ID: 19
TITLE: CORRECTION OF APOPTOSIS OF LYMPHOCYTES INHALATION NITROGEN OXIDE IN NEWBORNS ON MECHANICAL VENTILATION.
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AFFILIATIONS: Department of Anesthesiology and Critical Care Medicine, State Medical University, Rostov-on-Don, Russia.

CONTENT:

Introduction. Activation of apoptosis of lymphocytes at the newborns with respiratory pathology, who are on mechanical ventilation of lungs, is followed by decrease in blood of concentration of endogenous nitrogen oxide (NO) and confirms high probability of development of bacterial complications.

Research objective. Decrease in frequency of development of sepsis by correction of apoptosis of lymphocytes by inhalation NO.

The randomized controlled blind clinical trial was performed on 97 full-term newborns with respiratory pathology on mechanical ventilation; no clinical signs of bacterial infection were diagnosed, with the content in blood of lymphocytes AnnexinV-FITC+PL≤10,6%, AnnexinV-FITC+PL≤0,56%. Patients of group I (n=44) received inhalations by NO (10 ppm, 48 hours; «Pulmonox mini», Austria). Group of control - II (n=53).

On the 1th, 3th and 20th days after admission CD3+CD19-, CD3-CD19+, CD3+CD4+, CD3+CD8+, CD69+, CD71+, CD95+, HLA-DR+, CD34+, CD14+, CD3-CD56 + , lymphocytes with expression AnnexinV-FITC+PI-, AnnexinV-FITC+PI+ were determined by method of a flowing phenotyping.

In I group (n=44) development of sepsis is confirmed at 4 newborns; in control group (n=53) - at 13 newborns (p1=0,04; p2=0,05, Fischer-Earvin,s test, bilateral alternative, 5% significance value). Lethal outcome in I group – 6 newborns; in II group - 10 (p1=0,37; p2=0,59; Fischer-Irvin,s test). Median of the transfer to independent breath in I group- 5 days, in II – 10 (p=0,00007); hospitalization duration in resuscitation in I group - 11 days, in II – 15 (p=0,02610); Kaplan-Major,s method, Gekhana-Vilkokson,s criterion.

For 3th days in I group on comparison II group with relative contents increased CD3+CD19-, CD3+CD4+, CD14+ (p<0,05); decrease CD3+CD69+, CD3+ CD95+, lymphocytes with expression AnnexinV-FITC+PI-, AnnexinV-FITC+PI+ (p<0,05).

Correction of apoptosis of lymphocytes inhalation NO reduces the frequency of development of sepsis, duration of artificial ventilation of lungs and hospitalization in resuscitation, forms a tendency of decrease in frequency of a lethal outcome.

Inhalation NO increases activity of monocytes and decrease activity of apoptosis of lymphocytes.

COI: "none declared"
ID: 110

TITLE: Meconium peritonitis is caused by leakage of meconium into the fetal peritoneal cavity due to intestinal perforation. Since meconium is sterile, it is regarded as a unique non-infectious inflammatory disease. However, its pathophysiology is not well understood due to lack of animal models that accurately mimic the condition. Recently, a technique using “cecal slurry (CS)” has been established to non-surgically induce neonatal sepsis, and involves the intraperitoneal (IP) administration of adult cecal contents suspended in dextrose to newborn pups. To generate a neonatal mouse model of meconium peritonitis via IP administration of human meconium suspension or “slurry” (MS) by applying the CS methodology.

Under the approval of our Institutional Animal Care and Use Committee (P170103) and obtaining parental consent, fresh meconium from healthy term newborns was taken via the rectal stimulation and then suspended in PBS to 500 mg/mL and stored at -80°C. 200 μL of MS (meconium) or PBS (control), or of CS at the LD40 dose (1.5 mg/g, suspension of cecal contents from adult mice in 15% glycerol-PBS to 100 mg/ml) was administered IP to 4d-old wild-type FVB mice pups. Blood gas/electrolyte levels at 3h, weight at 24h post-administration were measured and survival up to 5 days was monitored.

Administration of MS resulted in significant decreases in weight gain and survival (0.8±7.5% (n=26), and 58.8% (n=34), respectively) compared with PBS controls (18.6±4.8% (n=10) and 100% (n=10), respectively, p<0.05 for both). These findings were comparable to those found in age-matched CS-treated pups (-3.1±5.2% (n=11) and 58.3% (n=12), respectively, Fig. 1, 2). At 3h post-sepsis induction, significant changes in Na+, K+, anion gap, lactate, base excess, and HCO3- were found in both MS and CS groups compared with controls. In contrast, pCO2, pO2, and osmolarity levels were different in in MS-treated pups only. Interestingly, blood glucose levels were significantly increased in CS-treated pups (Table).

IP administration of MS from human infants resulted in significant mortality and weight loss to 4d-old newborn pups, and affects blood gasses and electrolytes. Therefore, we conclude that this MS model can be used to study the pathophysiology and treatment of meconium peritonitis.

IMAGES: https://www.eiseverywhere.com/eselectv3/v3/events/351149/submission/files/download?fileID=bb9b5b60b5461c6605f80cf1b783bea4-MjAxOS0wNSM1Y2UyNjY2YmQwNGNh

Figure 1. Kaplan-Meier survival plots of 4d-old pups given MS (n=34), CS (n=12), or Veh (n=10). The survival rate was significantly lower in the MS group (58.8%) and CS group (58.3) than in the Veh groups (100%).

Figure 2. Body weight change 24h post-administration of MS (0.8±7.5%, n=26), CS (-3.1±5.2%, n=11), or Veh (18.6±4.8%, n=10). The BW changes of MS and CS groups were significantly lower than those of Veh groups. *p <0.0001

COI: None declared
ID: 300

**TITLE:** ASSOCIATION OF AGE AT FIRST RESPIRATORY SYNCTIAL VIRUS HOSPITALISATION (RSVH) AND SUBSEQUENT RISK OF ASTHMA

**AUTHORS:** Jonathan Coutts 1; Richard Thwaites 2; John Fullarton 3; ElizaBeth Grubb 4; Carole Morris 5; Barry Rodgers-Gray 3; Xavier Carbonell-Estrany 6

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**CONTENT:**

RSV in early childhood is becoming increasingly well-recognised as a significant risk factor for the subsequent development of asthma. Whether the risk for developing asthma varies with age at first RSVH has yet to be fully explored. A recently published Australian study reported, perhaps somewhat surprisingly, that the burden of subsequent asthma was higher in children with RSVH at ≥6 months than <6 months of age (Homaira et al. J Infect Dis. 2018). The aim of this study was to determine the association between age at first RSVH and subsequent development of asthma.

All live births between 1996-2011 from NHS Scotland Information Services Division (ISD) databases were followed until 18 years of age or until the study period ended in 2014, whichever came sooner. Those who died or moved away from Scotland during the study period were excluded. The rate of asthma-related hospitalisations (ICD-10 codes J45 and J46) and use of asthma medications (bronchodilators, corticosteroids, cromoglycate and related therapy, leukotriene receptor antagonists, and phosphodiesterase type-4 inhibitors) were assessed in children with first RSVH (ICD-10 codes J12.1, J20.5 & J21.0) at <6 months, 6 to <12 months, 12 to <18 months, and 18-24 months. A composite outcome of ‘confirmed asthma’ was defined as a child with an asthma admission and requirement for asthma medication.

Of 740,418 children, 15,791 (2.1%) had ≥1 RSVH at ≤2 years (median age at first RSVH: 143 [IQR 64-274] days). 58.8% (9,281) of first RSVHs occurred at <6 months, 26.5% (4,191) at 6 to <12 months, 10.2% (1,603) at 12 to <18 months, and 4.5% (716) at 18-24 months. The asthma admission rate in those with a RSVH was 148.8/1000 at <6 months, 225.0/1000 at 6 to <12 months, 301.3/1000 at 12 to <18 months, and 342.2/1000 at 18-24 months (p<0.0001 across age groups). Similar trends were found for asthma medication use (<6: 23.1%, 6 to <12: 27.9%, 12 to <18: 28.5%, 18-24: 34.6%; p<0.0001) and confirmed asthma (92.5, 134.3, 188.4 & 215.1/1000; p<0.0001). Compared with the overall RSVH group, children without RSVH had significantly fewer asthma admissions (193.2 vs 46.0/1000; p<0.0001), lower asthma medication use (25.5% vs 14.7%; p<0.0001), and less confirmed asthma (117.6 vs 29.5/1000; p<0.0001).

This study provides further confirmation of the association between RSVH in early childhood and subsequent asthma. Interestingly, older age at first RSVH was associated with higher asthma rates, which may reflect a more competent immune system. It should be noted, however, that due to the declining incidence of RSVH with age, numerically, the largest clinical burden for asthma related to RSV comes from those infants subject to RSVH early in life.

**COI:**

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Disclosures
Financial support for this study was provided by AbbVie. AbbVie participated in analysis and interpretation of data, drafting, reviewing, and approving the publication. All authors contributed to the development of the publication and maintained control over the final content.

RT, JC and XCE have received research funding and/or compensation as advisor/lecturer from AbbVie.

BRG and JF, working for Strategen, have previously received payment from AbbVie for work on various projects.

EG is an employee of AbbVie and may hold stock in AbbVie.

CM, working for ISD Scotland, has received payment from AbbVie for work on this project.
ID: 302

TITLE: HUMAN PARECHOVIRUS (HPEV) MENINGOENCEPHALITIS IN INFANTS: A DESCRIPTIVE REGIONAL Study

AUTHORS: Luciana Romaniello 1, Rosa Lapolla 2, Giambattista Gallicchio 3, Michele Grisolia 4, Giorgio Madonna 5, Simona Pesce 6, Giulio Strangio 7, Anna Curci 8, Teresa Lopizzo 9, Camilla Gizzi 10

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CONTENT:

Human parechovirus (HPEV) is increasingly being recognized as a potentially severe viral infection in neonates and young infants. HPEV belongs to the family Picornaviridae and is currently divided into 19 genotypes. HPEV-3 is clinically the most important genotype due to its association with severe disease in younger infants. HPEV are an increasingly recognized cause of meningo-encephalitis in young children and causes adverse neurodevelopmental outcomes. We report children who presented with suspected encephalitis who had laboratory confirmed HPEV infection. We describe the key clinical features of this disease and its outcome at discharge and 3 months follow-up.

Clinical records of infants with diagnosis of HPEVmeningoencephalitis were reviewed. Encephalitis was diagnosed as per “International Encephalitis Consortium definition and Brighton criteria”. FilmArray parechovirus molecular testing was used to identify HPEV on CSF. Demographic details, clinical features, medical imaging, laboratory tests, treatment and outcome were recorded.

7 infants (BW3430±808g, GA39.2±2.4w, 6M) were identified. Age upon admission was 18(6-28)d, and length of stay was 11(7-52)d. All infants presented: fever, irritability, erythema or maculopapular rash. 4 infants showed decreased response to external stimuli and disinterest in feeding. HPEV was detected in all infants’ CSF in absence of pleocytosis and with normal protein and glucose levels. All infants received IVIG. Brain MRI was performed at 8±2d. 2 infants showed small altered signal areas; one also showed hyperintense spots on cortex-subcortex region of the left frontal and right parietal-occipital regions. The female infant showed diffuse severely altered signal at 10d and malacic multiple areas at 41d. She had seizures. Neurodevelopmental follow-up at 3m revealed cramped synchronized general movements and poor repertoire in the female and axial hypotonia in one male infant.

According with the literature, the most severe case of HPEV encephalitis occurred in a female infant. Overall, 43% of infants showed MRI alterations. Given the absent CSF pleocytosis and the need for specific testing, HPEV could be a missed cause of encephalopathy while it should be considered in all infants with fever, irritability and rash. Neurodevelopmental follow-up is necessary.

COI: None declared.
ID: 305

TITLE: ANALYZING THE EFFECT OF NEONATAL ANTIBIOTIC TREATMENT IN THE ABSOLUTE NUMBER OF IMMUNE CELL POPULATIONS IN PRETERM INFANTS

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CONTENT:

Preterm infants are highly susceptible to infectious and inflammatory diseases due to the immaturity of their immune and gastrointestinal systems. Neonatal sepsis, necrotizing enterocolitis (NEC) and pneumonia, are common diseases in this population which are treated with antibiotics. Antibiotic treatment has been associated with intestinal microbiome dysbiosis and linked to the increased risk of NEC, sepsis and death in neonates, and allergy, asthma, overweight and obesity in childhood and adulthood. The aim of our study was to analyze the effect of neonatal antibiotic treatment in the absolute number of immune cell populations in preterm infants.

The study included 90 preterm infants equal or less than 32 weeks gestation, untreated or treated with antibiotics during hospitalization in the NICU at the National Institute of Perinatology in Mexico City. Venous peripheral blood was collected at birth, 15 days of life, and discharge, and complete blood counts were performed upon parental written informed consent. Infants were classified as: Control Group (not antibiotic treated), Group A1 (treated once with ampicillin/amikacin), Group A2 (treated once with tazobactam-piperacillin/vancomycin), Group A3 (treated with two or more antibiotic schemes), Group A4 (treated with two or more antibiotic schemes including clarithromycin). Maternal infectious history, and neonatal anthropometric, clinical and laboratory data were analyzed.

Study groups were integrated as follows: control group (n=16), group A1 (n=15), group A2 (n=5), group A3 (n=14), and group A4 (n=40). There were not significant differences in gestational weeks and anthropometric data at birth among study groups, except for a lower weight in group A4 compared to controls. Chorioamnionitis and premature rupture of membranes were more frequent in neonates from groups A3 and A4, respectively. The most frequent clinical diagnoses per group were: group A1 (early-onset sepsis), group A2 (late-onset sepsis and NEC), group A3 (late-onset sepsis, septic shock and NEC), group A4 (early- and late-onset sepsis, and pneumonia caused by atypical pathogens). The absolute number of leukocytes, lymphocytes, monocytes, neutrophils and platelets from birth to discharge were equivalent between untreated and antibiotic-treated preterm infants.

Neonatal antibiotic treatment did not alter the absolute number of leukocytes, lymphocytes, neutrophils, monocytes and platelets in preterm infants suggesting antibiotics do not affect neonatal immune cell compartments at short-term. Nevertheless, in order to confirm these results, detailed analysis of the phenotype and function of T cell, B cell, NK cell and monocyte subpopulations are required.

COI: None declared
ID: 365

TITLE: EPIDEMIOLOGY OF BLOOD CULTURE PROVEN EARLY-ONSET NEONATAL SEPSIS: 8-YEAR EXPERIENCE FROM A UK CENTRE

AUTHORS: Sunitha Vimalasvaran 1
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AFFILIATIONS: 1 & 3 Neonatal Department, West Hertfordshire Hospitals NHS Trust, United Kingdom
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CONTENT:

Neonatal sepsis remains a major cause of mortality, with an estimated 400,000 annual deaths worldwide. The incidence of neonatal sepsis varies in different geographic regions; reflecting differences in resources, maternal and infant risk factors and prevention strategies. It remains one of the most common neonatal diseases, even in high-income countries. We aimed to determine the incidence and etiology of early-onset sepsis (EOS) using positive blood cultures in our centre. We defined EOS as infection occurring <72 hours after birth. We also examined trends of antibiotic treatment episodes in neonates <72 hours old, within the same time period.

This was an 8-year, retrospective single-centre observational cohort study. This study was registered with hospital clinical audit service and conformed to local information governance standards. Epidemiological, clinical and microbiological data from all infants with culture-proven sepsis over an 8-year period (Jan 2011-Dec 2018) was collected. Positive blood cultures, which were deemed to be contaminant, were excluded. Data on antibiotic treatment episodes was extracted from the neonatal electronic patient database. Descriptive statistics were performed on demographic data. Hospital live birth denominators were used to calculate incidence rates (per 1000 live births). Chi-square test was used to assess for statistical significance (p<0.05) of categorical variables.

We identified 47 cases of EOS between 2011 and 2018. GBS was the leading cause (n=34, 0.8/1000 live births) followed by E.Coli (n=9, 0.21/1000 live births). Demographic data is shown in Table 1. Relative to our live birth cohort, the EOS population had significantly higher preterm (p<0.05) and very low birth weights (p<0.05) babies. The highest incidence of EOS was in 2018 (2.8/1000 live births), with a statistically significant increase in trend, p=0.02. There was an unusual rise in incidence of EOS in 2018. E. Coli sepsis was higher in preterm babies (n=5, 44%) compared to term babies (n=5, 13%). Incidence of GBS sepsis is notably rising with 10 cases in 2018, compared to 3 in 2011. Overall mortality rate was 6.4%.

We also report an increase in number of infants treated with antibiotics for suspected EOS (2011: 121/1000 live births versus 2018: 217/1000 live births) during study period.

We report a high burden of neonatal EOS at our centre compared to national average (0.7/1000 live births). GBS and E. coli are the most common causes of EOS in our term and preterm babies, respectively. This data allows us to benchmark against national standards and drive research/quality improvement. There are ongoing efforts at our centre to try sepsis prediction tools such as Kaiser Permanente Sepsis calculator to reduce antibiotic exposure.

IMAGES:

Table 1: Demographic and EOS Incidence Data

COI: None declared
ID: 402

TITLE: PRENATAL ENDOTOXIN EXPOSURE ADVERSELY AFFECTS KIDNEY DEVELOPMENT IN PRETERM PIGS

AUTHORS: Tik Muk1; Ping-Ping Jiang1,2; Allan Stensballe3; Per Torp Sangild1,4,5; Duc Ninh Nguyen1

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CONTENT:

Intrauterine bacterial infection predisposes to preterm birth and is associated with dysregulated development of several organs, including gut, lungs and brain. However, it is unclear if such neonatal organ complications result from immaturity alone, (e.g. reduced gestational age) or from prenatal insults (e.g. inflammation induced by chorioamnionitis, CA). Using preterm pigs as a model for preterm infants, we investigated plasma proteomic responses after preterm birth, with and without exposure to endotoxin. Plasma proteomic profiling was employed to search for unrecognized organ responses to prenatal inflammation, reflected by changes in the composition of plasma proteins.

Preterm pigs were exposed to intra-amniotic endotoxin (LPS, 1 mg/fetus, n=37) or saline (SAL, n=32) three days before preterm delivery by cesarean section at 90% gestation. Blood and organs were collected at birth and after five days of rearing in incubators. Mass spectrometry (MS)-based label-free proteomics was applied to indicate plasma parameters affected for each group at d 1 (n=26-28) and 5 (n=12). mRNA and protein levels of selected genes in tissue or plasma were validated by qPCR, ELISA and Western blot analyses.

Fetal endotoxin induced inflammation (higher amniotic fluid cytokines and immune cell infiltration), together with higher plasma creatinine levels at birth and urinary α1-microglobulin levels at d 5, indicating renal dysfunction. Plasma proteomics also revealed LPS effects on several proteins related to kidney function. Levels of leucine-rich alpha-2-glycoprotein 1 (LRG1) were increased and correlated with creatinine levels, while inhibitor of carbonic anhydrase (ICA) and angiotensin-converting enzyme (ACE) levels decreased. In kidney tissue, the density of MPO-positive cells and expression of genes related to injury and inflammation (KIM-1, NGLA, HIF1A, CASP3, TLR2, TLR4, IL8, LTF, S100A9, LYZ, IFNG, TBET) were increased at birth. MPO cell density and TLR2/TLR4 expression remained elevated until day 5.

Prenatal inflammation after endotoxin exposure induces kidney injury in preterm pigs. Immature epithelial barriers (e.g. lung, gut, skin) may explain that intra-amniotic endotoxin exposure induces both local and systemic (e.g. kidney) effects. Short-term prenatal infections may contribute to acute kidney injury (AKI) at preterm birth and LRG1 may be an early biomarker of AKI in preterm infants.

COI: None declared
ID: 512

TITLE: THE EFFECT OF SEX ON PRETERM INNATE AND ADAPTIVE IMMUNITY

AUTHORS: Matthew McGovern1, Rebecca Finnegan3, Ashanty M. Melo2,4, Ana Moreno-Olivera2,4, Derek G. Doherty2,4, Eleanor J Molloy1,3,5,6

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CONTENT:

Preterm male neonates are at higher risk of sepsis and have poorer outcomes following sepsis episodes than females. Sex differences in innate and adaptive immunity may account for some of the differences in sepsis outcomes which are seen clinically. Our aim was to study sex difference in innate and adaptive immunity between term and preterm infants and examine the immunomodulatory effect of estrogen and progesterone treatment.

Whole blood samples were obtained from 13 preterm infants (4 female, 9 male) and 20 healthy term infants (10 males and 10 females). Granulocytes, monocytes and lymphocyte subsets were enumerated by flow cytometry based on light scattering properties and cell surface markers. Whole blood was treated with endotoxin (LPS; 10ng/mL), 17-β estradiol (E2; 10−8M) and progesterone (10−8 M), alone and in combination. Granulocyte and Monocyte activation was quantified by analysis of CD11b and Toll-like receptor (TLR)-2 expression.

Lymphocyte percentages were similar between preterm and term infants of both sexes. Preterm infants had robust immune responses following LPS stimulation. Preterm female granulocytes and monocytes had lower CD11b expression following LPS stimulation compared to term controls (p<0.05). Hormone treatments did not significantly alter immune cell activity or TLR2 expression.

CD11b was significantly decreased in preterm females compared to term controls. Lymphocyte populations were similar in preterm and term infants of both sexes. These results suggest a sex difference in innate immune function but do not completely account for the difference in clinical outcome between the sexes.

COI: None declared
**ID:** 531  
**TITLE:** TYPE 2 IMMUNITY IS A HALLMARK OF MURINE NEONATAL CARDIOPULMONARY DISEASE  
**AUTHORS:** Christine B Bui 1,2; Arvind Sehgal 2,3; James T Pearson 4,5,6; Anton Maksimenko 7; Ina Rudloff 1,2; Steven X Cho 1,2; Kirstin Elgass 8; Morag Young 9; Alex Veldman 1,2; Philip J Berger 1,2; Marcel F Nold 1,2; Claudia A Nold-Petry 1,2.  
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**CONTENT:**

Bronchopulmonary dysplasia (BPD) is a chronic inflammatory lung disease that affects extremely preterm infants. Pulmonary hypertension secondary to BPD (BPD-PH) is its gravest complication and contributes to significant morbidity and mortality. Due to the multifactorial nature of BPD and BPD-PH, its pathogenesis remains poorly characterised despite considerable research efforts. We discovered that the type 2 immune response plays a role in the development of BPD and BPD-PH. By using STAT6-KO mice, which have limited type 2 immune responses, we employed a clinically relevant murine model of disease to investigate the underlying immune responses driving BPD and BPD-PH.

At day 14 of gestation, pregnant C57BL/6J (WT) and STAT6-KO dams received an i.p. injection of LPS (150 µg/kg) to induce systemic maternal inflammation. Within 24h of birth, WT and STAT6-KO pups were randomised to either continuous hyperoxia (65% O2) or room air (21% O2) as a control. Pulmonary inflammation was characterised by the abundance of cytokines (IL-1β, IL-6, IL-13, IL-33) and chemokines (eotaxin) in lung lysates on postnatal day 5 (P5) by ELISA. Lung structure was assessed by histology. To assess the effects of inflammation and hyperoxia on the pulmonary vasculature at P28, we used echocardiography to measure pulmonary artery pressure and synchrotron micro-CT imaging to visualise pulmonary vasculature remodelling.

Perinatal exposure to inflammation and hyperoxia caused lung tissue injury in WT pups, characterised by fewer (36% reduction) and enlarged alveoli (29% increase) with reduced surface area-to-volume ratio (18% decrease) compared to WT animals reared in room air. The lung parenchymal structure was protected from injury in STAT6-KO pups. Protein abundance of pro-inflammatory mediators was significantly increased in lung lysates of hyperoxia WT pups at P5 but was prevented in STAT6-KO mice. Furthermore, micro-CT imaging revealed substantial changes in pulmonary vascular morphology in hyperoxia-WT mice at P28, as evidenced by 84% fewer small vessels (4-7µm diameter) and 9-fold more large vessels (30-60µm diameter), which were accompanied by PH (TPV/RVET 0.26 for hyperoxia vs 0.32 for controls by echocardiography). The changes in the pulmonary vasculature were abrogated in STAT6-KO mice.

We observed that a deficiency in the type 2 immune response is protective for the lung parenchymal structure and pulmonary vascular remodelling in a murine model of BPD and BPD-PH. Our findings suggest that type 2 immunity plays a major role in the pathogenesis of BPD and BPD-PH and that targeting type 2 key mediators may have a therapeutic benefit.

**COI:** None declared
ID: 562

TITLE: BREASTFED NEONATES SHOW INCREASED IMMUNE TOLERANCE AGAINST MATERNAL ANTIGENS.

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AFFILIATIONS: Neonatal Intensive Care Unit, Birmingham Women’s and Children’s NHS Foundation Trust, Birmingham, UK. Institute of Immunology and Immunotherapy, University of Birmingham, UK.

CONTENT:

During pregnancy, a unique symbiosis must be maintained between the maternal and fetal immune systems to accommodate the fetus. These systems present as immunologically distinct entities to one another and the maternal immune system is known to be suppressed in pregnancy. The neonatal immune response to infection is reduced and significantly contributes to morbidity and mortality worldwide. We hypothesised that immune suppression in pregnancy may be extended to the neonatal immune system in a bidirectional manner.

Our study investigates the interaction and adaptation of the maternal and neonatal immunological systems by analysing T cell responsiveness in the early postnatal period.

20 dyads of mothers and neonates delivered by elective caesarean section at term following an uncomplicated pregnancy were recruited. Maternal peripheral blood samples were taken prior to caesarean section. Cord blood was collected at birth followed by a neonatal peripheral blood sample at three weeks of age. T cells were isolated and mixed lymphocyte reactions (MLRs) were performed over 5 days. MLRs were setup for cord blood responders versus maternal antigens and vice versa, and neonatal responders versus maternal antigens and vice versa. Positive and negative controls were included. Cells were stained for CD3, CD4 and CD8 prior to flow cytometry.

The percentage of proliferating maternal responder cells to cord blood antigens and neonatal antigens show a stable response between birth and 3 weeks for all subsets. Conversely, neonatal responder cells show a decreased response to maternal antigens at 3 weeks in all subsets. This finding is in opposition to our original hypothesis. We therefore considered the influence of feeding on this. Of the 20 neonates, 11 were exclusively breastfed and 4 mixed fed (breastfed with formula top ups). The combined effect in these 15 neonates receiving any breastmilk shows the decreased response in CD3 cells at 3 weeks. However, in the 5 exclusively formula fed there is an increased response at 3 weeks (Figure 1).

Neonates receiving breastmilk show a decreased CD3 response to maternal antigens at 3 weeks of age compared to birth. However, this reduction was not observed in exclusively formula fed neonates. Interestingly, a neonate only needs some breastmilk to show the same response as an exclusively breastfed neonate. This response could be due to on-going antigen load via breastmilk and may reflect persisting immune tolerance towards maternal antigens.

IMAGES:
https://www.eiseverywhere.com/eselectv3/v3/events/351149/submission/files/download?fileID=37b28231c0b2d459d8d8d81d07ab0728-MjJAxOS0wNSM1Y2UyNjyY2YzkxNWMw

Figure 1 - Mixed lymphocyte reactions showing the response of CD3 cord blood/neonatal responders at birth and 3 weeks of age according to the method of feeding.

COI: None declared
**ID:** 709  
**TITLE:** CLINICAL MANIFESTATIONS AND RESISTANCE PATTERNS OF STAPHYLOCOCCUS AUREUS INFECTION IN THE NEONATAL PERIOD  
**AUTHORS:** Maria Tsirigotaki 1, Sofia Maraki 2, Emmanouil Athanasopoulos 1, Eleftheria Hatzidaki 1  
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**CONTENT:**

Staphylococcus aureus (S. aureus) is a common cause of neonatal infections worldwide. MRSA is associated with increased morbidity and mortality, especially in the premature neonates. Aim of this study was to evaluate the clinical manifestations, resistance patterns and incidence of culture proven S. aureus infection in neonates admitted to a tertiary-care neonatal intensive care unit (NICU).

We performed an 11-year retrospective cohort study in neonates admitted at a level III NICU with culture-proven, invasive and non-invasive, methicillin resistant (MRSA) or susceptible (MSSA) S. aureus infection between January 2008 and December 2018. Community-acquired (CA), community-onset healthcare associated (COHA) and hospital-acquired (HA) infection was defined according to CDC criteria. Logistic regression analysis was performed to identify risk factors for MRSA infections in the neonatal period.

A total of 59 clinical isolates of S. aureus were identified (46 CA, 12HA, 1 COHA) among neonates 1 to 30 days old, mean birth weight 3278gr [range 1020-5050gr]. Skin and soft tissue infections were the most common (54/59) while invasive infections were rare (5/59, CNS infection: 1, septicemia: 4). A total of 35.5% (21/59) were MRSA, erythromycin and clindamycin resistance were seen in 27.1% (16/59) and 16.9% (10/59) of isolates respectively. 80.9% of neonates received intravenous antibiotics (vancomycin 31/34, cloxacillin 5/34). The incidence of S.aureus infections increased during the study period from 3.76 per 1000 admissions in 2008-2012 to 19.75 per 1000 in 2014-2018. In logistic regression analysis, there was decreased risk of MRSA in neonates born by caesarian section (OR 0.015-0.902, p 0.03). A 7-fold rise of MSSA was noted from 1.88 to 13.31/1000 in the second half of the study.

The burden of S.aureus infections is considerable in the neonatal period. Rising trends of CA infections were noted along with an increase in methicillin sensitive strains.

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**TITLE:** NEONATAL OUTCOMES OF PREMATURE INFANTS OF WOMEN WITH PRETERM PREMATURE RUPTURE OF THE MEMBRANES

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**CONTENT:**

There is limited and conflicting data about the effect of preterm premature rupture of the membranes (pPROM) on neonatal morbidities in premature infants. The aim of this study was to determine the neonatal morbidities in infants born to mothers with pPROM and to compare it with non-pPROM premature infants.

This retrospective study included 140 premature babies with a maternal history of pPROM and 140 premature babies who had no maternal history of pPROM. Maternal data (age, parity, duration of pPROM, antibiotic usage, duration of hospitalization), neonatal demographics, neonatal morbidities (RDS, PDA, IVH, NEC, BPD) and mortality were all recorded.

The mean gestational age and birth weight of infants were 28.8 ± 1.7 w and 1098 ± 67 grams, respectively. The rates of early sepsis and mechanical ventilation were significantly higher in infants born to mothers with pPROM. The urine/cervical swab culture was found to be positive in 60 (42.8%) mothers with pPROM including Gram negative (n=45), positive (n=10) and fungal organisms (n=7). The mean birth weight and gestational age of infants born to mothers with Gram negative bacteria were significantly lower and the duration of hospitalization, repeated dose surfactant requirement and mortality were significantly higher in these infants compared with Gram positive and fungal positivity (p <0.05).

Although neonatal outcomes of infants born to pPROM and non-pPROM mothers seem to be similar, maternal Gram negative infections caused preterm labor with lower gestational age and birth weight. These infants had higher surfactant requirement and mortality. Therefore, knowledge of maternal organism may be helpful for clinicians to determine the prognosis in infants born to mothers with pPROM.

**COI:** None declared