Cerebral palsy research news

Monday 9 May 2022

Cerebral Palsy Alliance is delighted to bring you this free weekly bulletin of the latest published research into cerebral palsy. Our organisation is committed to supporting cerebral palsy research worldwide - through information, education, collaboration and funding. Find out more at cerebralpalsy.org.au/our-research

Professor Nadia Badawi AM
CP Alliance Chair of Cerebral Palsy Research

Subscribe to CP Research News

Interventions and Management

1. Mirror movements after bimanual intensive therapy in children with unilateral cerebral palsy: A randomized controlled trial
Rodrigo Araneda, Enimie Herman, Louis Delcour, Anne Klöcker, Geoffroy Saussez, Julie Paradis, Daniela Ebner-Karestinos, Yannick Bleyenheuft

Dev Med Child Neurol. 2022 Apr 30. doi: 10.1111/dmcn.15257. Online ahead of print.

Aim: To investigate potential changes in mirror movements after Hand and Arm Bimanual Intensive Therapy Including Lower Extremity (HABIT-ILE) training in children with unilateral cerebral palsy (CP). Method: Thirty-one children with unilateral CP (mean age 9 years 4 months, SD 4 years 3 months; range 5 years 4 months-17 years 3 months; 14 females, 17 males) were randomized to either a control or treatment group. After allocation, children were assessed three times: before (T1, baseline) and after (T2) a 2-week interval and again at 3 months after T1 (T3) as follow-up. Between T1 and T2, the treatment group received 90 hours of HABIT-ILE training, while the control group continued their customary treatment. Mirror movements were assessed in all children using the Woods and Teuber Scale, as well as the Assisting Hand Assessment, Pediatric Evaluation of Disability Inventory, and Canadian Occupational Performance Measure. Results: Repeated measures analysis of variance indicated a significant decrease in mirror movements in the more-affected (mean difference = 0.97; 95% confidence interval [CI] = 0.51-1.42; $p < 0.001$) and less-affected (mean difference = 0.71; 95% CI = 0.37-1.0; $p < 0.001$) hands of children after HABIT-ILE; these improvements were maintained at the 3-month follow-up. Moreover, the mirror movement changes observed at the second assessment (T2) were inversely correlated with changes in the assessment of activities of daily living, especially in the less-affected hand. Interpretation: HABIT-ILE decreased the intensity of mirror movements in a group of children with CP. Furthermore, mirror movement changes were associated with bimanual performance and activities of daily living in these children.

PMID: 35489044

2. Dysphagia after occipital cervical fusion for retro-odontoid pseudotumor with ossification of the anterior longitudinal ligament
Hidenori Matsuoka, So Ohashi, Michihisa Narikiyo, Ryo Nogami, Hirokazu Nagasaki, Yoshifumi Tsuboi

Case Reports Surg Neurol Int. 2022 Apr 29;13:184. doi: 10.25259/SNI_286_2022. eCollection 2022.

Background: Ossification of the anterior longitudinal ligament (OALL) of the cervical spine is a relatively rare disease. If patients present with dysphagia, hoarseness, and/or dyspnea, they may require surgery. Case description: Over a 7-month period, a 55-year-old female with a history of cerebral palsy developed a progressive quadriparesis accompanied by diffuse sensory loss (i.e., clumsiness of the hand/legs and gait disturbance). The cervical spine X-rays showed atlanto-axial subluxation with instability, while the cervical MRI demonstrated "pseudotumor in the retro-odontoid" region. Following an occipital cervical fusion (C0-C2) surgery, her quadriparesis resolved. Nevertheless, she had persistent dysphagia that

worsened over 6 months. Video fluoroscopy revealed severe mechanical stenosis of the pharynx, which was attributed to OALL extending from the C3-C6 levels. Following OALL resection through a right anterior approach utilizing diamond burrs and an ultrasonic bone curette, the dysphagia rapidly resolved. Conclusion: We report a rare case of retro-odontoid pseudotumor successfully treated with a posterior C0-C2 cervical fusion. Additional symptomatic C3-C6 OALL, responsible for progressive dysphagia, was later managed with focal anterior OALL resection.

PMID: 35509553

3. The CPUP Hip Score predicts displacement of the hip in children with cerebral palsy
Mark S Gaston, Sarah J Wordie, Philippe Wagner, Gunnar Hägglund, James E Robb

Bone Joint J. 2022 May;104-B(5):640-644. doi: 10.1302/0301-620X.104B5.BJJ-2021-0301.R5.

Aims: The Uppföljningsprogram för cerebral pares (CPUP) Hip Score distinguishes between children with cerebral palsy (CP) at different levels of risk for displacement of the hip. The score was constructed using data from Swedish children with CP, but has not been confirmed in any other population. The aim of this study was to determine the calibration and discriminatory accuracy of this score in children with CP in Scotland. Methods: This was a total population-based study of children registered with the Cerebral Palsy Integrated Pathway Scotland. Displacement of the hip was defined as a migration percentage (MP) of > 40%. Inclusion criteria were children in Gross Motor Function Classification System (GMFCS) levels III to V. The calibration slope was estimated and Kaplan-Meier curves produced for five strata of CPUP scores to compare the observed with the predicted risk of displacement of the hip at five years. For discriminatory accuracy, the time-dependent area under the receiver operating characteristic curve (AUC) was estimated. In order to analyze differences in the performance of the score between cohorts, score weights, and subsequently the AUC, were re-estimated using the variables of the original score: the child's age at the first examination, GMFCS level, head shaft angle, and MP of the worst hip in a logistic regression with imputation of outcomes for those with incomplete follow-up. Results: The discriminatory accuracy of the score in the new population of 367 children was high (AUC 0.78 (95% confidence interval (CI) 0.71 to 0.86)). The calibration of the score was insufficient (slope 0.48 (95% CI 0.31 to 0.65)), and the absolute risks of displacement of the hip in this population were overestimated. The AUC increased with re-estimated weights (0.85 (95% CI 0.79 to 0.91)). Conclusion: The CPUP Hip Score had a high ability to discriminate between children at different levels of risk for displacement of the hip. The score overestimated the absolute risks of displacement in this population, which may have resulted from differences in the way children were initially registered in the two programmes. The results are promising, but the score weights may need re-estimation before its clinical application in Scotland. Cite this article: Bone Joint J 2022;104-B(5):640-644.

PMID: 35491586

4. Sacral-Alar-Iliac (SAI) Fixation in Patients With Previous Pelvic Osteotomy
Frederick Mun, Ashish Vankara, Krishna V Suresh, Adam Margalit, Paul D Sponseller

Clin Spine Surg. 2022 May 3. doi: 10.1097/BSD.0000000000001339. Online ahead of print.

Study design: This was a retrospective study. Objective: The purpose of this study was to investigate the technical challenges and outcomes of sacral-alar-iliac (SAI) fixation for scoliosis in patients who had previously undergone a pelvic osteotomy for hip dysplasia. Summary of background data: Patients with neuromuscular disease are at high risk for developing hip dislocation and scoliosis. Surgical correction of one may affect the other. Methods: We reviewed the records of patients aged 18 years and below who underwent spinal fusion using SAI screws after having undergone a pelvic osteotomy, with ≥2-year follow-up. We recorded the SAI screw dimensions, time from osteotomy to SAI fixation, type of osteotomy, and any complications performing SAI fixation due to the pelvic osteotomy. Bivariate statistics were used to analyze the data with statistical significance defined as P-value <0.05. Results: Thirty-two patients were included. The average age was 10.3±3.2 years at pelvic osteotomy and 13.5±3.4 years at SAI fixation. Most patients had cerebral palsy (87.5%) and a unilateral Dega osteotomy (78.1%). Average screw dimensions were significantly shorter on the side of the osteotomy (66 vs. 72 mm, P<0.05). SAI screw placement was technically challenging in 8 patients (25%), due to pelvic distortion from the pelvic osteotomy. The use of a curved awl helped to find the intracortical channel. No patients had complications due to the SAI screw, and there were no significant differences in pelvic obliquity and major coronal curve correction. Two patients (6.3%) had screw lucency >2 mm around the SAI screw on the side of the pelvic osteotomy but no clinical symptoms. Conclusions: SAI fixation in patients with previous pelvic osteotomy is technically challenging due to pelvic morphology and prior implants. Often, a shorter SAI screw is required on the side of the osteotomy. However, outcomes in this patient population are satisfactory, with no significant complications at a 2-year follow-up.

PMID: 35501910

5. [Dystonia in cerebral palsy; what are the treatment options?] [Article in Dutch]
Laura A van de Pol, Laura A Bonouvrié, R Jeroen Vermeulen, Marina A J de Koning-Tijssen, Martje E van Egmond, Michel A Willemsen, Annemieke I Buizer

Review Ned Tijdschr Geneeskd. 2022 Feb 16;166:D5868.

Cerebral palsy (CP) is the most common cause of motor disability in children. The largest group of children with CP present with spasticity. Dystonia is estimated to be present in approximately 15% of children with CP, referred to as dyskinetic CP. Still, dystonia in CP remains underdiagnosed. Dystonia and spasticity can occur together in a subgroup of children with CP as well. Dystonia is characterized by fluctuating hypertonia and involuntary movement and postures. Dystonia in children with CP can interfere with motor function, caregiving and comfort. It is important to recognize dystonia in children with CP as specific treatment is indicated. In this paper we describe three cases of children with dystonia in CP and we review the pharmacological treatment options for dystonia in CP and the surgical options including intrathecal baclofen pump and deep brain stimulation.

PMID: 35499589

6. Responsiveness of the Foot Profile Score in children with hemiplegia
Jennifer McCahill, Julie Stebbins, Robin J Prescott, Jaap Harlaar, Tim Theologis

Gait Posture. 2022 Apr 19;95:160-163. doi: 10.1016/j.gaitpost.2022.04.012. Online ahead of print.

Background: The Foot Profile Score (FPS) is a single score that summarises foot posture and dynamic foot motion during the gait cycle based on the kinematic data of the Oxford Foot Model. The FPS enables clinicians and researchers to quantify foot abnormalities during gait, to monitor change in foot/ankle motion over time, and to measure the outcome of intervention. With the creation of a new outcome measure, it is important to test its responsiveness in a clinical population for whom it may be sensitive to change. Aim: To evaluate the responsiveness of the FPS in a clinical population following isolated foot and ankle surgery. Methods: Using previous work completed to validate the FPS, we defined the minimal clinically important difference (MCID) for the FPS. Using this MCID, we applied it to a clinical population of 37 children with cerebral palsy, spastic hemiplegia, comparing their FPS before and after foot and ankle surgery. A regression analysis looked at potential relationships between the change in FPS and their pre-operative FPS, age at surgery, and time since surgery. Results: An MCID of 2.4 degrees was calculated through regression analysis. The mean change from the pre-operative FPS to the post-operative FPS was 4.6 (SD 3.7 with a range from -0.1 to 13.4). Twenty-eight children (76%) had a change in their FPS greater than the MCID. A regression analyses only showed a clear regression between pre-operative FPS and change in FPS ($R2 = 0.58$ $p < 0.01$).

PMID: 35500365

7. Age related progression of clinical measures and gait in ambulant children and youth with bilateral cerebral palsy without a history of surgical intervention
C Daly, H McKeating, D Kiernan

Gait Posture. 2022 Apr 25;95:141-148. doi: 10.1016/j.gaitpost.2022.04.018. Online ahead of print.

Background: Age related progression needs to be considered when assessing current status and treatment outcomes in cerebral palsy (CP). Research question: What is the association between age, gait kinematics and clinical measures in children with bilateral CP? Method: A retrospective database review was conducted. Subjects with bilateral CP with baseline and follow-up 3D gait analyses, but no history of intervening surgery were identified. Clinical and summary kinematic measures were examined for age related change using repeat measures correlation. Interactions with GMFCS classification and whether surgery was recommended were examined using robust linear regression. Timeseries kinematic data for baseline and most recent follow-up analyses were analysed using statistical parametric mapping. Results: 180 subjects were included. 75% of participants were classified as GMFCS I or II at baseline. Mean time to follow-up was 4.89 (2.8) years (range 1-15.9 years) with a mean age of 6.4 (2.4) at baseline and 11.3 (3.4) at final follow-up. 15.5% of subjects demonstrated an improvement in GMFCS classification while GDI remained stable. Age related progression was noted across many clinical measures with moderate correlations ($r \geq 0.5$) noted for reduced popliteal angle, long lever hip abduction and internal hip rotation range. In gait, there was reduced hip extension in late stance ($p < 0.001$), increased knee flexion in mid-stance ($p < 0.001$), reduced peak

knee flexion in swing ($p < 0.001$) and increased ankle dorsiflexion in stance ($p < 0.001$). In the coronal plane, there was reduced hip abduction in swing ($p < 0.001$). In the transverse plane, increased external rotation of the knee ($p < 0.001$) and reduced external ankle rotation were noted in early stance and through swing ($p < 0.001$). There were no changes in foot progression or hip rotation. Significance: Individuals with CP show age related progression of clinical and kinematic variables. Treatment can only be deemed successful if outcomes exceed or match these age-related changes.

PMID: 35489226

8. Correction: Effect of Pilates Exercises on Standing, Walking, and Balance in Children With Diplegic Cerebral Palsy
Hanaa Mohsen Abd-Elfattah, Dina Othman Shokri Morsi Galal, Mahmoud Ibrahim Elsayed Aly, Sobhy M Aly, Tamer Emam Elnegamy

Published Erratum Ann Rehabil Med. 2022 Apr;46(2):110. doi: 10.5535/arm.21148.e. Epub 2022 Apr 30.

No abstract available

PMID: 35508931

9. Study protocol for Running for health (Run4Health CP): a multicentre, assessor-blinded randomised controlled trial of 12 weeks of two times weekly Frame Running training versus usual care to improve cardiovascular health risk factors in children and youth with cerebral palsy
Sarah E Reedman, Leanne Sakzewski, Lynda McNamara, Catherine Sherrington, Emma Beckman, Kerry West, Stewart G Trost, Rachel Thomas, Mark D Chatfield, Iain Dutia, Alix Gennen, Bridget Dodds, Zoë Cotton, Roslyn N Boyd

BMJ Open. 2022 Apr 29;12(4):e057668. doi: 10.1136/bmjopen-2021-057668.

Introduction: Children and youth with moderate-severe (Gross Motor Function Classification System (GMFCS) levels II-V) cerebral palsy (CP) participate less frequently in physical activities compared with peers without CP and have elevated risk of cardiorespiratory morbidity and mortality in adulthood. Frame Running (RaceRunning) is a new athletics discipline that is an accessible option for physical activity participation for people with moderate-severe CP. There is no high-quality evidence for the effect of Frame Running on cardiovascular disease in children and young people with CP. The primary aim of this study is to conduct a randomised controlled trial of the effect of 12 weeks of Frame Running training on risk factors for cardiovascular disease. Methods and nalysis: Sixty-two children and youth with CP (age 8-20 years) in GMFCS levels II-V will be recruited across four sites and randomised to receive either 12 weeks of Frame Running training two times weekly for 60 min, or usual care. Outcomes will be measured at baseline, immediately postintervention (primary endpoint) and 12 weeks later for retention of training effects. The primary outcome is cardiorespiratory fitness as measured by distance covered on Six Minute RaceRunner Test with 1 min heart rate recovery. Other outcomes include blood pressure, objectively measured physical activity, body mass index, waist circumference, percentage body fat, gross motor function capacity, community participation, feasibility, tolerability and safety. Adverse events will be monitored, and participants and their caregivers will be interviewed to discern their experiences of participation in Frame Running. Ethics and dissemination: The Children's Health Queensland Hospital and Health Service and the University of Queensland Human Research Ethics Committees have approved this study. Results will be disseminated in peer-reviewed journals and scientific conferences; through professional and athletic organisations; and to people with CP and their families.

PMID: 35487751

10. Risk Factors for High-Arched Palate and Posterior Crossbite at the Age of 5 in Children Born Very Preterm: EPIPAGE-2 Cohort Study
Sandra Herrera, Véronique Pierrat, Monique Kaminski, Valérie Benhammou, Laetitia Marchand-Martin, Andrei S Morgan, Elvire Le Norcy, Pierre-Yves Ancel, Alice Germa

Front Pediatr. 2022 Apr 15;10:784911. doi: 10.3389/fped.2022.784911. eCollection 2022.

Introduction: Children born very preterm have an immature sucking reflex at birth and are exposed to neonatal care that can impede proper palate growth. Objectives: We aimed to describe the frequency of high-arched palate and posterior crossbite at

the age of 5 in children born very preterm and to identify their respective risk factors. Methods: Our study was based on the data from EPIPAGE-2, a French national prospective cohort study, and included 2,594 children born between 24- and 31-week gestation. Outcomes were high-arched palate and posterior crossbite. Multivariable models estimated by generalized estimation equations with multiple imputation were used to study the association between the potential risk factors studied and each outcome. Results: Overall, 8% of children born very preterm had a high-arched palate and 15% posterior crossbite. The odds of high-arched palate were increased for children with low gestational age (24-29 vs. 30-31 weeks of gestation) [adjusted odds ratio (aOR) 1.76, 95% confidence interval (CI) 1.17, 2.66], thumb-sucking habits at the age of 2 (aOR 1.53, 95% CI 1.03, 2.28), and cerebral palsy (aOR 2.18, 95% CI 1.28, 3.69). The odds of posterior crossbite were increased for children with pacifier-sucking habits at the age of 2 (aOR 1.75, 95% CI 1.30, 2.36). Conclusions: Among very preterm children, low gestational age and cerebral palsy are the specific risk factors for a high-arched palate. High-arched palate and posterior crossbite share non-nutritive sucking habits as a common risk factor. The oro-facial growth of these children should be monitored.

PMID: 35498807

11. Cognitive, academic, executive and psychological functioning in children with spastic motor type cerebral palsy: Influence of extent, location, and laterality of brain lesions
R Jeroen Vermeulen

Editorial Eur J Paediatr Neurol. 2022 Apr 25;S1090-3798(22)00063-0. doi: 10.1016/j.ejpn.2022.04.007. Online ahead of print.

No abstract available

PMID: 35491355

12. Pain trajectories and well-being in children and young people with cerebral palsy: A cohort study
Heather M Shearer, Pierre Côté, Sheilah Hogg-Johnson, Patricia Mckeever, Darcy L Fehlings

Dev Med Child Neurol. 2022 Apr 30. doi: 10.1111/dmcn.15252. Online ahead of print.

Aim: To identify 5-week pain intensity trajectories and their association with physical and psychological well-being in children/young people with cerebral palsy (CP). Method: A cohort study was conducted with 101 Canadian children/young people with CP, of whom 49 were female, with an overall mean age of 12 years 11 months (SD 3 years 1 month), range of 8 to 18 years, and classified in any Gross Motor Function Classification System level. Self-reported pain intensity (Faces Pain Scale - Revised) was collected weekly for 5 weeks and physical and psychological well-being (KIDSCREEN-27) at baseline and 5 weeks. Statistical analyses included latent class growth and general linear models. Results: All Gross Motor Function Classification System levels were represented (I = 40.6%; II = 15.8%; III = 20.8%; IV = 13.9%; V = 8.9%). Five pain intensity trajectories were identified. Three trajectories had very low (35.4%), low (32.4%), or high (4.9%) mean stable pain. Two trajectories had moderate changing pain (16.8%) and high pain decreasing to moderate levels (10.5%) respectively. Trajectory participants with stable high pain had the lowest physical well-being (adjusted β = -10.01; 95% confidence interval [CI] = -19.37 to -0.66). Those in the three trajectories with the highest mean baseline pain intensity (>3 out of 10) had the lowest psychological well-being (adjusted β = -8.27, 95% CI = -14.84 to -1.70; β = -6.74, 95% CI = -12.43 to -1.05; β = -5.82, 95% CI = -15.34 to 3.71). Interpretation: Almost one-third of participants had moderate-to-high pain intensity trajectories. Membership in the higher pain intensity trajectories was associated with lower physical and psychological well-being.

PMID: 35489074

13. Postsurgical pain assessment in children and adolescents with cerebral palsy: a scoping review
Débora Sierra-Núñez, Esperanza Zuriguel-Pérez, Alejandro Bosch-Alcaraz

Review Dev Med Child Neurol. 2022 Apr 30. doi: 10.1111/dmcn.15259. Online ahead of print.

Aim: To investigate factors that influence the assessment of postoperative pain in children and adolescents with cerebral palsy (CP) and the tools available to determine pain intensity. Method: The search was performed in January 2022 using six databases. Articles focused on paediatric patients with CP; we included instruments for postsurgical pain assessment in this population published in the last 11 years. Results: Eight of 441 studies were included. Males and females behave differently;

their families can be called on to describe their pain responses. Seven instruments for pain assessment were identified: the Non-Communicating Children's Pain Checklist and its Postoperative Version; the Paediatric Pain Profile; the revised Face, Legs, Activity, Cry and Consolability (FLACC) pain scale; the Douleur Enfant San Salvador scale; the Pain Indicator for Communicatively Impaired Children; the University of Wisconsin Children's Hospital Pain Scale; and the Individualized Numeric Rating Scale. Interpretation: The revised FLACC pain scale is suited to postsurgical units because of its ease of use and the fact that parental collaboration is not required. More studies are needed to demonstrate the clinical utility of these scales in postsurgical units and the factors that influence pain assessment.

PMID: 35490248

14. A case of transvaginal lithotripsy for a giant vaginal calculus
Shunsuke Owa, Shigenori Yonemura, Masaki Sakurai, Takahiro Inoue

Case Reports IJU Case Rep. 2022 Feb 21;5(3):157-160. doi: 10.1002/iju5.12421. eCollection 2022 May.

Introduction: Primary vaginal calculi are relatively rare, compared with secondary calculi. Primary calculi are often a result of urogenital sinus abnormalities, neurogenic bladder, or chronic incontinence. Case presentation: Forty-seven years old female with cerebral palsy since infancy had longstanding urinary incontinence. She visited her doctor for a fever and was referred to us with a urinary tract infection. Imaging revealed a large vaginal calculus. It was not possible to remove the calculus vaginally without crushing it, so we performed rigid cystoscopy with lithotripsy, using a pneumatic lithotripsy device. The calculus was completely removed without complications. Conclusion: We were able to remove a large primary vaginal calculus using ultrasonic and pneumatic lithotripsy through a rigid cystoscope. Minimally invasive surgery is a good option for patients with large vaginal calculi.

PMID: 35509778

15. Validation of a new Equinometer device for measuring ankle range of motion in patients with cerebral palsy: An observational study
Axel Horsch, Saskia Kleiber, Maher Ghandour , Matthias Christoph Michael Klotz, Pit Hetto, Stefanos Tsitlakidis, Merkur Alimusaj, Marco Götze

Observational Study Medicine (Baltimore). 2022 Apr 29;101(17):e29230. doi: 10.1097/MD.0000000000029230.

The goniometer is the gold-standard measurement tool of ankle range of motion (ROM). However, several studies have questioned its inter- and intra-rater reliability. Therefore, we conducted this validation study to assess the reliability of a different tool, named Equinometer, as a measurement device of ankle ROM in addition to comparing the reproducibility of their results.Sixteen healthy individuals were included. They underwent both goniometer and Equinometer measurements in knee extension and 90° knee flexion (Silfverskjöld Test). Three raters reported the values of dorsiflexion (DF) and plantarflexion (PF) in each session using both measurement tools. Intra-rater reliability was assessed between 2 raters on another study group of 24 participants. Intraclass correlation coefficients were used to determine the reliability of the used device.The age of study subjects ranged from 22 to 85 years. Fifty percent were males, and the right ankle joint was the most examined side (68.75%). In terms of DF and PF during knee extension and flexion, our analysis revealed that the measurements recorded by the Equinometer were equivalent to the goniometer. Of note, the intra-rater reliability of the Equinometer was excellent for both DF and PF assessment during both knee flexion and extension (Intraclass correlation coefficient ranged from 0.90 to 0.98), with minimal mean differences from goniometer measurements. Subgroup analysis based on age did not reveal any significant differences ($P > .05$).Given the high intra-rater correlations of the Equinometer, we suggest that it is reliable and precise in recording ankle ROM in outpatient clinics, particularly to obtain reproductive, comparable and unbiased data from different observers.

PMID: 35512083

16. Predictors of hospitalisation and death due to SARS-CoV-2 infection in Finland: A population-based register study with implications to vaccinations
Heini Salo, Toni Lehtonen, Kari Auranen, Ulrike Baum, Tuija Leino

Vaccine. 2022 Apr 22;S0264-410X(22)00495-9. doi: 10.1016/j.vaccine.2022.04.055. Online ahead of print.

Introduction: The aim of this study was to investigate how age and underlying medical conditions affect the risk of severe outcomes following SARS-CoV-2 infection and how they should be weighed while prioritising vaccinations against COVID-19. Methods: This population-based register study includes all SARS-CoV-2 PCR-test-positive cases until 24 Feb 2021, based on the Finnish National Infectious Diseases Register. The cases were linked to other registers to identify presence of predisposing factors and severe outcomes (hospitalisation, intensive care treatment, death). The odds of severe outcomes were compared in those with and without the pre-specified predisposing factors using logistic regression. Furthermore, population-based rates were compared between those with a given predisposing factor and those without any of the specified predisposing factors using negative binomial regression. Results: Age and various comorbidities were found to be predictors of severe COVID-19. Compared to 60-69-year-olds, the odds ratio (OR) of death was 7.1 for 70-79-year-olds, 26.7 for 80-89-year-olds, and 55.8 for ≥ 90-year-olds. Among the 20-69-year-olds, chronic renal disease (OR 9.4), malignant neoplasms (5.8), hematologic malignancy (5.6), chronic pulmonary disease (5.4), and cerebral palsy or other paralytic syndromes (4.6) were strongly associated with COVID-19 mortality; severe disorders of the immune system (8.0), organ or stem cell transplant (7.2), chronic renal disease (6.7), and diseases of myoneural junction and muscle (5.5) were strongly associated with COVID-19 hospitalisation. Type 2 diabetes and asthma, two very common comorbidities, were associated with all three outcomes, with ORs from 2.1 to 4.3. The population-based rate of SARS-CoV-2 infection decreased with age. Taking the 60-69-year-olds as reference, the rate ratio was highest (3.0) for 20-29-year-olds and < 1 for 70-79-year-olds and 80-89-year-olds. Conclusion: Comorbidities predispose for severe COVID-19 among younger ages. In vaccine prioritisation both the risk of infection and the risk of severe outcomes, if infected, should be considered.

PMID: 35489984

17. Mental, Neurological, and Somatic Comorbidities and Their Treatment in Persons With Intellectual Disability-an Analysis of Outpatient Billing Data for the Year 2018
Markus Weih, Sabine Köhler, Norbert Schöll, Mandy Schulz, Ramona Hering

Dtsch Arztebl Int. 2022 Jun 17;(Forthcoming):arztebl.m2022.0193. doi: 10.3238/arztebl.m2022.0193. Online ahead of print.

Background: Persons with intellectual disability (ID) often suffer from significant comorbidities. As data have been lacking until now, the present report is the first one containing outpatient data on the prevalence of ID in Germany, its comorbidities, and outpatient (drug) treatment. Methods: This study is based on the nationwide outpatient billing data and drug prescription data of all SHI-insured adults (SHI, statutory health insurance) (age 18-109) who were seen at least once in an outpatient medical practice in 2018. Patients with at least two F70-F79 diagnoses in two quarters were included in the study group (SG) (n = 324 428). A random sample of patients without ID served as the control/comparison group (CG) (n = 648 856). The odds ratios (SG vs. CG) for comorbidities, prescriptions of selected classes of drugs, and involvement of medical specialties were each analyzed by multivariate logistic regression. Results: The prevalence of ID was 0.55%. ID was found to be associated with a variety of comorbidities. The highest odds ratios [OR] were for infantile cerebral palsy (OR: 121.71; 95% confidence interval: [111.67; 132.67]), autism spectrum disorders (OR: 83.85 [75.54; 93.08]), and developmental disabilities (OR: 61.34 [58.86; 63.94]). The most frequently prescribed drug categories (as classified by the anatomic-therapeutic-chemical (ATC) convention) were psychoactive drugs (antipsychotic, anxiolytic, and hypnotic drugs and sedatives) and antiepileptic drugs (OR: 10.40 [10.27; 10.53] and 9.90 [9.75; 10.05], respectively). Both general practitioners (OR: 2.64 [2.59; 2.69]) and medical specialists were consulted by the SG more frequently than by the CG; the type of specialist most commonly consulted was in the neuropsychiatric field, i.e., a neurologist or psychiatrist (OR: 6.85 [6.77; 6.92]). Conclusion: A diagnosis of ID frequently appears in outpatient billing data. Future analyses should be devoted to the specific care of people with intellectual disability, who constitute an especially multimorbid and vulnerable patient group.

PMID: 35506265

18. Identification of a novel homozygous intron 3 splice site (A>T) mutation in the ARG1 gene in cerebral palsy pediatric cases from Odisha, India
Chinmay Kumar Behera, Amit Ranjan Rup, Sagnika Samal, Biswadeep Das

Mol Biol Rep. 2022 May 3. doi: 10.1007/s11033-022-07499-7. Online ahead of print.

Background: Arginase enzyme is essential for the catalysis of the last step of the urea cycle, resulting in the conversion of L-arginine to L-ornithine and urea. Arginase deficiency could lead to hyperarginemia, an autosomal recessive disorder of the urea cycle that could result in developmental manifestations after the first year of life, followed by gradually progressive atonic cerebral palsy, spastic quadriplegia, and mental decline. ARG1 mutations have been reported in hyperarginemia patients of Western countries because they exhibited reduced arginase activity. Hence, it is important to assess ARG1 mutations in cerebral palsy cases with hyperarginemia in different populations. Methods and results: This study involved two unrelated

pediatric patients from two non-consanguineous East Indian families, exhibiting a range of manifestations, including hypotonia of all limbs, mental retardation, and multiple episodes of seizure. The onset of the disease ranged from 1 to 3 years of age. Hyperammonemia (> 250 micromoles) and serum hyperarginemia (> 350 micromoles) were observed in both the patients. Whole-genome sequencing, followed by Sanger sequencing of both the patients confirmed the presence of a homozygous 3' splice site variation in intron 3 of the ARG1 gene (chr6: g.131902357A>T) that affects the invariant AG acceptor splice site of exon 4 (c.330-2A>T; ENST00000356962.2). Conclusion: The study reported the identification of a novel ARG1 mutation in two different unrelated pediatric cases from Odisha, India associated with hyperarginemia. The pathogenicity of the mutation was robustly supported by the clinical phenotype, complete co-segregation with the disease, and biochemical observations.

PMID: 35505270

19. Long-term follow-up of complicated monochorionic twin pregnancies: Focus on neurodevelopment
Patricia J C Knijnenburg, Enrico Lopriore, Femke Slaghekke, Jeanine M M van Klink

Review Best Pract Res Clin Obstet Gynaecol. 2022 Mar 31;S1521-6934(22)00053-0. doi: 10.1016/j.bpobgyn.2022.03.014. Online ahead of print.

Monochorionic twin pregnancies have an increased risk of morbidity and mortality. Due to the advancements in screening and treatment strategies, mortality rates have decreased. Improving survival rates demands a shift in scope toward long-term outcomes. In this review, we focus on neurodevelopmental outcome in survivors from complicated monochorionic twin pregnancies, including twin-twin transfusion syndrome (TTTS), twin anemia-polycythemia sequence (TAPS), acute peripartum TTTS, acute perimortem TTTS, selective fetal growth restriction (sFGR) and monoamnionicity. Our aim is to provide an overview of the current knowledge on the long-term outcome in survivors, including psychomotor development and quality of life, and provide recommendations for future research and follow-up programs.

PMID: 35491308

20. Maternal and fetal serum concentrations of magnesium after administration of a 6-g bolus dose of magnesium sulfate (MgSO 4) to women with imminent preterm delivery
Andrea Jonsdotter, Eridan Rocha-Ferreira, Henrik Hagberg, Ylva Carlsson

Acta Obstet Gynecol Scand. 2022 May 2. doi: 10.1111/aogs.14372. Online ahead of print.

Introduction: Magnesium sulfate is used world-wide to treat pregnant women at imminent risk of preterm delivery in order to protect the brain of the premature infant. Previous research has shown that magnesium sulfate decreases the risk of cerebral palsy by ~30% in infants born preterm. Despite this, the dosage required for optimal neuroprotection remains unknown. We aimed to investigate whether 6 g magnesium sulfate given as a single bolus dose was tolerable for the women and infants and whether the desired target concentration in the mother's blood was reached and non-toxic level in the infant could be ensured. Material and methods: In total, 49 women who were at risk of delivery prior to 32 weeks of gestation were recruited. They received a bolus dose of 6 g magnesium sulfate intravenously between 1 and 24 h prior to giving birth and were closely monitored during and after infusion. Blood samples from the patients were analyzed at different time-points (20-30 min after start of infusion, 1, 2, 6 and 24 h) post-administration. Blood samples from the umbilical cord were also taken directly after birth to assess the concentration of magnesium in the infant. Results: None of the women who received magnesium sulfate reached serum magnesium concentrations >3.3 mmol/L. In all, 72% of the women showed serum magnesium levels within the therapeutic interval (2.0-3.5 mmol/L) and no adverse events were observed during the infusion. The serum magnesium levels in the mothers declined to pre-bolus-levels within 24 h after delivery. Serum magnesium levels in the umbilical cord samples ranged from 0.87 to 1.4 mmol/L, which means that all but two were within the normal expected range for a newborn premature infant. Conclusions: A bolus dose of 6 g magnesium sulfate was well tolerated and without any serious side effects in either mother or infant. Most of our women reached the targeted concentration range of serum magnesium levels after infusion was completed. Their infants had magnesium levels within acceptable levels, regardless of gestational week or mother's body mass index.

PMID: 35501953

21. Acute Lymphoblastic Leukemia in Combined Methylmalonic Acidemia and Homocysteinemia (cblC Type): A Case Report and Literature Review
Jun Zhu, Shuisen Wan, Xueqi Zhao, Binlu Zhu, Yuan Lv, Hongkun Jiang

Case Reports Front Genet. 2022 Apr 14;13:856552. doi: 10.3389/fgene.2022.856552. eCollection 2022.

Background: Methylmalonic acidemia (MMA) can display many clinical manifestations, among which acute lymphoblastic leukemia (ALL) has not been reported, and congenital heart disease (CHD) is also rare. Case presentation: We report an MMA case with ALL and CHD in a 5.5-year-old girl. With developmental delay and local brain atrophy in MRI, she was diagnosed with cerebral palsy at 9 months old. Rehabilitation was performed since then. This time she was admitted to hospital because of weakness and widespread bleeding spots. ALL-L2 (pre-B-cell) was confirmed by bone marrow morphology and immunophenotyping. Echocardiography showed patent foramen ovale. The girl was treated with VDLD and CAML chemotherapy, during which she developed seizures, edema and renal insufficiency. Decrease of muscle strength was also found in physical examination. Screening for inherited metabolic disorders showed significantly elevated levels of methylmalonate-2, acetylcarnitine (C2), propionylcarnitine (C3), C3/C2 and homocysteine. Gene analysis revealed a compound heterozygous mutaion in MMACHC (NM_015,560): c.80A > G (p.Gln27Arg) and c.609G > A (p.Trp203*). CblC type MMA was diagnosed. Intramuscular injection of cyanocobalamin and intravenous L-carnitine treatment were applied. The edema vanished gradually, and chemotherapy of small dosage of vindesine was given intermittently when condition permitted. 2 months later, muscle strength of both lower limbs were significantly improved to nearly grade 5. The levels of methylmalonic acid and homocysteine were improved. Conclusion: Metabolic disease screening and gene analysis are very necessary for diseases with complex clinical symptoms. ALL can be a rare manifestation for MMA. Synopsis: We report a case of methylmalonic acidemia with acute lymphoblastic leukemia and congenital heart disease, which uncovered the importance of genetic testing and metabolic diseases screening in patients with multiple systemic organ involvement.

PMID: 35495149