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Interventions and Management

1. *Dev Med Child Neurol.* 2015 Feb 23. doi: 10.1111/dmcn.12715. [Epub ahead of print]

Relationships between activities of daily living, upper limb function, and visual perception in children and adolescents with unilateral cerebral palsy.

James S1, Ziviani J, Ware RS, Boyd RN.

AIM: This study examined relationships between activities of daily living (ADL) motor and process skills, unimanual capacity, bimanual performance, and visual perception in children with unilateral cerebral palsy (CP). **METHOD:** Participants were 101 children with unilateral CP (51 males, 50 females; mean age 11y 9mo [SD 2y 5mo; range 8-17y]; Manual Ability Classification System [MACS] level I=24; level II=76; level III=1). Measures were (1) Assessment of Motor and Process Skills (AMPS), (2) Jebsen-Taylor Test of Hand Function (JTTHF), (3) Assisting Hand Assessment (AHA), and (4) Test of Visual Perceptual Skills, 3rd edition (TVPS-3). Regression models were constructed with the AMPS motor scale and AMPS process as the dependent variables. **RESULTS:** The AHA and JTTHF dominant upper limb score together explained 57% of the variance in AMPS motor scale scores. TVPS-3 Visual Sequential Memory, TVPS-3 Visual Closure, and JTTHF dominant upper limb score together explained 35% of the variance in AMPS process scale scores. **INTERPRETATION:** Bimanual performance and unimanual capacity of the dominant upper limb are significantly associated with ADL motor skills in children with unilateral CP. Process skills of ADL are related to visual perceptual ability and dominant upper limb unimanual capacity, which may reflect motor planning required to perform daily tasks.

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2. *J Neurophysiol.* 2015 Feb 25;jn.00602.2014. doi: 10.1152/jn.00602.2014. [Epub ahead of print]

The Magnitude of Somatosensory Cortical Activity is related to the Mobility and Strength Impairments seen in Children with Cerebral Palsy.

Kurz MJ1, Heinrichs-Graham E2, Becker KM3, Wilson TW3.

The noted disruption of thalamocortical connections and abnormalities in tactile sensory function has resulted in a new definition of cerebral palsy (CP) that recognizes the sensorimotor integration process as central to the motor impairments seen in these children. Despite this updated definition, the connection between a child's motor impairments and somatosensory processing remains almost entirely unknown. In this investigation, we explored the relationship between the magnitude of neural activity within the somatosensory cortices, the strength of the

ankle plantarflexors, and the gait spatiotemporal kinematics of a group of children with CP and a typically-developing matched cohort. Our results revealed that the magnitude of somatosensory cortical activity in children with CP had a strong positive relationship with the ankle strength, step length and walking speed. These results suggest that stronger activity within the somatosensory cortices in response to foot somatosensations was related to enhanced ankle plantarflexor strength, and improved mobility in the children with CP. These results provide further support for the notion that children with CP exhibit not only musculoskeletal deficits, but also somatosensory deficits that potentially contribute to their overall functional mobility and strength limitations.

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3. Gait Posture. 2015 Jan 27. pii: S0966-6362(15)00021-1. doi: 10.1016/j.gaitpost.2015.01.018. [Epub ahead of print]

Patellar tendon shortening for flexed knee gait in spastic diplegia.

Sossai R1, Vavken P2, Brunner R3, Camathias C3, Graham HK4, Rutz E5.

We evaluated the outcome of three different approaches to the management of flexed knee gait patients with spastic diplegia. The three surgical procedures were patellar tendon shortening (PTS), PTS combined with rotational osteotomies of the femur and/or tibia, and PTS combined with supracondylar extension osteotomy (SEO) of the distal femur. The primary outcome measure was gait kinematics. The knee gait variable score (GVS) and the gait profile score (GPS) were derived from gait kinematics. 24 patients (16 male and 8 female), mean age 16.1 years (SD 5.8 years), who had surgery between 2002 and 2008, were followed for a mean of 22 months. Knee extension during gait improved by a mean of 20° throughout the gait cycle, with an improvement in the knee GVS of 14° ($p < 0.001$). The overall gait pattern improved with a mean decrease in GPS of 4.6°. Correction of patella alta was demonstrated by an improvement in the Koshino index from 1.34 pre-operatively to 1.10 post-operatively ($p < 0.001$). Knee and gait kinematics, physical examination measures and Koshino Index improved in all three surgical groups, suggesting that a tailored approach to the correction of flexed knee gait in spastic diplegia is both feasible and appropriate.

LEVEL OF EVIDENCE: Level III.

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4. Gait Posture. 2015 Feb 14. pii: S0966-6362(15)00035-1. doi: 10.1016/j.gaitpost.2015.02.001. [Epub ahead of print]

Do children with cerebral palsy change their gait when walking over uneven ground?

Malone A1, Kiernan D2, French H3, Saunders V3, O'Brien T2.

Independently ambulant children with Cerebral Palsy (CP) often report balance difficulties when walking in challenging settings. The aim of this study was to compare gait in children with CP to typically developing (TD) children walking over level ground and uneven ground, as an evaluation of dynamic balance. Thirty-four children participated, 17 with CP (10 hemiplegia and 7 diplegia, mean age 10 years) and 17 TD (mean age 10 years 1 month). Three-dimensional kinematic and kinetic data of the lower limbs and trunk were captured during walking over level and uneven ground using Codamotion®. Statistical analysis was performed using a mixed-effects model two-factor Analysis of Variance (Group×Surface). Over both surfaces, children with CP showed increased trunk movement in the sagittal (Group effect, $p < 0.001$) and transverse planes ($p < 0.001$), and increased pelvic movement in the coronal plane ($p = 0.008$), indicating impaired trunk control. Peak separation between the centre of mass and centre of pressure was reduced in CP, indicating impaired dynamic balance ($p = 0.027$). TD children made a number of significant adaptations to uneven ground, including reduced hip extension (mean difference 3.4°, 95% CI [-5.3, -1.0] $p = 0.006$), and reduced ankle movement in the sagittal (5.2°, 95% CI [0.01, 10] $p = 0.049$) and coronal planes (2.4°, 95% CI [0.3, 4.5], $p = 0.029$), but these adaptations were not measured in CP. A significant Group×Surface

interaction was detected for knee sagittal range ($p=0.009$). The findings indicate that children with CP walk show impaired control of trunk movement and are less able to adapt their gait to uneven ground, particularly at the ankle.

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5. Z Orthop Unfall. 2015 Feb;153(1):93-8. doi: 10.1055/s-0034-1396245. Epub 2015 Feb 27.

The Grice-Green Subtalar Arthrodesis using a Fibular Bone Graft - Follow-Up of 92 Patients [Article in German]

Bollmann C1, Franz A1, Raabe J1.

BACKGROUND: The Grice-Green subtalar arthrodesis is considered to be a valid treatment option of severe pes planovalgus deformity especially in children with cerebral palsy. The purpose of this study was to evaluate long term results using Grice-Green procedure with a fibular bone graft. **MATERIAL AND METHODS:** Between 3/07 and 11/12 92 patients (36 girls, 56 boys) with 127 feet underwent surgery. The average age of patients was 12.3 years (5-21 years). 68 patients had infantile cerebral palsy, 17 patients suffered from other neuromuscular diseases and 7 had idiopathic pes planovalgus deformities. The preoperative and postoperative radiographs with full weight bearing in the frontal and lateral planes were analysed. The mean follow-up was 22.6 months (6-64 months). In addition to that, 23 of the 92 patients (13 girls, 10 boys) were reviewed preoperatively, in the first year after operation and after more than 24 months. **RESULTS:** The mean lateral talocalcaneal angle was reduced from 49.52 to 31.49°. The calcaneal pitch angle changed from 2.95 to 7.55°. The mean lateral talo-first-metatarsal angle improved from -36.98 to -12.32°. The mean frontal talo-first-metatarsal-base-angle increased from -28.48 to -2.64° and the TMT index from -66.46 to -14.96°. All measured angles changed significantly ($p < 0.0001$). There was no significant change after 6-12 month and ≥ 24 month follow-up ($p > 0.05$). Eight feet were not corrected completely, three feet were overcorrected. In one case the fibular graft was reabsorbed. There were degenerative changes of the talus in three cases. 14 feet developed a dorsal bunion with extension deformity of the first metatarsal bone. **CONCLUSIONS:** The Grice-Green subtalar arthrodesis improves foot alignment and can achieve a significant correction also in long-term follow-up.

Georg Thieme Verlag KG Stuttgart · New York.

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6. Z Orthop Unfall. 2015 Feb;153(1):85-92. doi: 10.1055/s-0034-1396186. Epub 2015 Feb 27.

Causes and calculated predictors of a Duchenne gait in adolescents and young adults with cerebral palsy [Article in German]

Klum E1, Streicher H2, Böhm H1, Wagner P2, Döderlein L1.

BACKGROUND: Adolescents with cerebral palsy often complain about a Duchenne gait, which increases the load on the spine, the energy consumption and therefore decreases gait efficiency. However the underlying causes of a Duchenne gait in patients with CP are not clearly researched yet. Nevertheless there is an assumption that excessive trunk lean might assist foot clearance to compensate for muscle weakness or contractures of the legs. In particular weakness, secondary to surgical soft tissue muscle tendon lengthening in childhood, might predispose patients to greater compensatory movements of the trunk. Therefore the aim of this study was to estimate the prevalence, underlying causes and calculated predictors for a Duchenne gait on CP patients with and without previous muscle tendon lengthening. **PATIENTS, MATERIALS AND METHODS:** 50 CP patients between 12 and 22 years with diplegia and GMFCS II (GMFCS: Gross Motor Function Classification System) participated in this study. 25 patients had no previous surgeries (CP-0). 25 patients had previous calf, hamstrings and/or adductor muscle tendon lengthening surgeries (CP-1). Data of 20 typically developed adolescents served as controls (TD). Gait was analysed using an instrumented gait analysis system (Vicon, Oxford, UK) The parameter "thorax obliquity range" (TOR) investigated the dimension of Duchenne gait. **RESULTS:** CP-0 showed a prevalence of 72%, CP-1 of 66% for Duchenne gait. TOR was $5 \pm 2^\circ$, $16 \pm 8^\circ$ and $16 \pm 8^\circ$, for TD, CP-0 and CP-1, respectively. CP-0 and CP-1 showed significant differences in TOR between TD (both $p < 0.001$), but not between CP-0 and CP-1 ($p = 1.0$).

Passive hip abduction range of motion (ROM) showed no significant correlation to TOR in both groups, whereas hip abduction muscle strength revealed significant correlation ($r_s = -0.37$) in CP-0. Best gait predictors in CP-0 patients were increased hip generation work (stance = st) and ankle dorsi flexion (swing = sw), together explaining 47% of the variance in TOR. In CP-1 best gait predictors were increased hip generation work (st) as well as reduced knee flexion (sw) and ankle generation work (st), explaining 31% of the variance in TOR. **CONCLUSION:** With a prevalence of 66% or higher Duchenne gait is a serious gait pathology in CP. Neither the hypothesis that previous muscle tendon lengthening nor that hip adductor contractures increase Duchenne gait could be confirmed in this study. Weak hip abductor muscle strength only showed a small correlation in CP-0. Best predictor in both groups was hip generation work (st). Certain hip abductors (M. gluteus medius ventral; M. gluteus minimus; M. tensor fasciae latae) function also as hip flexors and internal rotators. This leads to the hypothesis that during stance the Duchenne gait unloads the hip abductor muscles and therefore decreases the effect of internal rotation and hip flexion which leads to improved dynamic power of the hip for propulsion. In consequence the resultant hip extension moment increases by reducing the hip flexion moment. Presumably this is due to the fact that patients with CP show a reduced selective muscle control. For CP patients the negative effects of the common pelvis drop and internal rotation of the hip during gait decrease.

Georg Thieme Verlag KG Stuttgart · New York.

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7. Gait Posture. 2015 Feb 2. pii: S0966-6362(15)00027-2. doi: 10.1016/j.gaitpost.2015.01.024. [Epub ahead of print]

Asymmetric pelvic and hip rotation in children with bilateral cerebral palsy: Uni- or bilateral femoral derotation osteotomy?

Niklasch M1, Döderlein L2, Klotz MC1, Braatz F3, Wolf SI1, Dreher T4.

Internal rotation gait is common among children with bilateral cerebral palsy. However, despite bilaterally increased femoral anteversion asymmetric internal rotation gait is often found. Femoral derotation osteotomy (FDO) is commonly performed bilaterally. Variable functional outcomes are reported especially in cases with mild internal hip rotation during gait and abnormal preoperative pelvic rotation. A major question is if a unilateral treatment of the more involved side in asymmetric cases leads to a comparable or even superior outcome. One hundred and nine children with spastic bilateral CP treated with FDO with pre- and 1-year postoperative 3D gait analysis were retrospectively collected. The asymmetry was calculated from the preoperative difference between both limbs in hip rotation obtained by 3D gait analysis. Twenty-eight children with asymmetry larger than 20° were selected and classified into two groups, according to whether they obtained a unilateral or bilateral FDO. Preoperative clinical examination and pre- and postoperative hip and pelvic rotation in gait analysis on the more and the less involved side did not differ significantly between both groups. Interestingly, in both groups, hip rotation did not change significantly in less-involved limbs, although intraoperative derotation averaged 25°. After unilateral FDO a significant change in pelvic rotation resulted, whereas this was not found after bilateral FDO. The results of this study suggest that unilateral FDO in children with asymmetric internal rotation gait leads to a comparable functional outcome compared to bilateral treatment. Furthermore, it was shown for the first time that considering the asymmetry has a positive effect on pelvic rotation.

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8. Laser Ther. 2014 Dec 27;23(4):243-7. doi: 10.5978/islsm.14-OR-17.

The effect of LLLT on bone metabolism in children with severe cerebral palsy (a secondary publication).

Asagai Y1.

BACKGROUND AND AIMS: It is said that the average frequency of bone fracture in hospitalized children with severe cerebral palsy (unable to remain seated) is 1% (0.2 to 2.0%). Cerebral palsy patients' bones are known to be vulnerable to fracture, and refractory bone atrophy may be observed. However, the effect of low level laser

therapy (LLLT) on bone density or bone metabolism has not been fully investigated. In recent years, tests for bone density or bone metabolism markers have become available. MATERIAL AND METHODS: In this study, we evaluated changes in bone density and bone metabolism markers in 4 children with severe cerebral palsy who underwent LLLT for an average of 22 days. RESULTS: B-ALP, a marker of ossification, increased 1 month after the start of irradiation in 3 of the 4 subjects and returned to a level close to the pre-irradiation level 2 months after the start of irradiation. In the remaining subjects in whom B-ALP failed to increase, B-ALP had been low before irradiation. Urinary N-terminal telopeptide (NTx) levels, a marker of bone resorption, decreased in 3 of the 4 subjects after the start of irradiation and remained low even 10 months later. Serum NTx levels tended to decrease in 3 of the 4 subjects. The levels of serum NTx/Crea, Deoxy-Pyridinoline (DPd) and DPd/Crea (DPd/Crea) also decreased in 3 of the 4 subjects. Transient decreases in intact parathyroid hormone (PTH) levels were observed in all 4 cases. Changes were particularly apparent in 2 cases: one with high NTx levels, which showed enhanced bone resorption, and one with high PTH levels, probably due to a vitamin D (VitD) deficiency. Although the metacarpal bone density measured by DIP was found to be lower than in normal children, there were no changes due to LLLT. CONCLUSION: These results suggest that LLLT has a positive influence on bone metabolism in that it temporarily increases bone formation and suppresses bone resorption while also tending to improve secondary hyperparathyroidism caused by VitD deficiency. Enhanced bone resorption in the case with high NTx levels was noteworthy, together with marked changes in the case with high PTH levels due to VitD deficiency. These positive influences on bone metabolism merit attention as potential new indications of LLLT.

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9. *Pediatr Neurol.* 2015 Mar;*52*(3):338-343.e1. doi: 10.1016/j.pediatrneurol.2014.11.009. Epub 2014 Dec 3.

Possible Linkage Between Visual and Motor Development in Children With Cerebral Palsy.

Lew H1, Lee HS2, Lee JY1, Song J2, Min K2, Kim M3.

AIM: The purpose of this study was to examine ophthalmic disorders associated with neurological disorders in children with cerebral palsy. METHODS: Children clinically diagnosed as cerebral palsy with supportive abnormal magnetic resonance imaging results were included in this prospective study. All participants were recommended to have comprehensive ophthalmic exams. To assess motor function, the Gross Motor Function Classification System and the Gross Motor Function Measure were used. To assess motor and cognitive function, the Bayley Scales of Infant Development-II was used. RESULTS: Forty-seven children completed all the evaluations and the data were analyzed. Ametropia was seen in 78.7% and strabismus was seen in 44.7% of the 47 children. When subjects were divided into severely impaired and mildly impaired groups based on Gross Motor Function Classification System level, ametropia was more prevalent in the severely impaired than the mildly impaired (95.8% versus 60.9%, $P < 0.05$). According to quantitative analysis, the severity of gross motor impairment correlated with the degree of refractive error in the subjects older than 36 months ($r = -0.65$ for the Bayley Scales of Infant Development-II motor scale, $P < 0.05$). INTERPRETATION: Based on these findings, children with cerebral palsy with poor gross motor function have a high possibility of severe refractive disorder that becomes evident from 36 months after birth. These results suggest that brain injury and impaired motor development negatively affect ophthalmic development. Hence, an ophthalmic examination is recommended for young children with cerebral palsy to start early management.

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10. *Front Neurol.* 2015 Feb *11*;6:24. doi: 10.3389/fneur.2015.00024. eCollection 2015.

Improving outcomes in cerebral palsy with early intervention: new translational approaches.

Basu AP1, Clowry G1.

[PMID: 25717317](#) [PubMed] Free full text

11. Augment Altern Commun. 2015 Feb 26:1-11. [Epub ahead of print]**Influence of message error type on Korean adults' attitudes toward an individual who uses augmentative and alternative communication.**

Kim JR1, Kim YT, Lee HJ, Park EH.

The aim of this study was to investigate the influence of types of message errors on the attitudes of Korean adults toward a person who uses AAC. The attitudes of 72 adults who speak native Korean were examined through attitude questionnaires completed after viewing videotaped conversations between a boy with cerebral palsy and an adult without disabilities. Each interaction video involved a message with one of six error types, including various types of syntactic, semantic, and pragmatic errors. The participants provided information on their attitude towards the person who used AAC, and ranked their preferences among the six messages. The results provide evidence that attitudes towards the individual using AAC were most positive (in comparison with other conditions) when a pragmatic error was observed. Messages containing a syntactic error were ranked most favorably. Spearman's correlation analyses revealed some relationship between attitudes rating and preferences ranking. Our results provide evidence that specific language and cultural contexts may play an important role in shaping attitudes toward those who use AAC.

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12. Int J Lang Commun Disord. 2015 Feb 19. doi: 10.1111/1460-6984.12151. [Epub ahead of print]**Spoken language comprehension of phrases, simple and compound-active sentences in non-speaking children with severe cerebral palsy.**

Geytenbeek JJ1, Heim MJ, Knol DL, Vermeulen RJ, Oostrom KJ.

BACKGROUND: Children with severe cerebral palsy (CP) (i.e. 'non-speaking children with severely limited mobility') are restricted in many domains that are important to the acquisition of language. **AIMS:** To investigate comprehension of spoken language on sentence type level in non-speaking children with severe CP. **METHODS & PROCEDURES:** From an original sample of 87 non-speaking children with severe CP, 68 passed the pre-test (i.e. they matched at least five spoken words to the corresponding objects) of a specifically developed computer-based instrument for low motor language testing (C-BiLLT), admitting them to the actual C-BiLLT computer test. As a result, the present study included 68 children with severe CP (35 boys, 33 girls; mean age 6;11 years, SD 3;0 years; age range 1;9-11;11 years) who were investigated with the C-BiLLT for comprehension of different sentence types: phrases, simple active sentences (with one or two arguments) and compound sentences. The C-BiLLT provides norm data of typically developing (TD) children (1;6-6;6 years). Binomial logistic regression analyses were used to compare the percentage correct of each sentence type in children with severe CP with that in TD children (subdivided into age groups) and to compare percentage correct within the CP subtypes. **OUTCOMES & RESULTS:** Sentence comprehension in non-speaking children with severe CP followed the developmental trajectory of TD children, but at a much slower rate; nevertheless, they were still developing up to at least age 12 years. Delays in sentence type comprehension increased with sentence complexity and showed a large variability between individual children and between subtypes of CP. Comprehension of simple and syntactically more complex sentences were significantly better in children with dyskinetic CP than in children with spastic CP. Of the children with dyskinetic CP, 10-13% showed comprehension of simple and compound sentences within the percentage correct of TD children, as opposed to none of the children with spastic CP. **CONCLUSION & IMPLICATIONS:** In non-speaking children with severe CP sentence comprehension is delayed rather than deviant. Results indicate the importance of following comprehension skills across all age groups, even beyond age 12 years. Moreover, the subtype of CP should be considered when establishing an educational programme for sentence comprehension, and augmentative and alternative communication support. In addition, educational programmes for children with severe CP should take into account the linguistic hierarchy of sentence comprehension when focusing on the input and understanding of spoken language comprehension.

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13. Qual Health Res. 2015 Feb 23. pii: 1049732315570122. [Epub ahead of print]

Parents' Experiences of Health Care for Their Children With Cerebral Palsy.

Hayles E1, Harvey D2, Plummer D3, Jones A2.

Although current health care service delivery approaches for children with cerebral palsy recognize the importance of including parents in the health care of their child, we do not yet understand how parents experience this phenomenon. In this study, we used grounded theory methodology to explore parents' experiences of health care for their children with cerebral palsy living in a regional area of Australia. Our findings indicate that parents experience health care for their child as a cyclical process of "making the most of their body and their life." Important aspects of care include "learning as you go," "navigating the systems," "meeting needs through partnership," "being empowered or disempowered," and "finding a balance." We suggest modifications to health care service delivery practices that might contribute to improved experiences of health care for this population.

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Prevention and Cure

14. Acta Paediatr. 2015 Feb 22. doi: 10.1111/apa.12983. [Epub ahead of print]

Genes determining the severity of cerebral palsy: the role of single nucleotide polymorphisms on the amount and structure of apolipoprotein E.

Lien E1, Andersen G, Bao Y, Gordish-Dressman H, Skranes JS, Blackman JA, Vik T.

AIM: ApolipoproteinE (apoE) influences repair and other processes in the brain and the apoE4 variant is a risk factor for Alzheimer's disease and for prolonged recovery following traumatic brain injury. We previously reported that specific single nucleotide polymorphisms in the APOE or TOMM40 genes affecting the structure and production of apoE were associated with epilepsy, more impaired hand function and gastrostomy tube feeding in children with cerebral palsy (CP). This study explored how various combinations of the same polymorphisms may affect these clinical manifestations. METHODS: Successful DNA analyses of APOE and TOMM40 were carried out on 227 children. The CP Register of Norway provided details of gross and fine motor function, epilepsy and gastrostomy tube feeding. Possible associations between these clinical manifestations and various combinations of the APOE ϵ 2, ϵ 3 or ϵ 4 alleles and of the rs59007384 polymorphism in the TOMM40 gene were explored. RESULTS: Epilepsy, impaired fine motor function and gastrostomy tube feeding were less common in children carrying the combination of rs59007384 GG and APOE ϵ 2 or ϵ 3 than in children with other combinations. CONCLUSION: Our findings suggest that specific combinations of genes influence the structure and production of apoE differently and affect the clinical manifestations of CP.

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15. Arch Dis Child. 2014 Nov 18. pii: archdischild-2014-307443. doi: 10.1136/archdischild-2014-307443. [Epub ahead of print]

The differential diagnosis of spastic diplegia.

Huntsman R1, Lemire E2, Norton J3, Dzus A4, Blakley P5, Hasal S1.

Spastic diplegia is the most common form of cerebral palsy worldwide. Many disorders mimic spastic diplegia, which can result in misdiagnosis for the child with resultant negative treatment and family counselling implications.

In this paper, the authors provide a brief review of spastic diplegia and the various disorders in the differential diagnosis. We also provide a diagnostic algorithm to assist physicians in making the correct diagnosis.

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16. Cell Transplant. 2015 Feb 2. doi: 10.3727/096368915X686931. [Epub ahead of print]

Current Proceedings of Cerebral Palsy.

Fan HC1, Ho LI, Chi CS, Cheng SN, Juan CJ, Chiang KL, Lin SZ, Harn HJ.

CP is a complicated disease with varying causes and outcomes. It has created significant burden to both affected families and societies, not to mention the quality of life of the patients themselves. There is no cure for the disease; therefore development of effective therapeutic strategies is in great demand. Recent advances in regenerative medicine suggest that the transplantation of stem cells, including embryonic stem cells (ESCs), neural stem cells (NSCs), bone marrow (mesenchymal stem cells; MSCs), induced pluripotent stem cells (iPSCs), umbilical cord blood (UCB) cells, and human embryonic germ (hEG) cells, focusing on the root of the problem, may provide the possibility of developing a complete cure in treating CP. However, safety is the first factor to be considered because some stem cells may cause tumorigenesis. Additionally, more preclinical and clinical studies are needed to determine the type of cells, route of delivery, cell dose, timing of transplantation, and combinatorial strategies to achieve an optimal outcome.

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17. Dev Neurosci. 2015 Feb 25. [Epub ahead of print]

Human Amnion Epithelial Cells Modulate Ventilation-Induced White Matter Pathology in Preterm Lambs.

Barton SK1, Melville JM, Tolcos M, Polglase GR, McDougall AR, Azhan A, Crossley KJ, Jenkin G, Moss TJ.

Background: Preterm infants can be inadvertently exposed to high tidal volumes (VT) during resuscitation in the delivery room due to limitations of available equipment. High VT ventilation of preterm lambs produces cerebral white matter (WM) pathology similar to that observed in preterm infants who develop cerebral palsy. We hypothesized that human amnion epithelial cells (hAECs), which have anti-inflammatory and regenerative properties, would reduce ventilation-induced WM pathology in neonatal late preterm lamb brains. **Methods:** Two groups of lambs (0.85 gestation) were used, as follows: (1) ventilated lambs (Vent; n = 8) were ventilated using a protocol that induces injury (VT targeting 15 ml/kg for 15 min, with no positive end-expiratory pressure) and were then maintained for another 105 min, and (2) ventilated + hAECs lambs (Vent+hAECs; n = 7) were similarly ventilated but received intravenous and intratracheal administration of 9×10^7 hAECs (18×10^7 hAECs total) at birth. Oxygenation and ventilation parameters were monitored in real time; cerebral oxygenation was measured using near-infrared spectroscopy. qPCR (quantitative real-time PCR) and immunohistochemistry were used to assess inflammation, vascular leakage and astrogliosis in both the periventricular and subcortical WM of the frontal and parietal lobes. An unventilated control group (UVC; n = 5) was also used for qPCR analysis of gene expression. Two-way repeated measures ANOVA was used to compare physiological data. Student's t test and one-way ANOVA were used for immunohistological and qPCR data comparisons, respectively. **Results:** Respiratory parameters were not different between groups. Interleukin (IL)-6 mRNA levels in subcortical WM were lower in the Vent+hAECs group than the Vent group ($p = 0.028$). IL-1 β and IL-6 mRNA levels in periventricular WM were higher in the Vent+hAECs group than the Vent group ($p = 0.007$ and $p = 0.001$, respectively). The density of Iba-1-positive microglia was lower in the subcortical WM of the parietal lobes ($p = 0.010$) in the Vent+hAECs group but not in the periventricular WM. The number of vessels in the WM of the parietal lobe exhibiting protein extravasation was lower ($p = 0.046$) in the Vent+hAECs group. Claudin-1 mRNA levels were higher in the periventricular WM ($p = 0.005$). The density of GFAP-positive astrocytes was not different between groups. **Conclusions:** Administration of hAECs at the time of birth alters the effects of injurious ventilation on the preterm neonatal brain. Further studies are required to understand the regional differences in the effects of hAECs on ventilation-induced WM pathology and their net effect on the developing brain. © 2015 S. Karger AG, Basel.

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18. J Matern Fetal Neonatal Med. 2015 Feb 25:1-6. [Epub ahead of print]

Hypoxic ischemic encephalopathy in newborns linked to placental and umbilical cord abnormalities.

Nasiell J1, Papadogiannakis N, Löf E, Elofsson F, Hallberg B.

Objective: Birth asphyxia and hypoxic ischemic encephalopathy (HIE) of the newborn remain serious complications. We present a study investigating if placental or umbilical cord abnormalities in newborns at term are associated with HIE. **Materials and methods:** A prospective cohort study of the placenta and umbilical cord of infants treated with hypothermia (HT) due to hypoxic brain injury and follow-up at 12 months of age has been carried out. The study population included 41 infants treated for HT whose placentas were submitted for histopathological analysis. Main outcome measures were infant development at 12 months, classified as normal, cerebral palsy, or death. A healthy group of 100 infants without HIE and normal follow-up at 12 months of age were used as controls. **Results:** A velamentous or marginal umbilical cord insertion and histological abruption was associated with the risk of severe HIE, OR = 5.63, p = 0.006, respectively, OR = 20.3, p = 0.01 (multiple-logistic regression). Velamentous or marginal umbilical cord insertion was found in 39% among HIE cases compared to 7% in controls. **Conclusions:** Placental and umbilical cord abnormalities have a profound association with HIE. A prompt examination of the placentas of newborns suffering from asphyxia can provide important information on the pathogenesis behind the incident and contribute to make a better early prognosis.

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Cognitive Outcomes After Neonatal Encephalopathy.

Pappas A1, Shankaran S2, McDonald SA3, Vohr BR4, Hintz SR5, Ehrenkranz RA6, Tyson JE7, Yolton K8, Das A9, Bara R2, Hammond J9, Higgins RD10; for the Hypothermia Extended Follow-up Subcommittee of the Eunice Kennedy Shriver NICHD Neonatal Research Network.

OBJECTIVES: To describe the spectrum of cognitive outcomes of children with and without cerebral palsy (CP) after neonatal encephalopathy, evaluate the prognostic value of early developmental testing and report on school services and additional therapies. **METHODS:** The participants of this study are the school-aged survivors of the National Institute of Child Health and Human Development Neonatal Research Network randomized controlled trial of whole-body hypothermia. Children underwent neurologic examinations and neurodevelopmental and cognitive testing with the Bayley Scales of Infant Development-II at 18 to 22 months and the Wechsler intelligence scales and the Neuropsychological Assessment-Developmental Neuropsychological Assessment at 6 to 7 years. Parents were interviewed about functional status and receipt of school and support services. We explored predictors of cognitive outcome by using multiple regression models. **RESULTS:** Subnormal IQ scores were identified in more than a quarter of the children: 96% of survivors with CP had an IQ <70, 9% of children without CP had an IQ <70, and 31% had an IQ of 70 to 84. Children with a mental developmental index <70 at 18 months had, on average, an adjusted IQ at 6 to 7 years that was 42 points lower than that of those with a mental developmental index >84 (95% confidence interval, -49.3 to -35.0; P < .001). Twenty percent of children with normal IQ and 28% of those with IQ scores of 70 to 84 received special educational support services or were held back ≥1 grade level. **CONCLUSIONS:** Cognitive impairment remains an important concern for all children with neonatal encephalopathy.

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