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Professor Nadia Badawi AM

Macquarie Group Foundation Chair of Cerebral Palsy

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Interventions and Management

1. Perspectives on tactile intervention for children with cerebral palsy: a framework to guide clinical reasoning and future research.

Auld ML, Johnston LM.

Disabil Rehabil. 2017 Apr 14:1-6. doi: 10.1080/09638288.2017.1312571. [Epub ahead of print]

PURPOSE: Many children with cerebral palsy (CP) are known to experience tactile impairments. Research evaluating specific interventions to manage this is, however, minimal. This paper seeks to consolidate current literature and provide a framework to help clinicians and researchers think strategically about tactile treatment selection and future research planning. **METHOD:** The framework is described via a novel analogy - "The Apartment Block Theory". The theory describes the relative effectiveness of three intervention strategies aimed at overcoming a poorly responsive tactile system: (1) Pressing the buzzer - providing repeated passive tactile stimulation at the periphery; (2) Sneaking in the door - providing active tactile-enhanced motor training that capitalises on the opportunity to provide high-dose tactile input during motor interventions; and (3) Connecting another way - providing visually enhanced touch strategies with the aim of enhancing tactile function, which can be compared to phoning the apartment as an alternative to using the buzzer. **RESULTS:** Using this theory, the paper describes which sub-groups of children with CP may benefit from each intervention strategy when considering their capabilities in visual, motor, and attention domains. **CONCLUSIONS:** This theory can assist clinicians to provide effective interventions and researchers to make informed future research decisions to optimise tactile function for children with CP. Implications for Rehabilitation Although tactile impairments are reported to be common in children with cerebral palsy, very few successful interventions are reported in the literature. Visually enhanced touch is a successful strategy for treating tactile impairments in children with cerebral palsy who have sufficient vision and attention. Combining intentional tactile input with upper limb movement training may improve tactile function in children with cerebral palsy who have sufficient movement and attention. In children who have complex co-morbidities, including both visual and movement impairments, it may be necessary to consider providing passive tactile stimulation in tactile intervention.

[PMID: 28407718](#)

2. Effects of Antigravity Treadmill Training on Gait, Balance, and Fall Risk in Children With Diplegic Cerebral Palsy.

El-Shamy SM.

Am J Phys Med Rehabil. 2017 Apr 13. doi: 10.1097/PHM.0000000000000752. [Epub ahead of print]

OBJECTIVE: The aim of this study was to investigate the effects of antigravity treadmill training on gait, balance, and fall risk in children with diplegic cerebral palsy. **DESIGN:** Thirty children with diplegic cerebral palsy were selected for this randomized controlled study. They were randomly assigned to (1) an experimental group that received antigravity treadmill

training (20 mins/d, 3 d/wk) together with traditional physical therapy for 3 successive mos and (2) a control group that received only traditional physical therapy program for the same period. Outcomes included selected gait parameters, postural stability, and fall risk. Outcomes were measured at baseline and after 3 mos of intervention. RESULTS: Children in both groups showed significant improvements in the mean values of all measured variables ($P < 0.05$), with significantly greater improvements in the experimental group than the control group. The posttreatment gait parameters (i.e., velocity, stride length, cadence, and percent of time spent in double-limb support) were 0.74 m/sec, 119 steps/min, 0.75 m/sec, 0.65 sec, and 55.9% as well as 0.5 m, 125 steps/min, 0.6 m/sec, 0.49 sec, and 50.4% for the experimental and control group, respectively. CONCLUSIONS: Antigravity treadmill training may be a useful tool for improving gait parameters, balance, and fall risk in children with diplegic cerebral palsy.

[PMID: 28410250](#)

3. Evaluation of Functional Mobility Outcomes Following Electrical Stimulation in Children With Spastic Cerebral Palsy.

Mukhopadhyay R, Lenka PK, Biswas A, Mahadevappa M.

J Child Neurol. 2017 Jan 1:883073817700604. doi: 10.1177/0883073817700604. [Epub ahead of print]

This study investigated the clinical feasibility of electrical stimulation in enhancing ankle dorsiflexion of the tibialis anterior muscle to improve mobility in children with spastic cerebral palsy. The intervention group received electrical stimulation therapy for 30 minutes and physiotherapy for another 30 minutes for 5 days a week, up to 12 weeks. Gait parameters, Gross Motor Function Measure, Physiological Cost Index, surface electromyogram, and electroencephalogram (EEG) data were recorded pre- and posttreatment. Data were compared with the control group, which received only conventional physiotherapy for 60 minutes. There was an increase in walking speed (17.67%) and Gross Motor Function Measure scores (2.1%) while the Physiological Cost Index value was decreased (19.7%). The analysis of features extracted from the surface electromyogram showed an increase in muscle strength and that of EEG showed increased motor activities. Hence, electrical stimulation combined with conventional physiotherapy improve gait, muscle strength, and motor activities in children with spastic cerebral palsy.

[PMID: 28393668](#)

4. Serial Casting as an Adjunct to Botulinum Toxin Type A Treatment in Children With Cerebral Palsy and Spastic Paraparesis With Scissoring of the Lower Extremities.

Dai AI, Demiryürek AT.

J Child Neurol. 2017 Jan 1:883073817701526. doi: 10.1177/0883073817701526. [Epub ahead of print]

The purpose of this study was to examine whether combination therapy of serial casting and botulinum toxin type A injection can further enhance the effects of botulinum toxin type A in children with cerebral palsy with scissoring of both legs. This study was a prospective and randomized trial. The children were divided into 2 groups, one of which received serial casting after botulinum toxin type A ($n = 40$), and the other which only received botulinum toxin type A ($n = 40$). Serial casting started 3 weeks after the botulinum toxin type A. Both groups received physiotherapy. Groups were assessed at baseline then compared at 6 and 12 weeks following the intervention. Significant improvements in Gross Motor Function Measure-66 and Caregiver Health Questionnaire were recorded in both groups ($P < .001$). The modified Ashworth scale improved significantly following botulinum toxin type A in the serial casting group ($P < .05$), but not in botulinum toxin type A only group. These results suggest that serial casting after botulinum toxin type A can enhance the benefits of botulinum toxin type A in children with cerebral palsy.

[PMID: 28393669](#)

5. Beneficial Effects of Childhood Selective Dorsal Rhizotomy in Adulthood.

Park TS, Edwards C, Liu JL, Walter DM, Dobbs MB.

Cureus. 2017 Mar 5;9(3):e1077. doi: 10.7759/cureus.1077.

BACKGROUND: Selective dorsal rhizotomy (SDR) has been used to treat children with spastic cerebral palsy (CP) for over three decades. However, little is known about the outcomes of childhood SDR in adults. **Objectives:** 1) To study the effects of childhood SDR on the quality of life and ambulatory function in adult life. 2) To determine late side effects of SDR in adults. **Methods:** Adults (> 17.9 years) who underwent SDR in childhood (2 - 17.9 years) between 1987 and 2013 were surveyed in 2015. Patients completed a survey, including questions on demographic information, quality of life, health, surgical outcomes, motor function, manual ability, pain, braces/orthotics, post-SDR treatment, living situation, education level, work status, and side effects of SDR. **Results:** In our study population of 294 patients (18.0 - 37.4 years), patients received SDR during the ages of 2.0 - 17.9 years and were followed up 2.2 to 28.3 years after surgery. Eighty-four percent had spastic diplegia, 12% had spastic quadriplegia, and 4% had spastic triplegia. The majority (88%) of patients reported improved post-SDR quality of life and 1% considered the surgery detrimental. Most (83%) would recommend the procedure to others and 3% would not. However, patients who would not recommend SDR to others ambulated with a walker or were not ambulatory at all prior to SDR. The majority (83%) of patients improved (30%) or remained stable (53%) in ambulation. Twenty-nine percent of patients reported pain, mostly in the back and lower limbs, with a mean pain level of 4.4 ± 2.4 on the Numeric Pain Rating Scale (NPRS). Decreased sensation in small areas of the lower limbs was reported by 8% of patients, though this did not affect daily life. Scoliosis was diagnosed in 28%, with 40% of these patients pursuing treatment. Whether scoliosis was related to SDR is not clear, though scoliosis is known to occur in patients with CP and also in the general population. Only 4% of patients underwent spinal fusion. Orthopedic surgeries were pursued by 59% of patients. The most common orthopedic surgeries were hamstring lengthenings (31%), Achilles tendon lengthenings (18%), adductor lengthenings (16%), and derotational osteotomies (16%). Twenty-four percent of all patients later underwent hip surgery and 8% had surgeries on their knees. **Conclusion:** Results of this study indicate that the beneficial effects of childhood SDR extend to adulthood quality of life and ambulatory function without late side effects of surgery.

[PMID: 28401027](#)

6. Risk Factors for Developing Scoliosis in Cerebral Palsy: A Cross-Sectional Descriptive Study.

Bertoncelli CM, Solla F, Loughenbury PR, Tsirikos AI, Bertoncelli D, Rampal V.

J Child Neurol. 2017 Jan 1:883073817701047. doi: 10.1177/0883073817701047. [Epub ahead of print]

This study aims to identify the risk factors leading to the development of severe scoliosis among children with cerebral palsy. A cross-sectional descriptive study of 70 children (aged 12-18 years) with severe spastic and/or dystonic cerebral palsy treated in a single specialist unit is described. Statistical analysis included Fisher exact test and logistic regression analysis to identify risk factors. Severe scoliosis is more likely to occur in patients with intractable epilepsy ($P = .008$), poor gross motor functional assessment scores ($P = .018$), limb spasticity ($P = .045$), a history of previous hip surgery ($P = .048$), and nonambulatory patients ($P = .013$). Logistic regression model confirms the major risk factors are previous hip surgery ($P = .001$), moderate to severe epilepsy ($P = .007$), and female gender ($P = .03$). History of previous hip surgery, intractable epilepsy, and female gender are predictors of developing severe scoliosis in children with cerebral palsy. This knowledge should aid in the early diagnosis of scoliosis and timely referral to specialist services.

[PMID: 28395573](#)

7. Cross-sectional study of urinary problems in adults with cerebral palsy: awareness and impact on the quality of life.

Yıldız N, Akkoç Y, Ersöz M, Gündüz B, Erhan B, Yesil H, Bardak AN, Ozdolap S, Tunç H, Koklu K, Alemdaroğlu E, Erden E, Sungur U, Satır O, Erdogan C, Alkan H.

Neurol Sci. 2017 Apr 7. doi: 10.1007/s10072-017-2948-z. [Epub ahead of print]

We aimed to assess the functional status, urinary problems, and awareness of these problems in adults with cerebral palsy (CP) and their relationship with the quality of life. One-hundred-seventeen adults with CP (53 women, 64 men) were included in this study. Subjects were asked to fill out a urological questionnaire which dealt with urinary symptoms, awareness of urinary

problems, and pharmacological treatment they received. Subjects were also assessed with the Gross Motor Function Classification System (GMFCS), Functional Independence Measures (FIM), Functional Mobility Scale (FMS), and King's Health Questionnaire (KHQ). The mean age of the subjects was 25.3 ± 7.8 years. Of the patients, 83.8% were currently unemployed, 95.7% were single, and 96.5% were living with family. Of the patients, 20.5% had experienced frequency, 38.5% had nocturia, 48.7% had urgency, and 36.8% had urge urinary incontinence. Approximately 80% of the patients did not refer to physician due to urinary problems, and 60% of patients were not recorded history about urinary problem by any physician. Urge urinary incontinence was statistically more frequent in females than males (54.7 and 21.9%, respectively, $p < 0.05$). Female patients had significantly higher KHQ incontinence impact, role limitation, physical limitation, emotion, incontinence severity measures, and symptom severity subgroup scores than male patients ($p < 0.05$). Urge urinary incontinence was most frequent (65.4%) in spastic quadriplegic CP ($p < 0.05$). All functional status scores (GMFCS, FIM-toilet transfer, and FMSs) were worse in spastic quadriplegic patients than other topographical involvement of CP ($p < 0.0125$). Although the urinary problems are common in adult with CP, it is yet an overlooked condition that could affect quality of life. Therefore, health care professionals, patients, and their caregivers should be aware of the increased risk of urinary problems in these patients.

[PMID: 28389939](#)

8. Cerebral palsy.

Dean E.

Nurs Child Young People. 2017 Apr 11;29(3):11. doi: 10.7748/ncyp.29.3.11.s11.

Essential facts Cerebral palsy, the term for several neurological conditions that affect movement and coordination, is the leading cause of physical disability in children and young people in the developed world. About one in 400 children in the UK is affected by the condition which can occur if the brain develops abnormally or is damaged before, during or shortly after birth.

[PMID: 28395607](#)

9. A model of Periventricular Leukomalacia (PVL) in neonate mice with histopathological and neurodevelopmental outcomes mimicking human PVL in neonates.

Zaghloul N, Patel H, Ahmed MN.

PLoS One. 2017 Apr 13;12(4):e0175438. doi: 10.1371/journal.pone.0175438. eCollection 2017.

Periventricular leukomalacia (PVL), a brain injury affecting premature infants is commonly associated with cerebral palsy. PVL results from hypoxia-ischemia (HI) with or without infection and is characterized by white matter necrotic lesions, hypomyelination, microglial activation, astrogliosis, and neuronal death. It is important to study a PVL mouse model that mimics human PVL in symptomatology, anatomic and molecular basis. In our neonate mice model, bilateral carotid arteries were temporary ligated at P5 followed by hypoxic exposure (FiO₂ of 8% for 20 min.). At P5 in mice, the white matter is more vulnerable to HI injury than the grey matter. In our PVL model, mice suffer from significant hind limb paresis, incoordination and feeding difficulties. Histologically they present with ventriculomegally, white matter loss, microglial activation and neuronal apoptosis. HI injury increases proinflammatory cytokines, activates NF- κ B, activates microglia and causes oxidative stress. All these inflammatory mediators lead to oligodendroglial injury and white matter loss. Neurobehavioral analysis in the PVL mice model at P60 showed that the HI group had a significant decrease in hind limb strength, worsening rotarod testing and worsening performance in the open field test. This new PVL model has great advantages far beyond just mimicking human PVL in clinical features and histopathology. Long term survival, the development of cerebral palsy and the ability of using this model in transgenic animals will increase our understanding of the mechanistic pathways underlying PVL and defining specific targets for the development of suitable therapeutics.

[PMID: 28406931](#)

Prevention and Cure

10. Outcomes of autologous bone marrow mononuclear cells for cerebral palsy: an open label uncontrolled clinical trial.

Nguyen LT, Nguyen AT, Vu CD, Ngo DV, Bui AV.

BMC Pediatr. 2017 Apr 12;17(1):104. doi: 10.1186/s12887-017-0859-z.

BACKGROUND: Stem cell therapy has emerged as a promising method for improving motor function of patients with cerebral palsy. The aim of this study is to assess the safety and effectiveness of autologous bone marrow mononuclear stem cell transplantation in patients with cerebral palsy related to oxygen deprivation. **METHODS:** An open label uncontrolled clinical trial was carried out at Vinmec International Hospital. The intervention consisted of two administrations of stem cells, the first at baseline and the second 3 months later. Improvement was monitored at 3 months and 6 months after the first administration of stem cells, using the Gross Motor Function Measure (GMFM) and Modified Ashworth Score which measures muscle tone. **RESULTS:** No severe complications were recorded during the study. After transplantation, 12 patients encountered fever without infections and 9 patients experienced vomiting which was easily managed with medications. Gross motor function was markedly improved 3 months or 6 months after stem cell transplantation than at baseline. The post-transplantation GMFM-88 total score, each of its domains and the GMFM-66 percentile were all significantly higher (p-value < 0.001). Muscle spasticity also reduced significantly after transplantation (p-value < 0.001). The therapy was equally effective regardless of sex, age and GMFCS level (p-value > 0.05). **CONCLUSION:** Autologous bone marrow mononuclear cell transplantation appears to be a safe and effective therapy for patients with cerebral palsy.

[PMID: 28403842](#)

11. Implicating Receptor Activator of NF- κ B (RANK)/RANK Ligand Signalling in Microglial Responses to Toll-Like Receptor Stimuli.

Kichev A, Eede P, Gressens P, Thornton C, Hagberg H.

Dev Neurosci. 2017 Apr 13. doi: 10.1159/000464244. [Epub ahead of print]

Inflammation in the perinatal brain caused by maternal or intrauterine fetal infection is now well established as an important contributor to the development of perinatal brain injury. Exposure to inflammatory products can impair perinatal brain development and act as a risk factor for neurological dysfunction, cognitive disorders, cerebral palsy, or preterm birth. Pre-exposure to inflammation significantly exacerbates brain injury caused by hypoxic/ischaemic insult. Tumour necrosis factor (TNF) is a family of cytokines largely involved in inflammation signalling. In our previous study, we identified the importance of TNF-related apoptosis-inducing ligand (TRAIL) signalling in the development of perinatal brain injury. We observed a significant increase in the expression levels of a soluble decoy receptor for TRAIL, osteoprotegerin (OPG). Besides TRAIL, OPG is able to bind the receptor activator of the NF- κ B (RANK) ligand (RANKL) and inhibit its signalling. The function of the RANK/RANKL/OPG system in the brain has not come under much scrutiny. The aim of this research study was to elucidate the role of RANK, RANKL, and OPG in microglial responses to the proinflammatory stimuli lipopolysaccharide (LPS) and polyinosinic-polycytidylic acid (Poly I:C). Here, we show that RANK signalling is important for regulating the activation of the BV2 microglial cell line. We found that LPS treatment causes a significant decrease in the expression of RANK in the BV2 cell line while significantly increasing the expression of OPG, Toll-like receptor (TLR)3, and the adaptor proteins MyD88 and TRIF. We found that pretreatment of BV2 cells with RANKL for 24 h before the LPS or Poly I:C exposure decreases the expression of inflammatory markers such as inducible nitric oxide synthase and cyclooxygenase. This is accompanied by a decreased expression of the TLR adaptor proteins MyD88 and TRIF, which we observed after RANKL treatment. Similar results were obtained in our experiments with primary mouse microglia. Using recently developed CRISPR/Cas9 technology, we generated a BV2 cell line lacking RANK (RANK^{-/-} BV2). We showed that most effects of RANKL pretreatment were abolished, thereby proving the specificity of this effect. Taken together, these findings suggest that RANK signalling is important for modulating the inflammatory activation of microglial cells to a moderate level, and that RANK attenuates TLR3/TLR4 signalling.

[PMID: 28402971](#)

12. [Modern principles of integrated diagnostics and rehabilitation of perinatal lesions of the nervous system and their consequences].

[Article in Russian; Abstract available in Russian from the publisher]

Nemkova SA.

Zh Nevrol Psikhiatr Im S S Korsakova. 2017;117(3):40-49. doi: 10.17116/jnevro20171173140-49.

The article is devoted to the comprehensive diagnosis and treatment of perinatal lesions of the nervous system and their consequences in children. Reflects modern approaches to data classification conditions, taking into account ideas on the etiology and pathogenesis of the disease, the clinical manifestations of the main syndromes (excitation and depression, hypertensive, convulsive, movement disorders) as the neonatal period, and in the formation of long-term effects (motor and mental delay and speech development, hyperkinetic syndrome, cerebral palsy and others). Considerable attention is paid to the modern principles of diagnosis (clinical, psychometric, instrumental) and comprehensive rehabilitation (medical, social and psycho-pedagogical) the effects of perinatal lesions of the nervous system. The results of the review of research on the use of the polypeptide and nootropic neurometabolic stimulator - cortexin - in the complex rehabilitation of perinatal lesions of the nervous system and their consequences in children. It is shown that the use of cortexin in treatment of critical conditions in newborns reduced the duration of intensive care and the length of stay of patients in a intensive care unit, the average period of hospital treatment and the stage of the primary neurological rehabilitation 2.5-3 times, but also reduces the frequency of detection of syndromes movement disorders in 2 times, hypertension-hydrocephalic disorders 3 times, vegetative-visceral dysfunctions 5 times. Application cortexin in the rehabilitation of children of the first years of life with the consequences of perinatal CNS indicates a significant improvement in their motor and cognitive functions, as well as predrechevogo and speech development. Application cortexin significantly improved the forecast recovery of motor, cognitive, and neurological status in general, with full compensation by the end of 1 year of life in 90% of patients, and was accompanied by a decline in disability in extremely premature newborns from 13.6% to 4.6% compared to the standard therapy, as well as reduced length of stay in hospital for 14.7 days of hospital stay. Revealed the cumulative effect of the drug: maintained for 6 to 18 months with repeated courses of therapy, his positive influence. High efficiency of cortexin due to a combination of nootropic, neurotrophic, neuroprotective, anticonvulsant and reparative effects, as well as antioxidant, metabolic and anti-stress action, which determines the need for wide application in complex regenerative treatment of perinatal lesions of the nervous system and their consequences.

[PMID: 28399095](#)

13. Effects of targeting lower versus higher arterial oxygen saturations on death or disability in preterm infants.

Askie LM, Darlow BA, Davis PG, Finer N, Stenson B, Vento M, Whyte R.

Cochrane Database Syst Rev. 2017 Apr 11;4:CD011190. doi: 10.1002/14651858.CD011190.pub2. [Epub ahead of print]

BACKGROUND: The use of supplemental oxygen in the care of extremely preterm infants has been common practice since the 1940s. Despite this, there is little agreement regarding which oxygen saturation (SpO₂) ranges to target to maximise short- or long-term growth and development, while minimising harms. There are two opposing concerns. Lower oxygen levels (targeting SpO₂ at 90% or less) may impair neurodevelopment or result in death. Higher oxygen levels (targeting SpO₂ greater than 90%) may increase severe retinopathy of prematurity or chronic lung disease. The use of pulse oximetry to non-invasively assess neonatal SpO₂ levels has been widespread since the 1990s. Until recently there were no randomised controlled trials (RCTs) that had assessed whether it is better to target higher or lower oxygen saturation levels in extremely preterm infants, from birth or soon thereafter. As a result, there is significant international practice variation and uncertainty remains as to the most appropriate range to target oxygen saturation levels in preterm and low birth weight infants.

OBJECTIVES: 1. What are the effects of targeting lower versus higher oxygen saturation ranges on death or major neonatal and infant morbidities, or both, in extremely preterm infants? 2. Do these effects differ in different types of infants, including those born at a very early gestational age, or in those who are outborn, without antenatal corticosteroid coverage, of male sex, small for gestational age or of multiple birth, or by mode of delivery? **SEARCH METHODS:** We used the standard search strategy of Cochrane Neonatal to search the Cochrane Central Register of Controlled Trials (CENTRAL 2016, Issue 4), MEDLINE via PubMed (1966 to 11 April 2016), Embase (1980 to 11 April 2016) and CINAHL (1982 to 11 April 2016). We also searched clinical trials databases, conference proceedings and the reference lists of retrieved articles for randomised controlled trials. **SELECTION CRITERIA:** Randomised controlled trials that enrolled babies born at less than 28 weeks' gestation, at birth or soon thereafter, and targeted SpO₂ ranges of either 90% or below or above 90% via pulse oximetry, with the intention of maintaining such targets for at least the first two weeks of life. **DATA COLLECTION AND ANALYSIS:** We

used the standard methods of Cochrane Neonatal to extract data from the published reports of the included studies. We sought some additional aggregate data from the original investigators in order to align the definitions of two key outcomes. We conducted the meta-analyses with Review Manager 5 software, using the Mantel-Haenszel method for estimates of typical risk ratio (RR) and risk difference (RD) and a fixed-effect model. We assessed the included studies using the Cochrane 'Risk of bias' and GRADE criteria in order to establish the quality of the evidence. We investigated heterogeneity of effects via pre-specified subgroup and sensitivity analyses. MAIN RESULTS: Five trials, which together enrolled 4965 infants, were eligible for inclusion. The investigators of these five trials had prospectively planned to combine their data as part of the NeOProm (Neonatal Oxygen Prospective Meta-analysis) Collaboration. We graded the quality of evidence as high for the key outcomes of death, major disability, the composite of death or major disability, and necrotising enterocolitis; and as moderate for blindness and retinopathy of prematurity requiring treatment. When an aligned definition of major disability was used, there was no significant difference in the composite primary outcome of death or major disability in extremely preterm infants when targeting a lower (SpO₂ 85% to 89%) versus a higher (SpO₂ 91% to 95%) oxygen saturation range (typical RR 1.04, 95% confidence interval (CI) 0.98 to 1.10; typical RD 0.02, 95% CI -0.01 to 0.05; 5 trials, 4754 infants) (high-quality evidence). Compared with a higher target range, a lower target range significantly increased the incidence of death at 18 to 24 months corrected age (typical RR 1.16, 95% CI 1.03 to 1.31; typical RD 0.03, 95% CI 0.01 to 0.05; 5 trials, 4873 infants) (high-quality evidence) and necrotising enterocolitis (typical RR 1.24, 95% CI 1.05 to 1.47; typical RD 0.02, 95% CI 0.01 to 0.04; 5 trials, 4929 infants; I² = 0%) (high-quality evidence). Targeting the lower range significantly decreased the incidence of retinopathy of prematurity requiring treatment (typical RR 0.72, 95% CI 0.61 to 0.85; typical RD -0.04, 95% CI -0.06 to -0.02; 5 trials, 4089 infants; I² = 69%) (moderate-quality evidence). There were no significant differences between the two treatment groups for major disability including blindness, severe hearing loss, cerebral palsy, or other important neonatal morbidities. A subgroup analysis of major outcomes by type of oximeter calibration software (original versus revised) found a significant difference in the treatment effect between the two software types for death (interaction P = 0.03), with a significantly larger treatment effect seen for those infants using the revised algorithm (typical RR 1.38, 95% CI 1.13 to 1.68; typical RD 0.06, 95% CI 0.01 to 0.10; 3 trials, 1716 infants). There were no other important differences in treatment effect shown by the subgroup analyses using the currently available data. AUTHORS' CONCLUSIONS: In extremely preterm infants, targeting lower (85% to 89%) SpO₂ compared to higher (91% to 95%) SpO₂ had no significant effect on the composite outcome of death or major disability or on major disability alone, including blindness, but increased the average risk of mortality by 28 per 1000 infants treated. The trade-offs between the benefits and harms of the different oxygen saturation target ranges may need to be assessed within local settings (e.g. alarm limit settings, staffing, baseline outcome risks) when deciding on oxygen saturation targeting policies.

[PMID: 28398697](#)

14. Magnesium sulfate for neuroprotection in the setting of chorioamnionitis.

Edwards JM, Edwards LE, Swamy GK, Grotegut CA.

J Matern Fetal Neonatal Med. 2017 Apr 11:1-8. doi: 10.1080/14767058.2017.1311312. [Epub ahead of print]

PURPOSE: We examined the effects of magnesium on premature neonatal outcomes complicated by chorioamnionitis. MATERIALS AND METHODS: We conducted a secondary analysis of data from the BEAM Trial, an RCT to determine if antenatal magnesium decreases the incidence of CP in preterm birth. We compared the effect of magnesium sulfate by the presence or absence of chorioamnionitis. Outcomes examined include CP, IVH, NEC, BPD, and assessments of mental and motor disability. Logistic regression was used to estimate adjusted odds ratios of each outcome. RESULTS: About 1944 women were included in this analysis of which 228 were diagnosed with chorioamnionitis. Demographic characteristics were similar between women randomized to receive magnesium or placebo. Magnesium therapy demonstrated no significant reduction in CP in the presence of chorioamnionitis (OR 0.76, CI: 0.19-2.76) but does demonstrate benefit in the absence of chorioamnionitis (OR 0.52, CI: 0.31-0.86). CONCLUSIONS: Antenatal magnesium did not show a clear neuroprotective effect in the setting of chorioamnionitis.

[PMID: 28395549](#)

15. Blocked, Delayed, or Obstructed: What Causes Poor White Matter Development in Intrauterine Growth Restricted Infants?

Tolcos M, Petratos S, Hirst JJ, Wong F, Spencer SJ, Azhan A, Emery B, Walker DW.

Prog Neurobiol. 2017 Apr 6. pii: S0301-0082(16)30023-5. doi: 10.1016/j.pneurobio.2017.03.009. [Epub ahead of print]

Poor white matter development in intrauterine growth restricted (IUGR) babies remains a major, untreated problem in neonatology. New therapies, guided by an understanding of the mechanisms that underlie normal and abnormal oligodendrocyte development and myelin formation, are required. Much of our knowledge of the mechanisms that underlie impaired myelination come from studies in adult demyelinating disease, preterm brain injury, or experimental models of hypoxia-ischemia. However relatively less is known for IUGR which is surprising because IUGR is a leading cause of perinatal mortality and morbidity, second only to premature birth. IUGR is also a significant risk factor for the later development of cerebral palsy, and is a greater risk compared to some of the more traditionally researched antecedents - asphyxia and inflammation. Recent evidence suggests that the white matter injury and reduced myelination in the brains of some preterm babies is due to impaired maturation of oligodendrocytes thereby resulting in the reduced capacity to synthesize myelin. Therefore, it is not surprising that the hypomyelination observable in the central nervous system of IUGR infants has similarly lead to investigations identifying a delay or blockade in the progress of maturation of oligodendrocytes in these infants. This review will discuss current ideas thought to account for the poor myelination often present in the neonate's brain following IUGR, and discuss novel interventions that are promising as treatments that promote oligodendrocyte maturation, and thereby repair the myelination deficits that otherwise persist into infancy and childhood and lead to neurodevelopmental abnormalities.

[PMID: 28392287](#)

16. Antenatal magnesium sulfate for both tocolysis and fetal neuroprotection in premature rupture of the membranes before 32 weeks' gestation.

Jung EJ, Byun JM, Kim YN, Lee KB, Sung MS, Kim KT, Shin JB, Jeong DH.

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OBJECTIVE: We aimed to assess the impact of antenatal MgSO₄ therapy given to women with PPROM before 32 weeks' gestation on latency, maternal outcomes, perinatal outcomes, and neurodevelopmental outcomes. **METHODS:** We undertook a retrospective cohort observational study of 184 singleton pregnancies complicated by PPROM at 23°-316 weeks who were hospitalized and received magnesium therapy for tocolysis (MgSO₄ group) or did not received tocolytic therapy (no MgSO₄ group) between 2005 and 2013. Furthermore, patients were subdivided into two groups based on the gestational age at the onset of PPROM (23°-276 weeks' gestation and 28°-316 weeks' gestation). **RESULTS:** We included 184 women, of whom 143 received magnesium therapy and 41 did not. The latency period was significantly longer in the MgSO₄ group compared with no MgSO₄ group (7.9 ± 9.0 vs 4.0 ± 6.0 days, P = 0.0017). Antenatal magnesium therapy was significantly associated with decreased stillbirth (1.4% vs 14.6%, P = 0.0012) and perinatal mortality (7% vs 19.5%, P = 0.0375) without significant increase in the risk of neonatal morbidities and chorioamnionitis. However, neonates who were exposed to antenatal MgSO₄ were associated with higher Mg levels (3.63 ± 1.05 mg/dl vs 2.13 ± 0.48 mg/dl, P < 0.0001) and phosphate levels (6.90 ± 1.36 mg/d vs 6.40 ± 1.01 mg/dl, P = 0.0459) than those who were not exposed. Neonates who were exposed to MgSO₄ showed significantly reduced risks of IVH (20.4% vs 58.3%; RR, 0.35; 95% CI, 0.17 to 0.71) and PVL (27.8% vs 58.3%; RR, 0.48; 95% CI, 0.25 to 0.91) in the subgroup of 23°-276 weeks' gestation. And the incidence of developmental delay in the subgroup of 23°-276 weeks' gestation was significantly lower in the MgSO₄ group (6.5% vs 36.4%; RR, 0.18; 95% CI, 0.05 to 0.69). However, there were no significant differences in the development of IVH, PVL, and developmental delay between the two groups for patients in the subgroup of 28°-316 weeks' gestation. A similar trend was observed for cerebral palsy, with 22.2% of unexposed children affected compared with only 7.0% of exposed children (RR, 0.31; 95% CI, 0.10 to 1.00). **CONCLUSION:** Antenatal magnesium therapy in women with PPROM before 32 weeks' gestation could prolong latency period, allowing for corticosteroid benefit. Moreover, MgSO₄ showed fetal neuroprotective effects for neonatal IVH and PVL, and for developmental delay in infancy while prolonging latency. However, these benefits were primarily limited to the subgroup of 23°-276 weeks' gestation and prolonged in utero exposure to MgSO₄ was associated bone mineralization in the neonates.

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