# 30th International Workshop on Surfactant Replacement

## *Scientific Programme*

*Stockholm, Sweden | June 5th - 6th, 2015*

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Chiesi
In neonatology for life

## SCIENTIFIC COMMITTEE

Tore Curstedt *(Stockholm, Sweden)*
Henry L. Halliday *(Belfast, UK)*
Mikko Hallman *(Oulu, Finland)*
Ola D. Saugstad *(Oslo, Norway)*
Christian P. Speer *(Würzburg, Germany)*

## CHAIRPERSONS

Sture Andersson *(Helsinki, Finland)*
Mats Blennow *(Stockholm, Sweden)*
Kajsa Bohlin *(Stockholm, Sweden)*
Giuseppe Buonocore *(Siena, Italy)*
Virgilio P. Carnielli *(Ancona, Italy)*
Tore Curstedt *(Stockholm, Sweden)*
Henry L. Halliday *(Belfast, UK)*
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Jan Johansson *(Stockholm, Sweden)*
Boris Kramer *(Maastricht, The Netherlands)*
Eren Özek *(Istanbul, Turkey)*
Richard Plavka *(Prague, Czech Republic)*
Rangasamy Ramanathan *(Los Angeles, USA)*
Ola D. Saugstad *(Oslo, Norway)*
Kris Sekar *(Okhlaoma City, USA)*
Eric Shinwell *(Tel Aviv and Tsfat, Israel)*
Christian P. Speer *(Würzburg, Germany)*
Ben Stenson *(Edinburgh, UK)*
Bo Sun *(Shanghai, China)*
David Sweet *(Belfast, UK)*
Maximo Vento *(Valencia, Spain)*
Luc Zimmermann *(Maastricht, The Netherlands)*

## INVITED SPEAKERS

Christopher Baker *(Denver, USA)*
Dirk Bassler *(Zurich, Switzerland)*
Mats Blennow *(Stockholm, Sweden)*
Kajsa Bohlin *(Stockholm, Sweden)*
Tore Curstedt *(Stockholm, Sweden)*
Henry L. Halliday *(Belfast, UK)*
Mikko Hallman *(Oulu, Finland)*
Aaron Hamvas *(Chicago, USA)*
Dominique Haumont *(Bruxelles, Belgium)*
Hugo Lagercrantz *(Stockholm, Sweden)*
Christian P. Speer *(Würzburg, Germany*
Rangasamy Ramanathan *(Los Angeles, USA)*
Ola D. Saugstad *(Oslo, Norway)*
Eric Shinwell *(Tsfat and Tel Aviv, Israel)*
Bernard Thébaud *(Ottawa, Canada)*
Frank van Bel *(Utrecht, The Netherlands)*

Dear Colleagues and Friends,

It is a great honour for me to invite you all to the 30th International Workshop on Surfactant Replacement which will be held in Stockholm, Sweden, June 5th-6th, 2015.

This annual meeting has been held in different places in Europe but we now return to the place where the research about Curosurf started. The meeting in 2015 will be in Aula Medica at Karolinska Institutet, Stockholm, in the lecture hall where the Nobel Lectures in Physiology or Medicine are given.

The most important topics in neonatology including basic and clinical surfactant research will be discussed during the meeting.

Well-known invited speakers from all over of the world will cover different neonatal topics, but as always free papers and posters from the participants are very important to obtain a highly qualitative program.

I am looking forward to meeting you in Stockholm.

Kindest Regards,

Tore Curstedt

# 30th International Workshop on Surfactant Replacement

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## Friday, June 5th

08.30 – 08.45 **WELCOME ADDRESS**
Anders Hamsten
*Vice-Chancellor of Karolinska Institutet, Stockholm, Sweden*

Tore Curstedt, *Stockholm, Sweden*

**Chairpersons: Tore Curstedt** *(Stockholm, Sweden)* **Henry L. Halliday** *(Belfast, UK)*

08.45 – 09.30 **7th Bengt Robertson Memorial Lecture**
**ETHICS OF BIRTH AT THE LIMITS OF VIABILITY: THE RISKY BUSINESS OF PREDICTION**
Eric Shinwell *(Tel Aviv and Tsfat, Israel)*

**Chairpersons: Ola D. Saugstad** *(Oslo, Norway)* **Mikko Hallman** *(Oulu, Finland)*

**Invited Lecture**

09.30 – 10.20 **A UNIQUE STORY IN NEONATAL RESEARCH: THE DEVELOPMENT OF A PORCINE SURFACTANT**
Tore Curstedt, *(Stockholm, Sweden), Henry* L. Halliday *(Belfast, UK),*
Christian P. Speer *(Würzburg, Germany)*

10.20 – 10.50 Coffee Break

**Chairpersons: Rangasamy Ramanathan** *(Los Angeles, USA)* **Virgilio Carnielli** *(Ancona, Italy)*

**Invited Lecture**

10.50 – 11.10 **SURFACTANT AND NON-INVASIVE VENTILATION**
Mats Blennow *(Stockholm, Sweden)*

**Oral Presentations**

11.10 – 11.20 **LESS INVASIVE SURFACTANT ADMINISTRATION (LISA) IS SAFE: TWO YEAR FOLLOW-UP OF 476 INFANTS**
E.Herting, A. Kribs, B. Roth, C. Härtel, W. Göpel *and members of the German Neonatal Network (GNN) (Cologne and Lübeck, Germany)*

11.20 – 11.30 **ATOMISED SURFACTANT IMPROVES OXYGENATION AND HOMOGENEITY OF VENTILATION IN SPONTANEOUSLY BREATHING PRETERM LAMBS RECEIVING CPAP**
I. Milesi, E. Zanin, R. Dellaca, A. Lavizzari, F. Mosca, P. Tagliabue, L. Ventura, F. Bianco, A. Rajapaksa, E. Zonneveld, D. Black, E. Perkins, M. Sourial, D.G. Tingay
*(Milan, Monza and Parma, Italy and Melbourne, Australia)*



11.30 – 11.40 **SUPRAGLOTTIC ATOMIZATION OF CUROSURF® VIA A NEW DELIVERY SYSTEM ALLOWS HIGH LUNG DEPOSITION**
A. Nord, R. Linner, I. Milesi, E. Zannin, R. Dellaca, F. Bianco, M. Di Castri, D. Cunha- Goncalves, V. Perez-de-Sa
*Lund, Sweden and Milan and Parma, Italy)*

11.40 – 11.50 **NEBULIZATION OF PORACTANT ALFA VIA A VIBRATING MEMBRANE NEBULIZER IN SPONTANEOUSLY BREATHING PRETERM LAMBS WITH BINASAL CONTINUOUS POSITIVE PRESSURE VENTILATION**
M. C. Hütten, E. Kuypers, D.R. Ophelders, M. Nikiforou, R.K. Jellema, H. Niemarkt, C. Fuchs, M. Tservistas, R. Razetti, F. Bianco, B. W. Kramer
*(Maastricht, The Netherlands, Aachen, Germany and Parma, Italy)*

11.50 – 12.05 **Discussion**

12.05 – 13.05 Lunch and Poster Viewing

13.05 – 14.25 **Poster Presentations 1**

**Chairpersons: David Sweet** *(Belfast, UK)* **Sture Andersson** *(Helsinki, Finland)*

Poster 1 **RETROSPECTIVE ANALISYS OF SURFACTANT ADMINISTRATION IN PRETERM INFANTS IN NON INVASIVE RESPIRATORY SUPPORT: LISA VS INSURE PROCEDURE**
F. Castoldi, P. Fontana, S. Martinelli, L. Ilardi, A. C. Marucco, P. Bastrenta, E. Lupo, S. Gatto, G. Lista *(Milan, Italy)*

Poster 2 **COMPARISON OF THE SURFACTANT ADMINISTRATION VIA THIN CATHETER DURING SPONTANEOUS BREATHING WITH THE INSURE PROCEDURE IN PRETERM INFANTS**
N. Akçay, A.S. Gokalp, A. Gunlemez, F. Kiliçbay, A.E. Arısoy, G. Turker
*(Kocaeli, Turkey)*

Poster 3 **NASAL CPAP VERSUS BI-LEVEL CPAP FOR EARLY RESCUE TREATMENT OF RESPIRATORY DISTRESS SYNDROME IN PRETERM INFANTS: PRELIMINARY REPORT**
S. Arayici, G. Kadioglu Simsek, E. Alyamac Dizdar, B. Say, M.Y. Oncel, F.N. Sari, N. Uras, S.S. Oguz, F.E. Canpolat, U. Dilmen *(Ankara, Turkey)*

Poster 4 **SURFACTANT TREATMENT COMPARED TO NASAL CONTINUOUS POSITIVE AIRWAY PRESSURE FOR THE MANAGEMENT OF RESPIRATORY DISTRESS SYNDROME IN THE NEWBORN BETWEEN 35 AND 41 WEEKS OF GESTATION (THE ASPEN STUDY)**
P. Tourneux, T. Blanc, B. Guillois, S. Klosowski, J. Mourdie, C. Lardennois, H. Boumecid, V. Datin Dorriere, G. Kongolo, G. Ramadan-Ghostine, L. Ghyselen, C. Fontaine, F. Morea *(Amiens, France)*

Poster 5 **EFFECTS OF SYNCHRONISED INTERMITTENT MANDATORY VENTILATION VS PRESSURE SUPPORT PLUS VOLUME GUARANTEE VENTILATION IN THE WEANING PHASE OF PRETERM INFANTS**
Aydin Erdemir, Zelal Kahramaner, Ebru Turkoglu, Hese Cosar, Sumer Sutcuoglu, Esra Arun Ozer (*Izmir Turkey)*

Poster 6 **VOLUME GUARANTEE ON HIGH FREQUENCY OSCILLATORY VENTILATION IN PRTERM INFANTS: IS IT NEW LUNG PROTECTIVE STRATEGY**
B. Iscan, N. Duman, F. Tuzun, A. Kumral, H. Ozkan *(Izmir, Turkey)*
A.Erdemir, Z. Kahramaner, E. Turkóglu, H. Cosar, S. Sutcuoglu, E.A. Ozer *(Izmir, Turkey)*

Poster 7 **EFFECT OF EXTERNAL INSPIRATORY LOADING ON DIAPHRAGMATIC FUNCTION OF PRETERM AND TERM INFANTS**
G. Dimitriou, S. Fouzas, A. Vervenioti, P. Pelekouda *(Patras, Greece)*

Poster 8 **EFFECTS OF BOLUS SURFACTANT THERAPY ON SERIAL PERIPHERAL PERFUSION INDEX AND TISSUE CARBON MONOXIDE MEASUREMENTS IN PRETERM INFANTS WITH SEVERE RESPIRATORY DISTRESS SYNDROME**
D. Terek, D. Gönülal, O. Koroglu, M. Yalaz, M. Akisu, N. Kultursay *(Izmir, Turkey)*

Poster 9 **PROTECTIVE EFFECTS OF VALPROIC ACID VIA SEVERAL MECHANISMS AGAINST HYPEROXIC LUNG INJURY IN A NEONATAL RAT MODEL**
M. Cetinkaya, M. Cansev, F. Cekmez, C. Tayman, F. E. Canpolat, I. M. Kafa, E. O. Yaylagul, B.W. Kramer, S.U. Sarici *(Istanbul, Turkey)*

Poster 10 **LUNG LAVAGE WITH DILUTE SURFACTANT VERSUS BOLUS SURFACTANT FOR MECONIUM ASPIRATION SYNDROME: A RANDOMISED CONTROLLED TRIAL**
S. Arayici, F. N. Sari, G. Kadioglu Simsek, E. Yarci, E. Alyamac Dizdar, N. Uras, S.S. Oguz, F.E. Canpolat, U. Dilmen *(Ankara, Turkey)*

Poster 11 **ANTENATAL STEROIDS AND PULMONARY OUTCOME IN NEONATES WITH A GESTATIONAL AGE ≤ 32 WEEKS**
E. Gulczyńska, M. K. Borszewska-Kornacka, M. Kostuch, I. Sadowska-Krawczenko, P. Korbal and the Polish study group *(Lódź, Poland)*

Poster 12 **NOVEL BIOMARKERS FOR THE ASSESSMENT OF INTRAAMNIOTIC INFECTION**
V. Stefanovic, A. Sánchez-Illana, J. Kuligowski, S. Andersson, J. Escobar, I. Torres-Cuevas, A. Nuñez, E. Cubells, M. Cernada, M. Vento, C. Chafer-Pericas *(Helsinki, Finland and Valencia, Spain)*

13.05 – 14.25 **Poster Presentations 2**

**Chairpersons: Eren Özek** *(Istanbul, Turkey)* ) **Kris Sekar** *(Oklahoma City, USA)*

Poster 13 **EVALUATION OF LUNG FUNCTION IN PRESCHOOL CHILDREN BORN LATE-PRETERM WITH IMPULSE OSCILLOMETRY**
I. Er, A. Gunlemez, Z.S. Uyan, M. Aydogan, O. Isik, M. Oruc, A.E. Arisoy, G. Turker, A.S Gokalp *(Kocaeli, Turkey)*

Poster 14 **THE EFFECT OF CLARITHROMYCIN PROPHYLAXIS ON DEVELOPMENT OF BRONCHOPULMONARY DYSPLASIA IN PRETERM INFANTS**
S. Yurttutan, R. Ozdemir, M.Y. Oncel, F.E. Canpolat, Ş.S. Oğuz, U. Dilmen *(Malatya and Ankara, Turkey)*

Poster 15 **DIAGNOSTIC ACCURACY OF LUNG ULTRASOUND IN THE CRASHINGINFANT: AN INTERNATIONAL, PROSPECTIVE STUDY**
F. Migliaro, J.R. Fanjul, S. Aversa, N. Youssef, I. Corsini, L. Grappone, A. Sodano, F. Raimondi *on behalf of the LUCI investigators (Naples, Italy)*

Poster 16 **EFFECT OF RECOMBINANT HUMAN ERYTHROPOIETIN ON TRACHEAL ASPIRATE INFLAMMATORY MARKERS IN VENTILATED PRETERM NEONATES**
K. Sarafidis, A. Thomaidou, V. Soubasi, A. Taparkou, E. Diamanti, V. Drosou *(Thessaloniki, Greece)*

Poster 17 **THE EFFECTS OF MATERNAL ANTICOAGULANT THERAPY ON CORD BLOOD ANGIOGENIC FACTORS AND NEONATAL RESPIRATORY MORBIDITY IN WOMEN WITH RECURRENT MISCARRIAGE**
S. Takci, S. Yigit, A. Korkmaz, M. Yurdakok *(Ankara, Turkey)*

Poster 18 **EARLY IMMUNOMODULATORY EFFECTS OF DIFFERENT NATURAL SURFACTANT PREPARATIONS IN PRETERM INFANTS WITH RESPIRATORY DISTRESS SYNDROME**
M. Yalaz, S. Tanrıverdi, O. Uygur, O. Altun Köroğlu, E. Azarsız, G. Aksu, N. Kültürsay *(Izmir, Turkey)*

Poster 19 **INTRANASAL SURFACTANT PROTEIN D AS NEUROPROTECTIVE RESCUE IN A NEONATAL RAT MODEL OF PERIVENTRICULAR LEUKOMALACIA**
A. Kumral, B. Iscan, D. Engur, F. Tuzun, S. Ozbal, B. U. Ergur, M. K. Turkmen, N. Duman, H. Ozkan *(Izmir, Turkey)*

Poster 20 **EFFECTS OF PERINATAL STEROID THERAPY ON DEVELOPING BRAIN AND GROWTH FACTORS: WHAT IS THE CRITICAL TIME WINDOW?**
B. Iscan, A. Kumral, F. Tuzun, S.C. Mıcılı, K. Tuğyan, N. Duman, H. Ozkan *(Izmir, Turkey)*

Poster 21 **ASSOCIATION OF E-NOS GENE POLYMORPHISM IN DEVELOPMENT OF BRONCHOPULMONARY DYSPLASIA**
M. Çetinkaya, I. Varturk, M. Korachi, S. Guven, I. Mungan Akın, C. Kaspar, T. Erener Ercan, G. Buyukkale, S. Sevuk Ozumut *(Istanbul, Turkey)*

Poster 22 **DEVELOPMENT OF A NEW METHOD TO DETERMINE F2-ISOPROSTANES IN NEWBORN SERUM AND PLASMA SAMPLES**
S. Andersson, C. Cháfer-Pericás, J. Kuligowski, J. Escobar, A. Sánchez-Illana, I. Torres-Cuevas, V. Stefanovic, E. Cubells, M. Cernada, A. Nuñez, M. Vento *(Helsinki, Finland and Valencia, Spain)*

Poster 23 **TARGETED NEXT GENERATION SEQUENCING FOR MUTATION DETECTION IN IDIOPATHIC NEONATAL AND PEDIATRIC DIFFUSE LUNG DISEASES**
O. Danhaive, D. Peca, R. Cutrera, A. Angioni *(San Francisco, Usa and Rome Italy)*



**Chairpersons: Giuseppe Buonocore** *(Siena, Italy)* **Luc Zimmermann** *(Maastricht, The Netherlands)*

**Invited Lecture**

14.30 – 15.10 **LUNGS, MICROBES AND THE DEVELOPING NEONATE**
Aaron Hamvas *(Chicago, USA)*

**Oral Presentations**

15.10 – 15.25 **MIXTURES OF CUROSURF AND POLYMYXIN E AND POLYMYXIN B ARE REDUCING PULMONARY AND SYSTEMIC BACTERIAL LOAD IN NEONATAL RABBIT PNEUMONIA**
G. Stichtenoth, M. Hägerstrand Björkman, B. Linderholm, E. Herting, T. Curstedt *(Stockholm, Sweden and Lübeck, Germany)*

15.25 – 15.40 **CAN SURFACTANT PREPARATIONS BE USED AS DRUG CARRIER?**
O. Basabe-Burgos, M. Haegerstrand-Björkman, B. Linderholm, K. Nordling, G. Stichtenoth, P. Bergman, T. Curstedt, J. Johansson, A. Rising *(Stockholm, Sweden and Lübeck, Germany)*

15.40 – 15.55 **EFFECTS OF THE NEW GENERATION SYNTHETIC SURFACTANT CHF5633 ON PRO- AND ANTI-INFLAMMATORY CYTOKINE RESPONSES IN CD14+ MONOCYTES AND CD4+ LYMPHOCYTES**
K. Glaser, M. Fehrholz, T. Curstedt, S. Kunzmann, S. Seidenspinner, C. P. Speer *(Würzburg, German and Stockholm, Sweden)*

15.55 – 16.25 Coffee Break

**Chairpersons: Richard Plavka** *(Prague, Czech Republic)* **Bo Sun** *(Shanghai, China)*

**Invited Lecture**

16.25 – 17.05 **IMPAIRED PULMONARY VASCULAR DEVELOPMENT IN BRONCHOPULMONARY DYSPLASIA**
Christopher Baker *(Denver, USA)*

**Oral Presentations**

17.05 – 17.20 **EARLY INTRAVENOUS PARACETAMOL AND PDA CLOSURE IN VERY PRETERM INFANTS; A RANDOMIZED, CONTROLLED TRIAL**
P. Härkin, A. Härmä, O. Aikio, M. Valkama, M. Leskinen, T. Saarela, M. Hallman *(Oulu, Finland)*

17.20 – 17.35 **PHYSICAL ACTIVITY AND THE RISK OF PRETERM BIRTH: A SYSTEMATIC REVIEW AND META-ANALYSIS OF EPIDEMIOLOGICAL STUDIES**
D. Aune, T. Henriksen, O.D. Saugstad, S. Tonstad, L.J. Vatten *(Oslo and Trondheim, Norway)*

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## Saturday, June 6th

**Chairpersons: Christian P. Speer** *(Würzburg, Germany)* **Ben Stenson** *(Edinburgh, UK)*

**Invited Lecture**

08.30 – 09.00 **ANTENATAL STEROID BEFORE PRETERM BIRTH**
Mikko Hallman *(Oulu, Finland)*

**Invited Lecture**

09.00 – 09.25 **INHALATION OR INSTILLATION OF STEROIDS FOR THE PREVENTION OF BRONCHOPULMONARY DYSPLASIA**
Dirk Bassler *(Zürich, Switzerland)*

**Oral Presentations**

09.25 – 09.40 **OPPOSITE EFFECTS OF PROGESTERONE AND DEXAMETHASONE (DEX) ON SURFACTANT-PROTEIN B (SP-B) PRODUCTION**
S. Kunzmann, M. Fehrholz, B. W. Kramer, C. P. Speer
*(Würzburg, Germany and Maastricht, The Netherlands)*

09.40 – 09.55 **DEXPANTHENOL THERAPY REDUCES LUNG DAMAGE IN A HYPEROXIC LUNG INJURY IN NEONATAL RATS**
R. Ozdemir, G. Demirtas, H. Parlakpinar, A. Polat, K. Tanbag, E. Taslidere, A. Karadag
*(Malatya, Turkey)*

09.55 – 10.10 **A BPD-MODEL IN NEWBORN MICE**
C. Revhaug, M Zasada, A.G. Rognlien, A. Madetko-Talowska, M. Bik-Multanowski, P. Kwinta, P. Pietzyk, O.D. Saugstad *(Krakow, Poland/Oslo, Norway)*

10.10 – 10.40 Coffee Break

**Chairpersons: Jan Johansson** *(Stockholm, Sweden)* **Boris Kramer** *(Maastricht, The Netherlands)*

**Invited Lecture**

10.40 – 11.20 **STEM CELLS FOR PREVENTION OF NEONATAL LUNG DISEASES**
Bernard Thébaud *(Ottawa, Canada)*

**Oral Presentations**

11.20 – 11.35 **MESENCHYMAL STEM- OR STROMAL CELLS (MSCS) FROM THE DEVELOPING HUMAN LUNG**
M.A. Möbius, S. Koss, D. Freud, R.K. Ohls, M. Rüdiger, B. Thébaud
(Dresden, Germany and Ottawa, Canada)

11.35 – 11.50 **SAFETY ASPECTS OF INTRAVENOUS MESENCHYMAL STEM CELL TRANSPLANTATION IN PRETERM INFANTS**
E. Henckel, G. Götherström, K. Le Blanc, B. Hallberg, K. Bohlin
*(Stockholm, Sweden)*

**Chairpersons: Kajsa Bohlin** *(Stockholm, Sweden)* **Max Vento** *(Valencia, Spain)*

**Invited Lecture**

11.50 – 12.20 **DELIVERY ROOM HANDLING OF TERM AND PRETERM NEWLY BORN INFANTS**
Ola D. Saugstad *(Oslo, Norway)*

**Oral Presentations**

12.20 – 12.35 **CHANGING PATTERNS OF SURFACTANT USE OVER TWO DECADES FOR BABIES <30 WEEKS GESTATION IN NORTHERN IRELAND'S REGIONAL INTENSIVE CARE UNIT**
J.C.A Courtney, B. McNaughton, D. G. Sweet *(Belfast, UK)*

12.35 – 12.50 **RELEVANCE OF URINARY LIPID PEROXIDATION BYPRODUCTS IN PRETERM INFANTS FOR PREDICTING NEONATAL CONDITIONS**
J. Kuligowski, M. Aguar, D. Rook, I. Lliso, I. Torres-Cuevas, J. Escobar, G. Quintás, M. Brugada, Á. Sánchez-Illana, J. B. van Goudoever, M. Vento
*(Valencia, Spain and Rotterdam and Amsterdam, The Netherlands)*

12.50 – 14.30 Lunch

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## Post Conference Workshop

**Chairpersons: Mats Blennow** *(Stockholm, Sweden)* **Eric Shinwell** *(Tel Aviv and Tsfat, Israel)*

14.30 – 15.00 **ONSET OF BREATHING AND EMERGENCE OF THE MIND AT BIRTH**
Hugo Lagercrantz *(Stockholm, Sweden)*

15.00 – 15.30 **NEUROMONITORING THE HIGH RISK PRETERM INFANTS. ITS CLINICAL RELEVANCE?**
Frank van Bel *(Utrecht, The Netherlands)*

15.30 – 15.50 Coffee Break

15.50 – 16.20 **USE OF IT TO MONITOR NOSOCOMIAL INFECTIONS AND PREVENTIVE STRATEGIES**
Dominique Haumont *(Bruxelles, Belgium)*

16.20 – 16.50 **FAMILY CENTRED CARE**
Kajsa Bohlin *(Stockholm, Sweden)*

16.50 – 17.00 **CLOSING REMARKS AND INVITATION TO NAPLES**
Tore Curstedt *(Stockholm, Sweden) )* Giuseppe Buonocore *(Siena, Italy)*

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# *Poster List*

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## Poster 1

***RETROSPECTIVE ANALISYS OF SURFACTANT ADMINISTRATION IN PRETERM INFANTS IN NON INVASIVE RESPIRATORY SUPPORT: LISA VS INSURE PROCEDURE***

Francesca Castoldi; Paola Fontana; Stefano Martinelli; Laura Ilardi; Annamaria Cirillo Marucco; Petrina Bastrenta; Enrica Lupo; Sara Gatto; Gianluca Lista
*NICU, V.Buzzi Children's Hospital ICP, Milan, Italy*

### BACKGROUND

Surfactant instillation via INtubation-SURfactant-Extubation (INSURE) method requires intubation; manual or mechanical ventilation (MV) can induce lung injury. Recently, a less invasive surfactant administration (LISA) method via a thin catheter inserted in trachea in spontaneously breathing infants in non invasive ventilation (NIV) has been developed.
The aim of this study is to report clinical and respiratory outcomes of preterm neonates in NIV for Respiratory Distress Syndrome (RDS) after administration of Surfactant through LISA compared to INSURE procedure.

### PATIENT AND METHODS

A retrospective study conducted in 2 NICUs (V.Buzzi and Niguarda Hospital, Milan,Italy) from 2/2012 to 10/2014; charts of infants undergoing NIV for RDS who required surfactant administration (200 mg/kg, Curosurf®) for FiO2 >35% were reviewed; the choice of INSURE or LISA was left to the neonatologist on duty; LISA was administered through a thin tracheal aspiration catheter or a umbilical catheter, depending on the center of birth. Clinical characteristics, respiratory outcomes as days of NIV, number of surfactant doses, need for MV within 72 hours, days of O2 support, were analyzed in the 2 groups. The two centers followed the same criteria for intubation and MV, and for discontinuation of MV and extubation.Statistical analysis of clinical data was perofrmed by Fisher exact test, Chi-squared test and t-Student's test.

### RESULTS

58 infants received INSURE and 28 infants LISA; clinical characteristics of infants (INSURE vs LISA BW 1341±478g vs 1308±584g; GA 29±2 vs 29±2 wks respectively) and antenatal steroids therapy (46/58 vs 25/28) were similar.
No adverse events occurred during surfactant administration. No differences were observed in : NIV failure, lenght of MV and oxygen support, PNX, IVH, significant PDA, BPD and death occurence. No differences were observed between the two centers. Infants who failed CPAP and needed MV in LISA group had lower BW vs INSURE group (845±179 g vs 1186±465g respectively; p=ns).

### CONCLUSIONS

In our study no differences in short and long term outcomes were observed between administration of surfactant via INSURE or LISA method to preterm infants in NIV for RDS.

## Poster 2

***COMPARISON OF THE SURFACTANT ADMINISTRATION VIA THIN CATHETER DURING SPONTANEOUS BREATHING WITH THE INSURE PROCEDURE IN PRETERM INFANTS***

N. Akçay; A.S. Gokalp; A. Gunlemez; F. Kiliçbay; A.E. Arısoy; G. Turker
*Department of Pediatrics, Division of Neonatology, University of Kocaeli, Turkey*

### BACKGROUND

The aim of this prospective study is to investigate the effectiveness of a technique of minimally invasive surfactant therapy (MIST) in preterm infants on continuous positive airway pressure (CPAP) and comparison of the results with the InSurE.

### PATIENT AND METHODS

78 preterm infants less than 32 weeks of gestational age need surfactant therapy were enrolled in this study. Infants who need resuscitation in the delivery room, major congenital anomalies, hidrops fetalis were excluded from the study . Preterm infants, who were less than 32 weeks and stabilized with nasal continuous positive airway pressure (nCPAP) in the delivery room, were randomized to receive early surfactant treatment either by via thin catheter (MİST) or InSurE technique. Tracheal instillation of 100 mg/kg poractant a via 5-F catheter during spontaneous breathing under nCPAP was performed in the MIST group (n 42). In the InSurE technique procedure, 36 infants were intubated, received positive pressure ventilation for 30 seconds after surfactant instillation, and placed on nCPAP immediately.

### RESULTS

There were no difference between the demographic data, needs of resuscitation in the delivery room and the Apgar scores of the MIST and InSurE group.
Need for intubation within the first 72 hours, readministration of surfactant, duration of nCPAP, incidence of pneumothorax, pulmonary hemorrhage, early sepsis, PDA, NEC, IVH, BPD and mortality were similar in both groups and there were no statistically significant difference between them (Table).
Blood pCO2 values were not different in both groups before surfactant administiration, whereas after treatment MIST group had significantly lower.

### CONCLUSIONS

MIST technique has been found as effective as InSurE technique The surfactant adminisration in preterm infants the InSurE method should be preferred because it is noninvasive and easy to apply.

## Table: Results of the MIST and EnSurE groups

| | MİST (n 42) | InSurE (n 36) | P value |
|---|---|---|---|
| Intub first 72 h, n (%) | 15 (35,7) | 14 (38,9) | 0,957 |
| Second dose surfactant | 8 (8,1) | 7 (6,9) | 1,0 |
| pH before, (mean) | 7,26 (0,06) | 7,27 (0,04) | 0,36 |
| pH after (mean) | 7,33 (0,05) | 7,32 (0,04) | 0,18 |
| pCO2 before (mean) | 55,4 (7,1) | 56 (6,7) | 0,507 |
| pCO2 after (mean) | 46,1 (5,6) | 50,9 (6,1) | 0,001 |
| Pneumothorax, n (%) | 2 (4,8) | 2 (5,6) | 1,0 |
| Pulmonary hemorrhage, n (%) | 4 (9,5) | 3 (8,3) | 1,0 |
| nCPAP day | 3 (2-6,25) | 3 (2-5) | 0,395 |
| O2 day | 15,5 (4-27) | 9 (5-23) | 0,371 |
| Early sepsis | 6 (14,3) | 9 (25) | 0,363 |
| İVH, n (%) | 7 (16,7) | 11 (30,6) | 0,849 |
| NEC, n (%) | 5 (11,9) | 7 (19,4) | 0,545 |
| PDA, n (%) | 15 (35,7) | 15 (41,7) | 0,76 |
| BPD, n (%) | 18 (42,9) | 10 (28,8) | 0,607 |
| Death , n (%) | 4 (9,5) | 2 (7,7) | 0,681 |

## Poster 3

### *NASAL CPAP VERSUS BI-LEVEL CPAP FOR EARLY RESCUE TREATMENT OF RESPIRATORY DISTRESS SYNDROME IN PRETERM INFANTS: PRELIMINARY REPORT*

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**BACKGROUND**
To compare the effectiveness of nasal continuous positive airway pressure (nCPAP) with variable flow and bi-level nasal CPAP (BiPAP) as primary mode of treatment for RDS in preterm infants.

**PATIENT AND METHODS**
In this prospective randomized study, preterm infants lower than 32 weeks of gestational age and 1500 gr who were admitted to the neonatal intensive care unit were screened for eligibility following parental consent. Enrolled infants were randomized into two study groups; nCPAP and BiPAP group. Non-invasive respiratory support was delivered using the infant flow-driver device (Viasys Corp, Care Fusion, CA). Surfactant therapy requirement was evaluated in all preterm infants after admission. Poractant alfa was administered using a non-invasive technique if necessary. Infants in both groups were compared with regard to failure of non-invasive respiratory support. Short and long-term neonatal outcomes were also evaluated.

**RESULTS**
A total of 52 patients were enrolled for the study. There was no significant difference between the nCPAP and BiPAP groups in terms of demographic characteristics. Statistically significant difference was observed between groups with regard to failure of non-invasive respiratory support (35% vs 8.3%; p=0.024). More patients in the nCPAP group required surfactant therapy compared to the BiPAP group (60.7% vs 16.7%; p=0.002). Four patients (14.3%) in the nCPAP group and 1 patient (4.2%) in the BiPAP group (p=0.33) required oxygen on day 28.

**CONCLUSIONS**
Preliminary results showed that fewer infants required mechanical ventilation and surfactant therapy in the BiPAP group compared to the nCPAP group. Neonatal outcomes will be more clearly defined after completion of the study.

## Poster 4

***SURFACTANT TREATMENT COMPARED TO NASAL CONTINUOUS POSITIVE AIRWAY PRESSURE FOR THE MANAGEMENT OF RESPIRATORY DISTRESS SYNDROME IN THE NEWBORN BETWEEN 35 AND 41 WEEKS OF GESTATION (THE ASPEN STUDY)***

Pierre Tourneux; Thierry Blanc; Bernard Guillois; Serge Klosowski; Julien Mourdie; Caroline Lardennois; Hocine Boumecid; Valérie Datin Dorriere; Guy Kongolo; Ghida Ramadan-Ghostine; Laurent Ghyselen; Cécile Fontaine; François Morea

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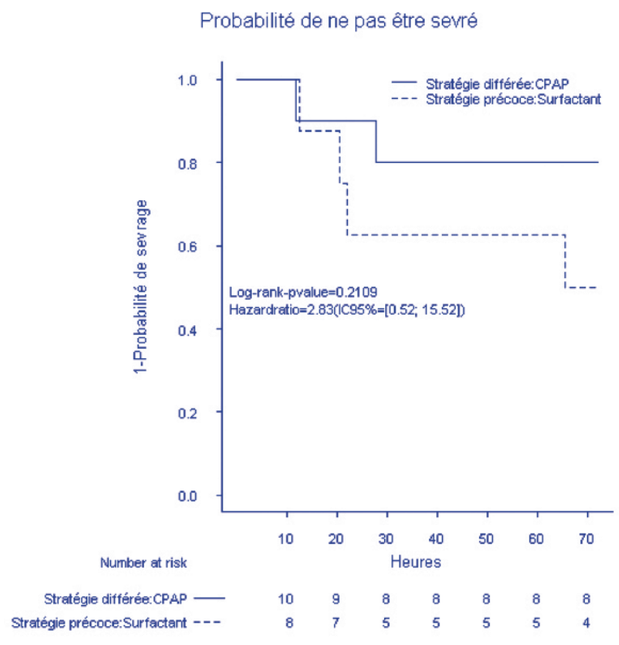
### BACKGROUND

Term and near-term newborns can present with acute respiratory distress syndrome (RDS). Surfactant treatment has been shown to be effective in reducing the duration of mechanical ventilation and oxygen treatment in preterm newborns. Whether surfactant treatment is also beneficial in term and near-term newborns is unknown. The purpose of this randomized trial was to compare surfactant treatment with nasal continuous positive airway pressure (nCPAP) in term and near-term newborns with RDS within the first 24 hours of life.




### PATIENT AND METHODS

Newborns born between 35 and 41 weeks of gestation, with RDS within the first 24 hours of life treated with nCPAP and with an FiO2 ≥ 30% but < 60% at enrolment were eligible. Newborns with nCPAP and an FiO2 >60%, polymalformative syndrome, heart disease, shock, blood gas pH 65 mmHg, or perinatal asphyxia were excluded.

Newborns were randomly assigned to two groups: "surfactant treatment after tracheal intubation" (Surfactant group) and "continuation of nCPAP" (nCPAP group). Rescue surfactant treatment was used in the second group if FiO2 reached > 60%. In each group, newborns were weaned from mechanical ventilation and oxygen treatment as soon as possible.

The primary outcome of the study was the success of the procedure, defined as "survival without oxygen treatment" at 72 hours of life.

The secondary endpoints were: death, surfactant treatment, pneumothorax, pulmonary hypertension, inhaled nitric oxide treatment, fluid loading, vasopressor amine treatment, duration of mechanical ventilation, duration of nCPAP treatment, duration of oxygen treatment, and oxygen treatment at 28

days of life.

administration of surfactant via INSURE or LISA method to preterm infants in NIV for RDS.

### RESULTS

Nineteen newborns were included: 10 in the nCPAP group and 9 in the Surfactant group. The study was stopped because of the low incidence of RDS in eligible newborns.

There was no significant difference between the two groups in terms of gestational age (36.1±2.23 gestational weeks in nCPAP vs. 36.1±2.03 gestational weeks in the Surfactant group), birth weight or Apgar score. The probability of "survival without oxygen treatment" at 72 hours of life was 50±18% in the Surfactant group vs. 20±13% in the nCPAP group (p=0.19). Five newborns (50%) in the nCPAP group required rescue surfactant treatment. Two newborns in the nCPAP group developed pneumothorax, compared to none in the Surfactant group (p = 0/47).

### CONCLUSIONS

We did not observe any significant difference between surfactant treatment vs. nCPAP in newborns between 35 and 41 weeks of gestation with RDS within the first 24 hours of life, probably due to the lack of power of the study. Five newborns (50%) in the nCPAP group required rescue surfactant treatment. The interest of using less invasive surfactant administration (LISA) in newborns with RDS treated with nCPAP and an FiO2 > 30% should be studied.

## Poster 5

***RESTROSPECTIVE ANALISYS OF SURFACTANT ADMINISTRATION IN PRETERM EFFECTS OF SYNCHRONISED INTERMITTENT MANDATORY VENTILATION VS. PRESSURE SUPPORT PLUS VOLUME GUARANTEE VENTILATION IN THE WEANING PHASE OF PRETERM INFANTS***

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### BACKGROUND

The aim of this study is to compare the effects and short-term outcomes of pressure support ventilation with volume guarantee (PSV+VG) vs. synchronized intermittent mandatory ventilation (SIMV) in the weaning phase of very low birth weight infants with respiratory distress syndrome (RDS).

### PATIENT AND METHODS

A total of 60 premature infants who were <33 weeks gestation and/or <1500 gram birth weight and received mechanical ventilation because of respiratory distress syndrome were included in this randomized, controlled, prospective study. All infants were ventilated from the time of admission with synchronized intermittent positive pressure ventilation (SIPPV) mode after surfactant treatment for RDS and then switched to PSV+VG or SIMV mode in the weaning phase. The ventilatory parameters and neonatal outcomes were recorded in each groups.

### RESULTS

The mean peak inflation pressure (PIP) was higher in SIMV group ($p<0.001$) and the mean airway pressure (MAP) was higher in PSV+VG group ($p=0.03$) whereas mean tidal volume and respiratory rates were similar in both groups. The incidence of post-extubation atelectasis was higher in SIMV group but the difference was not statistically significant ($p=0.08$). No differences were found in the incidence of re-entubation, patent ductus arteriosus, intraventricular hemorrhage, retinopathy of prematurity, bronchopulmonary dysplasia and pneumothorax between the groups.

### CONCLUSIONS

PSV+VG mode may be a safe and feasible mode during the weaning phase of very low birth weight infants on mechanical ventilation support for RDS in respect to reducing the frequency of post-extubation atelectasis and using less PIP.

## Poster 6

***VOLUME GUARANTEE ON HIGH FREQUENCY OSCILLATORY VENTILATION IN PRTERM INFANTS: IS IT NEW LUNG PROTECTIVE STRATEGY***

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### BACKGROUND

High frequency oscillatory ventilation (HFOV) theorically limits baro/volutrauma using subdeadspace volumes but lack of direct control over tidal volume resulting in fluctuating $PCO_2$ level. Volume guarantee plus high-frequency oscillatory ventilation (HFOV+VG) is a new ventilation mode allows the clinician to set a mean tidal volume to be delivered. This study aimed to investigate the feasibility and efficacy of this mode of ventilation in premature infants with respiratory distress syndrome (RDS).

### PATIENT AND METHODS

Inborn infants at less than 32 weeks of gestation with respiratory distress syndrome (RDS) were enrolled in the study if they required invasive mechanical ventilation. Patients were randomized to receive either HFOV plus VG or HFOV as the initial ventilator mode and then crossed over to the other mode of ventilation. HFOV was performed with "optimal lung volume strategy" during both study period.

### RESULTS

During the study period twenty-four infants ventilated for RDS were included in the study. There was no significant difference between ventilation mode in terms of mean amplitude and mean airway pressure (Paw) but high frequency tidal volume (VThf), minute ventilation (MVe) and carbon dioxide diffusion coefficient (DCO2) values were significantly higher in the HFOV+VG mode and hypocarbia and hypercarbia frequency was found to be less in HFOV+VG periods.

### CONCLUSIONS

This is the first prospective, randomized, crossover clinical study that compared HFOV with and without VG in infants with acute RDS. In this study, when used HFOV combined with VG demonstrated that equal airway pressure provides better ventilation and can achieve optimal gas exchange. HFOV combined with VG may be an effective and feasible for preterm infants.

## Poster 7

***EFFECT OF EXTERNAL INSPIRATORY LOADING ON DIAPHRAGMATIC FUNCTION OF PRETERM AND TERM INFANTS***

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### BACKGROUND

Newborns, especially those born prematurely, may present limited ability to adapt to additional respiratory loads, i.e during acute respiratory disease or upper airway obstruction. The diaphragmatic pressure-time product (PTPdi) reflects the energy expenditure of the diaphragm and has been used as a measure of the work of breathing. The diaphragmatic pressure-time index (PTIdi) describes the pressure-generating activity of the diaphragm and assesses the balance between the capacity of the diaphragm and the load imposed upon it. In adults, a PTIdi greater than 0.15-0.18 may indicate impending diaphragmatic fatigue.
The airm of this study is to compare the changes in diaphragmatic function after application of inspiratory flow-resistive loading in preterm and term infants.

### PATIENT AND METHODS

Sixteen preterm infants (median GA 32.5 weeks, range 30–34) and 16 term infants (median GA 38 weeks, range 37–40) were studied prior to discharge from the NICU. None of the preterm infants had chronic lung disease and all infants were breathing on room air when studied. PTPdi was calculated as the integral of transdiaphragmatic pressure over time. PTIdi was calculated as the product of the mean to the maximum transdiaphragmatic pressure ratio (Pdimean/Pdimax) and the inspiratory duty cycle (Ti/Ttot). The mean PTPdi and PTIdi were computed before and during application of an inspiratory flow resistance of 200 cmH2O for 120 seconds.

### RESULTS

Resistive loading resulted in significantly higher increase of PTPdi and PTI di in infants born preterm (PTPdi median [range] 58 [32-138]% vs. 35 [24-51]%, P<0.001 and PTIdi 67 [31-142]% vs. 35 [16-42]%, P<0.001, respectively). PTIdi became significantly higher in preterm infants after application of inspiratory resistance (0.102 [0.068-0.189] vs. 0.076 [0.044-0.119], P<0.001). Three preterm infants (18.8%) had post-resistance PTIdi higher than the reported adult fatigability threshold of 0.15. Multivariable linear regression analysis revealed that PTPdi and PTIdi increase after logarithmic transformation were inversely related to GA (P=0.001 and P=0.040, respectively), independently of gender, birthweight, days of mechanical ventilation and postconceptional age at the time of measurement.

### CONCLUSIONS

Under conditions that increase the inspiratory load, prematurity is associated with increased work of breathing and higher risk of diaphragmatic muscle fatigue.

## Poster 8

***EFFECTS OF BOLUS SURFACTANT THERAPY ON SERIAL PERIPHERAL PERFUSION INDEX AND TISSUE CARBON MONOXIDE MEASUREMENTS IN PRETERM INFANTS WITH SEVERE RESPIRATORY DISTRESS SYNDROME***

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### BACKGROUND

Exogenous bolus surfactant administration may affect hemodynamic parameters and peripheral perfusion. We aimed to investigate the effects of surfactant on perfusion index (PI) and transcutaneous carbon monoxide (TCO), hemodynamic and ventilatory parameters.

### PATIENT AND METHODS

PI and TCO values were measured before and 0, 5, 30, 60 and 360 minutes after surfactant administration in the first six hours of life in preterm infants with respiratory distress syndrome (RDS) treated with poractantalfa or beractant and preterms without RDS. Thirty preterm infants with RDS treated with poractantalfa (n=15) or beractant (n=15) and 18 preterms without RDS were enrolled to study.

### RESULTS

Study group had lower Tp PI and higher Tp TCO levels than controls. Both preparations improved mean arterial pressure, oxygenation index, pH and lactate levels. Median Tp PI value of 1.3 decreased to 0.86 at T0 (P < 0.001), and then increased to 0.99 at T5 (P < 0.001) and to 1.25 at T30 (P = 0.037). Median Tp TCO value of 3 decreased to 2, 1.5, 0 and 0 at T0, T5, T30, T60 respectively (P < 0.001). PI more quickly improved (30 versus 60 minutes) and reached control group values (30 versus 360 minutes) with beractant compared to poractantalfa. TCO improved similarly in both groups (5 versus 5 min).

### CONCLUSIONS

Peripheral perfusion improved with both preparations only after a decline in the first minute. TCO declined continuously and reached control group showing pulmonary function improvement or anti-inflammatory effect of surfactant. Noninvasive surfactant administration may prevent initial negative effect of bolus treatment on peripheral perfusion lasting for at least one minute.

## Poster 9

***PROTECTIVE EFFECTS OF VALPROIC ACID VIA SEVERAL MECHANISMS AGAINST HYPEROXIC LUNG INJURY IN A NEONATAL RAT MODEL***

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### BACKGROUND

Histone acetylation and deacetylation may play a role in the pathogenesis of inflammatory lung diseases. We evaluated the preventive effect of valproic acid (VPA); a histone deacetylase (HDAC) inhibitor; on neonatal hyperoxic lung injury.

### PATIENT AND METHODS

Forty newborn rat pups were randomized in normoxia; normoxia+VPA; hyperoxia and hyperoxia+VPA groups. Pups in the normoxia and normoxia+VPA groups were kept in room air and received daily saline and VPA (30 mg/kg) injections; respectively; while those in hyperoxia and hyperoxia+VPA groups were exposed to 95% O2 and received daily saline and VPA (30 mg/kg) injections for 10 days; respectively. Growth; histopathological; biochemical and molecular biological indicators of lung injury; apoptosis; inflammation; fibrosis and histone acetylation were evaluated.

### RESULTS

VPA treatment during hyperoxia significantly improved weight gain; histopathologic grade; radial alveolar count and lamellar body membrane protein expression; while it decreased number of TUNEL(+) cells and active Caspase-3 expression. Expressions of TGFβ3 and phospho-SMAD2 proteins and levels of tissue proinflammatory cytokines as well as lipid peroxidation biomarkers were reduced; while anti-oxidative enzyme activities were enhanced by VPA treatment. VPA administration also reduced HDAC activity while increasing acetylated H3 and H4 protein expressions.

### CONCLUSIONS

The present study shows for the first time that VPA treatment ameliorates lung damage in a neonatal rat model of hyperoxic lung injury. The preventive effect of VPA involves HDAC inhibition.

## Poster 10

***LUNG LAVAGE WITH DILUTE SURFACTANT VERSUS BOLUS SURFACTANT FOR MECONIUM ASPIRATION SYNDROME: A RANDOMISED CONTROLLED TRIAL***

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### BACKGROUND

To compare the effect of lung lavage with dilute porcine surfactant and bolus surfactant administration in the treatment of infants with meconium aspiration syndrome (MAS).

### PATIENT AND METHODS

In this prospective randomized controlled study; ventilated infants with MAS with a gestational age ≥ 36; birth weight ≥ 2000 g were included. Infants were randomized into two groups; in group 1; two sequential 15 mL/kg aliquots of dilute porcine surfactant (Curosurf; Chiesi Farmaceutici S.p.A.; Parma; Italy) with a phospholipid concentration of 5 mg/ml were instilled into the lung. In group 2; 100 mg/kg of porcine surfactant were administered as a bolus. The study groups were compared with regard to efficacy; morbidity and mortality.

### RESULTS

Thirty-three infants were randomized. Median duration of mechanical respiratory support was similar in infants who underwent lung lavage and bolus surfactant (3 versus 3.5 days; p=0.36). Similarly; duration of oxygen therapy and hospitalization were not significantly different between lung lavage and bolus surfactant group (5 versus 7 days; p=0.48; 12.5 versus 12 days p=0.88; respectively). There were no differences in high frequency ventilation and nitric oxide requirement between the groups. Mortality and pneumothorax also did not differ between the groups.

### CONCLUSIONS

Lung lavage with dilute surfactant therapy does not alter the neonatal outcomes in terms of the duration of respiratory support; need of high frequency ventilation and nitric oxide; mortality and duration of hospitalization in ventilated infants with MAS.

## Poster 11

### *ANTENATAL STEROIDS AND PULMONARY OUTCOME IN NEONATES WITH A GESTATIONAL AGE ≤ 32 WEEKS*

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#### BACKGROUND

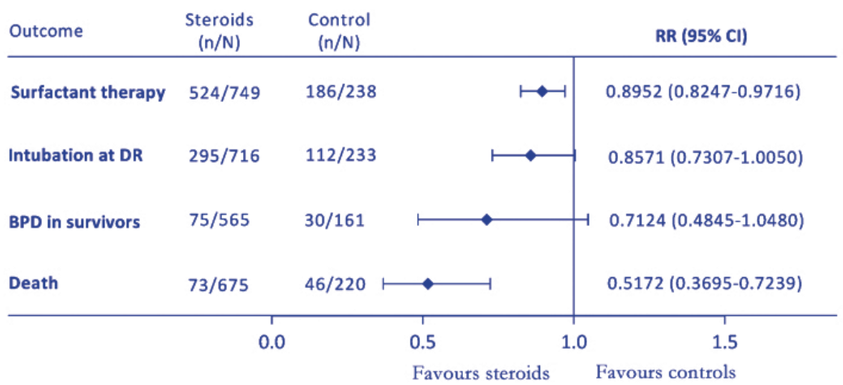
Antenatal corticosteroids are routinely used to promote lung maturity in premature neonates. The first Polish retrospective study aimed to evaluate the rate of antenatal use of corticosteroids and their effect on the incidence and treatment of respiratory disorders and survival rate.

#### PATIENT AND METHODS

Data of 987 neonates at gestational age of ≤ 32 weeks; treated at 54 centers; including tertiary (42) and secondary (12) referral centers; for the period of 6 months (between January 1; 2013 and June 30; 2013) were analyzed. The characteristics of both groups were similar according to: GA; BBW and gender.

#### RESULTS

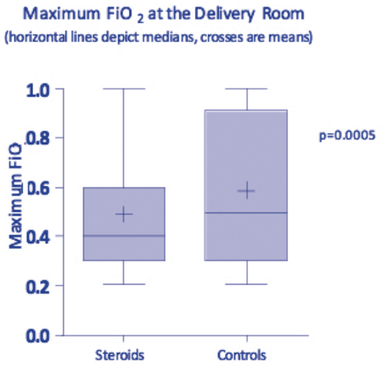
The percentage of glucocorticosteroids used in secondary and tertiary referral centers in Poland was only 76% (749 vs 238). We confirmed the effectiveness of antenatal corticosteroids on: lower fraction of inspired oxygen used for delivery room stabilization of preterm (FiO2 0;4 i 0;5; p=0;0005); reduced rate of surfactant treatment (69;9% vs. 78;1%; p=0;0143; RR=0;8952 [95%CI 0;8247 to 0;9716]); reduced rate of mechanical ventilation 55;7% vs 70;6%; p<0;0001; RR=0;7887 [95%CI 0;7108 to 0;8752] shorter duration of mechanical ventilation (5;7 ±1;4 days vs 7;9 ±12;7 days; p<0.0001); improved survival rate until 36 weeks of corrected gestational age (10;8% vs. 20;9%; p=0;0001; RR=0;5172 [95%CI 0;3695 - 0;7239]). We also observed trends toward reduced rate of BPD @36 CA; 13;2% vs 18;6%; p <0;09.

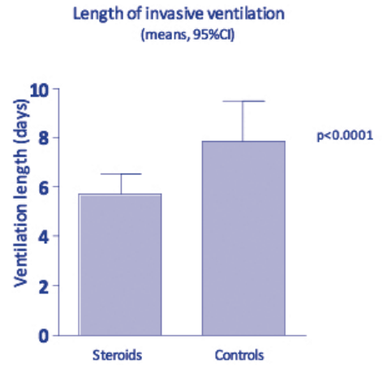



#### CONCLUSIONS

The percentage of glucocorticosteroids used in secondary and tertiary referral centers in Poland is still unsatisfactorily low (76%); We confirmed high efficacy of antenatal corticosteroid on reduced rate of surfactant therapy; duration of mechanical ventilation and mortality rates.

| Characteristics | Antenatal corticosteroids (N=749) | Controls (N=238) | P value |
|---|---|---|---|
| Birth weight; g; mean (5th; 95th percentile) | 1216 (600; 1980) | 1209 (520; 2021) | 0;6465 |
| GA; wk; mean (5th; 95th percentile) | 28;7 (24; 32) | 28;3 (23; 32) | 0;3191 |
| Sex; male; N(%) | 390 (52;0) | 124 (52;1) | 0;9933 |
| Outborn; N (%) | 38 (5;0) | 54 (22;7) | <0;0001 |
| Apgar at 1 min; median (IQR) | 6 (4-7) | 5 (2-6) | <0;0001 |
| Apgar at 5 min; median (IQR) | 7 (6-8) | 7 (6-8) | 0;0084 |
| Maximal FiO2 at DR; mean (5th; 95th percentile) | 0;49 (0;25; 1) | 0;59 (0;29; 1) | 0;0005 |
| Chest X-ray – degree of changes; median (IQR) | 2 (2-3) | 2 (2-3) | 0;1205 |
| Surfactant treatment; N(%) | 524 (69;9) | 186 (78;1) | 0;0143 |



## Poster 12

### *NOVEL BIOMARKERS FOR THE ASSESSMENT OF INTRAAMNIOTIC INFECTION*

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#### BACKGROUND

Intraamniotic infection/inflammation (IAI) and subsequent chorioamnionitis is a relevant factor triggering preterm birth; and is associated with adverse outcome (bronchopulmonary dysplasia; necrotizing enterocolitis; and brain white matter injury)1. However; there are limited data on oxidative stress and inflammation to the fetus after exposure to IAI. In sheep models; protein carbonyls were increased in plasma and airways; and myeloperoxidase in airways2.

Chorioamnionitis diagnosis is based on histological findings and/or clinical criteria. However; the histologic results do not always confirm the clinical diagnosis3. In this concern; important efforts have been carried out to modify obstetric diagnosis of chorioamnionitis and intervene in cases of silent IAI before clinical chorioamnionitis occurs4. Therefore; it is relevant to find new biomarkers that allow prompt diagnosis and optimize the timing of delivery.

#### OBJECTIVE

The aim of this work was to determine which biomarkers of oxidative stress; nitrosative stress; and inflammation could be used as early IAI biomarkers in amniotic fluid (AF) samples.

#### METHODS

35 AF samples collected from women grouped into three categories (normal; mild chorioamnionitis and intense chorioamnionitis) were analyzed following clinical and histological criteria.

The analytical methods employed consisted of liquid chromatography coupled to mass spectrometry5 (LC-MS/MS). The analytes determined were tyrosines (3-NO2-tyr; 3-Chloro-tyr; o-tyr; p-tyr; m-tyr; phenylalanine); glutathione (GSH); glutathione sulfonamide (GSA); 8-hydroxy-2'-deoxyguanosine (8OH-dG) and 2'-deoxyguanosine (2-dG).

#### RESULTS

GSH; 8OH-dG and 2-dG concentrations in AF were not relevant biomarkers for revealing the presence of chorioamnionitis. However; the concentrations of inflammation biomarkers; such as; GSA; 3-NO2-tyr and 3-Chloro-tyr showed significant differences among the three categories studied (Table). GSA and 3-NO2-tyr concentration in AF correlated well with the chorioamnionitis diagnosis; but did not discriminate upon severity of chorioamnionitis. Remarkably; 3-Chloro-tyr concentration was significantly increased in severe chorioamnionitis; but did not between mild chorio and normal AF samples.

Table. Comparison of biomarkers of oxidative stress & inflammation in amniotic fluid in patients with normal; mild or severe chorioamnionitis.

| | Normal | Severe Chorioamnionitis | Mild Chorioamnionitis |
|---|---|---|---|
| GSA (nM) | 5.0 ± 1.9 | 10±2** | 7.8±1.6** |
| 3-Chloro-tyr (nM) | 1.9±1.3 | 4.6±1.3** | 2.4±0.8 |
| 3-NO2-tyr (nM) | 200±80 | 700±200** | 400±200* |
| 8 -OH-dG (nM) | 4.4±1.8 | 5.4±0.7* | 5±3 |

*p<0.05; **p<0.01

#### CONCLUSIONS

We conclude that AF GSA and 3-NO2-tyr can be useful as early biomarkers of the presence of IAI; moreover; 3-Chloro-tyr can be used to detect the presence of severe chorioamnionitis necessitating urgent delivery.

## Poster 13

### *EVALUATION OF LUNG FUNCTION IN PRESCHOOL CHILDREN BORN LATE-PRETERM WITH IMPULSE OSCILLOMETRY*

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**BACKGROUND**

There is a paucity of data on lung physiology in late-preterm who may be exposed to a risk of decline in lung functions during childhood. In this study; we aimed to evaluate the lung function in preschool children born late-preterm using impulse oscillometry (IOS) and to compare the results with those obtained in healthy term-born children.

**PATIENT AND METHODS**

Children between 3 and 7 years of age born late-preterm who are currently being followed-up at the outpatient clinic were included as the late-preterm group. Age matched healthy term-born children served as controls. A total of 90 late-preterm and 75 healty children were included in the study. 15 of late-preterm (7%) had received surfactant postnatally. At 5-20 Hz; resistances (R5-R20); reactances (X5-X20) and resonant frequency were measured by IOS.

**RESULTS**

group ($p<0.05$). The mean values of R5; R10 and Z5 were statistically higher in late-preterms who had been hospitalized for pulmonary infections as compared to controls ($p<0.05$). The mean R5; R10; R15; R20 and Z5 were significantly higher and the mean X10 and X15 were significantly lower in late-preterms with passive smoking compared to late-preterms without passive smoking and controls ($p<0.05$).

**CONCLUSION**

Children born late-preterm exhibited signs of peripheral airway obstruction as evidenced by the results of our IOS-based comparison with healthy term-born controls. Besides the inherent disadvantages of premature birth; hospitalization for pulmonary infection and passive smoking also seemed to adversely impact the lung functions in children born late-preterm.

**Table I. Patient characteristcs of the late-preterm group**

| Late preterm n=90 | Mean±SD/ n(%) |
|---|---|
| Mean gestational week | 35.27±0.90 |
| Mean birth weight (g) | 2429.62±514.71 |
| Male; n(%) | 57(63.3) |
| Caesarean section; n(%) | 75(83.3) |
| Mean APGAR score at 5 min | 9.32±0.72 |
| Diagnosis | |
| Respiratory disorder; n(%) | 54(60) |
| Non-respiratory disorder; n(%) | 36 (40) |
| Respiratory support; n(%) | 37(41.1) |
| Surfactant treatment; n(%) | 13(14.4) |
| Mean duration of hospitalization (days) | 6.64±5.13 |
| Maternal asthma during pregnancy; n(%) | 5(5.6) |
| Passive smoking; n(%) | 53(58.9) |
| Hospitalization for pulmonary infection; n(%) | 27(30) |

**Table II. IOS results for late-preterm group and controls**

| IOS | Late-preterms (n=90) | | Controls (n=75) | | p |
|---|---|---|---|---|---|
| | Mean | SD | Mean | SD | |
| R5kPa/(L/s) | 0.96 | 0.29 | 0.88 | 0.25 | **0.028** |
| R10kPa/(L/s) | 0.82 | 0.20 | 0.75 | 0.19 | **0.037** |
| R15kPa/(L/s) | 0.76 | 0.18 | 0.72 | 0.18 | 0.158 |
| R20kPa/(L/s) | 0.70 | 0.17 | 0.67 | 0.17 | 0.197 |
| X5kPa/(L/s) | -0.27 | 0.11 | -0.26 | 0.11 | 0.719 |
| X10kPa/(L/s) | -0.15 | 0.09 | -0.12 | 0.07 | 0.079 |
| X15kPa/(L/s) | -0.09 | 0.08 | -0.07 | 0.06 | 0.091 |
| X20kPa/(L/s) | -0.00 | 0.08 | 0.01 | 0.05 | 0.337 |
| Resfreq 1/s | 19.57 | 3.72 | 18.52 | 4.69 | 0.240 |
| Z5kPa/(L/s) | 1.00 | 0.28 | 0.91 | 0.27 | **0.030** |

## Poster 14

***THE EFFECT OF CLARITHROMYCIN PROPHYLAXIS ON DEVELOPMENT OF BRONCHOPULMONARY DYSPLASIA IN PRETERM INFANTS***

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### BACKGROUND

Bronchopulmonary dysplasia (BPD) is a significant respiratory cause of morbidity and mortality in premature infants. Because of multifactorial etiology there is not any curative treatment in infants yet . In last years researches focused on uncontrolled and exagerrated inflammatory activity in preterm lung. Clarithromycin prophylaxis associated with diminished BPD rate in preterm infants colonisation with Ureaplasma urealyticum. We aimed to evaluate the efficacy of clarithromycin prophylaxis in preventing BPD in preterm infants with or without Ureaplasma urealyticum and Mycoplasma Hominis.

### PATIENT AND METHODS

Infants who were eligible for the study were determined as preterms with a birth week and weight under 30 week and 1250 gram respectively. In the first 24 hours of infants; we randomised and separate two groups after the take culture for Ureaplasma Urealyticum and Mycoplasma Hominis. First group treated with clarithromycin during 10 days. Second group treated with salin as same as clarithromycine volume during 10 days.The outcomes for this study were the composite mortalities and others comorbidities such as bronchopulmonary dysplasia; intracranial bleeding; patent ductus arteriosus; necrotizing enterocolitis and retinopathy of pretamurity. Exclusion criteria consisted of the presence of major congenital abnormalities; lack of parental informed consent; intrauterine growth retardation with a birth weight at the 10th percentile for gestational age and death in first 28 days of life.

### RESULTS

After the remove some patients because of exclusion criterias and death; 184 infants( 92 each group) were analysed. There was no significant difference between the clarithromycin and plasebo groups in terms of demographic characteristics. Mean gestational ages (27.4±1.3vs. 27.4±1.5 weeks) and birth weights (1009±154 vs. 992±170 g) were similar. At least 28 days oxygen requirement rate were high in plasebo group at 36 weeks PMA but statistically insignificant (51.1% vs. 41.3%; p=0.183). Moderate and severe BPD rate was significantly low in clarithromycin group compared with plasebo group (28.3% vs. 8.7%; p=0.01). Otherwise; Ureaplasma and Mycoplasma colonisation rate was not different between clarithromycin and plasebo groups.

### CONCLUSIONS

Our result showed that; clarithromycine prophlaxis was not changed total BPD rate ( mild; moderate and severe) in the study. At the same time; diminished moderate and severe BPD rate were reached in preterm infants treated with clarithromycine. We speculated that; clarithromycine prophlaxis provided decreased moderate and severe BPD rate in preterm infants with/without Ureaplasma urealyticum and Mycoplasma Hominis colonisation.



## Poster 15

***DIAGNOSTIC ACCURACY OF LUNG ULTRASOUND IN THE CRASHINGINFANT: AN INTERNATIONAL; PROSPECTIVE STUDY***

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### BACKGROUND

Pneumothorax is a common and potentially lethal emergency in the NICU. Adult emergency medicine data show that pneumothorax can be reliably diagnosed by ultrasound. Neonatal data are currently lacking.
The aim of this study is to evaluate the accuracy of lung ultrasound (LUS) for the differential diagnosis of pneumothorax in the suddenly decompensating newborn infant keeping the Chest X Rays as a reference standard.

### PATIENT AND METHODS

In a NICU setting; sudden deterioration was defined as a prolonged significant desaturation (Sat O2< 65% for over 40 seconds) and bradycardia OR sudden increment of oxygen requirement to meet a 50% increase in less than 10 minutes with a final FiO2 ≥ 0.7 to keep stable saturations. All eligible patients had a LUS scan before undergoing a CXR.

### RESULTS

19 infants (BW = 1878±933 grams; GA = 32 ±3 weeks) were enrolled in 6 centers; PNX was detected in 14 of them. LUS accuracy in diagnosing PNX: sensitivity; specificity; PPV and NPV were all 100%. Clinical evaluation of PNX showed sensitivity 92%; specificity 40%; VPP 81%; VPN 66%.After clinical crashing; LUS was performed in an averagetime of 6minutes versus a mean time of 22 minutes required for CXR. Emergency drainage was performed after LUS but before CXR in 6/14 cases. Chest transillumination was used only in two cases.

### CONCLUSIONS

These are the preliminary data of the LUCI study (Lung Ultrasound in the Crashing Infant). Lung ultrasound shows both absolute sensitivity and specificity in detecting pneumothorax in the crashing infant; outperforming clinical evaluation and reducing time to imaging diagnosis and often to drainage.

## Poster 16

***EFFECT OF RECOMBINANT HUMAN ERYTHROPOIETIN ON TRACHEAL ASPIRATE INFLAMMATORY MARKERS IN VENTILATED PRETERM NEONATES***

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### BACKGROUND

Existing evidence suggests a cytoprotective effect of erythropoietin (EPO) on various organs as a consequence of its multiple biological actions. OBJECTIVE: To test the hypothesis that recombinant human EPO (rhEPO) would ameliorate lung inflammation in ventilated preterm neonates.

### PATIENT AND METHODS

Preterm neonates (gestational age ≤ 30 weeks) with respiratory failure requiring mechanical ventilation on day of life 1 (T1) were eligible for this prospective pilot study. Enrolled neonates were randomly assigned to receive either rhEPO (1500 IU/kg s.c X 3 per day at T1 followed by 250 IU/kg s.c X 3 per week [EPO group]) or placebo (control group). Tracheal aspirate (TA) samples were collected at T1 as well as on days of life 4-5 (T2) and 7-10 (T3) if still intubated. Serum EPO was also measured at the above time points. TA samples were analyzed for EPO; interleukins-6; 8 and 18; macrophage inflammatory protein-1 alpha; and monocyte chemotactic protein 1. White blood cell count and differential as well neutrophil respiratory burst activity (RBA) were measured (Flow cytometry) on TA samples.

### RESULTS

Six and eight neonates comprised the EPO and control group; respectively. Serum and TA EPO levels were significantly increased at T2 in the EPO as compared to the control group. A significant correlation between serum and TA EPO levels was found at T1 and T2. However; TA levels of the cytokines studied as well as cell counts; differential and neutrophil RBA were comparable between groups.

### CONCLUSIONS

Our results do not support an amelioration of lung inflammation in ventilated preterm neonates with the rhEPO doses given in this study. However; a possible favorable effect with higher EPO doses cannot be excluded.

## Poster 17

***THE EFFECTS OF MATERNAL ANTICOAGULANT THERAPY ON CORD BLOOD ANGIOGENIC FACTORS AND NEONATAL RESPIRATORY MORBIDITY IN WOMEN WITH RECURRENT MISCARRIAGE***

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### BACKGROUND

Angiogenic imbalance of the placenta is one of the prominent pathophysiologic mechanism underlying pregnancy complications like recurrent miscarriage. Low molecular weight heparin and low dose aspirin are frequently used in the management of recurrent miscarriage. These treatments; mainly heparin has been shown to organize angiogenesis. Vascular endothelial growth factor (VEGF) and its soluble resector-sFlt-1-plays a major role in angiogenesis which has an impact on respiratory problems of newborns. The first aim of this study is to investigate whether maternal use of LMWH and low dose aspirin combination therapy can alter the circulatory profile of VEGF-A and sFlt-1 in cord blood of infants; and the second aim is to determine any association between respiratory morbidity of the newborn and maternal anticoagulant usage.

### PATIENT AND METHODS

Term newborns whose mothers were treated with LMWH and low dose aspirin due to recurrent miscarriage were prospectively included. A control group consisted of healthy gestational age matched infants without an adverse perinatal outcome who were born in the same period. The concentrations of VEGF-A and sFlt 1 in umbilical cord blood were assayed by ELISA and compared between study and control group. Short term neonatal outcomes and respiratory problems were also noted in two groups.

### RESULTS

Forty four infants with a maternal LMWH and low dose aspirin usage during pregnancy and 42 healthy infants as a control group were included in the study. Serum VEGF-A level was detected in all samples (n=86) whereas 23 samples were above the detection limit for sFLT-1. There were no significant differences between the demographics; serum VEGF-A and sFlt-1 levels. There were also no correlation between the cumulative LMWH dosage and serum levels of these angiogenic factors. Respiratory problems (transient tachypnea of the newborn and pulmonary maladaptation) were more common in the study group compared to control group (10/44 versus 2/42; $p<0.05$).

### CONCLUSIONS

LMWH and low dose aspirin treatment in mothers with recurrent miscarriage did not alter the circulatory profile of cord blood VEGF-A and sFlt-1 levels. These findings will contribute to improve our understanding the complex interactions of maternal anticoagulant therapy and angiogenic factors on fetal site. On the other hand the high frequency of respiratory problems in infants with maternal anticoagulant usage needs further evaluation.

## Poster 18

***EARLY IMMUNOMODULATORY EFFECTS OF DIFFERENT NATURAL SURFACTANT PREPARATIONS IN PRETERM INFANTS WITH RESPIRATORY DISTRESS SYNDROME***

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### BACKGROUND

Natural surfactant preperations are widely used for the treatment of respiratory distress syndrome (RDS). These preperations have either bovine or porcine surfactant proteins which may have immunoregulatory effects in the newborn lung. So far; little is known about the immunomodulatory effects of therapeutic surfactants. The aim of this study was to evaluate cytokine and chemokine response following three different regimens of natural surfactant treatment in preterm newborns with RDS.

### PATIENT AND METHODS

Forty five preterm newborns (gestational age ≤32wk) with RDS requiring intubation in the first hours of life were randomized into 3 study groups: Group 1= Beractant; 100mg/kg; Group 2=Poractant alfa; 100mg/kg; Group 3= Poractant alfa; 200mg/kg. Blood and tracheal aspirate samples were obtained prior to surfactant treatment. The same sampling procedures were repeated 6 hours after surfactant. Eosinophil count of the blood and tracheal aspirate (TA) samples were performed by Abbott Cell DYN 3700 counter. Commercially available enzyme-linked immunosorbent assay (ELISA) kits were used to determine ITaC (inducible T Cell alpha chemoattractant); MIP3b (macrophage inflammatory protein 3 beta); Il-5; IL-8; IL-9; IL-10; IL-13; IgE; IFN-gamma; TGFbeta1 levels in blood and TA samples. Antenatal and clinical variables of the study groups were recorded prospectively.

### RESULTS

Mean ±SD gestational age and birth weight of the study groups 1;2 and 3 were similar; 28;13 ±2;55 vs. 28;80±2;56 vs. 27;46±3;64 weeks and 1212;33±382;82 vs. 1319;80±390;952 vs. 1127;07±840;00 grams; respectively. Antenatal and clinical characteristics were also similar. No adverse effects related to surfactant treatment was observed in any study patients. TA samples: IFN-gamma concentration and eosinophil counts decreased after surfactant replacement in all groups; especially in the poractant-alfa treated infants. Eotaxin; TGF beta and IL8 concentrations increased significantly in poractant-alfa treated infants. TA IL9 levels decreased in the beractant group but increased in the poractant alfa groups. Blood samples: Blood levels of cytokines and chemokines showed significantly decreased levels of ITAC and MIP3b only in the beractant group; but were not informative for poractant alfa groups.

### CONCLUSIONS

Natural surfactants have different immunomodulatory effects in the newborn lungs. This initial response was more pronounced in the poractant alfa groups.

## Poster 19

***INTRANASAL SURFACTANT PROTEIN D AS NEUROPROTECTIVE RESCUE IN A NEONATAL RAT MODEL OF PERIVENTRICULAR LEUKOMALACIA***

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### BACKGROUND

Periventricular leukomalacia (PVL) is the leading cause of neurocognitive deficits in children with prematurity. Lipopolysaccharide (LPS) induced oligodendrocyte injury in the CNS occurs through toll-like receptors (TLR). We previously hypothesized that surfactant protein D (SPD) with its an ability to bind TLRs may have a possible ameliorating effect in PVL. To further explore our hypothesis; we introduced SPD in an established a rat model of PVL.

### PATIENT AND METHODS

Sprague-Dawley rats on day 18 of pregnancy were used for the study. To obtain live offspring for examination of neonatal brain injury; LPS was consecutively administered on gestation day 18 and 19 at a dose of 300 µg/kg. All newborn rats were randomly allocated to three groups: LPS administered and postnatal intranasal salin administered group; LPS administered and postnatal intranasal SPD treated group; and control group. Twenty-eight offspring rats were reared with their dams until their sacrifice for histological evaluation on day 7

### RESULTS

A significant loss of brain weight occurred in the LPS group compared with controls. We observed a significant increase in TUNEL-positive cells per field at P7 in the periventricular white matter of the LPS-treated group compared with control groups. The postnatal intranasal SPD treatment significantly reduced the number of TUNEL-positive cells in the periventricular white matter as compared with the LPS-treated group. Compared with the control group; LPS injection in the rat brain significantly reduced the MBP-positive staining. Postnatal SPD treatment greatly prevented LPS-stimulated loss of MBP staining.

### CONCLUSIONS

Present study demonstrated a neuroprotective effect of SPD in a rat model of PVL. When given intranasal route; SPD resulted in a remarkable reduction of apoptotic cell death and prevented endotoxin induced hypomyelination. Our results offer future implications towards increasing our understanding about multifactorial mechanisms underlying periventricular leukomalacia and developing plausible therapeutic strategies in order to prevent neurocognitive deficits in preterm infant.

## Poster 20

***EFFECTS OF PERINATAL STEROID THERAPY ON DEVELOPING BRAIN AND GROWTH FACTORS: WHAT IS THE CRITICAL TIME WINDOW?***

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### BACKGROUND

Growth factors play an important role in the development of the central nervous system (CNS). Evidences suggest that glucocorticoid exposure at certain developmental stages have considerable effects on the development of the central nervous system (CNS). This study thus aimed to evaluate the differential effects of glucocorticoid exposure on critical growth factor levels during different stages of brain maturation.

### PATIENT AND METHODS

Forty-two rat pups were divided into six groups according to the timing of betamethasone administration. Rats in the treatment groups were exposed to intraperitoneal bethamethasone injection beginning at different time points (postnatal days 1; 2; and 3). Rats in the placebo group were received the same volume of 0.9% saline via the same fashion. Pups were sacrificed at 24 hours after the last injection for neuronal density and immunohistochemical evaluation of Brain derived neurotrophic factor (BDNF); Transforming growth factor alpha (TGFα); Fibroblast growth factor 1 (FGF1); Platelet-derived growth factor receptor alpha (PDGFRα); and Vascular endothelial growth factor A (VEGFA).

### RESULTS

In the group treated with betamethasone the number of neurons in the CA1; CA2; CA3; and dentate gyrus regions of hippocampus were significantly lower than control groups on postnatal day 1 and on postnatal day 2; which correspond to 22-24 and 24-28 gestational weeks in humans in terms of brain growth. However; the number of the neurons in the hippocampus was not significantly different between the groups on postnatal day 3; corresponding to 28-32 weeks in humans. All of the evaluated growth factors except PDGF and VEGFA showed up-regulation in steroid exposed groups. A lineer relationship didn't exist between neuronal count and growth factors response.

### CONCLUSIONS

The present study demonstrates for the first time that steroid exposure during different stages of brain maturation showed differential effects on critical growth factors. Modulating effects of corticosteroids on growth factor response is depending on stage of brain development at the time of exposure and this may be one of the key determinants affecting the deleterious and beneficial effects of corticosteroids on central nervous system.

## Poster 21

***ASSOCIATION OF E-NOS GENE POLYMORPHISM IN DEVELOPMENT OF BRONCHOPULMONARY DYSPLASIA***

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### BACKGROUND

Nitric oxide is involved in multiple processes in the lung and all nitric oxide synthase (NOS) genes are expressed in airway epithelial cells The aim of this study was to investigate possible association of eNOS gene polymorphism in development of BPD in premature infants.

### PATIENT AND METHODS

This multi-center prospective study was performed in premature infants (≤ 32 weeks of gestation and/or ≤1500 g) who were admitted to the NICU with respiratory distress within the first 24 hours of life. Demographic and ventilation data of the infants were recorded. BPD was defined according to the National Institute of Child Health and Human Development/ National Heart; Lung; and Blood Institute and Office of Rare Diseases workshop definition. DNA isolation was carried out using the PureLinkTM Genomic DNA Mini Kit and the concentration of the DNA samples was measured by nanophotometerImplen P 300. For the SNP analysis of eNOS (rs1799983) optimized primers were used. Real Time Polymerase Chain Reaction(QRT-PCR) was carried out in a CFX96 thermocycler.

### RESULTS

A total of 122 infants were enrolled and 55 of them developed BPD; whereas 67 did not have BPD. The mean gestational age and birth weight of these infants were significantly lower than those who did not develop BPD. The mean ventilation and supplemental oxygen duration were also significantly higher in infants with BPD compared with non-BPD group. The presence of G allele of e-NOS gene was a highly significant risk factor for development of BPD. The frequency of GG and TT genotypes of eNOS gene were higher in babies with BPD. None of infants without BPD had GG genotype.

### CONCLUSIONS

This study shows for the first time that eNOS gene polymorphism is associated with development of BPD. GG ve TT genotypes of eNOS gene were found to be highly significant in infants with BPD.

## Poster 22

***DEVELOPMENT OF A NEW METHOD TO DETERMINE F2-ISOPROSTANES IN NEWBORN SERUM AND PLASMA SAMPLES***

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### BACKGROUND

Isoprostanes (IsoPs) are stable products resulting of a non-enzymatic oxidation of polyunsaturated fatty acids. IsoPs derived from arachidonic acid (AA) peroxidation are called F2-isoprostanes. They are considered as the most reliable markers of oxidative stress in vivo [1]; which is linked to severe neonatal conditions such as bronchopulmonary dysplasia; retinopathy of prematurity; hypoxic/ischemic encephalopathy.

Reported cord plasma levels are between 0.07 and 0.12 nM/mL [2]. Moreover; total F2-isoprostanes are significantly higher for term (0.73 nM) and especially preterm (1.02 nM) newborn comparing with adults (0.52 nM) [3]. F2-isoprostanes can be determined in urine; serum and plasma samples of newborn. However; few validated methods to determine F2-isoprostanes in plasma and serum samples can be found in literature.

### OBJECTIVE

The aim of this work was to validate a chromatographic-mass spectrometry method for the reliable determination of F2-isoprostanes within the limits of detection (LOD) that would be within levels usually found in healthy newborn plasma and serum samples.

Methods

Healthy term newborn infants' cord blood was used for the determinations (n=10). The analytical method employed consisted of liquid chromatography coupled to mass spectrometry (LC-MS/MS). The analytes determined were F2-isoprostanes (8-iso-15(R)-PGF2α; 1a1b-dihomo-PGF2α; 2;3-dinor-iPF2α-III; 8-iso-15-keto-PGE2; 8-iso-15-keto-PGF2α; 8-iso-PGE2; 5-iPF2α-VI; 8-iso-PGF2α; the PGs PGE2 and PGF2α). In addition to this; total parameters (isoprostanes; isofurans; neuroprostanes; neurofurans) were also determined.

### RESULTS

The limits of detection (LOD) obtained for 8-iso-15(R)-PGF2α; 8-iso-PGF2α; PGF2α; 5-iPF2α-VI; 2;3-dinor-iPF2α-III and 8-iso-15-keto-PGF2α were satisfactory to determinate these compounds in healthy adult human plasma or serum samples (range = 0.1-0.5 nM). In the table we can see ranges of assessed concentrations in newborn serum samples. As regards total parameters; important differences were observed for neurofurans and especially isofurans among the serum samples analyzed.

**Table. Limit of detection and assessed values of F2-isosprostanes by LC-MS/MS in healthy term newborn babies (n=10).**

| Parameter | LOD (nM) | Assessed concentrations (nM) |
|---|---|---|
| 8-iso-15(R)-PGF2α | 0.5 | 0.5-32 |
| 8-iso-PGF2α | 0.05 | 0.1-0.5 |
| PGF2α | 0.05 | 2-64 |
| 5-iPF2α-VI | 0.05 | 1-67 |
| 2;3-dinor-iPF2α-III | 0.2 | 0.4-2.3 |
| 8-iso-15-keto-PGF2α | 0.3 | 0.3-200 |

**LOD:** limit of detection.

### CONCLUSIONS

The method developed provides satisfactory sensitivity and accuracy to carry out reliable determination of F2-isoprostanes and total parameters in newborn serum and plasma samples. In comparison to previous methods; this method has some advantages; such as; simple sample treatment and high selectivity to determine a lot of compounds in just one analysis. In addition to this; ranges of F2-isoprostanes concentrations in newborn serum samples have been established.

## Poster 23

### *TARGETED NEXT GENERATION SEQUENCING FOR MUTATION DETECTION IN IDIOPATHIC NEONATAL AND PEDIATRIC DIFFUSE LUNG DISEASES*

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#### BACKGROUND

Next-Generation Sequencing (NGS) techniques allow fast; high-throughput mutation detection in cohorts of patients with heterogeneous genetic disorders. Unexplained acute and chronic diffuse lung disease in newborns and children are a heterogeneous group of rare diseases caused by genetic disorders of surfactant metabolism and by developmental vascular lung disorders such as alveolar capillary dysplasia; the molecular causes and mechanisms of which are still poorly understood.

#### OBJECTIVE

Our objectives were 1) to identify new and known disease-causing genetic variants in surfactant- or pulmonary vascular -related genes in a retrospective cohort of children 0-18 year-old with variable respiratory phenotypes ranging from neonatal hypoxic respiratory failure to chronic pulmonary hypertension or interstitial pneumonitis; and 2) to validate a targeted NGS panel using as a screening and diagnostic tool in these rare lung diseases.

#### METHODS

A custom-designed NGS panel including 9 surfactant-related genes (ABCA3; SFTPA1; SFTPA2; SFTPB; SFTPC; SFTPD; NKX2.1; CSF2Ra; CSF2Rb) and 15 developmental vascular genes (FOXF1; BMPR2; TBX4; MEOX2; TXNDC3; SMAD9; SMAD1; SMAD5; THBS1; ACVRL1; ENG; CBLN2; CRHBP; CRHR1; PPAR?); selected either by published data review or candidate gene approach; was applied in a subset of 17 cases aged 0-2 in a cohort of 127 cases referred from 2005 to 2014; 84 of which had been studied by Sanger exon sequencing in genes targeted for age of onset and clinical presentation. Copy number variation (CNV) analysis by array comprehensive genomic hybridization (aCGH) was performed in a subset of 8 cases.

#### RESULTS

Probable disease-causing genotypes were present in 24/84 cases (29%) analyzed by direct sequencing: ABCA3 (11 cases); SFTPC (8); NKX2.1 (2); FOXF1 (2) and TBX4 (1). In addition; single heterozygous mutations were present in ABCA3 (5 cases) and SFTPB (2 cases); of uncertain clinical significance since the related diseases are autosomal recessive. In the subset studied by NGS; 100% of the previously identified coding variants were confirmed; in addition; heterozygous coding variants were identified in other genes: CSF2Rb (4 cases); NKX2.1 (2); CRHR1 (1) and SMAD9 (1). Numerous non-coding variants of unknown significance were also present in all cases. aCGH revealed potentially disease-causing CNVs in 4 cases; involving TBX4 (1 case) and MEOX2 (1 case).

#### CONCLUSIONS

The wide clinical heterogeneity of pediatric diffuse lung diseases can be explained by the number of different genes involved and the variety of genetic mechanisms involved; including homozygosity; compound heterozygosity or; as suggested by these data; trans-heterozygosity. Targeted panel NGS appears to be a reliable method for mutation screening and complex phenotype identification; and should be integrated in combined genic and genomic strategies for comprehensive diagnosis and characterization of these rare diseases.



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Speakers are kindly requested to hand their presentations to the organizers or the congress technicians the day before their presentation or at least 15 minutes before the beginning of the Scientific Programme.

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***30th International Workshop on Surfactant Replacement has been organized with the unrestricted grant of Chiesi.***
*Also we would like to thank Ginevri for their collaboration.*

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| 1998 | Belfast, UK |
| 1999 | Skagen, Denmark |
| 2000 | Kos, Greece |
| 2001 | Edinburg, UK |
| 2002 | Cagliari, Italy |
| 2003 | Prague, Czech Republic |
| 2004 | Vienna, Austria |
| 2005 | Belfast, UK |
| 2006 | Oslo, Norway |
| 2007 | Ancona, Italy |
| 2008 | Brugge, Belgium |
| 2009 | Ljubljana, Slovenia |
| 2010 | Moscow, Russia |
| 2011 | Istanbul, Turkey |
| 2012 | Lisbon, Portugal |
| 2013 | Helsinki, Finland |
| 2014 | Valencia, Spain |
| 2015 | Stockholm, Sweden |
| 2016 | Naples, Italy |