**The 68th Congress of Japan Society for Neonatal Health and Development**

# The 6th Japan-Taiwan-Korea Joint Congress on Neonatology

## Management of Infants Born at 22-23 Weeks' Gestation

**November 9(Sat), 2024**
**HOTEL BUENA VISTA, Matsumoto, Japan**


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# Program at a glance

November 9(Sat), 2024

8:30-8:40

## Opening Remark

Naoto Takahashi (The University of Tokyo)

8:40-9:10

## Key Note Speech

Chairman Satoshi Kusuda (Neonatal Research Network Japan)



9:10-11:40

## Symposium：Management of Infants Born at 22-23 Weeks'Gestation

Chairman Hung-Chih Lin (China Medical University Children's Hospital)
Yun Sil Chang (Sungkyunkwan University School of Medicine)

11:40-13:20

## Lunch and Poster Viewing

13:20-14:10

## Oral Presentation 1

Chairman Kana Saito (Tokai University)
Kazumichi Fujioka (Kobe University)

14:10-15:00

## Oral Presentation 2

Chairman Saneyuki Yasuda (Kagawa University)
Shin Kato (Japanese Red Cross Aichi Medical Center)

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Toshihiko Ikuta (JPN) ……22

15:00-15:30

## MOU Ceremony and Closing

Master of Ceremony Hiroko Iwami (Osaka City General Hospital)

**San-Nan Yang** (Taiwan Neonatology Society)
**Min Soo Park** (Korean Society of Neonatology)
**Naoto Takahashi** (Japan Society for Neonatal Health and Development)

## Poster Presentation

# Key Note Speech

## Deliveries at 22-23 weeks' gestation: an international perspective on lessons learned

**Matthew Rysavy, MD, PhD**
**Department of Pediatrics, McGovern Medical School, UTHealth Houston**

Not long ago, in the 1960s and 70s, it was uncommon for babies born before 27 weeks to survive. However, neonatal intensive care has changed dramatically and, in many hospitals around the world, the majority of infants at 22-23 weeks' gestation now survive. Because of the knowledge that infants born at 22 and 23 weeks' gestation can survive, intensive care has increased substantially for babies born at these gestations in countries around the world. In the United States, for example, from 2008 to 2021, the number of infants born at 22 weeks in neonatal intensive care units increased more than 400%. However, while admission for intensive care has increased, specific intensive care intereventions remain understudied, with little scientific evidence to guide care decisions.

How should clinicians guide clinical care? A review of 10 years of clinical trials involving extremely preterm infants, including more than 200 clinical trials enrolling more than 32,000 babies, found that only 1.4% were 22 or 23 weeks' gestation. In the absence of robust scientific evidence about safe and effective treatment, many clinicians have relied on anecdotal information about treatments thought to be effective at hospitals with high rates of survival, such as many Japanese units, the University of Iowa in the United States, the University of Uppsala in Sweden, and the University of Cologne in Germany. Information from institutions such as these has been the basis of many protocols for caring for infants born at 22 and 23 weeks. However, notably, many approaches recommended by these institutions are quite different, some directly conflict, and few have been formally tested.

The Tiny Baby Collaborative (tinybabycollaborative.org) was established to collect data on clinical practices and outcomes at 22 and 23 weeks and to bring together interested clinicians and parents to identify and answer important research questions. The Collaborative has worked with hospitals in the U.S., Japan, Australia, U.K., Sweden, Germany, and Canada to elaborate what is known and unknown in areas of controversy.

# Symposium

## SY-1 Current status and prognosis of periviable premature infants in Taiwan

**Ming-Chih Lin, M.D., PhD**

**[1]Department of Post-Baccalaureate Medicine, College of Medicine, National Chung Hsing University, Taichung, Taiwan**

**[2]Children's Medical Center, Taichung Veterans General Hospital, Taichung, Taiwan**

Caring for periviable premature infants remains a challenging task, involving both medical and ethical considerations. According to data from the Taiwan Neonatal Network covering the years 2016 to 2023, the survival rates for these infants were reported as 23.7% at 22 weeks, 38.9% at 23 weeks, and 61.9% at 24 weeks gestational age. When excluding early deaths, the survival rates increase to 52.7% at 22 weeks, 58.7% at 23 weeks, and 68.7% at 24 weeks. The incidence of chronic lung disease was reported as 95.5% at 22 weeks, 83.5% at 23 weeks, and 79.7% at 24 weeks gestational age. Severe intraventricular hemorrhage (IVH) was observed in 44.9% of infants at 22 weeks, 38.8% at 23 weeks, and 26.1% at 24 weeks. Cystic periventricular leukomalacia (cPCL) occurred in 5.8% of cases at 22 weeks, 6.0% at 23 weeks, and 5.7% at 24 weeks. The prevalence of retinopathy of prematurity (ROP) was 75.0% at 22 weeks, 68.2% at 23 weeks, and 58.3% at 24 weeks. Additionally, the incidence of necrotizing enterocolitis (NEC) was 5.4% at 22 weeks, 7.2% at 23 weeks, and 8.7% at 24 weeks. Overall mortality and morbidity remain high, with rates of 100.0% at 22 weeks, 96.1% at 23 weeks, and 93.4% at 24 weeks gestational age. Pneumothorax and late sepsis are also significant concerns for these infants.

In a long-term follow-up study based on data from the Premature Baby Foundation of Taiwan, neurodevelopmental impairment was observed in 100% of infants born at 22 weeks, 53.9% of those born at 23 weeks, and 60.3% of those born at 24 weeks. Chronic lung disease was reported in 66.7% of infants at 22 weeks, 87.5% at 23 weeks, and 70.8% at 24 weeks. Additionally, retinopathy of prematurity occurred in 100% of infants born at 22 weeks, 69.7% at 23 weeks, and 63.5% at 24 weeks. Cesarean delivery may be associated with a decreased intraventricular hemorrhage (IVH) risk, however, without improvement in severe IVH, mortality, or neurodevelopment at 2-year corrected age.

In advanced economies and Northeast Asia, neonatologists tend to adopt a more conservative approach towards fluid management, maintain higher incubator humidity settings and inclined to perform surgical ligation for patent ductus arteriosus. IVH greater than grade II might be decreased after use of customized circulatory management.

# SY-2 The management and outcomes of infants born at 22–23 weeks' gestation in Korea

**Ga Won Jeon, MD, PhD**

**Department of Pediatrics, Inha University Hospital, Inha University College of Medicine, Incheon, Korea**

Survival rates for infants born at 22–23 weeks' gestation vary significantly by country and hospital, with differences particularly notable at these gestational ages. At more advanced gestational ages, survival rates tend to be more consistent. The reasons for the differences in survival rates are as follows.

The first reason for the difference in survival rates is the variation in proactive care across countries and hospitals, influenced by differing ethical or legal perspectives, which in turn can impact survival rates. Data from the Vermont Oxford Network show that the rate of proactive care for infants born at 22 weeks' gestation increased from 26% in 2007 to 58% in 2019. Consequently, the survival rate for these infants rose from 5% in 2007 to 17% in 2019. A positive correlation was observed between the rates of proactive care, neonatal intensive care unit admissions, assisted ventilation, antenatal corticosteroid administration, and the survival rate of infants born at 22 weeks' gestation.

The second reason for the difference in survival rates is the centralization of care. In 2014, Sweden recommended centralizing all extremely preterm births to six university hospitals. Following this recommendation, from 2014 to 2016, compared with the period from 2004 to 2007, the stillbirth rate at 22 weeks' gestation decreased from 65% to 35%, and the 1-year survival rate for all live-born infants at 22 weeks' gestation improved from 10% to 30%.

The third reason for the difference in survival rates is the variation in national guidance. In 2020, the British Association of Perinatal Medicine developed new consensus guidelines recommending that survival-focused care may include babies born at 22 weeks. After the release of these guidelines, the percentage of babies receiving survival-focused care increased from 11.3% to 38.4%, and survival to discharge rose from 2.5% to 8.2%. In Sweden, new national guidelines were introduced in 2014, recommending the centralization of care. At 22 weeks' gestation, a neonatologist should be present at birth and intensive care may be considered, while at 23 weeks' gestation, intensive care is recommended. Following the introduction of these guidelines, the mortality rate for infants born at 22 weeks' gestation decreased from 96% to 76%, and the 2-year survival rate increased from 4% to 24%. For infants born at 23 weeks, the mortality rate dropped from 56% to 27%, and the 2-year survival rate increased from 42% to 64%.

In conclusion, centralization of care to experienced hospitals with appropriate neonatal intensive care resources, such as adequate personnel and facilities, can improve the survival and outcomes of these vulnerable infants. National guidance for their treatment is essential.

# SY-3 Fluid management in infants born at ≤24 weeks gestation: The DOs and DON'Ts

**Johan Agren MD, PhD**
**Uppsala University, Department of Women's and Children's Health**
**University Children's Hospital, Neonatology Division**
**Uppsala, Sweden**

While the evidence-base to guide fluid management in tiny babies is very limited, a few fundamentals need to be taken into account when providing fluids and electrolytes during the first 1-2 weeks. Firstly, a general understanding of the fetal/postnatal physiology of body water content and distribution is required. Secondly the relative deficiency of skin barrier function and renal regulatory capacity needs to be taken into account. Thirdly it is important to consider the interplay with the environment (skin barrier), how fluid and electrolyte status changes with the postnatal transition and beyond (renal function), and how/when these factors impact the care provided. Fluid management benefit from knowledge about what to expect, implementation of protocols for care environment, initial prescription of water and salt, and standardized monitoring with pre-defined targets. The presentation aims to cover aspects simplistically expressed as treatment recommendations (the Dos) and pitfalls that should be avoided (the DON'Ts).

**DOs**

- Provide starting fluid intakes in a range tailored to gestational age and the level of incubator humidity used.
- Standardize the types of fluids used, and the rates of infusion. "Separate" nutrition from adjustable fluids.
- Minimize initial intake of sodium (include ALL sources) to allow postnatal loss of extracellular water.
- Monitor body weight, urine output, and serum sodium closely.
- Know what to expect, and when, and adjust in relation to set management targets.

**DON'Ts**

- Inadvertently provide too much sodium in to-keep-open fluids, flushes, transfusions, PN etc.
- Blindly trust balance calculations from charts - weigh the baby!
- Disregard diapers weighed with stools - it's (almost) all urine!
- Frequently adjust PN and/or fluids with high dextrose content - hyperglycemia
- Think that rapid weight gain = growth!
- Use highly humidified incubation for several weeks.

# SY-4 Management and outcomes of periviable infants born at 22 to 23 weeks of gestation: experience-based medicine in Japan

**Fumihiko Namba MD, PhD**
**Department of Pediatrics, Saitama Medical Center, Saitama Medical University**

Despite the existence of recommended guidelines for the resuscitation of premature infants in major developed countries, no such guidelines currently exist in Japan. A survey of Japanese neonatal intensive care units (NICUs) revealed that approximately half of these units actively resuscitate infants born at 22 weeks' gestation. The in-hospital survival rate for infants born at 22 weeks' gestation who have undergone active resuscitation has been 70% in Japan.

At present, delayed cord clamping is advised for infants born extremely prematurely, given the elevated risk of severe intraventricular hemorrhage (IVH) associated with intact cord milking. In Japan, the predominant method of cord management is cut cord milking. In 90% of Japanese NICUs, cord milking is performed at 22-23 weeks.

A systematic review of the respiratory management of preterm infants in the delivery room demonstrated that continuous positive airway pressure for respiratory distress in very preterm infants reduced the incidence of death or bronchopulmonary dysplasia (BPD) compared with tracheal intubation. Furthermore, catheter-based administration of surfactant for respiratory distress syndrome in preterm infants has been demonstrated to reduce the risk ratio of death or BPD, death, tracheal intubation, BPD, and severe IVH in comparison with endotracheal tube administration. In contrast, tracheal intubation is performed in the delivery room in 94% of Japanese NICUs, either shortly after birth, after heart rate recovery, or after heart rate and SpO2 stabilization.

In 88% of Japanese NICUs, echocardiography is performed more than twice a day within the first three days of life. In approximately 60% of Japanese NICUs, steroids, dopamine/dobutamine, and volume loading are used for more than 50% of infants born at 22-23 weeks of gestation to maintain blood pressure during the acute phase.

A Cochrane review of high-frequency ventilation (HFOV) for respiratory failure in preterm infants demonstrated that HFOV reduced the incidence of BPD and retinopathy of prematurity compared to conventional mechanical ventilation. In Japanese NICUs, the initial ventilation mode is synchronized intermittent mandatory ventilation, which is subsequently replaced by HFOV. Following the initial seven-day period, HFOV is employed in approximately 60% of Japanese NICUs.

A synthesis of the findings of a Cochrane review of pharmacologic analgesia and sedation for the prevention of IVH in preterm infants requiring respiratory support revealed that none of the tested drugs demonstrated a protective effect against IVH when compared with a placebo. With regard to acute sedation, over 70% of NICUs utilize sedation during the acute phase, with fentanyl being the most frequently employed drug.

In Japan, probiotics are utilized in 90% of NICUs. Enemas are employed in the majority of Japanese NICUs. The survival rate of premature infants in Japan is notably superior to that observed in other countries. However, the incidence of severe neurodevelopmental impairment among extremely premature infants has been on the rise over the past decade. In Japan, the discourse has now transitioned from merely enhancing survival rates to exploring strategies for improving survival rates without impairment and enhancing the quality of life for these vulnerable infants and their families.

# Oral Presentation 1

## O-1 Factors influencing weight percentile at discharge in very low birth weight infants from the Taiwan Neonatal Network (TNN) Database

**Hsiu-Lin Chen[1,2] MD, Yu Hsien Wei[3] MD**

**[1]Department of Pediatrics, Kaohsiung Medical University Hospital, Kaohsiung, Taiwan**

**[2] School of Medicine, College of Medicine, National Sun Yat-sen University, Kaohsiung, Taiwan**

**[3] School of Medicine, College of Medicine, Kaohsiung Medical University, Kaohsiung, Taiwan**

**Objective**: Extrauterine growth retardation (EUGR), defined as a weight percentile below the 10th percentile at discharge, is a significant concern for very low birth weight (VLBW) premature infants. This study aims to analyze the factors influencing weight percentile at discharge using the Fenton growth chart based on data from the Taiwan Neonatal Network (TNN) database.

**Methods**: Data on maternal, neonatal characteristics, and nutritional factors of VLBW preterm infants were collected from the TNN database from 2019 to 2023. Univariate and multivariate multiple regressions were used to determine significant factors influencing weight percentile at discharge.

**Results**: The study included 790 VLBW preterm infants (396 males, 394 females) with a mean gestational age of 28.7 weeks and a mean birth weight (BBW) of 1115.2 grams. At discharge, 49.9% of the infants were classified as EUGR. Univariate analysis revealed significant maternal, neonatal, and nutritional factors influencing weight percentile at discharge, including cesarean section, multiple births, pregnancy-induced hypertension, chorioamnionitis, prenatal MgSO4 exposure, BBW percentile, 5th Apgar score, length of stay, retinopathy of prematurity, highest weight loss percentage after birth, amount of trophic feeding, growth rates after regaining BBW to 36 weeks of postmenstrual age (PMA), and weight percentile at 36 weeks of postmenstrual age (PMA). Multivariate analysis identified BBW percentile, highest weight loss percentage after birth, length of stay, growth rates after regaining BBW to 36 weeks of PMA, and weight percentile at 36 weeks of PMA as significant factors affecting weight percentile at discharge. Additionally, the rate of regaining BBW from the lowest weight by day was found to be the most crucial factor influencing weight percentile at 36 weeks of PMA.

**Conclusion**: This study highlights the importance of the rate of regaining birth weight from the lowest weight by day on the weight percentile at 36 weeks of PMA in VLBW preterm infants during their stay in the neonatal intensive care unit.

# O-2 Impact of hydrogen gas inhalation during therapeutic hypothermia on cerebral hemodynamics and oxygenation in the asphyxiated piglet

**Shinji Nakamura MD., DMSc.[1], Yasuhiro Nakao MD.[1], DMSc., Yinnmon Htun MD., DMSc.[1], Tsutomu Mitsuie DMSc.[2], Kosuke Koyano MD., DMSc.[3], Aya Morimoto MD., DMSc.[3], Yukihiko Konishi MD., DMSc.[1], Makoto Arioka MD., DMSc.[1], Sonoko Kondo MD., DMSc.[1], Ikuko Kato MD., DMSc.[1], Saneyuki Yasuda MD., DMSc.[4], Takashi Kusaka MD., DMSc.[1]**

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**[3]Maternal Perinatal Center, Faculty of Medicine, Kagawa University, Kagawa, japan**

**[4]Postgraduate Clinical Education Center, Kagawa University Hospital, Kagawa, Japan**

**Background &Aim**: We previously reported the neuroprotective potential of combined hydrogen (H2) gas ventilation therapy and therapeutic hypothermia (TH) by assessing the short-term neurological outcomes and histological findings of 5-day neonatal hypoxic-ischemic (HI) encephalopathy piglets. However, the effects of H2gas on cerebral circulation and oxygen metabolism and on prognosis were unknown. Here, we used near-infrared time-resolved spectroscopy to compare combined H2 gas ventilation and TH with TH alone.

**Methods**: Piglets were divided into three groups: HI insult with normothermia (NT, n = 10), HI insult with hypothermia (TH, 33.5 ± 0.5 °C, n = 8), and HI insult with hypothermia plus H2 ventilation (TH + H2, 2.1–2.7%, n = 8). H2 ventilation and TH were administered and the cerebral blood volume (CBV) and cerebral hemoglobin oxygen saturation (ScO2) were recorded for 24 h after the insult.

**Results**: CBV was significantly higher at 24 h after the insult in the TH + H2 group than in the other groups. ScO2 was significantly lower throughout the 24 h after the insult in the TH + H2 group than in the NT group.

**Conclusion**: Combined H2 gas ventilation and TH increased CBV and decreased ScO2, which may reflect elevated cerebral blood flow to meet greater oxygen demand for the surviving neurons, compared with TH alone.

# O-3 Perceptions on family-centered care among health care providers of Korean neonatal intensive care units

**[1]Eunhye Lee, RN, [2]Nawon Oh, MD, [2]Juyoung Lee, MD. PhD**

**[1]College of Nursing, Inha University, Incheon, Korea**

**[2]Department of Pediatrics, Korea University Anam Hospital, Seoul, Korea**

**Background**: Family-centered care (FCC) is a method in which parents are actively involved and their opinions are respected in the care of their baby. It is not known to what extent the FCC is implemented in Korean neonatal intensive care units (NICUs). Staff perceptions of FCC may influence clinical practice and management strategies of FCC in NICUs.

**Objectives**: To identify staff perceptions and current practice of FCC in Korean NICUs.

Methods: The family-centered care questionnaire-revised (FCCQ-R)@it-NICU was used from 344 staff of 70 NICUs of Korea. A total of 44 questions of 9 areas were asked using a Likert scale ranging from 1 to 5 about both current state and necessity of FCC. Paired t-test, independent t-test, and ANOVA were used to analyze the data.

**Results**: The total mean (±SD) scores of the necessary dimension was significant higher than those of the current dimension of FCCQ-R@it-NICU (3.91±0.20 vs. 3.33±0.27; $p<0.001$), and the biggest difference between Necessary and Current dimension was found in the area of providing support to staff (4.1±0.39 vs. 3.0±0.60; $p<0.001$). The answers for Necessary dimension showed significant higher scores among staff with parental experience ($p=0.026$), receiving education sessions on FCC ($p=0.012$), and who worked in NICUs more than 10 years ($p=0.045$).

**Conclusion**: Medical staff in Korean NICUs are aware of the need to implement FCC and seem to recognize that the current state falls short of the ideal FCC. Their parental experience, training on FCC, and work experience over 10 years positively influence the perception of what is required for FCC practice within NICUs.

# O-4 Machine learning approaches for predicting perinatal brain injury using early birth data

**Ga Won Jeon, MD, PhD, Yeong Seok Lee, MD, Won-Ho Hahn, MD, PhD, Yong Hoon Jun, MD, PhD**

**Department of Pediatrics, Inha University Hospital, Inha University College of Medicine, Incheon, Korea**

**Background/Objective**: It is difficult to predict perinatal brain injury, and performing brain magnetic resonance imaging (MRI) based on suspected injury remains a clinical challenge. Therefore, we aimed to develop a reliable method for predicting perinatal brain injury using a machine learning model with early birth data.

**Methods**: Neonates admitted to our institution from January 2017 to June 2024 with a gestational age of ≥36 weeks, a birth weight of ≥1,800 grams, admission within 6 hours of birth, and who underwent brain MRI to confirm perinatal brain injury were included. Perinatal brain injury was defined as the presence of HIE, perinatal arterial ischemic stroke, intracranial hemorrhage, or cerebral sinovenous thrombosis confirmed on a sub-sequent brain MRI. Various machine learning models, including gradient boosting, were trained using early birth data to predict perinatal brain injury. Synthetic Minority Over-sampling and Adaptive Synthetic Sampling (ADASYN) were applied to address class imbalance. Model performance was evaluated using accuracy, F1 score, and ROC curves. Feature importance scores and SHapley Additive exPlanations (SHAP) values were also calculated.

**Results**: Among 179 neonates, 39 had perinatal brain injury. There were significant differences between the injury and non-injury groups in mode of delivery, apgar scores, capillary pH, lactate dehydrogenase (LDH) levels, and whether therapeutic hypothermia was performed. The gradient boosting model with ADASYN method achieved the best performance. In terms of feature importance scores, the 1-minute Apgar score was the most influential predictor. Additionally, SHAP analysis showed that LDH levels had the highest SHAP values.

**Conclusion**: The gradient boosting model with ADASYN oversampling effectively predicts perinatal brain injury, potentially improving early detection for predicting long-term outcomes, reducing unnecessary MRI scans, and lowering healthcare costs.

This paper will be presented as a poster at the 74th Conference of the Korean Pediatric Society in 2024.

# O-5 A nationwide survey of Neonatal Pseudohypoaldosteronism Type-1 in Japan

**Kazumichi Fujioka MD, PhD, Yuki Nakata MD, Masafumi Fujimoto MD, Yukihito Imagawa MD, Yu masuda MD, Keisuke Shirai MD, Takumi Kido MD, PhD, Mariko Ashina MD, PhD, Kandai Nozu MD, PhD**
**Department of Pediatrics, Kobe University Graduate School of Medicine**

**Background:** Pseudohypoaldosteronism type 1 (PHA-1) is a disorder caused by renal tubular resistance to aldosterone and is characterized by problems with sodium regulation. PHA-1 is typically divided into primary PHA-1, which is caused by genetic mutation, and secondary PHA-1, which is associated with urinary tract abnormality. However, data on the clinical features of PHA-1 among newborn infants are limited.

**Methods:** We conducted a nationwide prospective surveillance study of neonatal PHA in Japan from 1 April 2019 to 31 March 2022 as part of a rare disease surveillance project of the Japan Society for Neonatal Health and Development.

**Results:** Fifteen cases (male:female = 7:8), including four primary, four secondary, and seven non-classified cases, were reported during the study period. The median gestational age and birthweight were 34 weeks (28-41) and 1852 g (516-4610), respectively. At the onset, the median serum Na and K levels were 132 mEq/L (117-137) and 6.3 mEq/L (4.7-8.3), respectively. The median plasma renin activity was 45 ng/mL/h (3.1-310, n = 9), active renin concentration was 1017 pg/mL (123-2909, n = 6), and serum aldosterone concentration was 5310 pg/mL (3250-43,700).

**Conclusions:** Neonatal PHA-1 was more common among preterm infants with no male predominance. It developed immediately after birth in cases without genetic or renal complications.

# Oral Presentation 2

## O-6 Exploring the NEC-necroptosis link: insights from in vivo and enteroids models

**Hsiang-Yu Lin [1,2], Chu-Han Chang [3], Yi-xue Yeow [3], Shu-Wei Lin [3], Ya-Huey Chen [2,3]**

**[1]China Medical University Children's Hospital [2]China Medical University, Graduate Institute of Biomedical Sciences [3]China Medical University Hospital**

**Objective**: Despite neonatal care advances, necrotizing enterocolitis (NEC) remains a severe complication in premature infants. We explore the role of necroptosis, a regulated cell death form, in NEC development using both in vivo and enteroid models. Recent studies link necroptosis to inflammatory diseases, with RIPK1, RIPK3, and MLKL as key regulators. We propose necroptosis as a significant factor in NEC, offering potential therapeutic strategies. Methods: We used an established mouse NEC model (3-6 day-old C57BL/6J mice) involving hypoxia, hypothermia, and reoxygenation, with LPS administration. An in vitro NEC model using enteroids was developed. We assessed enteroid viability under various conditions and evaluated necroptosis-associated gene expression and protein activation.

**Results**: Histological examination showed disrupted villous structure in the NEC group. Quantitative assessment confirmed exacerbated NEC in treated mice. RIPK1 expression was upregulated in disease groups with increased pRIP1 levels, suggesting necroptosis pathway activation. RIPK3 expression remained high in all tissues, while MLKL expression was elevated in disease samples. The enteroid model showed disrupted epithelial architecture and increased necroptosis-related protein expression upon LPS exposure.

**Conclusions**: We established a positive correlation between NEC and necroptosis in both mouse and enteroid models. Increased expression and phosphorylation of RIP1 were detected in NEC-afflicted mouse intestines, with heightened necroptosis-related protein expression in diseased enteroids. These findings demonstrate necroptosis activation in NEC, highlighting its potential as a treatment target.

# O-7 Maternal and neonatal risk factors of sepsis in preterm infants: nationwide population based study

**Chih-Sung Lan[1] MD, Hsiao-Han Yang[1] MD, Hao-Wen Cheng[1] MD, Ming-Luen Tsai[1,2] MD, Shang-Po Shen[1] MD, Yin-Ting Chen[1] MD, Hsiao-Yu Chiu[1] MD, Hsiang-Yu Lin[1,2] MD, Hung-Chih Lin[1,3] MD**

**[1] Division of Neonatology, China Medical University Children's Hospital**

**[2] Graduate Institute of Biomedical Sciences, China Medical University**

**[3] Department of Pediatrics, Asia University Hospital, Asia University**

**Background**: The Global Burden of Disease estimated neonatal sepsis incidence was 2.82 cases per 100 live births, of which estimated 17.6% died. Identifying risk factors may offer opportunities for early intervention. We aim to design the nationwide study about preterm neonatal sepsis.

**Methods**: We paired pregnant individuals and their preterm offspring between 1 January 2010 and 31 December 2019 from the National Health Insurance Research Database. We collected sepsis cases within three months after birth and excluded unlikely cases whom did not have blood culture, antibiotics treatment or hospitalized less than 10 days. Control group is selected by matching 1:5 numbers ratio from all live births excluding those ever diagnosed as sepsis, and ever admitted in the sick baby room or ICU. Risk analyses were performed, and a multivariate logistic regression analysis was conducted to adjust for covariates.

**Results**:Among 176681 preterm neonates born from 2010 to 2019, a total of 5521 newborns (3.12%) suffered from sepsis. More than a half (82.9%) neonates with sepsis was found within three days after birth. By adjusted stepwise logistic regression, full-term young infants with sepsis correlated with maternal fever, chorioamnionitis, maternal pneumonia, PPROM, maternal antibiotics usage, gestational age < 32wks , LBW, perinatal infections, insertion of endotracheal tube, previous antibiotics usage, previous TPN usage, admission in NICU (all above P <0.001), previous UTI (P = 0.005), maternal bacteremia (P = 0.007), delivered by C/S (P = 0.012), maternal DM (P = 0.02), previous steroids usage (P = 0.03), maternal steroids usage (P = 0.042), previous pneumonia (P = 0.042).

# O-8 The mechanism of hyperglycemia in a non-obese diabetes mouse model born with small-for-gestational age

**Nobuhiko Nagano MD, PhD, Ichiro Morioka MD, PhD**
**Department of Pediatrics and Child Health, Nihon University School of Medicine, Tokyo, Japan**

**Background**: Fetuses exposed to undernutrition may be born small-for-gestational age (SGA) and have a higher risk of developing diabetes if they become obese later in life, but some cases develop diabetes without significant obese after birth.

Objective: This study aimed to develop a non-obese hyperglycemic mouse model born SGA to investigate its pathogenesis.

**Methods**: At 16.5 days of gestation, transient intrauterine ischemia, blocked blood flow in both uterine arteries for 15 min, was performed in a subgroup of pregnant mice (I). Non-occluded dams were used as sham controls (C). After birth, female pups from each group reared on the normal diet until 8 weeks of age (n=7 for each group). Fasting blood glucose, serum insulin (IRI), homeostasis model assessment of insulin resistance (HOMA-IR), body composition, and metabolite analyses of the liver tissues were compared at 8 weeks of age.

**Results**: Birthweight was lower in group I compared to group C at birth (I: 1.5g, C: 1.9g, $p<0.05$), confirming SGA. The mice in group I remained underweight and exhibited hyperglycemia at 8 weeks of age (I: 36.9g, 213.0mg/dL, C: 41.2g, 72.0mg/dL, respectively, $p<0.01$). IRI and HOMA-IR were higher in group I (3.9μIU/mL, 2.08 vs. 1.0μIU/mL, 0.16, $p<0.05$). Fat mass was similar between groups (I: 16.6g, C: 17.7g, $p=0.95$), but lean body mass was lower in group I (19.1g vs. 22.6g, $p<0.05$), indicating a reduced muscle mass. Metabolite analyses from group I showed a significant reduction in adenosine triphosphate (I: 16.0nmol/g, C: 37.0nmol/g, $p<0.05$) and an increase in lactic acid compared to group C (I: 14.9nmol/g, C: 5.7nmol/g, $p<0.05$). indicating a mitochondrial dysfunction.

**Conclusion**: The pathogenesis of our non-obese hyperglycemic mouse model may be due to increased myogenic insulin resistance based on mitochondrial dysfunction and reduced muscle mass.

# O-9 Factors associated with response after systemic corticosteroid treatment in invasively ventilated preterm infants

**Gyeong Eun Yeom, MD[1]., Seung Han Shin, MD,PhD*[1,2], Ee-Kyung Kim, MD,PhD[1,2]**
**Ju sun Heo, MD.PhD[1,2], Han Suk Kim, Md.PhD[1,2]**
**Seoul National University Children's Hospital Department of Pediatrics[1]**
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**Objective** This study evaluated the factors associated with extubation failure after systemic corticosteroid (CS) therapy in preterm infants with established or evolving bronchopulmonary dysplasia (BPD).

**Study design** In this retrospective study, preterm infants with gestational age (GA) <32 weeks and/or birthweight <1500g, who admitted to Seoul National University Children's Hospital in 2013 and 2023, and received systemic CS therapy for BPD were included. Participants were classified as responders when they were extubated within 14 days after first dose of CS therapy. Perinatal and neonatal characteristics, as well as the respiratory severity score at the time of CS therapy and thereafter, were collected. Multivariate logistic regression analysis for non-responder was conducted.

**Results** Among the 62 infants, 32 were responders, and 30 were non-responders. There were no significant differences in GA (25.9 vs. 25.4 weeks, p=0.262) and birth weight (753.6 vs. 698 grams, p=0.132) between the groups. Non-responders began CS therapy at a younger postmenstrual age (PMA) (29.2 vs. 31.0 weeks, p=0.011) and earlier postnatal day (PND) (27.6 vs. 37.0 days, p=0.016). Non-responders had higher rates of iNO therapy for pulmonary hypertension (15.6% vs. 66.7%, p=0.001), more hemodynamically significant PDA (hsPDA) (3.1% vs. 30.0%, p=0.005), and higher RSS scores (4.54 vs. 6.87, p=0.001) at treatment initiation. RSS change (%) between day 1 and 4 was greater in responders (31.51 vs. 14.07, p=0.036). Multivariate analysis identified hsPDA (aOR 22.97, 95% CI 1.53-345.73, p=0.024), pulmonary hypertension treatment (aOR 3.00, 95% CI 0.85-10.55, p=0.089), day 1 RSS (aOR 3.16, 95% CI 1.39-7.17, p=0.006), and difference RSS between day 1 and day 3 (aOR 0.91, 95% CI 0.86-0.94, p=0.026) as significant factors.

**Conclusion** hsPDA, treatment of pulmonary hypertension, day 1 RSS, and difference RSS between day 1 and day 3 were crucial predictors of response after systemic CS therapy. The percentage difference in RSS between days 1 and 3 was critical in distinguishing treatment responses.

# O-10 Trends in serum albumin levels over the first two months of life in preterm infants

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**Background:** In preterm infants, hypoalbuminemia is associated with increased risks of mortality, respiratory distress syndrome, necrotizing enterocolitis, infection, and jaundice. However, evaluating human serum albumin (HSA) levels in preterm infants is challenging, since HSA levels vary with gestational age (GA) and postnatal day (PD). In a previous study (Neonatology, 2022), we have reported a linear increase in HSA levels at birth with GA based on cord blood data from 2,917 singleton infants without congenital anomalies. The current study aims to elucidate the postnatal changes in HSA levels in preterm infants.

**Methods:** In this single-center cohort study, all singletons born at 22-36 weeks of GA in a tertiary perinatal center between January 2017 and December 2022 were retrospectively investigated. Infants with congenital anomalies, those who died before discharge, or those who received albumin infusions were excluded. Minimum HSA levels measured on PD 0, 1-2, 3-6, 7-13, 14-20, 21-27, 28-41, and 42-55 were extracted, and compared using Kruskal-Wallis test followed by Dunnett's multiple-comparison tests. These analyses were also performed by stratifying into 22-26, 27-31, and 32-36 weeks of GA. Data was expressed as median (range).

**Results:** Of 463 singletons, 257 infants (55.5%) with 1,114 measurements were analyzed after exclusions. GA and birth weight were 33.4 (23.7-36.9) weeks and 1,846 (560-3,138) g, respectively. HSA levels (g/dL) were 2.8 (1.7-3.8) at PD 0, 2.9 (2.0-3.8) at PD 1-2, 3.1 (1.9-3.9) at PD 3-6, 3.2 (2.3-4.0) at PD 7-13, 3.3 (2.3-4.0) at PD 14-20, 3.2 (2.5-3.8) at PD 21-27, 3.2 (2.4-3.8) at PD 28-41, and 3.0 (2.5-3.6) at PD 42-55. HSA levels were significantly higher at PD 14-20 compared to PD 0 ($p < 0.001$) and lower at PD 42-55 compared to PD 14-20 ($p = 0.017$). Similar trends were observed even after stratifying by GA group.

**Conclusion:** HSA levels in preterm infants increase from birth to PD 14-20 and then gradually decrease until PD 42-55. These findings may provide valuable insights for assessing HSA levels in preterm infants.

# Poster Presentation

## P-1 Gut microbiota transition during the first week of age in healthy newborns

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The development and maturation of gut microbiome after birth has significant impact on infant health with life-long consequences. The gut microbiome undergoes a maturation process with great shifts in both composition and diversity during the early life. To determine the transition during the first week of life, we analyzed stool samples of first-pass meconium and 7 days of age from 27 healthy newborns using 16s rRNA sequencing. Our results showed the similar compositions of first-pass meconium with the most abundant genus Pseudomonas. Enterococcus, Bifidobacterium, Streptococcus and Lactobacillus were found enrichment in stool samples of 7-day of age. Shannon diversity indices were 1.38 and 1.62 in first-pass meconium and 7-day stool samples, respectively. It showed a significant upward trend with increasing age ($p=0.0129$), suggesting an increase in diversity during first week of life. In conclusion, gut microbiota composition showed great transition with increasing diversity in the early life.

# P-2 Navigating the complexities of sirolimus in neonatal hemangioma: a case study of klippel-trenaunay syndrome

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**Foreword**

Sirolimus, known for its ability to bind and regulate the mTOR enzyme, inhibits cellular vascular activation and proliferation. Commonly used to prevent organ rejection post-transplant, it has also been applied to treat hemangiomas. This case discusses sirolimus use for a newborn with Klippel-Trenaunay syndrome, a rare condition, highlighting a unique clinical scenario and the need for careful pharmaceutical management.

**Case**

The subject is a preterm infant born at 35+1 weeks gestation, weighing 2800 g. The newborn exhibited a lymphangioma in the right chest, swelling in the left arm, and purple patches on the trunk. Diagnosed with suspected Klippel-Trenaunay syndrome (excluding Kasabach-Merritt phenomenon), initial treatment involved intravenous methylprednisolone and oral propranolol.

Since symptoms did not improve, sirolimus 1 mg/m²/day was introduced after five days, alongside enoxaparin to prevent venous thromboembolism. The recommended first steady-state trough concentration was to be measured 10–14 days post-initiation. One week later, sirolimus levels were 25.5 ng/mL, exceeding the target range of 5-15 ng/mL. A one-compartment pharmacokinetic model suggested reducing the dose to 0.5 mg/m²/day after a 24-hour drug holiday. Despite this, sirolimus levels remained above 30 ng/mL, prompting a temporary cessation of the drug for three days. Sirolimus caused adverse effects including neutropenia (WBC: 0.7 x10^3 /ul, ANC: 335 /uL), thrombocytopenia (Platelets: 31 x10³/μL), and toxic shock syndrome from Methicillin Resistant Staphylococcus Aureus (MRSA), with concurrent acute hepatitis. The drug was discontinued, and shock was managed promptly.

One month later, at corrected age of 43+5 weeks,sirolimus was reintroduced at a lower dose of 0.2 mg/m²/day, which was adjusted to 0.25 mg/m²/day after one week, resulting in a stable concentration of 5.84 ng/mL. The infant was eventually discharged with good control of the condition and outpatient follow-up.

**Comment**

Sirolimus inhibits the PI3K/AKT pathway, affecting angiogenesis and lymphangiogenesis, making it useful for treating hemangiomas. Challenges in this case included: **(1)Scarcity of Newborn Cases**: Sirolimus use in neonates is rare, with limited dosing information available. Recommended doses may lead to severe complications. **(2)Pharmacokinetic Variability**: Neonates have distinct pharmacokinetic profiles and tissue metabolism, making drug metabolism unpredictable. The lack of specific pharmacokinetic parameters for sirolimus in neonates complicates dosing and monitoring.

Despite stable drug concentrations in subsequent treatments, past cases have reported complications with sirolimus use in infants, necessitating caution and thorough evaluation.

**Conclusion**

Sirolimus has been used for hemangiomas, but individual variability requires careful consideration. This case underscores the importance of pharmaceutical care services, emphasizing the need for collaborative efforts in assessing dosage, monitoring drug concentrations, pharmacokinetics, and side effects.

**Keywords**

Sirolimus, hemangioma, mTOR(mammalian target of rapamycin),Klippel-Trenaunay syndrome, phosphatidylinositol 3-kinase (PI3K)/AKT

# P-3 Lower mortality in units with prophylactic indomethacin in preterm infants <25 weeks: a national network study

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[**Background**] Prophylactic indomethacin (PIND) halves mortality in very preterm infants <25w, but there is variability in the unit rates of administration.

**[Methods**] In the NRNJ dataset (2003-2019), the correlation between PIND rate, survival rate, and 3-year outcomes was examined for each unit of infants at 22-24 weeks' gestation. The t-test and Pearson's product-moment correlation coefficient test were used in R.

[**Results**] 112 centers performed PIND and there were 1,321 infants in the PIND group. The mean number of PIND infants per center was 12.2, and the mean PIND rate was 15.9%. The correlation between the unit PIND rate and survival was r=0.36, 95% CI [0.18-0.52] (P<0.001). The mean survival rate of 80.0% for units with a PIND rate greater than 0.2 was greater than the survival rate of 74.7% for units with a PIND rate less than 0.2 (P=0.014). Higher PIND rates were associated with lower CP rates, r= -0.298, 95%CI[-0.594-0.0699], P= 0.11 (excluding units: (CP+ No CP)≦23 & PIND rate = 0). The CP rate of 0.151(±0.053) for units with a PIND rate above 0.25 was lower than the CP rate of 0.195(±0.073) for units with a PIND rate below 0.25(P=0.13). The mean DQ at 3 years was 83.2 for units with PIND rates above 0.25 and 75.6 for units with PIND rates below 0.25.

[**Conclusions**] Among preterm infants at 22-24 weeks' gestation, mortality was significantly lower in units with higher rates of indomethacin prophylaxis and may have improved neurodevelopmental outcomes at 3 years.

# P-4 Development of an application that analyzes baby cries using AI technology to estimate emotions and propose interventions

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**Background**: One in seven mothers suffers from postpartum depression. Leaving postpartum depression untreated may lead to an increased risk of child abuse and attachment disorders, making it essential to address this issue.

**Objective**: We developed an application that estimates emotions based on recordings of baby cries and proposes appropriate interventions for each emotion. The goal is to prevent postpartum depression and promote more relaxed parenting. Additionally, by making the app accessible to people other than mothers, we aim to create a society where anyone can actively participate in child-rearing.

**Methods**: Using proprietary technology, we developed an app that estimates five types of emotions (hunger, discomfort, hot/cold, sleepiness, and pain) from baby cries and displays appropriate interventions. The technology is based on sound analysis and deep learning, utilizing a custom-designed sound signal classification framework to create an AI model that recognizes the melodic patterns of infant vocalizations.

**Results**: As of February 2024, the accuracy of emotion estimation is 87.17%. The app has achieved 4,575 downloads and 84,000 impressions annually. User feedback has been overwhelmingly positive, with many stating that the app is genuinely helpful in parenting.

**Conclusion**: The application, which analyzes baby cries using AI technology to estimate emotions and propose interventions, shows potential to prevent postpartum depression and promote more stress-free parenting through its widespread use.

# P-5 Risk factors for mortality in infants born at 22-23 weeks of gestation using the cox proportional hazards model

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**Objective:** To identify risk factors for mortality in infants born at 22-23 weeks of gestation using the Cox proportional hazards model.

**Methods:** This retrospective cohort study included 185 infants born at 22–23 weeks of gestation and admitted to the neonatal intensive care unit (NICU) of Kagoshima City Hospital between January 2006 and December 2023. Infants with congenital anomalies, specifically those diagnosed with critical pulmonary stenosis (PS) or tetralogy of Fallot (TOF), were excluded. The study cohort consisted of 57 infants born at 22 weeks and 128 infants born at 23 weeks, with a median birth weight of 547 g (interquartile range, 475–601 g). Maternal characteristics, placental pathology, incidence of out-of-hospital births, and neonatal characteristics were compared between the mortality group (n = 64, 34.6%) and the survival group (n = 121, 65.4%). Comparisons between groups were performed using Chi-square tests or Fisher's exact tests, as appropriate. A Cox proportional hazards model was employed to identify risk factors for mortality, with mortality as the dependent variable. Explanatory variables included intrauterine growth restriction (IUGR; birth weight below the 10th percentile), twin-to-twin transfusion syndrome (TTTS), mode of delivery (cesarean section), 5-minute Apgar score, occurrence of bacteremia, tension pneumothorax, focal intestinal perforation (FIP), and necrotizing enterocolitis (NEC).

**Results:** In the univariate analysis, the mortality group had significantly higher incidences of IUGR (14/64 cases, 21.9%), TTTS (6/64 cases, 9.4%), bacteremia (26/64 cases, 40.6%), intraventricular hemorrhage (IVH; 43/64 cases, 67.2%), tension pneumothorax (16/64 cases, 25%), FIP (14/64 cases, 21.9%), and NEC (12/64 cases, 18.8%). Additionally, the mortality group showed a significantly lower rate of cesarean delivery (37/64 cases, 57.8%) and lower 5-minute Apgar scores (median: 6, 95% CI: 4-7). There were no significant differences between the groups in maternal characteristics, fetal heart rate monitoring, placental pathology, out-of-hospital birth, and other neonatal data. The Cox proportional hazards model identified the following as risk factors for mortality: IUGR (below the 10th percentile) with a hazard ratio (HR) of 3.41 [95% CI: 1.27-9.12], TTTS with HR of 1.37 [95% CI: 0.12-4.27], cesarean delivery with HR of 0.58 [95% CI: 0.38-0.89], bacteremia with HR of 1.68 [95% CI: 1.04-2.74], tension pneumothorax with HR of 1.11 [95% CI: 0.55-2.23], FIP with HR of 2.42 [95% CI: 1.14-5.11], and NEC with HR of 3.0 [95% CI: 0.54-16.7].

**Conclusion:** This study suggests that intrauterine growth restriction, vaginal delivery, bacteremia, and focal intestinal perforation may be significant risk factors for mortality in infants born at 22-23 weeks of gestation.

# P-6 Using situational language teaching to reduce blood culture contamination rate in neonatal intensive care unit

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**Abstract**

Blood culture collection is a routine nursing technology in the NICU. However, blood culture contamination can easily cause indirect harm to patients. In view of the unit's 2023 blood culture contamination rate of 3.51%, which far exceeds the set threshold of 3%, it affects the progress of patient treatment., delayed discharge from hospital.

This project improved by simulating the real situation of blood drawing, conducting on-the-job education, implementing five opportunities for hand washing, revising the standard blood drawing operation process, and replacing disinfectant solutions. The blood contamination rate dropped to 1.27% from January to August 2024.

**Method**

The director of pediatrics simulated the situation of a newborn being admitted to the NICU due to illness. Each nursing staff carried out the preparation, physical assessment, blood drawing, medication, etc. in a practical way. From this, it was found that the missing points in blood culture collection are: (1) Nursing staff failed to follow the five timings of hand washing (before performing aseptic techniques), (2) the blood collection site was left too short after disinfection, (3) the blood culture bottle was left too long after disinfection.

**Improvement strategy**

(1) Use situational language teaching language to teach nursing staff to correctly collect blood cultures through practical demonstrations, response interactions, evaluations, etc.
(2) Together with the laboratory department, we organize blood culture collection education courses every six months.
(3) Promote nursing staff to count the seconds when performing disinfection.
(4) Develop handwashing quality monitoring and incorporate it into daily management of the unit.
(5) Replace the disinfectant solution in the blood culture bottle, and regulate the nursing staff to sterilize the blood culture bottle after collection.

**Result**

Beginning in January 2024, improvement strategies were implemented:
(1) In February and August, two educational training sessions were held with the laboratory team leader as the lecturer, and the participation rate was 82.4%.
(2) The compliance rate for unit handwashing quality monitoring in January, April and July was 98.3%.
(3) The blood contamination rate from January to August was 1.27%.

**Conclusion**

The blood culture collection process is the most important factor affecting the quality of blood specimens. Through the design of situational language teaching and simulating the real situation of receiving patients, compared with traditional classroom teaching methods, the teaching is concrete and the impression is deepened through practical operations, and different situations can also be formulated according to the needs and characteristics of different nursing staff to promote learning motivation and effectiveness.

# P-7 Enhancing pig-tail drainage tube care competency in NICU: a quality improvement initiative

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**Background**: Pig-tail drainage tubes are infrequently used in our Neonatal Intensive Care Unit (NICU), with only 8-10 cases annually. A severe adverse event in 2011, classified as Severity Assessment Code (SAC) level 3, resulted from misconnection of a pig-tail pipeline, prolonging an infant's pneumothorax and hospitalization. This incident highlighted the need for improved care practices.

Objective: To enhance the competency of NICU nursing staff in pig-tail drainage tube care and reduce associated adverse events.

**Methods**: We implemented a multifaceted quality improvement initiative from 2012 to 2013. Interventions included: 1) Developing and conducting in-service education courses on pig-tail drainage tube care; 2) Creating an audit form and model teaching materials for pig-tail drainage tube management; 3) Collaborating with the Nursing Department to produce illustrated instructions for single and double-chamber drainage bottle management; 4) Incorporating pig-tail pipeline care information into the NICU pocket manual. We conducted biannual audits of each staff member's competency and monitored adverse events.

**Results**: Following implementation, no adverse events related to pig-tail drainage tubes occurred in 2012 or 2013. The average audit scores improved from 99.2 points in 2012 to 99.5 points in 2013. Any deductions or scores below 100 prompted immediate feedback and review.

**Conclusion**: Our quality improvement initiative successfully enhanced staff competency and eliminated adverse events related to pig-tail drainage tube care. Given the infrequent use of this technique and staff turnover, ongoing monitoring is crucial to maintain care quality and patient safety. Future research should assess long-term sustainability of these improvements and explore potential applications in other clinical settings.

# P-8 Standardizing neonatal transport protocols: enhancing care quality and safety by NICU nursing staff

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**Background**: Neonatal transport is critical for vulnerable newborns, yet challenging due to limited resources. Our NICU conducts approximately 18 transports monthly, each managed by only one physician and one nurse during the hour-long journey. This minimal staffing, coupled with the complexity of neonatal care, poses significant risks. A review of past transports revealed inconsistencies in care practices, emphasizing the urgent need for standardized protocols to ensure safety and quality care despite resource constraints.

**Objective**: To evaluate the impact of implementing a comprehensive, evidence-based neonatal transport protocol on the quality and safety of care provided during inter-hospital transfers, with a focus on optimizing nursing interventions in resource-limited settings.

Methods: Methods: From January 2023 to June 2024, we implemented a quality improvement initiative comprising: 1) A "Neonatal Transport Care Completeness Rate" audit tool; 2) Equipment function confirmation procedures; 3) Criteria for transport personnel qualification; 4) Biannual competency assessments; 5) Standardized handover documentation; and 6) A pre-transport checklist.

**Results**: During the 18-month study period, 326 neonatal transports were conducted (229 in 2023, 97 in the first half of 2024). Adherence to the new standardized protocols reached 100%, with no adverse events reported during transfers. Staff competency scores improved significantly ($p<0.01$) from baseline.

**Conclusion**: Standardized neonatal transport protocols significantly improved care quality and safety. Regular audits and checklists enhanced staff and equipment preparedness. Future research should examine long-term outcomes and protocol applicability in diverse settings.

# P-9 Association between subjective stress levels and learning effectiveness: a study using the Perceived Stress Scale during high-fidelity simulation

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**Objective:** Appropriate stress reportedly has an effect on increased memory. This study was conducted to determine whether changes in trainees' vital signs and stress scores affect the effectiveness of Neonatal Resuscitation Program (NRP) training conducted using high-fidelity simulation (HFS) training.

**Study design:** This training was conducted as a single-blind randomized controlled study for medical staff in charge of neonatal care. The trainees selected training days according to their schedules and sequentially completed NRP theory training and practical training during one session; the training order was randomly assigned. The vital signs and Perceived Stress Scale (PSS) scores of the trainees were measured and determined before, during, and after each training session, and the results were analyzed.

**Results:** Heart rate (HR) and the PSS score significantly increased after practical training, but there was no difference between the groups in terms of the final confirmed test result or PSS score. However, as a result of multiple regression analysis, the difference between the PSS scores measured at the beginning and end of training showed a statistically significant correlation with the increase in the final test score.

**Conclusion:** Training through simulation increased the PSS score and HR, and the degree of increase in stress was proportional to the degree of increase in memory; however, there was no significant correlation with the difference in HR. Learning accompanied by appropriate stress could improve working memory function.

# P-10 Renal function analysis of preterm newborns treated with Anti-VEGF antibodies for retinopathy

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**Background and Objective:** Intravitreal injection of anti-vascular endothelial growth factor (VEGF) antibodies is used to treat retinopathy of prematurity, but its systemic effects remain unclear. Since VEGF plays a crucial role in maintaining glomerular homeostasis, concerns exist regarding potential renal side effects of anti-VEGF therapy. This study aimed to investigate the renal effects of anti-VEGF therapy (ranibizumab) by longitudinally measuring urinary biomarkers in preterm infants.

**Methods:** Preterm infants were divided into two groups: those receiving anti-VEGF therapy (VEGF group) and controls. Urinary biomarkers, including angiotensinogen, liver-type fatty acid binding protein (L-FABP), albumin, and podocalyxin, were compared between the two groups at three time points: before treatment, one month after treatment, and two months after treatment.

**Results:** The study included 30 infants in the VEGF group and 12 in the control group. The mean gestational age and birth weight were 24.9 weeks/664g in the VEGF group and 26.8 weeks/845.6g in the control group. The mean postnatal age at treatment was 68.8 days, and the corrected gestational age was 34.8 weeks. No significant differences were observed in the four urinary biomarkers between the groups at one and two months after treatment.

**Conclusion:** No significant impact of anti-VEGF therapy on urinary biomarkers was observed. Given the lack of renal effects, the systemic impact of intravitreal anti-VEGF injections appears to be limited.

# P-11 Associations between surgical interventions and mortality and healthcare device use at 3 years of age in infants with trisomy 18: a population-based cohort study in Japan

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**Background**: More than 70% of children with trisomy 18 have congenital malformations that require surgery. However, surgical interventions for these patients are controversial due to their poor long-term prognosis. Although some studies reported improvement in survival of these infants after surgical interventions, national-level data are limited, especially in Japan.

**Methods**: This retrospective cohort study included children with trisomy 18 born between 2010 and 2016 who were captured in the Japanese national database (NDB). The NDB contains detailed information of medical claims data in Japan. The database captures approximately 100 % of all the population in Japan. The associations between the surgical interventions and death or healthcare device use in the home at 3 years of age were examined by multivariate logistic regression analyses adjusted for preterm birth, severe neonatal asphyxia, gastrointestinal or cardiac malformation.

**Results**: There were 935 trisomy 18 children born between 2010 and 2016, 360 in the surgery-group and 575 in the control-group. Infants in the surgery-group had higher incidence of preterm birth (26 vs. 17%), severe gastrointestinal malformation (36 vs. 12%), and severe cardiac malformation (80 vs. 77%) than the control group. After adjustment for the above-mentioned confounders, the surgery-group had significantly lower mortality (57 vs. 78%, aOR 0.21 [95%Cl 0.15-0.29]) and higher rates of the use of home health care device (67 vs. 56%, aOR 2.22 [1.44-3.45]) at 3 years of age.

**Conclusions**: Surgical intervention reduced mortality while increasing the rate of home health care device by age 3 years. This information can be used when parents or guardians and health care providers discuss the indication of surgical interventions for infants with trisomy 18.

# P-12 Interdisciplinary collaboration optimizes IV medication safety in NICU: a quality improvement initiative

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**Background**: Enhancing medication safety is a key patient safety goal in Taiwan for 2024, particularly for intravenous infusions. Our NICU primarily treats preterm infants (<32 weeks), whose fragile vasculature makes them susceptible to irreversible harm from improper medication dilution. The lack of standardized dilution methods and flow rate settings prompted improvement. We developed "NICU Precautions" in collaboration with multidisciplinary teams, outlining dilution methods and infusion times.

**Methods**: We implemented a comprehensive approach to enhance IV medication safety in our NICU. This included developing an "IV Medication Administration" audit checklist, collaborating with multidisciplinary teams (ward director, physicians, nurses, and pharmacists) to establish standardized dilution methods and infusion times, and integrating "NICU Precautions" into the medication system. Weekly interdisciplinary rounds ensured continuous protocol updates. The precautions were also included in the unit's pocket guide for easy staff reference.

**Results**: By August 2024, the average audit score reached 99 points. Prompt feedback was provided for any scores below 100. Staff satisfaction with the "NICU Precautions" system averaged 4.9 out of 5.

**Conclusion**: The implementation of "NICU Precautions" through interdisciplinary collaboration effectively enhanced medication infusion safety and reduced risks for infants. This standardized approach ensures safe medication processes. Future improvements include integrating dilution methods and flow rate information directly into physician orders, further minimizing potential errors and improving infant care.

# P-13 Case series of very preterm babies with diffuse with bubbly/cystic appearances on chest X-ray

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**Introduction**: Among very preterm babies with chronic lung disease (CLD), those with chorioamnionitis (CAM), respiratory distress syndrome (RDS), or diffuse bubbly/cystic appearances on chest X-ray images are at high risk for home oxygen therapy (HOT) introduction and considered more severe. In this study, we examined cases of very preterm babies born in Osaka City General Hospital (OCGH) with bubbly/cystic appearance on chest X-ray images within 28 days of birth.

**Methods**: Of 112 cases of very preterm babies (born at less than 28 weeks of gestational age) born in OCGH between 2018 and 2023, we excluded cases of death at <7 days of age, congenital anomalies, and out-of-hospital births, and 86 cases were included. A retrospective review was performed based on medical records. Chest X-ray images were taken when necessary, but images taken within 28 days of birth were all included, and read by several doctors in our department.

**Results**: Of 86 cases, 14 showed bubbly/cystic appearances. All that findings were detected within 14 days of birth. All patients required systemic hydrocortisone administration, and 11 patients received inhaled nitric oxide in the acute or chronic phase. 13 of the 14 patients were type III in the new japan CLD classification. the median number of weeks of gestation in the bubbly/cystic group was significantly earlier than in the group without bubbly/cystic findings. The mortality rate was also significantly higher in the bubbly/cystic group than in the group without bubbly/cystic findings (29% vs. 8%, $p<0.05$). The median length of hospital stay in the bubbly/cystic group was 197 days (120-369 days), and 90% of patients were discharged with HOT introduction.

**Conclusion**: The cases with bubbly/cystic findings in very preterm babies born at our hospital were considered to be the most severe cases of CLD.

# P-14 Successful management of pneumopericardium in a very low birth weight preterm infant using a 22-gauge intravenous catheter as a pericardial drain

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Pneumopericardium is relatively rare but potentially fatal in premature babies. When a massive pneumopericardium leads to cardiac tamponade, emergent pericardiocentesis is often required to save lives. In some cases, the placement of a pericardial drain for continuous drainage may be necessary.

However, for very low birth weight or extremely low birth weight preterm babies, there is a lack of appropriately sized pericardial drain tubes, posing a clinical challenge. We report a case of a very low birth weight preterm infant with birth body weight 1016 grams, who developed pneumopericardium.

We successfully treated the pneumopericardium using a 22-gauge intravenous catheter as a pericardial drainage tube.

# P-15 Postnatal weight loss and neurodevelopmental outcomes at age 3 years in extremely preterm infants: a cohort study

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**Background**: Previous research has suggested a correlation between postnatal maximum weight loss (MWL) and both neonatal mortality and morbidities in extremely preterm infants. However, the relationship between MWL and neurodevelopmental outcomes remains underexplored.

**Methods**: In a single-center retrospective cohort study, we evaluated data from extremely preterm infants admitted to the NICU from 2010 to 2020. Infants who died within the first 10 days of life were excluded. MWL in the first 10 days was the main exposure, categorized into three groups: >15%, 5%–15%, and <5%. The primary outcome evaluated was the occurrence of death or neurodevelopmental impairment (NDI) at age 3 years, defined as developmental impairments (developmental quotient [DQ] <85), cerebral palsy, hearing impairments, or visual impairments. Data analysis involved robust Poisson regression, adjusted for perinatal confounders, with a restricted cubic spline function to examine the dose-response relationship.

**Results**: Among 135 infants assessed for neurodevelopmental outcomes, 40 were in the >15% MWL group, 71 in the 5%–15% group, and 24 in the <5% group. Median gestational ages and birth weights were 25.9 weeks and 821 g for >15% MWL; 26.1 weeks and 818 g for 5%–15% MWL; and 26.0 weeks and 734 g for <5% MWL. Compared with the 5%–15% MWL group, the <5% group exhibited a higher risk of death or NDI at age 3 years (62.8% vs. 80.8%, RR 1.36, 95% CI 1.04–1.79) and NDI alone (59.2% vs. 79.2%, RR 1.43, 95% CI 1.06–1.94). Furthermore, higher risks of developmental impairment were also noted in the >15% (RR 1.32, 95% CI 1.00–1.75) and <5% (RR 1.46, 95% CI 1.08–1.98) groups. Spline analyses confirmed these associations.

**Conclusions**: MWL within the first 10 days of life is associated with increased risks of NDI and developmental impairments by age 3 years in extremely preterm infants.

# P-16 Association between labor regional analgesia and neonatal outcomes up to 1 month

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**Background**: Regional analgesia (RA) is a common and effective method for the management of pain during labor. Nevertheless, there is a paucity of evidence regarding the potential association between RA and adverse neonatal outcomes, particularly after the early neonatal period.

**Aims**: To examine the association between RA and neonatal outcomes up to 1 month postpartum.

**Materials and Methods**: A retrospective cohort study of singleton term births at a tertiary perinatal center in 2017. A comparison was made between maternal characteristics and neonatal outcomes up to 1 month in deliveries with and without RA. Multivariable logistic and linear regression analyses were used.

**Results**: Of the 403 deliveries, 77 were induced with RA. Women who received RA had a higher risk of instrumental delivery compared with those who did not (adjusted odds ratio = 2.36, 95% CI: 1.22–4.54). Despite the observed lower Apgar score at 1 minute in neonates of mothers who received RA (β-coefficient = 0.31, 95% CI: 0.29–0.34), no significant differences were identified between the two groups with regard to other neonatal outcomes in the first month after birth, including the admission rate to the neonatal intensive care unit or pediatric ward and the change in Z-score of body weight from birth to 1 month.

**Conclusion**: The results of this study indicate that RA is associated with adverse neonatal outcomes in the short term, but not at 1 month after birth. These findings contribute to the ongoing risk-benefit discussion on RA during labor and be helpful for shared decision-making.

# P-17 Comparison of clinical practices and neonatal outcomes between infants born at 22 and 23 gestational weeks ― a retrospective observational study in tertiary centres in Japan―

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**Background:** Infants born at 22–23 gestational weeks (GW) remain a challenge in perinatal medicine. The survival rate has improved, but they frequently survive with several complications. This study aimed to clarify the differences of clinical practices and neonatal outcomes between infants born at 22 GW and 23 GW using the Neonatal Research Network of Japan (NRNJ) database.

**Methods:** Using the NRNJ database, this observational study compared clinical practices and neonatal outcomes of infants born at 22 GW with those of 23 GW during 2018–2020. The primary outcome was a composite of death or bronchopulmonary dysplasia (BPD). The secondary outcomes were major and minor morbidities associated with prematurity.

**Results:** The NRNJ involved 229 infants born at 22 GW (birth weight of 476.8 ± 70.2 g) and 588 infants at 23 GW (546.1 ± 93.9 g). Statistical differences were observed in multiple births (22 GW: 9.6% vs. 23 GW: 20.1%, P <0.001), light-for-dates (7.9% vs. 16.0%, P = 0.002), and resuscitation withholding (5.2% vs. 0.2%, P <0.001). As to the clinical practices, there were differences in the use of antenatal corticosteroids (59.4% vs. 68.2%, P = 0.023), cesarean section (45.8% vs. 77.4%, P <0.001), and PDA ligation (11.9% vs. 19.1%, P = 0.026). Regarding neonatal outcomes, differences were demonstrated as follows: death/BPD (94.4% vs. 84.8%, P <0.001), mortality (39.7% vs. 19.9%, P <0.001), BPD (90.7% vs. 81.1%, P = 0.01), persistent pulmonary hypertension of neonate (31.1% vs. 21.6%, P = 0.009), patent ductus arteriosus (48.5% vs. 58.9%, P = 0.015), and sepsis (31.8% vs. 22.3%, P = 0.010).

**Conclusions:** Several discrepancies in clinical practices exist between infants born at 22 GW and 23 GW in Japan. There may be room for improvement in perinatal management to improve the prognosis of neonates born at 22 GW, particularly in obstetric interventions.

# P-18 The clinical course of subependymal cysts in healthy neonates

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**Background**

Subependymal cysts (SECs) are commonly identified in neonatal cranial sonography and especially in preterm infants. However, the clinical correlation with other perinatal complications and the prognosis of SECs in healthy neonates remain unclear. The objective of our study is aimed to evaluate the clinical course of SECs in healthy neonates and to correlate the findings with perinatal data.

**Objective**

To investigate the association between subependymal cyst and clinical characteristics and the prognosis of children with subependymal cyst in a birth cohort study.

**Methods**

We conducted a retrospective cohort study with neonates, who received cranial sonography in the first week after birth, born from 2015 to 2019 in our hospital located at Northern Taiwan. Clinical characteristics were collected by chart review and those with abnormal scan results will have next follow-up cranial sonography exam in 1-2 month later. They were tracked through until the brain lesions were completely resolved, closed anterior fontanelle or loss follow-up. We performed T test, chi-square test, survival analysis and Kaplan-Meier method to determine the association of SECs and clinical characteristics.

**Results**

A total of 1,016 neonates received cranial sonography after birth during this period. 99 (9.74%) of them had SECs, 16 (1.57%) neonates had choroid plexus cysts, and 14 (1.38%) neonates had ventriculomegaly. In children with SECs, 64 neonates had regular follow-up in our hospital and 55 (86%) of them had completed resolution before 4-month-old. Female neonates, later gestation age, and higher birth body weight are correlated with SECs significantly. Delivery modes, head circumference, maternal age, or small for gestational age are not associated with the development of SECs. Unilateral/bilateral cysts and single/multiple cysts are both independent with perinatal data. For neonates with SECs, none of them had hearing impairment.

**Conclusion**

Our findings suggest that neonates with SECs had good prognosis and most of them may resolve before 4-month-old. Female neonates, later gestation age, and higher birth body weight may have higher risk of SECs. Further study to elucidate the association between SECs and long-term neurodevelopment is needed.

# P-19 Pentoxifylline use in treatment of distal ischemic injury after arterial line insertion

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**Introduction**

Extremely premature infants, particularly those born before 28 weeks of gestation, are at high risk for various complications, including vascular injuries associated with arterial line insertion. Ischemic injuries due to compromised blood flow following arterial catheterization can lead to significant morbidity, particularly in amputation of extremities such as toes and fingers. Therapeutic options including pharmacological treatments for improving microcirculation might be considered. Sildenafil (Viagra) is commonly used for its vasodilatory effects and sometimes with fully recovery. However, in cases not response to Sildenafil, Pentoxifylline, a phosphodiesterase inhibitor known for improving blood flow and oxygenation in ischemic tissues, may be an alternative treatment option.

**Case Report**

We present a case of a 24-week gestational age preterm infant, weighing 770 grams at birth, who developed ischemic injury to the left toes following arterial line insertion for blood pressure monitoring when he was 23-day-old (PMA 27 weeks). Despite initial treatment with topical Sildenafil (Viagra, 2mg/ml, wet dressing one course for 30 minutes then resting for 15 minutes, until resolving of ischemic change) to promote vasodilation, the ischemic injury persisted with no significant improvement in tissue perfusion. As an alternative, we gave systemic therapy with Pentoxifylline (17mg/kg/day PO in Q8H, for 5-day treatment course), aimed at enhancing microcirculation and reducing the ischemic damage. Over the course of treatment, the patient demonstrated gradual improvement in peripheral perfusion, with eventual resolution of the ischemic injury. And no bleeding event was noted during treatment course.

**Discussion**

Arterial catheterization in extremely preterm infants is crucial for blood pressure monitoring and laboratory examination. However, risk of peripheral extremities ischemic injury could not be neglected. While Sildenafil is often utilized for its vasodilatory properties, its efficacy in treating ischemic injuries in neonates is variable. Pentoxifylline is commonly utilized to treat peripheral ischemic injuries due to its ability to improve blood flow by reducing blood viscosity and increasing red blood cell flexibility. Its mechanism includes inhibiting pro-inflammatory cytokines like TNF-α and IL-6, reducing oxidative stress, and enhancing tissue perfusion. Thus, Pentoxifylline might be beneficial in peripheral arterial disease (PAD) and might be helpful in neonatal ischemic injury, where microcirculation is compromised. Although

only few case reports, most neonates with pentoxifylline use with tolerated condition, we still noticed about side effect like gastrointestinal disturbances or bleeding tendency.

**Conclusion**

In conclusion, Pentoxifylline appears to be a promising alternative treatment for peripheral ischemic injury in extremely preterm infants, especially in cases where Sildenafil is ineffective. Its ability to enhance microcirculation and reduce inflammation contributes to tissue recovery, with minimal adverse effects noted in the presented case. Further studies are needed to confirm its broader efficacy in neonates.


Day 0


Day 0


Day 0

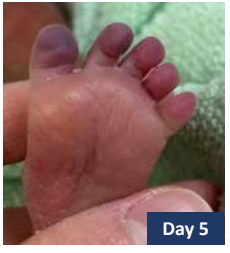

Day 1


Day 1


Day 2


Day 3


Day 4


Day 5

# P-20 Rapid bedside measurement of Reactive Oxygen Species (ROS) in neonates

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**Introduction**: Reactive oxygen species (ROS), including hypochlorite ions (OCl−), are produced upon neutrophil activation. Although C-reactive protein (CRP) is a valuable biomarker in neonatal medicine, some crucial patients get worse preceding elevated levels of CRP. ROS measurements can be a useful biomarker for early detection of serious medical conditions in neonates, as well as infectious diseases in adults. This study aims to establish a baseline of OCl− level in neonates using our novel technique with only 3μL of whole blood.

**Methods**: Neonates included in this study were born at Chiba University Hospital between June 2023 and March 2024. OCl− levels were measured in NICU-admitted neonates using residual blood samples collected between days 3 and 5 of life. OCl− levels were measured using samples from neonatal mass screening on day 4 for non-NICU neonates.

**Results**: Written informed consent was obtained from the parents of 20 neonates. No additional blood sampling was needed. The OCl- levels for full-term infants were 31.3×103 (±1.1×103), and those of preterm infants were 26.0×103 (±11.4×103) ($p = 0.35$). The correlation coefficient between the ratio of maternal milk and the OCl- levels at 4 days of age was -0.27 ($p = 0.06$). Discussion and conclusion: This is the first report showing that ROS can be measured at the bedside in neonates. Compared to adults, newborns have higher ROS levels, which is thought to be due to the increased exposure to oxygen after birth. Due to the small number of cases, we could not find significant correlations with CRP or bilirubin, known confounding factors in existing reports. Breastfeeding may reduce oxidative stress. We plan to investigate the relationship between ROS and newborn diseases and the correlation between ROS and severity and prognosis.

# P-21 Higher caffeine reduced lung injury in a respiratory distress and ventilatory-induced lung injury newborn animal model

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**Background**: Ventilatory-induced lung injury (VILI) and exposure to high oxygen in preterm infants with respiratory distress syndrome (RDS) cause the development of bronchopulmonary dysplasia (BPD). Available randomized control trials (RCT) showed that higher loading and maintenance doses of caffeine had several potential benefits.

To further explore these findings, we studied the effect of a higher caffeine loading dose on a respiratory distress and ventilatory-induced lung injury model in a newborn animal model.

**Methods:** Fifteen 1 to 2 day old piglets, anesthetized and mechanically ventilated, underwent lung lavage with saline to induce respiratory distress. Followed by injurious ventilation using high PIP, low PEEP, and high respiratory rate. After which, the animals were placed in a maintenance setting with an FIO2 to maintain saturations above 90%. Five piglets received a loading of 20 mg / kg, caffeine, five received 40 mg/kg and five served as controls. Lung ultrasounds were taken at 1, 3, and 6 hours (hrs) after VILI induction.

The lung ultrasound score (LUS) was determined for each lung and a respiratory distress score was calculated[1]. The highest being 18 and lowest 0. The animals were scarified after 6 hours.

Lung histology and lung tissue Krebs von den Lungen-6 (KL-6) were evaluated. Lung injury and inflammation scores were evaluated from lung histology.

**Results:**

LUS increased in the control from before to 1, 3 and 6 hours. LUS was significantly lower in the two caffeine groups compared to the control at 3 and 6 h. A trend for fewer lung injury and inflammatory scores were observed in the 20 mg/kg and 40 mg/kg groups compared to the control. KL-6 was significantly lower in the 40 mg/kg groups compared to the 20 mg/kg group and the control.

**Conclusion(s)**: In a characterized neonatal model of RDS and VILI in a newly born piglet, caffeine reduced LUS scores and a higher caffeine loading dose of 40 mh/kg reduced lung injury marker KL-6.

**References:** [1] Brat R, Yousef N, Klifa R, et al. Lung Ultrasonography Score to Evaluate Oxygenation and Surfactant Need in Neonates Treated With Continuous Positive Airway Pressure. JAMA Pediatr 2015;169:e151797–e151797.

# P-22 Early-life adverse respiratory exposure affects motor development is mediated by brain dysmaturation

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**Rationale**: Few studies have untangled the relationship between adverse respiratory exposures in the neonatal intensive care unit (NICU), altered brain development by term-equivalent age (TEA), and neurodevelopment outcome in extremely preterm infants.

**Objective:** To investigate the mediating effect of brain dysmaturation at TEA in association between early-life adverse respiratory exposure and neurodevelopmental outcome in extremely preterm infants.

**Methods:** 89 infants born less than 29 weeks' gestation received neuroimaging by MRI at TEA. Patterns of daily assisted ventilation in the first 8 postnatal weeks were analyzed using k-means clustering analyses, and neurodevelopment evaluated at age 6 and 12 months. The mediation effects of brain structural volume for the link between early-life respiratory exposures and neurodevelopmental outcome were explored.

**Measurements and Main Results:** Two distinct respiratory patterns with differential severity were found: improving (n=35, 39%) and delayed improvement (n=54, 61%). Using improving pattern as reference, delayed improvement pattern was associated with a significant mean reduction in the parietal lobe volume residuals (−4.9 cm3, 95% confidence interval −9.4 to −0.3) and motor composite scores (−8.7, −14.2 to −3.1) at age 12 months. Mediation analysis revealed that association between delayed respiratory improvement and inferior motor performance (total effect −8.7, −14.8 to −3.3) was partially mediated by reduction in the parietal lobe volume (natural indirect effect −1.8, −4.9 to −0.01, proportion mediated = 20%).

**Conclusions:** Dysmaturation of parietal lobe mediated the link between adverse respiratory exposure and inferior motor development in preterm infants. Optimizing respiratory critical care may mitigate the consequences of brain dysmaturation and neurodevelopmental delay.

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