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Interventions and Management

1. Eur J Paediatr Neurol. 2016 Apr 22. pii: S1090-3798(16)30012-5. doi: 10.1016/j.ejpn.2016.04.008. [Epub ahead of print]

Safety profile of incobotulinum toxin A [Xeomin®] in gastrocnemius muscles injections in children with cerebral palsy: Randomized double-blind clinical trial.

Carraro E, Trevisi E, Martinuzzi A.

BACKGROUND: The only two preparations of botulinum toxin A for which there are published evidences of efficacy in children with cerebral palsy are onabotulinum toxin A (Botox®) and abobotulinum toxin A (Dyport®); these toxins should be considered generally safe and appropriate in the treatment for localized upper and lower limb spasticity. **AIMS:** To establish the safety profile of incobotulinum toxin A (Xeomin®) in children with cerebral palsy and muscle spasticity. **METHODS:** Randomized double-blind controlled trial that involved the recruitment of children of both sexes with spastic hemiplegia or diplegia in cerebral palsy, aged between 3 and 18 years. Children were randomized to either the study group (SG, incobotulinum toxin A) or the control group (CG, onabotulinum toxin A) both to be injected with 5units/kg on gastrocnemius (medialis and lateralis) muscles. The occurrence of adverse events at baseline, after 48 h, 10 days and 3 months was recorded by the caregivers in a checklist that listed both common and uncommon side effects. **RESULTS:** 35 patients were treated (CG = 18; SG = 17); the 2 groups were well balanced regarding demographics and anthropometry characteristics. At least 1 adverse event occurred in 49% of patients within first 2 days, 46% between 2 and 10 days, and 12% between 10 and 90 days. All the reported events were minor; no serious adverse event was recorded. Fatigue was the most frequent complaint. There was no significant difference in frequency and type of events between the 2 groups. **CONCLUSION:** Incobotulinum toxin A and onabotulinum toxin A share similar profile of safety in the treatment of lower limb spasticity in CP children.

[PMID: 27177451](#)

2. Explore (NY). 2016 Apr 19. pii: S1550-8307(16)30025-8. doi: 10.1016/j.explore.2016.04.004. [Epub ahead of print]

The Effects of a Home-Based Connective Tissue Targeting Therapy on Hip Development in Children With Cerebral Palsy: Six Case Reports.

Drewes E, Driscoll M, Blyum L, Vincentz D.

Hip subluxation in children with Cerebral Palsy (CP) has an incidence of 10-30 %, and children with severe CP having the highest incidence. The condition deteriorates if left untreated. Surgery is the most common method used in managing hip subluxation because standard conservative therapies do not improve it. Surgery may have to be repeated and comes at a biological cost to the child. A new home-based CAM, Advanced Biomechanical Rehabilitation (ABR), has shown encouraging results leading to improved spinal stability and stability in sitting in children with severe CP. This case report examines hip development over time in six children with severe CP in the ABR Program. Changes in their clinical picture and pelvic X-Rays are reported. ABR appeared to help stabilize and improve hip subluxation, resulting in these children not

requiring further surgical intervention. These findings warrant further investigation of ABR as a noninvasive therapy for hip subluxation.

[PMID: 27198038](#)

3. J Child Orthop. 2016 May 13. [Epub ahead of print]

Correlation between the Gait Deviation Index and gross motor function (GMFCS level) in children with cerebral palsy.

Malt MA, Aarli Å, Bogen B, Fevang JM.

AIM: The Gait Deviation Index (GDI) is a score derived from three-dimensional gait analysis (3DGA). The GDI provides a numerical value that expresses overall gait pathology (ranging from 0 to 100, where 100 indicates the absence of gait pathology). The aim of this study was to investigate the association between the GDI and different levels of gross motor function [defined as the Gross Motor Function Classification System (GMFCS)] and to explore if age, height, weight, gender and cerebral palsy (CP) subclass (bilateral and unilateral CP) exert any influence on the GDI in children with unilateral and bilateral spastic CP. **METHODS:** We calculated the GDI of 109 children [73 % boys, mean age 9.7 years (standard deviation, SD 3.5)] with spastic CP, classified at GMFCS levels I, II and III. Twenty-three normally developing children were used as controls [61 % boys, mean age 9.9 years (SD 2.6)]. Multiple linear regression analysis was performed. **RESULTS:** The mean GDI in the control group was 100 (SD 7.5). The mean GDI in the GMFCS level I group was 81 (SD 11), in the GMFCS level II group 71 (SD 11) and in the GMFCS level III group 60 (SD 9). Multiple linear regression analysis showed that gender, age and CP subclass had no significant correlation with the GDI, whereas height and weight had a slight impact. **CONCLUSION:** This study showed a strong correlation between the GDI and GMFCS levels. The present data indicate that calculation of the GDI is a useful tool to characterise walking difficulties in children with spastic CP.

[PMID: 27177476](#)

4. J Pediatr Orthop. 2016 May 19. [Epub ahead of print]

Proximal Femoral Growth Modification: Effect of Screw, Plate, and Drill on Asymmetric Growth of the Hip.

d'Heurle A, McCarthy J, Klimaski D, Stringer K.

BACKGROUND: Guided growth has long been used in the lower extremities but has not been applied to varus or valgus deformity in the hip, as may occur in children with cerebral palsy or developmental dysplasia of the hip. The purpose of this study was to determine if screw, plate, or drilling techniques decreased the femoral neck-shaft angle (NSA) and articular trochanteric disease (ATD), as well as describe growth plate structural changes with each method. **METHODS:** Twelve 8-week-old lambs underwent proximal femoral hemiepiphyseodesis (IACUC approved) using either a screw (n=4), plate (n=4), or drilling procedure (n=4). Postoperative time was 6 months. Radiographs taken after limb harvest were used to measure NSA and ATD. Differences between treated and control sides were determined by 1-tailed paired t tests and Bonferroni ($\alpha=0.05/3$). Histology was obtained for 1 limb pair per group. Proximal femurs were cut in midcoronal plane and the longitudinal growth plates were examined for structural changes. **RESULTS:** The mean NSA measured 7 degrees less than controls in this model using the screw technique, and this difference was statistically significant. Differences between the control and the treated groups did not reach statistical significance for either the plate or the drill group. Differences in ATD were not statistically significant, although there was a trend for larger ATD measurements using the screw technique. Histologically, physal changes were observed on the operative sides in screw and plate specimens, but not drill specimens, compared with contralateral sham control. The screw specimen exhibited the most severe changes, with growth plate closure over half the section. The plate specimen showed focal loss of the physis across the section, but with no evidence of closure. **CONCLUSIONS:** This study builds on previous work that indicates screw hemiepiphyseodesis can effectively alter the shape of the proximal femur, and result in a lower neck-shaft angle (or lesser valgus). This study suggests that implantation of a screw is likely to be more effective than a plate or drilling procedure in decreasing the NSA in skeletally immature hips. **CLINICAL SIGNIFICANCE:** If further preclinical, and later clinical, studies demonstrate reproducible efficacy, guided growth of the proximal femur may eventually become a viable option for treatment or prevention of hip deformity in select patients.

[PMID: 27203823](#)

5. J Phys Ther Sci. 2016 Apr;28(4):1387-91. doi: 10.1589/jpts.28.1387. Epub 2016 Apr 28.

Clinical usefulness of augmented reality using infrared camera based real-time feedback on gait function in cerebral palsy: a case study.

Lee BH.

[Purpose] This study investigated the effects of real-time feedback using infrared camera recognition technology-based augmented reality in gait training for children with cerebral palsy. [Subjects] Two subjects with cerebral palsy were recruited. [Methods] In this study, augmented reality based real-time feedback training was conducted for the subjects in two 30-minute sessions per week for four weeks. Spatiotemporal gait parameters were used to measure the effect of augmented reality-based real-time feedback training. [Results] Velocity, cadence, bilateral step and stride length, and functional ambulation improved after the intervention in both cases. [Conclusion] Although additional follow-up studies of the augmented reality based real-time feedback training are required, the results of this study demonstrate that it improved the gait ability of two children with cerebral palsy. These findings suggest a variety of applications of conservative therapeutic methods which require future clinical trials.

[PMID: 27190489](#)

6. Front Hum Neurosci. 2016 May 4;10:203. doi: 10.3389/fnhum.2016.00203. eCollection 2016.

Increased Adaptation Rates and Reduction in Trial-by-Trial Variability in Subjects with Cerebral Palsy Following a Multi-session Locomotor Adaptation Training.

Mawase F, Bar-Haim S, Joubran K, Rubin L, Karniel A, Shmuelof L.

Cerebral Palsy (CP) results from an insult to the developing brain and is associated with deficits in locomotor and manual skills and in sensorimotor adaptation. We hypothesized that the poor sensorimotor adaptation in persons with CP is related to their high execution variability and does not reflect a general impairment in adaptation learning. We studied the interaction between performance variability and adaptation deficits using a multi-session locomotor adaptation design in persons with CP. Six adolescents with diplegic CP were exposed, during a period of 15 weeks, to a repeated split-belt treadmill perturbation spread over 30 sessions and were tested again 6 months after the end of training. Compared to age-matched healthy controls, subjects with CP showed poor adaptation and high execution variability in the first exposure to the perturbation. Following training they showed marked reduction in execution variability and an increase in learning rates. The reduction in variability and the improvement in adaptation were highly correlated in the CP group and were retained 6 months after training. Interestingly, despite reducing their variability in the washout phase, subjects with CP did not improve learning rates during washout phases that were introduced only four times during the experiment. Our results suggest that locomotor adaptation in subjects with CP is related to their execution variability. Nevertheless, while variability reduction is generalized to other locomotor contexts, the development of savings requires both reduction in execution variability and multiple exposures to the perturbation.

[PMID: 27199721](#)

7. Neuromodulation. 2016 May 18. doi: 10.1111/ner.12449. [Epub ahead of print]

Intrathecal Baclofen Therapy in a Child With Severe Scoliosis: Report of 2 Cases.

Sasaki N, Ogiwara H.

OBJECTIVE: Scoliosis is commonly found in children with cerebral palsy. Many patients with cerebral palsy and scoliosis undergo intrathecal baclofen (ITB) pump placement. The authors report 2 cases with cerebral palsy and severe scoliosis treated with intrathecal baclofen. **METHOD:** The case of a 7-year-old boy with shunted hydrocephalus required surgical revision of the intrathecal catheter, while the other patient without shunt did not require revision. In the patient with shunted hydrocephalus, after the initial placement of baclofen pump and catheter at Th3 level, spasticity of lower extremities did not improve. The Indium111 diethylenetriamine pentaacetic acid (In111 DTPA) scintigraphy with injection of In111 DTPA through the pump did not demonstrate distribution of the tracer to the lumbosacral area. Conversely, by direct injection of In111 DTPA through lumbar puncture, the tracer distributed in the whole spinal canal. **RESULT:** Replacement of the tip of the catheter caudal to the curve of the scoliosis improved the symptom. **CONCLUSION:** The authors suggest that, in patients with severe scoliosis and shunted hydrocephalus, it may be necessary to place the tip of the catheter caudal to the curve of the scoliosis for correction of spasticity of lower extremities.

[PMID: 27191796](#)

8. Front Psychol. 2016 May 3;7:643. doi: 10.3389/fpsyg.2016.00643. eCollection 2016.

A Perceptual Motor Intervention Improves Play Behavior in Children with Moderate to Severe Cerebral Palsy.

Ryalls BO, Harbourne R, Kelly-Vance L, Wickstrom J, Stergiou N, Kyvelidou A.

For children with moderate or severe cerebral palsy (CP), a foundational early goal is independent sitting. Sitting offers additional opportunities for object exploration, play and social engagement. The achievement of sitting coincides with important milestones in other developmental areas, such as social engagement with others, understanding of spatial relationships, and the use of both hands to explore objects. These milestones are essential skills necessary for play behavior. However, little is known about how sitting and play behavior might be affected by a physical therapy intervention in children with moderate or severe CP. Therefore, our overall purpose in this study was to determine if sitting skill could be advanced in children with moderate to severe CP using a perceptual motor intervention, and if play skills would change significantly as sitting advanced. Thirty children between the ages of 18 months and 6 years who were able to hold prop sitting for at least 10 s were recruited for this study. Outcome measures were the sitting subsection of the Gross Motor Function Measure (GMFM), and the Play Assessment of Children with Motor Impairment play assessment scale, which is a modified version of the Play in Early Childhood Evaluation System. Significant improvements in GMFM sitting scores ($p < 0.001$) and marginally significant improvement in play assessment scores ($p = 0.067$) were found from pre- to post-intervention. Sitting change explained a significant portion of the variance in play change for children over the age of 3 years, who were more severely affected by CP. The results of this study indicate that advances in sitting skill may be a factor in supporting improvements in functional play, along with age and severity of physical impairment.

[PMID: 27199868](#)

9. Augment Altern Commun. 2016 May 17:1-11. [Epub ahead of print]

Mastery motivation in children with complex communication needs: longitudinal data analysis.

Medeiros KF, Cress CJ, Lambert MC.

This study compared longitudinal changes in mastery motivation during parent-child free play for 37 children with complex communication needs. Mastery motivation manifests as a willingness to work hard at tasks that are challenging, which is an important quality to overcoming the challenges involved in successful expressive communication using AAC. Unprompted parent-child play episodes were identified in three assessment sessions over an 18-month period and coded for nine categories of mastery motivation in social and object play. All of the object-oriented mastery motivation categories and one social mastery motivation category showed an influence of motor skills after controlling for receptive language. Object play elicited significantly more of all of the object-focused mastery motivation categories than social play, and social play elicited more of one type of social-focused mastery motivation behavior than object play. Mastery motivation variables did not differ significantly over time for children. Potential physical and interpersonal influences on mastery motivation for parents and children with complex communication needs are discussed, including broadening the procedures and definitions of mastery motivation beyond object-oriented measurements for children with complex communication needs.

[PMID: 27184193](#)

10. Child Care Health Dev. 2016 May 19. doi: 10.1111/cch.12350. [Epub ahead of print]

Treatment with botulinum toxin in children with cerebral palsy: a qualitative study of parents' experiences.

Lorin K, Forsberg A.

BACKGROUND: In children with cerebral palsy everyday movements such as walking, standing and using one's hands can be difficult to perform because of spasticity. Botulinum neurotoxin type A (BoNT-A) are often used to reduce spasticity. The aim of this study was to describe how parents of children with cerebral palsy experienced the child's treatment with BoNT-A, how the child was affected by the treatment and how spasticity affected the child. **METHODS:** A qualitative study in which 15 parents of children (6-13 years old) with cerebral palsy were interviewed about their experiences of the BoNT-A treatment. The children had received several BoNT-A treatments. An interview guide was used with topics: the child's functions before and after the treatment, the outcomes of the treatment and how they valued the BoNT-A treatment. Content analysis was used to analyse the interviews. **RESULTS:** The analyses resulted in two themes: 'When softness comes and goes' and 'Both want and do not want'. The reduction of spasticity - softness - was described to promote motor functions, and facilitate the next step in

motor development. The children were described as being more active out of their own initiative and having a happier mood. Spasticity, described as stiffness, was described to make walking more strenuous as well as interfering with activities. The BoNT-A injection procedure was perceived as troublesome and painful for the child, and sometimes traumatic for both children and parents. CONCLUSIONS: Treatment with BoNT-A was described as facilitating motor development and activity. The children's and the parents' negative experiences of the injection procedure should be addressed.

[PMID: 27198886](#)

Prevention and Cure

11. *Nat Rev Dis Primers*. 2016 Jan 7;2:15082. doi: 10.1038/nrdp.2015.82.

Cerebral palsy.

Graham HK, Rosenbaum P, Paneth N, Dan B, Lin JP, Damiano DL, Becher JG, Gaebler-Spira D, Colver A, Reddihough DS, Crompton KE, Lieber RL.

Cerebral palsy is the most common cause of childhood-onset, lifelong physical disability in most countries, affecting about 1 in 500 neonates with an estimated prevalence of 17 million people worldwide. Cerebral palsy is not a disease entity in the traditional sense but a clinical description of children who share features of a non-progressive brain injury or lesion acquired during the antenatal, perinatal or early postnatal period. The clinical manifestations of cerebral palsy vary greatly in the type of movement disorder, the degree of functional ability and limitation and the affected parts of the body. There is currently no cure, but progress is being made in both the prevention and the amelioration of the brain injury. For example, administration of magnesium sulfate during premature labour and cooling of high-risk infants can reduce the rate and severity of cerebral palsy. Although the disorder affects individuals throughout their lifetime, most cerebral palsy research efforts and management strategies currently focus on the needs of children. Clinical management of children with cerebral palsy is directed towards maximizing function and participation in activities and minimizing the effects of the factors that can make the condition worse, such as epilepsy, feeding challenges, hip dislocation and scoliosis. These management strategies include enhancing neurological function during early development; managing medical co-morbidities, weakness and hypertonia; using rehabilitation technologies to enhance motor function; and preventing secondary musculoskeletal problems. Meeting the needs of people with cerebral palsy in resource-poor settings is particularly challenging.

[PMID: 27188686](#)

12. *Am J Obstet Gynecol*. 2016 May 10. pii: S0002-9378(16)30199-5. doi: 10.1016/j.ajog.2016.05.004. [Epub ahead of print]

Proximity of magnesium exposure to delivery and neonatal outcomes.

Turitz AL, Too GT, Gyamfi-Bannerman C.

BACKGROUND: In infants delivered preterm, magnesium sulfate reduces cerebral palsy in survivors. The benefit of magnesium given remote from delivery is unclear. **OBJECTIVE:** Our objective is to evaluate the association of time from last exposure to magnesium with cerebral palsy. **STUDY DESIGN:** Secondary analysis of a multicenter trial evaluating magnesium for neuroprotection. For this study, we included women with live, non-anomalous, singleton gestations who received magnesium. Pregnancies with missing information at 2-year follow-up were excluded. Women were divided into 2 groups based on exposure timing: last infusion of magnesium <12 hours and last infusion of magnesium ≥12 hours prior to delivery. The primary outcome was cerebral palsy of any severity at 2 years of life. Secondary outcomes were moderate/severe cerebral palsy and moderate/severe cerebral palsy or death. Chi-squared, Student's t-test, and Mann Whitney U were used for bivariate associations. We fit a multivariable logistic regression model to adjust for confounders. **RESULTS:** 906 infants were analyzed. 568 were last exposed to magnesium <12 hours prior to delivery and 338 were last exposed ≥12 hours. Cerebral palsy occurred in 28 offspring (3%), 2.3% of those last exposed <12 hours vs. 4.4% last exposed ≥12 hours prior to delivery, p=0.07. On adjusted analyses, last exposure to magnesium <12 hours prior to delivery was associated with a significant reduction in cerebral palsy compared to last exposure ≥12 hours (adjusted odds ratio 0.41, 95% confidence interval 0.18-0.91, p=0.03). There was no difference in secondary outcomes. **CONCLUSION:** Exposure to magnesium proximal to delivery (<12 hours) is associated with reduced odds of cerebral palsy compared to more remote exposure. This highlights the importance of timing of magnesium for neuroprotection for women at risk of preterm delivery.

[PMID: 27177525](#)

13. Eur J Paediatr Neurol. 2016 May 6. pii: S1090-3798(16)30020-4. doi: 10.1016/j.ejpn.2016.04.016. [Epub ahead of print]

A change in temporal organization of fidgety movements during the fidgety movement period is common among high risk infants.

Sæther R, Støen R, Vik T, Fjørtoft T, Vågen RT, Silberg IE, Loennecken M, Møinichen UI, Lydersen S, Adde L.

AIM: General movement assessment (GMA) at 9-20 weeks post-term, can effectively predict cerebral palsy. Our aim was to evaluate intra-individual variability of the temporal organization of fidgety movements (FMs) in high risk infants. MATERIAL AND METHODS: 104 High risk infants (66 males) with at least two video recordings from the FMs period participated. 45 of the infants had GA <28 weeks and/or BW ≤800 g. Mean post-term age at first and second assessments was 11.0 (8-16) and 14.0 (11-17) weeks, respectively, and median time-difference between the assessments was 2.0 (range: three days to six weeks) weeks. Video recordings were analyzed according to Prechtl's GMA. RESULTS: 33 (32%) Infants were classified differently at first and second assessments. Six infants (6%) changed from normal to abnormal, and 10 (10%) changed from abnormal to normal FMs. Seven of the ten who changed classification from abnormal to normal were born before GA 26 weeks. A change between intermittent and continual, which are both considered normal, was observed in 17 (16%) infants. CONCLUSION: A change in temporal organization of FMs is common in high risk infants. Especially in extremely preterm infants with abnormal FMs, more than one assessment should be performed before long-term prognosis is considered.

[PMID: 27185580](#)

14. Front Neurol. 2016 Apr 25;7:57. doi: 10.3389/fneur.2016.00057. eCollection 2016.

Rodent Hypoxia-Ischemia Models for Cerebral Palsy Research: A Systematic Review.

Rumajogee P, Bregman T, Miller SP, Yager JY, Fehlings MG.

Cerebral palsy (CP) is a complex multifactorial disorder, affecting approximately 2.5-3/1000 live term births, and up to 22/1000 prematurely born babies. CP results from injury to the developing brain incurred before, during, or after birth. The most common form of this condition, spastic CP, is primarily associated with injury to the cerebral cortex and subcortical white matter as well as the deep gray matter. The major etiological factors of spastic CP are hypoxia/ischemia (HI), occurring during the last third of pregnancy and around birth age. In addition, inflammation has been found to be an important factor contributing to brain injury, especially in term infants. Other factors, including genetics, are gaining importance. The classic Rice-Vannucci HI model (in which 7-day-old rat pups undergo unilateral ligation of the common carotid artery followed by exposure to 8% oxygen hypoxic air) is a model of neonatal stroke that has greatly contributed to CP research. In this model, brain damage resembles that observed in severe CP cases. This model, and its numerous adaptations, allows one to finely tune the injury parameters to mimic, and therefore study, many of the pathophysiological processes and conditions observed in human patients. Investigators can recreate the HI and inflammation, which cause brain damage and subsequent motor and cognitive deficits. This model further enables the examination of potential approaches to achieve neural repair and regeneration. In the present review, we compare and discuss the advantages, limitations, and the translational value for CP research of HI models of perinatal brain injury.

[PMID: 27199883](#)

15. JAMA. 2016 May 17;315(19):2079-85. doi: 10.1001/jama.2016.5504.

Effect of Early Prophylactic High-Dose Recombinant Human Erythropoietin in Very Preterm Infants on Neurodevelopmental Outcome at 2 Years: A Randomized Clinical Trial.

Natalucci G, Latal B, Koller B, Rügger C, Sick B, Held L, Bucher HU, Fauchère JC; Swiss EPO Neuroprotection Trial Group.

IMPORTANCE: Very preterm infants are at risk of developing encephalopathy of prematurity and long-term neurodevelopmental delay. Erythropoietin treatment is neuroprotective in animal experimental and human clinical studies. OBJECTIVE: To determine whether prophylactic early high-dose recombinant human erythropoietin (rhEPO) in preterm infants improves neurodevelopmental outcome at 2 years' corrected age. DESIGN, SETTING, AND PARTICIPANTS: Preterm infants born between 26 weeks 0 days' and 31 weeks 6 days' gestation were enrolled in a randomized, double-blind, placebo-controlled, multicenter trial in Switzerland between 2005 and 2012. Neurodevelopmental assessments at age 2 years were completed in 2014.

INTERVENTIONS: Participants were randomly assigned to receive either rhEPO (3000 IU/kg) or placebo (isotonic saline, 0.9%) intravenously within 3 hours, at 12 to 18 hours, and at 36 to 42 hours after birth. **MAIN OUTCOMES AND MEASURES:** Primary outcome was cognitive development assessed with the Mental Development Index (MDI; norm, 100 [SD, 15]; higher values indicate better function) of the Bayley Scales of Infant Development, second edition (BSID-II) at 2 years corrected age. The minimal clinically important difference between groups was 5 points (0.3 SD). Secondary outcomes were motor development (assessed with the Psychomotor Development Index), cerebral palsy, hearing or visual impairment, and anthropometric growth parameters. **RESULTS:** Among 448 preterm infants randomized (mean gestational age, 29.0 [range, 26.0-30.9] weeks; 264 [59%] female; mean birth weight, 1210 [range, 490-2290] g), 228 were randomized to rhEPO and 220 to placebo. Neurodevelopmental outcome data were available for 365 (81%) at a mean age of 23.6 months. In an intention-to-treat analysis, mean MDI was not statistically significantly different between the rhEPO group (93.5 [SD, 16.0] [95% CI, 91.2 to 95.8]) and the placebo group (94.5 [SD, 17.8] [95% CI, 90.8 to 98.5]) (difference, -1.0 [95% CI, -4.5 to 2.5]; $P = .56$). No differences were found between groups in the secondary outcomes. **CONCLUSIONS AND RELEVANCE:** Among very preterm infants who received prophylactic early high-dose rhEPO for neuroprotection, compared with infants who received placebo, there were no statistically significant differences in neurodevelopmental outcomes at 2 years. Follow-up for cognitive and physical problems that may not become evident until later in life is required.

[PMID: 27187300](#)

16. Neuro Endocrinol Lett. 2016 May 15;37(2):79-96. [Epub ahead of print]

Neonatal brain injury as a consequence of insufficient cerebral oxygenation.

Placha K, Luptakova D, Baciak L, Ujhazy E, Juranek I.

Neonatal brain hypoxic-ischemic injury represents a serious health care and socio-economical problem since it is one of the most common causes of mortality and morbidity of newborns. Neonatal hypoxic-ischemic encephalopathy is often associated with signs of perinatal asphyxia, with an incidence of about 2-4 per 1,000 live births and mortality rate up to 20%. In about one half of survivors, cerebral hypoxic-ischemic insult may result in more or less pronounced neuro-psychological sequelae of immediate or delayed nature, such as seizures, cerebral palsy or behavioural and learning disabilities, including attention-deficit hyperactivity disorder. Hypoxic-ischemic injury develops as a consequence of transient or permanent restriction of blood supply to the brain. Severity of hypoxic-ischemic encephalopathy varies depending on the intensity and duration of hypoxia-ischemia, on the type and size of the brain region affected, and on the maturity of the foetal/neonatal brain. Though a primary cause of hypoxic-ischemic injury is lack of oxygen in the neonatal brain, underlying mechanisms of subsequent events that are critical for developing hypoxic-ischemic encephalopathy are less understood. Their understanding is however necessary for elaborating effective management for newborns that underwent cerebral hypoxic-ischemic insult and thus are at risk of a negative outcome. The present paper summarizes current knowledge on cerebral hypoxic-ischemic injury of the neonate, fundamental processes involved in etiopathogenesis, with a special focus on cellular and molecular mechanisms and particular attention on certain controversial aspects of oxidative stress involvement.

[PMID: 27179569](#)

17. Physiol Meas. 2016 May 20;37(6):751-764. [Epub ahead of print]

In vivo quantification of intraventricular hemorrhage in a neonatal piglet model using an EEG-layout based electrical impedance tomography array.

Tang T, Weiss MD, Borum P, Turovets S, Tucker D, Sadleir R.

Intraventricular hemorrhage (IVH) is a common occurrence in the days immediately after premature birth. It has been correlated with outcomes such as periventricular leukomalacia (PVL), cerebral palsy and developmental delay. The causes and evolution of IVH are unclear; it has been associated with fluctuations in blood pressure, damage to the subventricular zone and seizures. At present, ultrasound is the most commonly used method for detection of IVH, but is used retrospectively. Without the presence of adequate therapies to avert IVH, the use of a continuous monitoring technique may be somewhat moot. While treatments to mitigate the damage caused by IVH are still under development, the principal benefit of a continuous monitoring technique will be in investigations into the etiology of IVH, and its associations with periventricular injury and blood pressure fluctuations. Electrical impedance tomography (EIT) is potentially of use in this context as accumulating blood displaces higher conductivity cerebrospinal fluid (CSF) in the ventricles. We devised an electrode array and EIT measurement strategy that performed well in detection of simulated ventricular blood in computer models and phantom studies. In this study we describe

results of pilot in vivo experiments on neonatal piglets, and show that EIT has high sensitivity and specificity to small quantities of blood (<1 ml) introduced into the ventricle. EIT images were processed to an index representing the quantity of accumulated blood (the 'quantity index', QI). We found that QI values were linearly related to fluid quantity, and that the slope of the curve was consistent between measurements on different subjects. Linear discriminant analysis showed a false positive rate of 0%, and receiver operator characteristic analysis found area under curve values greater than 0.98 to administered volumes between 0.5, and 2.0 ml. We believe our study indicates that this method may be well suited to quantitative monitoring of IVH in newborns, simultaneously or interleaved with electroencephalograph assessments.

[PMID: 27206102](#)

18. Ultrasound Obstet Gynecol. 2016 May 17. doi: 10.1002/uog.15961. [Epub ahead of print]

Increased nuchal translucency thickness and the risk of neurodevelopmental disorders.

Hellmuth SG, Pedersen LH, Miltoft CB, Petersen OB, Kjaergaard S, Ekelund C, Tabor A.

OBJECTIVE: To investigate the association between fetal nuchal translucency thickness (NT) and neurodevelopmental disorders in euploid children. **METHOD:** This study included 222,505 euploid children, with a routine first trimester screening. They were divided into three groups by NT thickness: NT <95th percentile, 217,103 (97.6%), NT 95th -99th percentile, 4,760 (2.1%), and NT >99th percentile 642 (0.3%). All children were followed-up through national patient registries at a mean age of 4.4 years. We obtained information on diagnoses of mental retardation, autism spectrum disorders (ASDs), cerebral palsy, epilepsy and febrile seizures. **RESULTS:** There was no excess risk of neurodevelopmental disorders among euploid children with a NT between 95th and 99th percentile. For children with a NT >99th percentile, there were increased risks of mental retardation (OR=6.16, 95% confidence interval (CI): 1.51-25.0, 2 cases) and ASDs (OR=2.48, 95%CI: 1.02-5.99, 5 cases) compared to children with a NT<95th percentile (110 and 686 cases of mental retardation and ASDs, respectively). There was no detected increased risk of cerebral palsy (OR= 1.91, 95%CI: 0.61-5.95, 3 cases), epilepsy (OR= 1.51, 95%CI: 0.63-3.66, 5 cases) or febrile seizures (OR=0.72, 95%CI: 0.44-1.16, 17 cases) among children with a NT >99th percentile. **CONCLUSION:** In a large unselected cohort, euploid fetuses with a NT 95th -99th percentile had no increased risk of neurodevelopmental disorders. Among euploid fetuses with a NT >99th percentile there was an increased risk of mental retardation and ASDs but the absolute risk was low (<1%) and thus reassuring.

[PMID: 27183961](#)