Semmelweis Gyermekklinika

Klinikai PhD napok

2026. március 19–20.

Minden kutatás mögött egy beteg gyermek áll.
Mutasd meg te is, min dolgozol!

Xue Andrea

A rapid liquid chromatography – tandem mass spectrometry method for the assessment of bile acid profile in human sera

In the first part of the research, we aimed to evaluate cystic fibrosis screening in Hungary and fine-tune the CF NBS process according to the experiences gained in the first years. In patients with cystic fibrosis, excessively thick mucus forms a plug at the outlet of the bile ducts, obstructing bile flow into the intestine. Therefore, bile flows back into the bloodstream and aggregates in the liver, which is toxic to the organ.

Our present research aims to investigate bile acid levels in newborn and older cystic fibrosis patients. As first step we developed a liquid chromatography – tandem mass spectrometry (LC-MS/MS) method to measure bile acids from serum samples. In order to optimise the method, we set up the analytical (column flow rate, gradient elution) and mass spectrometric (temperature, IS voltage, gas pressures, ion mode, MS/MS transitions) parameters and measured single analytically pure bile acids. As second step, we optimised the sample preparation method to purify the sample and gain bile acid free matrices to quantify patients' bile acid level, furthermore enrich the bile acid concentration in the sera. For internal quantification, we used isotope-labelled bile acids (CA and CDCA), and validation according to CLSI relative to LC-MS is in progress.

The developed method will be applied to assess the variation of different bile acids in cystic fibrosis patients.

Bokrossy Péter

Extracelluláris Vezikulák Koronaképződésének Vizsgálata Jelölésmentes Optikai Hullámvezető Fénymódus Spektroszkópiás Módszerrel

Bevezetés
Az extracelluláris vezikulák (EV-k) lipid kettősréteggel határolt nanorészecskék, amelyeket szinte minden sejttípus termel. Képződésük és felszabadulásuk során biomolekulákból – például fehérjékből álló réteg képződik a felszínükön, amelyeket EV koronának nevezünk. Jelen tanulmányban egy új módszert dolgoztunk ki az EV-k immobilizálására és a fehérjekorona képződésének vizsgálatára humán szérumalbumint (HSA) használva modellfehérjeként.

Módszerek
Az EV–HSA kötődést optikai hullámvezető fénymódus-spektroszkópián (OWLS) alapuló áramlásos injektálásos analizátorral vizsgáltuk. A méréseket tris pufferben (42 mM, pH 7,4), különböző áramlási sebességek és hőmérsékletek mellett végeztük. Az EV-k immobilizálását és a felület passziválását különböző molekulatömegű, pH-jú és koncentrációjú poli-L-lizin (PLL) alkalmazásával optimalizáltuk. Az optimális fehérjekoncentráció-tartományt a beállított felületi feltételek mellett, különböző HSA-koncentrációk használatával határoztuk meg. Matematikai modellezéssel becsültük az EV-k maximális HSA-kötő kapacitását, majd ezt kísérletileg ellenőriztük.

Eredmények
Az optimális mérési körülmények meghatározását követően a matematikai modell ellenőrzésére validációs méréseket végeztünk. Az eredmények összhangban voltak az elméleti maximális HSA-mennyiséggel, ezáltal megerősítve az OWLS módszer pontosságát.

Támogatás
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Zrufkó Réka

The role of PARK7 in sepsis-induced acute kidney injury

Aims
Sepsis-induced acute kidney injury (AKI) is a condition associated with significant morbidity and mortality, for which there is no effective therapy. A central elements of its pathomechanism are oxidative stress and inflammation. The antioxidant and anti-inflammatory role of the Parkinson's disease 7 (PARK7) molecule is known, but it has not been investigated as a potential therapeutic target in sepsis-induced AKI. Therefore, our aim was to explore the role of PARK7 in the pathomechanism of the disease.

Methods
We investigated the effect of the compound Comp23, which activates the protective functions of PARK7, on apoptosis induced by bacterial lipopolysaccharide (LPS) and H2O2 in HEK293 kidney epithelial cells. We also examined the effect of Comp23 on oxidative stress induced by LPS and H2O2 and its molecular markers in HEK293 cells. We explored the anti-inflammatory effect of the compound Comp23 on LPS and H2O2 activated immune cells. We investigated the effect of PARK7 activation on inflammation, oxidative stress, and kidney function damage (creatinine, BUN) during LPS-induced acute kidney injury in vivo.

Results
We demonstrated that PARK7 activation with Comp23 reduces LPS and H2O2-induced cell death and oxidative stress in HEK293 cells. Our results showed that Comp23 activation decreases the production of inflammatory cytokines induced by LPS and H2O2 in immune cells. We also showed that the Comp23 decreased inflammation and oxidative stress in the kidneys during LPS-induced sepsis. Additionally, treatment with Comp23 reduced serum creatinine and BUN levels in LPS-treated animals.

Conclusion
Our studies have pointed out that the PARK7 molecule is a potential therapeutic target in sepsis-induced acute kidney injury (AKI) through the activation of antioxidant and anti-inflammatory mechanisms.

Kelemen Hanga

Sex-dependent long-term behavioural and microglial consequences of perinatal neuroinflammation in mice

Hypoxic–ischaemic encephalopathy (HIE) following perinatal asphyxia (PA) is a major contributor to later neurodevelopmental disorders. Outcomes can be substantially worse when PA occurs in the context of systemic inflammation that may already be present in utero, yet the neurobiological mechanisms driving this “double-hit” interaction remain poorly defined, limiting the development of targeted therapies. Shared inflammatory signalling pathways involving microglia are a plausible point of convergence and may induce long-lasting changes in higher-order brain networks. Here, we examined the long-term, region-specific effects of PA alone and in combination with pre-existing systemic inflammation on adult behaviour and microglial alterations, with an emphasis on sex differences. Mice received subcutaneous IL-1β injections on postnatal days 2-6, and a subset was exposed to a PA insult on postnatal day 7 by inhalation of a hypoxic-hypercapnic gas mixture (4% O_2, 10% CO_2). In adulthood, animals underwent a comprehensive behavioural battery assessing cognitive and affective domains. Brains were then processed for Iba1 immunohistochemistry to label microglia. Atlas-registered histological sections were used to quantify microglia across nearly 500 brain regions, and morphology was analysed in regions identified as most relevant to the behavioural phenotype to probe persistent functional shifts. Across both sexes, all treatment groups showed behavioural disruptions, with the strongest and most consistent effects in the IL-1β + PA double-hit condition. Males exhibited spatial learning deficits and increased impulsivity, whereas anxiety-like behaviour was elevated in both sexes. In brain regions implicated in these behavioural changes, microglial density was significantly increased, including in the mediodorsal thalamus, nucleus reuniens, and amygdalar nuclei. These alterations were accompanied by robust, long-lasting microglial morphological changes in the analysed amygdala subregion. Overall, early-life systemic inflammation induced by IL-1β heightened vulnerability to PA and worsened long-term outcomes in a sex-dependent manner. The findings further indicate sustained microglial dysregulation in behaviourally relevant circuits, supporting microglia-linked inflammatory pathways as a key substrate of the synergism between PA and systemic inflammation.
Buzogány Zsuzsanna Fluvoxamine-mediated Sigma-1 receptor activation suppresses TGF-β1,2 and PDGF-induced corneal fibroblast activation and extracellular matrix remodeling “Introduction: Corneal fibrosis, a major cause of vision impairment and blindness in diabetes and external injuries, is driven by TGF-β and PDGF-mediated myofibroblast activation. We previously showed that the Sigma-1 receptor (S1R) agonist fluvoxamine (FLU) reduces fibrotic damage in the trabecular meshwork. S1R’s pharmacological activation represents a promising, yet unexplored therapeutic strategy to mitigate the fibrotic cascade in the corneal stroma.

Aims
To elucidate the effects of FLU on TGF-β and PDGF-driven fibroblast activation, focusing on proliferation, extracellular matrix (ECM) remodeling, and the expression profile of key fibrotic markers at both mRNA and protein levels.

Methods
Primary human corneal fibroblasts were isolated enzymatically and cultured in DMEM:F12 with 10% FBS. Cells were treated with TGF-β1,2 or PDGF ± FLU (10 µM) for 48–72 h. Viability and proliferation were assessed by MTT/LDH; β-SMA, F-actin, Ki67, and Fibronectin by immunocytochemistry; and Col1A1, FN, CTGF, MMP9, and S1R by qPCR or Western blot.

Results
FLU and PDGF were non-toxic within the tested concentration ranges. FLU increased S1R expression and reduced β-SMA, Fibronectin, MMP9, Col1A1, and CTGF levels, indicating suppression of fibroblast activation and ECM remodeling.

Conclusion
FLU attenuates TGF-β1,2 and PDGF-driven fibroblast activation and promotes S1R expression, supporting its potential as a novel anti-fibrotic candidate in corneal wound healing.

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Pomlényi Petra

Sedation, Circadian Disruption, and Propofol Practice in the PICU: Preliminary Findings

Introduction
Sedation in the Pediatric Intensive Care Unit (PICU) is a complex but essential element of intensive therapy, with significant impact on short- and long-term outcomes. Pediatric sedation strategies differ from adult practice, particularly regarding propofol use. Appropriate sedative selection is crucial for therapeutic success; however, sedation is associated with important adverse effects, including delirium, tolerance, dependence, and withdrawal, which may increase morbidity and mortality. In addition, sedation contributes to circadian rhythm disruption during critical illness, potentially further worsening patient outcomes.

Methods
Our research investigates pediatric sedation from two complementary perspectives. In a prospective cohort study, we evaluate the effects of different sedative agents on circadian rhythmicity in mechanically ventilated children. Circadian disruption is assessed using actigraphy and urinary melatonin measurements, comparing sedated, ventilated patients with controls. In a retrospective observational study, we analyze the use of continuous propofol infusion in areas where current recommendations remain unclear. Patients receiving continuous plus bolus propofol are compared with those treated with bolus-only administration, using multivariable regression models to assess variables related to potential adverse effects.

Results
Preliminary results show that mechanically ventilated patients had significantly lower daytime activity values than controls (OR = 0.33; 95% CI [0.14–0.76]; p < 0.01), adjusted for age, PRISM mortality score, and PICU days before actigraphy. Among 70 patients receiving continuous propofol infusion, dosing exceeded guideline recommendations in 36 cases (51.43%), and infusion duration surpassed recommended limits in 13 cases (18.57%).

Conclusion
These findings suggest that sedation negatively affects circadian rhythmicity and highlight the need to optimize pediatric sedation strategies. Continuous propofol use warrants further investigation to support clearer and safer clinical recommendations.

Csekő Anna

Therapeutic hypothermia and its association with mortality in 30- to 35-week gestation preterm infants after a severe hypoxic-ischemic event: A patient registry study

Introduction
Therapeutic hypothermia (TH) reduces the risk of death, brain injury and neurodevelopmental impairment in infants >35 weeks' gestation. Only limited data are available in preterm infants <36 weeks' gestation. Here we report the short-term outcomes of <36 weeks' gestation asphyxiated preterm infants who received TH.

Methodology
In this retrospective study, we reviewed the Hungarian Perinatal Registry for preterm infants born between 2005-2023 with a gestational age between 30- to 35-weeks. Subjects were selected based on having concurrent 5-minute Apgar score ≤7, base deficit (BD) ≥14 mmol/L and a serum lactate level of ≥7.0 mmol/L. Provision of TH was determined by the attending neonatologist.

Results
336 patients met inclusion criteria and 70 underwent TH. The hypoxic-ischemic insult was more severe in the TH-treated group [5-minute Apgar score 3 (0;5) vs.5 (3;7) and BD 21(18;25) vs. 19 (17;23) mmol/L], and these infants were born more mature [34 (33;35) vs. 33 (31;34) weeks]. TH-treated infants were ventilated longer [5 (4;7) vs. 2 (1;7) days], received fresh-frozen plasma (FFP) (52% vs. 31%), hydrocortisone (49% vs. 17%) and vasopressor/inotropic support (83% vs. 66%) more frequently. Occurrence of mortality and severe intraventricular haemorrhage (IVH) were similar between the groups.

Conclusion
TH-treated preterm infants suffered from more severe hypoxic-ischemic insults, received more FFP and cardiovascular support during care, yet mortality and the incidence of severe IVH were similar. Prospective studies are required to better determine the potential short and long-term risks and benefits of TH in 30- to 35-week's gestation preterm infants with perinatal asphyxia.

Tarjányi Eszter

Early Enteral Feeding in Neonates with Hypoxic–Ischemic Encephalopathy Undergoing Therapeutic Hypothermia

Introduction
Therapeutic hypothermia (TH) is the standard neuroprotective treatment for neonates with hypoxic–ischemic encephalopathy (HIE). Enteral feeding has traditionally been withheld during TH due to concerns about necrotizing enterocolitis (NEC). However, early human milk feeding may provide immunological and trophic benefits, potentially facilitating feeding progression and improving long-term neurodevelopmental outcomes.

Objective
To evaluate the feasibility and safety of starting enteral feeding with the mother's own milk during TH. Secondary outcomes included the time to reach full enteral feeding and the rate of human milk feeding at discharge.

Methods
In this single-centre retrospective study, neonates treated with TH for HIE from 2019 to 2023 were analysed. Between 2019 and 2021, enteral feeding was withheld during cooling (control group), while in 2022 and 2023, feeding with mother's own milk was started within the first 72 hours. Statistical analyses included the Mann–Whitney U test and Fisher's exact test.

Results
A total of 198 neonates were included. Demographic and clinical characteristics did not differ significantly between the groups. NEC occurred in two infants (1.8%) in the control group and none in the early feeding group (p = 0.5). Early feeding was associated with earlier initiation of enteral nutrition (median 87 vs. 66 hours, p < 0.001) and a shorter time to full enteral feeding (median day 9 vs. 8, p < 0.002). The proportion of infants receiving human milk at discharge increased significantly (44% vs. 62%, p < 0.02).

Conclusion
Early enteral feeding with mother's own milk during TH in neonates with HIE is feasible and safe. It reduces the time to full enteral feeding and increases human milk feeding at discharge, with possible long-term developmental benefits.

Pál Vanda

Neuro-Cool Project – Neurointensive monitoring in neonates with hypoxic ischaemic encephalopathy undergoing therapeutic hypothermia

Background
Moderate-severe hypoxic ischaemic encephalopathy (HIE) is a devastating condition that may cause neurodevelopmental injury in up to 50% of the cases. In recent years, research efforts to ameliorate outcome has shifted from population-level interventions to individualized treatment options. This necessitates continuous brain monitoring to implement physiology-guided neonatal neurocritical care.

Aims
To set up a multimodal neurointensive monitoring system for patients with HIE and to describe the relationship between dynamically changing physiological parameters related to brain function.

Methods
A multimodal monitoring system was assembled for research purposes. The Philips MP40 patient monitor (Philips, Amsterdam, Netherlands) was connected to a Moberg electroencephalography based system (Natus Medical, Middleton, WI, USA), that integrated time-synchronized data collected from multiple sources. A microstream capnograph and the INVOS 5100C (Medtronic, Dublin, Ireland) for near-infrared spectroscopy were also connected. Here we report the first experience with the system in neonates with moderate-severe HIE.

Results
Between August 2025 and January 2026, we have recorded 10 patients during hypothermia with the multimodal monitoring system. Several technical difficulties have been identified and solved including monitor programming, implementation of mainstream then sidestream capnography, and cooling device intergation for temperature measurement. Of the 10 patients, complete timeseries data was registered from 3 patients. In one case we noted a strong temporal relationship between regional cerebral oxygen saturation values and end-tidal CO2 trends that will be presented as a case report.

Conclusion
Multimodal neurointensive monitoring is feasible in patients with HIE and may provide insights into brain physiology and cerebral autoregulation.

Kerekes Ramona

Volumetric Absorptive Microsampling: A Novel Technique for Neonatal Blood Sample Collection for Steroid Measurement

Background
Hydrocortisone (HC) is widely used as rescue therapy in infants with hypoxic-ischemic encephalopathy (HIE) and vasopressor-resistant hypotension. Relative adrenal insufficiency (serum cortisol <15 µg/dL) is often considered an underlying cause; however, little is known about endogenous cortisol levels in this population, and the relationship between HC administration and long-term neurological outcomes remains unclear.

Methods
We conducted a retrospective cohort study of 104 infants with moderate-to-severe HIE treated with therapeutic hypothermia between 2016 and 2021. All patients had early serum cortisol measurements. Hydrocortisone use was determined at the discretion of the attending physicians. Brain injury was assessed using the Weeke MRI scoring system1, and multi-organ injury was evaluated with the MODE score2. Neurodevelopmental outcomes were assessed at 2 years of age using the Bayley Scales of Infant Development, 2nd Edition (BSID-II). Adverse neurodevelopmental outcome was defined as a score <70 on either the Mental Development Index (MDI) or the Psychomotor Development Index (PDI), or death.

Results
Median [interquartile range] serum cortisol level was 7.7 [2.7; 31.9] µg/dL, measured at 11 [6; 21] hours of life. Of the total cohort, 42 (40%) infants had an adverse outcome, including 11 (10%) deaths, and 62 (60%) had a favorable outcome. Infants with adverse outcomes had higher median initial cortisol levels compared with those with favorable outcomes (15.6 vs. 4.1 µg/dL, p=0.06), and higher MODE (10 vs. 8, p<0.001) and Weeke scores (15 vs. 2, p<0.001), reflecting more severe multi-organ and brain injury. Hydrocortisone was administered to 71 infants (68%) for hemodynamic instability. Baseline cortisol levels were higher in infants who received HC compared to those who did not (12.3 vs. 3.2 µg/dL, p=0.03). Importantly, among adverse and favourable outcome groups, the rate of HC use was similar [28/42 (67%) vs. 43/62 (69%), p=0.83]. In addition, no serum cortisol threshold could be identified above which HC administration negatively influenced neurodevelopmental outcomes. Finally, in multivariable regression adjusted for socioeconomic and clinical factors, only the Weeke MRI score remained an independent predictor of outcome, while initial cortisol levels and HC use were not associated with neurodevelopmental results.

Conclusion
In this retrospective cohort, we found no evidence that HC administration influences long-term neurodevelopmental outcomes in infants with moderate-to-severe HIE. The commonly used definition of relative adrenal insufficiency may not be clinically meaningful in this patient population. HC may be used for acute hemodynamic stabilization without regard to initial cortisol levels, though prospective studies are warranted to confirm these findings.

Bogner Luca

NeoTracker, the digital event log for delivery room neonatal care

Introduction
Delivery room care of a newborn has crucial impact on short- and long-term outcome. International recommendations include critical and time-sensitive interventions based on the assessment of physiological parameters and monitoring data. Since real-time, structured, unbiased data are much needed for successful decision support and quality improvement, we have developed a digital delivery room event log called “NeoTracker”.

Objective
Our aim is to design a proof of concept study in order to validate the feasibility and the punctuality of data registration in the “NeoTracker” application.

Method
In this proof of concept study, the current gold standard documentation method—retrospective data entry performed hours after delivery based on the neonatologist’s recollection—will be compared with real-time data recording using NeoTracker. Parallel documentation will be conducted in 50 cases. Three predefined time slots will be included: 08:00–16:00, 17:00–23:00 and 24:00–07:00, with an equal number of cases recorded in each period. We will assess (1) the time interval between patient care and documentation in the retrospective method, and (2) the proportion of missing predefined data points. These outcomes will be compared with the completeness and timeliness of NeoTracker recordings.

Results
Fifty parallel documentations will be analyzed. Primary outcomes include documentation delay and frequency of missing data in the retrospective method, compared with real-time NeoTracker recordings.

Conclusions
This proof of concept study represents a key step towards clinical implementation of NeoTracker. By providing objective data on current documentation delays and data gaps, the study may support staff acceptance and demonstrate the added value of structured real-time documentation in the delivery room. Ultimately, improved data accuracy and completeness may enhance quality improvement initiatives and decision support in neonatal care.

Muzslay Eszter

Overweight worsens the metabolic presentation of type 1 diabetes mellitus in children

Introduction
The prevalence of both obesity and type 1 diabetes mellitus (T1DM) has increased globally over the last decades. Overweight and obesity affect individuals with T1DM and influence not only the autoimmune pathogenesis but also the long-term complications of T1DM. This study aimed to investigate the effect of excess body weight on the clinical presentation of T1DM.

Methods
We conducted a retrospective, single-center cohort study. Data were collected from children diagnosed with T1DM between 2014 and 2023. A total of 994 patients' presentation parameters and anthropometric data were analyzed. Based on BMI Z-scores, patients were categorized into three groups (normal-weight, overweight, and obese). Metabolic parameters at diagnosis were compared between groups.

Results
The combined ten-year prevalence of overweight and obesity was found to be 15.9%. Significant between-group differences were observed in pH (p=0.005), HCO3- (p=0.018), pCO2 pressure (p=0.018), and C-peptide levels (p< 0.001). Lower pH, pCO2 and HCO3- levels were found among those who were overweight, and higher C-peptide levels in children with obesity. Diabetic ketoacidosis (DKA) and severe DKA were seen at a significantly higher rate among children with overweight and obesity (p=0.013; p< 0.001).

Discussion
Children with overweight presented with more severe metabolic derangement at T1DM onset. Overweight children have a higher risk of having DKA at presentation despite elevated C-peptide levels, which suggest a greater residual β-cell function. These findings support the hypothesis that other factors may contribute to T1DM manifestation and the impact of overweight and obesity on the presentation of T1DM.

Kovács Janka

Life-changing Treatments in Central Nervous System Diseases- Ventriculoperitoneal-shunt and Targeted Therapies

Background
Modern pediatric care increasingly relies on precision-based strategies aiming not only to improve survival but also to reduce treatment-related complications. This thesis investigates two complementary aspects of precision medicine: prevention of device-related infections in pediatric neurosurgery and pharmacokinetically guided individualization of targeted therapy in pediatric oncology.

Methods
The first study was a systematic review and meta-analysis evaluating the effectiveness of antibiotic-impregnated ventriculoperitoneal shunt catheters compared with standard catheters. Electronic databases were searched up to July 2023, and randomized and observational studies reporting infection outcomes were included.

The second study was a prospective observational pilot study analysing the pharmacokinetics of selumetinib in paediatric patients with neurofibromatosis type 1. Serial blood samples were collected at steady state, plasma concentrations were measured using LC-MS/MS, and exposure–toxicity relationships were evaluated.

Results
The meta-analysis included 27 studies comprising more than 27,000 shunt procedures. Antibiotic-impregnated shunts significantly reduced infection risk compared with standard catheters (OR ≈ 0.42; 95% CI 0.30–0.58), with the greatest benefit observed in paediatric and infant populations. Evidence quality was moderate, and several studies suggested reduced healthcare costs due to fewer revisions.

In the pharmacokinetic study, 22 paediatric NF1 patients were analysed. Substantial interindividual variability in selumetinib exposure was observed despite body-surface-area–based dosing. Higher drug exposure was associated with increased toxicity, particularly dermatologic and muscular adverse effects. Therapeutic drug monitoring proved feasible in clinical practice, and a preliminary therapeutic AUC range was identified to support individualized dosing.

Conclusions
The results demonstrate that precision medicine in pediatric care must address both prevention of avoidable complications and optimization of drug exposure. Antibiotic-impregnated shunts represent an effective strategy to reduce infection risk, while therapeutic drug monitoring may enable safer and more effective use of targeted therapies. Integrating evidence-based prevention with pharmacokinetic individualization may improve outcomes and support a more patient-centred approach in pediatric neurosurgery and oncology.

Höbőr Bence

Retrospective Survival Analysis of Paediatric Patients with First Relapse of Acute Lymphoblastic Leukaemia in the ALL-IC REL Study Group

Introduction
Approximately 15% of paediatric patients with acute lymphoblastic leukaemia (ALL) relapse during or after frontline therapy. The long-term overall survival (OS) rate in primary ALL drops from over 90% to approximately 30% to 50% in the relapse settings. The ALL-IC REL Protocol is a best practice treatment guidance for high-middle income countries to harmonise management of first relapse across the ALL-IC network and improve survival outcomes.

Materials and Methods
Data were collected in a pseudonymus online register (REDCap). Patients aged ≤18 years who experienced a first relapse between November 2017 and December 2021 were included in this retrospective analysis. Statistical analyses were performed using IBM SPSS Statistics. Event-free survival (EFS) and overall survival (OS) were estimated using the Kaplan–Meier method. The log-rank test was used to compare different groups.

Results
Among 370 patients (mean age 9 years; 33.2% female) diagnosed with first relapse between 2017 and 2021, 90.5% had received ALL-IC-Berlin-Frankfurt-Münster (BFM) 2009 treatment initially. Upon relapse, 46.8% were classified as SR and 53.2% as HR. Complete remission rates post-induction were 84% (SR) and 56% (HR). MRD < 0.1% was achieved by 53% (SR) and 29% (HR). Five-year

overall survival was 50.5% (74% SR, 32% HR). HR outcomes were adversely affected by disease progression, treatment toxicity, and posttransplant complications.

Conclusion
Our analysis demonstrates promising SR outcomes, comparable to findings from the International Study for the Treatment of Childhood Relapsed ALL (IntReALL). However, outcomes remain poor in HR patients treated with standard chemotherapy. Novel therapeutic strategies are urgently needed in upcoming ALL-IC-BFM REL protocols.

Pfeffer Anita

Efficacy and Safety of Growth Hormone Therapy for Pediatric Brain Tumor Survivors Based on Real-World Data

Background
Among survivors of childhood brain tumors, the prevalence of endocrine complications approaches 40%, with growth hormone deficiency (GHD) representing the most common disorder. Early initiation of growth hormone therapy (GHT) is particularly important to prevent impaired linear growth and metabolic abnormalities associated with GHD. However, in clinical practice, initiation of therapy is often delayed due to concerns raised by in vitro studies suggesting that GHT may increase the risk of tumor recurrence and secondary malignancies.

Aim
The primary objective of this study was to assess the impact of growth hormone replacement initiated at different time points following completion of oncological treatment on growth outcomes and safety.

Methods
We conducted a retrospective analysis of 235 patients diagnosed with brain tumors between 2013 and 2023 at the Neurooncology Department, Semmelweis University. Growth outcomes were evaluated using height standard deviation scores (SDS). To assess safety, recurrence-free survival was analyzed. Hazard ratios were estimated using Cox proportional hazards regression modeling. Statistical significance was defined as a p-value <0.05 with 95% confidence intervals.

Results
GHD was identified in 25 patients, of whom 20 received GHT at a mean of 37 months following the completion of oncological treatment. Among untreated GHD patients, the mean height SDS at the end of oncological therapy was −2.58, declining further to −3.62 by the third year of follow-up. In contrast, patients receiving GHT demonstrated an annual improvement in height SDS of 0.27. Tumor recurrence was documented in 32 patients, including 2 cases occuring after the initiation of GHT. No secondary malignancies were observed within the cohort.

Conclusion
Our findings support the early initiation of GHT to ensure optimal growth in pediatric brain tumor survivors. GHT was not associated with an increased risk of tumor recurrence or secondary malignancy, indicating a favorable safety profile in this population. Despite this, initiation of therapy in routine clinical practice frequently remains delayed compared with current guideline recommendations, resulting in clinically significant progression of growth failure.

Szilágyi Ádám

Efficacy and Safety Comparison of CAR T-cell Therapy vs Standard Care in Hematological Malignancies

Chimeric antigen receptor (CAR) T-cell therapy has been compared with conventional non-CAR T treatments in hematological malignancies, but the magnitude and robustness of benefit across diseases and comparators remain unclear. We performed a systematic review and meta-analysis of comparative studies in non-Hodgkin lymphoma (NHL), acute lymphoblastic leukemia (ALL), and multiple myeloma (MM).

Randomized and comparative observational studies evaluating CAR T-cell therapy versus non-CAR T comparators were included. Outcomes were analyzed by disease type. Treatment effects were summarized using odds ratios (ORs) for response and hazard ratios (HRs) for survival with random-effects models.

In NHL, mainly large B-cell lymphoma (LBCL), CAR T-cell therapy improved complete response and overall survival versus standard chemo-immunotherapy (OR=2.48, 95% CI=1.35-4.57; HR=0.61, 95% CI=0.48-0.78). Progression-free survival was prolonged in second-line LBCL, whereas no consistent advantage was observed over targeted therapies or transplantation. In follicular lymphoma, CAR T-cell therapy extended progression-free survival, while overall survival differences varied by comparator. In MM, CAR T-cell therapy reduced progression risk versus standard or targeted therapies (HR=0.30, 95% CI=0.11-0.77), without a significant overall survival difference. In ALL, CAR T-cell therapy improved overall survival versus chemotherapy or donor lymphocyte infusion (HR=0.30, 95% CI=0.25-0.36) and was associated with fewer grade III–IV graft-versus-host disease events after transplantation (OR=0.25, 95% CI 0.06-0.98).

CAR T-cell therapy confers disease- and comparator-specific efficacy advantages without clear evidence of increased toxicity, with the most consistent benefits seen in LBCL, MM, and ALL.

Szabó Patrik

Associations Between Gut Microbiome Composition and the Development of Therapy-Induced Neutropenic Fever

Background
Neutropenia-related infections remain important causes of morbidity and mortality in children with solid tumors.

Methods
By analyzing fecal samples collected at diagnosis and after each of the initial phases of chemotherapy, we evaluated the role of gut microbiota in predicting infections in children with newly diagnosed solid malignancies. The bacterial 16S rRNA gene was analyzed by high-depth sequencing to determine the diversity and composition of the microbiome.

Results
After the induction of chemotherapy, microbial diversity decreased significantly relative to the prechemotherapy value. After chemotherapy, the relative abundance of certain bacterial taxa (eg, Bacteroidetes) decreased significantly, whereas that of other taxa (eg, Clostridiaceae and

Streptococcaceae) increased. A baseline gut microbiome characterized by Proteobacteria predicted febrile neutropenia. Adjusting for the chemotherapy phase and cancer risk level, Enterococcaceae dominance (relative abundance ≥30%) predicted significantly greater risk of subsequent febrile neutropenia and diarrheal illness, whereas Streptococcaceae dominance predicted significantly greater risk of subsequent diarrheal illness.

Conclusions
In children undergoing therapy for newly diagnosed solid tumors, the relative abundance of Proteobacteria before chemotherapy initiation predicts the development of febrile neutropenia, and domination of the gut microbiota by Enterococcaceae or Streptococcaceae at any time during chemotherapy predicts infection in subsequent phases of chemotherapy.

Horváth Fanni

Screening for Associated Autoimmune Diseases in Pediatric Celiac Disease

Introduction
The association between celiac disease and autoimmune disorders, particularly type 1 diabetes mellitus (T1DM) and autoimmune thyroid disease (AITD), is well established; however, screening strategies remain inconsistent. Early detection may prevent severe complications.

Objectives
To assess the prevalence of associated autoimmune diseases in asymptomatic children with celiac disease and in a control group.

Methods
We analyzed laboratory data of asymptomatic patients under 20 years of age with biopsy-proven celiac disease and no other autoimmune disorders, evaluated since March 2024 at the Bókay Street Department, Pediatric Centre, Semmelweis University. T1DM screening included GAD, IAA, IA-2, and ZnT8 autoantibodies; thyroid autoimmunity was assessed by anti-TPO and anti-TG antibodies. A non-autoimmune control group was also screened. The study is ongoing.

Results
Among 218 children with celiac disease (59.6% female; mean age 12.1 years), diabetes-related autoantibodies were detected in 14 (6.4%), with ≥2 antibodies in 4 cases. Thyroid autoantibodies were found in 26 patients (11.9%). Female sex was a significant risk factor for thyroid autoimmunity (OR=0.0483; 95% CI: 0.0046–0.2695; p=0.0001). Longer disease duration (β=0.0118; p=0.0153) and older age (β=0.0147; p=0.0026) increased the risk. In the control group (n=187), 22 (11.8%) were positive for diabetes-related and 7 (3.7%) for thyroid autoantibodies.

Conclusions
Screening for associated autoimmune diseases is justified not only in children with celiac disease but may also be considered in a broader population. Early identification may prevent complications such as diabetic ketoacidosis and improve long-term outcomes.

Papik Flóra

Virtual reality-based preparation of children undergoing MRI examination

Magnetic resonance imaging (MRI) can be a stressful and fear-inducing experience for children, often requiring general anaesthesia to ensure image quality. Prior research suggests that appropriate preparation may reduce stress and the need for anaesthesia. Virtual reality (VR), offering a 360-degree immersive experience, may represent a promising preparatory tool.

The aim of this study is to investigate the effects of a self-developed VR-based preparation tool on anaesthesia use and psychological outcomes in children.

We conduct a randomized controlled trial, where children aged 4–18 years scheduled for MRI under general anaesthesia are assigned to one of three groups. In the VR group, participants explore a virtual MRI environment, then take part in an acceptance and commitment therapy-based experience. In the booklet group, children receive an illustrated educational brochure. The control group receive standard care. Nervousness, fear, mood, and familiarity is assessed using visual analogue scales at three time points: before the intervention, after the intervention, and post-MRI. Data are analysed using regression models and two-way repeated measures ANOVA.

Preliminary analyses of data from 199 children showed higher proportion of children in the booklet group requested anaesthesia compared to VR or control group. Children receiving preparation via VR or booklet reported higher fear levels than the control group prior to MRI. However, VR-based preparation was associated with a significant reduction in nervousness.

In conclusion, VR-based preparation appears to be a useful tool for reducing anxiety in children undergoing MRI. We plan to investigate this effect further in children undergoing MRI without anaesthesia and identify subgroups for whom this intervention is most beneficial.

Antics Dorottya

Should we screen children with obesity for nocturnal hypoventilation?

Background
Sleep-disordered breathing (SDB) is an increasingly recognized co-morbidity in childhood obesity but is still often overlooked as it can appear insidiously. SDB can lead to a decline in school performance and quality of life. Most pediatric studies exclusively focus on obstructive sleep apnea. The prevalence of nocturnal hypoventilation and obesity hypoventilation syndrome (OHS) in children is unknown.

Aims and objectives
To determine whether transcutaneous carbon dioxide monitoring (tcCO2) as a part of the polysomnographic assessment (PSG) is beneficial for children with obesity if SDB-related symptoms are present.

Methods
Retrospective study: the clinical, PSG, and tCO2 data of symptomatic children with overweight and obesity (BMI Z-score ≥1; 5-18 yrs) were collected between 2021 and 2024. PSG recordings, including tcCO2 monitoring, were analyzed according to the American Association of Sleep Medicine guideline. The frequency of nocturnal hypoventilation and OHS and the introduction of non-invasive ventilation (NIV) were established.

Results
Out of 41 children, 23 met the criteria for nocturnal hypoventilation. In four patients, nocturnal hypoventilation was present without an increase in the obstructive apnea-hypopnea index (oAHI). Seventeen children were diagnosed with OHS, and NIV was initiated in 18 children.

Conclusions
Polysomnography with continuous monitoring of the CO2 level is of key importance in this population, especially if SDB-related symptoms are present, to provide diagnosis and early NIV if needed. Hypoventilation can be present without increased oAHI, highlighting the need for tcCO2 monitoring as part of the routine PSG.

Petes Cintia

Mitigating Cardiovascular Risk of Children with Chronic Conditions

Background
Children living with chronic conditions face a substantially increased risk of premature cardiovascular disease due to accelerated vascular aging. Disease-specific mechanisms, lifelong exposure to vascular-damaging therapies, unfavorable lifestyle factors, and socioeconomic disadvantages together contribute to early atherosclerosis and microvascular dysfunction.

Objectives
We initiated a 10-year prospective observational cohort study at Semmelweis University Pediatric Center to systematically evaluate cardiovascular health in children and young adults with chronic diseases. Our goal is to to develop improved cardiovascular risk assessment tools, targeted prevention and treatment strategies of this population.

Methods
Children and adolescents aged 6–25 years receiving care are eligible for enrollment. The pilot phase focuses on kidney transplant recipients. Participants undergo a comprehensive vascular evaluation, using non-invasive measurement of vascular function (carotid–femoral pulse wave velocity, carotid intima–media thickness, flow-mediated dilation, and retinal microcirculation imaging). Additional data include clinical history, treatment exposure, lifestyle characteristics, and socioeconomic status. Annual follow-up visits are planned.

Preliminary Results
To date, 35 patients have been enrolled in the pilot cohort. Initial findings confirm the feasibility of recruitment and the successful implementation of the vascular assessment protocol.

Bodócs Dóra

Rationale and design of the SANE study, evaluating the Speech of children After Neonatal Encephalopathy

Background
Language development is a key determinant of academic achievement and psychosocial outcome.Due to the therapeutic hypothermia procedure, 60% of children diagnosed with moderate to severe hypoxic-ischaemic encephalopathy (HIE) survive without serious neurological sequelae. Several studies have already revealed the overall cognitive deficits of these infants, however their long-term language developmental specificities and its early risk markers remain underinvestigated.

Objectives
With a comprehensive neuropsychological approach, we aim to investigate whether children's language impairment in this population occurs alongside age-appropriate cognition, or reflects a more global cognitive developmental vulnerability. Developmental Language Disorder (DLD) can be diagnosed from 4 years onwards. According to the DLD definition, this diagnosis is valid within the normal IQ range. We have planned three studies along the following research questions: Which neonatal clinical, laboratory and neuroradiological markers predict the risk of DLD? (Study 1). What are the long-term overall cognitive, language, and neurobehavioral outcomes in HIE survivors without moderate/severe cognitive delay and without cerebral palsy? (Study 2). How do early (2 years) overall cognitive and language outcomes relate to later (4–8 years) outcomes, and what environmental factors influence these developmental trajectories? (Study 3).

Methods and analyses
Into our single-center cohort study, we will involve only those children with perinatal asphyxia who meet the stepwise criteria of the TOBY study. The included HIE survivors cared for in the Level III NICU of the Pediatric Center, Semmelweis University, Budapest, Hungary, were born between 2017 and 2022. Clinical, laboratory, electrographic, and neuroimaging data will be extracted from medical records. Patients are followed-up to assess overall cognitive and language development at 2 years of age (short-term outcome) and between 4–8 years (long-term outcome). The association between neonatal biomarkers and DLD will be analyzed with binary logistic regression models. Machine learning (ML) techniques will be used to develop predictive models for DLD. For modeling the longitudinal changes between early (2-year) and later (4–8-year) cognitive and language status, mixed effects models will be applied.

Discussion
Our approach will allow us to explore how early risk factors interact with childhood environmental influences to shape long-term language outcomes. Establishing early predictors of DLD could enable earlier identification of children likely to benefit from targeted intervention.

Pekli-Tóth Fanni

Endogenous Cortisol, Hydrocortisone Use, and Long-Term Neurodevelopment in Infants with Hypoxic-Ischemic Encephalopathy

Background
Hydrocortisone (HC) is widely used as rescue therapy in infants with hypoxic-ischemic encephalopathy (HIE) and vasopressor-resistant hypotension. Relative adrenal insufficiency (serum cortisol

<15 µg/dL) is often considered an underlying cause; however, little is known about endogenous cortisol levels in this population, and the relationship between HC administration and long-term neurological outcomes remains unclear.

Methods
We conducted a retrospective cohort study of 104 infants with moderate-to-severe HIE treated with therapeutic hypothermia between 2016 and 2021. All patients had early serum cortisol measurements. Hydrocortisone use was determined at the discretion of the attending physicians. Brain injury was assessed using the Weeke MRI scoring system1, and multi-organ injury was evaluated with the MODE score2. Neurodevelopmental outcomes were assessed at 2 years of age using the Bayley Scales of Infant Development, 2nd Edition (BSID-II). Adverse neurodevelopmental outcome was defined as a score <70 on either the Mental Development Index (MDI) or the Psychomotor Development Index (PDI), or death.

Results
Median [interquartile range] serum cortisol level was 7.7 [2.7; 31.9] µg/dL, measured at 11 [6; 21] hours of life. Of the total cohort, 42 (40%) infants had an adverse outcome, including 11 (10%) deaths, and 62 (60%) had a favorable outcome. Infants with adverse outcomes had higher median initial cortisol levels compared with those with favorable outcomes (15.6 vs. 4.1 µg/dL, p=0.06), and higher MODE (10 vs. 8, p<0.001) and Weeke scores (15 vs. 2, p<0.001), reflecting more severe multi-organ and brain injury. Hydrocortisone was administered to 71 infants (68%) for hemodynamic instability. Baseline cortisol levels were higher in infants who received HC compared to those who did not (12.3 vs. 3.2 µg/dL, p=0.03). Importantly, among adverse and favourable outcome groups, the rate of HC use was similar [28/42 (67%) vs. 43/62 (69%), p=0.83]. In addition, no serum cortisol threshold could be identified above which HC administration negatively influenced neurodevelopmental outcomes. Finally, in multivariable regression adjusted for socioeconomic and clinical factors, only the Weeke MRI score remained an independent predictor of outcome, while initial cortisol levels and HC use were not associated with neurodevelopmental results.

Conclusion
In this retrospective cohort, we found no evidence that HC administration influences long-term neurodevelopmental outcomes in infants with moderate-to-severe HIE. The commonly used definition of relative adrenal insufficiency may not be clinically meaningful in this patient population. HC may be used for acute hemodynamic stabilization without regard to initial cortisol levels, though prospective studies are warranted to confirm these findings.

Wakil Mir

The Deceptive Nature of Neonatal Cerebral Sinovenous Thrombosis: Subtle Onset with Long-term Shadow – A Population-Based Cohort Study

Introduction & Aim
Neonatal cerebral sinovenous thrombosis (CSVT) is a rare but critical condition often presenting with subtle symptoms that leaves its profound long-term impact. While previous research has focused on short-term outcomes, little is known about the trajectory into later age. This population-based study aimed to describe the clinical characteristics and long-term neurodevelopmental outcomes of term and near-term neonates with CSVT and to identify specific predictors of adverse sequelae.

Methods
We conducted a retrospective cohort study of term and near-term neonates (≥32 weeks) diagnosed with MRI-confirmed CSVT in the Central-Hungarian Region between 2007 and 2024. Clinical data were collected from medical records, and long-term neurodevelopmental outcomes were assessed using standard evaluations at a median follow-up age of 7 years (84 months).

Results
We identified 43 neonates with CSVT incidence: 1 per 11,665 live births(prevalence 8.57 cases per 100,000 live births). The mortality rate was 26%. Among the survivors with long-term follow-up, 63% experienced adverse neurodevelopmental outcomes, most frequently language delays and behavioral problems.

Our analysis identified distinct predictors for mortality versus morbidity
Predictors of Mortality: Congenital Heart Disease (CHD) was the strongest predictor (OR 81.3), followed by concomitant ischemic or hemorrhagic strokes (OR 14.9).
Predictors of Adverse Neurodevelopment: Emergency C-section (OR 12.9) and involvement of the deep venous system (OR 9.7) were independent predictors of poor long-term outcome.
Hypoglycemia: 100% of infants presenting with hypoglycemia had a poor outcome (death or adverse sequelae), and every child who developed cerebral palsy had a history of neonatal hypoglycemia.

Conclusion
Neonatal CSVT carries a significant burden of mortality and long-term morbidity that extends well into school age. While CHD and concomitant strokes drive mortality, the “”long-term shadow”” of neurodevelopmental impairment is predicted by deep venous system occlusion, emergency C-sections, and hypoglycemia. These findings underscore the need for vigilance regarding deep vein thrombosis on MRI and strict glucose management in affected neonates.


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