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**Professor Nadia Badawi AM**

Macquarie Group Foundation Chair of Cerebral Palsy

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## Interventions and Management

1. *Acta Orthop Traumatol Turc.* 2015;49(1) :51-6. doi: 10.3944/AOTT.2015.14.0078.

**Improvement of popliteal angle with semitendinosus or gastrocnemius tenotomies in children with cerebral palsy.**

Sarıkaya İA(1) , İnan M(2) , Şeker A(3) .

(1) Department of Orthopedics and Traumatology, Muş State Hospital, Muş, Turkey. (2) Department of Orthopedics and Traumatology, Cerrahpaşa Faculty of Medicine, İstanbul University, İstanbul, Turkey. (3) Department of Orthopedics and Traumatology, Medipol Mega Hospital, İstanbul Medipol University, İstanbul, Turkey.

**OBJECTIVE:** The aim of this study was to determine the efficacy of semitendinosus and gastrocnemius tenotomies on popliteal angle presenting knee flexion spasticity in children with cerebral palsy (CP). **METHODS:** The study included 44 patients (25 males, 19 females; mean age: 8.1 years, range: 4 to 14 years) with spastic CP who underwent surgery for knee flexion spasticity. A total of 78 semitendinosus tenotomies and 28 associated gastrocnemius tenotomies were performed. Popliteal angle was measured under general anesthesia before and after surgery. Patients were divided into groups according to age (younger and older than 7 years), severity of deformity and type of CP. **RESULTS:** Mean popliteal angles decreased by 14.3° (30.1%) following semitendinosus tenotomy and by 6.1° (12%) following gastrocnemius tenotomy ( $p=0.0001$ ). The change in popliteal angle was not statistically significant according to age, severity of flexion spasticity, and type of CP palsy. There was a significant difference following gastrocnemius tenotomy between groups with a popliteal angle of greater or lesser than 50° ( $p=0.0001$ ). **CONCLUSION:** Semitendinosus and gastrocnemius tenotomies improved popliteal angle by 30.1% and 12%, respectively. Age, preoperative popliteal angle or anatomical disease classification did not significantly affect popliteal angle.

[PMID: 25803254](#) [PubMed - in process]

2. *J Child Orthop.* 2015 Mar 24. [Epub ahead of print]

**Cannulated, locking blade plates for proximal femoral osteotomy in children and adolescents.**

Zhou L(1) , Camp M, Gahukamble A, Khot A, Graham HK.

(1) Department of Paediatrics, The University of Melbourne, Carlton, VIC, 3052, Australia.

**BACKGROUND:** Proximal femoral osteotomy is the most common major reconstructive surgery in the region of

the hip joint in children and adolescents. Given that it may be required across a wide range of ages and indications, appropriate instrumentation is necessary to ensure a technically satisfactory result. Recent developments in fixation include cannulation of the blade plate and locking screw technology. **METHODS:** We conducted a prospective audit of our first 25 patients who had a unilateral or bilateral proximal femoral osteotomy using a recently available system which combines cannulation and locking plate technology. The principal outcome measures were the radiographic position of the osteotomy at the time of union and surgical adverse events. **RESULTS:** Forty-five proximal femoral osteotomies were performed in 25 patients, mean age 8 years (range 3-17 years), for a variety of indications, the most common of which was hip subluxation in children with cerebral palsy. All osteotomies were soundly united by 6 weeks in children and by 3 months in adolescents, in the position achieved intra-operatively. There were no revision procedures and the technical goals of surgery were achieved in all patients. There was one adverse event, a low-grade peri-prosthetic infection, diagnosed at the time of implant removal. **CONCLUSIONS:** In this prospective audit of our first 25 patients, the new system performed well across a wide range of ages, body weights and surgical indications. Further comparative studies will be required to determine whether it offers additional advantages over more traditional systems.

[PMID: 25802189](#) [PubMed - as supplied by publisher]

### 3. *Dev Med Child Neurol.* 2015 Mar 22. doi: 10.1111/dmcn.12739. [Epub ahead of print]

#### **Botulinum toxin A injections and occupational therapy in children with unilateral spastic cerebral palsy: a randomized controlled trial.**

Lidman G(1) , Nachemson A, Peny-Dahlstrand M, Himmelmann K.

(1) Institute of Neuroscience and Physiology at the Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden; Regional Rehabilitation Center, Queen Silvia's Children's Hospital, Sahlgrenska University Hospital, Gothenburg, Sweden.

**AIM:** To investigate the effects of repeated botulinum toxin A (BoNT-A) injections combined with occupational therapy, including a splint, compared with occupational therapy alone on hand function in children with unilateral spastic cerebral palsy (USCP), in all International Classification of Functioning, Disability and Health (ICF) domains. **METHOD:** This was a randomized controlled study, population-based and evaluator-blinded for primary outcome (October 2004 to September 2010). Twenty children (14 males; median age 3y 1mo) with USCP, recruited at a rehabilitation centre in Sweden, were assigned to one of two parallel groups using concealed allocation. In the course of one year, 10 children received occupational therapy, while 10 received repeated BoNT-A plus occupational therapy (BoNT-A/OT). Primary outcome (Assisting Hand Assessment [AHA]), and secondary outcome measures (range of movement [ROM], and Canadian Occupational Performance Measure), were measured at baseline, 3, 6, 9, and 12 months. **RESULTS:** AHA revealed a superior effect in the BoNT-A/OT group at 12 months: 6 out of 10 improved compared with 1 out of 10 in the occupational therapy group ( $p < 0.03$ ). A 95% Peskun exact confidence interval for the difference in proportions is given as 0.01 to 0.81. Secondary outcomes improved in both groups. **INTERPRETATION:** Repeated BoNT-A/OT appeared superior to occupational therapy alone for bimanual performance in young children with USCP. Active ROM and goal performance improved in both groups.

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[PMID: 25808577](#) [PubMed - as supplied by publisher]

### 4. *Rehabil Res Pract.* 2015;2015:196395. doi: 10.1155/2015/196395. Epub 2015 Feb 23.

#### **Perceived cause, environmental factors, and consequences of falls in adults with cerebral palsy: a preliminary mixed methods study.**

Morgan P(1) , McDonald R(2) , McGinley J(3) .

(1) Department of Physiotherapy, School of Primary Health Care, Monash University, Frankston, VIC 3199, Australia. (2) Department of Occupational Therapy, School of Primary Health Care, Monash University, Frankston, VIC 3199, Australia. (3) Department of Physiotherapy, School of Health Sciences, The University of Melbourne, Parkville, VIC 3010, Australia.

**Objective.** Describe perceived cause, environmental influences, and consequences of falls or near-falls in ambulant adults with cerebral palsy (CP). **Methods.** Adults with CP completed postal surveys and follow-up semistructured interviews. Surveys sought information on demographic data, self-nominated Gross Motor Function Classification Score (GMFCS-E&R), falls, and near-falls. Interviews gathered additional information on falls experiences, near-falls, and physical and psychosocial consequences. **Results.** Thirty-four adults with CP participated. Thirty-three participants reported at least one fall in the previous year. Twenty-six participants reported near-falls. Most commonly, falls occurred indoors, at home, and whilst engaged in nonhazardous ambulation. Adults with CP experienced adverse falls consequences, lower limb injuries predominant (37%), and descriptions of fear, embarrassment, powerlessness, and isolation. **Discussion.** Adults with CP may experience injurious falls. Further investigation into the impact of falls on health-related quality of life and effective remediation strategies is warranted to provide comprehensive falls prevention programs for this population.

PMCID: PMC4352903 [PMID: 25802759](#) [PubMed]

##### **5. J Indian Soc Periodontol. 2015 Jan-Feb;19(1) :78-82. doi:10.4103/0972-124X.145800.**

#### **Comparison of oral health status between children with cerebral palsy and normal children in India: A case-control study.**

Sinha N(1) , Singh B(2) , Chhabra KG(3) , Patil S(4).

(1) Department of Conservative Dentistry and Endodontics, Jodhpur Dental College General Hospital, Jodhpur, Rajasthan, India. (2) Department of Prosthodontics, Jodhpur Dental College General Hospital, Jodhpur, Rajasthan, India. (3) Department of Public Health Dentistry, Jodhpur Dental College General Hospital, Jodhpur, Rajasthan, India. (4) Department of Oral Medicine and Radiology, Jodhpur Dental College General Hospital, Jodhpur, Rajasthan, India.

**BACKGROUND:** The aim of the present research was to describe and compare the oral health of children with cerebral palsy (CP) with the normal children in India. **MATERIALS AND METHODS:** Fifty children with CP of the age range 7-17 years and fifty normal children were selected for the study. An oral examination was carried out and decayed, missing, and filled teeth (dmft/DMFT) index, oral hygiene index-simplified (OHI-S) index, Angles malocclusion were charted along with other significant dental findings. Data were analyzed using Student's t-test and Kruskal-Wallis one-way ANOVA test. **RESULTS:** The mean dmft/DMFT of the CP group was  $4.11 \pm 2.62$ , while that of controls was  $2.95 \pm 2.75$ , which showed higher caries prevalence in the CP group. There was a significant association between the dmft/DMFT ( $P = 0.03$ ), OHI-S ( $P = 0.001$ ), and Angles Class 2 malocclusion and CP. **CONCLUSIONS:** Cerebral palsy group had higher caries, poor oral hygiene and Class 2 malocclusion when compared to controls primarily because of their compromised general health condition and also less dental awareness. Effort should be made for better organization of preventive dental care and promoting dental health of this challenged population.

[PMID: 25810598](#) [PubMed]

##### **6. Dev Med Child Neurol. 2015 Mar 24. doi: 10.1111/dmcn.12740. [Epub ahead of print]**

#### **Variation in health care for children and young people with cerebral palsies: a retrospective multicentre audit study.**

Horridge K(1) , Tennant PW, Balu R, Rankin J.

(1) City Hospitals Sunderland NHS Foundation Trust, Sunderland Royal Hospital, Sunderland, UK.

**AIM:** To explore the provision and variations in care for children and young people with cerebral palsies (CP) registered with the population-based North of England Collaborative Cerebral Palsy Survey (NECCPS). **METHOD:** This is a retrospective multicentre record audit of 389 children with CP (220 males, 148 females, 21 no data; median age at time of audit 12y 3mo), born between 1995 and 2002. Data were collected on cranial magnetic resonance imaging (MRI), hip and spine surveillance and management, and pain presence and management. Variations over time and between the districts in the north of England (Northumberland, North and West Cumbria,

North and South Tyneside, Newcastle-upon-Tyne, Gateshead, Sunderland, Durham, Darlington, Bishop Auckland, Hartlepool, Stockton-on-Tees, Middlesbrough, Redcar, and Cleveland), and by socio-economic status (SES) (estimated from the Index of Multiple Deprivation [IMD] 2004) were estimated by generalized estimating equations. RESULTS: There was significant variation between districts in access to MRI ( $p < 0.001$ ), orthopaedic surgeons ( $p = 0.005$ ), recording state of spine ( $p < 0.001$ ), and discussions about pain ( $p < 0.001$ ). Fifty-seven per cent (95% CI 52-62) had evidence of a reported MRI brain scan, the proportion of which increased over time ( $p < 0.001$ ). Sixty-seven per cent (95% CI 62-71) had a discussion about pain recorded. Of those in pain, 87% (95% CI 80-93) had a pain management plan. The proportion with documented discussion about pain increased with increasing SES ( $p = 0.04$ ). INTERPRETATION: The provision of care for children with CP in the north of England varies between districts. Internationally agreed, evidence-based standards are urgently needed to ensure more equitable health care and improved outcomes for all.

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[PMID: 25808699](#) [PubMed - as supplied by publisher]

## 7. No To Hattatsu. 2015 Jan;47(1) :23-7.

### A nationwide survey on the uses of melatonin and ramelteon in Japanese children [Article in Japanese]

Fukumizu M, Hayashi M, Miyajima T, Ishizaki A, Tanaka H, Kohyama J.

OBJECTIVE: We carried out a questionnaire survey to investigate the uses of melatonin and ramelteon in Japanese children. METHODS: We sent a questionnaire to councilors of the Japanese Society of Child Neurology by e-mail, and sent the same questionnaire to members of the Japanese Society of Pediatric Psychiatry and Neurology by postal mail. RESULTS: During the first phase of the survey, 220 responses were obtained, and 45% of the respondents prescribed melatonin. Imported supplements and chemical reagents were used by 64% and 29% of melatonin prescribers, respectively. Some prescribed melatonin without patient consent or institutional approval. In patients with pervasive developmental disorder, cerebral palsy, attention-deficit hyperactivity disorder, Rett syndrome, and visual disturbance, melatonin was prescribed by 37%, 29%, 10%, 6%, and 6% of the respondents, respectively. In terms of sleep disorders, melatonin was prescribed by 49% and 42% of respondents in patients with circadian rhythm disorders and insomnia, respectively. Ramelteon was prescribed by 52% of respondents. Regarding types of target diseases and sleep disorders, the use of ramelteon differed little from that of melatonin. In the second phase of the survey on the use of melatonin, 23 doctors prescribed the drug for 254 patients. The daily effective dose ranged from 0.2 mg to 8 mg in patients aged 2 months to 37 years. In more than 60% of the patients who took melatonin, PDD was diagnosed. In the patients with melatonin for insomnia, 90% and 25% had difficulty falling asleep and disorders in circadian rhythm, respectively. CONCLUSIONS: Both melatonin and ramelteon were widely prescribed in Japanese children. Melatonin tended to be used without sufficient ethical consideration in Japan, indicating the necessity of melatonin as medicine. Then, careful determination of an applicable dose are required in future studies.

[PMID: 25803907](#) [PubMed - in process]

## 8. J Registry Manag. 2014 Winter;41(4):182-9.

### Exclusion of progressive brain disorders of childhood for a cerebral palsy monitoring system: a public health perspective.

Olney RS, Doernberg NS, Yeargin-Allsop M.

BACKGROUND: Cerebral palsy (CP) is defined by its nonprogressive features. Therefore, a standard definition and list of progressive disorders to exclude would be useful for CP monitoring and epidemiologic studies. METHODS: We reviewed the literature on this topic to 1) develop selection criteria for progressive brain disorders of childhood for public health surveillance purposes, 2) identify categories of disorders likely to include individual conditions that are progressive, and 3) ascertain information about the relative frequency and natural history of candidate disorders. RESULTS: Based on 19 criteria that we developed, we ascertained a total of 104 progressive brain disorders of childhood, almost all of which were Mendelian disorders. DISCUSSION: Our list is meant for CP surveillance programs and does not represent a complete catalog of progressive genetic conditions, nor is the list

meant to comprehensively characterize disorders that might be mistaken for cerebral palsy. The criteria for progressive disorders that we developed could be applied by public health investigators in the future, as more children with very rare conditions are followed and new candidate disorders are identified.

[PMID: 25803631](#) [PubMed - in process]

**9. Dev Med Child Neurol. 2015 Apr;57 Suppl 3:48-50. doi: 10.1111/dmcn.12727.**

**The long-term health, social, and financial burden of hypoxic-ischaemic encephalopathy.**

Eunson P(1) .

(1) Department of Paediatric Neurosciences, Royal Hospital for Sick Children, Edinburgh, UK.

Infants who suffer hypoxic-ischaemic encephalopathy (HIE) at term are at risk of dying or developing severe cerebral palsy (CP). Children with severe CP often have other neurodevelopmental disabilities, which may affect their quality of life as much as the CP itself. New treatments for HIE, such as cooling, may improve motor outcomes, but affected infants may still have significant cognitive or communication problems. Infants who have experienced HIE and develop CP will require significant medical input throughout childhood and adult life. The costs of this medical input are high, but the indirect costs to the child, his or her family, and the relevant social services and education systems are many times greater. When demonstrating the cost-effectiveness of interventions aimed at preventing or treating HIE, these additional costs should be taken into account.

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[PMID: 25800493](#) [PubMed - in process]

## Prevention and Cure

**10. Clin Obstet Gynecol. 2015 Mar 24. [Epub ahead of print]**

**Intrapartum Fetal Monitoring.**

Cahill AG(1) , Spain J.

(1) Department of Obstetrics and Gynecology, Washington University School of Medicine, St. Louis, Missouri.

Intrapartum fetal monitoring to assess fetal well-being during the labor and delivery process has been a central component of intrapartum care for decades. Today, electronic fetal monitoring (EFM) is the most common method used to assess the fetus during labor without substantial evidence to suggest a benefit. A Cochrane review of 13 trials, which included over 37,000 women, found that continuous EFM provided no significant improvement in perinatal death rate [riskratio (RR) 0.86; 95% confidence interval (CI), 0.59-1.23] or cerebral palsy rate (RR 1.75; 95% CI, 0.84-3.63) as compared with intermittent auscultation; however, there was a significant decrease in neonatal seizures (RR 0.50; 95% CI, 0.31-0.80). In addition, there was a significant increase in cesarean delivery (RR 1.63; 95% CI, 1.29-2.07) and operative vaginal delivery (RR 1.15; 95% CI, 1.01-1.33). Despite the lack of scientific support to suggest that EFM reduces adverse neonatal outcomes, its use is almost universal in the hospital setting and very likely has contributed to the rise in cesarean rate.

[PMID: 25811127](#) [PubMed - as supplied by publisher]

**11. Infect Disord Drug Targets. 2015 Mar 20. [Epub ahead of print]****Neuroimaging findings in a series of children with cerebral palsy and congenital cytomegalovirus infection.**

Smithers-Sheedy H, Raynes-Greenow C, Badawi N, Reid SM, Meehan E, Gibson CS, Dale RC, Jones CA(1) .

(1) The Children's Hospital at Westmead, Locked Bag 4001, Westmead NSW 2145 Australia.  
cheryl.jones@health.nsw.gov.au.

Congenital cytomegalovirus (cCMV) is a contributing cause of neurodevelopmental disabilities including cerebral palsy (CP). In this case series we reviewed the neuroimaging findings of children with CP and cCMV infection in the context of the children's clinical profile. PARTICIPANTS: Children with CP and laboratory confirmed cCMV (n=12) reported to the Australian CP Register, born South Australia and Victoria, 1993-2006, with magnetic resonance imaging (MRI) and/or computerized tomography (CT) report available. Clinical details and neuroimaging findings were tabulated and compared to published literature. Children in this series were mostly born at term (n=8), with symptoms or signs of cCMV (n=10) and had spastic quadriplegia (n=9), epilepsy (n=8), intellectual (n=12), communication (n=10) and hearing impairments (n=9). All but one had abnormal neuroimaging findings reported on MRI or CT (n=11): most commonly brain malformations including disorders of neuronal migration (n=10), such as lissencephaly, pachygyria and polymicrogyria, and cerebellar hypoplasia (n=5). Other findings included ventricular dilatation (n=8), calcifications (n=7) and white matter abnormalities (n=6). This study suggests that brain malformations, calcifications, ventricular dilatation and cerebellar hypoplasia are common neuroimaging patterns in children with CP and cCMV infection. The presence of these findings should prompt investigations for congenital cytomegalovirus.

[PMID: 25809629](#) [PubMed - as supplied by publisher]

**12. PLoS One. 2015 Mar 25;10(3) :e0122034. doi: 10.1371/journal.pone.0122034. eCollection 2015.****Association between Antibiotic Prescribing in Pregnancy and Cerebral Palsy or Epilepsy in Children Born at Term: A Cohort Study Using The Health Improvement Network.**

Meeraus WH(1) , Petersen I(2) , Gilbert R(3) .

(1) UCL Institute of Child Health, Population Policy and Practice Programme, London, United Kingdom; UCL Research Department of Primary Care and Population Health, London, United Kingdom. (2) UCL Research Department of Primary Care and Population Health, London, United Kingdom. (3) UCL Institute of Child Health, Population Policy and Practice Programme, London, United Kingdom; Farr Institute of Health Informatics Research, London, United Kingdom.

**BACKGROUND:** Between 19%-44% pregnant women are prescribed antibiotics during pregnancy. A single, large randomised-controlled-trial (ORACLE Childhood Study II) found an increased risk of childhood cerebral palsy and possibly epilepsy following prophylactic antibiotic use in pregnant women with spontaneous preterm labour. We ascertained whether this outcome could be reproduced across the population of babies delivered at term and prospectively followed in primary-care using data from The Health Improvement Network. **METHODS:** We determined the risk of cerebral palsy or epilepsy in children whose mothers were prescribed antibiotics during pregnancy using a cohort of 195,909 women linked to their live, term-born, singleton children. We compared the effect of antibiotic class, number of courses and timing of prescribing in pregnancy. Analyses were adjusted for maternal risk factors (e.g. recorded infection, age, chronic conditions, social deprivation, smoking status). Children were followed until age seven years or cessation of registration with the primary-care practitioner. **RESULTS:** In total, 64,623 (33.0%) women were prescribed antibiotics in pregnancy and 1,170 (0.60%) children had records indicating cerebral palsy or epilepsy. Adjusted analyses showed no association between prescribing of any antibiotic and cerebral palsy or epilepsy (adj.HR 1.04, 95%CI 0.91-1.19). However, compared with penicillins, macrolides were associated with an increased risk of cerebral palsy or epilepsy (adj.HR 1.78, 95%CI 1.18-2.69; number needed to harm 153, 95%CI 71-671). **CONCLUSIONS:** We found no overall association between antibiotic prescribing in pregnancy and cerebral palsy and/or epilepsy in childhood. However, our finding of an increased risk of cerebral palsy or epilepsy associated with macrolide prescribing in pregnancy adds to evidence that macrolide use is associated with serious harm.

[PMID: 25807115](#) [PubMed - in process]

**13. *Pediatr Ann.* 2015 Mar 1;44(3) :e53-7. doi: 10.3928/00904481-20150313-09.**

**A 9-month-old boy with right-hand preference.**

Kastner K, Rust L, Kelley K, Msall M, Hageman JR.

We present a case of a 9-month-old boy with a history of unequal hand movements, right-hand preference on physical examination, and cortical dysplasia on brain magnetic resonance imaging who was eventually diagnosed with cerebral palsy (CP). Although spasticity involving one or more limbs is the most common neurologic sign of CP, there can be a variety of other presenting symptoms including early hand preference, hypotonia, and oral motor dysfunction. In addition, traditional risk factors of premature birth and intrapartum complications are not always present. Given the wide clinical spectrum of CP, it is important for primary care providers to maintain a high index of suspicion to ensure appropriate diagnosis and early access to interventions. [*Pediatr Ann.* 2015;44(3) :e53-e57.].

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[PMID: 25806730](#) [PubMed - in process]

**14. *Georgian Med News.* 2015 Feb;(239):69-75.**

**The role of lactate acidosis in the development and treatment of various neurologic syndromes in children and adolescents [Article in Russian]**

Arveladze G(1) , Geladze N(1) , Sanikidze T(1) , Khachapuridze N(1) , Bakhtadze S(1) .

(1) Tbilisi State Medical University, Department of Child Neurology; EPR laboratory, Georgia.

The aim of the study was to detect the role of lactate acidosis, also to find the share of mitochondrial insufficiency in development of various neurologic syndromes in children and adolescents. The detection of cellular energetic metabolism and acid based imbalance is also important for finding the specific method of management. We have studied 200 patients with various degree of neurodevelopment delay with epilepsy and epileptic syndromes, headache, vertigo, early strokes, floppy infant syndrome, atrophy of ophthalmic nerve, cataracta, neurosensory deafness, systemic myopathy, cerebral palsy. In 27% of cases with various ages we have detected lactate acidosis and increase level of pyruvate. Mitochondrial insufficiency was seen in 8% of cases which gives us opportunity to find the specific method of treatment in this group of patients. Each patient with neurological symptoms requires correction of parameters of energetic and oxidative metabolism.

[PMID: 25802453](#) [PubMed - in process]

**15. *Dev Med Child Neurol.* 2015 Apr;57 Suppl 3:17-28. doi: 10.1111/dmcn.12723.**

**Inflammation-induced sensitization of the brain in term infants.**

Fleiss B(1) , Tann CJ, Degos V, Sigaut S, Van Steenwinckel J, Schang AL, Kichev A, Robertson NJ, Mallard C, Hagberg H, Gressens P.

(1) Inserm, U1141, Paris, France; University Paris Diderot, Sorbonne Paris Cité, UMRS 1141, Paris, France; Department of Child Neurology, APHP, Robert Debré Hospital, Paris, France; PremUP, Paris, France; Division of Imaging Sciences, Department of Perinatal Imaging and Health, King's College London, King's Health Partners, St. Thomas' Hospital, London, UK.

Perinatal insults are a leading cause of infant mortality and amongst survivors are frequently associated with neurocognitive impairment, cerebral palsy (CP), and seizure disorders. The events leading to perinatal brain injury are multifactorial. This review describes how one subinjurious factor affecting the brain sensitizes it to a second injurious factor, causing an exacerbated injurious cascade. We will review the clinical and experimental evidence, including observations of high rates of maternal and fetal infections in term-born infants with neonatal encephalopathy and cerebral palsy. In addition, we will discuss preclinical evidence for the sensitizing effects of inflammation on injuries, such as hypoxia-ischaemia, our current understanding of the mechanisms underpinning

the sensitization process, and the possibility for neuroprotection.

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**16. Dev Med Child Neurol. 2015 Apr;57 Suppl 3:2-7. doi: 10.1111/dmcn.12725.**

**Does aetiology of neonatal encephalopathy and hypoxic-ischaemic encephalopathy influence the outcome of treatment?**

Mcintyre S(1) , Badawi N, Blair E, Nelson KB.

(1) Cerebral Palsy Alliance, University of Notre Dame, Darlinghurst, NSW, Australia.

Neonatal encephalopathy, a clinical syndrome affecting term-born and late preterm newborn infants, increases the risk of perinatal death and long-term neurological morbidity, especially cerebral palsy. With the advent of therapeutic hypothermia, a treatment designed for hypoxic or ischaemic injury, associated mortality and morbidity rates have decreased. Unfortunately, only about one in eight neonates (95% confidence interval) who meet eligibility criteria for therapeutic cooling apparently benefit from the treatment. Studies of infants in representative populations indicate that neonatal encephalopathy is a potential result of a variety of antecedents and that asphyxial complications at birth account for only a small percentage of neonatal encephalopathy. In contrast, clinical case series suggest that a large proportion of neonatal encephalopathy is hypoxic or ischaemic, and trials of therapeutic hypothermia are specifically designed to include only infants exposed to hypoxia or ischaemia. This review addresses the differences, definitional and methodological, between infants studied and investigations undertaken, in population studies compared with cooling trials. It raises the question if there may be subgroups of infants with a clinical diagnosis of hypoxic-ischaemic encephalopathy (HIE) in whom the pathobiology of neonatal neurological depression is not fundamentally hypoxic or ischaemic and, therefore, for whom cooling may not be beneficial. In addition, it suggests approaches to future trials of cooling plus adjuvant therapy that may contribute to further improvement of care for these vulnerable neonates.

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[PMID: 25800486](#) [PubMed - in process]

**17. Ann Anat. 2015 Feb 25;200:66-72. doi: 10.1016/j.aanat.2015.02.003. [Epub ahead of print]**

**Immunoreactivity of neurogenic factor in the guinea pig brain after prenatal hypoxia.**

Chung Y(1) , So K(2) , Kim E(3) , Kim S(4), Jeon Y(5).

(1) Department of Anatomy, School of Medicine, Chosun University, Gwangju, South Korea. (2) Department of Anesthesiology and Pain Medicine, Chosun University Hospital, Gwangju, South Korea. (3) Department of Pediatrics, Chosun University Hospital, Gwangju, South Korea. (4) Department of Neurosurgery, Chosun University Hospital, Gwangju, South Korea. (5) Department of Anatomy, School of Medicine, Chosun University, Gwangju, South Korea. Electronic address: [jyh1483@chosun.ac.kr](mailto:jyh1483@chosun.ac.kr).

Chronic prenatal hypoxia is considered to cause perinatal brain injury. It can result in neurological disorders such as cerebral palsy or learning disabilities. These neurological problems are related to chronic placental insufficiency (CPI), which leads to chronic hypoxemia and hypoglycemia. The effects of hypoxia on neurogenesis during development have been a matter of controversy. We therefore investigated the effect of chronic prenatal hypoxia in the brain of the fetal guinea pig using the guinea pig CPI model. Chronic placental insufficiency was induced by unilateral uterine artery ligation at 30-32 days of gestation (dg: with term defined as ~67dg). At 50 and 60dg, fetuses were sacrificed and assigned to either the growth-restricted (GR) or control (no ligation) group. Immunohistochemistry was performed with HIF-1 $\alpha$ , PCNA, NeuN and BDNF antibodies in the cerebral cortex and dentate gyrus. The number of NeuN-IR and BDNF-IR cells was lesser in GR fetuses than in controls in the cerebral cortex and dentate gyrus at 60dg ( $p < 0.05$ ). The growth of the developing brain is dependent upon the availability of



growth factors such as BDNF. The reduction in the number of neuronal cells observed in our GR group was associated with the observed reduction in BDNF protein found at 60dg. There was no significant difference between control and GR fetuses in the densities of PCNA-IR cells in the subventricular zone and subgranular zone at 50 and 60dg. These findings suggest that the survival of neurons in the cerebral cortex is decreased by chronic prenatal hypoxia at 60dg.

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