examined patients presented relatively mild phenotype (3a and 3b), apart from one sibling with Werdnig-Hoffmann syndrome. Using direct sequencing, we identified one missense mutation (T274I) in SMN1, connected with mild phenotype (3a). The rest of analysed group could carry mutations in SMN promoter region or is unlinked to 5q13.

P 1181

**Apolipoprotein E genetic polymorphism and stroke subtypes**

M. Baranska-Gieruszczak<sup>1</sup>, G. Gromadzka<sup>2</sup>, A. Ciesielska<sup>1</sup>, I. Sarzynska-Dlugosz<sup>1</sup>, T. Mendel<sup>1</sup>, A. Czlonkowska<sup>2</sup>  
<sup>1</sup>Institute of Psychiatry and Neurology, 2nd Dept. of Neurology, Warsaw, POLAND, <sup>2</sup>1-Institute of Psychiatry and Neurology, 2nd Dept. of Neurology; 2-Medical University of Warsaw, Dept. of Experimental and Clinical Pharmacology, Warsaw, POLAND

The association between apolipoprotein E (apoE) genetic polymorphism and stroke has not been completely understood.

We investigated the association between ApoE genotypes and stroke subtypes in 244 patients included into the study. The diagnosis in all cases has been established on the basis of history and full neurological examination, standardized blood tests, CT scan of the brain, Doppler sonography of the carotid arteries and a cardiac analysis that included echocardiography. Cerebral infarction was classified anatomically into cortical and penetrating region and etiologically into thrombosis and embolism. Cerebral haemorrhage was considered as a whole in all analyses.

PCR RFLP method has been used to determine ApoE genotypes.

**Results** The most frequent genotype was E3/3 (66.4%) followed by E3/4 (17.2%), E2/3 (14.8%) and E2/4 (1.6%). We observed differences in the frequencies of ApoE genotypes between groups of patients with different stroke subtypes, infarction volume, number and pathology of lesions.

In the univariate logistic regression analysis, E4 allele carriage conferred an increased risk for cardio embolic stroke (OR=3.04, 95% CI 0.8–11.3, p=0.07), carotid artery occlusion (OR=1.13, 95% CI 0.39–3.2, p=0.05) and hemorrhagic stroke (OR=2.57, 95% CI 0.98–6.73, p=0.05). Epsilon 4 carriage presented a tendency to be associated with increased risk of death during 30-days period following stroke (OR=1.99, 95% CI 0.9–4.4, p=0.08).

**Conclusion** Results of our study suggest that genetic variation at the ApoE locus in Polish stroke patients population is a genetic factor that influence the risk of embolic stroke, hemorrhagic stroke, carotid artery occlusion and can establish a risk factor of death during 30-days period.

P 1182

**Paraoxonases genes polymorphisms in ischemic stroke of different aetiology**

P. Szermer, A. Slowik, J. Pera, L. Glodzik-Sobanska, A. Szcudlik  
 Jagiellonian University, Krakow, POLAND

**Background** Paraoxonases genes polymorphisms play an important role in determining the anti-atherogenic action of paraoxonases. This function in humans has been demonstrated in the coronary artery disease. The impact of paraoxonases genes variability on risk of ischemic stroke is still not certain. The aim of this study was to assess the M/L54 of PON1 and

C/S311 of PON2 polymorphisms in patients with ischemic stroke of different aetiology, based on TOAST criteria (Adams, Stroke 1993).

**Material and methods** The study population included 48 patients with small vessel disease, 49 patients with large vessel disease, 59 patients with cardioembolic stroke and 122 healthy control subjects. The genotyping was carried out with the restriction enzyme digestion pattern after PCR amplification.

**Results** Genotype distribution and allele frequencies of M/L54 and C/S311 were similar among the patients and control group. There were also no significant differences among stroke subgroups.

Our study indicates that probably neither M/L54 nor C/S311 polymorphisms are involved in pathogenesis of ischemic strokes due to large vessel disease, small vessel disease or cardioembolism.

P 1183

**Hypokalemic periodic paralysis, age of onset in Iranian patients**

M. Harirchian  
 Tehran University, Tehran, ISLAMIC REPUBLIC OF IRAN

**Objective** To investigate the age of first attack of primary hypokalemic periodic paralysis in our patients and know whether there is any difference between them and other studies about the age of onset of this disease.

**Background** Primary hypokalemic periodic paralysis is a familial channelopathy inherited as an autosomal dominant trait. The first attack of paralysis may be evolved at any age, but several studies indicate that its onset (first attack) is most common in second decade, so that some authorities believe that an episodic weakness beginning after age 25 is almost never due to primary periodic paralysis.

**Design and methods** In a retrospective study, we reviewed the patients admitted in two hospitals of Tehran University of Medical Science during 1992–2001. We reviewed the medical data's of 50 patients with flaccid weakness and hypokalemia and 27 patients were excluded due to deficits in documents and inclusion and exclusion criteria. Twenty-three patients remained with the diagnosis of primary hypokalemic paralysis.

**Results** First attack was beyond age 20 in 13 patients (56.5%) and beyond 25 in 9 patients (39%). Two patients were below age 15, 8 in 15–20, 4 in 20–25, 3 in 25–35, 4 in 35–45, and 2 were more than 45.

**Conclusion** Age of first attack is much more than other studies and it seems to be a difference between our epidemiological characteristics with west.

P 1184

**The spread and clinical development of myasthenia gravis in the Republic of Belarus**

T. Korbut, E. Ponomareva  
 Research Institute of Neurology, Neurosurgery and Physiotherapy, Minsk, BELARUS

**Introduction** Myasthenia gravis (MG) was considered to be a very rare disease. But for the last few years, it has increased in the world and now it is one of the most widespread nervous and muscular pathology.

**Methods** In the Republic of Belarus 769 people who suffer from MG (67% of women and 33% of men aged from 2.5 to 92 years) have been under observation for more than 20 years. The disease was diagnosed on the basis of a medical examination,

diagnosis myasthenic tests, and electroneuromyography. The results have been analysed.

**Results** The first cases of MG were reported in 1980 and accounted for 0.031 per 100000 people, in 1983 there were 0.230 cases, in 1990–0.343, in 1996–0.561 and in 2001–0.630. The age group has also changed. The number of people over 60 has increased while the number of children and teenagers has decreased. There prevails a generalized form of the disease (59%). In 56% of cases, treatment with anticholinesterase medicines doesn't give full compensation. 271 patients underwent thymectomy, 39.6% of them had a benign tumour of the thymus and 2.6% – a malignant tumour.

**Conclusion** In the Republic of Belarus there has been reported a significant growth of MG, increasing of tumour of the thymus. It might be connected with the ecological situation in the country and the Chernobyl disaster consequences in particular.

#### P 1185

##### **Risk of cancer in patients with Parkinson's disease**

P. Ragonese<sup>1</sup>, M. D'Amelio<sup>1</sup>, G. Salemi<sup>1</sup>, M. Ruggirello<sup>1</sup>, A. Epifanio<sup>2</sup>, L. Morgante<sup>2</sup>, G. Savettieri<sup>1</sup>

<sup>1</sup>University of Palermo, Palermo, ITALY, <sup>2</sup>University of Messina, Messina, ITALY

**Introduction** Several surveys reported lower cancer risk in Parkinson's disease (PD) patients compared to the general population. Most of these studies were however based on death certificates, which are not representative of the general occurrence of cancer. We estimated the risk of cancer in people with PD through means of a case-control study.

**Methods** Cases: PD patients from two Neurological Departments. Controls: PD free individuals, matched by age (+/-2 years) and sex, randomly selected from all residents of the municipalities of residence of cases. Occurrence of cancer was assessed through a structured questionnaire. Cancer was categorized as follows: benign, malignant or of uncertain classification tumours and, endocrine related or not. Odds Ratios (OR) were calculated using conditional logistic regression and adjusted for gender, cancer categories, and known cancer risk factors.

**Results** We included 211 PD patients (123 women, 88 men). Mean age at PD onset was 59.5 years. Frequency of cancer was 11.4% for PD patients, 24.7% for controls. Patients with Parkinson's disease had a significantly decreased risk for cancer (OR 0.3; CI 0.2, 0.6). Risk was reduced for women (OR 0.3; CI 0.1, 0.6) and for men (OR 0.5, CI 0.2, 1.2). PD patients had a decreased risk for malignant compared to non-malignant neoplasm (OR 0.6, 95% CI 0.2, 1.7). Still, risk was increased for endocrine related tumours compared to non-endocrine related malignancies (OR 1.8, 95% CI 0.6, 5.3).

**Conclusions** Our study confirms the lower risk of cancer among PD patients reported in previous epidemiological studies.

#### P 1186

##### **Epidemiological studies on patients with persistent vegetative state/apallic syndrome in Vienna – a study of the prevalence**

C. Stepan

*Otto Wagner Hospital, Vienna, AUSTRIA*

Searching for data concerning the prevalence of persistent vegetative state/ apallic syndrome (PVS/AS), international literature does not contain exact information. That depends on several reasons as variable diagnostic criteria in different countries or

that health agencies do not include PVS/AS as a codable diagnosis.

Due to the insufficient information on prevalence of PVS/AS, a survey on this topic was conducted in Vienna in November 2001. The aim was to register all patients with the diagnosis PVS/AS in a defined area during an exact period of time. The defined area was the city of Vienna with an exact recorded number of inhabitants (1.6 Mio.). November 28th was determined as the day of the examination.

To exclude all source of error, all reported patients, under consideration of epidemiological rules, were examined by a neurologist. Leading the evaluation of all patients by one person, problems based on different examiners were excluded.

32 patients with the diagnosis PVS/AS could be observed. 13 of the patients were treated in a hospital and 19 in a nursing home. 7 patients had a traumatic and 25 patients a non-traumatic aetiology for developing a PVS/AS.

The prevalence of PVS/AS in the area of Vienna was 2.1/100 000 citizens. A longitudinal examination was started to observe the result in its course.

#### P 1187

##### **Diabetic neuropathy in Satu Mare district (Romania) – epidemiological data**

Z. A. Bzduch<sup>1</sup>, M. G. Bzduch<sup>2</sup>, I. Szilagy<sup>2</sup>, A. M. Mos<sup>3</sup>

<sup>1</sup>Caritas Medical Center Satu Mare, Satu Mare, ROMANIA,

<sup>2</sup>Satu Mare, ROMANIA, <sup>3</sup>Oradea, ROMANIA

The importance of diabetic neuropathy is widely recognised. Our study is to determinate the real epidemiological status in the district of Satu Mare, Romania.

Our material consists from a lot of 4351 diabetic patients evaluated for the presence of diabetic neuropathy and other manifestations such as form, gravity, clinical signs, and localization of neuropathy. Patients were selected by function of type of diabetes, age, sex, and age of onset. Another selection of the patients was made function of the affected nervous system, either peripheral or autonomic. Epidemiological data will be represented graphically. In our study, we obtained a main prevalence of 38.1% for neuropathy. In the group of type 1 diabetic patient, the main prevalence of the neuropathy was 15.4%, and in the group of type 2 diabetic patients, this value were of 43.9%, respectively. Other epidemiological data will be presented in our study.

In conclusion, our data shows a higher prevalence of diabetic neuropathy, comparing with the general data found in literature. Our data underlines the importance of new and effective measures for evaluation and treatment of diabetic and neuro-pathic patients.

#### P 1188

##### **Is TGA a seasonal disorder? Evidence from a hospital based population**

C. Agosti, N. Maalikj Akkawi, B. Borroni, A. Padovani

*Clinica Neurologica Spedali Civili, Brescia, ITALY*

**Introduction** Transient global amnesia (TGA) has been defined as the abrupt onset of transient inability to form new memories, repetitive queries and retrograde amnesia without neurological symptoms or sign. Many precipitants factors have been described. We observed that patients affected by TGA were admitted at our hospital especially in cold days, so we investigated whether there is a relationship between lower temperature and admittance of TGA patients.

**Materials and methods** 225 patients affected by TGA and 225 patients by transient ischemic attack (TIA) were admitted to the Department of Neurology, Spedali Civili, Brescia, Italy. The two groups were matched by sex and age. We evaluated: maximum temperature (Tmax), minimum temperature (Tmin), mean temperature ( $T = [T \text{ recorded at 8 am} + T \text{ recorded at 7 pm} + T_{\text{min}} + T_{\text{max}}]/4$ ), excursion temperature ( $DT = T_{\text{max}} - T_{\text{min}}$ ), mean atmospheric pressure reduced to the sea level (P), mean relative humidity (RH), mean water vapour pressure (e). The meteorological station of the "Pastori Technical Institute", Brescia, collected these parameters.

**Results** The mean values of Tmax, Tmin, DT and Tmean were significantly lower in the days of admittance of TGA and the frequency of TGA decreased with the increasing of the temperature. There were no correlations with the other parameters considered. The difference in frequency of TGA and TIA respect to the mean temperatures classified in quartiles was highly significant ( $p < 0.02$ ).

**Conclusion** The frequency of TGA increases with the lowering temperature while barometric pressure, mean water vapour and humidity do not influence the incidence of TGA.

P 1189

**Epidemiological study of multiple sclerosis among people suffering from Chernobyl disaster in Mogilev region (Belarus)**

G. Naumova, M. Klimova, A. Naumov  
Vitebsk Regional Centre for Medical Diagnostics, Vitebsk, BELARUS, Branch of Clinical Research Institute for Radiation Medicine and Endocrinology, Vitebsk, BELARUS

In the context of a national Project "Health status evaluation of population, suffering from the Chernobyl disaster", a descriptive epidemiology of multiple sclerosis on the Mogilev region (Belarus) was done.

The aim of our investigation was to carry out an epidemiological study on multiple sclerosis checking out the epidemiological hypothesis concerning the action of low dose radiation exposure.

We performed a population-based case ascertainment of all available sources of medical care including the State Belarussian Register of people subjected to radiation exposure after Chernobyl disaster.

The study was conducted since May 1986 to December 2000. The total number of inhabitants in the area (29,100 km<sup>2</sup>) was 1,200,000.

The average annual incidence was between 1.5–9.5 per 100,000 (1.1–9.0/100,000 in men and 2.9–12.6/100,000 in women).

There was an apparent peak of the incidence in 1986, which was clearly the result of improved case detection due to obligatory universal clinic system for such people initiated since that time. Clinical profiles of these patients in most respects were similar to those commonly observed in the multiple sclerosis population. The initial remitting-relapsing of multiple sclerosis was the prevalent type of clinical course of the disease.

The mean age of the patients at onset was 32.6 years.

54% of the patients suffering from multiple sclerosis were disabled persons.

P 1190

**Neurological and psychiatric forms of adult metachromatic leukodystrophy: phenotype/genotype relationships.**

J. Turpin<sup>1</sup>, N. A. Baumann<sup>2</sup>, M. Lefevre<sup>2</sup>, B. Colsch<sup>2</sup>  
<sup>1</sup>Salpêtrière Hospital, Paris, FRANCE, <sup>2</sup>INSERM Unit 495 and Salpêtrière Hospital, Paris, FRANCE

Metachromatic leukodystrophy is due to a deficiency in aryl-sulfatase which hydrolyses sulfogalactosylceramides and other sulfated glycolipids (sulfatides). In function of age, the clinical manifestations are different. The infantile form is characterized by a regression of acquired motor and later of mental activities. There are also adult forms, which do not occur, in the same families. Moreover, in the adult, there are two clinical variants, one in which motor signs are predominant, the other in which psychiatric symptoms dominate, although secondarily the patients become bedridden and demented. The evolution in the adult forms may be of several decades. In all those cases in the adult, the enzyme deficiency is identical as well as sulfatiduria, which relates to the absence of the catabolic enzyme for sulfated glycolipids. Interestingly, it is well known from the work of V. Gieselmann (reviewed in *Human Mut.* 4: 233–243, 1994). That the mutations in infantile forms are different from those occurring in the adult, which may explain homochrony. There seem to be specific mutations according to the motor and psycho cognitive types in the adult, i.e. P426L for motor forms in a homozygote form and in the psychiatric forms a specific I179S mutation as a compound heterozygote. Studies are in progress to determine the precise clinical characteristics of the psychiatric forms and whether the I179S mutation of arylsulfatase A could be a susceptibility factor of schizophrenia.

P 1191

**A female carrier of Fabry disease with multi-infarct encephalopathy and extrapyramidal symptoms. A case report.**

S. Büchner<sup>1</sup>, S. Ramat<sup>1</sup>, A. Pupi<sup>2</sup>, W. Borsini<sup>1</sup>  
<sup>1</sup>Department of Neurology, Hospital of Careggi/University of Florence, Florence, ITALY, <sup>2</sup>Department of Nuclear Medicine, Hospital of Careggi/University of Florence, Florence, ITALY

**Introduction** Fabry disease is a lysosomal storage disease, X-linked, secondary to deficiency of alpha-galactosidase A ( $\alpha$ -GAL A), which results in progressive accumulation of globotriaosylceramide in endothelia. Cerebrovascular manifestations (strokes of early onset) frequently complicate Fabry, also in some female carriers. Extrapyramidal signs are unusual. We report a case of a 54 y. o. female Fabry patients with cerebrovascular alterations in brain MRI and extra pyramidal symptoms.

**Case report** A 46-year-old female developed bradykinesia and rigidity on the left hemi soma. Her past medical history included acroparesthesias in childhood, spontaneous miscarriages and thrombophlebitis. Cornea verticillata was detected. Brain MRI showed lacunar infarctions in the basal ganglia and in the periventricular white matter. Her  $\alpha$ -GAL A-activity was reduced and she presented a point mutation in the  $\alpha$ -GAL A-gene; the diagnosis of Fabry disease with cerebrovascular complications was done. She started treatment with L-Dopa. The extrapyramidal symptoms initially had a good response, but then they showed a rapid and progressive course. Since 51 years, she has been suffering for on-off symptoms.

**Discussion** It's difficult to say if the extrapyramidal symptoms are caused by the cerebrovascular complications of Fabry disease or by an idiopathic Parkinson. The clinical history and the response to L-Dopa suggest an idiopathic form; brain MRI positive for infarction in the basal ganglia a secondary form.

**Conclusion** A female carrier of Fabry disease presented cerebrovascular complications and extrapyramidal symptoms. The extrapyramidal symptoms are of uncertain pathogenesis and need further evaluations like brain PET/SPECT, with studying the metabolism and the neurotransmitter of the basal ganglia.

P 1192

**Genotype study of Steinert's myotonic dystrophy in men and women in Bashkortostan (Russia)**

L. Akhmadeyeva<sup>1</sup>, R. Magzhanov<sup>1</sup>, R. Fatkhislamova<sup>2</sup>, E. Khusnutdinova<sup>2</sup>

<sup>1</sup>Bashkirian State Medical University, Ufa, RUSSIAN FEDERATION, <sup>2</sup>Institute of Biochemistry & Genetics, Ufa, RUSSIAN FEDERATION

For the last decade since the mutation associated with Steinert's myotonic dystrophy (DM1) was discovered, scientists are analysing the length of expansion of CTG-repeats at 19q13.1 in patients of both genders. The results vary from study to study. Our **purpose** was to perform genotype study in populations of DM1 patients living in Bashkortostan Republic (Russia) and to compare the data from males and females.

We used standard **methods** for DNA extraction and analyses including PCR and Southern blot.

The mutation was detected in 52 DM1 patients (28 men and 24 women) aged from 5 up to 74 (mean 44.63, standard error of mean -2.12, standard deviation -15.17, median -43.00). In 67% of patients, the size of expansion in different blood cells was different and here we are using the biggest numbers counting in base pairs (bp). The mean length of mutation in our patients was 2503±229 bp and it did not have significant difference in both genders (2388±332 bp in men and 2558±331 bp in women, p=0.71). Both men and women had approximately equal proportion of small (less than 1000 bp), medium (1000–3000 bp) and large (over 3000 bp) expansions (mean -27%, 36% and 37% accordingly) with no statistical difference between the groups.

This study allows us to **conclude** that the size of DM1 mutation in male and female patients in Bashkortostan does not differ significantly. To continue our study we will analyse our population by pairs "affected parent - affected child".

Supported by Russian Foundation for Basic Research.

P 1193

**Clinical epidemiology of aneurysmal subarachnoid haemorrhage at tertiary level hospitals in Latvia**

I. Macane, M. Buks, V. Keris, Z. Kalnina, A. Vetra, N. Jurjane  
*Medical Academy of Latvia, Riga, LATVIA*

**Introduction** Aneurysmal subarachnoid haemorrhage (ASAH) is a devastating event associated with significant morbidity and mortality. The aim of study was to obtain incidence rates, clinical course and case fatality of ASAH for health care services of tertiary level in Latvia.

**Methods** A retrospective population-based study included Latvian residents aged 20 to 79 yrs. Inclusion criteria was ASAH confirmed either by computed tomography or magnetic resonance imaging and cerebral angiography or autopsy. Hunt-

Hess grade at admission and modified Rankin disability scale score, at discharge, have estimated clinical condition of each patient.

**Results** A total of 546 ASAH patients were registered from the beginning of 1996 till the end of 2000. The mean age (±SD) of study population was 51.0±0.8 y. regarding referral territory, 47% was from Riga (the capital of Latvia). The mean annual incidence rates were 6.4 per 100 000 population in Latvia and 10.0 per 100 000 - in Riga. There were not significant differences between age-specific incidence rates in men and women. The mean age-adjusted incidence rate was 5.8 per 100 000 per year. The annual hospital fatality fluctuated from 28% to 42%. The mortality rate was 32% for all hospitalised patients and 15% for operated patients.

**Conclusions** The ASAH incidence rates for Latvia were consistent with other north European region countries. The case fatality at level III hospitals was high without tendency to decrease. The view woman have a higher risk of subarachnoid haemorrhage does not correspond to ASAH in Latvian population.

P 1194

**The analysis of the beginning of multiple sclerosis (MS) in the group of patients in Lublin (Poland)**

A. J. Lobinska<sup>1</sup>, T. Hasiec<sup>2</sup>, Z. Stelmasiak<sup>2</sup>

<sup>1</sup>Neurological Polyclinic, Swidnik, POLAND, <sup>2</sup>Neurological Clinic, Lublin, POLAND

The aim of the study was to analyse the beginnings of MS with patients in Lublin, in 2001. The average age of developing the illness was 30.11 years; 30.34 years for women; 29.88 years for men. The earliest age of the disease development was 5 years (it was a girl); the latest was 52 years (it was a woman too). There was a period of 3.8 years, on the average, between the appearance of the first symptoms and the diagnosis. Most often, the beginning of the illness was monosymptomatic, 155 patients (75.98%). The polysymptomatic beginning was with 37 patients (18.14%). The most common first symptom was sensory impairment. For the relapsing-remitting (RR) and secondary progressive (SP) forms the illness usually started in the spring. The sufferers reported a cold and virus infection of the respiratory tract that most often precede the first symptoms of multiple sclerosis.

P 1195

**Trends in mortality from cerebrovascular disorders in Moldova**

R. Baltag

*Scientific and Practical Centre of Neurology and Neurosurgery, Chisinau, REPUBLIC OF MOLDOVA*

**Objective** Cerebrovascular disorders are viewed as a concerning problem, both medically and socially. This is due to the big burden and high incidence of severe consequences owing to this group of diseases: high fatality coupled with a prolonged disability. The purpose of this paper is to evaluate the level of mortality from stroke in the Republic of Moldova.

**Material and methods** Deaths due to stroke have been defined as those classified with ICD-9 codes 430–436 and ICD-10 I60–I64.

**Outcomes** The mortality rate from stroke in Moldova accounted for 169.56 per 100,000 population in 1999, ranking cerebrovascular conditions I60–I69 second after the "ischemic heart disease I20–I25" with 422.5 cases of deaths per 100,000 inhabitants. There is an insignificant increase in the indicator

figures, and not a soothing one, as compared to 1998 (161.74 per 100,000 people).

**Discussion** Figures show stroke ranking second as the main cause of death countrywide. The mortality rates owing to strokes in the Republic of Moldova is 5 to 6 times higher than those in other European countries, but more alarming is that this indicator displays no trends in slowing down and reversing.

**Conclusions** Stroke ranks second as the main cause of death in adult population of Moldova.

There is a trend in stroke mortality rates up-going over the last several years in the mainstream population of Moldova.

P 1196

**The role that circulatory disorders play in the general mortality rates of population of the Republic of Moldova**

R. Baltag<sup>1</sup>, C. Etco<sup>2</sup>, N. Istrati<sup>1</sup>

<sup>1</sup>Scientific and Practical Centre of Neurology and Neurosurgery, Chisinau, REPUBLIC OF MOLDOVA, <sup>2</sup>Health Management Dept., Chisinau, REPUBLIC OF MOLDOVA

**Introduction** The main cause of death in adult population of the Republic of Moldova, much alike in developed European countries and USA, is due to circulatory system conditions, entailing almost 12m death cases in Europe alone yearly. The given paper aims at assessing levels of mortality owing to circulatory system disorders in the overall mortality.

**Materials and methods** Deaths have been defined as those classified under ICD 10.

**Results** 53% out of 1,093.1 deaths per 100,000 population occurred throughout 1998 were due to circulatory system disorders; whereas in 1999 this share was even higher nationwide – 55% from the overall number of death cases, in absolute figures coming as high as 1,133.7 per 100,000 people. Thus, the mortality due to circulatory system disorders (made up of three components: strokes, ischemic heart disease, and other cardiovascular disorders) accounted for 623.8 per 100,000 people in Moldova in 1999, that is 48.2 per 100,000 people more vs. 1998.

**Discussions** The study carried out proved that the burden of circulatory system disorders in the overall mortality of population is very high.

**Conclusions** Sharing of experience that developed countries gained in decreasing the level of mortality due to circulatory system disorders needs to be implemented to develop national preventive programs.

P 1197

**The natural history of initial subarachnoid haemorrhage (SAH) in unselected patients**

E. V. Barabanova<sup>1</sup>, I. P. Antonov<sup>1</sup>, E. K. Sidorovich<sup>2</sup>, I. M. Pralyhina<sup>1</sup>, O. M. Kondratjeva<sup>3</sup>

<sup>1</sup>Belarussian Research Institute of Neurology, Minsk, BELARUS, <sup>2</sup>Clinical Hospital N 5, Minsk, BELARUS, <sup>3</sup>Belarussian State University, Minsk, BELARUS

A common practice in our country is admission of patients with the initial SAH to a neurological department, where diagnose is made and neurological/neurosurgical observation is performed. A case-series study of SAH was carried out from 1997–2001 in the Neurological Department of our Clinic, which provides health maintenance for more than 400,000 inhabitants.

The database included 137 symptomatic and laboratory and/or computed tomography proved SAH patients (58 men, 79 women). The mean age for men was 52.2±1.4, for women - 57.8±1.4 years old. 54.8% of all patients were in the age inter-

val of 30–60 years (75.3% men, 40.7% women). An age peak for men was from 40 to 50 years, for women – from 60 to 70 years. An average case fatality rate was 21.2% (25.9% in men, 17.7% in women). The age distribution of short-term mortality showed the peak in men of 50–60 and in women of 60–70 years old; 80% of fatal cases were observed in men of 40–60 years old instead of 28.6% in women of the same age. Saccular aneurysms as a cause of SAH were diagnosed by cerebral vessels angiography in 21.9% of patients (24.1% in men, 20.3% in women). A frequency of aneurysmal SAH was significantly higher in younger patients. In 56.2% of the cases, SAH was associated with arterial hypertension.

The results of this study and previous data on population study of SAH showed, that standard risk of initial SAH corresponds to 40–60 year old men and 60–70 year old women.

P 1198

**Disability pension of patients with multiple sclerosis (MS) in Lublin (Poland)**

A. J. Lobinska<sup>1</sup>, Z. Stelmasiak<sup>2</sup>, T. Hasic<sup>2</sup>

<sup>1</sup>Neurological Polyclinic, Swidnik, POLAND, <sup>2</sup>Neurological Clinic, Lublin, POLAND

The aim of our study was to evaluate the problem of disability pension among MS sufferers. 204 patients living in Lublin in 2001 were examined. The average age in the group was 45.5 years. Out of the group of 204 patients, the pension was assigned to 172 people (84.14%), 119 (69.2%) women and 53 (30.8%) men.

The average disability degree according to the Kurtzke's scale – EDSS was 3.5; 3.4 for women, 3.6 for men.

The disease form, its course, EDSS of the patient, his education status, was of no influence to obtaining the pension.

From the first symptoms of the disease to the pension assignment, there was an average period of 5 years. The majority of the disability pensions were assigned in the 90-ties (47.6%), 28.6% in the 80-ties and 23.8% in the 70-ties. If the patient developed the illness in the 60-ties, he obtained the pension after the average 9.5 years. If he fell sick during the 70-ties, the pension was assigned to him after 8 years. If the illness started in the 80-ties he was due to get the pension after 5.4 years, and if it began in the 90-ties, after 3.25 years.

P 1199

**The trends in incidence and survival of primary CNS tumours in the population of Primorje-Gorski Kotar region-Croatia (1977–2000)**

L. Tuskan Mohar<sup>1</sup>, M. Weiner Crnja<sup>1</sup>, I. Antoncic<sup>1</sup>, K. Willheim<sup>1</sup>, A. Jurjevic<sup>1</sup>, E. Materljan<sup>2</sup>

<sup>1</sup>KBC Rijeka, Rijeka, CROATIA, <sup>2</sup>Dom zdravlja, Labin, CROATIA

**Introduction** Descriptive epidemiology of primary CNS tumours has been the subject of several studies, indicating a possible increase in CNS tumour rates. The aim of this study was to evaluate incidence and survival of patients with primary CNS tumours diagnosed between 1977 and 2000 in our Region.

**Methods** Between 1977 and 2000, 911 registered patients with diagnosis of primary CNS tumours were reviewed. The incidence rates by gender, age, tumour location and histological type were calculated for whole and for two times period of investigation (1977–1986 and 1991–2000). Temporal trends were analysed. Survival rates at 1 and 5 years were also estimated.

**Results** Eighty-six percent of the tumours were pathohistologically confirmed and 14% were clinically verified. Total

annual incidence of all CNS primary tumours was 11.5/100 000/year, (10.7 for intracranial and 0.5 for intarsia location). Mean age at diagnosis year was 50.7 the most common tumour types were glioblastoma (26.1%). It was an increasing trend of incidence rate from 9.69/100 000/year (1977–1986) to 12.19/100 000/year (1991–2000). The most increase incidence was noted for meningiomas (from 1.0 to 3.17). The 1-year survival for all tumours was 60.5% (95% CI=57.2–65.8) and the 5 years survival was 52.2% (95% CI=48.7–55.7). Comparing the first and the second time period, significant improvements occurred in survival for all tumours.

**Conclusion** The results of this study confirm the observation made in other countries that the incidence of primary brain tumours is increasing, and the further research into their aetiology and treatment is required.

## P 1200

### **Hereditary thrombophilia in cerebral venous thrombosis in Pécs (Hungary)**

Á. Klabuzai<sup>1</sup>, J. Czopf<sup>1</sup>, I. Gáti<sup>1</sup>, Á. Nagy<sup>2</sup>, B. Melegh<sup>3</sup>, L. Szapáry<sup>1</sup>

<sup>1</sup>Department of Neurology of Pécs University, Pécs, HUNGARY, <sup>2</sup>Department of Haematology, Pécs, HUNGARY, <sup>3</sup>Department of Human Genetics, Pécs, HUNGARY

**Introduction** In the last few years several studies suggested that the most frequent hereditary risk factors for cerebral venous thrombosis (CVT) are the mutations of factor V Leiden (FVL)(11–24%) and prothrombin (PTR)(6–20%) genes. The aim of this study is to compare Hungarian data with the data of those studies.

**Methods** 41 CVT patients have been treated at the Department of Neurology of Pécs University (Hungary) (1995–2001). 37 patients were screened for hereditary thrombophilia (antithrombin III (ATIII), protein C (PRC), S, (PRS) deficiency, FVL, and PTR gene mutation).

**Results** 10 hereditary thrombophilia have been verified in 8 patients (5 FVL heterozygous (HZ), 1 homozygous (HO), 1 PTR gene mutation and 1 ATIII, 2 PRS deficiency have been found). In 2 patients, combined hereditary thrombophilia was found. (ATIII + PRS and FVL HO + PRS)

**Conclusion** While regarding the frequency of FVL (16%) and inhibitor deficiency (8%) the results are in accordance with the results of the relevant previous studies, the occurrence of PRT gene mutation in this study (2.7%) is lower than in other populations.