

Monday 17 January 2011

This free weekly bulletin lists the latest research on cerebral palsy (CP), as indexed in the NCBI, PubMed (Medline) and Entrez (GenBank) databases. These articles were identified by a search using the key term "cerebral palsy".

To subscribe, please email Robyn Cummins rcummins@tscnsw.org.au with 'Subscribe to CP Research News' in the subject line, and your name and email address in the body of the email.

You may unsubscribe at any time by emailing Robyn with your 'unsubscribe' request.

Interventions

1. *Am J Phys Med Rehabil.* 2011 Feb;90(2):137-49.

Improved gait after repetitive locomotor training in children with cerebral palsy.

Smania N, Bonetti P, Gandolfi M, Cosentino A, Waldner A, Hesse S, Werner C, Bisoffi G, Geroin C, Munari D.

From the Neuromotor and Cognitive Rehabilitation Center, Department of Neurological, Neuropsychological, Morphological and Motor Sciences, University of Verona, Italy (NS, PB, MG, CG, DM); Rehabilitation Unit "C. Santi," Polyfunctional Centre Don Calabria, Verona, Italy (AC); Villa Melitta, Bolzano, Italy (AW); Medical Park Berlin, Charité-University Medicine, Berlin, Germany (SH, CW); and Statistics Unit, University Hospital of Verona, Italy (GB).

OBJECTIVE: The aim of this study was to evaluate the effectiveness of repetitive locomotor training with an electromechanical gait trainer in children with cerebral palsy. **DESIGN:** : In this randomized controlled trial, 18 ambulatory children with diplegic or tetraplegic cerebral palsy were randomly assigned to an experimental group or a control group. The experimental group received 30 mins of repetitive locomotor training with an applied technology (Gait Trainer GT I) plus 10 mins of passive joint mobilization and stretching exercises. The control group received 40 mins of conventional physiotherapy. Each subject underwent a total of 10 treatment sessions over a 2-wk period. Performance on the 10-m walk test, 6-min walk test, WeeFIM scale, and gait analysis was evaluated by a blinded rater before and after treatment and at 1-mo follow-up.

RESULTS: The experimental group showed significant posttreatment improvement on the 10-m walk test, 6-min walk test, hip kinematics, gait speed, and step length, all of which were maintained at the 1-mo follow-up assessment. No significant changes in performance parameters were observed in the control group. **CONCLUSIONS:** Repetitive locomotor training with an electromechanical gait trainer may improve gait velocity, endurance, spatio-temporal, and kinematic gait parameters in patients with cerebral palsy.

PMID: 21217461 [PubMed - in process]

2. *BMC Pediatr.* 2011 Jan 7;11(1):1. [Epub ahead of print]

Becoming and staying physically active in adolescents with cerebral palsy: protocol of a qualitative study of facilitators and barriers to physical activity.

Claassen AA, Gorter JW, Stewart D, Verschuren O, Galuppi BE, Shimmell LJ.

BACKGROUND: Adolescents with cerebral palsy (CP) show a reduced physical activity (PA). Currently there are no interventions for adolescents with CP in this critical life phase that optimise and maintain the individuals' physical activity in the long term. To develop such a program it is important to fully understand the factors that influence physical activity behaviours in adolescents with CP. The aim of this study is to explore what makes it easy or hard for adolescents with CP to be and to become physically active. **METHODS:** A qualitative research method is cho-

sen to allow adolescents to voice their own opinion. Because we will investigate the lived experiences this study has a phenomenological approach. Thirty ambulatory and non-ambulatory adolescents (aged 10-18 years) with CP, classified as level I to IV on the Gross Motor Function Classification System and 30 parents of adolescents with CP will be invited to participate in one of the 6 focus groups or an individual interview. Therapists from all Children's Treatment Centres in Ontario, Canada, will be asked to fill in a survey. Focus groups will be videotaped and will approximately take 1.5 hours. The focus groups will be conducted by a facilitator and an assistant. In preparation of the focus groups, participants will fill in a demographic form with additional questions on physical activity. The information gathered from these questions and recent research on barriers and facilitators to physical activity will be used as a starting point for the content of the focus groups. Recordings of the focus groups will be transcribed and a content analysis approach will be used to code the transcripts. A preliminary summary of the coded data will be shared with the participants before themes will be refined. **DISCUSSION:** This study will help us gain insight and understanding of the participants' experiences and perspectives in PA, which can be of great importance when planning programs aimed at helping them to stay or to become physically active.

PMID: 21214908 [PubMed - as supplied by publisher]

3. Dev Med Child Neurol. 2011 Jan 14. doi: 10.1111/j.1469-8749.2010.03849.x. [Epub ahead of print]

Immediate effect of a wrist and thumb brace on bimanual activities in children with hemiplegic cerebral palsy.

Louwers A, Meester-Delver A, Folmer K, Nollet F, Beelen A.

Department of Rehabilitation, Academic Medical Center, University of Amsterdam, Amsterdam, the Netherlands. Rehabilitation Center 'De Trappenberg', Huizen, the Netherlands.

Aim: The aim of this study was to determine the immediate effect of wearing a wrist and thumb brace on the performance of bimanual activities in children with spastic hemiplegic cerebral palsy. **Method:** In a pre- and post-test cohort study of 25 children (age range 4-11y; mean age 8y 4mo [SD 2y 2mo]; 16 males, 9 females) with spastic hemiplegic cerebral palsy with a Zancolli classification hand score of I, IIA, or IIB (mild and moderate hand dysfunction; children with a Zancolli classification of III - severe hand dysfunction - were excluded from this study), performance of bimanual activities was evaluated with the Assisting Hand Assessment (AHA) on three occasions: one assessment with a static wrist and thumb brace placed on the affected hand and two other assessments without a brace. The differences between AHA scores obtained at the three assessments were evaluated using the repeated measures analysis of variance. **Results:** Performance of bimanual activities while wearing the brace improved significantly compared to performance without the brace ($p < 0.001$). With the brace, the mean AHA score increased by 3.2 (95% confidence interval 2.1-4.3) from 59.1 to 62.3. The scores of the two assessments without the brace did not differ significantly. **Interpretation:** In children with spastic hemiplegic cerebral palsy, bracing of the wrist and thumb immediately improves spontaneous use of the affected upper limb in bimanual activities, possibly because bracing permits a more functional hand position.

© The Authors. Journal compilation © Mac Keith Press 2011.

PMID: 21232053 [PubMed - as supplied by publisher]

4. Dev Med Child Neurol. 2011 Jan 14. doi: 10.1111/j.1469-8749.2010.03848.x. [Epub ahead of print]

Time demands of caring for children with cerebral palsy: what are the implications for maternal mental health?

Sawyer MG, Bittman M, LA Greca AM, Crettenden AD, Borojevic N, Raghavendra P, Russo R.

Children, Youth and Women's Health Service, Adelaide, Australia. University of Adelaide, Australia. University of New England, New South Wales, Australia. University of Miami, Florida, USA. Novita Children's Services, Adelaide, Australia. Flinders University, Adelaide, Australia. University of South Australia, Adelaide, Australia.

Aim: To examine the relationship between maternal mental health problems and the time required by mothers to care for children with cerebral palsy (CP). **Method:** Cross-sectional study of 158 mothers of children with cerebral

palsy (98 males, 60 females; mean age 11y 3mo, range 6-17y). Gross Motor Function Classification System levels of the children were 37% level I, 20% level II, 9% level III, 12% level IV, and 22% level V. Manual Ability Classification System levels were 19% level I, 27% level II, 22% level III, 13% level IV, and 19% level V. Maternal mental health problems were assessed using the General Health Questionnaire. Depressive symptoms were assessed using the Center for Epidemiological Studies Depression Scale. A time-diary was used to measure caregiving time. Experience of time pressure was assessed using the Time Crunch Scale. Results: On average, mothers spent 6.0 hours per 24 hours on weekdays and 8.3 hours per 24 hours on weekends caring for children with CP. There was a significant positive relationship between maternal psychological problems and both caregiving time required per 24 hours ($p=0.03$) and mothers' experience of time pressure ($p<0.001$). There was also a significant positive association between maternal depressive symptoms and experience of time pressure ($p=0.003$). Interpretation: It is important to support mothers to find ways of reducing the real and perceived impact of caregiving. This might include identifying sources of 'respite' support for caregivers, training in stress and time management, and appropriate treatment of mental health problems.

© The Authors. Journal compilation © Mac Keith Press 2011.

PMID: 21232052 [PubMed - as supplied by publisher]

5. Gait Posture. 2010 Dec 4. [Epub ahead of print]

Editorial: Strength, Gait and Function in Cerebral Palsy.

Shortland A.

Guy's and St Thomas' Foundation NHS Trust, King's Health Partners, London, UK.

PMID: 21131204 [PubMed - as supplied by publisher]

6. Med Arh. 2010;64(6):359-61.

Application of botulinum toxin in treatment of spasticity and functional improvements for children suffering from cerebral palsy.

Meholjic A, Madjar D.

Pediatric Clinic, Clinical Centre of Sarajevo University, Patriotske Lige 81,71000 Sarajevo, Bosnia and Herzegovina.

Application of Botulin toxin type A in children with cerebral palsy is represent targeted antispasm treatment for relaxation of spastic muscles. GOAL: The goal of this study was to determine the significance of the application of Botulin toxin in the treatment of spasticity and functional progress of children suffering from cerebral palsy. MATERIAL AND METHODS: At the Department of Developmental diagnosis, habilitation and rehabilitation of children in the Pediatric Clinic, Clinical Center of Sarajevo University study included 20 patients aged 4-18 years. Data were obtained by examining the patient's records. Selected patients are diagnosed with cerebral palsy and were treated with Botulin toxin. The study was retrospective, and data are presented in tables and charts using descriptive statistics. As a measurement scale, we used the "gross motor function measurement"-GMFM, based on which the children were scored by the "Gross Motor Function Classification System"--the GMFCS. RESULTS: Of 20 children, 11 or 55% were boys and 9 or 45% of girls. The largest number of children in the sample had 9 +/- 4.03 years (5 or 25%), with an average age of 9 years (range: 4-18 years). 80% of children suffering from cerebral palsy for the first time received botulin toxin at the age of 2-6 years, 40% of children had 2 applications of Botulin toxin, and for 45% of children the time interval between repeated applications was from 3-6 months. Measuring gross motor function before and after botulin toxin application registered significant functional improvement. CONCLUSION: Botulin toxin is beneficial in the treatment of spasticity in children suffering from cerebral palsy.

PMID: 21218755 [PubMed - in process]

7. Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz. 2010 Aug;53(8):783-90.**Neural prostheses and neuromodulation : Research and clinical practice in therapy and rehabilitation [Article in German]**

Stieglitz T.

Lehrstuhl für Biomedizinische Mikrotechnik, Institut für Mikrosystemtechnik IMTEK, Albert-Ludwigs-Universität Freiburg, Deutschland. thomas.stieglitz@imtek.uni-freiburg.de

Stimulation of the nervous system with the aid of electrical active implants has changed the therapy of neurological diseases and rehabilitation of lost functions and has expanded clinical practice within the last few years. Alleviation of effects of neurodegenerative diseases, therapy of psychiatric diseases, the functional restoration of hearing as well as other applications have been transferred successfully into clinical practice. Other approaches are still under development in preclinical and clinical trials. The restoration of sight by implantable electronic systems that interface with the retina in the eye is an example how technological progress promotes novel medical devices. The idea of using the electrical signal of the brain to control technical devices and (neural) prostheses is driving current research in the field of brain-computer interfaces. The benefit for the patient always has to be balanced with the risks and side effects of those implants in comparison to medicinal and surgical treatments. How these and other developments become established in practice depends finally on their acceptance by the patients and the reimbursement of their costs.

PMID: 20700777 [PubMed - indexed for MEDLINE]

8. Zhonghua Er Ke Za Zhi. 2010 Nov;48(11):860-864.**Clinical characteristics of 14 critically ill children with 2009 influenza A (H1N1). [Article in Chinese]**

Bai ZJ, Ji W, Xie MH, Li Y, Hua J, Ren Y.

Pediatric Intensive Care Unit, Children's Hospital Affiliated to Soochow University, Suzhou 215003, China.

OBJECTIVE: To summarize characteristics and outcomes of critically ill children with 2009 influenza A (H1N1). **METHOD:** A prospective observational study of 14 critically ill children with 2009 influenza A (H1N1) in pediatric intensive care unit (PICU) in Suzhou between Oct. 1(st) 2009 and Dec. 25(th) 2009. The primary outcome measures included frequency and duration of mechanical ventilation and duration of ICU stay. **RESULT:** Critical illness occurred in 14 patients with confirmed (n = 14), community-acquired 2009 influenza A virus (H1N1) infection. The mean (SD) age of the 14 patients with confirmed 2009 influenza A (H1N1) was (4.91 ± 4.14) years, 7 were female (50.0%). The median duration from symptom onset to hospital admission was (3.09 ± 1.30) days and from hospitalization to ICU admission was (0.95 ± 0.96) day. All the patients were severely hypoxemic [mean (SD) ratio of PaO₂/FiO₂ was (191.27 ± 80.58) mm Hg] at ICU admission. ARDS occurred in 11 cases (78.6%). Mechanical ventilation was applied for 10 patients (71.4%). The median duration of ventilation was (12.51 ± 10.03) days and ICU stay was (12.58 ± 10.65) days. The median length of time during which the real-time RT-PCR test results were positive was (17.27 ± 5.57) days; Comorbidities such as iron deficiency anemia, cerebral palsy and congenital heart disease were found in 8 cases (57.1%). The longer length of mechanical ventilation and ICU stay were found in cases with higher admission PRISM III Score and lower Pediatrics Critical Illness Score. **CONCLUSION:** Critical illness due to 2009 influenza A (H1N1) in Suzhou occurred rapidly after hospital admission and was associated with severe hypoxemia, ARDS, a condition that required prolonged mechanical ventilation. There were myocardial damages in critically ill children with severe 2009 influenza A (H1N1).

PMID: 21215032 [PubMed - as supplied by publisher]

Epidemiology / Aetiology / Diagnosis & Early Treatment

9. *Annu Rev Public Health*. 2010 Sep 29. [Epub ahead of print]

Prematurity: An Overview and Public Health Implications.

McCormick MC, Litt JS, Smith VC, Zupancic JA.

Department of Society, Human Development, and Health, School of Public Health, Harvard University, Boston, MA 02115 and Department of Neonatology, Beth Israel Deaconess Medical Center, Boston, MA 02215; email: mmccormi@hsph.harvard.edu.

The high rate of premature births in the United States remains a public health concern. These infants experience substantial morbidity and mortality in the newborn period, which translate into significant medical costs. In early childhood, survivors are characterized by a variety of health problems, including motor delay and/or cerebral palsy, lower IQs, behavior problems, and respiratory illness, especially asthma. Many experience difficulty with school work, lower health-related quality of life, and family stress. Emerging information in adolescence and young adulthood paints a more optimistic picture, with persistence of many problems but with better adaptation and more positive expectations by the young adults. Few opportunities for prevention have been identified; therefore, public health approaches to prematurity include assurance of delivery in a facility capable of managing neonatal complications, quality improvement to minimize interinstitutional variations, early developmental support for such infants, and attention to related family health issues. Expected final online publication date for the Annual Review of Public Health Volume 32 is March 17, 2011. Please see <http://www.annualreviews.org/catalog/pubdates.aspx> for revised estimates.

PMID: 21219170 [PubMed - as supplied by publisher]

10. *Dev Med Child Neurol*. 2011 Jan 14. doi: 10.1111/j.1469-8749.2010.03880.x. [Epub ahead of print]

Magnetic resonance imaging of the brain in children and young people with cerebral palsy: who reports matters?

Horridge KA, Johnston J, Phatak V, Guadagno A.

Paediatrics, Sunderland Royal Hospital, Sunderland, UK Medical School, University of Newcastle upon Tyne, Newcastle upon Tyne, UK.

Retrospective case note audits were undertaken of children with clinically diagnosed cerebral palsy known to paediatricians and physiotherapists in Sunderland (UK). Evidence of brain magnetic resonance imaging (MRI) was recorded, including expert opinions requested, in order to quantify the perceived mismatch between local, general radiological and regional, specialist neuroradiological reporting, towards ensuring the best possible yield to inform clinical practice and accurate information-sharing with families. One hundred and ninety-seven out of 214 (92%) had documented neuroimaging; 111 out of 197 (56.3%) were dual reported. Only 34 out of 111 reports were concordant overall. Sixty per cent of brain MRI reported as normal locally, were found not to be normal on specialist review. Clinicians requesting brain MRI in children with disordered development must be mindful of the expertise of those reporting. Those based in district settings must network closely with specialists in expert centres, if disabled children and young people are to receive equitable care of the highest standard.

© The Authors. Journal compilation © Mac Keith Press 2011.

PMID: 21232056 [PubMed - as supplied by publisher]

11. Dev Med Child Neurol. 2011 Jan 14. doi: 10.1111/j.1469-8749.2010.03877.x. [Epub ahead of print]**Effects of constraint-induced movement therapy on neurogenesis and functional recovery after early hypoxic-ischemic injury in mice.**

Rha DW, Kang SW, Park YG, Cho SR, Lee WT, Lee JE, Nam CM, Han KH, Park ES.

Department and Research Institute of Rehabilitation Medicine, Yonsei University College of Medicine, Seoul, Korea. Department of Rehabilitation Medicine, Rehabilitation Institute of Muscular Disease, Yonsei University College of Medicine, Seoul and Korea. Department of Anatomy, Yonsei University College of Medicine, Seoul, Korea. Department of Biostatistics, Yonsei University College of Medicine, Seoul, Korea. Department of Research Affairs, Yonsei University College of Medicine, Seoul, Korea.

Aim: Constraint-induced movement therapy (CIMT) has emerged as a promising therapeutic strategy for improving affected upper limb function in children with hemiplegic cerebral palsy (CP). However, little is known about the changes in the brain that are induced by CIMT. This study was designed to investigate these changes and behavioural performance after CIMT intervention in mice with neonatal hypoxic-ischemic brain injury. **Method:** We utilized the neonatal hypoxic-ischemic brain injury model established in mice pups. Three weeks after the injury, the mice were randomly assigned to the following three groups: the control group (n=15), the enriched-environment group (n=17), and the CIMT with an enriched-environment group (CIMT-EE, n=15). 5-bromo-2-deoxyuridine (BrdU) was injected daily to label proliferating cells during the 2 weeks of intervention. **Results:** The CIMT-EE group showed better fall rate in the horizontal ladder rung walking test (mean 5.4%, SD 3.6%) than either the control (mean 14.3%, SD 7.3%; p=0.001) or enriched-environment (mean 12.4%, SD 7.7%; p=0.010) groups 2 weeks after the end of intervention. The CIMT-EE group also showed more neurogenesis (mean 7069 cells/mm³, SD 4017 cells/mm³) than either the control group (mean 1555 cells/mm³, SD 1422 cells/mm³; p<0.001) or enriched-environment group (mean 2994 cells/mm³, SD 3498 cells/mm³; p=0.001) in the subventricular zone. In the striatum, neurogenesis in the CIMT-EE group (mean 534 cells/mm³, SD 441 cells/mm³) was greater than in the control group (mean 95 cells/mm³, SD 133 cells/mm³; p=0.001). **Interpretation:** There was CIMT-EE enhanced neurogenesis in the brain along with functional benefits in mice after early hypoxic-ischemic brain injury. This is the first study to demonstrate the effects of CIMT on neurogenesis and functional recovery after experimental injury to an immature brain.

© The Authors. Journal compilation © Mac Keith Press 2011.

PMID: 21232055 [PubMed - as supplied by publisher]

12. J Leg Med. 2010 Jul;31(3):249-86.**Neurologic birth injury. Protecting the legal rights of the child.**

Conason RL, Pegalis SE.

Gair, Conason, Steigman, Mackauf, Bloom & Rubinowitz, New York, NY, USA.

PMID: 20830638 [PubMed - indexed for MEDLINE]

13. J Neurosci. 2011 Jan 12;31(2):538-48.**Regulation of oligodendrocyte development and myelination by glucose and lactate.**

Rinholm JE, Hamilton NB, Kessar N, Richardson WD, Bergersen LH, Attwell D.

Department of Neuroscience, Physiology, and Pharmacology, and Wolfson Institute for Biomedical Research, Department of Cell and Developmental Biology, University College London, London WC1E 6BT, United Kingdom, and The Brain and Muscle Energy Group, Department of Anatomy and Centre for Molecular Biology and Neuroscience, University of Oslo, N-0317 Oslo, Norway.

In the gray matter of the brain, astrocytes have been suggested to export lactate (derived from glucose or glycogen)

to neurons to power their mitochondria. In the white matter, lactate can support axon function in conditions of energy deprivation, but it is not known whether lactate acts by preserving energy levels in axons or in oligodendrocytes, the myelinating processes of which are damaged rapidly in low energy conditions. Studies of cultured cells suggest that oligodendrocytes are the cell type in the brain that consumes lactate at the highest rate, in part to produce membrane lipids presumably for myelin. Here, we use pH imaging to show that oligodendrocytes in the white matter of the rat cerebellum and corpus callosum take up lactate via monocarboxylate transporters (MCTs), which we identify as MCT1 by confocal immunofluorescence and electron microscopy. Using cultured slices of developing cerebral cortex from mice in which oligodendrocyte lineage cells express GFP (green fluorescent protein) under the control of the Sox10 promoter, we show that a low glucose concentration reduces the number of oligodendrocyte lineage cells and myelination. Myelination is rescued when exogenous L-lactate is supplied. Thus, lactate can support oligodendrocyte development and myelination. In CNS diseases involving energy deprivation at times of myelination or remyelination, such as periventricular leukomalacia leading to cerebral palsy, stroke, and secondary ischemia after spinal cord injury, lactate transporters in oligodendrocytes may play an important role in minimizing the inhibition of myelination that occurs.

PMID: 21228163 [PubMed - in process]

14. J Voice. 2011 Jan 11. [Epub ahead of print]

Histopathologic Investigations of the Unphonated Human Child Vocal Fold Mucosa.

Sato K, Umeno H, Nakashima T, Nonaka S, Harabuchi Y.

Department of Otolaryngology-Head and Neck Surgery, Kurume University School of Medicine, Kurume, Japan.

OBJECTIVES: Vocal fold stellate cells (VFSCs) in the maculae flavae (MFe) located at both ends of the vocal fold mucosa are inferred to be involved in the metabolism of extracellular matrices. MFe are also considered to be an important structure in the growth and development of the human vocal fold mucosa. Tension caused by phonation (vocal fold vibration) is hypothesized to stimulate VFSCs to accelerate production of extracellular matrices. Human child vocal fold mucosae unphonated since birth were investigated histologically. **STUDY DESIGN:** Histologic analysis of human child vocal fold mucosa. **METHODS:** Vocal fold mucosae, which have remained unphonated since birth, of two children (7 and 12 years old) with cerebral palsy were investigated by light and electron microscopy and compared with normal subjects. **RESULTS:** Vocal fold mucosae and MFe were hypoplastic and rudimentary and did not have a vocal ligament, Reinke's space, or the layered structure. The lamina propria appeared as a uniform structure. Some VFSCs in the MFe showed degeneration and not many vesicles were present at the periphery of the cytoplasm. The VFSCs synthesized fewer extracellular matrices, such as fibrous protein and glycosaminoglycan. The VFSCs appeared to have decreased activity. **CONCLUSION:** Vocal fold vibration (phonation) after birth is an important factor in the growth and development of the human vocal fold mucosa.

Copyright © 2010 The Voice Foundation. Published by Mosby, Inc. All rights reserved.

PMID: 21227641 [PubMed - as supplied by publisher]

15. Pediatr Neurol. 2011 Feb;44(2):88-96.

Cerebral palsy, developmental delay, and epilepsy after neonatal seizures.

Garfinkle J, Shevell MI.

Division of Pediatric Neurology, Montreal Children's Hospital-McGill University Health Center, Montreal, Quebec, Canada; Department of Neurology and Neurosurgery and Department of Pediatrics, McGill University, Montreal, Quebec, Canada.

This study sought to identify clinical prognostic factors for cerebral palsy, global developmental delay, and epilepsy in term infants with neonatal seizures. We completed a retrospective analysis of 120 term infants who experienced clinical neonatal seizures at a single academic pediatric neurology practice. Logistic regression analysis determined the significant independent prognostic ($P < 0.05$) indicators of cerebral palsy, global developmental delay, and epilepsy. Fifty-four (45%) infants were never diagnosed with a neurodevelopmental abnormality, whereas 37 (31%)

manifested cerebral palsy, 51 (43%) manifested global developmental delay, and 38 (32%) manifested epilepsy. Global developmental delay was present in 92% of the children who manifested spastic quadriparetic cerebral palsy. Seizure type, seizure onset, electroencephalographic background findings, and 5-minute Apgar scores constituted independent predictors of cerebral palsy. None of the children who manifested less than two predictors developed the disorder. For global developmental delay, predictors included method of delivery, seizure onset, electroencephalographic background findings, and etiology. Only one infant (2%) who manifested less than two predictors exhibited global developmental delay. For epilepsy, predictors included seizure type and administration of a second antiepileptic drug. Only one infant (3%) who manifested neither predictor developed the disease.

Copyright © 2011 Elsevier Inc. All rights reserved.

PMID: 21215907 [PubMed - in process]

16. *Pediatr Res.* 2011 Jan 10. [Epub ahead of print]

Adverse and Protective Influences of Adenosine on the Newborn and Embryo: Implications for Preterm White Matter Injury and Embryo Protection.

Rivkees SA, Wendler CC.

Department of Pediatrics, Yale Child Health Research Center, Yale University School of Medicine, New Haven, Connecticut 06520.

Few signaling molecules have the potential to influence the developing mammal as the nucleoside adenosine. Adenosine levels increase rapidly with tissue hypoxia and inflammation. Adenosine antagonists include the methylxanthines caffeine and theophylline. The receptors that transduce adenosine action are the A1, A2a, A2b, and A3 adenosine receptors (ARs). In the postnatal period, A1AR activation may contribute to white matter injury in the preterm infant by altering oligodendrocyte (OL) development. In models of perinatal brain injury, caffeine is neuroprotective against periventricular white matter injury (PWMI) and hypoxic-ischemic encephalopathy (HIE). Supporting the notion that blockade of adenosine action is of benefit in the premature infant, caffeine reduces the incidence of broncho-pulmonary dysplasia and cerebral palsy in clinical studies. In comparison with the adverse effects on the postnatal brain, adenosine acts via A1ARs to play an essential role in protecting the embryo from hypoxia. Embryo protective effects are blocked by caffeine, and caffeine intake during early pregnancy increases the risk of miscarriage and fetal growth retardation. Adenosine and adenosine antagonists play important modulatory roles during mammalian development. The protective and deleterious effects of adenosine depend on the time of exposure and target sites of action. ABBREVIATIONS::

PMID: 21228731 [PubMed - as supplied by publisher]

16. *Pediatrics.* 2011 Jan 10. [Epub ahead of print]

Inhaled Nitric Oxide in Preterm Infants: A Systematic Review.

Donohue PK, Gilmore MM, Cristofalo E, Wilson RF, Weiner JZ, Lau BD, Robinson KA, Allen MC.

Context: Studies of the efficacy of inhaled nitric oxide (iNO) to prevent or treat respiratory failure in preterm infants have had variable and contradictory findings. Objectives: To systematically review the evidence on the use of iNO in infants born at ≤ 34 weeks' gestation who receive respiratory support. Methods: Medline, Embase, the Cochrane Central Register of Controlled Studies, PsycInfo, ClinicalTrials.gov, and proceedings of the 2009 and 2010 Pediatric Academic Societies meetings were searched in June 2010. Additional studies from reference lists of eligible articles, relevant reviews, and technical experts were considered. Two investigators independently screened search results and extracted data from eligible articles. We focus here on mortality, bronchopulmonary dysplasia (BPD), the composite outcome of death or BPD, and neurodevelopmental impairment. Results: Fourteen randomized controlled trials, 7 follow-up studies, and 1 observational study were eligible for inclusion. Mortality rates in the NICU did not differ for infants treated with iNO compared with controls (risk ratio [RR]: 0.97 [95% confidence interval (CI): 0.82-1.15]). BPD at 36 weeks for iNO and control groups also did not differ for survivors (RR: 0.93 [95% CI: 0.86-1.003]). A small difference was found in favor of iNO in the composite outcome of death or BPD (RR: 0.93 [95% CI: 0.87-0.99]). There was no evidence to suggest a difference in the incidence of cerebral palsy (RR: 1.36 [95% CI: 0.88-

2.10]), neurodevelopmental impairment (RR: 0.91 [95% CI: 0.77-1.12]), or cognitive impairment (RR: 0.72 [95% CI: 0.35-1.45]). Conclusions: There was a 7% reduction in the risk of the composite outcome of death or BPD at 36 weeks for infants treated with iNO compared with controls but no reduction in death alone or BPD. There is currently no evidence to support the use of iNO in preterm infants with respiratory failure outside the context of rigorously conducted randomized clinical trials.

PMID: 21220391 [PubMed - as supplied by publisher]