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### A RANDOMIZED CONTROLLED TRIAL OF LOW VS HIGH HEMOGLOBIN THRESHOLDS FOR TRANSFUSION IN EXTREMELY LOW-BIRTH-WEIGHT INFANTS

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**Background:** Infants of extremely low-birth-weight (ELBW, or <1000g) are frequently exposed to multiple transfusions of packed red blood cells. Our objective was to evaluate the effects of using low vs. high levels (thresholds) of blood hemoglobin concentration for transfusion of ELBW infants on mortality or severe morbidity until discharge.

**Methods:** We selected infants <1000 g birth-weight and <48 hr of age, excluding infants with established blood disease, shock or sepsis. We randomized 451 (223 low, 228 high) infants to transfusion threshold algorithms of low vs. high hemoglobin. The algorithms differed by 10–20 g/l and were adjusted for age and need for respiratory support (low from 115 to 75 g/l, high from 135 to 85 g/l). These were maintained until discharge. Additional transfusions were permitted for shock, sepsis or surgery.

**Results:** Maternal and infant prognostic factors were similar between the groups. Median (IQR) birth-weight was 770 (670–887) g and gestational age 26 (25–27) wk. *Transfusion and Hematologic Outcomes:* Comparing infants in the low vs. high threshold group, the time to first transfusion was delayed by a median of two days, fewer infants were exposed to any transfusion (194 (87%) vs. 214 (94%), p<0.01), and fewer transfusions were given (means 4.8 vs. 5.5, p=0.09). Hemoglobin levels fell faster from admission to discharge (from 164 to 101g/l vs. from 165 to 111g/l; mean difference after first week was 11 g/l, p<0.0001). *Clinical Outcomes:* There were no significant differences between low and high threshold groups respectively in mortality (22% vs. 18%, OR 1.3 95% c.i. 0.8–2.2), bronchopulmonary dysplasia as oxygen supplementation at 36 wk (59% vs. 56%, OR 1.2 c.i. 0.7–1.8), retinopathy of prematurity of stage 3 or worse (18% vs. 17%, OR 1.2 c.i. 0.7–2.0) or periventricular leukomalacia/ventriculomegaly by ultrasound (19% vs. 21% OR 0.8 c.i. 0.5–1.4). Rates of combined death or severe morbidity were not significantly different (74% vs. 70% (OR 1.3 c.i. 0.8–2.0). Overall, 28% of all infants (or 35% of survivors) survived with no severe morbidity to discharge.

**Conclusion:** Using a regimen of low rather than high hemoglobin transfusion thresholds results in a reduced exposure to blood transfusion for infants of extremely low birth weight with postnatal hemoglobin levels approximately 11 g/l lower. There is no difference in mortality or severe morbidity in these very high-risk infants managed with low vs. high hemoglobin thresholds.

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### DECISION-MAKING IN THE PAEDIATRIC ONCOLOGY SETTING: PARENTS' PERSPECTIVES

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**Background:** Decision-making is just one of the many challenges parents face in caring for their child with cancer. Although parents are increasingly involved in decision-making, research in this area is limited especially within the paediatric oncology setting. This study examined 12 parents' experiences of caring for their ten children aged six months to 12 years with cancer as they progressed through the illness trajectory.

**Methods:** This longitudinal study was guided by the constructivist paradigm. This approach enabled the researcher as instrument to interpret the reality of parenting a child with cancer through the meanings these parents attached to their experience. The study was conducted in a children's hospital in western Sydney. In-depth interviews, documentary evidence and observations were the strategies used to collect data.

**Results:** Throughout the treatment period parents were faced with multiple decisions that impacted on their child's care and treatment. Parents involvement in decision making was primarily determined by the nature of the decision and differed for day-to-day care decisions and treatment-related decisions. Parents assumed an active role in day-to-day care decisions, while most parents were happy to assume a collaborative or passive rather than active role in treatment-related decisions

**Conclusion:** It is important that health professionals provide sufficient information and support to parents to enable them to partake in the decision-making process to the degree to which they feel able.

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### NIRS DETECTS CEREBRAL OXYGENATION CHANGES INDUCED BY TACTILE, AUDITORY AND VISUAL STIMULATION IN TERM NEONATES

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**Background:** Near-infrared spectrophotometry (NIRS) can be used to reliably assess changes in cerebral oxy- and deoxyhaemoglobin (O2Hb and HHb) concentrations associated with normal and pathologic processes. It is well suited for the purpose of functional brain analysis. However, in the term and preterm infant, normal oscillatory fluctuations in cerebral haemodynamics can obscure functional activation changes and complicate data analysis.

**Aim:** 1. To improve visualization of functional activation changes in the term and preterm infant. 2. To establish a method to detect functional impairments based on NIRS using different functional stimuli.

**Methods:** The NIRS instrument consists of a measuring system, stimulation unit and sensors. To allow for mapping of different brain regions, 8 locations were analyzed simultaneously. Several different stimulation tasks were performed: *tactile* (vibration motor), *auditory* (headphones), and *visual* (light emitting diodes). Four sensors were placed over either the C3 or C4 area (tactile), T3 or T4 area (auditory), or the occipital O1 area (visual). Left and right sides were alternately stimulated for 20s. Each stimulation period was followed by 10 seconds of rest. Stimulation-rest cycles were repeated for a minimum of 10min.

**Results:** For *tactile* stimulation, a total of 29 measurements in 15 neonates were recorded. For *auditory* stimulation a total of 27 measurements in 14 neonates, and for *visual* stimulation a total of 30 measurements in 10 neonates were recorded. Without application of specialized data analysis techniques, separated, localized, functional activations were visible in 10% of the measurements. In the remaining 90% haemodynamic changes in O2Hb and HHb, resulting from non-localized, slow vasomotion, obscured the functional signal. The amplitude of this vasomotion in the visual cortex was smaller compared to the other areas, but much larger in neonates than in adults. The latter due to immature autoregulation. Novel data analysis methods, such as an automated movement recognition algorithm and adaptive filter, allowed suppression of the slow vasomotion signal and improved the visualization of functional activation changes.

**Conclusions:** Suppression of the slow vasomotion signal enables us to more clearly visualize the local changes in cerebral oxygenation due to tactile, auditory and visual stimulation.

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### NEAR INFRARED SPECTROPHOTOMETRY DETECTS THE NEURONAL ACTIVATION INDUCED BY TACTILE, AUDITORY AND VISUAL STIMULATION IN TERM NEONATES

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**Background:** Near infrared spectrophotometry (NIRS) can be used to non-invasively measure changes in optical properties during functional activation. Because these changes originate from differences in optical properties between activated and non-activated neurons, the spatial localization and temporal resolution of this signal make it a promising tool for studying the time course of neuronal activity in localized brain areas. So far no normative data exist in neonates.

**Aim:** 1. To detect neuronal activation and observe its time course in healthy term and preterm infants. 2. To get normative data in order to establish a NIRS optical encephalogram.

**Methods:** The NIRS instrument consists of a measuring system, stimulation unit and sensors. To allow for mapping of different brain regions, 8 locations were analyzed simultaneously. The following stimulation tasks were performed: *tactile* (vibration motor), *auditory* (headphones), and *visual* (light emitting diodes). Four sensors were placed over either the C3 or C4 area (tactile), T3 or T4 area (auditory), or the occipital O1 area (visual). Left and right sides were alternately stimulated for 20s. Stimuli were pulsed using random on/off cycles ranging from 300 to 500ms. Each stimulation period was followed by 10 seconds of rest. Stimulation-rest cycles were repeated for a minimum of 10min. Novel adaptive spectral filters were applied to extract the neuronal signal from the optical intensity signal. A time triggered, folded average allowed isolation of the time course of the neuronal signal.

**Results:** For *tactile* stimulation a total of 29 measurements in 16 neonates were recorded. For *auditory* stimulation a total of 27 measurements in 14 neonates, and for *visual* stimulation a total of 30 measurements in 10 neonates were recorded. Preliminary results indicate that visualization of the neuronal response to *tactile* stimulation was possible in 13 infants and to *auditory* stimulation in 11 infants. No clear signal could be observed during *visual* stimulation. The latter might be due to immaturity, as only the subcortical visual region is activated in term newborns.

**Conclusions:** Our observations show that it is possible to detect neuronal activation from the optical NIRS signal in healthy term infants. The NIRS system thus, may provide an inexpensive tool for cerebral functional diagnostics in the neonatal intensive care unit.

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### ANTIMICROBIAL PEPTIDE ACTIVITY OF AMNIOTIC FLUID WITH AND WITHOUT PROLONGED RUPTURE OF MEMBRANE

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**Aim:** Antimicrobial peptides are widespread in nature and play a critical role in host defense however, their role in innate immunity of newborn infants is not clarified. Our aim is to examine antimicrobial peptide activity of amniotic fluid comparing with and without prolonged rupture of membrane (PROM). **Material and methods:** Amniotic fluids from six term infants without PROM and four ones with PROM were examined. All samples of amniotic fluid were obtained at elective caesarean section. The gestational ages and birth weights of the former and later groups were 38 ± 1.5w and 3551 ± 479g, 39 ± 0.9w and 3605 ± 443g, respectively. The collected amniotic fluid was adjusted with 0.1% trifluoroacetic acid (TFA). For enrichment of proteins/peptides these solutions were passed through OASIS columns at 4°C and eluted peptides/proteins were typhosphilized. All these samples were analyzed for antimicrobial activity against *Bacillus megaterium*, (strain Bm11), using an inhibition zone assay. **Result and conclusion:** The diameters of inhibition zone assay for amniotic fluid against Bm11 with PROM (14.4 ± 1.8mm) were larger than those without PROM (11.1 ± 0.89mm). Antimicrobial peptide in amniotic fluid may play a more intrinsic role in a condition with PROM.

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### EPITHELIAL REPAIR IN THE PRETERM LUNG IS DECREASED IN THE EARLY PHASE OF BRONCHOPULMONARY DYSPLASIA

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**Background:** In the early phases bronchopulmonary dysplasia (BPD) is characterized by epithelial and endothelial damage and inflammation. A recent study showed an absent or decreased concentration of keratinocyte growth factor, a factor contributing to epithelial repair, in early BPD (Danan C et al, Am J Respir Crit Care Med. 2002;165:1384–7).

**Aim:** To investigate whether bronchoalveolar lavage fluid (BALF) from preterm infants who develop BPD has a decreased capacity to stimulate epithelial repair compared to BALF from infants who recover from respiratory distress syndrome (RDS).

**Methods:** A standardized blind bronchoalveolar lavage was performed with 2x1 ml/kg saline in ventilated preterm infants with a gestational age <30 weeks on day 2 to 4 of life. Infants who recovered from RDS were all extubated within the first week of life. BPD was defined as oxygen requirement at 28 days of life. A bronchial epithelial cell line (BEAS) was grown to confluence and a scratch of known surface area was made in the epithelium (Geiser et al, Am J Physiol Lung Cell Mol Physiol 2000;279:L1184–90). BALF (or control medium without serum) was added to the cell cultures for 18 hours and the closure of the epithelial wound was assessed (expressed as % closure above control medium).

**Results:** BALF from infants who developed BPD (n=13) had a significantly lower capacity to stimulate epithelial wound closure than BALF from infants who recovered from RDS (n=10): 25±5% versus 48±4.5% closure above control medium (p=0.02 by t-test) (mean±SEM).

**Conclusion:** BALF on day 2 to 4 from preterm infants who develop BPD has a decreased capacity to stimulate epithelial repair in an in vitro assay compared to BALF from infants who recover from RDS. This suggests that besides epithelial injury also decreased epithelial repair plays a role in the early phase of BPD development. Further investigations are necessary to elucidate which growth factors or other factors are important for the decreased epithelial repair in the early phase of BPD development.