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Interventions and Management

1. Rebalancing the Spastic Wrist by Transposition of Antagonistic Muscle-Tendon Complex

Silvia Schibli, Jan Fridén

Tech Hand Up Extrem Surg. 2021 Oct 27. doi: 10.1097/BTH.0000000000000371. Online ahead of print.

Upper limb spasticity and spasticity-induced deformities after upper motor neuron lesions because of traumatic brain injury, encephalitis or cerebral palsy inhibit activities of daily living, result in impaired self-care and often dependence on assistance of carers. A key element of the dysfunction is wrist hyper-flexion and ulnar deviation deformity. Traditionally, this deformity has been corrected by transfer of the spastic flexor carpi ulnaris to the extensor carpi radialis brevis. Instead, this study emphasizes the causative role of the palmar subluxation of extensor carpi ulnaris and describes a surgical correction strategy detailing transfer of extensor carpi ulnaris-to-extensor carpi radialis brevis. This surgery re-establishes and maintains a more favorable muscle-tendon-joint mechanics and hand position. Patient satisfaction is high, time and effort in daily care for patients and caregivers are less, and incidence of complications is low.

PMID: [34711790](#)

2. Active Joint Position Sense in Children With Unilateral Cerebral Palsy

Nikolaos Chrysagis, George A Koumantakis, Eirini Grammatopoulou, Emmanouil Skordilis

Cureus. 2021 Sep 18;13(9):e18075. doi: 10.7759/cureus.18075. eCollection 2021 Sep.

Objective The aim of the study was to examine the differences in joint position sense at the elbow joint between 15 children with unilateral cerebral palsy (CP) and 15 typically developing (TD) controls without neurological or other health deficits. **Methodology** Joint position sense, a major proprioceptive component, was evaluated actively using a Kin Com 125 AP isokinetic dynamometer (Chattanooga Group, Chattanooga, TN). **Results** A significant interaction was found ($p < 0.05$) between disability and side, with respect to the active reproduction movement scores. Post-hoc independent t-tests, with Bonferroni adjustments, revealed significant differences for the dominant ($t = -3.63$, $p = 0.001$) and non-dominant sides respectively ($t = -6.19$, $p = 0.000$). Repeated measures t-test revealed wider errors with the non-dominant (affected side) in the active reproduction test, compared to the dominant (nonaffected) side for the CP group of children ($t = -4.73$, $p = 0.000$). A positive correlation was evident between the level of spasticity and joint position sense ($Rho = 0.71$, $p = 0.003$). **Conclusions** Based on our findings, joint position sense is impaired at the elbow joint in children with spastic hemiplegia. The proprioceptive deficit is present at both the affected and unaffected sides and is related to the level of spasticity.

PMID: [34671539](#)

3. Measurement properties of the box and block test in children with unilateral cerebral palsy

Kai-Jie Liang, Hao-Ling Chen, Jeng-Yi Shieh, Tien-Ni Wang

Sci Rep. 2021 Oct 25;11(1):20955. doi: 10.1038/s41598-021-00379-3.

This study aimed to examine the reliabilities (test-retest reliability and measurement error), construct validity, and the interpretability (minimal clinically important difference) of the Box and Block Test (BBT) to interpret test scores precisely for children with UCP. A total of 100 children with UCP were recruited and 50 children from the whole sample assessed the BBT twice within 2-week interval. The BBT, the Melbourne Assessment 2, the Bruininks-Oseretsky Test of Motor Proficiency, 2nd Edition, and the Pediatric Motor Activity Log Revised were measured before and immediately after a 36-h intensive neurorehabilitation intervention. Measurement properties of the BBT were performed according to the CONsensus-based Standards for the selection of health Measurement INSTRuments checklist. The test-retest reliability of the BBT was high (intraclass correlation coefficient = 0.98). The measurement error estimated by the MDC95 value was 5.95. Construct validity was considered good that 4 of 4 (100%) hypotheses were confirmed. The interpretability estimated by the MCID ranged from 5.29 to 6.46. The BBT is a reliable and valid tool for children with UCP. For research and clinical applications, an improvement of seven blocks on the BBT is recommended as an indicator of statistically significant and clinically important change.

PMID: [34697312](#)

4. Does spasticity affect the postural stability and quality of life of children with cerebral palsy?

Mostafa S Ali

J Taibah Univ Med Sci. 2021 Jun 11;16(5):761-766. doi: 10.1016/j.jtumed.2021.04.011. eCollection 2021 Oct.

Objectives: Cerebral palsy is a unique physical disability that primarily affects children's gross motor functions and postural control. Cerebral palsy has a direct impact on children's daily activities and quality of life. This study aims to determine the relationship between spasticity, motor function, postural stability, and the quality life of children with cerebral palsy. **Methods:** Forty-five children (age range 4-6 years) diagnosed with spasticity from cerebral palsy participated in this study. Spasticity was evaluated by the modified Ashworth scale; the children's functions were evaluated by gross motor functional measures, postural stability was evaluated by biodex balance system, and quality of life was measured with the pediatric quality of life inventory. **Results:** There was a strong positive correlation between the degree of spasticity and quality of life. Additionally, there was a significantly strong association between spasticity and gross motor function. In contrast, there was no correlation between spasticity and postural stability indices. Moreover, there was a strong positive correlation between quality of life and gross motor function. Lastly, there was no association between quality of life and the postural stability index. **Conclusion:** The findings highlight the impact of spasticity on motor function and the quality of life of a cohort of children with cerebral palsy. These findings may determine therapeutic interventions and priorities to plan physical therapy programs. Such measures may overcome the main cause of disorders that delay and undermine the daily routines of the affected children.

PMID: [34690659](#)

5. Range of hip abduction after preventive and reconstructive surgery in cerebral palsy: a longitudinal registry study of 307 children

Gunnar Hägglund, Philippe Wagner

Acta Orthop. 2021 Oct 25;1-4. doi: 10.1080/17453674.2021.1995813. Online ahead of print.

Background and purpose - Hip dislocation in cerebral palsy (CP) is caused by altered muscle forces on the joint during typical hip positioning in adduction-flexion-inward rotation. Preventive surgery includes adductor-psoas lengthening (APL) or varus derotation osteotomy (VDRO) of the proximal femur. We assessed the changes in the hip abduction range after these operations. **Patients and methods** - Data were obtained from the Swedish Surveillance Programme for CP. The range of hip abduction before and up to 18-36 months after surgery was assessed for all children who underwent APL or VDRO. Data for 1 hip per child was assessed. Ordinary linear regression was used. **Results** - In the 150 children who underwent APL, the mean range of abduction increased from 29° (95% confidence interval [CI] 28-32) preoperatively to 37° (CI 35-39) at 18-36 months. In the 157 children who underwent VDRO, the respective mean values were 30° (CI 29-32) and 29° (CI 28-31). The mean

difference in preoperative abduction between sides was greater in children who underwent unilateral (9.4°, CI 7.8-11) than bilateral (5.5°, CI 3.4-7.6) VDRO. At 18-36 months postoperatively, the differences between sides were almost unchanged. Interpretation - The range of hip abduction increased after APL but remained unchanged after VDRO. This may explain the normal development of hip displacement after these operations. Differences in abduction between sides were not substantially affected by whether VDRO was performed uni- or bilaterally.

PMID: [34694202](#)

6. Blood loss in hip reconstructive surgery in children with cerebral palsy: when do I need to be prepared for blood transfusion?

Afolayan K Oladeji, Arya Minaie, Andrew J Landau, Pooya Hosseinzadeh

J Pediatr Orthop B. 2021 Oct 20. doi: 10.1097/BPB.0000000000000926. Online ahead of print.

Objective: The hip is the second most common joint involved in pediatric patients with cerebral palsy (CP). Hip reconstructive procedures are performed to improve function and comfort level. Blood loss can occur leading to blood transfusion in close to 1/3 of children with CP undergoing hip reconstruction. The purpose of this study was to report the rate and risk factors for blood transfusion after hip reconstruction in a large cohort of children with CP. **Methods:** We conducted a retrospective chart review of pediatric patients at our tertiary referral children's hospital who underwent reconstructive hip osteotomy over an 8-year period. Binary logistic regression was employed to compare and model differences in transfusion between age greater than 4 or 6 years and the number of osteotomies. **Results:** A total of 180 patients met our inclusion criteria. Thirty-seven patients (20.6%) received blood transfusion. Incidence of transfusion increased as number of osteotomies increased from 1 to 4 (3.7%, 7.3%, 34.0%, 58.3%, respectively). We did not find a significant effect of age greater than 4 or 6 years on the rate of blood transfusion ($P = 0.676$ and $P = 0.323$, respectively). The number of osteotomies was a significant factor in the rate of blood transfusion in both models ($P < 0.001$). **Conclusion:** Number of osteotomies and not age was a significant risk factor in the rate of blood transfusion. This data can help the orthopedic surgeons in preoperative planning for the possibility of blood transfusion in these patients.

PMID: [34678853](#)

7. Effects of Ankle Foot Orthoses on the Gait Patterns in Children with Spastic Bilateral Cerebral Palsy: A Scoping Review

Diogo Ricardo, Maria Raquel Raposo, Eduardo Brazete Cruz, Raul Oliveira, Filomena Carnide, António Prieto Veloso, Filipa João

Review Children (Basel). 2021 Oct 10;8(10):903. doi: 10.3390/children8100903.

Background: Cerebral palsy (CP) is the most common cause of motor disability in children and can cause severe gait deviations. The sagittal gait patterns classification for children with bilateral CP is an important guideline for the planning of the rehabilitation process. Ankle foot orthoses should improve the biomechanical parameters of pathological gait in the sagittal plane. **Methods:** A systematic search of the literature was conducted to identify randomized controlled trials (RCT) and controlled clinical trials (CCT) which measured the effect of ankle foot orthoses (AFO) on the gait of children with spastic bilateral CP, with kinetic, kinematic, and functional outcomes. Five databases (Pubmed, Scopus, ISI Web of SCIENCE, SciELO, and Cochrane Library) were searched before February 2020. The PEDro Score was used to assess the methodological quality of the selected studies and alignment with the Cochrane approach was also reviewed. Prospero registration number: CRD42018102670. **Results:** We included 10 studies considering a total of 285 children with spastic bilateral CP. None of the studies had a PEDro score below 4/10, including five RCTs. We identified five different types of AFO (solid; dynamic; hinged; ground reaction; posterior leaf spring) used across all studies. Only two studies referred to a classification for gait patterns. Across the different outcomes, significant differences were found in walking speed, stride length and cadence, range of motion, ground force reaction and joint moments, as well as functional scores, while wearing AFO. **Conclusions:** Overall, the use of AFO in children with spastic bilateral CP minimizes the impact of pathological gait, consistently improving some kinematic, kinetic, and spatial-temporal parameters, and making their gait closer to that of typically developing children. Creating a standardized protocol for future studies involving AFO would facilitate the reporting of new scientific data and help clinicians use their clinical reasoning skills to recommend the best AFO for their patients.

PMID: [34682168](#)

8. Comparison of body structure, function, activity, and participation levels according to ankle foot orthosis wearing time in children with spastic cerebral palsy

Sefa Unes, Gursoy Coskun, Mintaze Kerem Gunel

Prosthet Orthot Int. 2021 Oct 22. doi: 10.1097/PXR.000000000000048. Online ahead of print.

Background: Ankle foot orthoses (AFOs) are usually recommended to prevent deformities and to increase the standing and walking performance in children with spastic cerebral palsy (CP). **Objective:** To compare the body functions and structures, activity and participation levels, and environmental factors according to AFO-wearing time in children with spastic CP. **Study design:** Prospective, cross-sectional-observational-clinical study. **Methods:** Eighty children with spastic CP (Gross Motor Function Classification System I-III; mean age 7.3 ± 3.9 years) were divided into two groups with equal ages and duration of AFO usage, which is provided as a part of routine clinical care: 6-12 hours per day group ($n = 40$) and 12-24 hours per day group ($n = 40$). The outcomes measured were calf muscle's spasticity with the modified Ashworth Scale (MAS), passive ankle dorsiflexion angle (DA), 66-item Gross Motor Function Measurement, Pediatric Berg Balance Scale, and Pediatric Quality of Life Inventory (PedsQL). Parental satisfaction was measured with a Visual Analog Scale. Multifactorial ANOVA was used to compare the groups, corrected for 66-item Gross Motor Function Measurement. **Results:** No significant differences for the Pediatric Berg Balance Scale, MAS, and DA were found between the groups. Significant differences for the PedsQL (76.99 vs. 57.63; mean difference [MD], 15.60; 95% confidence interval [CI], 10.99~20.22), daily living activities (65.30 vs. 35.92; MD, 25.72; 95% CI, 17.58~33.86), fatigue (76.9 vs. 56.85; MD, 23.11; 95% CI, 16.87~29.35), and satisfaction (8.08 vs. 5.21; MD, 2.46; 95% CI, 1.64~3.27) were found between the groups; 6-12 hour group had superiority for each outcome ($P < 0.001$). Wearing time was significantly correlated with PedsQL ($r = -0.524$, $P < 0.001$) and satisfaction ($r = -0.521$, $P < 0.001$) but not with MAS or DA. **Conclusions:** AFO-wearing time seems to depend on the child's activity and participation levels rather than body functions and structures in children with spastic CP. Prolonged AFO-wearing time was negatively correlated with both the activity-participation level and parental satisfaction.

PMID: [34693939](#)

9. Effects of the Combination of Music Therapy and Physiotherapy in the Improvement of Motor Function in Cerebral Palsy: A Challenge for Research

Maria Jesus Vinolo-Gil, Esteban Casado-Fernández, Veronica Perez-Cabezas, Gloria Gonzalez-Medina, Francisco Javier Martín-Vega, Rocío Martín-Valero

Review Children (Basel). 2021 Sep 29;8(10):868. doi: 10.3390/children8100868.

Background: There are different therapeutic strategies such as physiotherapy and music therapy for the treatment of cerebral palsy. Intervention protocols using both therapies to unify the measurement of motor function have not been investigated. **Aims and scope:** To summarize the effects of the treatment of cerebral palsy through the use of both for the improvement of motor function, analyse the challenges encountered, and submit proposals for improving them. **Methods:** The systematic review was conducted following PRISMA guidelines and registered in the PROSPERO database (CRD42020162493). Clinical trials that described the results obtained in terms of motor function through physiotherapy and music therapy were included. **Results:** Eight clinical trials with 234 participants were considered with a significant improvement in motor function. Results of meta-analysis suggested improvements in gait velocity in favour of the control group for cerebral palsy (mean differences = 0.03; 95% confidence interval = 0.01, 0.04, $p = 0.001$; $I^2 = 97\%$). However, high heterogeneity was identified in the meta-analysis due to the small number of studies included. **Conclusions:** The combination can be effective in subjects with cerebral palsy to improve motor function, although due to the diversity of studies analysed, it is complex to extrapolate results.

PMID: [34682132](#)

10. A scoping review of oral health outcomes for people with cerebral palsy

Karen Lansdown, Michelle Irving, Kimberly Mathieu Coulton, Hayley Smithers-Sheedy

Spec Care Dentist. 2021 Oct 27. doi: 10.1111/scd.12671. Online ahead of print.

Introduction: Good oral health is important for good overall health. Studies have reported poorer oral health outcomes for

people with cerebral palsy, but there has been no synthesis of the evidence surrounding this and, there are no clear oral health recommendations for people with cerebral palsy globally. This review synthesizes the existing knowledge base on oral health in people with cerebral palsy and provides recommendations for future research. Methods: A scoping review was conducted to assess the current literature. Databases were searched using relevant search terms. Study outcomes were synthesized according to their reported outcomes. Results: One hundred seventy three studies were included in this review. Children with cerebral palsy have an increased risk for dental caries and untreated caries. Higher saliva osmolality is a major contributor to increased dental caries. People with cerebral palsy are more likely to experience tooth wear and bruxism. Children and their care-givers have poor oral health related quality of life. There is a large unmet need for oral healthcare in this group. There is no suggested plan for the prevention of poor oral health for this group. A high number of studies included related to research is conducted in low- and middle-income countries, care should be taken in applying results outside this context. There is a lack of research conducted in people with cerebral palsy, 18 years and over. Conclusion: There is a higher risk for poor oral health in people with cerebral palsy and there is a large unmet need to dental care in this group. This study highlights the need for further research to focus on adults with cerebral palsy and an of understanding the oral health care outcomes in the context of settings. The authors recommend the inclusion of classification systems and the integration of disability inclusive language in future studies.

PMID: [34706111](#)

11. Spontaneous Swallowing Frequency, Dysphagia and Drooling in Children with Cerebral Palsy

M A Cray, G D Carnaby, L Mathijs, S Maes, G Gelin, E Ortibus, N Rommel

Arch Phys Med Rehabil. 2021 Oct 26;S0003-9993(21)01494-5. doi: 10.1016/j.apmr.2021.09.014. Online ahead of print.

Objective: To evaluate relationships between spontaneous swallowing frequency, dysphagia, and drooling in children with cerebral palsy. Spontaneous swallowing frequency was predicted to be inversely related to both dysphagia and drooling among children with cerebral palsy. A secondary objective compared patterns among spontaneous swallowing frequency, drooling, and age in healthy children vs. children presenting with cerebral palsy. Design: Cross sectional study. Setting: Children with cerebral palsy were tested at a Cerebral Palsy Reference Center within a university hospital. Healthy children were tested in their home setting. Participants: Twenty children with cerebral palsy were recruited from the local registry for cerebral palsy children and purposive sampling among parents. A group of 30 healthy children was recruited by purposive sampling among family, friends, and the local community. Children below 1 year of age up to 5 years of age were included in the healthy group. This age range was targeted to maximize the potential for drooling in this group. Main outcome measures: Both groups provided data on spontaneous swallowing frequency (swallows per minute: SPM), dysphagia, and drooling. Motor impairment was documented in the children with cerebral palsy. Results: SPM was significantly lower in children with cerebral palsy. Among children with cerebral palsy, SPM correlated significantly with dysphagia severity and trended toward a significant correlation with drooling at rest. In this subgroup SPM was not correlated with age or degree of motor impairment. Dysphagia was significantly correlated with drooling at rest and both dysphagia and drooling at rest were correlated with degree of motor impairment. The two groups did not differ in the degree of drooling at rest. Among healthy children, age but not SPM demonstrated a significant inverse correlation with DQr. Conclusions: Spontaneous swallowing frequency is related to dysphagia and drooling in children with cerebral palsy. The pattern of relationships among spontaneous swallowing frequency and drooling is different between children with cerebral palsy and younger healthy children.

PMID: [34715081](#)

12. Cytomegalovirus infections in pregnant women as a risk of congenital deafness in a child

Wiesław Konopka, Małgorzata Śmiechura-Gańczarczyk, Renata Pepaś

Prz Menopauzalny. 2021 Sep;20(3):122-126. doi: 10.5114/pm.2021.109391. Epub 2021 Sep 24.

Introduction: One per cent of live births are affected by cytomegalovirus infection, but 90% of neonates with perinatal infection do not show symptoms of disease. Symptomatic cytomegalovirus (CMV) is present in 5-10% of children. Typical clinical signs of congenital cytomegalovirus infection are microcephalia, mental retardation, progressive major amblyacousia, and neuromuscular infection. Hypoacusis is present in 30-60% of children with congenital symptomatic CMV - in most cases it is bilateral and applies to high-frequency hearing loss. Material and methods: A group of 70 children had serological and genetic screening of viral DNA using the polymerase chain reaction method in urine and blood. In this group, 52 children were diagnosed with congenital CMV, and 10 children were diagnosed with acquired CMV. Audiological examinations including

pure-tone audiometry, auditory brainstem response, transiently evoked otoacoustic emission, and immittance audiometry were performed. Results: Bilateral sensorineural hearing loss was in 9 children associated with mental and physical retardation, brain malformation, and microcephalia. Unilateral hearing loss was observed in 3 children. In 40 cases, we did not observe hearing loss, although the level of bilirubin was high, as well as splenomegaly, hepatomegaly, and facial nerve paralysis. Conclusions: Congenital cytomegalovirus infection often caused hearing loss. Children with congenital and acquired CMV should be under the permanent care of an audiologist. The growing problem of CMV infections and their late diagnosis suggests the need to prepare screening tests and increase the education of gynaecologists, neonatologists, paediatricians, and general practice doctors about CMV problems.

PMID: [34703412](#)

13. Evaluation of Pain in Adults With Childhood-Onset Disabilities and Communication Difficulties

Taylor Jersak, Garey Noritz

Review Front Neurol. 2021 Oct 5;12:722971. doi: 10.3389/fneur.2021.722971. eCollection 2021.

Adults with childhood-onset disabilities, particularly those with central nervous system impairment, commonly experience pain. Because many such individuals have difficulties in communication, caregivers and medical professionals must identify and interpret non-verbal behaviors as indicators of pain. This process is challenging and can lead to poor outcomes through delayed or incorrect diagnosis and treatment. Most research in the evaluation of pain in individuals with neurologic impairment has focused on the pediatric population, and evidence-based guidelines do not exist for adults. The purpose of this paper is to review current recommendations for pain assessment in adults with communication impairment. This approach includes guidance for history-taking, pharmacologic review, physical examination, and the judicious use of laboratory and imaging tests. Finally, we discuss adult-specific diagnoses to consider when evaluating pain in adults with childhood-onset disabilities and communication difficulties.

PMID: [34675866](#)

14. Clinical changes as a result of dynamic seating in a young adult with cerebral palsy

Michelle L Lange

Disabil Rehabil Assist Technol. 2021 Oct 21;1-6. doi: 10.1080/17483107.2021.1984593. Online ahead of print.

Purpose: This case study follows a single participant with cerebral palsy through 15 years of wheelchair seating interventions. Positioning challenges within the wheelchair seating system included significantly increased muscle tone, extension patterns, extraneous movement, loss of body position in relation to the seating system, loss of alignment with other assistive technologies, high energy expenditure, client injury and pain, and equipment damage. The purpose of this article is to present clinical changes seen in this participant during a progression of dynamic seating interventions. Case description: includes four separate seating and wheeled mobility evaluations over an eight-year time frame and subsequent equipment recommendations. A key intervention was the application of dynamic seating. No standardized assessments for wheeled seating and mobility evaluation are available, at this time. Outcomes: the recommended interventions resulted in reduced extension patterns, extraneous movement, loss of position and alignment with other assistive technologies, energy expenditure, client injury and pain, and equipment damage. Further, functional gains and increased seating tolerance were noted. Conclusion: dynamic seating may address numerous positioning challenges in clients with increased muscle tone in conjunction with an appropriate seating system and mobility base. IMPLICATIONS FOR REHABILITATION: Dynamic seating may: •Dissipate client forces to reduce active extension. •Protect a client from injury by reducing intermittent and sustained forces. •Protect wheelchair seating, mounting hardware, and the frame from loss of alignment and damage. •Provide movement to decrease agitation and increase alertness.

PMID: [34672910](#)

15. A Systematic Multidisciplinary Process for User Engagement and Sensor Evaluation: Development of a Digital Toolkit for Assessment of Movement in Children With Cerebral Palsy

Lisa Kent, Ian Cleland, Catherine Saunders, Andrew Ennis, Laura Finney, Claire Kerr

Front Digit Health. 2021 Jun 24;3:692112. doi: 10.3389/fdgth.2021.692112. eCollection 2021.

Objectives: To describe and critique a systematic multidisciplinary approach to user engagement, and selection and evaluation of sensor technologies for development of a sensor-based Digital Toolkit for assessment of movement in children with cerebral palsy (CP). **Methods:** A sequential process was employed comprising three steps: Step 1: define user requirements, by identifying domains of interest; Step 2: map domains of interest to potential sensor technologies; and Step 3: evaluate and select appropriate sensors to be incorporated into the Digital Toolkit. The process employed a combination of principles from frameworks based in either healthcare or technology design. **Results:** A broad range of domains were ranked as important by clinicians, patients and families, and industry users. These directly informed the device selection and evaluation process that resulted in three sensor-based technologies being agreed for inclusion in the Digital Toolkit, for use in a future research study. **Conclusion:** This report demonstrates a systematic approach to user engagement and device selection and evaluation during the development of a sensor-based solution to a healthcare problem. It also provides a narrative on the benefits of employing a multidisciplinary approach throughout the process. This work uses previous frameworks for evaluating sensor technologies and expands on the methods used for user engagement.

PMID: [34713169](#)

16. Maternal intake of folate during pregnancy and risk of cerebral palsy in the MOBAND-CP cohort

Jonathan Groot, Tanja G Petersen, Pål Suren, Anne Lise Brantsæter, Peter Uldall, Torben Martinussen, Charlotta Granström, Sjurður F Olsen, Allen J Wilcox, Katrine Strandberg-Larsen

Am J Clin Nutr. 2021 Oct 23; nqab351. doi: 10.1093/ajcn/nqab351. Online ahead of print.

Background: Folate prevents neural tube defects and may play a role in some neurodevelopmental disorders. **Objective(s):** To investigate whether higher intakes of periconceptual or midpregnancy folate as recommended were associated with a reduced risk of offspring cerebral palsy (CP). **Methods:** We included participants from the Nordic collaboration cohort consisting of mother-child dyads in the Danish National Birth Cohort and the Norwegian Mother, Father and Child Cohort Study (MOBAND-CP). A total of 190 989 live-born children surviving the first year of life were included. Missing covariate data were multiply imputed. Our exposures were defined as any or no folic acid supplementation in gestational weeks (GWs) -4 to 8 (periconceptual), GWs 9 to 12, and -4 to 12, and supplemental, dietary, and total folate during midpregnancy (GWs 22 to 25). CP overall and the unilateral and bilateral spastic subtypes, as well as CP with low or moderate/high gross motor function impairment were our outcomes of interest. **Results:** Periconceptual folic acid supplementation was not associated with CP (adjusted odds ratio (aOR) 1.02; 95% confidence intervals (CI) 0.82, 1.28). However, supplementation in GWs 9 to 12 was associated with a reduced risk of CP (aOR 0.74; 0.57, 0.96), and inverse associations were indicated for both the unilateral (aOR 0.68; 0.46, 1.02) and bilateral (aOR 0.70; 0.49, 1.02) spastic subtypes, although not statistically significant. Supplemental or dietary folate in midpregnancy alone were not associated with CP. Strong inverse associations were observed with low gross motor function impairment (aOR 0.49; 0.29, 0.83), while for unilateral CP the aOR was 0.63 (0.34, 1.22) for intakes of ≥ 500 compared to ≤ 199 dietary folate equivalents/day during midpregnancy. **Conclusions:** Our findings suggested that folate intakes in GWs 9 to 12 and midpregnancy were associated with a lower risk of CP, while no association was observed for periconceptual supplementation.

PMID: [34687208](#)

17. The multifaceted care-seeking practices among caregivers of children with cerebral palsy: Perspectives from mothers and providers in Ghana

Victoria Fonzi, Blessed Sheriff, Sarah Dalglish, Adote Anum, Emmanuella Dwomo Agyei, Devin Diggs, Loretta Eboigbe, Prince Gyebi Owusu, Kwame S Sakyi

PLoS One. 2021 Oct 27;16(10):e0258650. doi: 10.1371/journal.pone.0258650. eCollection 2021.

Background: Research on cerebral palsy (CP) has lacked emphasis on knowledge and treatment practices among caregivers, particularly in low- and middle-income countries where socio-cultural contexts encourage a variety of treatment alternatives. In this study, we explored the beliefs and experiences that motivate care-seeking practices among caregivers of children with CP in Ghana. **Methods:** Semi-structured interviews were conducted with 25 caregivers, 10 medical providers, and 5 alternative providers in the Greater Accra Region. Participant interviews were analyzed using principles adapted from grounded theory. A conceptual model was constructed to illustrate salient patterns and motivational factors influencing care-seeking practices. **Results:** Participants' experiences showed that caregivers initially sought physiotherapy and prescription medications from medical providers. Many of them then transitioned to alternative methods to search for a cure or address specific CP symptoms. Over time, most caregivers discontinued both medical and alternative care in favor of at-home treatment. A few withdrew completely from all forms of care. Cost of treatment, caregiver burden, and stigma strongly inhibited care-seeking outside the home. **Conclusion:** Although caregivers were open to exploring a variety of treatment options, at-home treatment was preferred by long-time caregivers for its convenience, low cost, and adaptability to patient and caregiver needs.

PMID: [34705843](#)

18. Spatial accessibility to health care services among children with cerebral palsy in Johor, Peninsular Malaysia

Mohd Azmeer Abu Bakar, Narimah Samat, Nik Soriani Yaacob

Geospat Health. 2021 Oct 19;16(2). doi: 10.4081/gh.2021.987.

Cerebral palsy (CP) is one of the most common causes of disability in childhood, leading to functional limitations and poor nutritional status. Families with CP children face challenges in providing proper care. Thus, accessibility of CP patients to health facilities is important to ensure that they can maintain regular visits to health facilities for proper treatment and care. The current study aimed to map the spatial distribution of CP in Johor, Malaysia and measure the accessibility of CP patients to nearby hospitals, health clinics and community-based rehabilitation centres. The study is based on CP cases in 2017 obtained from the Department of Social Welfare, Malaysia and analysed using the average nearest neighbour, buffer analysis and Kernel Density Estimation. Results indicate that there is generally good access to health care services for many of the CP children in Johor, but for 25% of those living more than 10 km away from the health clinics or community-based rehabilitation centres, regular visits can be a problem. This information should be used for targeted intervention and planning for health care strategies. Furthermore, information on hospital accessibility of CP children would allow for planning of proper and regular treatment for these patients. The study has shown that it is possible to improve the understanding of the distribution of CP cases by integrating spatial analysis using geographical information systems without relying on official information about the density of populations.

PMID: [34672180](#)

19. Factors associated with mortality of pediatric sepsis patients at the pediatric intensive care unit in a low-resource setting

Desy Rusmawatiningtyas, Arini Rahmawati, Firdian Makrufardi, Nurul Mardhiah, Indah Kartika Murni, Cuno S P M Uiterwaal, Ary I Savitri, Intan Fatah Kumara, Nurnaningsih

BMC Pediatr. 2021 Oct 25;21(1):471. doi: 10.1186/s12887-021-02945-0.

Background: Sepsis is the leading cause of death worldwide in pediatric populations. Studies in low-resource settings showed that the majority of pediatric patients with sepsis still have a high mortality rate. **Methods:** We retrospectively collected records from 2014 to 2019 of patients who had been diagnosed with sepsis and admitted to PICU in our tertiary hospital. Cox proportional hazard regression modeling was used to evaluate associations between patient characteristics and mortality. **Results:** Overall, 665 patients were enrolled in this study, with 364 (54.7%) boys and 301 (46.3%) girls. As many as 385 patients (57.9%) died during the study period. The median age of patients admitted to PICU were 1.8 years old with interquartile range (IQR) ± 8.36 years and the median length of stay was 144 h (1-1896 h). More than half 391 patients (58.8%) had a good nutritional status. Higher risk of mortality in PICU was associated fluid overload percentage of $> 10\%$ (HR 9.6, 95% CI: 7.4-12.6), the need of mechanical ventilation support (HR 2.7, 95% CI: 1.6-4.6), vasoactive drugs (HR 1.5, 95% CI: 1.2-2.0) and the presence of congenital anomaly (HR 1.4, 95% CI: 1.0-1.9). On the contrary, cerebral palsy (HR 0.3, 95% CI: 0.1-0.5) and post-operative patients (HR 0.4, 95% CI: 0.3-0.6) had lower mortality. **Conclusion:** PICU mortality in pediatric patients with sepsis is associated with fluid overload percentage of $> 10\%$, the need for mechanical ventilation support, the need of vasoactive drugs, and the presence of congenital anomaly. In septic patients in PICU, those with cerebral palsy and

admitted for post-operative care had better survival.

PMID: [34696763](#)

20. Autosomal dominant ADAR c.3019G>A (p.(G1007R)) variant is an important mimic of hereditary spastic paraplegia and cerebral palsy

Hannah F Jones, Marion Stoll, Gladys Ho, Dugald O'Neill, Velda X Han, Simon Paget, Kirsty Stewart, Jennifer Lewis, Kavitha Kothur, Christopher Troedson, Yanick J Crow, Russell C Dale, Shekeeb S Mohammad

Case Reports Brain Dev. 2021 Oct 23;S0387-7604(21)00185-6. doi: 10.1016/j.braindev.2021.10.001. Online ahead of print.

Background: The type 1 interferonopathy, Aicardi-Goutières syndrome 6 (AGS6), is classically caused by biallelic ADAR mutations whereas dominant ADAR mutations are associated with dyschromatosis symmetrica hereditaria (DSH). The unique dominant ADAR c.3019G>A variant is associated with neurological manifestations which mimic spastic paraplegia and cerebral palsy (CP). Case summaries: We report three cases of spastic paraplegia or CP diagnosed with AGS6 caused by the ADAR c.3019G>A variant. Two children inherited the variant from an asymptomatic parent, and each child had a different clinical course. The youngest case demonstrated relentless progressive symptoms but responded to immunomodulation using steroids and ruxolitinib. Conclusion: The ADAR c.3019G>A variant has incomplete penetrance and is a likely underrecognized imitator of spastic paraplegia and dystonic CP. A high level of clinical suspicion is required to diagnose this form of AGS, and disease progression may be ameliorated by immunomodulatory treatment with selective Janus kinase inhibitors.

PMID: [34702576](#)

21. Fetal Reduction and Twins

Mark I Evans, Jenifer Curtis, Shara M Evans, David W Britt

Review Am J Obstet Gynecol MFM. 2021 Oct 23;100521. doi: 10.1016/j.ajogmf.2021.100521. Online ahead of print.

Infertility treatments have benefited millions of couples to have their own children, but resultant multiple pregnancies with their increased morbidity and mortality have been a significant complication. Fetal reduction (FR) was developed to ameliorate those. Over 30 years of publications show that FR has been highly successful in substantially reducing both mortality and morbidity. As with most radically new techniques, initial cases were in the "nothing to lose" category. With experience, indications liberalize, and quality of life issues increase as a proportion of cases. Overall risks for twins are not twice singletons; they are about 4 - 5 x higher. In experienced hands, the combination of genetic testing by CVS followed by FR has made most multiples behave statistically as if they were originally the lower number. Use of microarray analysis to better determine fetal genetic health before deciding on which fetus(es) to keep or reduce further improves pediatric outcomes. With increasing experience and lower average starting numbers, the proportion of FRs to a singleton has increased considerably. Twins to a singleton FR now constitute an increasing proportion of cases performed. Data on such cases show improved outcomes, and we believe FR should be at least discussed and offered to all patients with a dichorionic twin pregnancy or higher. With increasing reliance upon elective single embryo transfer (eSET), monochorionic twins have substantially increased which have much higher complication rates than dichorionic twins. Furthermore, monochorionic twins cannot be readily, safely reduced so the adverse perinatal statistics of eSET are a major set-back for good outcomes. While eSET is appropriate for some, we believe that for many couples, transfer of 2 embryos is generally a more rational approach.

PMID: [34700026](#)

22. Regional Oxygenation and Perfusion Monitoring to Optimize Neonatal Packed Red Blood Cell Transfusion Practices: A Systematic Review

Pranav Jani, Kiran Balegarvirupakshappa, James E Moore, Nadia Badawi, Mark Tracy

Transfus Med Rev. 2021 Sep 29;S0887-7963(21)00047-X. doi: 10.1016/j.tmr.2021.07.005. Online ahead of print.

Contemporary packed red blood cell transfusion practices in anaemic preterm infants are primarily based on measurement of hemoglobin or haematocrit. In neonatal intensive care units, most preterm infants receive at least 1 packed red cell transfusion as standard treatment for anaemia of prematurity. Clinicians are faced with a common question "at what threshold should anaemic preterm infants receive packed red blood cell transfusion?". While evidence from interventional trials offers a range of haemoglobin levels to clinicians on thresholds to initiate red cell transfusion, it does not offer identification of exact haemoglobin level at which regional oxygenation and perfusion gets compromised. Assessment of regional oxygenation using near infrared spectroscopy and perfusion using ultrasound could offer a personalized transfusion medicine approach to optimize transfusion practices. We conducted a systematic review of the literature to identify the role of both regional oxygenation and/or ultrasound-based perfusion monitoring as a potential trigger to initiate packed red blood cell transfusion in anaemic preterm infants. MEDLINE, Embase, Maternity and Infant Care database were searched up to March 2021. Publications identified were screened and relevant data was extracted. Changes to regional oxygenation and/or perfusion monitoring before and after packed red blood cell transfusion were the primary outcomes. 44 out of 755 studies met the inclusion criteria and were included in the final analysis. Most were prospective, observational studies in stable preterm infants. Overall, studies reported an improvement in regional oxygenation and/or ultrasound-based perfusion after packed red blood cell transfusion. These changes were more consistently observed when hemoglobin <9.6g/dL or hematocrit was <0.30. Significant variation was found for patient characteristics, postnatal age at the time of monitoring, criteria for diagnosis of anaemia, and period of monitoring as well as regional oxygenation monitoring methodology. Regional oxygenation and/or perfusion monitoring can identify at-risk anaemic preterm infants and are promising tools to individualize packed red blood cell transfusion practices. However, there is lack of evidence for incorporating this monitoring, in their present form, into standard clinical practice. Additionally, consistency in reporting of study methodology should be improved.

PMID: [34702614](#)

23. Editorial: Experimental and Clinical Approaches in the Pursuit of Novel Therapeutic Strategies for Perinatal Brain Injury and Its Neurological Sequelae

Changlian Zhu, Chao Chen, Claire Thornton

Editorial Front Cell Neurosci. 2021 Oct 11;15:762111. doi: 10.3389/fncel.2021.762111. eCollection 2021.

PMID: [34707483](#)

24. Early (< 7 days) systemic postnatal corticosteroids for prevention of bronchopulmonary dysplasia in preterm infants

Lex W Doyle, Jeanie L Cheong, Susanne Hay, Brett J Manley, Henry L Halliday

Review Cochrane Database Syst Rev. 2021 Oct 21;10(10):CD001146. doi: 10.1002/14651858.CD001146.pub6.

Background: Bronchopulmonary dysplasia (BPD) remains a major problem for infants born extremely preterm. Persistent inflammation in the lungs is important in its pathogenesis. Systemic corticosteroids have been used to prevent or treat BPD because of their potent anti-inflammatory effects. Objectives: To examine the relative benefits and adverse effects of systemic postnatal corticosteroids commenced within the first six days after birth for preterm infants at risk of developing BPD. Search methods: We ran an updated search of the following databases on 25 September 2020: CENTRAL via CRS Web and MEDLINE via OVID. We also searched clinical trials databases and reference lists of retrieved articles for randomised controlled trials (RCTs). We did not include cluster randomised trials, cross-over trials, or quasi-RCTs. Selection criteria: For this review, we selected RCTs examining systemic (intravenous or oral) postnatal corticosteroid treatment started within the first six days after birth (early) in high-risk preterm infants. We included studies that evaluated the use of dexamethasone, as well as studies that assessed hydrocortisone, even when the latter was used primarily for management of hypotension, rather than for treatment of lung problems. We did not include trials of inhaled corticosteroids. Data collection and analysis: We used standard Cochrane methods. We extracted and analysed data regarding clinical outcomes that included mortality, BPD, mortality or BPD, failure to extubate, complications during the primary hospitalisation, and long-term health and neurodevelopmental outcomes. We used the GRADE approach to assess the certainty of evidence. Main results: Use of the GRADE approach revealed that the certainty of evidence was high for the major outcomes considered, except for BPD at 36 weeks for all studies combined, which was downgraded one level to moderate because of evidence of publication bias. We included 32 RCTs (4395 infants). The overall risk of bias of included studies was low; all were RCTs, and most trials used rigorous methods. Early systemic corticosteroids overall have little or no effect on mortality to the latest reported age (risk ratio (RR) 0.95, 95% confidence interval (CI) 0.85 to 1.06; 31 studies, 4373 infants; high-certainty evidence), but hydrocortisone alone reduces mortality (RR 0.80, 95% CI 0.65 to 0.99; 11 studies, 1433 infants; high-certainty evidence). Early systemic corticosteroids overall probably reduce BPD at 36 weeks' postmenstrual age (PMA) (RR 0.80, 95% CI 0.73 to 0.88; 26 studies,

4167 infants; moderate-certainty evidence), as does dexamethasone (RR 0.72, 95% CI 0.63 to 0.82; 17 studies, 2791 infants; high-certainty evidence), but hydrocortisone has little to no effect (RR 0.92, 95% CI 0.81 to 1.06; 9 studies, 1376 infants; high-certainty evidence). Early systemic corticosteroids overall reduce the combined outcome of mortality or BPD at 36 weeks' PMA (RR 0.89, 95% CI 0.84 to 0.94; 26 studies, 4167 infants; high-certainty evidence), as do both dexamethasone (RR 0.88, 95% CI 0.81 to 0.95; 17 studies, 2791 infants; high-certainty evidence) and hydrocortisone (RR 0.90, 95% CI 0.82 to 0.99; 9 studies, 1376 infants; high-certainty evidence). Early systemic corticosteroids overall increase gastrointestinal perforation (RR 1.84, 95% CI 1.36 to 2.49; 16 studies, 3040 infants; high-certainty evidence), as do both dexamethasone (RR 1.73, 95% CI 1.20 to 2.51; 9 studies, 1936 infants; high-certainty evidence) and hydrocortisone (RR 2.05, 95% CI 1.21 to 3.47; 7 studies, 1104 infants; high-certainty evidence). Early systemic corticosteroids overall increase cerebral palsy (RR 1.43, 95% CI 1.07 to 1.92; 13 studies, 1973 infants; high-certainty evidence), as does dexamethasone (RR 1.77, 95% CI 1.21 to 2.58; 7 studies, 921 infants; high-certainty evidence) but not hydrocortisone (RR 1.05, 95% CI 0.66 to 1.66; 6 studies, 1052 infants; high-certainty evidence). Early systemic corticosteroids overall have little to no effect on the combined outcome of mortality or cerebral palsy (RR 1.03, 95% CI 0.91 to 1.16; 13 studies, 1973 infants; high-certainty evidence), nor does hydrocortisone (RR 0.86, 95% CI 0.71 to 1.05; 6 studies, 1052 infants; high-certainty evidence). However, early dexamethasone probably increases the combined outcome of mortality or cerebral palsy (RR 1.18, 95% CI 1.01 to 1.37; 7 studies, 921 infants; high-certainty evidence). In sensitivity analyses by primary intention for treatment with hydrocortisone (lung problems versus hypotension), there was little evidence of differences in effects on major outcomes of mortality, BPD, or combined mortality or BPD, by indication for the drug. Authors' conclusions: Early systemic postnatal corticosteroid treatment (started during the first six days after birth) prevents BPD and the combined outcome of mortality or BPD. However, it increases risks of gastrointestinal perforation, cerebral palsy, and the combined outcome of mortality or cerebral palsy. Most beneficial and harmful effects are related to early treatment with dexamethasone, rather than to early treatment with hydrocortisone, but early hydrocortisone may prevent mortality, whereas early dexamethasone does not. Longer-term follow-up into late childhood is vital for assessment of important outcomes that cannot be assessed in early childhood, such as effects of early corticosteroid treatment on higher-order neurological functions, including cognitive function, executive function, academic performance, behaviour, mental health, motor function, and lung function. Further RCTs of early corticosteroids, particularly of hydrocortisone, should include longer-term survival free of neurodevelopmental disability as the primary outcome.

PMID: [34674229](#)

25. Long-term cognitive outcomes in term newborns with watershed injury caused by neonatal encephalopathy

Bo Lyun Lee, Dawn Gano, Elizabeth E Rogers, Duan Xu, Stephany Cox, A James Barkovich, Yi Li, Donna M Ferriero, Hannah C Glass

Pediatr Res. 2021 Oct 26. doi: 10.1038/s41390-021-01526-2. Online ahead of print

Background: We previously reported that increasing severity of watershed (WS) injury in neonatal magnetic resonance imaging (MRI) is associated with worse language outcomes in early childhood. In the present study, we investigated the relationship between neonatal injury patterns and cognitive profile in adolescents with neonatal encephalopathy. **Methods:** Term neonates with encephalopathy were prospectively enrolled and imaged using brain MRI from 1999 to 2008. Neonatal brain injury was scored according to the degree of injury in WS and basal ganglia/thalamus (BG/T) areas. The children underwent a neurocognitive assessment and follow-up brain MRI at the age of 10-16 years. The relationship between neonatal brain injury patterns and adolescent cognitive outcomes was assessed. **Results:** In a cohort of 16 children, neonatal MRI showed WS injury in 7, BG/T injury in 2, and normal imaging in 7. Children with WS injury had lower estimated overall cognitive ability than those with normal imaging. Increasing WS injury score was associated with decreasing estimated overall cognitive ability, Perceptual Reasoning Index, and digit span score. **Conclusions:** Children with the WS injury are at an increased risk of having problems in long-term intellectual ability. These cognitive outcomes may underlie early language difficulties seen in children with neonatal WS injury. **Impact:** Adolescents with a history of neonatal encephalopathy and watershed pattern of injury on neonatal brain magnetic resonance imaging (MRI) had lower overall cognitive ability, perceptual reasoning skills, and auditory working memory than those with normal neonatal imaging. Children with post-neonatal epilepsy and cerebral palsy had the worst cognitive outcomes. Watershed pattern of injury confers high long-term differences in intellectual ability.

PMID: [34702974](#)

26. Impact of the Coronavirus Pandemic on High-Risk Infant Follow-Up (HRIF) Programs: A Survey of Academic Programs

Sanjeet Panda, Rashmi Somu, Nathalie Maitre, Garrett Levin, Ajay Pratap Singh

Children (Basel). 2021 Oct 6;8(10):889. doi: 10.3390/children8100889.

Objective: The impact of the COVID-19 pandemic on the functioning and services of academic high-risk infant follow-up (HRIF) clinics throughout North America. **Study design:** Prospective 25-question questionnaire survey through REDCAP links that was sent over 10 weeks, to 105 US and 10 Canadian programs. Finally, 59 of 105 US programs and 5 of 10 Canadian responses were analyzed using SAS version 9.4. **Results:** In the US, 67% of programs reported closures between 1-5 months, whereas in Canada 80% of programs closed for 1-3 months. In the US 86% of programs provided telemedicine visits and only 42.5% provided multidisciplinary HRIF telemedicine visits. We enumerated innovative approaches specifically for the conduct of Telemedicine visits, the need for the standardization of various tests and services in a telemedicine setting, and to emphasize the urgent need for more government funding to improve follow-up and developmental services to this fragile group of newborns.

PMID: [34682154](#)

27. The use of neuroimaging, Prechtl's general movement assessment and the Hammersmith infant neurological examination in determining the prognosis in 2-year-old infants with hypoxic ischemic encephalopathy who were treated with hypothermia

Umut Apaydın, Erkan Erol, Ayşe Yıldız, Ramazan Yıldız, Şebnem Soysal Acar, Kıvılcım Gücüyener, Bülent Elbasan

Early Hum Dev. 2021 Oct 14;163:105487. doi: 10.1016/j.earlhumdev.2021.105487. Online ahead of print.

Background: The use of neuroimaging, the General Movement Assessment (GMA), and the Hammersmith Infant Neurological Examination (HINE) to identify the risk of neurodevelopmental delay in early infancy is recommended. **Aim:** The aim of this study was to examine the predictive power of neuroimaging, GMA and HINE for neurodevelopmental delay and cerebral palsy (CP) in infants with hypoxic ischemic encephalopathy (HIE) who were treated with hypothermia. **Study design:** Retrospective cohort. **Subjects and outcome measures:** This retrospective study included 47 (18 female and 29 male) infants who were treated with hypothermia due to HIE. Neonates with a diagnosis of HIE were followed and assessed using neuroimaging, GMA, HINE and the Bayley Scales of Infant and Toddler Development-II (Bayley II) between 3 m and 2 years of age. **Results:** Out of the 47 infants with HIE, no fidgety movements were observed in 5 infants. The sensitivity and specificity in determining the psychomotor developmental index (PDI) score were 97% and 100%, respectively, for MRI; 92.9% and 100% for GMA; and 91.9% and 80% for the HINE. The sensitivity and specificity in determining the mental developmental index (MDI) score were 95% and 85.7%, respectively, for MRI; 90.5% and 80% for GMA; and 91.9% and 50% for HINE. The sensitivity and specificity in determining CP diagnosis at the age of 2 years were 83.3% and 95%, respectively, for MRI; 83.3% and 100% for GMA; and 83.3% and 87.8% for HINE. **Conclusion:** The interpretation of MRI, GMA, and HINE that are performed within the early period of life may be the gold standard for the early detection of neurodevelopmental risks in 2-year-old infants with HIE. Clinical implementation of these methods in the early period in the follow-up of these infants offers useful information for the early identification of neurodevelopmental risk and for planning early intervention.

PMID: [34673463](#)

28. Immunological effects of cerebral palsy and rehabilitation exercises in children

Oleksandra Sharova, Oleksandr Smiyan, Thomas Borén

Brain Behav Immun Health. 2021 Oct 9;18:100365. doi: 10.1016/j.bbih.2021.100365. eCollection 2021 Dec.

Cerebral palsy (CP) is a group of motor disorders caused by non-progressive lesions of the premature brain with lifelong pathophysiological consequences that include dysregulation of innate immunity. Persistent inflammation with increased levels of circulating pro-inflammatory tumor necrosis factor alpha (TNF- α) is negatively associated with rehabilitation outcome in children with CP. Because of the crosstalk between innate and adaptive immunity, we investigated the effect of CP and rehabilitation exercises on the adaptive immune system in children with CP by measuring the levels of CD3⁺, CD4⁺, CD8⁺ T-cells, and CD22⁺ B-cells and the levels of immunoglobulins. Children with CP had higher levels of CD3⁺, CD4⁺, CD8⁺ T-cells, and CD22⁺ B-cells compared to healthy children, and the rehabilitation exercise programs produced better outcomes in terms of increased gains in motor function at an earlier age. Rehabilitation exercises performed over a month resulted in significantly decreased levels of IgA in serum and reduced numbers of B-lymphocytes and reduced IgM levels. Our study suggests that rehabilitation programs with a focus on neuroplasticity and physical exercises in children with CP can reduce both

cellular and humoral immune responses.

PMID: [34704080](#)

29. Shared Physiologic Pathways Among Comorbidities for Adults With Cerebral Palsy

Daniel G Whitney, Mary Schmidt, Edward A Hurvitz

Front Neurol. 2021 Oct 4;12:742179. doi: 10.3389/fneur.2021.742179. eCollection 2021.

Objective: Aging with cerebral palsy is accompanied by a declining health and function status across neurological and non-neurological systems. There is a need to understand the shared pathophysiology among comorbidities for adults with cerebral palsy, to inform clinical assessment and guidelines for interventions to improve healthful aging. To begin defining multimorbidity, this study identified the most common comorbidity combinations and their association with mortality among a representative sample of adults with cerebral palsy. **Methods:** Data from 2016 to 2018 were used from a random 20% sample from the fee-for-service Medicare database. Adults ≥ 18 years with cerebral palsy and 25 neurological and non-neurological comorbidities were obtained from 2016. Principal component (PC) analysis identified the most common comorbidity combinations, defined as individual PCs. Cox regression estimated the hazard ratio (HR) of 2-year mortality including all PCs and demographics in a single model. To facilitate comparisons, PC scores were transformed into quintiles (reference: lowest quintile). **Results:** Among the 16,728 adults with cerebral palsy, the most common comorbidity combinations (PCs) in order were: cardiorespiratory diseases, dysphagia, and fluid/electrolyte disorders; metabolic disorders (e.g., diabetes, renal disease, hypertension); neurologic-related disorders (e.g., dementia, cerebrovascular disease); gastrointestinal issues; and orthopedic-related disorders. During the 2-year follow-up, 1,486 (8.9%) died. In the adjusted model, most PCs were associated with an elevated mortality rate, especially the first PC (5th quintile HR = 3.91; 95%CI = 3.29-4.65). **Discussion:** This study identified the most common comorbidity combinations for adults with cerebral palsy, many of them were deadly, which may inform on the underlying pathophysiology or shared characteristics of multimorbidity for this population.

PMID: [34671312](#)

30. Health service use among adults with cerebral palsy: a mixed-methods systematic review

Manjula Manikandan, Claire Kerr, Grace Lavelle, Michael Walsh, Aisling Walsh, Jennifer M Ryan

Review Dev Med Child Neurol. 2021 Oct 27. doi: 10.1111/dmcn.15097. Online ahead of print.

Aim: To determine the proportion of adults with cerebral palsy (CP) using health services and frequency of use, and to explore experiences and perceptions of health services for this population. **Method:** A mixed-methods systematic review was conducted using the Joanna Briggs Institute methodology. Five databases were searched to September 2020. Observational and qualitative studies were included. Two reviewers screened titles, abstracts, and full texts; extracted data; and assessed the quality of included studies. Separate meta-analyses were used to pool the proportion of adults using each service and frequency of use. A meta-aggregation approach was used to synthesize qualitative data. Quantitative and qualitative findings were integrated using the Andersen and Newman Model of health care utilization. **Results:** Fifty-seven studies (31 quantitative, 26 qualitative) of 14 300 adults with CP were included. The proportion of adults using services ranged from 7% (95% confidence interval [CI]: 2-13%) for urologists to 84% (95% CI: 78-90%) for general practitioners. Incidence of visits ranged from 67 (95% CI: 37-123) hospital admissions to 404 (95% CI: 175-934) general practitioner visits per 100 person-years. Qualitative themes highlighted issues regarding accessibility, caregivers' involvement, health workers' expertise, unmet ageing needs, transition, and health system challenges. **Interpretation:** Adults with CP used a wide range of health services but faced context-specific challenges in accessing required care. Appropriate service delivery models for adults with CP are required. This review emphasizes a need to develop an appropriate service model for adults with CP to meet their needs.

PMID: [34705276](#)

31. Recent Advances in the Treatment of Spasticity: Extracorporeal Shock Wave Therapy

En Yang, Henry L Lew, Levent Özçakar, Chueh-Hung Wu

Review J Clin Med. 2021 Oct 14;10(20):4723. doi: 10.3390/jcm10204723.

Spasticity is a common sequela of the upper motor neuron lesions. For instance, it often occurs in the first 4 weeks after stroke and is seen in more than one-third of stroke survivors after 12 months. In recent years, extracorporeal shock wave therapy (ESWT) has been recognized as a safe and effective method for reducing muscle spasticity. Possible/relevant mechanisms include nitric oxide production, motor neuron excitability reduction, induction of neuromuscular transmission dysfunction, and direct effects on rheological properties. There are two types of ESWT, focused and radial, with the radial type more commonly applied for treating muscle spasticity. Concerning the optimal location for applying ESWT, the belly muscles and myotendinous junction seem to produce comparable results. The effects of ESWT on spasticity are known to last at least four to six weeks, while some studies report durations of up to 12 weeks. In this review, the authors will focus on the current evidence regarding the effectiveness of ESWT in spasticity, as well as certain technical parameters of ESWT, e.g., the intensity, frequency, location, and number of sessions. The pertinent literature has been reviewed, with an emphasis on post-stroke upper limbs, post-stroke lower limbs, cerebral palsy, and multiple sclerosis. In short, while ESWT has positive effects on parameters such as the modified Ashworth scale, mixed results have been reported regarding functional recovery. Of note, as botulinum toxin injection is one of the most popular and effective pharmacological methods for treating spasticity, studies comparing the effects of ESWT and botulinum toxin injections, and studies reporting the results of their combination, are also reviewed in this paper.

PMID: [34682846](#)**32. Stimuli for Adaptations in Muscle Length and the Length Range of Active Force Exertion-A Narrative Review**

Annika Kruse, Cintia Rivas, Guido Weide, Markus Tilp, Richard T Jaspers

Review Front Physiol. 2021 Oct 8;12:742034. doi: 10.3389/fphys.2021.742034. eCollection 2021.

Treatment strategies and training regimens, which induce longitudinal muscle growth and increase the muscles' length range of active force exertion, are important to improve muscle function and to reduce muscle strain injuries in clinical populations and in athletes with limited muscle extensibility. Animal studies have shown several specific loading strategies resulting in longitudinal muscle fiber growth by addition of sarcomeres in series. Currently, such strategies are also applied to humans in order to induce similar adaptations. However, there is no clear scientific evidence that specific strategies result in longitudinal growth of human muscles. Therefore, the question remains what triggers longitudinal muscle growth in humans. The aim of this review was to identify strategies that induce longitudinal human muscle growth. For this purpose, literature was reviewed and summarized with regard to the following topics: (1) Key determinants of typical muscle length and the length range of active force exertion; (2) Information on typical muscle growth and the effects of mechanical loading on growth and adaptation of muscle and tendinous tissues in healthy animals and humans; (3) The current knowledge and research gaps on the regulation of longitudinal muscle growth; and (4) Potential strategies to induce longitudinal muscle growth. The following potential strategies and important aspects that may positively affect longitudinal muscle growth were deduced: (1) Muscle length at which the loading is performed seems to be decisive, i.e., greater elongations after active or passive mechanical loading at long muscle length are expected; (2) Concentric, isometric and eccentric exercises may induce longitudinal muscle growth by stimulating different muscular adaptations (i.e., increases in fiber cross-sectional area and/or fiber length). Mechanical loading intensity also plays an important role. All three training strategies may increase tendon stiffness, but whether and how these changes may influence muscle growth remains to be elucidated. (3) The approach to combine stretching with activation seems promising (e.g., static stretching and electrical stimulation, loaded inter-set stretching) and warrants further research. Finally, our work shows the need for detailed investigation of the mechanisms of growth of pennate muscles, as those may longitudinally grow by both trophy and addition of sarcomeres in series.

PMID: [34690815](#)**33. IFN γ -Producing γ/δ T Cells Accumulate in the Fetal Brain Following Intrauterine Inflammation**

Emma L Lewis, Natalia Tulina, Lauren Anton, Amy G Brown, Paige M Porrett, Michal A Elovitz

Front Immunol. 2021 Oct 4;12:741518. doi: 10.3389/fimmu.2021.741518. eCollection 2021.

Intrauterine inflammation impacts prenatal neurodevelopment and is linked to adverse neurobehavioral outcomes ranging from cerebral palsy to autism spectrum disorder. However, the mechanism by which a prenatal exposure to intrauterine inflammation contributes to life-long neurobehavioral consequences is unknown. To address this gap in knowledge, this study investigates how inflammation transverses across multiple anatomic compartments from the maternal reproductive tract to the fetal brain and what specific cell types in the fetal brain may cause long-term neuronal injury. Utilizing a well-established mouse model, we found that mid-gestation intrauterine inflammation resulted in a lasting neutrophil influx to the decidua in the absence of maternal systemic inflammation. Fetal immunologic changes were observed at 72-hours post-intrauterine inflammation, including elevated neutrophils and macrophages in the fetal liver, and increased granulocytes and activated microglia in the fetal brain. Through unbiased clustering, a population of Gr-1+ γ/δ T cells was identified as the earliest immune cell shift in the fetal brain of fetuses exposed to intrauterine inflammation and determined to be producing high levels of IFN γ when compared to γ/δ T cells in other compartments. In a case-control study of term infants, IFN γ was found to be elevated in the cord blood of term infants exposed to intrauterine inflammation compared to those without this exposure. Collectively, these data identify a novel cellular immune mechanism for fetal brain injury in the setting of intrauterine inflammation.

PMID: [34675929](#)

34. Fibroblast growth factor 19 as a countermeasure to muscle and locomotion dysfunctions in experimental cerebral palsy

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Background: Cerebral palsy (CP) associates cerebral function damages with strong locomotor defects and premature sarcopenia. We previously showed that fibroblast growth factor 19 (FGF19) exerts hypertrophic effects on skeletal muscle and improves muscle mass and strength in mouse models with muscle atrophy. Facing the lack of therapeutics to treat locomotor dysfunctions in CP, we investigated whether FGF19 treatment could have beneficial effects in an experimental rat model of CP. **Methods:** Cerebral palsy was induced in male Wistar rat pups by perinatal anoxia immediately after birth and by sensorimotor restriction of hind paws maintained until Day 28. Daily subcutaneous injections with recombinant human FGF19 (0.1 mg/kg bw) were performed from Days 22 to 28. Locomotor activity and muscle strength were assessed before and after FGF19 treatment. At Day 29, motor coordination on rotarod and various musculoskeletal parameters (weight of tibia bone and of soleus and extensor digitorum longus (EDL) muscles; area of skeletal muscle fibres) were evaluated. In addition, expression of specific genes linked to human CP was measured in rat skeletal muscles. **Results:** Compared to controls, CP rats had reduced locomotion activity (-37.8% of distance travelled, $P < 0.05$), motor coordination (-88.9% latency of falls on rotarod, $P < 0.05$) and muscle strength (-25.1%, $P < 0.05$). These defects were associated with reduction in soleus (-51.5%, $P < 0.05$) and EDL (-42.5%, $P < 0.05$) weight, smaller area of muscle fibres, and with lower tibia weight (-38%, $P < 0.05$). In muscles from rats submitted to CP, changes in the expression levels of several genes related to muscle development and neuromuscular junctions were similar to those found in wrist muscle of children with CP (increased mRNA levels of Igfbp5, Kcnn3, Gdf8, and MyH4 and decreased expression of Myog, Ucp2 and Lpl). Compared with vehicle-treated CP rats, FGF19 administration improved locomotor activity (+53.2%, $P < 0.05$) and muscle strength (+25.7%, $P < 0.05$), and increased tibia weight (+13.8%, $P < 0.05$) and soleus and EDL muscle weight (+28.6% and +27.3%, respectively, $P < 0.05$). In addition, it reduced a number of very small fibres in both muscles ($P < 0.05$). Finally, gene expression analyses revealed that FGF19 might counteract the immature state of skeletal muscles induced by CP. **Conclusions:** These results demonstrate that pharmacological intervention with recombinant FGF19 could restore musculoskeletal and locomotor dysfunction in an experimental CP model, suggesting that FGF19 may represent a potential therapeutic strategy to combat the locomotor disorders associated with CP.

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35. Spinal Tuina Improves Cognitive Impairment in Cerebral Palsy Rats through Inhibiting Pyroptosis Induced by NLRP3 and Caspase-1

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Cerebral palsy (CP) is a severe cerebral disease with high mortality and morbidity, which leads to great challenges for the suffering children and their families. Hence, the need for the efficacious and safe treatments is urgent. As a physical therapy arising from traditional Chinese medicine (TCM), Tuina has shown multiple effects on various diseases, including cerebral palsy. Nevertheless, the detailed mechanisms of Tuina on CP remain unknown, which impedes its further clinical application. Herein, we explored the effects of Tuina on CP and its potential mechanisms. Thirty Sprague Dawley (SD) male rats were randomly divided into sham, model, and Tuina groups (model + Tuina). CP rat model was established by hypoxia-ischemia via permanent occlusion of left common carotid artery and hypoxia for 2.5 hours caused by anaerobic environment, which was subsequently followed by onset of Tuina treatment from postnatal day 7 (P7) to P49. After completion of Tuina treatment, the behavioral tests showed that Tuina treatment not only improved the retarded body weight and impaired motor balance function, but also ameliorated weakened learning and memory function of CP rats. Moreover, immunohistochemistry and western blot also revealed a reduced expression of NLRP3 inflammasome and corresponding pyroptosis-related molecules induced by NLRP3 in CP rats after Tuina treatment. Therefore, our study indicated that Tuina treatment may improve impaired neurocognitive function of CP rats, which was possibly realised via inhibiting NLRP3-induced pyroptosis.

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