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## Interventions and Management

### 1. Adductor Tenotomy Combined with Palmar Capsulodesis for Spastic Thumb-in-Palm Deformity in Cerebral Palsy: Description of a Surgical Technique and Clinical Results.

Luis-Alejandro G, Bárbara G.

J Hand Surg Asian Pac Vol. 2017 Sep;22(3):315-319. doi: 10.1142/S0218810417500368.

**BACKGROUND:** Spastic thumb deformity in cerebral palsy significantly impedes hand function. Flexion-adduction forces across the first ray is the result from imbalance between intrinsic and extrinsic muscles. Multiples surgeries have been devised for the treatment of this condition such as contracture release and by tendon transfers for balancing the muscles forces. We report the results of a less demanding surgical technique, intended to avoid hyperextension of the metacarpophalangeal joint previously described in other series. **METHODS:** Five patients with cerebral palsy who underwent a surgical correction for their thumb-in-palm deformity between January 2013 and August 2014 were included. All patients were assessed postoperatively with a minimum follow up of six months. Three criteria were chosen to evaluate functional ability: capacity to perform pinch, volitional muscle control and usefulness of the hand in daily life activities. **RESULTS:** Patients who had surgery for spastic thumb deformity were reviewed. The thumb was maintained out of the palm in all patients. Three patients were able to perform correct pinch, achieved volitional muscle control and a more functional hand. One patient had limitation to achieve one of the evaluated daily life activities and one patient lacked active thumb movement for pinch, motor control and achieved no daily life activities. No postoperative complications were recorded. **CONCLUSIONS:** We present a less challenging technique that should be taken into account for the treatment of thumb-in-palm deformity. Appearance and functional improvement can be achieved with this

[PMID: 28774242](#)

### 2. J Effects of Transcutaneous Electrical Acupoint Stimulation on Motor Functions and Self-Care Ability in Children with Cerebral Palsy.

Zhang B, Zhu Y, Jiang C, Li C, Li Y, Bai Y, Wu Y.

Altern Complement Med. 2017 Aug 2. doi: 10.1089/acm.2016.0111. [Epub ahead of print]

**OBJECTIVES:** To observe the effects of transcutaneous electrical acupoint stimulation (TEAS) in improving motor functions and self-care abilities in children with cerebral palsy in their early childhood. **DESIGN:** A preliminary, prospective, cohort study. **SETTINGS/LOCATION:** Multicenter. **SUBJECTS:** Children aged 2-6 years old. **INTERVENTIONS:** Twenty-three children were included in the study and randomly assigned to a control group ([CG] N = 11) or a therapeutic group ([TG] N = 12). In the TG, children were treated with TEAS (Shousanli [LI10] and Waiguan [SJ5]) plus the exercise therapy, while in the control group, they were treated with sham TEAS plus exercise therapy. Therapies were performed five days per week for eight weeks. **OUTCOME MEASURES:** The Gross Motor Function Measure (GMFM) and the Functional Independent Measurement for children (WeeFIM) were used to evaluate motor functions and self-care abilities before and after the

therapies. RESULTS: Greater improvements were observed in the TG concerning all the measurements, although without statistical differences. The increments of the GMFMS score and the WeeFIM motor, self-care and total scores were  $36.08 \pm 18.34$  (26%),  $16.17 \pm 8.21$  (33%),  $7.67 \pm 3.42$  (40%) and  $20.33 \pm 10.08$  (28%) in the TG, while  $22.73 \pm 16.54$  (17%),  $9.09 \pm 9.43$  (19%),  $5.64 \pm 6.73$  (29%) and  $12.82 \pm 11.77$  (18%) in the CG, respectively. No statistically significant correlations were shown between functional improvements and the demographics in the TG or the CG. The GMFMS improvement was not statistically correlated with the improvements of the WeeFIM motor, self-care or total scores. However, the WeeFIM motor, self-care and total score were significantly positively correlated with one another in both groups ( $P < 0.01$ ). No adverse effect was recorded during the study. CONCLUSION: TEAS may be effective in improving motor functions and self-care abilities in children with cerebral palsy, in addition to conventional exercise therapy. Larger samples are required to confirm the efficacies.

[PMID: 28767271](#)

### 3. Upper Limb Function, Kinematic Analysis, and Dystonia Assessment in Children With Spastic Diplegic Cerebral Palsy and Periventricular Leukomalacia.

Pons R, Vanezis A, Skouteli H, Papavasiliou A, Tziomaki M, Syrengelas D, Darras N.

J Child Neurol. 2017 Jan 1;883073817722451. doi: 10.1177/0883073817722451. [Epub ahead of print]

Assessment of upper limb function, kinematic analysis, and dystonia in patients with spastic diplegia cerebral palsy and periventricular leukomalacia. Seven children with spastic diplegia cerebral palsy and 8 controls underwent upper limb kinematics. Movement duration, average and maximum linear velocity, index of curvature, index of dystonia, and target accuracy and stability were analyzed. In the patients with spastic diplegia, Gross Motor Function and Manual Ability Classification Systems were determined, and spasticity and dystonia were rated using the Modified Ashworth and the Burke-Fahn-Marsden Dystonia scales respectively. Children with spastic diplegia demonstrated a tendency toward higher index of dystonia reflecting overflow, higher index of curvature, lower velocities, and poor target accuracy and stability. All patients showed clinical evidence of dystonia in the upper limbs. Dystonia scores correlated with the Manual Ability Classification System ( $r = 0.86$ ,  $P = .01$ ) and with the index of dystonia ( $r = 0.82$ ,  $P = .02$ ). Children with spastic diplegia cerebral palsy present dystonia in the upper limbs. This is functionally relevant and can be measured with kinematic analysis.

[PMID: 28776460](#)

### 4. Treadmill interventions in children under six years of age at risk of neuromotor delay.

Valentín-Gudiol M, Mattern-Baxter K, Girabent-Farrés M, Bagur-Calafat C, Hadders-Algra M, Angulo-Barroso RM.

Cochrane Database Syst Rev. 2017 Jul 29;7:CD009242. doi: 10.1002/14651858.CD009242.pub3.

BACKGROUND: Delayed motor development may occur in children with Down syndrome, cerebral palsy, general developmental delay or children born preterm. It limits the child's exploration of the environment and can hinder cognitive and social-emotional development. Literature suggests that task-specific training, such as locomotor treadmill training, facilitates motor development. OBJECTIVES: To assess the effectiveness of treadmill interventions on locomotor development in children with delayed ambulation or in pre-ambulatory children (or both), who are under six years of age and who are at risk for neuromotor delay. SEARCH METHODS: In May 2017, we searched CENTRAL, MEDLINE, Embase, six other databases and a number of trials registers. We also searched the reference lists of relevant studies and systematic reviews. SELECTION CRITERIA: We included randomised controlled trials (RCTs) and quasi-RCTs that evaluated the effect of treadmill intervention in the target population. DATA COLLECTION AND ANALYSIS: Four authors independently extracted the data. Outcome parameters were structured according to the International Classification of Functioning, Disability and Health model. MAIN RESULTS: This is an update of a Cochrane review from 2011, which included five trials. This update includes seven studies on treadmill intervention in 175 children: 104 were allocated to treadmill groups, and 71 were controls. The studies varied in population (children with Down syndrome, cerebral palsy, developmental delay or at moderate risk for neuromotor delay); comparison type (treadmill versus no treadmill; treadmill with versus without orthoses; high- versus low-intensity training); study duration, and assessed outcomes. Due to the diversity of the studies, only data from five studies were used in meta-analyses for five outcomes: age of independent walking onset, overall gross motor function, gross motor function related to standing and walking, and gait velocity. GRADE assessments of quality of the evidence ranged from high to very low. The effects of treadmill intervention on independent walking onset compared to no treadmill intervention was population dependent, but showed no overall effect (mean difference (MD) -2.08, 95% confidence intervals (CI) -5.38 to 1.22, 2 studies, 58 children; moderate-quality evidence): 30 children with Down syndrome benefited from treadmill training (MD -4.00, 95%

CI -6.96 to -1.04), but 28 children at moderate risk of developmental delay did not (MD -0.60, 95% CI -2.34 to 1.14). We found no evidence regarding walking onset in two studies that compared treadmill intervention with and without orthotics in 17 children (MD 0.10, 95% CI -5.96 to 6.16), and high- versus low-intensity treadmill interventions in 30 children with Down syndrome (MD -2.13, 95% CI -4.96 to 0.70). Treadmill intervention did not improve overall gross motor function (MD 0.88, 95% CI -4.54 to 6.30, 2 studies, 36 children; moderate-quality evidence) or gross motor skills related to standing (MD 5.41, 95% CI -1.64 to 12.43, 2 studies, 32 children; low-quality evidence), and had a negligible improvement in gross motor skills related to walking (MD 4.51, 95% CI 0.29 to 8.73, 2 studies, 32 children; low-quality evidence). It led to improved walking skills in 20 ambulatory children with developmental delay (MD 7.60, 95% CI 0.88 to 14.32, 1 study) and favourable gross motor skills in 12 children with cerebral palsy (MD 8.00, 95% CI 3.18 to 12.82). A study which compared treadmill intervention with and without orthotics in 17 children with Down syndrome suggested that adding orthotics might hinder overall gross motor progress (MD -8.40, 95% CI -14.55 to -2.25). Overall, treadmill intervention showed a very small increase in walking speed compared to no treadmill intervention (MD 0.23, 95% CI 0.08 to 0.37, 2 studies, 32 children; high-quality evidence). Treadmill intervention increased walking speed in 20 ambulatory children with developmental delay (MD 0.25, 95% CI 0.08 to 0.42), but not in 12 children with cerebral palsy (MD 0.18, 95% CI -0.09 to 0.45). **AUTHORS' CONCLUSIONS:** This update of the review from 2011 provides additional evidence of the efficacy of treadmill intervention for certain groups of children up to six years of age, but power to find significant results still remains limited. The current findings indicate that treadmill intervention may accelerate the development of independent walking in children with Down syndrome and may accelerate motor skill attainment in children with cerebral palsy and general developmental delay. Future research should first confirm these findings with larger and better designed studies, especially for infants with cerebral palsy and developmental delay. Once efficacy is established, research should examine the optimal dosage of treadmill intervention in these populations.

[PMID: 28755534](#)

##### **5. Selective dorsal rhizotomy: A multidisciplinary approach to treating spastic diplegia.**

Al-Shaar HA, Imtiaz MT, Alhalabi H, Alsubaie SM, Sabbagh AJ.

Asian J Neurosurg. 2017 Jul-Sep;12(3):454-465. doi: 10.4103/1793-5482.175625.

**BACKGROUND:** Spasticity is a motor disorder that interferes with mobility and affects the quality of life. Different approaches have been utilized to address patients with spastic diplegia, among which is selective dorsal rhizotomy (SDR). Although SDR has been shown to be efficacious in treating spastic patients, many neurologists and neurosurgeons are not well aware of the procedure, its indications, and expected outcomes due to the limited number of centers performing this procedure. **OBJECTIVES:** The aim of this study is to describe the collaborative multidisciplinary approach between neurosurgeons, neurophysiologists, and physiotherapists in performing SDR. In addition, we delineate three illustrative cases in which SDR was performed in our patients. **MATERIALS AND METHODS:** A retrospective review and analysis of the clinical records of our three patients who underwent SDR was conducted and reported. Patients' outcomes were evaluated and compared to preoperative measurements based on clinical examination of power, tone (Ashworth scale), gait, and range of motion, as well as subjective functional assessment, gross motor function classification system, and gross motor function measure with follow-up at 6, 12, and 24 months postoperatively. A detailed description of our neurosurgical technique in performing SDR in collaboration with neurophysiology and physiotherapy monitoring is provided. **RESULTS:** The three patients who underwent SDR using our multidisciplinary approach improved both functionally and objectively after the procedure. No intraoperative or postoperative complications were encountered. All patients were doing well over a long postoperative follow-up period. **CONCLUSION:** A multidisciplinary approach to treating spastic diplegia with SDR can provide good short-term and long-term outcomes in select patients suffering from spastic diplegia.

[PMID: 28761524](#)

##### **6. Lumbosacral Dorsal Rhizotomy for Spastic Cerebral Palsy: A Health Technology Assessment.**

Health Quality Ontario. Pron G, Chan B, Tu HA, Xie X, Weir M, Wells D, Higgins C.

Ont Health Technol Assess Ser. 2017 Jul 6;17(10):1-186. eCollection 2017.

**BACKGROUND:** Cerebral palsy, a spectrum of neuromuscular conditions caused by abnormal brain development or early damage to the brain, is the most common cause of childhood physical disability. Lumbosacral dorsal rhizotomy is a neurosurgical procedure that permanently decreases spasticity and is always followed by physical therapy. The objectives of this health technology assessment were to evaluate the clinical effectiveness, safety, cost effectiveness, and family perspectives of dorsal rhizotomy. **METHODS:** We performed a systematic literature search until December 2015 with auto-alerts until

December 2016. Search strategies were developed by medical librarians, and a single reviewer reviewed the abstracts. The health technology assessment included a clinical review based on functional outcomes, safety, and treatment satisfaction; an economic study reviewing cost-effective literature; a budget impact analysis; and interviews with families evaluating the intervention. RESULTS: Eighty-four studies (1 meta-analysis, 5 randomized controlled studies [RCTs], 75 observational pre-post studies, and 3 case reports) were reviewed. A meta-analysis of RCTs involving dorsal rhizotomy and physical therapy versus physical therapy confirmed reduced lower-limb spasticity and increased gross motor function (4.5%,  $P = .002$ ). Observational studies reported statistically significant improvements in gross motor function over 2 years or less (12 studies, GRADE moderate) and over more than 2 years (10 studies, GRADE moderate) as well as improvements in functional independence in the short term (10 studies, GRADE moderate) and long term (4 studies, GRADE low). Major operative complications, were infrequently reported (4 studies). Bony abnormalities and instabilities monitored radiologically in the spine (15 studies) and hip (8 studies) involved minimal or clinically insignificant changes after surgery. No studies evaluated the cost effectiveness of dorsal rhizotomy. The budget impact of funding dorsal rhizotomy for treatment of Ontario children with cerebral palsy was \$1.3 million per year. Families reported perceived improvements in their children and expressed satisfaction with treatment. Ontario families reported inadequate medical information on benefits or risk to make an informed decision, enormous financial burdens, and lack rehabilitation support after surgery. CONCLUSIONS: Lumbrosacral dorsal rhizotomy and physical therapy effectively reduces lower-limb spasticity in children with spastic cerebral palsy and significantly improves their gross motor function and functional independence. Major peri-operative complications were infrequently reported. Families reported perceived improvements with dorsal rhizotomy, and surgery and post-operative rehabilitation were intensive and demanding.

[PMID: 28757906](#)

### **7. Explicit and implicit motor learning in children with unilateral cerebral palsy.**

van der Kamp J, Steenbergen B, Masters RSW.

Disabil Rehabil. 2017 Jul 30:1-8. doi: 10.1080/09638288.2017.1360403. [Epub ahead of print]

OBJECTIVES: The current study aimed to investigate the capacity for explicit and implicit learning in children with unilateral cerebral palsy. PARTICIPANTS: Children with left and right unilateral cerebral palsy and typically developing children shuffled disks toward a target. DESIGN: A prism-adaptation design was implemented, consisting of pre-exposure, prism exposure, and post-exposure phases. Half of the participants were instructed about the function of the prism glasses, while the other half were not. MEASURES: For each trial, the distance between the target and the shuffled disk was determined. Explicit learning was indicated by the rate of adaptation during the prism exposure phase, whereas implicit learning was indicated by the magnitude of the negative after-effect at the start of the post-exposure phase. Results No significant effects were revealed between typically developing participants and participants with unilateral cerebral palsy. Comparison of participants with left and right unilateral cerebral palsy demonstrated that participants with right unilateral cerebral palsy had a significantly lower rate of adaptation than participants with left unilateral cerebral palsy, but only when no instructions were provided. The magnitude of the negative after-effects did not differ significantly between participants with right and left unilateral cerebral palsy. CONCLUSIONS: The capacity for explicit motor learning is reduced among individuals with right unilateral cerebral palsy when accumulation of declarative knowledge is unguided (i.e., discovery learning). In contrast, the capacity for implicit learning appears to remain intact among individuals with left as well as right unilateral cerebral palsy. Implications for rehabilitation Implicit motor learning interventions are recommended for individuals with cerebral palsy, particularly for individuals with right unilateral cerebral palsy Explicit motor learning interventions for individual with cerebral palsy - if used - best consist of singular verbal instruction.

[PMID: 28756681](#)

### **8. Ocular Motor Function in Children with Spastic Hemiplegia Evaluated by the Ocular Motor Score.**

Rydberg A, Ygge J, Olsson M.

Strabismus. 2017 Aug 3:1-4. doi: 10.1080/09273972.2017.1350727. [Epub ahead of print]

PURPOSE: To assess the ocular motor functions in children with spastic hemiplegia by using the Ocular Motor Score (OMS). MATERIAL: This study included 34 children, median age 11 years. The children were divided into 3 groups according to the underlying brain lesion; group 1 malformations, group 2 white matter damage of immaturity (WMDI), and group 3 cortical/subcortical lesions. METHODS: The OMS protocol consists of 15 different subtests evaluating ocular motor functions. The

OMS is divided into 2 parts, a static and a dynamic. The results from each subtest are scored 0, 0.3, 0.5, or 1, according to the level of disturbance, where 0 corresponds to normal function and 1 represents the maximum disability in the certain subtest. A total OMS (tOMS) between 0 and 15 can be obtained. RESULTS: The median tOMS in the whole spastic hemiplegia group was 2.5 (range 1.3-5.8). The highest median tOMS 5.2 was seen in group 1, in the children with malformations. Strabismus was found in 45% (15/34) of the children, with an equal percentage in all 3 groups. CONCLUSIONS: The children with spastic hemiplegia had a median tOMS of 2.7 and the highest median tOMS was seen in children with malformations. The OMS protocol is easy to use clinically and gives a quick overview of the patient's ocular motor functions.

[PMID: 28771056](#)

## 9. [Feeding, eating, and swallowing disorders in infants and children : An overview].

[Article in German]

Schwemmler C, Arens C.

HNO. 2017 Jul 31. doi: 10.1007/s00106-017-0388-y. [Epub ahead of print]

Swallowing is a dynamic process that requires more than 30 muscles in the recruitment/coordination of the lips, tongue, palate, pharynx, larynx and esophagus. The eating and swallowing procedure is learned in sensitive or critical periods: when a certain degree of maturation has been achieved, the appropriate stimulus permits a certain milestone of development to occur. The swallowing procedure occurs in three main stages oral, pharyngeal, and esophageal. Therefore, swallowing disorders may present in any, some, or all of these stages in addition to feeding problems. Adult dysphagia, or difficulty swallowing, has long been reported in the literature. Infants and children also experience feeding disorders and swallowing problems, either because of developmental disorders, syndromes, behavioral or neurological conditions, respiratory problems, and/or gastroesophageal reflux, eosinophilic esophagitis or anatomical deficits. Feeding problems or dysphagia are seen in up to 25% of all children; approximately 40% of prematurely born infants have swallowing disorders, up to 64-78% with developmental disorders and up to 99% with cerebral palsy. Diagnostic options include health status, broad social environment, parent-child interactions, and parental concerns. Evaluation of dysphagia and feeding disorders involves a multifactorial approach. Imaging studies may include videofluoroscopy and/or fiberoptic evaluation of swallowing (FEES). Successful oral feeding must be measured in quality of meal time experiences with best possible oral sensorimotor skills and safe swallowing while not jeopardizing a child's functional health status or the parent-child relationship. An interdisciplinary team approach enables coordinated global assessment and therapy planning.

[PMID: 28761970](#)

## Prevention and Cure

### 10. Identifying relevant biomarkers of brain injury from structural MRI: Validation using automated approaches in children with unilateral cerebral palsy.

Pagnozzi AM, Dowson N, Doecke J, Fiori S, Bradley AP, Boyd RN, Rose S.

PLoS One. 2017 Aug 1;12(8):e0181605. doi: 10.1371/journal.pone.0181605. eCollection 2017.

Previous studies have proposed that the early elucidation of brain injury from structural Magnetic Resonance Images (sMRI) is critical for the clinical assessment of children with cerebral palsy (CP). Although distinct aetiologies, including cortical maldevelopments, white and grey matter lesions and ventricular enlargement, have been categorised, these injuries are commonly only assessed in a qualitative fashion. As a result, sMRI remains relatively underexploited for clinical assessments, despite its widespread use. In this study, several automated and validated techniques to automatically quantify these three classes of injury were generated in a large cohort of children (n = 139) aged 5-17, including 95 children diagnosed with unilateral CP. Using a feature selection approach on a training data set (n = 97) to find severity of injury biomarkers predictive of clinical function (motor, cognitive, communicative and visual function), cortical shape and regional lesion burden were most often chosen associated with clinical function. Validating the best models on the unseen test data (n = 42), correlation values ranged between 0.545 and 0.795 (p<0.008), indicating significant associations with clinical function. The measured prevalence

of injury, including ventricular enlargement (70%), white and grey matter lesions (55%) and cortical malformations (30%), were similar to the prevalence observed in other cohorts of children with unilateral CP. These findings support the early characterisation of injury from sMRI into previously defined aetiologies as part of standard clinical assessment. Furthermore, the strong and significant association between quantifications of injury observed on structural MRI and multiple clinical scores accord with empirically established structure-function relationships.

[PMID: 28763455](#)

### **11. Activation of Neonatal Microglia can be Influenced by Other Neural Cells.**

Turano A, Lawrence JH, Schwarz JM.

Neurosci Lett. 2017 Jul 31. pii: S0304-3940(17)30624-9. doi: 10.1016/j.neulet.2017.07.052. [Epub ahead of print]

During development, microglial progenitor cells migrate into the brain from the periphery, a process critical to the maturation of the developing brain. Although they perform functions similar to mature, adult microglia, immature microglia are distinct from mature microglia. Activation of immature microglia, via an early-life immune challenge, can lead to persistent changes in microglial function, resulting in long-term neuronal and cognitive dysfunction. Early-life immune activation is associated with multiple neurodevelopmental disorders, including autism, ADHD, schizophrenia, and cerebral palsy - disorders with known or suspected immune etiologies, and strong sex biases for males. Activation of immature microglia requires further examination to determine its potential role in these neurodevelopmental disorders. More work is also necessary to better understand the relationship between developing microglia and other developing neural cells during this critical period of development. Thus, we treated freshly isolated, sex-specific microglia from the rat hippocampus with lipopolysaccharide (LPS) on P4, in either the presence or absence of other neural cells. Mixed and microglial-specific cultures were analyzed for inflammatory gene expression to determine whether immature microglia exhibited a sex-specific response to immune activation, and if the presence of all other neural cells influenced that response. We found that the microglial response to an LPS-induced immune activation differed depending on the presence of other neural cells in the culture. We found very few sex differences in the cytokine response, except that the microglial expression of IL-6 following immune activation was more robust in male microglia that were in the presence of other neural cells than female microglia in the same condition.

[PMID: 28774571](#)

### **12. De novo and rare inherited copy-number variations in the hemiplegic form of cerebral palsy.**

Zarrei M, Fehlings DL, Mawjee K, Switzer L, Thiruvahindrapuram B, Walker S, Merico D, Casallo G, Uddin M, MacDonald JR, Gazzellone MJ, Higginbotham EJ, Campbell C, deVeber G, Frid P, Gorter JW, Hunt C, Kawamura A, Kim M, McCormick A, Mesterman R, Samdup D, Marshall CR, Stavropoulos DJ, Wintle RF, Scherer SW.

Genet Med. 2017 Aug 3. doi: 10.1038/gim.2017.83. [Epub ahead of print]

**Purpose**Hemiplegia is a subtype of cerebral palsy (CP) in which one side of the body is affected. Our earlier study of unselected children with CP demonstrated de novo and clinically relevant rare inherited genomic copy-number variations (CNVs) in 9.6% of participants. Here, we examined the prevalence and types of CNVs specifically in hemiplegic CP.**Methods**We genotyped 97 unrelated probands with hemiplegic CP and their parents. We compared their CNVs to those of 10,851 population controls, in order to identify rare CNVs (<0.1% frequency) that might be relevant to CP. We also sequenced exomes of "CNV-positive" trios.**Results**We detected de novo CNVs and/or sex chromosome abnormalities in 7/97 (7.2%) of probands, impacting important developmental genes such as GRIK2, LAMA1, DMD, PTPRM, and DIP2C. In 18/97 individuals (18.6%), rare inherited CNVs were found, affecting loci associated with known genomic disorders (17p12, 22q11.21) or involving genes linked to neurodevelopmental disorders.**Conclusion**We found an increased rate of de novo CNVs in the hemiplegic CP subtype (7.2%) compared to controls (1%). This result is similar to that for an unselected CP group. Combined with rare inherited CNVs, the genomic data impacts the understanding of the potential etiology of hemiplegic CP in 23/97 (23.7%) of participants.**GENETICS IN MEDICINE advance online publication, 3 August 2017; doi:10.1038/gim.2017.83.**

[PMID: 28771244](#)

### 13. Two unrelated children with overlapping 6q25.3 deletions, motor speech disorders, and language delays.

Peter B, Lancaster H, Vose C, Fares A, Schrauwen I, Huentelman M.

Am J Med Genet A. 2017 Aug 2. doi: 10.1002/ajmg.a.38385. [Epub ahead of print]

Interstitial and terminal 6q25 deletions are associated with developmental delays, hypotonia, eye pathologies, craniofacial dysmorphologies, and structural brain anomalies. In most cases, speech and language deficits are not described in detail. We report on a case (Patient 1, age 7 years) with a de novo 6q25.3-qter deletion, 11.1 Mb long and encompassing 108 genes, and a case (Patient 2, age 5 years) with an inherited interstitial 6q25.3 deletion, located within Patient 1's deletion region and 403 kb long, the smallest 6q25 deletion reported to date. Both children have hypotonia, motor speech disorders, and expressive language delays. Patient 1's speech was characterized by childhood apraxia of speech (CAS) and dysarthria. Other findings include developmental delay, ataxic cerebral palsy, optic nerve dysplasia, and atypical brain morphologies regarding the corpus callosum and gyration patterns, a clinical profile that closely matches a previously reported case with a nearly identical deletion. Patient 2 had speech characterized by CAS and typical nonverbal processing abilities. His father, a carrier, had typical speech and language but showed difficulties with complex motor speech and hand motor tasks, similar to other adults with residual signs of CAS. The small deletion in this family contains the IGF2R-AIRN-SLC22A2-SLC22A3 gene cluster, which is associated with imprinting and maternal-specific expression of IGF2R, Slc22a2, and Slc22a3 in mice, whereas imprinting in humans is a polymorphic trait. The shared phenotypes in the two patients might be associated with the deletion of the gene cluster.

[PMID: 28767196](#)

### 14. Fluid supplementation for neonatal unconjugated hyperbilirubinaemia.

Lai NM, Ahmad Kamar A, Choo YM, Kong JY, Ngim CF.

Cochrane Database Syst Rev. 2017 Aug 1;8:CD011891. doi: 10.1002/14651858.CD011891.pub2. [Epub ahead of print]

**BACKGROUND:** Neonatal hyperbilirubinaemia is a common problem which carries a risk of neurotoxicity. Certain infants who have hyperbilirubinaemia develop bilirubin encephalopathy and kernicterus which may lead to long-term disability. Phototherapy is currently the mainstay of treatment for neonatal hyperbilirubinaemia. Among the adjunctive measures to compliment the effects of phototherapy, fluid supplementation has been proposed to reduce serum bilirubin levels. The mechanism of action proposed includes direct dilutional effects of intravenous (IV) fluids, or enhancement of peristalsis to reduce enterohepatic circulation by oral fluid supplementation. **OBJECTIVES:** To assess the risks and benefits of fluid supplementation compared to standard fluid management in term and preterm newborn infants with unconjugated hyperbilirubinaemia who require phototherapy. **SEARCH METHODS:** We used the standard search strategy of Cochrane Neonatal to search the Cochrane Central Register of Controlled Trials (CENTRAL; 2017, Issue 5), MEDLINE via PubMed (1966 to 7 June 2017), Embase (1980 to 7 June 2017), and CINAHL (1982 to 7 June 2017). We also searched clinical trials databases, conference proceedings, and the reference lists of retrieved articles for randomised controlled trials and quasi-randomised trials. **SELECTION CRITERIA:** We included randomised controlled trials that compared fluid supplementation against no fluid supplementation, or one form of fluid supplementation against another. **DATA COLLECTION AND ANALYSIS:** We extracted data using the standard methods of the Cochrane Neonatal Review Group using the Covidence platform. Two review authors independently assessed the eligibility and risk of bias of the retrieved records. We expressed our results using mean difference (MD), risk difference (RD), and risk ratio (RR) with 95% confidence intervals (CIs). **MAIN RESULTS:** Out of 1449 articles screened, seven studies were included. Three articles were awaiting classification, among them, two completed trials identified from the trial registry appeared to be unpublished so far. There were two major comparisons: IV fluid supplementation versus no fluid supplementation (six studies) and IV fluid supplementation versus oral fluid supplementation (one study). A total of 494 term, healthy newborn infants with unconjugated hyperbilirubinaemia were evaluated. All studies were at high risk of bias for blinding of care personnel, five studies had unclear risk of bias for blinding of outcome assessors, and most studies had unclear risk of bias in allocation concealment. There was low- to moderate-quality evidence for all major outcomes. In the comparison between IV fluid supplementation and no supplementation, no infant in either group developed bilirubin encephalopathy in the one study that reported this outcome. Serum bilirubin was lower at four hours postintervention for infants who received IV fluid supplementation (MD -34.00  $\mu\text{mol/L}$  (-1.99 mg/dL), 95% CI -52.29 (3.06) to -15.71 (0.92); participants = 67, study = 1) (low quality of evidence, downgraded one level for indirectness and one level for suspected publication bias). Beyond eight hours postintervention, serum bilirubin was similar between the two groups. Duration of phototherapy was significantly shorter for fluid-supplemented infants, but the estimate was affected by heterogeneity which was not clearly explained (MD -10.70 hours, 95% CI -15.55 to -5.85; participants = 218; studies = 3;  $I^2 = 67\%$ ). Fluid-supplemented infants were less likely to require exchange transfusion (RR 0.39, 95% CI 0.21 to 0.71; RD -0.01, 95% CI -0.04 to 0.02; participants = 462; studies = 6;  $I^2 = 72\%$ ) (low quality of evidence, downgraded one level due to

inconsistency, and another level due to suspected publication bias), and the estimate was similarly affected by unexplained heterogeneity. The frequencies of breastfeeding were similar between the fluid-supplemented and non-supplemented infants in days one to three based on one study (estimate on day three: MD 0.90 feeds, 95% CI -0.40 to 2.20; participants = 60) (moderate quality of evidence, downgraded one level for imprecision). One study contributed to all outcome data in the comparison of IV versus oral fluid supplementation. In this comparison, no infant in either group developed abnormal neurological signs. Serum bilirubin, as well as the rate of change of serum bilirubin, were similar between the two groups at four hours after phototherapy (serum bilirubin: MD 11.00  $\mu\text{mol/L}$  (0.64 mg/dL), 95% CI -21.58 (-1.26) to 43.58 (2.55); rate of change of serum bilirubin: MD 0.80  $\mu\text{mol/L/hour}$  (0.05 mg/dL/hour), 95% CI -2.55 (-0.15) to 4.15 (0.24); participants = 54 in both outcomes) (moderate quality of evidence for both outcomes, downgraded one level for indirectness). The number of infants who required exchange transfusion was similar between the two groups (RR 1.60, 95% CI 0.60 to 4.27; RD 0.11, 95% CI -0.12 to 0.34; participants = 54). No infant in either group developed adverse effects including vomiting or abdominal distension. AUTHORS' CONCLUSIONS: There is no evidence that IV fluid supplementation affects important clinical outcomes such as bilirubin encephalopathy, kernicterus, or cerebral palsy in healthy, term newborn infants with unconjugated hyperbilirubinaemia requiring phototherapy. In this review, no infant developed these bilirubin-associated clinical complications. Low- to moderate-quality evidence shows that there are differences in total serum bilirubin levels between fluid-supplemented and control groups at some time points but not at others, the clinical significance of which is uncertain. There is no evidence of a difference between the effectiveness of IV and oral fluid supplementations in reducing serum bilirubin. Similarly, no infant developed adverse events or complications from fluid supplementation such as vomiting or abdominal distension. This suggests a need for future research to focus on different population groups with possibly higher baseline risks of bilirubin-related neurological complications, such as preterm or low birthweight infants, infants with haemolytic hyperbilirubinaemia, as well as infants with dehydration for comparison of different fluid supplementation regimen.

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