Academia, 1 3-OH-metilglutaric aciduria, 1 glutaric aciduria type 1, 1 metilglutaric acidemia, 1 trimethylaminuria, 1 proponic acidemia, 2 tyrosinemia and 3 homocystinuria. Ventilatory support needed in 13/20, vasoactive agents 11/20, peritoneal dialysis 8/20, continuous veno-venous haemofiltration 4/20. 8 patients died; among survivors, 2/12 madurative failure, 5/12 serious neurological sequelae, 1/12 liver failure, needing transplantation.

Conclusions Aminoacidopathies diagnosed by Ms/Ms start early with treatment. Wide range of presentation symptoms and findings.

Background and Aims The Suspicion Index (SI) screening tool was developed to identify suspected patients with Niemann-Pick disease type C (NP-C, Neurology, 2012). The SI provides Risk Prediction Score (RPS) based on NP-C symptoms within and across domains (visceral, neurological, and psychiatric). To further examine a) discriminatory power of the SI by age and b) symptom-associations by NP-C suspicion-level and leading symptoms.

Methods The original retrospective data were split into three age groups, where NP-C positive cases were: >16 years (n=30), 4–16 years (n=18), and < 4 years (n=23), and patients’ RPS was analysed by logistic regression. Co-occurrence of symptoms within groups of suspicion-level (low, medium, and high) and leading symptoms (presence/absence of ataxia, cognitive decline, psychosis, and sple-enomegaly) were analysed descriptively.

Results NP-C positive cases vs. controls showed strong discriminatory power of RPS. Area under the Receiver Operating Characteristic curve was 0.964 (>16 years) and 0.981 (4–16 years) but a weaker 0.562 for infants (< 4 years). Patients with RPS < 70 were characterised by a lack of psychiatric symptoms and low levels of neurological involvement, suggestive of a more visceral phenotype. In patients >4 years, prominent leading symptoms’ associations were: ataxia with “dystonia, dysarthria/dysphagia and cognitive decline”; psychosis with “dysarthria/dysphagia”; and psychotic symptoms with “cognitive decline and treatment-resistant psychiatric symptoms”.

Conclusions The SI tool maintains strong discriminatory power in patients >4 years but is not as useful for infants < 4 years. The SI is informative regarding the association and co-occurrence of symptoms in patients with NP-C.

Background The differential diagnosis of respiratory alkalosis (RA) includes a state called central neurogenic hyperventilation (CNH). In the few reported cases of CNH the etiology was a stimulation of the respiratory center by an infiltrative tumor in the cerebral pons. In some cases, a shift in the cerebral pH to acidic range was also hypothesized.

Case Report We report the case of a six year-old boy with a known Pearson syndrome, a mitochondrial disorder affecting bone marrow, pancreas and renal tubules. He was admitted to our PICU with deteriorating mental status and compensated metabolic acidosis (lactic, hyperchoremic and tubular). On admission, blood gas analysis showed a pH of 7.30 with a disproportionately low compensating pCO₂ of 10 mmHg (HCO₃ 4.9 mmol/L). Serum HCO₃ was normalized by substitution (21.0 mmol/L), when he developed a RA (pH 7.51, pCO₂ 24 mmHg) persisting over 48 hours, even during sleeping periods. After reviewing his previous blood gas results, this phenomenon was present for years. After excluding known etiologies of RA, we suspected CNH caused by intra-cerebral acidosis. The pH and HCO₃ were lower, while lactate was higher in cerebro-spinal fluid than in serum. An MR spectroscopy confirmed cerebral lactate accumulation, showing a peak in the posterior cerebrum. Encephalopathy is not among the classic manifestations of Pearson syndrome.

Conclusion We were able to demonstrate elevated local lactate level leading to intra-cerebral acidosis, stimulation of the respiratory center and causing long-standing hyperventilation. This phenomenon adds a new aspect to the complex clinical picture of mitochondrial disorders.

Background Methylene tetrahydrofolate reductase (MTHFR) deficiency is a rare autosomal recessive disorder, caused by mutated alleles of the MTHFR gene. Since this enzyme catalyzes the conversion of 5,10-methylene tetrahydrofolate to 5-methyltetrahydrofolate, its deficiency results in hyperhomocysteinemia, homocystinuria and hypomethionemia. The clinical manifestations vary from asymptomatic to fatal disease with severe neurodevelopmental delay and epileptic encephalopathy.

Case Our patient was a two-month old female born from consanguineous parents presenting with infantile spasms, hypotonia and microcephalus. She was transferred to our pediatric intensive care unit for respiratory failure. The biochemical work-up revealed low vitamin B12 level: 152.6 pg/ml (197–866 pg/ml), close to lower limit of folate: 4.62 ng/ml (3.1–17.5 ng/ml), increased homocysteine level: 9.85 nmol/ml (0–1 nmol/ml), and very low methionine level: 7.32 nmol/ml (19–51 nmol/ml). Magnetic resonance imaging of the brain showed white matter changes of the frontal lobes, posterior legs of capsula interna, pons and nucleus dentatus consistent with demyelination. MTHFR deficiency was suspected, and treatment with folic acid, vitamin B12, methionine and betaine was initiated. The peripheral blood DNA analysis of the patient demonstrated a homozygous mutation of c.1015T>G in MTHFR gene. Both parents were confirmed to be asymptomatic heterozygote carriers. Despite treatment, the prognosis was fatal.

Conclusions As related reports suggest better prognosis with early treatment, pediatricians need to consider MTHFR deficiency in similar cases. Prenatal diagnosis is available and should be encouraged for the future pregnancies.
Background and Aim An international disease registry was started in September 2009 to evaluate the long-term disease course of NP-C in clinical settings.

Methods Descriptive data from enrolment are presented for all patients with available data who were included in the Registry as of 19th August 2011.

Results 121 patients have been enrolled. The median (range) age at enrolment was 16.9 (0.9–56.6) years, age at onset of neurological manifestations was 8.2 (1–48.0) years (n=100), and age at diagnosis was 11.8 (0.1–53.9) years (n=110). A history of neonatal jaundice was recorded in 4/4 evaluable patients with early-infantile (EI) onset of neurological manifestations (at age < 2 years; n=9), 6/21 (29%) with late-infantile (LI) onset (at 2 to < 6 years; n=31), 6/21 (29%) with juvenile (JUV) onset (at 6 to < 15 years; n=15), and 3/20 (15%) with adolescent/adult (AA) onset (at ≥ 15 years; n=29).

Miglustat therapy at enrolment was recorded in 88/121 (73%) patients; mean (SD) exposure 1.69 (1.85) years (n=86). Neurological manifestations included weakness, gait ataxia, ambulation, and/or swallowing.

Conclusions Over two-thirds of this NP-C cohort had infantile or juvenile onset of neurological manifestations; neonatal jaundice was observed more frequently in these patients versus adolescent/ adult-onset patients.

GRACLE SYNDROME IN A TURKISH NEWBORN INFANT CAUSED BY A HOMOZYGOUS MUTATION (P99L) IN COMPLEX III ASSEMBLY FACTOR BCS1L

Background and Aim GRACLE syndrome, a neonatal, autosomal recessive disorder found in Finland, featuring growth retardation, aminoaciduria, cholestasis, iron overload, lactic acidosis and early death, is caused by a homozygous mutation (S78G) in BCS1L, which is the assembly factor for respiratory chain complex III. We investigated a newborn Turkish girl with similar symptoms. Her two sisters with low birth weight, metabolic acidosis, cholestasis, iron overload, lactic acidosis and early death, were caused by a homozygous mutation (S78C) in BCS1L. Hence, we hypothesized that a Turkish newborn with similar symptoms might have a homozygous BCS1L mutation.

Methods and results A Turkish girl born at 37 weeks gestation and weighing 2550 g presented with tachypnea and metabolic acidosis on day one. Lactic acidosis, jaundice with direct hyperbilirubinemia, nonspecific aminoaciduria, high phosphaturia, proteinuria and glucosuria were detected. Serum iron (190 mcg/dl), ferritin (2819 ng/ml) and transferrin saturation (99.4%) were increased. Metabolic, cardiological and sonographic workup were otherwise normal. Because of similarities with GRACLE syndrome, the BCS1L gene was sequenced, revealing a homozygous mutation in the protein.

Conclusions The mutation identified in this Turkish newborn caused a similar clinical presentation, with a homozygous BCS1L mutation. This supports the hypothesis that GRACLE syndrome is a genetically heterogeneous disorder.