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Selected Abstracts of the 9th International Workshop on Neonatology

LEARNED LESSONS, CHANGING PRACTICE AND CUTTING-EDGE RESEARCH

CAGLIARI (ITALY) • OCTOBER 23RD-26TH 2013

The Workshop has been organized on behalf of Union of European Neonatal and Perinatal Societies, Union of Mediterranean Neonatal Societies, Italian Society of Neonatology, UNICEF, and under the High Patronage of the President of the Italian Republic.

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ABS 1

AETIOLOGY AND TYPE OF REFERENCE HOSPITAL FOR NEONATAL TRANSPORT IN GREECE DURING 2012

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OBJECTIVE

To record and analyze the main reasons for neonatal transport (NS) and admission to Neonatal Intensive Care Units (NICU) in tertiary hospitals, in Athens Greece, over a period of one year, as well as the type of reference hospital (with or without NICU).

MATERIALS AND METHODS

According to the Hellenic National Centre of Emergency Care (HNCEC), 742 NS were performed in 2012. Transports of neonates scheduled for a consultation (radiological, cardiological) were not included. Analysis was performed using SPSS-17.

RESULTS

742 NS were performed in 2012 The ratio male:female was 435(58.7%):307(41.3%). Mean gestational age was 35.3 ± 3.6 weeks (mean ± SD) and mean birth weight was 2,521 ± 879 g (mean ± SD). 667 neonates (90%) were transported during the 1st week of life, while 554 neonates (74.7%) on the 1st day of life. 440 neonates were transported by the flying squad of the HNCEC from hospitals in the region of Attica and comprised 59.3% of the total number of neonatal transports. Out of 440 neonates, 70 (9.4%) and 5 (0.7%) were born in private maternity hospitals with and without NICU respectively, while 218 (29.2%) and 148 (19.9%) in maternity hospitals of the public sector with and without NICU respectively. 171 neonates (23%) were transported from regional hospitals without neonatal transport unit and 131 neonates (17.7%) were picked-up from the air transport unit, especially from hospitals without NICU (107 neonates).

Concerning the aetiology for transport, respiratory distress was the main reason (57.1%), followed by prematurity (35.4%), no availability of cot in the NICU (18.6%), congenital heart disease (11.2%), gastrointestinal tract congenital defects and necrotizing enterocolitis (4.7% and 1.6% respectively), sepsis (3.9%), feeding disorders (2.8%), hypoglycemia (2.4%) and jaundice (2%).

CONCLUSIONS

NS is performed at a high percentage in Greece. As the majority of NS comes from public maternity hospitals with or without NICU, staffing with specialized personnel and increase in beds would lead to NS reduction.

ABS 2

CHANGES IN NEONATAL OUTCOMES OF VERY LOW BIRTH WEIGHT INFANTS IN HOSPITAL OF LITHUANIAN UNIVERSITY OF HEALTH SCIENCES

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OBJECTIVE

To compare the survival and morbidity of very low birth weight (VLBW) infants born in two time periods: 2003-2005 and 2010-2012.

METHODS

All VLBW infants (birth weight ≤ 1,500 and gestational age (GA) ≤ 32 weeks) admitted to a single level III unit were included. Perinatal and neonatal data were collected prospectively from birth until discharge home or death. In each time period two groups of GA infants were analyzed: extremely preterm 22-27 weeks GA and very preterm 28-32 weeks GA. Newborns with lethal congenital malformations were excluded.

RESULTS

Similar number of VLBW infants were admitted for care (2003-2005, n = 326 and 2010-2012, n = 331), with the same proportion of extremely preterm infants (2003-2005, n = 155 and 2010-2012, n = 150). Overall survival to discharge home increased from 73% in 2003-2005 to 87% in 2010-2012, including a higher proportion of extremely preterm survivors in 2010-2012 (76% v 53.5% respectively; $p < 0.01$). The 2003-2005 cohort had lower proportion of cesarean sections (33% v

40.5% respectively; p < 0.05) and use of antenatal steroids (60% v 82.5% respectively; p < 0.01). The incidence of morbidities, including severe/moderate bronchopulmonary dysplasia (6.3% v 2.8% respectively, p < 0.05), retinopathy of prematurity requiring treatment (4.2% v 2.8% respectively, p = 0.2), intracerebral and intraventricular hemorrhage grade III (10.9% v 5.6% respectively, p < 0.05), cystic periventricular leukomalacia (8% v 13.6% respectively, p = 0.4) was lower in 2010-2012.

CONCLUSIONS

Improvements in perinatal and neonatal care led to an increase survival and to a decrease of neonatal morbidities.

ABS 3

AUTOIMMUNE LIVER DISEASE IN CHILDHOOD

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Autoimmune liver disease (AILD) represents a spectrum of liver diseases characterized by a likely autoimmune pathogenesis, target cells being represented by hepatocytes (hepatitis) and bile duct cells (cholangitis). Multiple pathological entities may be included within the AILD spectrum: autoimmune hepatitis (AIH), primary sclerosing cholangitis (PSC), primary biliary cirrhosis (PBC), autoimmune cholangitis (AIC), and IgG4-related sclerosing cholangitis (IgG4-RSC). In pediatric clinical practice, the borders between these entities are only rarely sharp [1]. Overlap syndromes, with clinical, serological and pathological markers of different diseases including AIH/AIC, and AIH/PSC also called autoimmune sclerosing cholangitis (ASC) are frequently observed, often causing relevant diagnostic and therapeutic problems. In childhood, about 25-50% of patients presenting with AIH show insurgence of ASC. In these complex cases, needle liver biopsy may give relevant data, that may be extremely useful for reaching a precise differential diagnosis in the AILD spectrum. ASC is characterized, at tissue level, by the finding of a onion-like periductal fibrous obliterative cholangitis, affecting both small intrahepatic ducts as well as large peri-hylar and extrahepatic bile ducts. In about 25% of cases, pediatric patients affected by ASC are also affected by idiopathic bowel disease, more frequently ulceratice cholitis. In recent years, a new entity, IgG4-RSC has been reported even in children [2]. This disease is frequently associated with autoimmune pancreatitis and acalculous cholecystitis. IgG4-RSC should be considered a multi-organ disease, affecting thyroid, salivary glands, lymph nodes, and less frequently many of the organs, in which inflammatory pseudotumors may arise. The typical pathological findings in liver biopsy from patients affected by IgG4-RSC are: strong and diffuse plasma cell portal and periportal infiltration, with predominance at immunohistochemistry of IgG4-positive plasma cells; obliterative phlebitis affecting the small branches of the portal vein; periportal inflammatory nodules (**Fig. 1**); biliary interface activity, with proliferating biliary cells leading to disruption of the periportal limiting plate, which may be easily identified by cytokeratin 7 immunostaining. The absence of periductal onion-like fibrous obliterative cholangitis, typical of PSC, of portal epithelioid granulomas surrounding damaged bile ducts, typical of PBC, and of biliary tombstones, typical of ductopenia in PSC and PBC, may be useful in confirming the diagnosis of IgG4-RSC. The finding of segmentary strictures in the distal third of the common bile duct at magnetic resonance cholangiography, and the absence of the beaded and pruned-tree appearance typical of PSC, may confirm the histological diagnosis of IgG4-RSC (**Fig. 2**). In conclusion, in the differential diagnosis of autoimmune liver disease occurring in pediatric patients, liver biopsy may play a relevant role, by evidencing the presence of some peculiar morphological and immunohistochemical features which are characteristic, and sometimes specific, of each single entity in the spectrum of pediatric AILD. The high frequency in children affected by AILD of overlap syndromes, clearly increases the diagnostic value of liver biopsy in the differential diagnosis between AIH and the different types of autoimmune cholangities, liver biopsy interpretation being able,

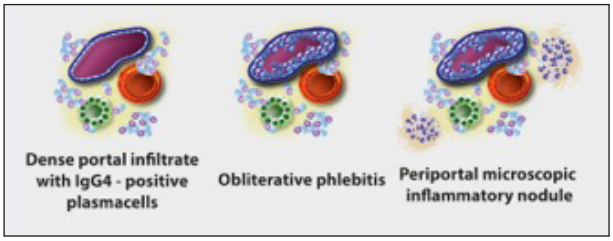

Figure 1. IgG4-related sclerosing cholangitis.

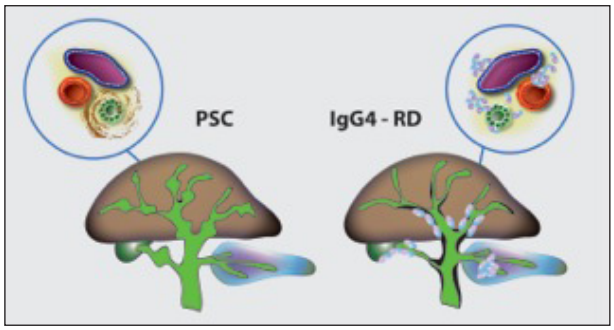

Figure 2. Difference between primary sclerosing cholangitis and IgG4-related sclerosing cholangitis.

in these complex cases, of revealing that both hepatocytes and bile duct cells represent the target of the autoimmune pathological process.

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ABS 4

LACTOFERRIN ATTENUATES INTESTINAL INJURY AFTHER PERINATAL HYPOXIA AND HYPOTHERMIA

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INTRODUCTION

Several biological effects (anti-microbial, anti-inflammatory and proinflammatory, antiapoptotic, promytogenic, etc.) are attributed to lactoferrin (LF). Those effects are expressed through various mechanisms of action. Protective effects of LF on hypoxia/reperfusion injury are assessed only in a few recent studies.

AIM

The objective of this study was to investigate whether oral administration of LF could attenuate intestinal injury induced by perinatal hypoxia and global hypothermia.

MATERIALS AND METHODS

Experimental animal population encompassed adult females and newborn pups of Wistar rats. The uterus was removed from the female rats by caesarean section on the last day of gestation. Perinatal asphyxia was induced by immersing the uterus (still containing the pups) into the water (38°C) during a period of 15 min. After birth pups were exposed to global hypothermia for 1 h. Then, the pups were randomly distributed into two groups of 10 cubs: LG – the pups that orally received LF during 7 days (20 mg/day), KG-L – control group; the pups that orally received normal saline during 7 days. On the 7th day of life the rats were sacrificed and macroscopic examination of the bowels and pathohistological analyses of tissue samples have been performed. Samples for microscopic analysis were taken from the distal part of the ileum (the last 2 cm proximal to the ileocecal valve). Three tissue samples were taken from each animal. Mucosal injury was assessed and graded by pathologists, in a blinded manner. Mucosal injury was quantified using the scale (mucosal injury score) previously described by Chiu et al. [1]. To assess and compare the severity of intestinal damage between animals, we used absolute injury score – defined as the highest value of mucosal injury score among three tissue samples taken from the same animal.

RESULTS

In LG group, discoloration of the intestine was observed in 20% of animals. In the KG-L group intestinal discoloration was present in 80% of animals. The incidence of intestinal discoloration was lower in LG group comparing with KG-L, and that difference was highly statistically significant ($p < 0.01$). Bleeding, intestinal distension or stenosis were not observed in any animal.

The average value of mucosal injury score in the LG group was 1.03. The average value of mucosal injury score in the KG-L group was 2.57. The difference of values of mucosal injury scores between animals in LG and KG-L groups was statistically significant ($p < 0.05$). The distribution of the values of mucosal injury scores in the groups is shown in **Fig. 1**.

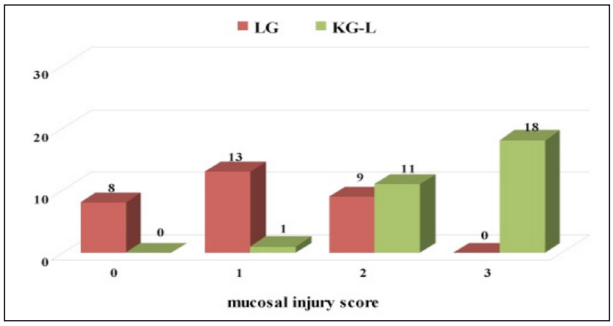

Figure 1. The distribution of the values of mucosal injury scores.

None of the animals in the LG group had absolute injury score corresponding with grade 0. Half of the animals in the LG group had absolute injury score corresponding to grade 1, and the other half of the animals had an absolute injury score corresponding with grade 2. The highest value of the absolute injury score in the LG group was 2. In the KG-L group, there were no animals with normal histology findings in all three tissue specimens. In this group, only one animal (10%) had absolute injury score corresponding to grade 2 and that was the lowest value of this score in the KG-L group. Total of 90% of the animals in this group had an absolute injury score corresponding to grade 3 (severe damage with villous degeneration). Statistical analysis of absolute injury scores in LG and KG-L groups showed statistical significance ($p < 0.05$). The distribution of absolute injury scores between the groups is shown in **Fig. 2**.

DISCUSSION

In animals that received LF, macroscopic changes were less frequentely observed. Also, values of mucosal injury scores and absolute injury scores were significantly lower in the LG group, indicating less severe degree of intestinal damage. The results of our study showed that intestinal injury induced by perinatal hypoxia and hypothermia was significantly attenuated in animals that were supplemented with oral LF.

LF exerts multiple effects on cells. LF may accelerate apoptosis of cells that are, in some way, previously damaged or modified. For example, LF can induce apoptosis and inhibit the growth of altered malignant cells [2]. On the other hand, LF may interference with the processes of DNA transcription and thus, may stimulate proliferation and suppress proapoptotic processes in healthy cells, like it has been shown on enterocytes [3]. This effect is dose-dependent. LF stimulates proliferation and migration of functional and healthy cells, as demonstrated on keratinocytes of skin and cornea [4].

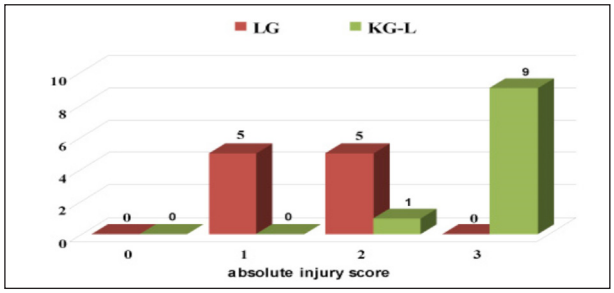

Figure 2. The distribution of the values of absolute injury scores.

Presumably, LF achieves its protective effects coordinating the processes that lead to apoptosis, and at the same time, processes that stimulate proliferation and migration of enterocytes, thus favouring efficient and prompt repair of the intestinal lining. Positive effects of LF on damaged intestinal mucosa may be contributed to other mechanisms: LF inhibits the production of proinflammatory cytokines such as interferon-gamma, tumor necrosis factor-alpha (TNF alpha) and interleukin-1 beta (IL-1SS), interleukin 2 (IL-2) and interleukin-6 (IL-6) [5, 6]. Also, in the intestinal lumen, LF binds to a large number of microorganisms or their toxic products, directly regulating the composition of the intestinal microflora. Acting as an antioxidant – directly, and binding to toxic proinflammatory microbial products (eg lipolysaccharides) and their receptors – indirectly, LF controls and limits over extensive inflammation of the intestinal mucosa [7, 8]. With all this features, LF creates more favorable environment and provides less exposure of injured intestinal mucosa to extra stress at a time when such help is most needed, ie. when all of their metabolic resources need to be focused on the fast repair of damage caused by hypoxia.

CONCLUSION

Lactoferrin has protective effect on intestinal mucosa and attenuates intestinal injury induced by hypoxia and hypothermia in newborn rats.

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ABS 5

OSTEOPENIA IN PREMATURITY: CASE REPORT

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INTRODUCTION

Neonatal osteopenia is a well-known condition that predisposes to pathological fractures in premature newborns. Mineral deficiency leading to abnormal bone formation is the commonest cause of neonatal osteopenia and preterm infants are at increased risk of developing this condition. Other risk factors of neonatal osteopenia such as prolonged parenteral nutrition, chronic diseases such as bronchopulmonary dysplasia and short bowel syndrome have also been implicated. In neonates, especially those born prematurely or of extremely low birth weight (ELBW), osteopenia is a common cause of pathological fractures.

CASE DESCRIPTION

A female neonate was born at 24 weeks of gestation and birth weighed 646 g. She was born vaginally, by breech delivery. Apgar scores were 3 at the 1st minute and 6 at the 5th minute. She was intubated in delivery room and transported to NICU. Apart from preterm labor, the mother had no symptoms or signs of infection. The infant's initial clinical course was complicated by respiratory distress syndrome, treated with surfactant, jaundice and patent ductus arteriosus. At third day ibuprofen was started, but the duct remained open and 2 weeks after birth was ligated. Suppuration of operative wound was noted on 32 day of life and vancomycin was started. Parenteral nutrition (PN) was started on day 1 and suspended after 6 days. Oral feeding was introduced in the second day of life. She required ventilatory support until day 26 and CPAP for 40 days. Because of hypocalcemia (Ca^{2+} 0.78-1.07 mmol/l) calcium gluconate was started at day 9 and was continued for 2 weeks together with furosemide. At the age of 47 days fracture of the right humerus was diagnosed on X-ray and was immobilized. Basic serum biochemical tests were carried out, in which serum calcium (Ca: 2.39 mmol/l), ionized calcium (Ca^{2+}: 1.36 mmol/l), phosphorus (P: 1.64 mmol/l) and alkaline phosphatase (ALP: 218 IU/L) activity were measured. The patient in NICU was treated for 68 days. He was discharged home on day 107 with weight of 2,304 g.

DISCUSSION

Owing to the lack of a sufficiently sensitive diagnostic test and the fact that the disease may disclose different biochemical abnormalities, diagnosis of osteopenia in premature infants is difficult.

ELBW infants, who were treated with corticosteroids, diuretics or received long term parenteral nutrition are at high risk of bone fractures and they should be monitored for bone disease.

ABS 6

NEONATAL BARTTER SYNDROME: CASE REPORT OF A VERY UNUSUAL ENTITY

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INTRODUCTION

Bartter syndrome is a rare genetic disorder affecting several ion channel in the renal tubule. The neonatal type of the disorder is more unusual and should be suspected during the antenatal period, when hydramnios and electrolyte disorders in the amniotic fluid occur.

CASE DESCRIPTION

We report on a preterm infant with intrauterine growth restriction whose gestation was complicated by hydramnios. The infant was born prematurely at 31+3 weeks of gestation and since her first days of life she suffered marked polyuria and electrolyte disorders such as hypokalemia, hyponatremia, hypochloremia and hypocalcemia with excessive loss of the same elements in the urine. The infant gradually lost weight and came to nonoliguric acute renal failure exacerbated by a concurrent infection.

The history of hydramnios, the electrolyte disorders and the persisting polyuria put strongly the suspicion of Bartter syndrome. This diagnosis was confirmed by the high plasma levels of renin (74,220 pg/ml) and aldosterone (> 150 ng/dl) with normal blood pressure. Metabolic alkalosis did not appear until fluid equilibrium and renal function were restored.

Despite the early suspicion and diagnosis, treatment with indomethacin was postponed for a few weeks until renal function tests were normalized. The first sign of response to treatment was the acute remission of polyuria. At that time nephrocalcinosis had already occurred so hydrochlorothiazide was added to treatment.

DISCUSSION

We suggest that, although treatment with indomethacin interferes with the pathophysiologic pathway of Bartter syndrome, it cannot reverse all of the affected functions, so the management of these patients remains a complicated task.

ABS 7

PLACENTAL GROWTH FACTOR (PLGF) AND PLACENTAL FUNCTION

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INTRODUCTION

Placental Growth Factor (PlGF) is an angiogenic protein secreted by the placenta. Low levels of PlGF are a marker of preeclampsia and reduced placental function. The study aimed to confirm whether the plasma PlGF levels in pregnant women are related with the placental function and morphology. A second end point of the study was to evaluate the relationship between PlGF levels with the timing of childbirth and the newborn's weight.

MATERIALS AND METHODS

219 plasma samples of pregnant women between the 20th and 35th week of gestation were evaluated. Symptoms of preeclampsia, Doppler velocimetry of uterine artery and umbilical artery and the timing of delivery were evaluated. Later the delivery infant weight at the birth and the macroscopic evaluation of the placenta were also performed. Several placentas were sent to Pathology Department for hystologic examination. Statistical analysis used is chi-square test.

RESULTS

In the study group, the percentage of preterm births, abnormal flow meters, preeclampsia, and low birth weight infants was significantly higher (p-value < 0.001) than in the control group. In the control group the percentage of macroscopically and microscopically normal placentas was significantly higher (p-value < 0.0002) than in the study group.

CONCLUSIONS

These preliminary data suggest that PlGF is a good indicator of placental function. PlGF values below the cut-off for gestational age is related with histological alterations of the placenta, commonly reported in chronic hypoxia. In addition, the results of the study suggest that low PlGF levels are a marker of a earlier timing of delivery and low newborn weight at the birth.

ABS 8

NEONATAL ECMO: INITIAL EXPERIENCE OF HOSPITAL DE SÃO JOÃO

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The purpose of this series is to report the initial ECMO experience of the Neonatal Intensive Care Unit of Hospital de São João. The first three clinical cases are reported.

CASE REPORT 1

A 39 weeks gestational age girl with severe lung hypoplasia secondary to a bilateral congenital diaphragmatic hernia underwent a 16 days, unsuccessful, VA-ECMO run.

CASE REPORT 2

A 39 weeks gestational age girl with a right congenital diaphragmatic hernia with liver up was treated on VA-ECMO for respiratory failure. The surgical repair was done with protesis on day four of life, and weaning from ECMO was sucssessfull in day seven of life. On day eight of life, she developed a worsening clinical course marked by respiratory failure and pulmonary hypertension. A 3D chest tomography revealed a tracheal stenosis. The child deceased and the autopsy revealed an anel of the left pulmonary artery as the cause of a tracheal stenosis.

CASE REPORT 3

On day 61 of life, a 34 weeks gestational age boy was transferred to Hospital de São João NICU,

because of *B. pertussis* pneumonia with severe pulmonary hypertension, shock, hyperleukocytosis and seizures. He went an eight days VA-ECMO run, successfully weaned, although with neurological damage secondary to *pertussis* encephalopathy, hypoxemia and shock.

CONCLUSIONS

Our small series has shown that ECMO is an effective technique for respiratory and cardiovascular support. A correct evaluation of fetuses with congenital diaphragmatic hernia, with an as appropriate as possible assessment of the degree of pulmonary hypoplasia and associated congenital anomalies is mandatory before starting ECMO.

ABS 9

GCMS-BASED METABOLOMICS ANALYSIS OF URINES IN HYPOXIC NEONATAL PIGLETS

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OBJECTIVE

The neonatal hypoxia is the major cause of mortality or morbidity in infants. Resuscitation therapy with pure oxygen, hyperoxia, following the hypoxic condition, can generate a condition of oxidative stress and damage to several organs. In this work, the metabolomic approach has been used to characterize the metabolic profiles of some newborn piglets submitted to induced hypoxia and resuscitation.

MATERIALS AND METHODS

Urine samples of pigs in hypoxia and subsequently exposed to resuscitation with 100% oxygen have been analyzed by mass spectrometry. For the present study, 10 male newborn pigs (Landrace/Large, ELPEN of Research and Experimental Centre, Athens, Greece) with a weight in the range between 2.3 and 3.8 kg were analysed at room air and after 100% oxygen resuscitation. All piglets were obtained from the same breeder (N. Validakis, Koropi, Greece) on the day of experimentation. The experimental protocol was approved by the General Directorate of Veterinary Services (permit No. 404/21-04-09) according to Greek Legislation regarding scientific and experimental procedures (Presidential Decree 160/1991, in compliance with the Directive 86/609/EEC). The procedures were as previously described [1].

RESULTS

This analysis provided the identification of the metabolites influenced by the basic mechanisms of hypoxia and resuscitation with pure oxygen treatment: a panel of six metabolites including lactate, aminomalonate, glucose, ribitole, ribose and erythropentose.

CONCLUSION

The GCMS-based metabolomic technique revealed a significant difference between the two metabolic state before and after hypoxia-reoxygenation with pure O_2. The clear division and the peculiarities of metabolite networks lead us to conclude that the metabolic damage is high [2].

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ABS 10

COMBINED ORAL SILDENAFIL AND BOSENTAN IN A EX-PRETERM INFANT WITH BRONCHOPULMONARY DYSPLASIA, SEPSIS AND SEVERE PULMONARY ARTERIAL HYPERTENSION REFRACTORY TO INHALED NITRIC OXIDE

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PURPOSE

Novel vasodilatator agents (i.e., Sildenafil and Bosentan) have been used to increase the overall efficacy of therapeutic interventions in pulmonary arterial hypertension.

METHODS

We report a case of a 5-month-old preterm infant with severe bronchopulmonary dysplasia, who developed sepsis from *S. Maltophilia* with

pulmonary involvement and severe pulmonary arterial hypertension refractory to inhaled nitric oxide and maximal ventilatory support. She was treated with either antibiotic and a combination of oral Sildenafil and Bosentan therapy.

RESULTS

Forty-eight hours after starting Sildenafil plus Bosentan, there was an improvement in her clinical condition, with a reduction in the oxygen requirement and a normalization of sepsis signs. An echocardiogram showed a substantial reduction in pulmonary hypertension. No complications or adverse effects related to long term Sildenafil or Bosentan therapy were noted.

CONCLUSION

This case illustrates the safety and efficacy of a combination treatment with oral Sildenafil and Bosentan in a infants with bronchopulmonary dysplasia and severe pulmonary hypertension refractory to inhaled nitric oxide.

ABS 11

THE IMPORTANCE OF THE NATIONAL ACADEMY OF SCIENCES, LETTERS AND ARTS OF MODENA FOR THE HISTORY OF PEDIATRICS

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The National Academy of Sciences, Letters and Arts of Modena is a cultural institution that is part of the National Academies as it was an institution of a sovereign state pre-unification. Its foundation dates back to about 1680 when it was the capital of the Duchy of Modena, Este [1].

In 1792 he founded the library, in the history of Pediatrics, which was of vital importance due to few publications at the time.

The collection is made according to the statutes of the Academy because each member must deliver a copy of its publications. Important pediatricians were members of the Academy and therefore submitted their works in the library. These are the three directors of the pediatric clinic of the University of Modena that worked from 1907 to 1951. They are: Riccardo Simonini (1865-1942), an ordinary member of the Academy since 1925, Giovanni De Toni (1895-1973), partner since 1940, honorary since 1951; Arrigo Colarizzi (1903-1974), full member since 1947. After Colarizzi, who left the direction of the clinic in 1951, among the successive directors, only Enrico Cheli (1916-1995) was a member of the Academy (ordinary member since 1990).

There is a fifth pediatrician who became a full member since 1952, Marco Bergamini (1892-1977), who was the deputy director volunteer at the pediatric clinic of the University of Modena, Parma, and Bari and then was director of the scientific journal *Il Lattante*. Bergamini produced about 150 publications and many are available only at the library of the Academy.

The library of the Academy is therefore an important source of bibliographic documentation, useful for the study of the history of Pediatrics.

It is also a demonstration of cultural resources in Italy represented by the institutions, often secular. They are a fundamental source of information as they have been able to preserve works and documents, ensuring cultural continuity.

In our case the pediatricians of the past help to serve as a model of though for today's Italian pediatricians.

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ABS 12

ALTERNATIVE USE OF PARACETAMOL IN PDA CLOSURE: THREE CASE REPORTS

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INTRODUCTION

PDA (patent ductus arteriosus) often complicates the clinical course of preterm infants, increasing the incidence's risk of other phathologies as chronic lung disease (CLD), necrotizing enterocolitis (NEC), and intraventricular hemorrhage (IVH) [1].

Indomethacin (a cyclo-oxygenase inhibitor) has been the first and most widely used drug in the therapy of PDA [2]. Its adverse effects, mainly related to the vasoconstrictor effect due to inhibition of prostaglandin synthesis, include transient renal failure [3], gastrointestinal

bleeding and perforation [4]; a reduced brain flow is associated [1]. Ibuprofen, a more recent cyclo-oxygenase inhibitor, is as effective as indomethacin in closing the ductus and has fewer renal sides effects [5].

There are also contra-indications for ibuprofen or indomethacin administration, that include thrombocytopenia with intracranical haemorrage, renal failure, necrotizing enterocolitis, coadaministration of corticosteroid (risk of intestinal perforation) or hyperbilirubinemia (competitive binding to albumin) [6-10].

The need for alternative medical treatments for PDA closure in preterm neonates is then urgent. In these last years, reports of an association between paracetamol exposure and PDA closure in a limited number of preterm neonates have been published. However, causality cannot be taken for granted because a link between the current knowledge of the clinical pharmacology of paracetamol and (patho)physiology of ductal closure is not known. In contrast to non-selective cyclo-oxygenase inhibitors, paracetamol has limited effects at peripheral sites, is a poor antithrombotic and anti-inflammatory drug and exerts its effects primarily within the central nervous system. Although paracetamol appears an effective and safe analgesic in term and near term neonates, its effectiveness and safety for PDA closure are uncertain because this drug is administered in high doses and a limited number of observations in this specific subpopulation have been reported so far. Prospective comparative trials are reasonable and are urgently needed to establish both the effectiveness and safety of paracetamol when used for this indication [11].

OBJECTIVE

We propose our experience of oral paracetamol therapy in 3 preterm infants with hemodynamically significant PDA (hsPDA), of which 2 had a intracranial haemorrhage. This report describes the effect and the results of this therapy.

The characteristics of the three newborns are showed in **Tab. 1**. They were treated with oral paracetamol (15 mg/kg every 6 h) for a period of 7 days. As said before, the all three patient had a hsPDA. In the first two patients we used paracetamol because both had a prior IVH, i.e. a contraindication for the use of ibuprofen. The third patient had not specific contraindications, but we decided for paracetamol as first choice drug for its less sides effects. We attempted to obtain a follow-up echocardiogram every two days and we stopped therapy when the ductus became hemodinamically insignificant or alternative we decided to change drug and start therapy with ibuprofen if the ductus was still hemodinacally significant.

In patients A and B we obtained a good result: after paracetamol therapy the ductus was still patent, but without any hemodinamically significance.

In patient C the ductus maintained its hemodinamically significance and we started ibuprofen after few days from the end of paracetamol administration.

No sides effects of paracetamol therapy were noticed in any of the three preterm babies.

CONCLUSION

In our opinion is worthwhile the choice of paracetamol as first drug in the therapy of PDA, when a contraindication for ibuprofen use is present.

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Table 1.

Infant	Sex	GA (w)	Birthweight (g)	Race	Age at diagnosis (d)	Age Paracetamol begun (d)	Current controindications to Ibuprofen	Duration therapy (d)
Infant A	F	25	770	Caucasian	4	8	IVH	6
Infant B	M	28	1,280	Caucasian	2	3	IVH	7
Infant C	M	25 + 4 d	900	African	2	11	NONE	8

W: weeks; d: days.

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ABS 13

MALES IN SARDINIA ARE THE HEALTHIEST OF ITALY

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ITALIAN DATA

In Italy 6% more males are born than females. The distribution of infants in Italy is fairly constant, 106 males compared to 100 females. At 43 years the number of males and females are equal, suggesting earlier onset of death in males (2009-2011) [1].

Overall, males of Southern Italy are more fragile, in fact, equality is reached early, unlike in North Italy where the survival of males is higher and equality is reached in late.

The first provinces that reach early parity (late twenties) are Palermo and Pistoia (24 years old), Lecce (25), Naples, Caserta and Catanzaro (27), Siena (28), Catania and Caltanissetta (29 years old).

SARDINIAN DATA

Data on the eight provinces of Sardinia have been analyzed and it is shown that a male Sardinian is among the most resistant in Italy. Male Sardinians live longer and the number of deaths over the years is much lower than the overall Italian one. Only two provinces can be found in the national average, Cagliari (where the overtaking of females occurs at 42-43 years) and Sassari.

Equality between males and females is reached in Ogliastra province at 53 years of age, while it is surprising that the other five provinces in Sardinia are among the top ten in which the males live longer in Italy. The record in Oristano along with Isernia, is reached at 66 years of age and the first place is ex aequo. The second one has the province of Medio Campidano (65 years), the third Cuneo (64), the fourth Olbia-Tempio and Carbonia-Iglesias together in Trento (63), the fifth Nuoro and Aosta, where equality is reached at age 62.

CONCLUSIONS

Research shows that despite the special anthropological genetics and exposure there is often a kinship, this additional risk factor, that affects females more than males. The phenomenon will be further studied in depth.

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ABS 14

RENAL PELVIS PERFORATION: A RARE COMPLICATION OF LONG LINE IN A PREMATURE INFANT

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INTRODUCTION

Percutaneous intravenous central catheters are commonly used in neonatal practice, however complications such as extravasation of the infusate into pericardial, pleural, and peritoneal cavities, have been described. The perforation of renal pelvis is a very rare complication, previously reported in few cases of neonates with abdominal malformation.

CASE REPORT

We report the perforation of percutaneous intravenous central catheters (PICC) into the right renal pelvis in a premature infant without malformations. Despite positioning of PICC in the inferior vena cava is considered safe, serious and insidious complications can occur. The effusion of parenteral nutrition in the renal pelvis with the appearance of milky urine is an extremely rare occurrence.

CONCLUSION

To our knowledge, this is the first report of renal pelvis perforation caused by PICC in premature infant without malformations.

ABS 15

THE CHAIR OF CHILDCARE IN FLORENCE WAS ESTABLISHED BY THE SOVEREIGN MILITARY ORDER OF MALTA

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Assistance to the poor, the sick, the weak, and defenseless is part of the specific tasks of the Sovereign Military Order of Malta (SMOM) as stated in His motto: *tuitio fidei et obsequium pauperum*. The charitable activity is managed by the Association of Italian Knights of the Sovereign Military Order of Malta (ACISMOM). During the 1960's the field of neonatology development was entrusted to the SMOM, through the ACISMOM, whose initiatives have enabled a fundamental development of neonatology. In our study, we reported the establishment of the chair of child welfare at the University of Rome, but in demonstration of the continuity of the SMOM for neonatology there is also the chair of the establishment of childcare University of Florence [1]. On October 29, 1968 at 11:30 in a hall of the refectory of the University, in St. Mark's Square, an agreement was stipulated between the University of Florence, represented by Vice Rector Carlo Alberto Smokestacks and ACISMOM, represented by the Deputy Commissioner of 'Association, Armando Morini, for the establishment of a post of professor of the role of childcare at the faculty of medicine and surgery. The decree was published in the Official Gazette of the Italian Republic n° 259 of 11.10.1969 p. 6427-8. A song reiterates the commitment of the SMOM to protect children, "that the parties have determined to be necessary for the establishment of this Chair, for his decisive importance for study and to enhance the methods of protection of the child during its development and particularly to give a real boost to the development and in particularly to give a real boost to the study of congenital diseases, metabolic, and those acquired". The chair was given to Lelio Nassi (1911-1985) who held it until 1981: he is known for strengthening neonatal intensive care.

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ABS 16

NURSE LED CLINIC: WELLBEING FOR MOTHER AND SON

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BACKGROUND

Mother's caring for her baby and breastfeeding are to be understood as a harmonious communication. Breastfeeding promotes the so-called dialogue of glances, a non-verbal language which is divided into moments that lead to the formation of the first mental structures of the newborn.

Breastfeeding is a source of well-being for both mother and the child concerned the physiological and perfect nourishment for the baby and a social and psychological aspect for themselves and for their little ones.

OBJECTIVES

The Nurse Led Clinic was born to provide continuity of care after discharge from the nursery with the main objective to promote breastfeeding (exclusive) according to the guidelines issued by WHO/UNICEF.

Continuity of care, particularly oriented to support first-time mothers in caring and for management of the physiological newborn.

The objectives of the ambulatory nursing infant are:

- support for exclusive breastfeeding;
- support of the mother-infant-father;
- information: health education, childcare;
- a moment of transition up to take charge of the family pediatrician;
- to promote parent-infant contact through the teaching of infant massage.

METHODS

The satisfaction questionnaires on the promotion of breastfeeding, offered to mothers during childbirth in the hospital have suggested the idea of activating the surgery neonatal nursing.

The counseling nurses: is the tool used by the operator with the order to seize any doubts and difficulties experienced by parents in the first

few days after discharge, besides, any maternal discomfort by supporting and safeguarding the mother in all the new relational aspects that characterize the first sensitive period after birth. The father is always involved in the interview.

The self-report questionnaire: "Postnatal Attachment Inventory" (adapted form of the "Prenatal Attachment Inventory").

The questionnaire aims to investigate thoughts, emotions, feelings and situations that mothers may have felt or experienced in the first period of post-partum.

RESULTS

The data concerning the mode of feeding (**Tab. 1**) were collected during the meeting in the clinic 4-5 days after hospital discharge.

The predominant mode of breastfeeding is a trend that after the meeting evolves very frequently in exclusive breastfeeding.

Postnatal Attachment Inventory Responses are on a Likert scale from 1 to 4. The sum of individual items may be between a minimum score of 20 and a maximum score of 80, the higher the score, the greater will be the involvement in maternal attachment bond with her child (**Fig. 1** and **Fig. 2**).

Item 3: "I like to see the baby moving".
Item 5: "I like other people touching my baby".
Item 6: "I know that the child is affected by the things I do".
Item 9: "I love watching him when he sleeps".
Item 11: "I buy/do things for the baby".
Item 13: "I try to imagine what the child is doing when I'm gone".
Item 14: "I like to be in his company".
Item 15: "I dream the child".
Item 16: "I know why my baby is crying".
Item 19: "I know that the child listens to me".

The sample of this study consists of 50 mothers enrolled in the Nurse Led Clinic. The age of mothers is between 15 and 41 years, the average age was 32.29 (SD: 3.56). Regarding marital status, 72% of mothers were married, 27% cohabitants and 1% unmarried. With regard to the socio-economic level, 83% of the respondents fall into a medium level, estimated on the basis of education and employment.

Table 1. Breastfeeding during a three years period.

	Year 2011	Year 2012	Jan-June 2013 (6 months)
Esclusive breastfeeding	(198) 68.5%	(209) 70%	(108) 65%
Predominant breastfeeding	(14) 2%	(18) 6%	(18) 6%
Complementary breastfeeding	(52) 18%	(63) 21%	(28) 16.7%
Formula	(25) 9%	(7) 2.5%	(2) 1%
Total mothers	289	297	167

CONCLUSIONS

In order to offer a better response to the parents care, it is particularly interesting to promote the organizational model of the Nurse Led Clinic. With this capability of nursing care and continuity of care after discharge it is possible to encourage, facilitate and strengthen the parent-child bond. Promoting and supporting breastfeeding, underlying the nutritional benefits, psychological,

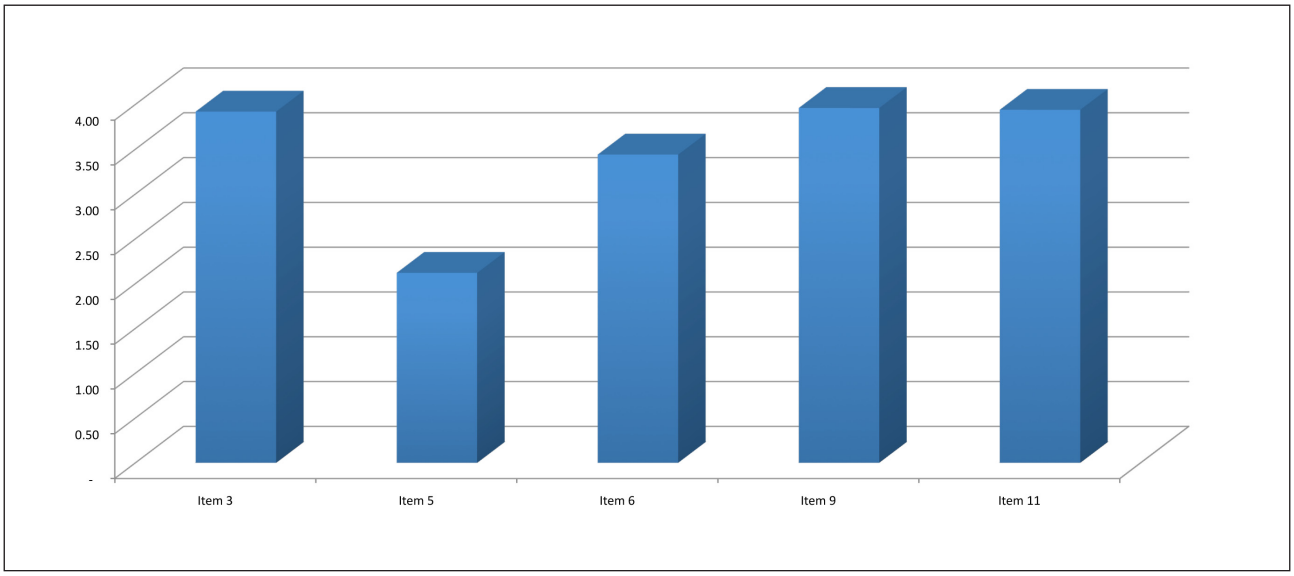

Figure 1. Results of the questionnaires administered in the Nurse Led Clinic, year 2012. Postnatal Attachment Inventory Responses (Likert scale from 1 to 4).

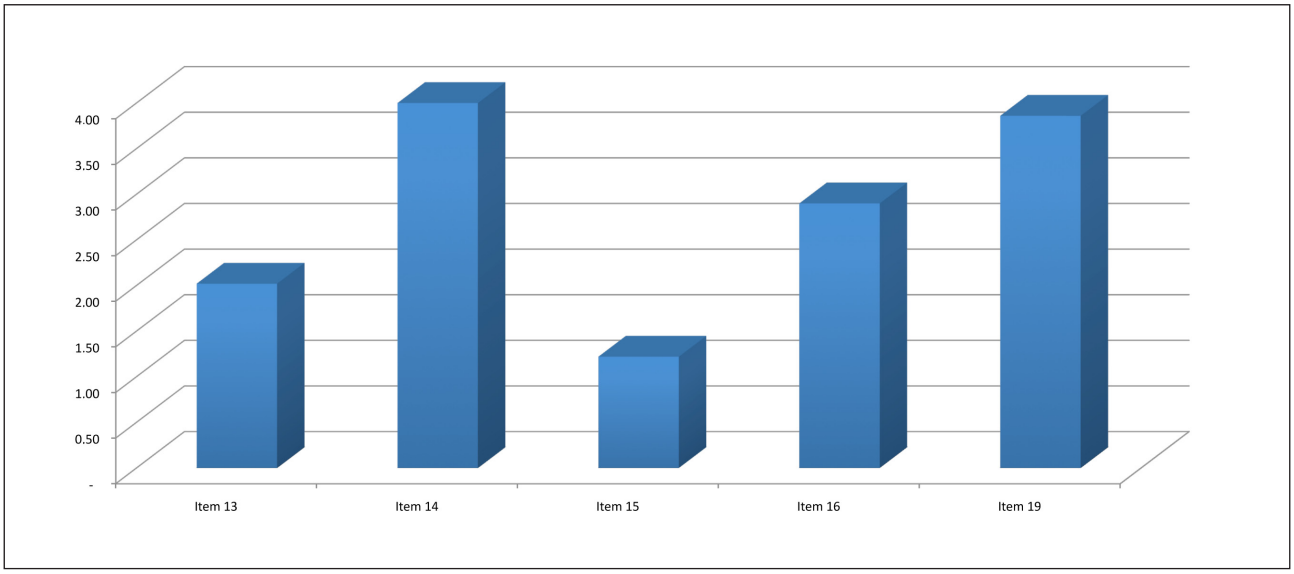

Figure 2. Results of the questionnaires administered in the Nurse Led Clinic, year 2012. Postnatal Attachment Inventory Responses (Likert scale from 1 to 4).

emotional and social skills, improve the mothers's self-esteem. The counseling nurses, the ability to receive and communicate in a simple and clear, sometimes using an informal and spontaneous style helps the relationship and listening to the family dynamics that snap in the sensitive period postpartum.

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ABS 17

EMOTIONAL STATES OF MOTHERS OF PREMATURE BABIES THREE MONTHS AFTER DISCHARGE

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The object of this research is to explore the sensation and the possible presence of emotional disorders in mothers of premature babies, assessed after three months from the discharge.

The sample is composed of a group of 30 subjects.

MATERIALS AND METHODS

The test used is the symptom checklist-90 (scl-90 [1]) and consists of 90 items, which assess the presence and the severity of symptoms of mental health problems in different symptomatological domains.

The test assesses the disturbances in case felt during the last period; the subject provides an assessment from 0 (a mere nothing) to 5 (very severe) on Likert scale, the results identify symptomatological dimensions of different meaning for each of them the relative score is calculated as the average of the questions with answer. In general, we consider to be of clinical interest the average scores equal or greater than 1.00.

In order to observe how the dynamics can evolve, and the possible psychopathological areas develop, were examined the average scores obtained by the different examined subjects.

PRELIMINARY RESULTS

A partial analysis detects the presence of moderate or severe mental illness.

The psychopathological concerned areas are: somatic activation, interpersonal sensitivity, depression, general anxiety, hostility, sleep disorders.

The test is processing. The partial results obtained, therefore, put in evidence the persistence of a condition of emotional distress in mothers of premature babies after three months from the discharge from NICU.

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ABS 18

RECURRENT BENIGN PNEUMOPERITONEUM IN A MODERATELY PRETERM NEWBORN INFANT

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CASE REPORT

A male infant, Caucasian, was born after an unremarkable pregnancy and labour at 32 weeks of gestational age. The preterm delivery was due to premature rupture of the membranes and spontaneous onset of labour (mother with suspected myopathy). At birth the baby was apnoeic and profoundly hypotonic. Respiratory effort was insufficient, poorly responsive to bag and mask ventilation and pressure support. We electively proceeded to endotracheal intubation.

The abdomen was soft. A chest and abdomen X-ray film of control showed a striking diffuse pneumoperitoneum, associated with a marked bilateral lung derecruitment (**Fig. 1**).

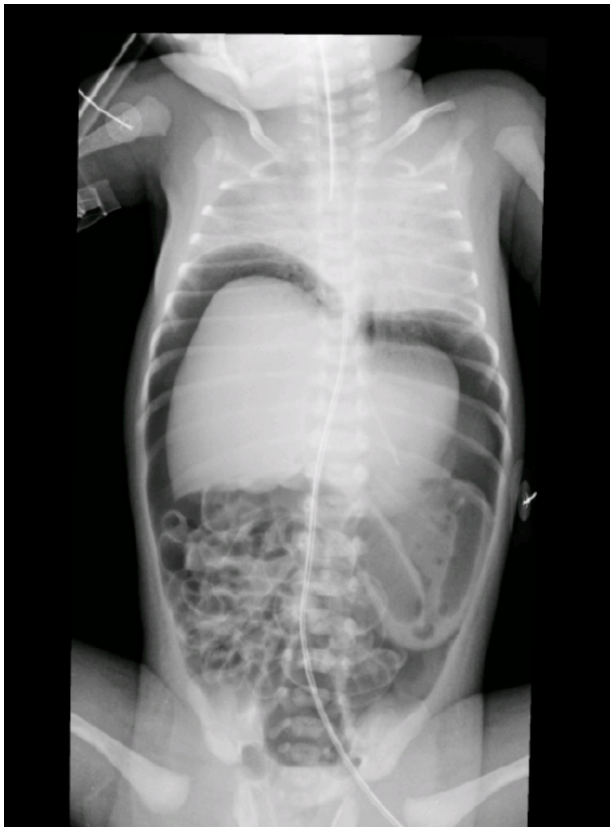

Figure 1. A chest and abdomen X-ray film showing a striking diffuse pneumoperitoneum, associated with a marked bilateral lung derecruitment.

A needle cannula was placed in emergency, in order to decrease the volume of air-leak. An urgent paediatric surgical consult made the decision to maintain a conservative approach.

Few days later, after an accidental extubation and the consequent need of bag and mask ventilation, a new episode of pneumoperitoneum was noticed. Recovered spontaneously without any invasive treatment.

DISCUSSION

Peritoneal air-leak is generally due to acute intestinal perforation; rarely is deemed as secondary to intrathoracic air-leak. However, pneumoperitoneum without any documented gastrointestinal leak in infants with respiratory distress and mechanical respiratory support has been reported in the literature.

The first cause is the dissection of air from the mediastinum along the course of the aorta and vena cava through the diaphragm, with caudal rupture into the peritoneal cavity. Preterm patients with severe respiratory distress may actually develop clinical and radiological signs of pneumoperitoneum, particularly while under mechanical ventilation [1, 2].

In our patient as possible risk factors we propose both the moderate prematurity and the need for mechanical respiratory support, in addition to the manual bag and mask ventilation performed in emergency conditions.

Given the self-limiting clinical course in the absence of any bowel lesion, the diagnosis of benign pneumoperitoneum was made.

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ABS 19

DOSIMETRIC ISSUES IN A NEONATAL INTENSIVE CARE UNIT

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INTRODUCTION

Preterm children, hospitalized in Neonatal Intensive Care Unit due to respiratory and digestive diseases, undergo numerous chest and abdomen X-rays [1]. The use of X-rays as an aid in diagnosis and in subsequent follow-up, along with an undoubted benefit, also involves an intrinsic biological damage [2]. In addition, for the same dose of ionizing radiation, babies have on average a higher risk of developing cancer than adults, mainly due to a greater sensitivity of the organs and tissues in rapid development and to an increased life expectancy [3].

AIM

The aim of this study was to compare different dosimetric methods to verify the most suitable one for accuracy and practicality of measuring doses of radiation entering the patient (Entrance Skin Dose – ESD), and also for later evaluation of Diagnostic Reference Levels (DRLs) [4] which represent the ESD under clinical conditions.

MATERIALS AND METHODS

The measurement of the ESD was performed with two methods: the direct method, using three different types of dosimeters; the indirect method, by measuring the output of the X-ray tube [5] and the Dose Area Product (DAP) [6].

All measurements were performed on a mobile X-ray unit type MOBILETT HP Plus (SIEMENS), in use at the Neonatal Intensive Care Unit of Cagliari.

For the evaluation of the radiological technique, data of about 75 patients were collected. They are summarized in **Tab. 1**.

The dosimeters we used for the measurements with the direct method, were: 1) solid state photodiode; 2) thermoluminescence dosimeters (TLD); 3) optically stimulated luminescence dosimeters (OSLD). For the indirect method we used: 4) X-ray tube output; 5) transmission ionization chamber for DAP measurements.

RESULTS AND CONCLUSIONS

From the comparison of the measurements (**Fig. 1**), one can observe that, excluding those obtained with TLD dosimeter, the others were perfectly valid

Table 1. Patient data and exposure parameters.

Patients	Total no.	75
	Female	24
	Male	51
Weight	MAX	3820
	AVERAGE	1633
	MIN	510
Gestational age (weeks)	MAX	36
	AVERAGE	32
	MIN	22
Peak voltage (kV)	MAX	85
	75%	70
	MIN	63
Tube load (mAs)	MAX	3.2
	75%	2.5
	MIN	2.0

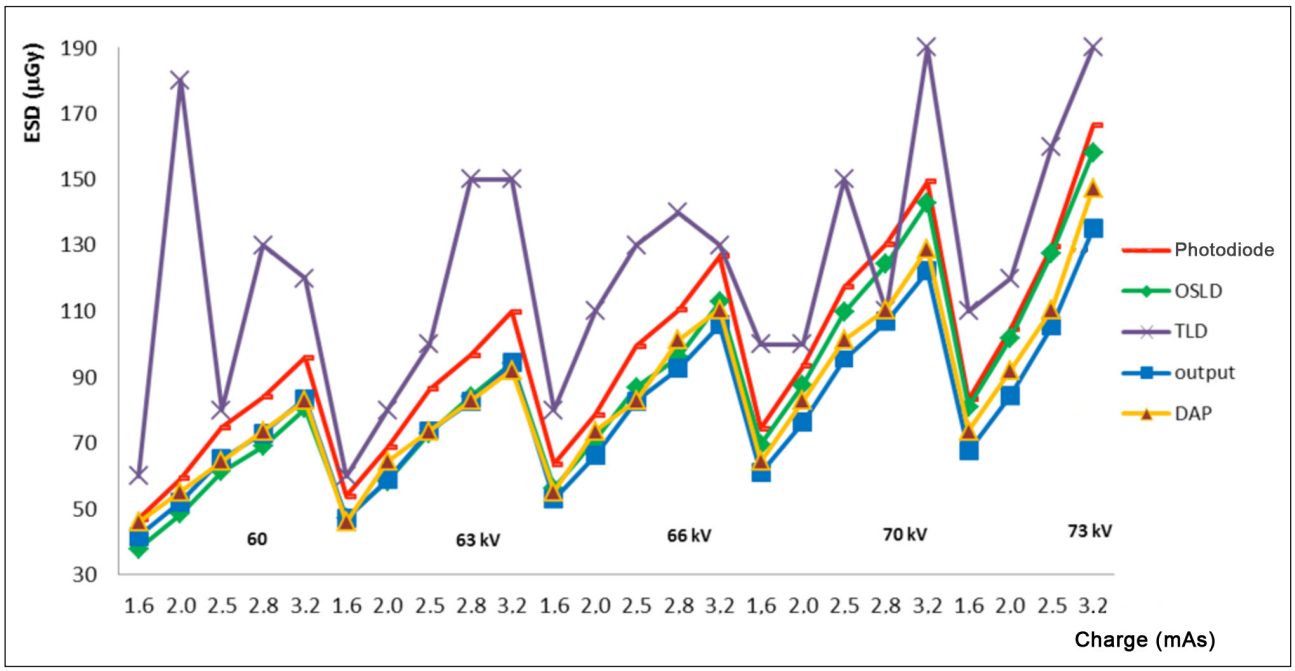

Figure 1. Comparison of Entrance Skin Dose (ESD) measurement with different methods.

and comparable. The type of TLD we used had a sensitivity which was not good enough for the dose range of interest.

The most accurate method but especially the most practical one for the measurement of the ESD and for the assessment of the DRLs, is therefore the tube output method. It is also advantageous for its simplicity of calculation. In fact, when the tube output curve of the device and the exposure values set for each patient are known (**Fig. 2**), it is possible to determine the relative value of DRL and to estimate the absorbed dose [7].

This evaluation shows that, in clinical radiological practice, voltages higher than the range indicated in the European guidelines (60-65 kV) are used in a systematic way. This fact, together with the use of high X-ray tube workloads, leads to frequently exceed the limit of DRL indicated by national and international regulations (DRL < 80 μGy) [8, 9] (**Tab. 2**).

The conclusions of this study lead us to suggest a particular attention to the radiological practice in order to obtain an optimal imaging while keeping the dose to the patient as low as possible.

Table 2. Diagnostic Reference Level (DRL) in Neonatal Intensive Care Unit of Cagliari.

Peak voltage (kV)	Tube load (mAs)	Output: DRL (μGy)
63	2.0	58.96
63	2.5	73.70
63	3.2	94.33
70	2.0	76.38
70	2.5	95.47
70	3.2	122.20
85	2.0	120.44
85	2.5	150.55
85	3.2	192.71

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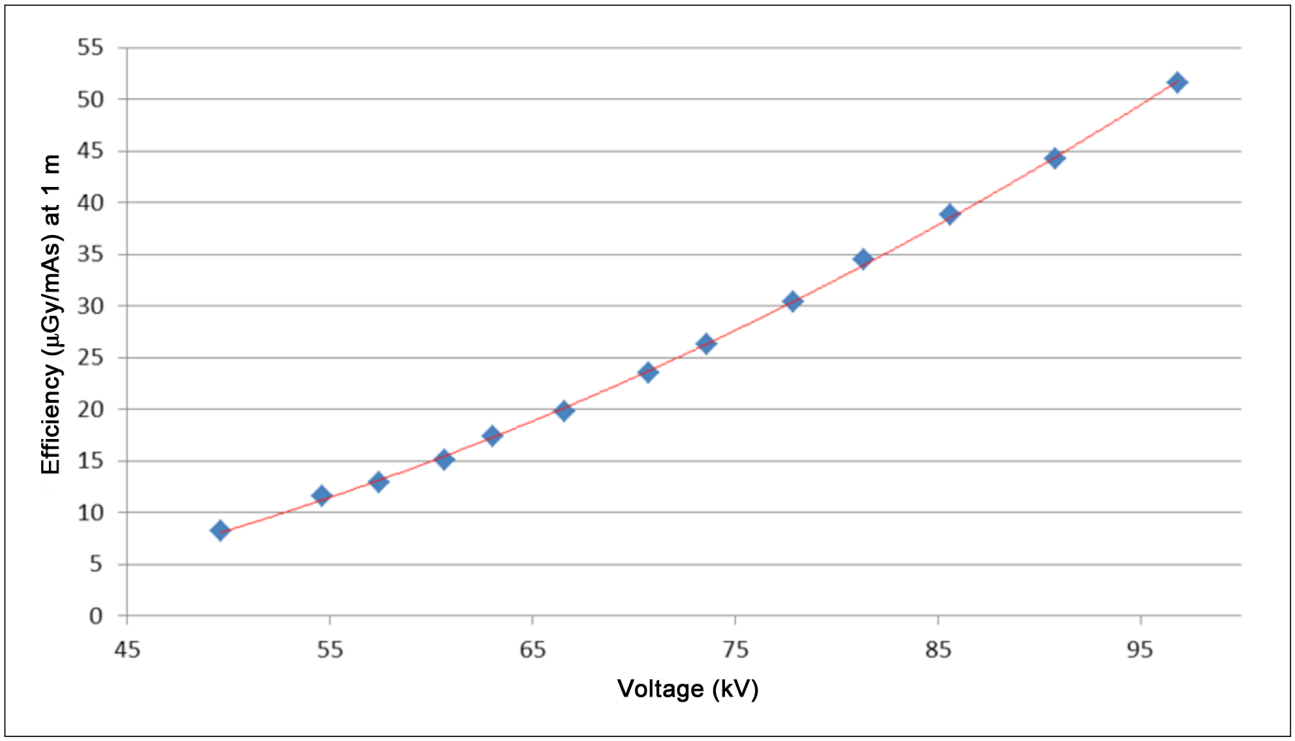

Figure 2. X-ray tube output curve.

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ABS 20

SELF-HEALING LANGERHANS CELL HISTIOCYTOSIS (HASHIMOTO-PRITZKER DISEASE) IN A 5-MONTH-OLD CHILD

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INTRODUCTION

"Self-healing" Langerhans cell histiocytosis (SHLCH) is a rare self-limited variant of Langerhans cell histiocytosis first described by Hashimoto and Pritzker in 1973 that presents at birth or during the neonatal period [1]. We report here a case of SHLCH occurring in infancy.

CLINICAL DATA

A male infant, born at term, presented at the age of 5 months multiple skin lesions, consisting of papules of variable size, sometimes with ulcerations and scabs. The lesions were distributed mainly over the trunk. The child had fever but was otherwise healthy.

MICROSCOPIC FINDINGS

A skin biopsy revealed a massive infiltration of mononuclear cells in the superficial epidermis. The cells had eccentric, pale, oval nuclei, and abundant eosinophilic cytoplasm (**Fig. 1**) with sparse mitotic figures. Infiltrating histiocytes made micro-abscess-like clusters within the epidermis, which was focally ulcerated (**Fig. 2**). Immunohistochemistry demonstrated that most infiltrating cells were S-100- and CD1a- immunoreactive (**Fig. 3** and **Fig. 4**). Based on histological and immunohistochemical findings, the lesions was categorized as Langerhans cell istiocytosis (LCH).

Due to the absence of involvement of internal organs, a follow-up was performed without any treatment. Within some months, skin lesions regressed.

CONCLUSIONS

LCH is a generic term that identifies several clinical diseases characterized by proliferation of distinctive

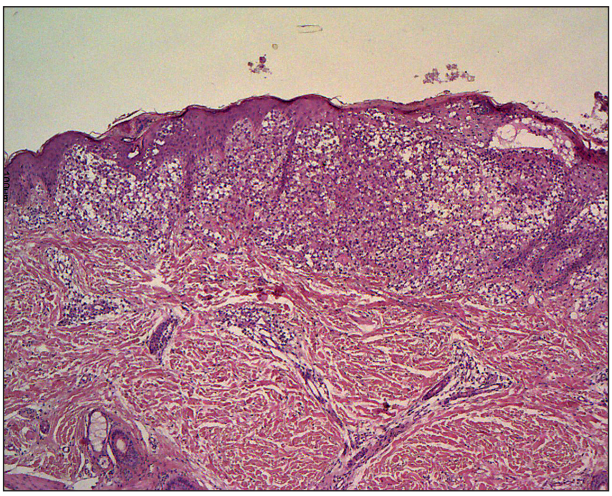

Figure 1. Massive infiltration of superficial dermis and epidermis by mononuclear cells (H&E, Bar scale 100 μm).

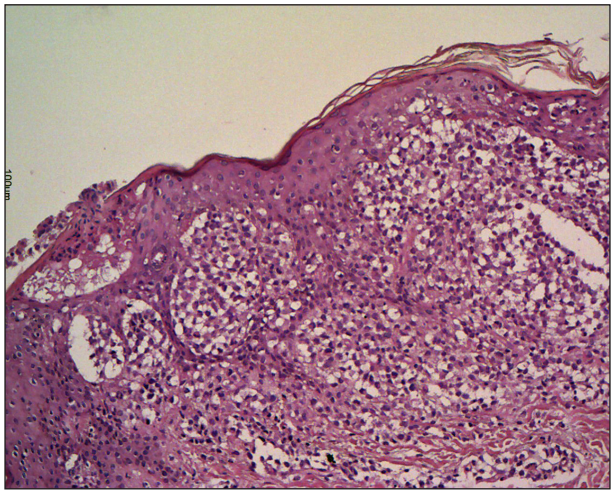

Figure 2. Infiltrating Langerhans cells give rise to micro-abscess-like clusters within the epidermis (H&E, Bar scale 100 μm).

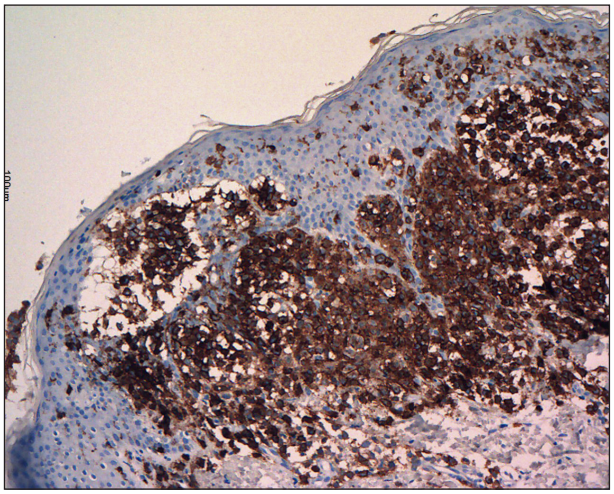

Figure 3. Cytoplasmic immunoreactivity for CD1a characterizes Langerhans cells (Bar scale 100 μm).

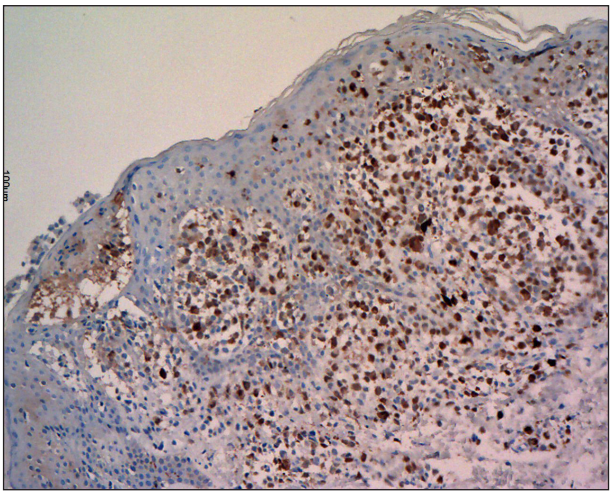

Figure 4. Nuclear immunostaining for S100 in Langerhans cells (Bar scale 100 μm).

cells that are S100- and CD1a-positive and contain Birbeck granules in their cytoplasm [2, 3]. SHLCH should be differentiated from the malignant form of other LCHs, such as Letterer-Siwe disease. However, the healthy general condition, the lack of multiorgan involvement, and the spontaneous regression of the lesions in our child suggest the diagnosis of SHLCH.

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ABS 21

RECURRENT PRETERM DELIVERY AND HISTOLOGICAL CHORIOAMNIONITIS: A CASE REPORT

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INTRODUCTION

Chorioamnionitis (CA) is an intrauterine status of inflammation of fetal-maternal tissues generally caused by a polimicrobial infection of the amniotic cavity by organisms ascending from the lower genital tract. CA is a major risk factor for preterm birth (preterm labor and preterm prelabor rupture of membranes [PPROM]) especially between 20 and 30 weeks of gestation. Clinical diagnosis is variably defined by maternal fever, tachycardia, leucocytosis, uterine tenderness, foul-smelling vaginal discharge, fetal tachycardia. Nonethless CA is often clinically inapparent and the diagnosis is made on the basis of pathological examination of the placenta showing polymorphonuclear leucocytes infiltration of placental tissues (histological chorioamnionitis-HCA). Preterm birth is a major cause of perinatal mortality and morbidity, both short- and long-term. Consequences of intraamniotic infection can affect the development of vital organs and have been strongly associated with perinatal brain damage (intraventricular haemorrhage, periventricular leucomalacia, cerebral palsy). Evidence exist that association with adverse neurological outcome might be related to the fetal inflammatory response syndrome (FIRS), caused by the release of inflammatory cytokines.

CASE REPORT

We here report the case of a black woman with two previous preterm deliveries (one CS and one spontaneous vaginal delivery), at 23 and 22 weeks of gestation respectively, followed by the death of both babies, normal and liveborn, due to the extremely low birth weight and the consequences of severe prematurity. Pathological exam of the placenta revealed in both cases a severe neutrophilic infiltrate in the chorionic plate with vasculitis of the chorial and umbilical vessels (chorioamnionitis with funisitis) (**Fig. 1** and **Fig. 2**). In light of the poor past obstetric history, the woman now at her third pregnancy was carefully monitored and investigated for the presence of infection. At 21 weeks, vaginal and cervical swabs revealed colonization by *U. urealyticum*, *M. hominis*, *K. pneumoniae* and *E. coli*, treated with administration of a strong polyantibiotic therapy with josamycin, ceftazidime, azithromycin and simultaneous probiotic therapy. Meanwhile ultrasound vaginal cervicometry showed an abnormal shortening of the cervix. PPROM occurred at 23 w + 6 d followed by spontaneous vaginal delivery at 25 w + 4 d of a liveborn male baby weighing 900 grams with Apgar score 6-7-8.

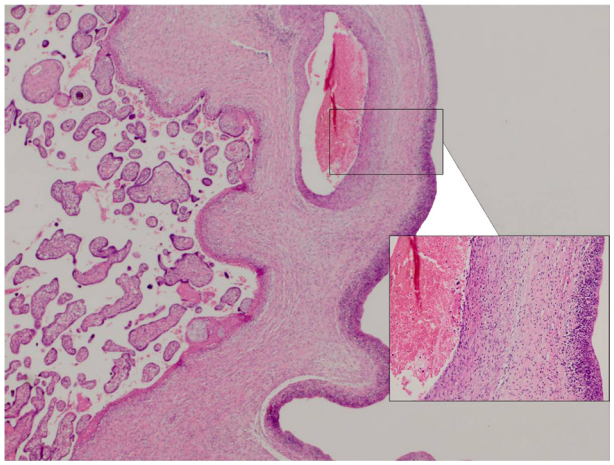

Figure 1.

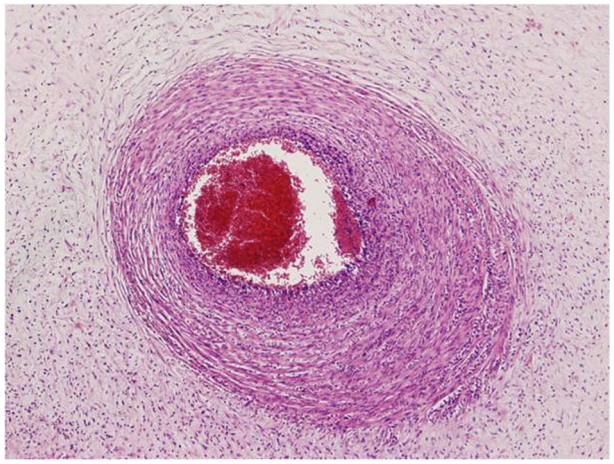

Figure 2.

Again, pathological examination of the placenta showed a neutrophilic infiltrate in fetal membranes, this time milder in grade and without any evidence of fetal vasculitis and funisitis (absence of fetal inflammatory response).

DISCUSSION

CA is strongly associated with preterm birth and with high rates of perinatal mortality and morbidity. There is still controversy if gestation-independent effects of CA on neonatal outcome do exist. The clue to predict neonatal outcome seems to be the development of a fetal inflammatory response syndrome (FIRS). Clinically, FIRS is defined by fetal plasma levels of IL-6 > 11 pg/mL, whilst subclinical FIRS is defined histologically by funisitis and fetal vasculitis. *Mycoplasma spp.* and *Ureaplasma spp.* are commonly associated with infection of the amniotic cavity and are usually low virulence organisms. Animal models demonstrate that the host genetic background has a strong impact on disease outcome, determining the strength of the inflammatory response. In the case here reported, an aggressive polyantibiotic therapy likely succeeded in delaying preterm delivery and reducing the fetal inflammatory response, improving fetal outcome.

CONCLUSIONS

Fetal inflammatory response, besides the severity of neutrophilic exudate in fetal membranes, seems the most reliable predictor of fetal outcome. Histological subclinical chorioamnionitis is much more common than clinical chorioamnionitis and cannot be predicted by clinical findings and infectious markers in mother or infant. Therefore, placental histopathology may play a role in predicting neonatal outcome in premature deliveries, especially below 30 weeks.

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ABS 22

BCL-2 IMMUNOREACTIVITY IN THE NEWBORN KIDNEY: A NEW MARKER FOR CAP MESENCHYMAL CELLS

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INTRODUCTION

Bcl-2 (B cell lymphoma 2) is an integral membrane protein of the mitochondrial, nuclear and endoplasmic reticular membranes that plays a crucial role in preventing apoptosis and maintaining cell survival. The Bcl-2-mediated block of apoptosis is the result of its influence on the release of cytochrome c from mitochondria (**Fig. 1**). Bcl-2 protein prevents Bax from perforating the outer mitochondrial membrane and from causing cytochrome c leakage, thus

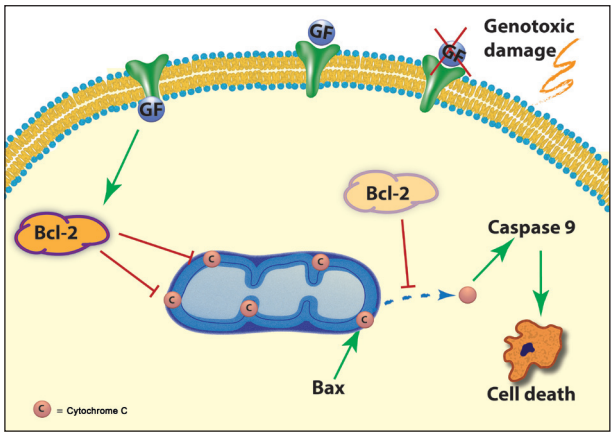

Figure 1. Bcl-2 prevents Bax from inducing leakage from mitochondria of cytochrome C, thus bloching apoptosis.

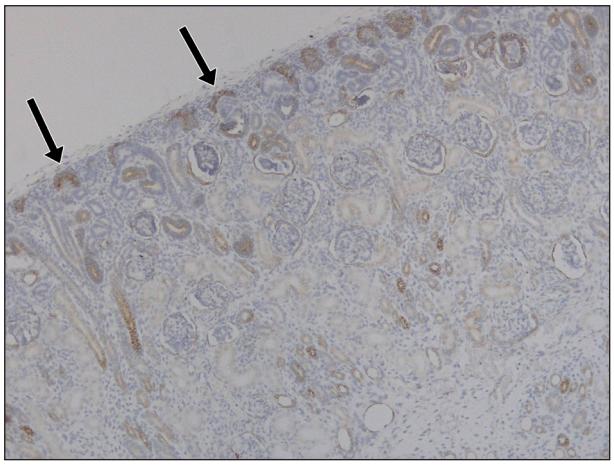

Figure 2. At low power, immunoreactivity for Bcl-2 was mainly localized in the nephrogenic zone in close proximity of the renal capsule (arrows).

blocking activation of caspase cascade and halting apoptosis. Recently it has become evident that the function of the members of the Bcl-2 family is not restricted to the regulation of apoptosis, Bcl-2 being also involved in regulation of mitochondrial fusion and fission, and thereby in morphogenesis of multiple developing human organs [1-2], including ureteral bud cells and metanephrogenic mesenchymal progenitor cells [3].

MATERIALS AND METHODS

The expression of Bcl-2 was evaluated in kidneys of 14 human fetuses and newborns, ranging from 20 up to 36 weeks of gestation. Kidney samples were 10% formalin-fixed, routinely-processed and paraffin-embedded. Immunoistochemical staining was performed using antibodies against Bcl-2 (polyclonal anti Bcl2 antibody, Dako, 1:50 dilution) on 4 µ-thick sections, incubated for 30 minutes at room temperature.

RESULTS

At low power, immunoreactivity for Bcl-2 was mainly localized in the nephrogenic zone in close proximity of the renal capsule (**Fig. 2**). At higher power, the highest levels of Bcl-2 immunostaining was restricted to cap mesenchymal cells encircling the ureteric bud tips (**Fig. 3**). Moreover, focal and mild reactivity for Bcl-2 was also detected in parietal epithelial cells (PECs) of the Bowman's capsule and in distal tubules.

CONCLUSIONS

Our study clearly evidences that Bcl-2 immunostaining selectively marks cap mesenchymal cells in the nephrogenic zone of the developing human kidney. Given the anti-apoptotic function of Bcl-2 in human cells, we

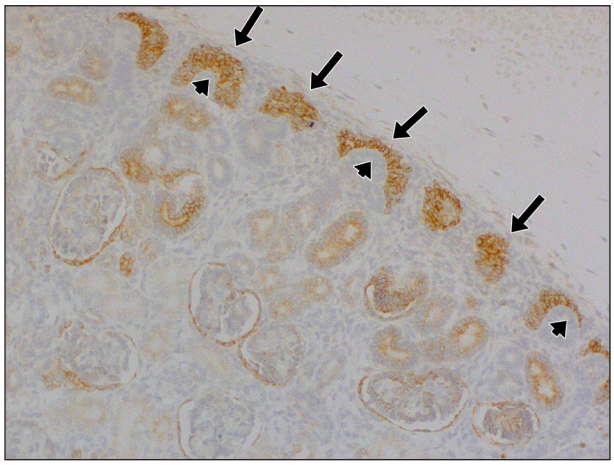

Figure 3. At higher power, Bcl-2 immunostaining was restricted to cap mesenchymal cells (arrows) encircling the ureteric bud tips (arrowheads).

may hypothesize that overexpression of Bcl-2 in this peculiar renal progenitor cell compartment might underly the necessity of protecting these cells in order to allow nephron formation and kydney development. From a pratical point of view, immunoreactivity for Bcl-2 appears as a useful tool for the identification of cap mesenchymal cells in the nephrogenic zone of the fetal and newborn human kidney.

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ABS 23

RELEVANT CHANGES IN NEPHROGENESIS IN DOWN SYNDROME

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INTRODUCTION

Cap mesenchymal cells in the subcapsular blue strip represent the nephron progenitor population in fetal kidney. Recent studies on the preterm neonatal kidney showed the existence of a marked interindividual variability in the amount of stem cells although without correlation between the blue strip width and radial glomerular count [1]. The aim of our study was to analyze morphological aspects of nephrogenesis (blue strip width and mean glomerular size) in fetuses with chromosome 21 trisomy.

PATIENTS AND METHODS

7 fetuses from therapeutic abortions for chromosome 21 trisomy (Down Syndrome, DS) and 5 age-matched controls with normal karyotype (NK) from pregnancies interrupted for maternal reasons have been selected. Macroscopic examination of all the fetuses included did not show any congenital malformation. Tissue samples from different organs were formalin–fixed and paraffin-embedded to obtain 4 µm-thick histologic sections that were H&E-stained. Cases and controls were matched according to gestational age and subdivided in three groups: 14 weeks (4 DS, 3 NK), 17 weeks (1 DS, 1 NK), 20 weeks (2 DS, 1 NK). Histological sections of the kidneys were digitally scanned at 100X magnification. The blue strip width (µm) was estimated by measurement of the length of orthogonal segments to the capsule line in 20-25 different sites for each kidney, to avoid misinterpretation due to morphological variability of the subcapsular zone. The mean glomerular size (µm^2) was estimated on a variable number of fully-developed glomeruli (range: 19-49) at different levels in the renal cortex. The obtained values were analyzed with a specific algorithm developed with MatLab software.

RESULTS

Blue strip width and mean glomerular size values were higher in kidneys of DS fetuses in each gestational age group considered, with greater differences at 14 weeks (**Fig. 1** and **Fig. 2**; **Fig. 3a**, DS 14 w; **Fig. 3b**, NK 14 w). A strong linear correlation between blue strip width and mean glomerular size was recorded: larger glomerular structures are found in kidneys with a wider blue strip. Relevant histopathological features of DS fetal kidneys were glomerular changes consisting in glomerular hypertrophy and fusion, producing larger structures due to confluence of two or three vascular tufts.

CONCLUSIONS

The blue strip width, representing the mesenchymal pluripotential renal cell burden, is highly variable and might be a predictor of the potential for residual nephrogenesis in a developing fetal kidney. Our study shows that the blue strip width and mean glomerular size values are greater in DS kidneys compared to those with normal karyotype. A range of renal

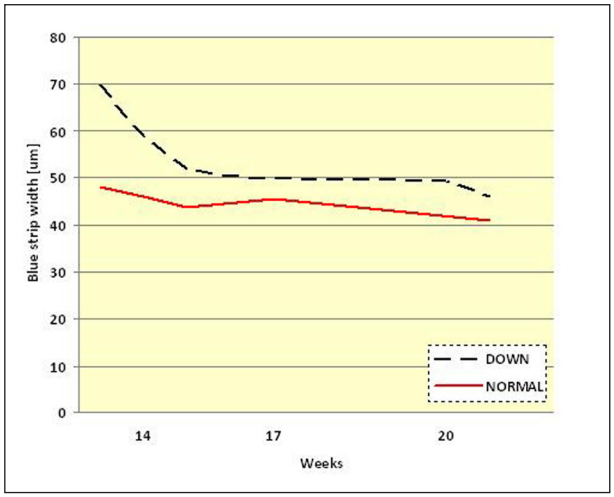
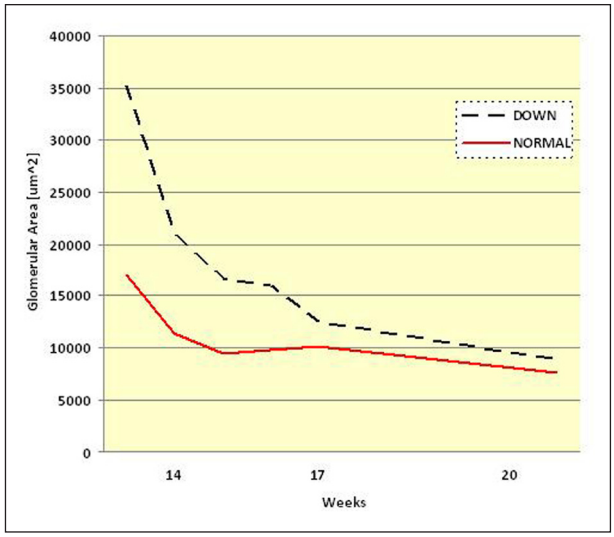


Figure 1.



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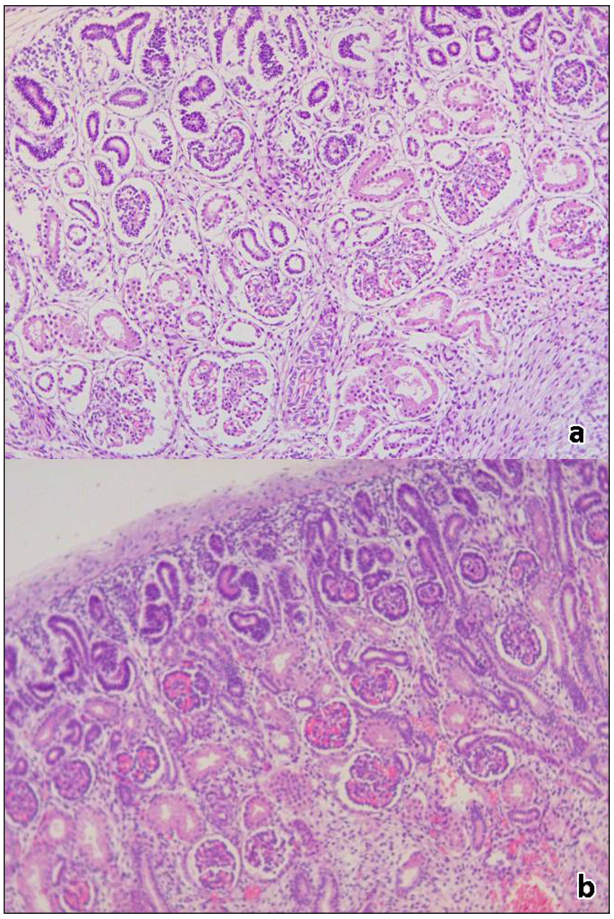

Figure 3.

diseases have been described in patients with Down syndrome, increased survival being associated with growing number of these patients presenting with chronic renal failure. The underlying causes are still poorly understood. Further studies on larger series and on wider gestational age range are needed to validate the differences here recorded and to comment the functional reflection of the morfphological features described.

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ABS 24

INTERINDIVIDUAL VARIABILITY IN LANGERHANS ISLET BURDEN IN NEWBORN PANCREAS AT BIRTH

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BACKGROUND

Human pancreas is a complex organ constituted by an endocrine and an exocrine compartment and with an intricate development, characterized by epithelial and mesenchymal interactions depending on multiple molecular signals [1]. Perinatal programming is fundamental in determining the health or the disease status in adulthood, since the predisposition to many pathologies may start in the first stages of life. The aim of the present work was to study pancreatic histology in fetuses and in preterm of different gestational age, in order to correlate the degree of pancreas development and in particular Langerhans islet burden at birth [2].

DESIGN

10 pancreatic samples were obtained for legal interruption of pregnancy and 10 from autopsies. Gestational age ranged from 12 up to 36 weeks. All living newborns were admitted to the Neonatal Intensive Care Unit or Obstetrics and Gynaecology Division of the San Giovanni di Dio University Hospital, Cagliari. Pancreatic samples were formalin-fixed, paraffin-embedded and routinely processed. 4 μ-thick sections were stained with H&E and examined by two pathologists (G.L.; S.N.) without any knowledge of gestational age and of other clinical or laboratory data. In each pancreas the number of Langerhans islets was evaluated, by counting the number of islet cells in 5 consecutive histological fields at X 20.

RESULTS

Pancreatic samples under 20 weeks of gestational age didn't show any organized Langerhans islet, endocrine cells forming small clusters distributed in the whole parenchyma, indistinguishable at H&E from other surrounding cell types (**Fig. 1**). Pancreas count evidenced a peak in islet development around 28th w (**Fig. 2**). 27 w and 36 w samples, belonging to multiple organ failure affected newborns, had a lower islet burden when compared with patients of inferior gestational age (**Fig. 3**). Moreover, we observed two twin samples of 27 w of gestation that didn't show marked interindividual variability in Langerhans islets burden.

CONCLUSIONS

Our data show that Langerhans islets are distinguishable in human pancreas starting from 20th w. Islet burden is strictly influenced by

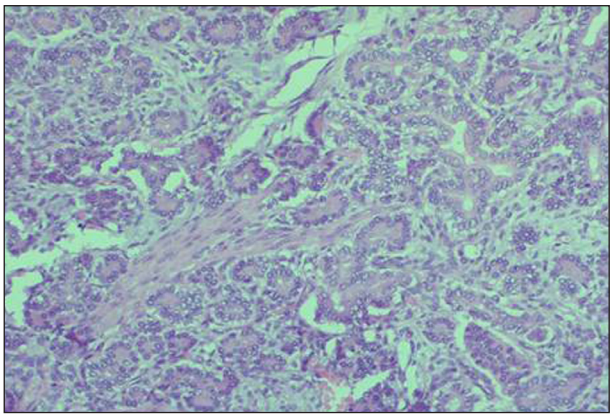

Figure 1. Human pancreas at 16 weeks of gestation: no organized Langerhans islet is evident.

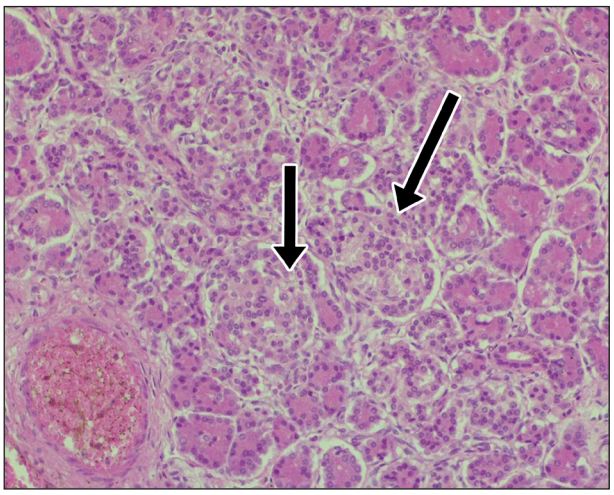

Figure 2. Human newborn pancreas: two large well organized islets are shown (arrows).

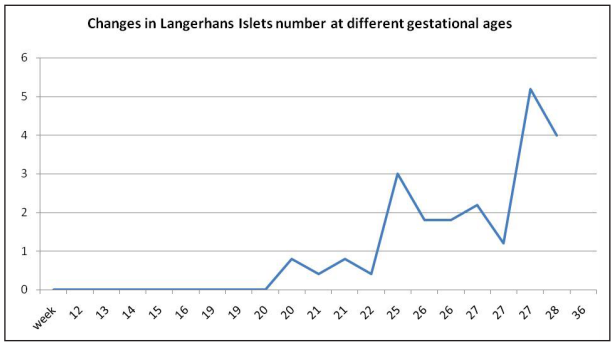

Figure 3. Interindividual variability in Langerhans islets burden during gestational weeks.

gestational age, as demonstrated by the increasing number of islets that reach an adult conformation at 26th w. The incomplete pancreatogenesis caused by various intrauterine injuries, including asphyxia and multiple organ failure, can result in a reduction of quantity and quality of the endocrine compartment, potentially representing a risk factor for pancreas disease insurgence in adulthood. Further studies are needed in order to better understand relevance of fetal programming and Langerhans islet burden at birth on the predisposition to develop diabetes in childhood and adulthood.

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ABS 25

G6PD DEFICIENCY IN SARDINIAN NEWBORN: THE UTILITY OF MOLECULAR TEST

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INTRODUCTION

The G6PD deficiency is a common enzyme deficiency responsible for two clinical syndromes: episodic hemolytic anemia (caused by infections, medications, ingestion of fava beans) and spontaneous chronic hemolytic nonspherocytic anemia. G6PD is an enzyme of the cycle of pentoses, metabolic pathway that regenerates NADPH, indispensable for obtaining GSH. Subjects with G6PD deficiency are not able to maintain an adequate level of GSH in their erythrocytes, so the SH groups are oxidized Hb and Hb tends to precipitate inside the cell forming the bodies of Heinz. There are more than 400 variants of G6PD divided into 5 classes based on residual activity of the enzyme. In Sardinia the most common variant is the Mediterranean, associated with acute hemolytic anemia due to assumption of fava beans or medication. The enzyme deficiency is transmitted with X-linked mode and is more severe in males that, being hemizygous, possess only mutated allele. Females heterozygous present clinical variables justified by the fact that the lionization allows a population of red cells either lacking enzymatic activity, either with normal activity. Homozygous females with unbalanced

lionization will have a framework similar to that of the hemizygous males.

OBJECTIVES OF THE STUDY

In our study we assessed the impact of the lack of G6PD Mediterranean variant and sought the newborn in order to compare the results with those of the analysis of biochemical molecular parameters. The study was approved by the Ethics Committee of the AOU of Cagliari.

PATIENTS AND METHODS

Patient: term infants of both sexes, apparently healthy, with adequate weight for gestational age, whose parents have signed a informed consent. For each patient were collected 2 samples of peripheral blood, first and third day. On the first sample enzymatic analysis of G6PD was performed; on the second the molecular survey was carried out.

RESULTS

The dosage G6PD/6PGD was performed on 211 infants. It was deficient in 14 (13 M – 1 F), intermediate in 44 (12 M – 32 F) and normal in 153 (90 M – 63 F) newborns. Performing the research of the Mediterranean G6PD variant, it was sought in 96 females. Among them:

- 32 (33.3%) were heterozygous for the Mediterranean variant in agreement with the biochemical parameters;
- 1, who appeared to be heterozygous at molecular analysis, showed a ratio of the enzyme typical of homozygotes or male hemizygotes, highlighting a unfavorable lionization;
- 3, heterozygotes from the molecular point of view, showed a normal enzymatic ratio, due to a favorable lionization.

CONCLUSIONS

The results of the molecular test stress the importance of analysis in females in case of doubt and discrepancy of inheritance within the family.

ABS 26

MORPHOGENESIS AND MOLECULAR MECHANISMS INVOLVED IN HUMAN EXOCRINE AND ENDOCRINE PANCREAS DEVELOPMENT

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INTRODUCTION

Early pancreas development, given its peculiar complexity, is generally considered as a paradigm for branching morphogenesis and for the development of two organs in one: the endocrine one, programmed to secrete hormones into the bloodstream, and the exocrine pancreas, devoid to secrete enzymes into the gut [1, 2]. As a consequence, the development of the human pancreas is a composite process, that requires the fusion between two buds emerging from the endoderm germ layer (**Fig. 1**) and necessitates molecular interactions between the pancreatic endoderm and the adjacent notochord, eventually leading to the coordinate development of multiple highly specialized stromal, vascular, acinar, ductal and endocrine cell types, a peculiar feature of the pancreas architectural and functional complexity. (**Fig. 2**).

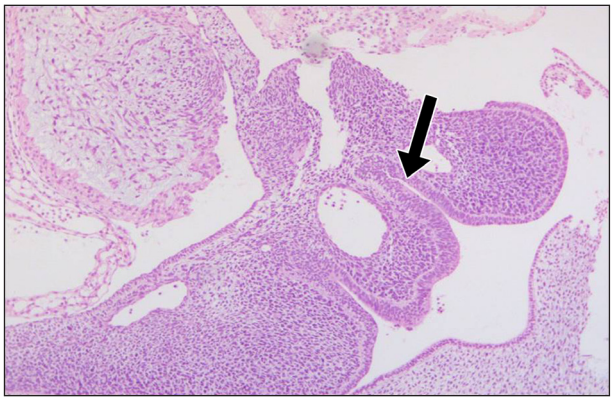

Figure 1. Human embryo. Fusion between two buds emerging from the endoderm germ layer at 7th w of gestation.

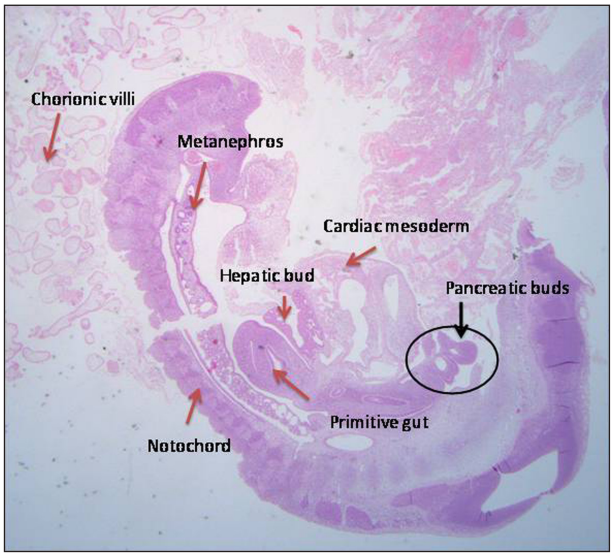

Figure 2. Human embryo at 7th w of gestation: pancreas development and the interactions with adjacent endodermal structures.

DESIGN

The aim of this work was to review pancreas organogenesis, with particular emphasis on morphological events occurring in the human organ, starting from the differentiation of pancreatic stem/progenitor cells within the embryonic gut endoderm that, eventually, give origin to all the numerous differentiated cell types whose coordinate behavior characterizes the complexity of the mature human pancreas. In particular, we shall focus on morphological and immunohistochemical peculiarities of pancreatic progenitor populations, on the specific markers of each cell type undergoing the exocrine or the endocrine fate, and on the main molecular pathways regulating human pancreas organogenesis.

RESULTS

Our preliminary data carried out on 20 pancreas of fetuses and newborns ranging from 7 up to 38 weeks of gestation, evidence that human pancreas morphogenesis shows some peculiarities as compared with other mammals. Morpho-molecular changes occurring during human pancreatic development, reflect up- and down-regulation of genes expressed in the endoderm-derived pancreatic buds and in pancreatic progenitors during development. This complex picture shows that even subtle changes in the complex reciprocal interactions between the multiple cell types involved in pancreas organogenesis may have severe consequences on the ultimate morphogenesis of this organ [1, 2].

CONCLUSIONS

Further studies are needed in order to better realize the correlation between embryogenic cell fate and the predisposition to pancreatic diseases in adulthood life. Understanding the differentiation pathways of stem cells to insulin producing cells can be an important turn in diabetes therapy and other pancreatic diseases.

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ABS 27

MASSIVE MYOCARDIAL INFARCTION IN A NEWBORN WITH IDIOPATHIC INFANTILE ARTERIAL CALCIFICATION

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INTRODUCTION

Calcification of heart and vessels in fetuses and newborns is a very rare condition. An extremly rare form of vascular calcification, first described by Bryant and White in 1901, has been termed Idiopathic Arterial Calcification of Infancy (IACI). This inherited autosomal recessive disorder due to an inactivating mutation of the ENPP1 gene on chromosome 6p22 is usually diagnosed postmortem. The antemortem diagnosis is made in only a few cases on the radiographic or sonographic demonstration of arterial calcification. Only about 160 cases are reported in the literature to date, with about 85% of the patients diagnosed in infancy and dying before 6 months of age because the difficulty of an early diagnosis and the absence of an effective treatment. Because of this, there are only very few survivors reported in literature. An extremely rare case of massive myocardial infarction in a newborn with IACI, diagnosed at autopsy in our hospital, is here reported.

CASE REPORT

A female preterm infant, weighing 2,480 g, was born in a first level Hospital, with caesarean section performed for acute fetal distress. The mother, a 34 years old woman, had a previous healthy child. At birth the general conditions were good. At cardiological examination a patent ductus arteriosus was diagnosed. Laboratory values were within normal range. The newborn was discharged after 11 days, in good general conditions and with spontaneous feeding.

During a planned cardiologic follow-up control at day 50, cardiac ultrasounds revealed an increase of volume of left atrium and ventriculus, which appears severely hypokinetic. The baby was urgently transferred in a NICU, where she died after 12 hours for heart insufficiency.

RESULTS

The external examination revealed no dysmorphic features in a baby of 2,595 grams of body weight, crown-heel length 47.5 cm, foot length 6.8 cm, cephalic perimeter 33.5 cm. At the internal examination the heart (35 grams) showed left

ventricular hypertrophy and dilatation. The pericardium, endocardium, valvular apparatus, pulmonary, and systemic venous drainage were normal. The coronary arteries showed a normal anatomical pattern. Coarctaction of the abdominal aorta was seen. On sectioning, the major branches of the coronary arteries were patent with no significant macroscopically apparent luminal narrowing, but the anterior coronary artery was gritty on cut, consistent with calcification. Histology showed significant changes, predominantly in aorta and in the major arteries of heart, lungs, kidneys, thymus, adrenal glands. There was calcification in the internal elastic lamina and media of medium-sized arteries (**Figs. 1-4**), with focal intimal fibrous proliferation. Moreover, we observed significant changes in the endothelial layer of cardiac arteries, like loss of endothelial cells, a finding associated with thrombosis and heart infarction (**Fig. 5**). No inflammatory infiltration was seen in the arterial walls. An acute myocardial infarction of the left ventricle wall, associated with stenosis and calcification of the anterior coronary artery is demonstrated (**Fig. 6** and **Fig. 7**).

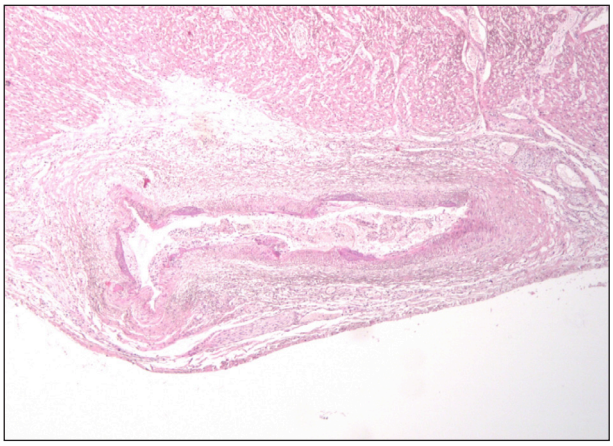
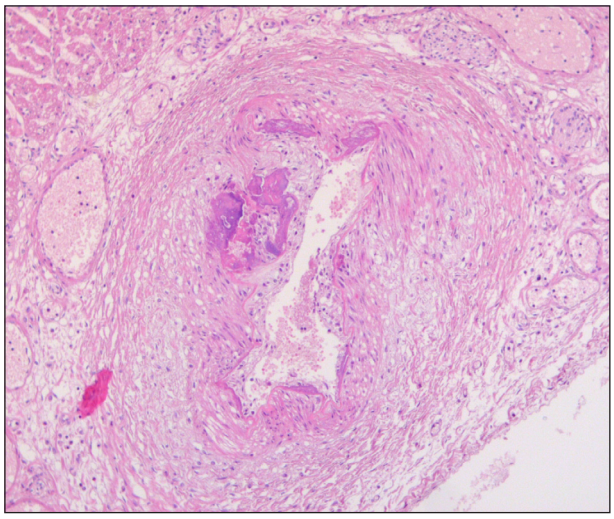


Figure 1.



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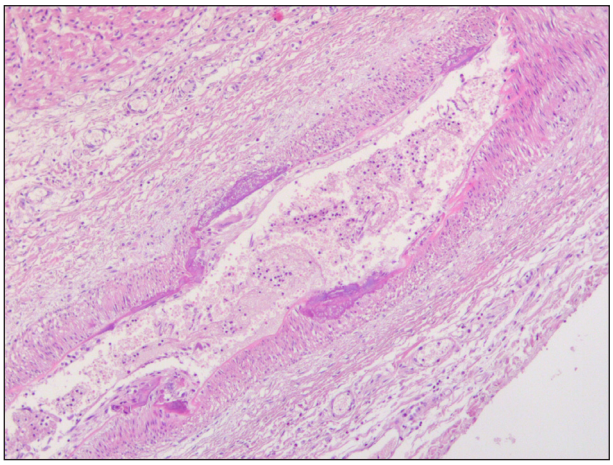

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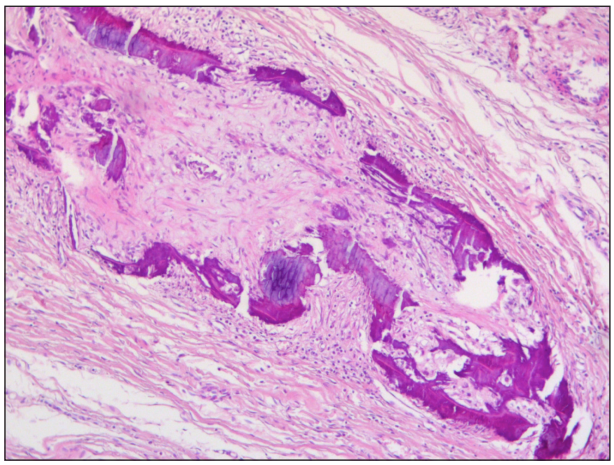

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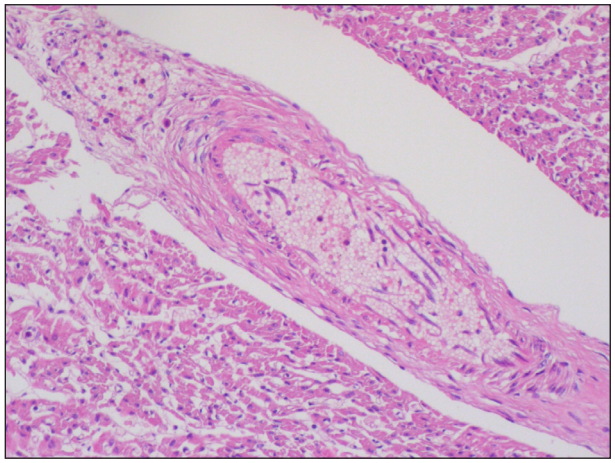

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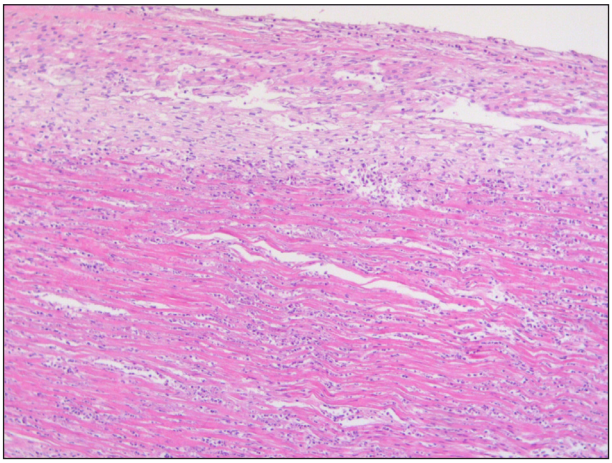

Figure 6.

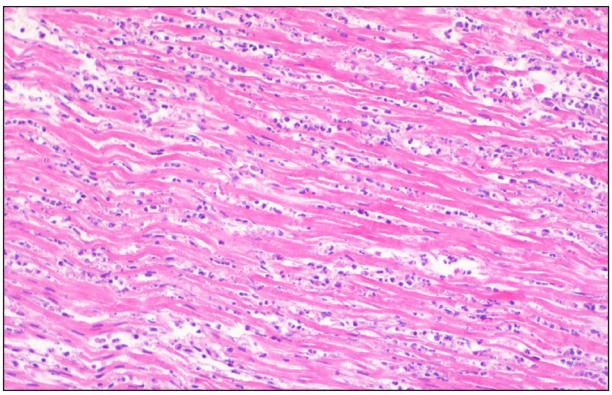

Figure 7.

DISCUSSION

IACI is characterized by widespread and extensive calcification and stenosis of large and medium sized arteries due to the deposition of calcium hydroxyapatite in the arterial internal elastic lamina layer. This is responsible of several symptoms that usually occur in utero or at birth, most important of which are decreased fetal activity, gestation with an antenatal diagnosis of hydrops fetalis, polyhydramnios, low biophysical profile, marked cyanosis, edema, severe hypertension, no or fade pulses, refusal of feeds, tachypnea, vomiting, abdominal distension, general arterial rigidity, cardiac failure (most common clinical finding), strain pattern. Biochemical investigations are usually in the normal range and there is no detectable abnormality of calcium metabolism. In the patient here described, heart involvement was particularly massive, with branchs of coronary arteries mainly affected by calcium depositions. Myocardial infarction has been demonstrated in infancy as a relatively common lesion [1], predominantly associated with congenital heart disease, perinatal asphyxia, coronary artery abnormalities and sepsis. IACI is an extremely rare disease and so, myocardial infarction in a newborn with IACI, especially if the infarction is massive as in the present case, is exceedingly rare.

In conclusion, our case underlines the relevance of myocardial necrosis and infarction as a consequence of arterial calcification in patients affected by IACI.

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ABS 28

VITAMIN D STATUS AND TYPE OF FEEDING IN A GROUP OF 50 UNSUPPLEMENTED INFANTS (1 MONTH – 2 YEARS)

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BACKGROUND

Vitamin D is a key hormone in the regulation of calcium and phosphorus metabolism. Hypovitaminosis D is widespread in children in Europe [1] but data on Italian infants are scarce. A sufficient vitamin D status should be warranted during childhood, particularly during the first two years of age when growth velocity is high [1, 2]. Breastfeeding is a known risk factor for hypovitaminosis and vitamin D deficiency in infancy [3]. The aim of the study was to evaluate vitamin D status and the role of the type of feeding in a group of unsupplemented Italian infants.

METHODS

We evaluated 50 children (males = 35, mean age 1.1 years, range 0.1-2.0) admitted at the Pediatric Unit, Department of Pediatrics, S. Chiara University-Hospital, University of Pisa, Italy between February 2011 and October 2012 for pathological conditions not related to vitamin D metabolism. None of the infants was taking vitamin D supplementation at the time of enrollment. Serum 25-hydroxyvitamin D (25-OH-D)levels were evaluated in all children by radioimmunoassay (25-OH-D^{125}I RIA Kit, DiaSorin). Vitamin D status was defined as follows: severe deficiency = 25-OH-D < 10.0 ng/ml; deficiency = 25-OH-D < 20.0 ng/ml; insufficiency = 20.0-29.9 ng/ml;

sufficiency = 25-OH-D ≥ 30.0 ng/ml; hypovitaminosis = 25-OH-D < 30.0 ng/ml. The type of feeding (breastfeeding/formula feeding) as reported by parents was investigated as a determinant of vitamin D status. Statistics were carried out using JMP 9.0 Software and non-parametric tests (Wilcoxon, Kruskal-Wallis) or chi-squared test.

RESULTS

The median serum 25-OH-D level was 15.3 ng/ml (range = 0.0-48.0 ng/ml), with a prevalence of vitamin D deficiency, insufficiency, and sufficiency of 66.0% (n = 33), 30.0% (n = 15), and 4.0% (n = 2), respectively. 32.0% (n = 16) of all children showed severe vitamin D deficiency.

Information on the type of feeding was available for 34 infants (median 25-OH-D level = 15.5 ng/ml, range = 0.0-29.1). The type of feeding significantly influenced vitamin D status: 25-OH-D levels were significantly lower in breastfed infants (n = 21/34, median 25-OH-D = 15.1 ng/ml) than in formula-fed infants (n = 13/34, median 25-OH-D = 21.0 ng/ml; p = 0.049 by Wilcoxon test). Breastfed infants were at a 5-times and 7-times higher risk of being vitamin D deficient and severely vitamin D deficient than formula-fed infants (OR = 4.95, confidence interval = 1.26-23.15, p = 0.035; OR = 7.38, confidence interval = 0.80-68.12, p = 0.050). None of the infants in this subgroup showed sufficient 25-OH-D levels.

CONCLUSIONS

Hypovitaminosis was highly prevalent in a group of 50 Italian infants who were not receiving vitamin D supplementation. The type of feeding influenced 25-OH-D levels and breastfed infants were at a 5-times higher risk of vitamin D deficiency and at a 7-times higher risk of severe vitamin D deficiency than formula-fed infants. Formula-fed infants had higher but nevertheless suboptimal 25-OH-D levels. These results were obtained in hospitalized children and may not be representative of the healthy infants population. Nevertheless, vitamin D supplementation should be provided in infants to guarantee an optimal vitamin D status in this age group, independently of the type of feeding.

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ABS 29

MULTIDISCIPLINARY CARE TO ACHIEVE HUMANIZATION IN PREGNANCY AT HIGH RISK OF PRETERM BIRTH

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INTRODUCTION

The word "humanization"derives from the definition of human health proposed by the World Health Organization. It means the process of centralization of the person with its values, its identity, its dignity, its needs and rights to ensure health and safety.

Preterm birth still represents the first cause of perinatal mortality and morbidity.

Many efforts are worldwide made to reduce preterm births and to improve neonatal outcomes.

Recent studies are focusing not only on survival rates or short term adverse outcomes associated to the most common complications (intra-ventricular haemorrhage, necrotizing enterocolitis, sepsis, respiratory distress, cerebral palsy, etc.) but also on long term outcomes and neurologic and cognitive development.

We consider of great relevance taking into account feelings, beliefs and values of each woman during hospitalization and healthcare.

We propose an integrated approach to offer appropriate treatment and medical management associated with psychological support and multidisciplinary care involving obstetricians, midwives, psychologist, neonatologist and Clinical Ethics and Medical Humanities (CEMH) consultant.

PATIENTS AND METHODS

Patients are recruited among pregnant women admitted to our High Risk Pregnancy Ward at Azienda Ospedaliero Universitaria of Cagliari at risk of preterm birth.

Each one of them receives:

- Care and treatment by caregivers who are already specifically trained but also receiving a continuous on-the-job training,

- Personalized treatment and timing of birth,
- Written tailored treatment management plan, exhaustively explained, based on each one's clinical condition;
- Psychological support during hospitalization, before and after delivery;
- Counselling about individualized risk of prematurity and both short and long term possible adverse outcomes by obstetricians together with neonatologists and the CEMH consultant.

To generate data pregnant women involved in the study will be asked to give a first psychological interview at the first meeting with the psychologist, a second one later, during hospitalization and a third in the postnatal period during premature baby hospitalization to neonatal intensive care unit (NICU).

PRELIMINARY RESULTS

Preliminary data show that this approach seems to improve the compliance at prolonged hospitalization and to reinforce the therapeutic alliance not only during pregnancy but even later during preterm newborn admission at NICU.

DISCUSSION

Hospitalization for pregnant women at high risk of spontaneous or iatrogenic preterm delivery (threatened preterm labour, preterm premature rupture of membranes, intrauterine growth restriction, placenta praevia, preeclampsia) can be so traumatic that it may change their life.

The dream of pregnancy is broken. They experiment an extremely stressful event and they meet other women with pregnancy related health problems never imagined before.

Moreover preterm birth may pose some ethical challenge for both healthcare professionals and parents, especially in those cases at risk of extremely high prematurity.

We're strongly convinced of the importance of supporting pregnant women in case of preterm birth and of offering, as much as possible, a chance of a positive experience to each woman and her partner.

The first results of our approach are encouraging and we hope that it may help parents to bring up their baby, improving its affective and cognitive development, even if affected by disabilities.

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ABS 30

AN UNEXPECTED CASE OF GBS EARLY-ONSET MENINGO-SEPSIS

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INTRODUCTION

B Group streptococcus is a gram positive bacteria responsible for early and late onset sepsis in the newborn. Early onset sepsis occurs within the first week of life, while late onset sepsis occurs between the first week and the third month of life. The main risk factor for the early onset form is represented by maternal colonization of vaginal-rectal mucosa (vertical transmission in the birth call during the delivery). A positive GBS (S. Agalactiae) vaginal-rectal swab occurs in about 30% of pregnant women. Since the state of maternal colonization changes during the pregnancy the execution of vaginal and rectal swab is recommended at 35 and 37 week of gestational age (GA). Preterm birth (GA < 37 week), prolonged rupture of membranes (> 12 hours), chorioamnionitis, maternal fever (> 38 °C) represents other risk factors for early onset GBS sepsis in the newborn. The intra-partum antibiotic prophylaxis with Ampicillin is actually the only therapeutic option to prevent GBS infection in vaginal-rectal swab positive pregnant women and has led to a reduction of 80% cases of neonatal infection.

CASE-REPORT

M. (39 weeks, 3,360 g), is a second son born by natural childbirth. Apgar scores were 10-10. Pregnancy history was negative for TORCH. Vaginal-rectal swab tests performed at 35 and repetead at 37 weeks of gestation were negative. Nor PROM, neither chorioamnionitis or maternal fever during the labour were referred. The child was discharged from Nursery in good general conditions at 3 days of life.

Nevertheless the day after she was admitted to the Puericulture Division (4th day of life) for eating disorder, vomiting and seizure episodes.

At the medical examination she presented spoiled general condition, marbled skin, moaning crying, spleen mood, tremors and hypotonia. Temperature was 37.5°C. Normal the bregmatic fontanelle. The baby presented several clinical seizure episodes, some of which were registered at the EEG. She suddenly started therapy with Midazolam, then passed to barbiturate. Routine blood test and coltures were performed, together with cerebrospinal fluid colture. A triple empirical antibiotic therapy was started with Ampicillin, Gentamicin and Ceftadizime. The day after cerebral-MRI was performed and showed: multiple intersecting areas of ischemic nature into the basal and paraventricular anteriors ganglia and bilateral ventriculitis. Again several seizure episodes at the EEG were registered. Meanwhile blood colture and liquor, faringeal and nasal specimens, resulted positive for GBS. A GBS meningitis and sepsis was diagnosed and therapy with Ampicillin was implemented at high doses (400 mg/kg/die), while Gentamicin and later on Ceftazidime were interrupted. In 5 days we observed a clinical improvement with better general conditions, reduction in number of seizures, no fever, and a restart in feeding. The control cerebral MRI showed: evolution toward cavitation of the previous restricted loci with bilateral and symmetrical pattern. Slight perihemispheric layers. Light enlargement of the lateral ventricles, no high pressure.

She was discharged after 24 days, in good general conditions and put into a follow-up program. At 1 and 3 months distance controls she showed normal clinical features, normal growth, appropriate psychological motor skills.

CONCLUSIONS

Even though the prevention strategy based on execution of vaginal and rectal swab at 35 and 37 weeks of gestation and intra partum antibiotical prophylaxis (in vaginal-rectal swab positive women or with other maternal risk factors) has led to a significant reduction in GBS sepsis, unfortunately early onset cases are still diagnosed. This especially occurs in newborns from vaginal-rectal swab negative women even in absence of risk factor. The causes should be related to undetected maternal GBS infection due to lack of precision of laboratory tests or to colonization after performing the vaginal-rectal swab test. The clinical practice plays a pivotal role especially in the first 48 hours of life, to detect early signs of GBS infections and to start the antibiotic therapy. The child, though, can develop the disease even after being discharged at home in good clinical conditions. Therefore, being time of action vital, it becomes essential the watchful eye of the parents in detecting any clinical changes in their baby, so that when necessary a medical examination is performed and an antibiotic therapy is started as soon as possible.

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ABS 31

RELEVANT HYSTOLOGICAL ALTERATIONS IN NEONATAL KIDNEY: 5 CASE REPORTS

C. Loddo[1], M. Puddu[1], S. Puddu[1], C. Gerosa[2], D. Fanni[2], C. Fanni[1], G. Ottonello[1], E. Trudu[1], P. Van Eyken[3], V. Fanos[1], G. Faa[2]

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INTRODUCTION

Many causes of kidney damage in the newborn can play in the immediate perinatal period (just before or just after birth), such as perinatal asphyxia, infections, drugs (especially antibiotics) or before birth, such as drugs during pregnancy, antenatal infections, intrauterine growth retardation (IUGR)-correlated events [1].

OBJECTIVE

The aim of our study is the description of relevant renal histological alterations in 5 infants ≥ 32 weeks of gestational age (GA) (who are just a part of a wider case record used for other scientific purposes), deceased in a period between 7 hours and 2 months of age, and their subsequent correlation with the possible exposure to harmful factors during or at the end of the nephrogenetic process.

CASE REPORTS

Fig. 1: Expansion of glomerular loops (**a**) and thrombosis of the afferent artheriole (**b**) in a 39 weeks-old male died 8 hours after birth for a severe perinatal asphyxia associated with multiple organ failure and with meconium aspiration syndrome.

Fig. 2: Degeneration of glomeruli with polycystic glomerulus aspects characterized by dilated and

often confluent capillaries (**a**), mixed with normal glomeruli in a 38 weeks-old female died 16 hours after birth for a severe perinatal asphyxia associated with multiple organ failure.

In the two at term infants previously described, the observed histological alterations may be attributed to the severe perinatal asphyxia associated with multiple organ failure, resulting in an ischemic damage of nephrons. In fact, the association between perinatal asphyxia [2] and severe impairment of renal parameters is well known. These laboratory abnormalities (especially those affecting the glomerulus) are likely to reflect renal histological abnormalities, even if the few literature data on this subject.

Fig. 3: Severe hemorrhages of the cortex, presence of multiple glomeruli with dismorfisms, dilated and congested glomerular loops (**a**) in a 34 weeks-old male, died 7 hours after birth for a severe respiratory distress due to pulmonary hemorrhage in the context of a disseminated intravascular coagulation (DIC).

Fig. 4: Enlarged and cystic glomeruli, with frequent hyaline cylinders, microthrombosis of the afferent arteriole, marked endothelial damage (**a**), glomerular thrombosis and medullary edema in a 33 weeks old female, diagnosed with a severe dilatative cardiomyopathy two months after delivery, who died 14 hours after her admission in NICU.

In the two cases described in **Fig. 3** and **Fig. 4**, in which glomerulogenesis was still active, histological alterations detected may be included within the group of glomerular dysmorphisms described by Rodriguez et al., who observed the presence of cystic dilation of Bowman's capsule in a group of preterm survived ≥ 40 days after birth, in particular those in which it was associated with a condition of kidney failure. The above-mentioned alterations may result in a long-term numerical and/or functional deficit of nephrons, with an increased risk of cardiovascular and renal disease [4]. Similarly, another study by Sutherland et al. noted, in renal histology of a group of preterm infants with postnatal survival between 2 and 68 days, the presence of a percentage from 0 to 13.7% of glomeruli with altered morphology at the level of the outer cortex and characterized by a primitive stage of development (fully formed glomeruli with at least half of the glomerular tuft lined with podocytes) [5].

Fig. 5: Abundant subcortical apoptotic elements (a), many subcortical eosinophils (b), intraglomerular lymphocytes (c) and eosinophils (b), cortical and medullary edema in a 32 weeks old female, died 16 hours after birth for pulmonary hemorrhage. The genesis of the numerous infiltrating lymphocytes and eosinophils is difficult to understand; we may assume, on the basis of the observation of a bronchial aspirate and a blood culture positive for *H. influenzae*, that it may be linked to the onset of an acute post-infectious glomerulonephritis, which could not be clinically evident given the premature exitus of the newborn.

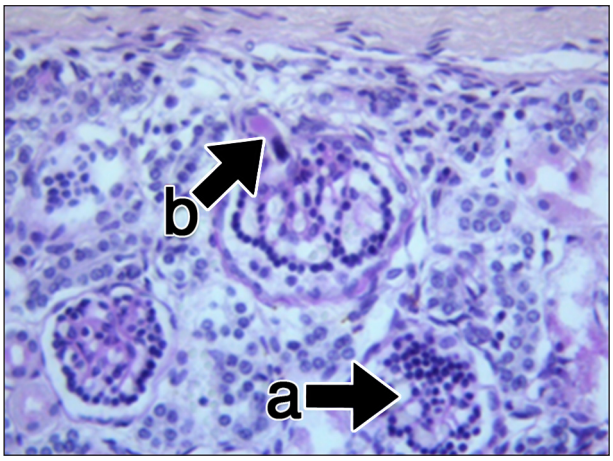


Figure 1.

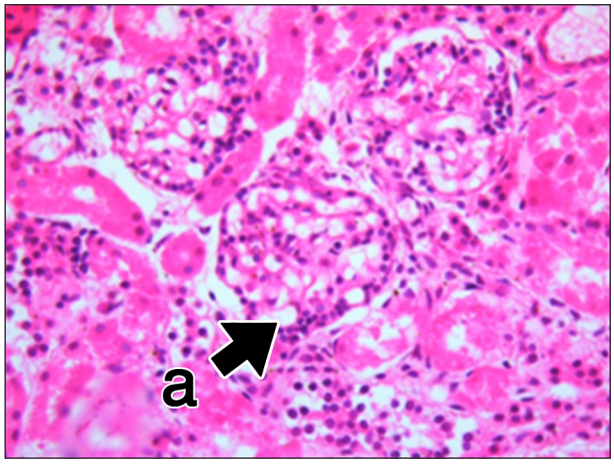
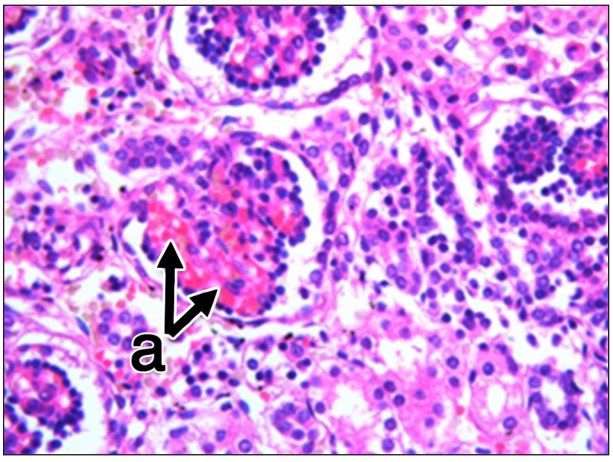


Figure 2.



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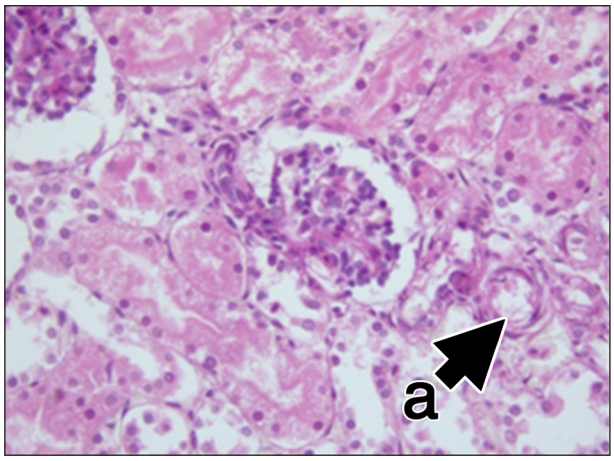

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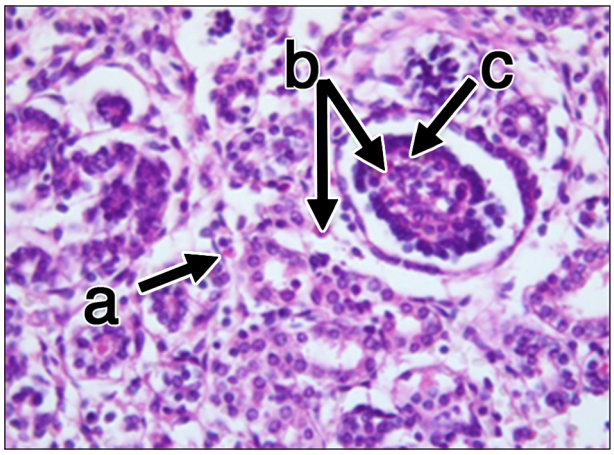

Figure 5.

CONCLUSIONS

The histological study of the kidneys of patients who died for various causes in the neonatal period should be a routine practice for the understanding of the pathological processes that occur at this stage, but also for the prediction of long-term kidney damage following exposure to harmful insults to the kidney during antenatal and perinatal period [6].

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ABS 32

VARIABILITY IN DRUG USE AMONG NEWBORNS ADMITTED TO NICUs: A PROPOSAL FOR AN EUROPEAN MULTICENTRE STUDY

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BACKGROUND

A great variability in the therapies employed by NICUs is a widespread phenomenon observed both within and between countries. Some authors underlined this aspect of variability in drug use among NICUs by reporting data on the treatment of neonatal sepsis [1] and PDA [2, 3] throughout Europe. Given the unique characteristics of neonatal population, the use of drugs on an individual basis should be justified in some situations. However, other factors could contribute to this variability, such as the lack of evidence-based guidelines and the common use of drugs in an off-label manner, with a higher risk of therapeutic errors and adverse reactions [4-6].

PROPOSAL OF AN EUROPEAN MULTICENTER STUDY

These differences in clinical practices between NICUs need to be addressed at a European level, therefore a multicentre study involving different NICUs of European countries could be useful to harmonize drug use in the neonate.

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ABS 33

GASTROINTESTINAL DISORDERS IN THE NEWBORN: PROPOSAL OF A PRACTICAL FLOW-CHART

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At the end of the '70s, Bell's classification of NEC [1] grouped, under a single denomination, various gastrointestinal disorders resulting in perforation. The fundamental difference between Bell's classification and Gordon's, published in 2007, is that the first is a staging classification, the second one is an etiological classification [2].

Gordon's concept of ANID (acquired neonatal intestinal disease) allows to formulate etiological hypotheses with reflection on prognosis and viable strategies to prevent perforation. The ANIDs do not necessarily lead to NEC. The premature infants suffer from inadequacies and environmental variables that justify the progression of the disease towards the ileum and the perforation, whilst the same does not occur for term infants, unless a major hypoxic-ischemic injury concurs.

The disease, therefore, requires different strategies for prevention and treatment [3]. With the exception of spontaneous intestinal perforation (SIP) [2, 4], and the meconium disease [5], we can assume for ANID a two stages path: an initial insult, hypoxic-ischemic or infectious, usually in the uterus, which corresponds to an impaired capacity of absorption and digestion [6]. It is caused by some food intolerance, which we can prevent progressing. Many strategies have been put in place for the purpose of avoiding the second step causing a NEC: preventing infections, the decrease of antibiotic prophylaxis to a minimum, the gradual introduction of food, preferably with breast milk [7], the probiotics [8]. We propose here a flow chart useful in daily clinical practice (**Fig. 1**).

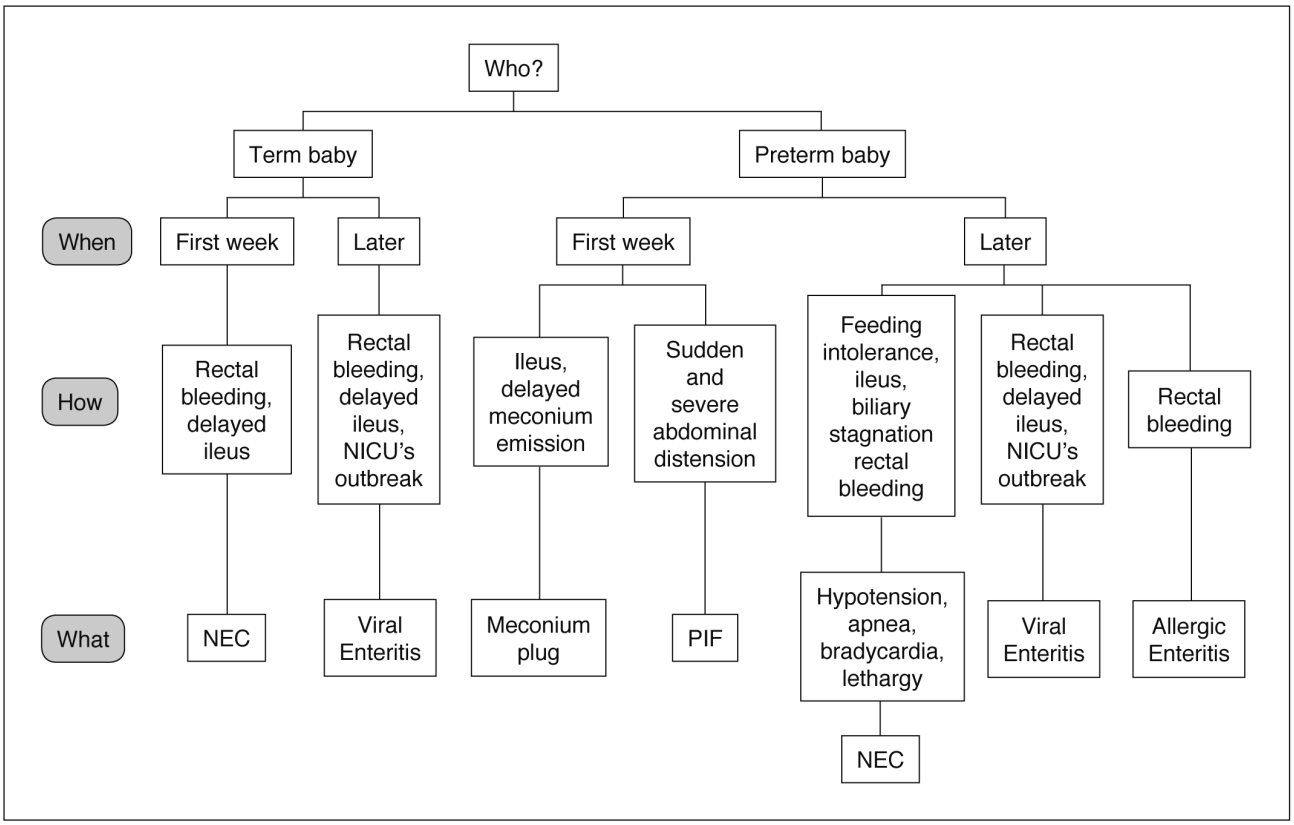

Figure 1. A practical flow-chart.

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ABS 34

SUDDEN INFANT DEATH SYNDROME AND THE RIGHT SLEEP POSITION: AN IRRATIONAL INFORMATION STRATEGY ON A VERY SERIOUS ISSUE

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INTRODUCTION

The "Back to Sleep" campaign in the early 1990s has led to decreased number of deaths from sudden infant death syndrome (SIDS).

AIM

To investigate the status of parental information regarding the right sleep position of infants in the Greek population.

MATERIAL AND METHOD

During the period 2008-2012 in a private provincial pediatric praxis, a multiple-choice questionnaire about the SIDS was filled in, by the parents. Analysis was performed using SPSS-16 and chi-square test. Statistical significance was set at $p < 0.05$.

Results

In total 647 questionnaires were answered by parents of neonates and infants with a mean age of 1.7 months (SD 1.92). The majority (54.9%) was born in maternity hospitals of the public sector. Instructions were given by a pediatrician/ neonatologist to 41.4% and by midwifes to 29.5% of the parents. Only 18.5% of parents (N = 120) mentioned that they were informed about the right sleep position (supine), 28.9% (N = 187) that they were not informed at all about the right sleep position and 52.6% (N = 340) that they were wrongly informed (N = 338 lateral, N = 2 prone) ($p < 0.001$).

The majority of parents (60.6%) placed their infants prone or lateral, while only the remaining 39.4% used the supine position. The vast majority of the parents (83.3%) who were informed that the right sleep position is the supine acted so, while the 64.7% and the 73.8% % of those who were not informed or informed wrongly respectively, used a wrong sleep position. Overall 94.9% of parents who finally used prone or lateral as the right sleep position, acted so after being wrongly or not informed ($p < 0.001$).

CONCLUSIONS

Guidelines given to parents concerning supine as the right sleep position for infants, are mainly either wrong or incomplete. This seems to lead to errors in everyday practice. We should strongly consider a campaign about the international issued guidelines addressed both to parents and healthcare professionals in order to achieve lower death rates from SIDS.

ABS 35

ATTENUATION MEASUREMENTS OF INFANT INCUBATORS IN RADIOLOGICAL PRACTICE

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INTRODUCTION

In a neonatal intensive care unit a frequent radiographic evaluation is often needed. This involves exposure to ionizing radiation whose biological effects can be especially problematic for

premature infants, due to their intrinsic sensitivity to environmental and iatrogenic detriment. The minimization of the dose to the patient, while maintaining a satisfactory quality of the image is a fundamental aspect [1].

AIM

The aim of this work was to test the characteristics of three types of incubators used in the Neonatal Intensive Care Unit (NICU) of the AOU of Cagliari. In particular we wanted to assess the variation of the attenuation strength of the various components such as cassette-holder, mats and scale, as a function of different exposure parameters [2]. In the radiological practice the image receptor (imaging plate) is placed in an incubator housing located under the tray. On the tray there is a soft mattress on which the infant lies. Depending on the model of the incubator, a further support for the scale can also be present. The radiant beam must therefore cross the cover of the incubator, the mat, the tray and, possibly, the support [3].

The attenuating characteristics of each component have an impact on both the quality of the image and on the dose to the patient. In fact, in order to balance a worsening in the image quality, the exposure parameters are often increased, with a consequent increase of the dose [4].

MATERIALS AND METHODS

The characteristics of the three types of incubators present in the NICU are shown in **Tab. 1**.

All measurements were performed with a mobile X-ray unit type MOBILETT Plus HP (SIEMENS). A solid-state detector (semiconductor photodiode model RTI 'Piranha Dose Probe"), placed at the center of the cassette holder was used to measure the attenuation of the X-ray beam. The distance between the X-ray source and the detector was set at 100 cm; the field size was 5cm x 5cm and the voltage (kV) and tube load (mAs) were varied under the following operating conditions:

1. measure of the attenuation of the cover only (A);
2. measure the attenuation of the cover plus the tray (B);
3. measure the attenuation of the cover plus the tray plus the mattress (C);
4. measure the attenuation of the cover plus the tray plus the mattress plus the support of the scale (D) (only for the incubator with support scale).

Table 1. Characteristics of the incubators.

Incubators	Accessories
(1)	Cassette holder
(2)	Cassette holder + scale support + scale
(3)	Cassette holder + scale

Table 2. Attenuation measurement for 2.5 mAs.

Operating conditions	kV	Attenuation of incubator (1)	Attenuation of incubator (2)	Attenuation of incubator (3)
A)	55	15.7%	15.7%	12.5%
	60	14.4%	14.4%	11.7%
	66	14.2%	14.2%	10.9%
	70	14.3%	14.3%	10.7%
B)	55	24.4%	21.8%	19.2%
	60	22.3%	18.4%	16.1%
	66	22.8%	19.0%	17.2%
	70	22.8%	19.3%	16.8%
C)	55	29.9%	30.0%	25.0%
	60	27.3%	26.4%	22.1%
	66	27.7%	26.7%	23.0%
	70	27.2%	26.3%	22.5%
D)	55		35.6%	
	60		32.4%	
	66		32.3%	
	70		31.9%	

Table 3. Attenuation measurement for 5 mAs.

Operating conditions	kV	Attenuation of incubator (1)	Attenuation of incubator (2)	Attenuation of incubator (3)
A)	55	15.0%	15.0%	11.2%
	60	14.2%	14.2%	10.3%
	66	14.1%	14.2%	9.9%
	70	14.5%	14.5%	10.2%
B)	55	23.9%	20.8%	17.8%
	60	22.5%	18.6%	16.4%
	66	22.7%	18.7%	16.8%
	70	22.4%	18.8%	16.5%
C)	55	29.6%	29.0%	24.3%
	60	27.6%	26.8%	22.3%
	66	27.5%	26.5%	22.3%
	70	27.0%	26.3%	22.4%
D)	55		34.9%	
	60		32.6%	
	66		31.9%	
	70		31.7%	

RESULTS AND CONCLUSIONS

In **Tab. 2** and **Tab. 3** the different attenuation values for the different layers, calculated as a percentage with respect to the measurements performed in air, are shown. In **Tab. 2** the data refer to a tube load of 2.5 mAs and in **Tab. 3** to a tube load of 5.0 mAs. The results show that the attenuation of the incubators is not negligible

and that, in order to get a good image quality, the radiological exposure values (kV, mAs), must be increased leading to an increased dose to the patient [5].

Since it is known that the radiosensitivity of children is very high, it would be desirable to raise awareness of manufacturing companies on the possibility of reducing the number of layers and to use materials with lower attenuation.

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ABS 36

IN VITRO KIDNEY EMBRYONIC CELL PROLIFERATION DURING INDOMETHACIN AND IBUPROFEN ADMINISTRATION

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INTRODUCTION

The kidney is particularly sensible to drugs, in particular during the neonatal period, when the impact of drugs on normal embryonic kidney growth and development may influence renal function not only during pregnancy but also after birth.

Indomethacin and ibuprofen are two drugs with a potentially nephrotoxic risk commonly used in neonates in Neonatal Intensive Care Unit (NICU) centers. The effect of these two drugs on the developing human kidney is not well known. A study in preterm baboons showed that ibuprofen is able to induce early cessation of nephrogenesis [1]. Recently it was suggested that these drugs might cause not only a block but even a derangement of nephrogenesis, giving raise to abortive ad maldeveloped kidney [2].

MATERIALS AND METHODS

In this work we used an embryonic kidney cell line as an in vitro experimental model in order to study a possible effect of ibuprofen and indomethacin in the normal rate of cell proliferation. Commercial human embrional kidney cell line 293T (ICLC HTL04001), were obtained from the Istituto Nazionale per la Ricerca sul Cancro c/o CBA (ICLC, Genova). The culture medium used for this purpose was a mixture of DMEM, 10% fetal bovine serum (FBS), 100 units/ml penicillin, 100 mg/ml streptomycin, 2 mM L-Glutamine, 1% non-essential amino acids.

Cells were plated on different glass coverslips at 37°C, 5% CO2. After 24 h of growth, in two different experimental groups drugs were added to the medium; the third group of control was maintained in normal medium. After 1.30 and 24hours all samples were washed with PBS and fixed with acetone for 20 min, air dried for 30 min and then stored at -20°C. Ki67 immunocytochemical analysis was performed using standard procedures.

RESULTS

Fig. 1 show Ki67 immunocytochemical analysis (**A** and **B**) and mitosis (**C** and **D**) in 293T kidney embryonic cells with (**B** and **D**) and without (**A** and **C**) drugs treatment.

After 24 h of growth with ibuprofen, 293T cell proliferation was similar to that of the control (8% versus 10% of Ki67 positive cells). On the contrary, cells treated with indomethacin for 24 h showed an evident inhibition of cell proliferation (4% versus 10%). When the presence of both drugs was limited to 1 h and half, cell proliferation was not affected.

CONCLUSIONS

In conclusion these preliminary data on kidney embryonic cells exposed to indomethacin (but not to ibuprofen) show an in vitro growth inhibitory effect suggesting a possible correlation with the block or the derangement of nephrogenesis previously described in vivo.

Therefore this in vitro model of kidney embryonic cells may be an useful experimental model for nephrogenesis studies on the influence of drugs utilized in therapy of newborns in NICU centers.

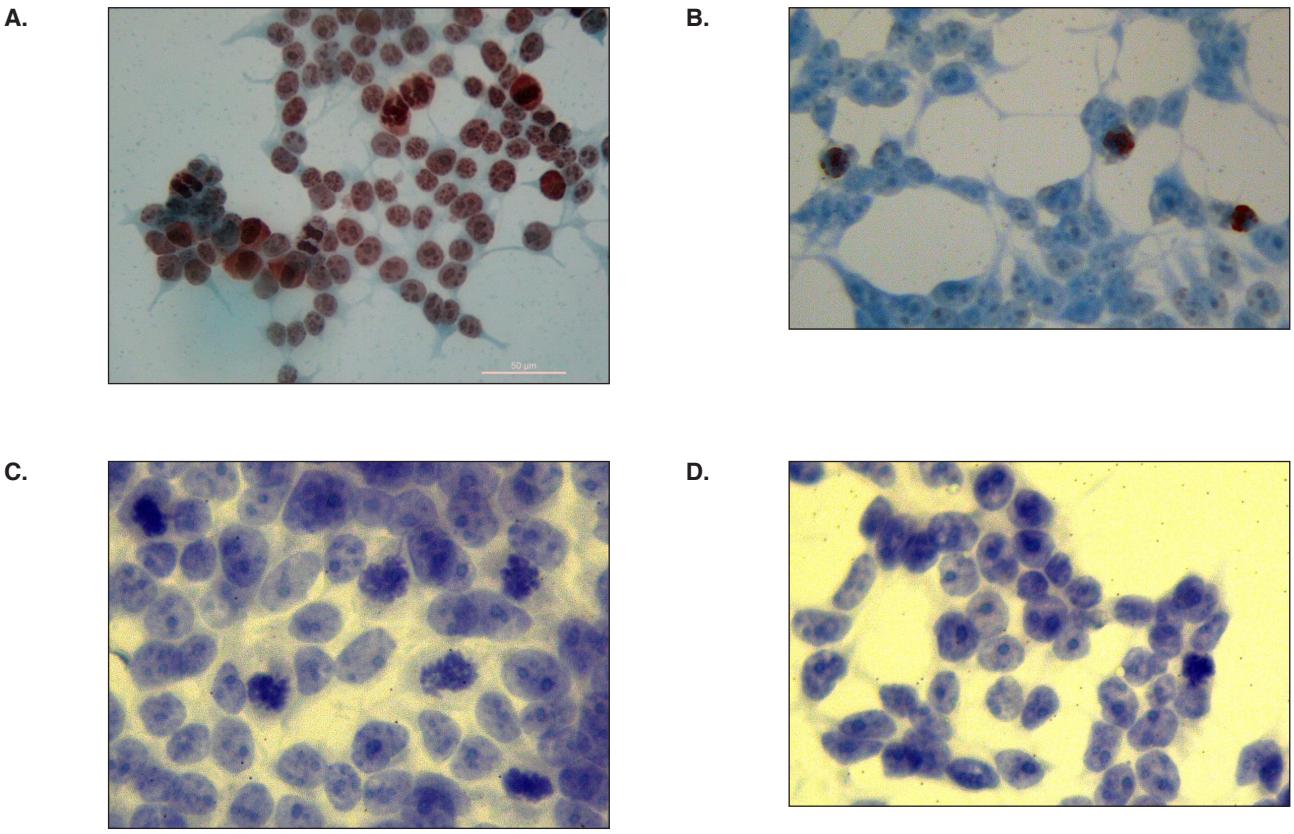

Figure 1. Ki67 immunocytochemical analysis (**A** and **B**) and mitosis (**C** and **D**) in 293T kidney embryonic cells with (**B** and **D**) and without (**A** and **C**) drugs treatment.

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ABS 37

CONGENITAL SYPHILIS IN BRAZIL: A PREVENTIVE CHALLENGE

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INTRODUCTION

Syphilis has represented a serious public health problem, particularly in developing countries. It is estimated that every year there are more than 12 million new infections by Treponema pallidum, of which over two million occur in pregnant women and the vertical transmission reaches 85% in non-treated pregnancies.

OBJECTIVE

To analyse the quality of treatment of pregnant women with syphilis diagnosed in the prenatal care and its impact on the incidence of congenital syphilis at a Public Maternity in Rio de Janeiro, Brazil.

METHODS

This retrospective study collected information on diagnosis by VDRL test and treatment of syphilis in pregnant women during prenatal care, the number of pregnant women with positive VDRL test at delivery and reported cases of congenital syphilis at a public maternity in Rio de Janeiro, in the period 2008-2012.

RESULTS

Among the 10,433 births, 292 (2.79%) of the pregnants had positive VDRL test and only 87 (29.7%) of these were followed up and treated properly in prenatal care. 166 (1.59%) cases of congenital syphilis, with a coefficient of 15.9/1,000 births, were reported.

CONCLUSION

The data show an alarming difficulty in care and treatment of pregnant women with syphilis, reflected in a high incidence of congenital syphilis. Therefore, a better involvement by health managers and

professionals in maternal and child health becomes imperative to change this scenario.

ABS 38

RELATIONSHIP BETWEEN INFECTIONS AND THE INVASIVE PROCEDURE IN VLBW PREMATURE: THE ROLE OF THE NURSE

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INTRODUCTION

In the last decades the technological and assistance progress in the obstetrical and neonatology fields has led to the birth and survival of premature babies, the VLBW (Very Low Birth Weight) characterized by a birthweight under 1.5 kg.

The functional and physical underdevelopment's characteristics of the preemies obligate their admittance to TIN and an intensive assistance that expose them to an increased danger to contract a hospital-acquired infection.

Among the many nosocomial risk factors linked to the assistance, the umbilical vein catheter (UVC) and central venous catheter (CVC) insertion and management become relevant.

The choice of the UVC insertion and medication types in particular, when UVC is maintained since birth for few days can represent an important prevention factor.

THE ROLE OF THE NURSE

The nurse is the main actor during this delicate assistance phase: he/she is responsible for high-risk infection procedures such as the substitution of the medication and the infusion ways and also for the checking of the insertion site in order to precociously recognize the presence of prognostic factors such as secretions and/or variations in the skin colour tone.

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ABS 39

RIGHT SIDED PULMONARY AGENESIS

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INTRODUCTION

Unilateral pulmonary agenesis is a is a rare congenital anomaly consisting of complete absence of the lung parenchyma, blood vessels as well as bronchia beyond the bifurcation [1]. The malformation occurs in isolation or in association with other anomalies, rarely it is associated with congenital tracheal stenosis [2].The true incidence of this disease is unknown, it occurs in 1 out of 10,000 autopsies [1, 3, 4]. Although the etiology is not entirely known, some cases have been linked to viral infections, deficiency of vitamin A, folic acid and intake of salicylates [5] and chromosomal abnormalities such as the duplication of the distal long arm of chromosome 2 (46, XX, 2p+) [6]. Right sided agenesis has been thought to have a worse prognosis than that of left [7] with death occurring earlier and with increasing frequency.

CASE REPORT

A. (35 weeks, 2,280 g) is a preterm infant born by natural childbirth in a peripheral hospital. Apgar score were 8-9. During pregnancy genital and rectal swab for the detection of a group B streptococcus (GBS) was positive and fetal echocardiography showed dextrocardia in situs solitus without structural heart disease. Within fifteenth minute of life she began to suffer from respiratory distress and consequently was transferred to the Neonatal Intensive Care Unit (NICU).

On admission to the NICU she was cyanotic, dyspnoic, required supplemental oxygen (Fraction of Inspired Oxygen concentration of 40% to achieve levels of Oxygen Saturation SaO2 of 90%) and ventilation with continuous positive airway pressure. Chest auscultation showed decreased breath sound on the right side and muffled heart sounds. Chest X-ray showed opacity at the right side of the chest with herniation of left lung to the right side, the mediastinum and heart were displaced to the right. The echocardiography confirmed dextrocardia with normal atrium and ventricular connections and pointed out a mild pulmonary hypertension and a small patent ductus arteriosus. No other congenital anomalies were identified. Chromosome Analysis, performed to detect abnormalities of the chromosome 2, was normal.

Following repeated apnea crisis associated with stridor together with expiratory dyspnea, the newborn underwent intravenous contrast-enhanced MRI scan of the chest which showed absence of

right lung and hyperexpansion of the contralateral lung (**Fig. 1** and **Fig. 2**). Morever MRI provided a more detailed description of the course of the aortic arch and its position in relation to the respiratory tree. Differently from the normal anatomical situation the hearth was rotated posteriorly and to the right, consequenly the aortic arch went from right to left passing antero-superiorly to the main bronchus of the left lung.

Lastly, since bronchoscopy revealed a severe tracheal stenosis that did not allow the progression of the bronchoscope beyond the 4-4.5 cm from the glottis rhyme, the newborn was sent to a specialized Surgery Unit where underwent tracheoplasty: this intervention performed at 3 months of life was preferred over other interventions like the injection of tissue expander into the affected chest.

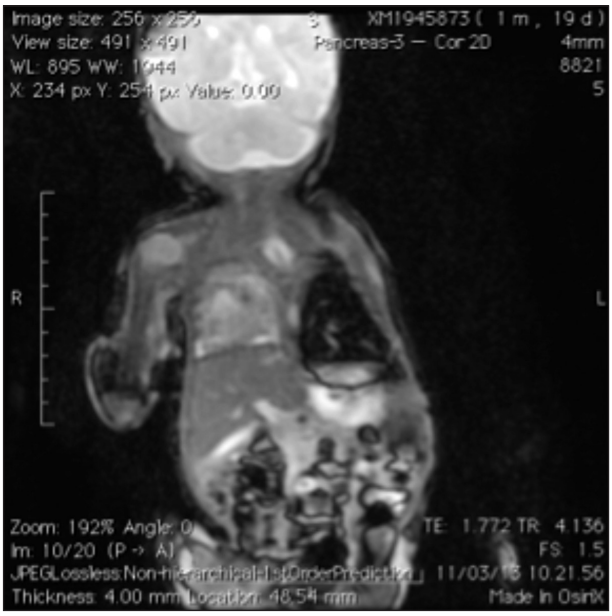

Figure 1. MR frontal image showing right pulmonary agenesis.

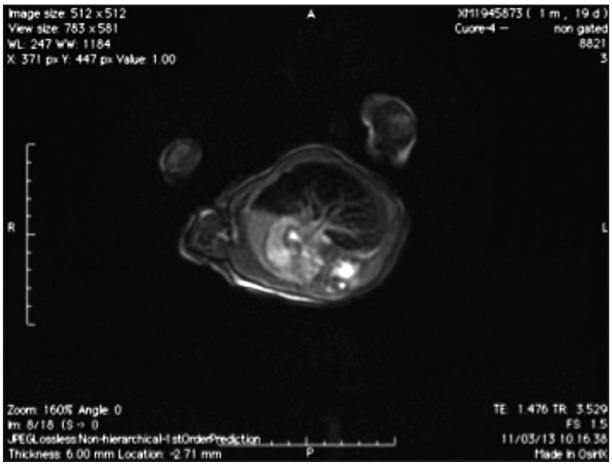

Figure 2. MR axial image showing right pulmonary agenesis.

CONCLUSION

In conclusion, right sided pulmonary agenesis is a very rare and serious condition which faces neonatologists to take delicate decisions.

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ABS 40

ENTERAL NUTRITION IN PRETERM INFANTS: CURRENT PRACTICAL ISSUES FOR THE DAILY PRACTICE

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INTRODUCTION

With improving survival rate and outcomes of extremely premature infants, nutritional practices in preterms are a growing concern for neonatologists. The best management of "the first golden minutes, hours, days, weeks" of a preterm infant's life is vital for its long-term development. Nutritional practices plays a key role in the management of all parameters (thermoregulation, cardiopulmonary support etc.).

Enteral nutrition should be preferred route for nutrition support, but there is no conclusive evidence about most aspects of enteral feeding practices. In a recent international survey, nutritional practices show marked differences in neonatal intensive care units in different countries. These clinical practices are not

largely evidence-based. There is limited evidence on current nutritional practices in preterm infants.

CURRENT PRACTICAL ISSUES ABOUT ENTERAL FEEDING IN PRETERMS

Minimal enteral nutrition

Early initiation of minimal enteral nutrition (MEN) or trophic feeding with very low volume feedings is highly recommended as a supplement to parenteral nutrition in the preterm infants hospitalized in NICU as soon as possible. There is no standardized practice for MEN, but the preterm infants may benefit from small volumes starting very slowly at 0.5-1 ml/kg two or three times a day. Colostrum may be administered in trophic feeds. Current data supports that MEN should be initiated within the first 2 days of life and advanced by 30 ml/kg/day in infants ≥ 1,000 g, but grade of recommendation is weak. Feeding volumes are gradually increased regardless of the gastric residuals or as gastric emptying improves. Since enteral nutrition is often not enough first days of life after birth, parenteral nutrition will be necessary.

Methods of feeding

Tube feeding is the most preferred and safest route in enteral nutrition. The orogastric route is better than the nasogastric one. Because the nasogastric tube increases airway resistance in preterm infants. The orogastric tube may displace more than nasogastric route and causes vagal stimulation.

There are two ways for administration of tube feeding: continuous drip using a pump or intermittent feedings, using gravity drip through a feeding tube. In the intermittent method, prescribed volume is usually given over 10 to 20 minutes every 2 or 3 hours. Intermittent feeding seems to be more physiological than continuous method. A new Cochrane systematic review analysis including 7 trials, involving 511 very low birth weight (VLBW) infants showed that there is no difference in time to reach full enteral feeds between the two feeding methods. Because of the conflicting results of the studies comparing continuous and intermittent bolus feeding, it is difficult to formulate general recommendations regarding the best tube feeding method for premature infants of less than 1,500 grams. The acute complications of tube feeding are reflux and aspiration, gastric perforation, vagal stimulation and bradycardia, as well as nasal erosion or palatal groove in long term period.

In the continuous feeding method, it must be keep in mind that it reduces fat delivery to the infant compared with intermittent bolus methods. If the use of continuous is clinically mandatory, following strategies will prevent the loss of fat. First, the syringe should be oriented with tip upright and be delivered first. Second, the feeding tube should be shortened, thus preventing loss of fat on tubing surfaces. Third, the syringe should be emptied completely at end of the infusion.

Enteral feeding for preterm infants may be administered in gastric or transpyloric tubes. In a meta-analysis of nine studies the two methods in preterm infants, there were no statistically significant differences in the incidence of adverse events (NEC, intestinal perforation, and aspiration pneumonia etc). The routine use of transpyloric feeding is not recommended in preterm infants.

Intermittent bolus feeds may be administered using a syringe to gently push milk into the stomach or using a syringe attached to the tube and allowing drip in gravity. In one small study, it was found higher respiratory rate in push method. To date, there is no sufficient evidence to recommend one of these methods.

During enteral feeding, the use of an umbilical catheter does not increase the risk of NEC.

Clinical monitoring of nutrition

In addition to monitoring of weight, length and occipitofrontal circumference must measured serially. Growth parameters are charted on specific growth curves for premature infants. To achieve targets of growth parameters is required 120 cal/kg/day enterally. The energy requirements of preterm infant may increase in some medical problems (bronchopulmonary dysplasia etc.). The preterm infant's nutritional evaluation includes weight, fluid and nutrient intake daily, length and head circumference weekly and biochemical markers such as Hb, Hct, BUN, Ca and P biweekly.

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ABS 41

ERYTHROPOIETIN ADIMINISTRATION EFFETCS ON HEART IN LANDRACE/LARGE WHITE PIGS EXPOSED TO VENTRICULAR FIBRILLATION

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OBJECTIVE
This study was aimed at evaluating the influence of erythropoietin administration in an experimental animal model of adult pig ventricular fibrillation and resuscitation.
METHODS
Twenty female Landrace/Large-White piglets were initially sedated; anaesthetized, intubated and mechanically ventilated. Right carotid artery and right internal jugular vein were catheterized for continuous measurement of right atrial pressure. After 30-minute stabilization, ventricular fibrillation (VF) was induced *via* a pacing wire forwarded into the right ventricle. Mechanical ventilation and administration of anaesthetics were discontinued simultaneously with the onset of VF and the animals were left untreated for 8 min. Ten of them (experimental group) were randomly treated with a bolus dose of erythropoietin; the other ten piglets received saline placebo (control group). Cardiopulmonary resuscitation (CPR) was activated immediately after erythropoietin administration. After 2 min of CPR, defibrillation was attempted with a 4 J/kg monophasic shock. CPR was resumed for another two minutes after each defibrillation attempt, continuing until return of spontaneous circulation (ROSC) or if asystole/pulseless electrical activity (PEA) occurred. After ROSC, animals were monitored, mechanically ventilated for six hours, extubated, observed for 48 hours and euthanized. At necroscopy, an heart sample from the left ventricle was 10% formalin-fixed, paraffin-embedded and routinely processed. 5-micron thick sections were stained with hematoxylin and eosin, and immunostained for S100B protein. Cardiac sections of treated and control animals were observed blindly by two pathologists (AF, DF) independently.
RESULTS
Histological examination of heart specimens showed the presence of pathological changes in cardiomyocytes and in vascular structures of all animals studied, both in the control and the experimental group. The most relevant lesions detected in cardiomyocytes were edema (69% in the control group versus 64% in the experiment group), wavy fibers (44% versus 53%), necrosis (17% versus 50%), apoptosis (28% versus 33%) and contraction band necrosis (11% versus 6%). The most relevant vascular lesions were endothelial loss and detachment (64% versus 61% and 50% versus 64% respectively), apoptosis (11% in the experimental group) and thrombosis (31% versus 56%). Furthermore we found immunostaining for S100B in all examined cases, both in the experimental and in the control group animals. When the frequency of cardiac changes was compared in control and experimental animals, significant statistical differences between the two groups were restricted to the incidence of cardiomyocyte necrosis, endothelial thrombosis, and to the degree of immunoreactivity for S100B. In particular the incidence of necrosis of cardiomyocytes and thrombosis was higher in the experimental group (17% and 31% versus 50% and 56% respectively), whereas the intensity of S100B expression was higher in control group animals (75% versus 58%).
CONCLUSIONS
Our data confirm that coagulative cardiomyocyte necrosis and thrombosis are the most predictive histological changes of cardiac damage, both in myocytes and in cardiac vessels. Interestingly, these lesions showed a higher incidence in erythropoietin-treated animals suggesting that the administration of erythropoietin was not able to halt cell death of cardiomyocytes, nor endothelial damage progression towards the insurgence of thrombosis. On the contrary, the inverse trend of the S100B protein expression as compared to important and irreversible cardiac changes like necrosis and thrombosis, confirm that S100B at cardiac level should be considered an early protective response to a cardiac insult.

ABS 42

A CASE OF NECROTIZING ENTEROCOLITIS (NEC) IN A FULL-TERM NEWBORN

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INTRODUCTION
NEC is a serious inflammatory disease of the bowel, uncommon in term infants (only 10% of the affected

newborns are full term) [1, 2]. NEC tends to occur in full term babies earlier than in preterm infants and it is associated with splanchnic hypo-perfusion and/or obstruction of the intestine [3]. Often there is a history of placental insufficiency, perinatal asphyxia, polycytemia and congenital heart disease. Differently from premature babies, where the jejunum and ileum are most affected, in the full-term newborn the colon is the preferred site of the disease [4]. NEC is a multi-factorial disease based on the hyper-reaction of the immune system to ischemic, infective insults which are possibly due to enteral feeding and translocation of normal enteric flora.

CLINICAL CASE

A. (38 weeks, 2,040 g) is a second child with intrauterine growth retardation, born by Caesarean section due to breech presentation. Apgar scores were 9-10. Pregnancy history was positive for oligohydramnios and negative for TORCH and TVR. She was admitted to the Puericulture Institute for Low Birth Weight. Blood and instrumental tests were normal. Within the fifth hour of life she began to be fed with formula milk. Suddenly, on the fourth day of life, despite negative CRP and procalcitonin, her clinical condition dramatically worsened. The girl had severe abdominal distension and tenderness associated with macroscopic evidence of blood in the stools. Abdominal ultrasound was performed and showed: portal air, distended bowel, free fluid in the right paracolic and splenic gutter. In addition the newborn had roetgenographic evidence of ileus and widespread colonic pneumatosis. NEC II-III stage was diagnosed and the newborn underwent surgery for total colectomy and terminal ileostomy. Operative details: on exploration there were multiple gangrenous and necrotic patches on the wall of the colon. Primary resection of the affected parts of the bowel with ileostomy was done. NEC was confirmed by histology. A postoperative complication occurred on the 6th day of life when the newborn had blood stools. Necrosis of the ileal loop ileostomy was suspected and the newborn was transferred to the Pediatric Surgery Department in Bambino Gesù Hospital in Rome where stenotic ileostomy was diagnosed and consequently the newborn underwent surgery to remove the stenotic part. As a result of the exams carried out in Rome, MTHFR (C677T) gene was found in homozygosis.

CONCLUSION

The MTHFR gene mutation is associated with thrombophilia. The MTHFR gene mutation is a risk factor in intrauterine growth retardation, miscarriage, late fetal death [5]. There are reports of a higher incidence of thrombophilic risk in selected cases of newborns affected by vascular complications such as IVH, ROP and la NEC. In addition NEC is associated with coagulopathies. Further research is needed in order to clarify whether NEC is brought on by these risk factors [6].

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ABS 43

A PILOT STUDY ON MATERNAL ATTACHMENT: A COMPARISON BETWEEN MOTHERS OF PRETERM BABIES AND MOTHERS OF FULL TERM BABIES

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INTRODUCTION

Maternal attachment is defined as a mother's emotional bond with the infant, including behavioral and emotional levels [1-4]. The early birth and separation of a preterm infant interrupt the mother's antenatal bonding to her child and arouse fear for the infant's safety, compromising the development of the postnatal attachment relationship [5-8].

METHODS

The aim of the present work was to assess the difference between maternal attachment in 54 mothers of preterm infants matched for age (mean:

32.7; SD: 3.38) and socio-economic level with 52 mothers of full-term infants. The quality of maternal attachment was evaluated through the administration of a 20 item adapted form of the Prenatal Attachment Inventory (PAI; [9]).

RESULTS

The performed one-way ANOVA showed that both groups of mothers formed an attachment relationship to their baby; nevertheless, preterm infants mothers resulted different on specific items, displaying a somewhat cautious affective engagement.

CONCLUSIONS

The study gives empirical evidence to the need that professionals working with preterm babies and their families strive to acknowledge parents' feelings and worries for their child in order to improve the quality of mother–infant interaction, therefore supporting their physical and mental health.

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ABS 44

INDIVIDUALIZED FORTIFICATION OF HUMAN MILK IN ELBW: GROWTH VELOCITY IN UTERO IS NOT THE IDEAL TARGET FOR PRETERM INFANTS (23-25 WEEKS GA) AFTER BIRTH

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INTRODUCTION

Human milk is the best food for all neonates; however, in pre-term infants, especially those with a an extremely low birth weight (ELBW), it may lead to insufficient intake of protein and energy. Besides guaranteeing nutrition, its components also have the short and long term effect of providing protection against infection and promoting psychomotor and behavioural development. To improve the nutritional management of pre-term infants ≤ 35 weeks' gestational age, an individualized human milk fortification system based on the analysis of maternal milk is performed in our unit from 2005.

Aim of our study was to evaluate the individualized human milk fortification in ELBW in NICU.

MATERIAL AND METHODS

In a cohort of 14 ELBW preterm neonates with a gestational age comprised between 23-25 weeks, we administered tailored fortification of maternal milk, previously analysed with a dairy infrared method (Milko Scan 93/133, Foss Electric, Denmark). We prospectively followed the growth of 14 ELBW pre-term with a mean gestational age of 31 ± 2.8 weeks (range 25-35 weeks). Newborns were recruited after a good gastrointestinal tolerance and a full enteral feeding. Exclusion criteria were: chromosomal diseases, malformations, gut pathology, renal failure. They received constant volumes of maternal milk between 150 and 170 ml kg–1 day–1; and FM85® (Nestlé) or BMF® (Milupa). The qualitative and quantitative analyses of milk samples were performed twice weekly with the Milko Scan 93/133 by Azienda Latte Arborea. Individualization of fortification was done to reach a protein apport of 3.5-4.0 g/kg/die.

RESULTS

Among the advantages was observed a marked improvement in growth,with a mean daily increase in weight of 15.71 ± 3.27 g/kg/d (range 10.99-21.6 g/kg/d, in the absence of effects on food tolerance or the incidence of necrotizing enterocolitis

However, at discharge only 21.4% of patients had a birth > 10th percentile.

DISCUSSION

In 1998, the American Academy of Pediatrics recommended that preterm neonates should receive sufficient nutrients to enable them to grow at a rate similar to that of foetuses of the same gestational age [1].

Feeding VLBW infants with unsupplemented maternal milk has been associated with delays

in growth and nutritional deficits both during hospitalization and after discharge. The minimum target for growth rate of 15 g/kg/day cannot be reached with the use of unfortified human milk. Our results confirm the importance of proper fortification of human maternal milk. Tailored fortification appears to be the most convenient method currently available for reaching recommended protein content, even in ELBW.

Our study, according with a large multicenter study of the literature, confirms that growth velocity in utero is not the ideal target for extremely preterm infants (23-25 weeks GA) after birth.

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ABS 45

ADOLESCENCE, PREGNANCY AND NEONATAL NURSING CARE FOR ADOLESCENT MOTHERS

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INTRODUCTION

The WHO has estimated that one in five people is a teenager and that teenagers represent about one billion of the world population. According to these studies, the majority of adolescents is healthy but a significant proportion of them develops health problems in adult life due to the unhealthy behaviours they exhibit precisely during adolescence. In particular, unprotected sex and the lack of information are the leading causes of unwanted pregnancies, and each year 15 million adolescent girls give birth to more than 10% of children worldwide. In addition, pregnancy can result in health problems for the mother and the child such as an increased rate of low birth weight or preterm children. Adolescent pregnancy is a complex event that takes place in an evolutionary moment when motherhood is not desired. It makes adolescence fragile; that is why this must be protected, in order for the teenager to reach adulthood in good health. To achieve this, an adolescence-focused nursing care is required.

OBJECTIVES

The object of this research was an investigation into adolescence, teenage pregnancy, and nursing care for adolescent mothers and the connections among these issues.

METHOD

This research involved the nursing care for adolescent mothers investigated through field research and the administration of questionnaires in the following hospital wards: Neonatal Intensive Care Unit, Puericulture Institute and Neonatal Section of University and AOU Cagliari. The questionnaire central theme was to assess what are the nurse' s skills necessary to approach to a teenage mother and what the main requirements of a teenage pregnancy are.

STUDY SAMPLE

The sample included 70 nurses of three neonatal units, who have worked on average for 14 years, 10 of which in neonatal units. 48 nurses and 10 pediatric nurses responded to the whole questionnaire.

CONCLUSIONS

The research demonstrated that the majority of nurses who took part in the survey had rarely received any training on adolescent mothers and knew little about the local services for teenagers. However, 60 nurses out of 70 expressed a keen interest in specific training and study sessions on the subjects of the care for adolescents mothers and teenage pregnancy. It also became evident that effective communication, listening skills, knowledge of the problems of adolescence are considered essential in the approach to adolescent mothers.

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ABS 46

MATERNAL PSYCHOLOGICAL HEALTH AND SOCIAL SUPPORT IN THE CONTEXT OF PRETERM BIRTH

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BACKGROUND

Transactional developmental theory [1] posits that development is a result of a complex interplay among child characteristics, family relationships and economic, social and community factors. Preterm birth is a psychologically distressing situation to mothers of preterm infants that needs to consider both the environmental complexity and the specificity of risk [2-4].

METHODS

On such basis, the present work aimed to study maternal psychological functioning and perceived support in the context of preterm births. For such purpose we administered to 46 mothers (mean age: 33.22; SD: 5.45) of preterm infants (corrected age: 6.32 months; SD: 3.14) the following measures: Edinburgh Postnatal Depression Scale (EPDS; [5, 6]); State-Trait Anxiety Inventory (STAI-Y1-2; [7-8]); Parent Stress Index – Short Form (PSI-SF; [9, 10]); Multidimensional Scale of Perceived Social Support (MSPSS; [11, 12]).

RESULTS

Descriptive and correlational analyses showed that the majority of mothers had a good level of psychological health; nevertheless, depressive risk, when present, seemed to be particularly linked both to anxiety and perceived parental stress.

CONCLUSIONS

Although support to all parents of preterm babies would be ideal, results highlight the need that professionals involved in the early intervention field strive to work especially with mothers who show an increased risk for depression and higher levels of perceived parental stress.

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ABS 47

PATIENT EDUCATION IN NEONATOLOGY: AN OPERATIVE PROPOSAL

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INTRODUCTION

One of the critical aspects in neonatology area with high risk hospitalized children is the necessity to perform a protected patient's discharge. Often parents do not possess the skills necessary for optimal care or sometimes live their own role with anxiety and emotion.

PURPOSES

The project was created with the intention of realizing a newborn overall care assistance, ensuring continuity and good home care.

METHODOLOGY

The educative approach chosen has been "Patient Education". Therapeutic education is a gradual process that contains a set of information and awareness activities that are designed to help the patient and his family understanding the disease and the treatment up to acquire the skills of manage conditions disease itself has brought and take of their health status. Therapeutic education is, therefore, a process supported by a method that involves four phases: the first one is to identify the needs of the patient, assessing all its potential and taking into consideration its requirements; the second one is the planning of the educational program by defining the goals to be achieved and the skills to be acquired; the third step is represented by the educational project activation according to the strategy previously chosen; concluding, the fourth and last phase is the final assessment which aims to measure the acquired competences and the short- and long-term changes produced in the behavior of the patient and his family.

MEANS

The pedagogical device chosen was a "Pre-discharge course", which is to be carried out with hospitalized children's parents at Puericulture Institute with at least 3 days of hospitalization. The course is focused on four principal areas:

1. breast-feeding and nutrition;
2. infectious diseases' prevention;
3. psycho-educational;
4. emergency management.

After the course in follow up ambulatory, a check is made which is designed to measure the skills acquired and the changes that these have resulted in the parents' behavior in the short and medium term.

DISCUSSION

The project started in April 2013. The results are, for the moment, very encouraging and the structuring of skills occurred in follow-up are constant; 97% of the sample also expressed appreciation and satisfaction with the initiative. Indeed, the course seems to show its importance and validity in the context of neonatal care. Further developments and details are currently in progress, which involve parents of infants after discharge from the NICU.

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ABS 48

THE NIDCAP: NURSING CARE SEEN THROUGH THE CHILDREN'S EYES

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The NIDCAP, Newborn Individualized Development Care Assessment Program, considers the management of preemies in the incubator exactly as if they were in in the womb, individualizing therapies, customizing and considering the child as a person and not as a patient.

This method allows the evolution of the nursing profession and assistance, obtaining relevant scientific results:

- decrease of mechanical ventilation time;
- less frequency of bronchopulmonary dysplasia and cerebral hemorrhage;
- early start of spontaneous nutrition;
- higher weight gain;
- improvement of the infant - parent relationship;
- more possibilities for the team to assess the infant condition;
- decreased length of hospital stay and costs of care.

That is why is important NIDCAP knowledge and application.

In the nursing care area it allows an assistance defined as relationship-oriented, that is based on relationships and communication, breaking with the more classic one based on the mere execution of tasks (task-oriented).

The poster will illustrate how the nurse solves the infant problems by applying the NIDCAP method. Starting from the knowledge of the five functional subsystems of the infant body, it will show which among the 91 behavioral typical signs he/she manifests. From this observation a card showing the signals of stability (organization, consolation, self-regulation) and instability (disorganization, stress and vacillation) of the infant body in relation to his competences will be filled.

In the next step the caregiver turns the card into a written report that provides information about abilities of the infant, its difficulties, the goals to

reach and the recommendations for care, in order to strengthen his strong points and reduce stress behaviors. Then, the conclusions provided by the observation become the basis for the specific intervention of Developmental-Care addressed to each infant in order to decrease as much as possible the negative effects produced by environment and cares in the NICU.

ABS 49

ESOPHAGEAL PERFORATION IN PRETERM BABY

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We will describe a case of a baby of 26th weeks of gestation. At birth she was intubated in delivery room for respiratory insufficiency, but she needed repeated attempt at endotracheal intubation. Baby was brought to Neonatal Intensive Care Unit and mechanical ventilation was started. The first X-Ray demonstrated a respiratory distress syndrome grade 2, without any other problem. She was extubated in the 3rd day of life and non invasive ventilation was started. She started a minimal enteral feeding on the first day of life, without any problem. At the end of the first week of life she presented a respiratory distress syndrome with increase oxygen need in NCPAP and abdominal distension with gastric residual. A chest X-Ray demonstrated the presence of right-sided pneumothorax with the nasogastric tube deviated from its normal course and with the distal end at the level of the diaphragm. Esophageal perforation is commonly a iatrogenic condition, which occurs rarely in the Neonatal Intensive Care Unit, but is life threatening. Perforation allows bacteria and digestive enzymes to spread into the mediastinum or subphrenic space leading to mediatinitis, empyema, abscesses or sepsis. Signs and symptoms depend on the site of perforation and can vary from respiratory distress, cough, hypersalivation. Diagnosis can be made with AP X-Ray; a finding suggestive of esophageal perforation is an abnormal location of nasogastic tube; it also may reveal pneumothorax or other complications. Contrast studies or endoscopic exams can be performed just in uncertain cases. Treatment is usually conservative, with bowel rest, nil per oral for 14 days and a course of prophylactic broad spectrum antimicrobial agents for 14 days. Surgical treatment is reserved to babies with clinical deterioration, persistence of esophageal leak despite treatment or complications. The outcome in our case was good. After penumothorax was drained, the baby was extubated and remained in NCPAP. Nasogastric tube was inserted after 14 days under radiologic guide and minimal enteral feeding was re-started. She never had any other problem.

ABS 50

A CASE OF POSTNATAL ONSET THALASSEMIA MAJOR

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A 6 month old infant came under our observation for fever and rhinitis. He was born by caesarean section at 35 weeks of GA and hospitalized in the Neonatal Intensive Care Unit (NICU) for prematurity and respiratory distress syndrome. He was admitted in bad general conditions presenting a 4/6 systolic heart murmur on centrum cordis, attributable to perimembranous ventricular septal defect diagnosed during hospitalization in NICU. Skin and mucous appeared intensely pale, inadequately hydrated. Spleen was palpable about 4 cm from costal margin and liver was palpable about 2 cm. Ultrasound examination confirmed hypochondriac organs enlarged size, detecting regular echostructure and echogenicity. Blood tests showed a microcytic anemia (Hb 6.9 g/dl and MCV 68 fl) and neutrophilic leukocytosis. During hospitalization infant general conditions worsened, presenting reactivity reduction and increasing hepatosplenomegaly. Cardiological examination detected signs of heart failure with cardiomegaly and increased pulmonary blood flow. Diuretic therapy and packed red blood cells transfusion were set, with improvement of infant clinical status. Peripheral blood smear showed an important anisopoikilocytosis with target cells and many erythroblasts at various stages of maturation. To prove the hypothesis of a major thalassemia Hb electrophoresis was performed demonstrating the presence of a HbF percentage of 97.5%, and the absence of HbA. Diagnosis was confirmed. The couple had not performed prenatal screening. The aim of this case report is to focus on clinical manifestation of homozygous beta thalassemia in Sardinian population, who are at

high risk (1:4) of having affected children, and the percentage of prenatal diagnosis doesn't cover the whole population. In fact, over the past decades in Sardinia there were more than 80 new diagnosis of homozygous beta-thalassemia, often accompanied by severe complications and bone alterations due to extramedullary erythropoiesis, typical of rare cases of postnatal clinical onset.

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ABS 51

EXTREMELY SEVERE NEONATAL ANAEMIA FROM FETAL-MATERNAL HAEMORRHAGE: A CASE REPORT

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INTRODUCTION

Anaemia of the newly born can be due to acute or chronic loss of foetal cells into maternal circulation. Even if the placenta does act as a barrier between the maternal and foetal circulations, the shunt of small amounts of blood from maternal to foetal circle is considered to be physiological. Although there is no universally accepted data in the literature, the fetal-maternal haemorrhage (FMH) occurs when the amount of foetal blood transfused is > 30 ml, the incidence being estimated to be about 1/300 normal pregnancies. In the most severe cases, with a volume of foetal blood transfused exceeding 150 ml, FMH is defined as massive, with an estimated incidence of 1/5,000 deliveries.

We report a case of massive FMH with important anomalies in the cardiotocographic monitoring and severe neonatal anaemia.

CASE REPORT

A 35 year-old second gravid woman was admitted in our hospital at 38+2 weeks of gestation, due to a decrease in foetal movements over the preceding 3-4 hours. A non stress-test revealed a sinusoidal heart rate pattern. Thus the patient underwent an emergency delivery by caesarean section of a 3,000 g male, with Apgar scores of 5/8/9 at 1/5/10 minutes, respectively. The newborn appeared markedly pale and hypotonic with irregular breathing. He was ventilated with positive pressure with improvement in tone and responsiveness of the respiratory drive, while severe pallor persisted. Cord blood gas analysis showed: pH: 7.15, pCO2 56.4, base excess -9.8. The blood count showed a markedly severe anaemia (Hb 2.6 g/dl, Ht 9.3%). An umbilical venous catheter was positioned then a bolus of saline and bicarbonates were immediately administered, waiting for an emergency blood transfusion. About 20 min after birth the newborn developed respiratory distress, he was intubated and transferred to our neonatal intensive care unit, while receiving a first packed red blood cells transfusion. Once in NICU, the baby received a second packed red blood cells transfusions (20 ml/kg) in the following hours.

Blood gas analysis at two hours of life was normal. Once stabilized, at 16th hour the infant was extubated. Other blood tests were normal, group 0 positive direct Coombs test negative, total bilirubin 62 mmol/L. The cytofluorimetry showed massive presence of foetal blood in the maternal blood. The neonatal haemoglobin values normalized on the second day of life (12.3 g/dl). Brain ultrasound and repeated neurologic evaluation did not reveal any pathological finding. The infant was discharged in good general conditions on the fifth day of life with a follow-up program.

DISCUSSION

The association between FMH and placenta previa, placental abruption, trauma, and amniocentesis is well known, but in many cases, the aetiology remains unknown. Clinically, this condition usually manifests with a marked decrease, up to complete absence, of foetal movements, sinusoidal CTG and foetal hydrops, even though this symptom triad may occur in a late stage of the disease. In most cases the clinical manifestations are scarce, and detection of neonatal severe anaemia or in uterus death may turn out as the only signs of the disease. The foetal tolerance to the FMH is certainly linked to the duration of haemorrhage. A shunt of more than 40% of the blood volume in the maternal circulation is hardly compatible with the survival the newborn.

If the diagnosis of FMH is performed in preterm infants, the intrauterine transfusion is a possible therapeutic choice, but particular attention must be paid to the amount of total blood transfused, which must correct the foetal anaemia without causing a volume overload. Usually 30 ml/Kg in base the estimated foetal weight are not exceeded. This procedure requires a degree of expertise that is not available in many centres.

Despite data of long-term neurological outcome are poor, it is estimated that live births from pregnancies complicated by FMH present about 30% incidence of neurological damage.
We believe that the responsibility of the neonatologist is not only the stabilization of the newborn in the first hours of life, but also the provision of an adequate long-term neurological follow-up.

ABS 52

AN INTEGRATED FOLLOW-UP PATH FOR PRETERM CHILDREN

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BACKGROUND

This report focuses on an outpatient follow-up path for preterm children, which provides for the integration of the physician, the nurse and the psychologist, within the Unit of Neonatology and Neonatal Intensive Therapy. This activity is contextualized within the testing of the Ce.S.I.P.P.U.O. (Experimental Multipurpose Interinstitutional Pediatric University Hospital Center) created through a partnership between the University of Palermo, "Villa Sofia-Cervello" Hospital of Palermo and Private Associations.

MATERIALS AND METHODS

The intervention model confirms the perspective of the developmental monitoring and control not only of the typical followup, also presents some innovative factors, like the co-conduction of the monitoring to focus on not only the areas of development, but also the possible psycho-developmental outcomes of preterm birth. This survey is facilitated by the use of the Griffiths Mental Development Scales.
Another innovative aspect is taking care of parents through an assessment related to different areas of their psychological functioning, which operates as a desensitizing parent's anxiety and stress moderation, that characterize the developmental control of a preterm child. In fact, it is created an appropriate condition to activate the intervention that allows the parent, through the use of narrative tools, to outline future planning hypotheses of the baby.
It should be emphasized that this intervention model provides an anticipation path of the same follow-up in an interview setup with the parental couple, at the time of discharge of the preterm child. This anticipation time (Time 1) as well as the Time 2 (management of follow-up) seem to have specific outcomes and impacts, which, in the case of 50 children involved, must be traced to a functional return about the developmental progressions, that the mother do in the further follow-up.
These progressions seem to be a resource to support children's development.

RESULTS AND CONCLUSIONS

It is, actually, going on a building of a catalog that allows to collect the aspects of this resource, within the Unit of Neonatology.

ABS 53

WHEN BREAST IS NOT THE BEST: A CASE OF SEVERE ALLERGIC PROCTOCOLITIS

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CASE REPORT

A two month old infant came under our observation for emission of a large amount of blood and mucus in stools, accompanied by failure to thrive and consequent reduction in food intake, all symptoms appeared 2 days before hospitalization. He was born at term by vaginal delivery, weight at birth was 3,070 g. He received only breastfeeding. On examination, the infant was in fairly good general conditions, anterior fontanelle was slightly depressed and skin turgescence and elasticity were reduced. He also had mild succulence of lower limbs, with normal remaining physical findings. Blood tests showed a progressive anemia, hypoproteinemia with hypoalbuminemia. Surgical consultation was negative, as well as stool cultures, autoimmunity and infectivological tests. Calprotectin progressively increased and numerous eosinophils in stool samples were found. Abdomen ultrasound documented dilated loops and the presence of semi-fluid material. During the hospitalization he had a progressive weight loss, recurrent vomit and mucus and blood in his stool. The nasogastric tube was placed and the colonoscopic exam was performed, showing an allergic pancolitis, with outbreaks of superficial erosion associated with reactive epithelial hyperplasia, recent hemorrhagic foci and numerous eosinophils in aggregates. The hystological exam documented marked aspects of

active cryptitis and some cryptic abscesses. The first line treatment was the maternal elimination diet, avoiding food containing cow's milk proteins, but later the breastfeeding was discontinued and the enteral nutrition (constituted by a mixture of aminoacids) was set, with a critical improvement of the clinical conditions.

CONCLUSIONS

Approximately 0.5-1% of exclusively breastfed infants develop allergic reactions to cow's milk proteins excreted in the mother's milk. Even if the breastfeeding should be promoted for primary prevention of allergy and breast-fed infants with allergy should be treated by allergen avoidance, in some cases the breastfeeding should also be stopped. Moreover in severe allergic proctocolitis if the hemoglobin or albumin level is significantly low, the use of a hypoallergenic formula may be considered.

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ABS 54

FETAL THROMBOTIC VASCULOPATHY (FTV) AND NEONATAL OUTCOME: THE IMPORTANCE OF HISTOLOGICAL EXAMINATION

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INTRODUCTION

Several fetal placenta vascular lesions, like fetal thrombotic vasculopathy (FTV), are predisposing conditions for obstetric/perinatal disease. FTV is characterized by chorionic plate and stem villi vessels thrombosis, numerous foci of degenerating or avascular villi (> 15 villi).

A retrospective cohort study of 2011 analyzed 24-months outcomes in newborns from mothers with placental FTV. 1,106 placentas were histological examined over 8,000 deliveries on obstetrician/neonatologist request.

RESULTS

- 27 FTV/1,106; incidence: 2.5% (literature: 2%);
- 6 intrauterine fetal death (IUFD) (18-39 w): 5 due to FTV, 1 due to Cornelia De Lange syndrome.

We excluded 2 placentas of twins and 3 gestational diabetes (higher perinatal pathologies).

Neonatal characters of 17 newborns with FTV:

- 2 malformations (Diaphragmatic hernia, Polycystic kidney disease), 1 chromosomal abnormality (trisomy 8);
- 6 IUGR;
- 3 newborns < 32 w, 6 late-preterms;
- 1 dead (Polycystic kidney disease);
- 4 cerebral diseases (2 IVH, 1 hydrocephalus, 1 mild cerebral retardation at 1 year);
- maternal thrombophilia screening, performed only 2/22 patients, was positive (both Factor V Leiden mutation). FTV was developed despite they received early antithrombotic therapy.

CONCLUSIONS

We confirm a high association of FTV with IUFD (6/22, 27%), IUGR (6/16, 37%), preterm (9/16, 56%), SNC-damage (4/16, 25%), and we find new association with chromosomal anomalies and malformations (4/22, 18%).

For these reasons is important placental histology, in explaining clinical diagnosis of neonatal disease and for future pregnancies management. Placental examination could clarify causes of neonatal pathologies or death in legal medicine trials. It is useful routinely placental storage for a week after birth, in order to obtain histological examination in case of complications.

If FTV is present we propose to perform maternal/neonatal thrombophilia, autoimmunity screening, as well as neonatal karyotype.

ABS 55

SURVEILLANCE OF FUNGAL COLONIZATIONS IN SURGICAL NEONATES IN NEONATAL INTENSIVE CARE UNIT

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INTRODUCTION

Invasive fungal infections are the third most common cause of late-onset infections in Neonatal

Intensive Care Units, particularly among neonates born with birth weight < 1,000 g and gestational age < 28 w. In most cases transmission occurs horizontally, through frequent contacts with healthcare workers. Hand washing is therefore the most important preventive procedure.
Other risk factors have been identified: prior antibiotic exposure, presence of a central line, endotracheal intubation, prior fungal colonization and major surgical procedures.
C. Albicans is the predominant specie, even if infections due to *C. Parapsilosis* have increased in the last years.

AIM OF THE STUDY

To evaluate the epidemiology and timing of colonization by *Candida spp.* among surgical neonates and the efficacy of antifungal prophylaxis.

METHODS

Between November 2012 and April 2013 we carried out an active surveillance program of fungal colonization in surgical neonates. We also planned prophylactic administration of fluconazole to prevent fungal colonization and invasive fungal infection in NICU. We enrolled all neonates that underwent abdominal or thoracic surgery. At admission in our unit we obtained rectal swab, auricular swab, nasopharyngeal swab/endotracheal tube aspirate and gastric aspirate from all patients. Before entering the operating room rectal swab, nasopharyngeal swab/endotracheal tube aspirate and gastric aspirate were repeated. Surveillance cultures (rectal swab, nasopharyngeal swab/endotracheal tube aspirate and gastric aspirate) were performed 48-72 hours after surgery and then once weekly. Prophylaxis with fluconazole 3 mg/kg/48h was administered for 21 days after surgery.

RESULTS

14 surgical neonates have been admitted in our NICU: 10/14 (71.4 %) had low birth weight; of these 10 % were ELBW, 30% were VLBW and 60% were LBW. In 3 neonates (21%) we found fungal growth (*C. Parapsilosis*) and in 2 we demonstrated invasive fungal infection.

CONCLUSIONS

Need for surgery is a strong risk factor for fungal colonization and infection. Active surveillance is a useful tool for prevention and early treatment. More extensive data are needed to evaluate efficacy of fluconazole prophylaxis in preventing fungal colonization and infection in surgical neonates.

ABS 56

FETAL MATERNAL ALLOIMMUNIZATION: THERAPY AND OUTCOMES IN A LARGE COHORT STUDY

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INTRODUCTION

Fetal-Maternal-Alloimmunization is the most frequent cause of fetal-neonatal anemia.
A retrospective observational cohort study was conduct to identify characteristics of Newborns (N) with alloimmunization of our center between January 2001 and June 2013.

RESULTS

149 N alloimmunized; Male: 53%; Foreign: 39%. Anti-D is the most frequent type of immunizations (65%, higher in foreign mothers). Median antibody-title: 1/256 (1/2-1/1,000,000). 61% Ig1 positive; 54% Ig2 positive.
Hb median at birth: 14 (3-26) g%; Median maximal bilirubin: 11(3-39 g%); GA median: 37(28-41) w; N weight 2,900 g (1,400-4,150).

THERAPIES

- 100% received phototherapy, and, if bilirubin increased rapidly, also intravenous-immunoglobulin;
- 11% intra-uterine-transfusions (TIU);
- 29% exanguino-transfusions (ET);
- 25% transfusions (but only 8% need transfusions after 21st days of life);
- 70% EPO (started if low reticulocytes + Coombs positive + low Hb). Median duration of EPO: 4 weeks (median beginning: 3 w, end 8 w). Median total reticulocytes at the end of EPO (140,000 mmc) was significant higher than at the beginning (70,000 mmc) (p = 0.000), as well as Hb at the end of EPO (11.2 mg%) and at the beginning of this therapy (10.7 mg%) (p = 0.03).

OUTCOME AT DISCHARGE

No deaths, no kernicterus; 2 IVH, one of them associated with neonatal thrombosis (TE). Follow up (performed up to Coombs test negativization or, if N was preterm, up to 3 years): patient with IVH and TE developed hemiplegia, normal outcome in every other.

CONCLUSION

Good outcome at discharge and during follow-up. EPO is good to reduce later transfusions: we have lower frequency of later transfusions, that means less discomfort to the patients, shorter hospitalizations and lower health-care-costs.

ABS 57

CORRELATION BETWEEN IMPEDANCE PATTERNS AND CLINICAL OUTCOME IN NEWBORNS WITH SYMPTOMS OF GASTROESOPHAGEAL REFLUX

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BACKGROUND

MII/pH is the recommended technique for gastroesophageal reflux (GER) detection in infants because of its ability to detect both acid and nonacid reflux. Currently, reflux events are analyzed considering pH values and quantitative parameters (number, duration and proximal extent); aim of this study was to realize a qualitative analysis, defining and classifying GER patterns, and assess the existence of a correlation between reflux patterns and duration of symptoms.

MATERIALS AND METHODS

Forty-eight infants with symptoms of GER and not receiving therapy underwent 24h-MII/pH study in the first month of life.

Ten GER patterns were described and classified according to the features of MII/pH tracings. Patients were divided into two groups according to symptom duration (cut off: 6 months) and MII/pH variables were compared between these groups.

RESULTS

The MII/pH variables obtained by a traditional MII/pH analysis showed that patients with prolonged symptoms had a significant increase in IBEI%, reflux frequency ($p < 0.001$), reflux duration, number of complete events and duration of acid episodes ($p < 0.005$).

All reflux patterns were identified and a higher frequency and percentage of intermittent refluxes ($p < 0.001$ and $p < 0.005$ respectively) and combined refluxes were observed in the same group.

CONCLUSIONS

In this study we introduced a new qualitative method for the analysis of MII/pH tracings. This method widens the potential of MII/pH. The ability to provide prognostic information by the qualitative analysis could influence clinical decision making as well as the detection of specific reflux patterns could give MII/pH a role in individualizing therapeutic strategy.

ABS 58

URINARY EXCRETION OF NGAL (NEUTROPHIL GELATINASE ASSOCIATED LIPOCALIN) AT BIRTH IS PREDICTIVE OF ACUTE KIDNEY INJURY (AKI) IN VERY LOW BIRTH WEIGHT INFANTS

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INTRODUCTION

Our ability to improve outcomes in infants with AKI is hampered by the inability to detect it early. Novel biomarkers, such as urinary NGAL, are emerging but their value as predictors of AKI in preterm infants has not yet been assessed. Aim of the study was to evaluate in a cohort of VLBWIs the urinary excretion of NGAL as early AKI biomarker during treatment with ibuprofen for PDA, which is an additional risk factor for renal damage.

STUDY POPULATION AND METHODS

We evaluated 50 VLBW infants (BW ≤ 1,500 g and/or GA ≤ 32 w) without congenital nephropaties, 19 treated with ibuprofen and 31 untreated. Renal function was assessed by serum creatinine (sCr) (IDMS) within 72 h from birth, at 1 w and 2 w and post ibuprofen (3 doses as standard).

eGFR was calculated with Schwartz formula (k 0.413). uNGAL was measured with an immunometric automatic assay at the same time of

sCr and within 24 h after each dose of ibuprofen. SCr and uNGAL are expressed as median with interquartile range.

RESULTS

Newborns requiring treatment (19) had lower GA (p 0.0045), lower APGAR score (p 0.0009) and required more ventilatory support (p < 0.001). At birth sCr and uNGAL were similar in both groups [uNGAL: 81.65 (22.48-198.90) treated vs 41.40 (13.30-215.10) untreated, p ns]. In treated infants uNGAL rose significantly after the first dose of ibuprofen (from 81.65 at birth to 188.00, p 0.0067) and decreased after 1 w to 52.96 (15.23-153.50) (p 0.03), still significantly higher than observed in untreated infants (52.96 vs 18.50, p 0.027). 9 infants (7 treated, 2 untreated) developed AKI according to AKIN criteria (Jetton and Askenazi 2012): 4 of stage 0, 3 of stage 1, 2 of stage 3 within the first 2 w of life. We found that uNGAL values at birth were predictive of AKI, being significantly higher in those infants who developed AKI [283.90 (81.18-787.20) vs 41.60 (13.30-101.60), p 0.03], while sCr was similar and not predictive. ROC analysis demonstrated that a cutoff of 122.4 ng/mL discriminated infants at risk for AKI with a specificity of 76.92%, sensibility of 75% and AUC values of 0.75 (p 0.03).

CONCLUSIONS

uNGAL is a sensible and specific biomarker to monitor AKI in preterm infants treated with ibuprofen. Its value at birth is an independent predictive factor of AKI in VLBWIs, with the advantage of being not invasive and repeatable.

ABS 59

INFLUENCE OF CIRCADIAN RHYTHMS ON GASTROESOPHAGEAL REFLUX IN NEWBORNS

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BACKGROUND

Recent studies showed a relationship between sleep-wake rhythm and gastroesophageal reflux in newborns. The sleep-awake circadian rhythms mature with growth, with a progressive increase of the phases of sleep during night. Accordingly, it is possible that the day and the night are distinguished by different frequencies and characteristics of refluxes.

Our aim was to evaluate reflux variations between day and night in gastroesophageal reflux disease (GERD) newborns.

METHODS

A group of newborns with symptoms of GERD, who underwent MII/pH in the first month of life, was studied.

Frequency and characteristics of refluxes were manually evaluated. Using a custom software the automatic count of reflux events was performed by dividing the events in day (hr. 08-20) and night (hr. 20-08).

On the basis of post-menstrual age (PMA) at MII/pH, 2 groups of patients were identified: PMA < 40 weeks and PMA ≥ 40 weeks.

Differences between groups were evaluated by Wilcoxon test.

RESULTS

Thirty-five infants had a PMA ≥ 40 weeks, 13 infants had a PMA < 40. In the group with PMA ≥ 40 weeks the frequency of non-acid liquid (p = 0.01) and gas refluxes (p < 0.001) were significantly higher in daytime, while acid-RI% was greater during night (p = 0.003). In the group with PMA < 40 weeks were not significant differences between day and night.

CONCLUSIONS

We found a circadian variability in refluxes of newborns with symptoms of GERD. This variability increases with increasing post-menstrual age and results in significant differences between day and night. This information could be useful for improving the therapeutic approach to GERD newborns.

ABS 60

IMPACT OF PREGNANCY AND LABOUR COMPLICATIONS ON NEONATAL OUTCOMES: A RETROSPECTIVE COHORT STUDY IN A RURAL HOSPITAL OF ETHIOPIA

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BACKGROUND

Despite relevant results Ethiopia is far from the Millennium Development Goal 4 target, with

Under 5 Mortality Rate of 88 and Neonatal Mortality Rate (NMR) of 37 per 1,000 live births. Focused Ante-Natal Care (ANC) is considered the first preventive measure to enhance Maternal Neonatal Child Health (MNCH) and reduce NMR.

OBJECTIVE

The study aim at exploring the main risk factors affecting neonatal health during pregnancy and delivery in Goba Hospital (Ethiopia) with the final goal of supporting the development of more effective interventions to enhance MNCH.

METHODOLOGY

The research is a retrospective cohort study including 1,283 women who delivered at Goba Hospital in 2011-12. Qualitative data were collected through interviews with health staff. Bivariate analysis was used for parametric variables.

RESULTS

The first negative neonatal outcome is preterm birth (18.5%), significant correlated with low ANC attendance (r -0.097), severe anaemia (r 0.304), hypertensive disorders (r 0.192), low Gestational Weight Gain (r -0.159), Urinary Tract Infection (UTI) (r 0.124), Caesarean Section (CS) delivery (r -0.103), obstructed delivery (r -0.101). It is followed by stillbirth rate (10.8%), correlated with low number of ANC visits (r -0.126), severe anaemia (r 0.251), AntePartum Haemorrhage (r0.140), hypotension (r 0.138), hypertensive disorders (r 0.109). A high prevalence of macrosomia was found (10.7%), correlated with CS (r 0.203), anaemia (r 0.132), UTI (r 0.123), obstructed labour (r 0.114).

CONCLUSION

Strengthening the quality of data management through Information and Communication Technology strategies is crucial to ensure continuous monitoring of provided services. Scaling up coverage and efficiency of ANC services seems to be the most pressing priority to enhance MNCH and community health education the most effective interventions to increase health services attendance. Crucial is a close collaboration among hospital staff, local authorities and MNCH stakeholders to ensure the supply of equipment and training. EBM approach should lead all future actions, therefore continuous investigations are needed; a special attention should be paid to anaemia, hypertensive disorders and, because of unexpected results, to macrosomia and hypotension during pregnancy.

ABS 61

ADMISSION CHEMISTRY BLOOD TESTS FROM UMBILICAL CORD AND FROM INFANT: ARE THEY COMPARABLE?

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BACKGROUND

In preterm infants early-onset anemia is mostly due to phlebotomies performed within the first hours or days after admission. In the smallest patients these initial samples might equal 10-20% of circulating blood volume. Umbilical cord blood drawing has been proposed to run the admission blood tests.

AIM

To assess the comparability between C-reactive protein (CRP), BUN, creatinine, electrolytes, transaminases, γGT, LDH, CPK, albumin, total proteins and alkaline phosphatase on cord and infant blood.

METHODS

A prospective cohort study comparing chemistry test results of paired samples of cord and infant blood.

Concordance between values was assessed using the Intraclass Correlation Coefficient (ICC) and the % of agreement on "in or out" reference intervals.

RESULTS

59 infants (GA 34 ± 3.3 wks; BW 1,990 ± 802 g) were studied. Cord samples were obtained within 10 min after birth, while median time for admission samples was 109 min. Cord and infant blood CRP, BUN, calcium and γGT showed a ICC > 0.8, while creatinine, phosphorus and magnesium showed an ICC 0.5-0.8 ($p < 0.001$), indicating a moderate yet significant concordance. The % of agreement was > 90% for CRP, BUN, calcium, γGT, phosphorus, magnesium, chlorum, LDH, albumin, alkaline phosphatase, total proteins and > 70% for the remaining values except for potassium. Potassium on cord was above the reference limit in 82% vs 5% of cases on infants ($p < 0.001$).

CONCLUSIONS

Cord blood is a potentially acceptable replacement source for admission tests in newborn infants. Experience and improved techniques may increase

the concordance between the results, in order to limit admission laboratory blood loss.

ABS 62

URINE METABOLOMIC SETTING IN NORMAL NEWBORN: METHODOLOGICAL APPROACH

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BACKGROUND

Metabolomics is a relatively young branch of "omics" science based on the systematic study of the complete set of metabolites in a biological sample. The metabolome is considered the best indicator of an organism's phenotype and is the most suitable for the study of epigenetic differences. The results of our pilot study (1) performed on 20 neonates showed strong differences on the metabolic status of the newborns' urine according to the type of delivery (vaginal or cesarean section). Urine is the favored biofluid for metabolomic analysis, but in newborns urine bags could be problematic (skin damage, loose of urine).

Aim of this study was to improve the knowledge of the metabolomic map in the neonate and to identify a harmless technique to collect the urine samples.

MATERIALS AND METHODS

After informed consent were enrolled 232 healthy infants at term and late preterm from 36 to 40 weeks of gestational age (GA 38.6 ± 1.1 wks, BW 3,145 ± 462 g), female/male ratio 0.9) admitted to the Pediatric Department. For each newborn we collected three samples of urine: the first within 24 hours of life, the second between 24-72 h and the third at one week, each sample in one or two tubes. Urine was collected using a cotton flock placed inside the diaper and then aspiring the urine using a syringe and storing it in Eppendorf tubes (1 cc) at -80°C. In many cases we obtained a good compliance by mothers.

RESULTS

Of 232 babies enrolled we obtained the first sample of urine from 227 (97.8%) and the second from 198 (85.3%). The third sample at one week was obtained from 165 (71.1%) although babies arrived from home. Two factors might have facilitated: the easy way of collection (cotton flock) and mothers collaboration.

CONCLUSION

The urinary metabolomic approach can hopefully be used to evaluate and quantify crucial metabolites and to identify biomarkers as early predictors of outcomes, which could lead to a "tailored" management of paediatric disorders. The "technique of cotton flock" to collect the urine turned out to be harmless, simple, quick and cheap. Shortly we will be able to confirm our data concerning the difference according to type of delivery as shown in our pilot study.

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ABS 63

UNIVERSAL NEONATAL HEARING SCREENING AND FOLLOW UP

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INTRODUCTION

Congenital hearing impairment is a common condition whose effects on language development and on the maintenance of verbal communication can be particularly crippling for the child. The first instrument for an early audiological diagnosis is the universal newborn hearing screening.

METHODS

From 2006 at the SCDU Neonatologia, AO Città della Salute e della Scienza of Turin, Italy, hearing screening is performed in all newborns (excluding transfers or exitus): up to September 2010 unilaterally, and then bilaterally. Newborns without risk factors for auditory neuropathy are tested between 24 and 48 hours from birth with TEOAEs. On the contrary, children with risk factors are evaluated with aABR by the discharge. The screening's results are classified into Pass (exited the screening) and Refer (suspected hearing loss unilateral or bilateral). All Refer results for TEOAEs are directed to a second evaluation. If the Refer result is confirmed, aABR are going to be performed within the 1st month of life. If aABR result Refer, babies are sent within the 3rd month of life in Audiology for a comprehensive evaluation aiming a

definition of the entity and characteristics of hearing loss and the possible therapeutic approach.

RESULTS

From May 2010 to August 2012, 9,299 infants were examined (6.2% admitted to the Neonatal Intensive Care Unit or Neonatal Subintensive Care Unit). 16.9% of the patients resulted Refer. Confirmed cases of Refer (to re-test and/or aABR) were referred for a complete diagnostic evaluation. 5 cases (3 unilateral, 2 bilateral) of severe or very severe hearing loss, 2 cases of unilateral anacusia and 2 cases of profound deafness were detected. All subjects are currently in follow-up. 3 patients after prosthetic rehabilitation and speech therapy implemented their hearing and verbal abilities.

CONCLUSIONS

The newborn hearing screening is a highly effective tool for the early diagnosis of congenital hearing loss and for the early implementation of rehabilitation measures. The identification of false negatives (1 case in our clinical records) is a crucial point and requires close collaboration between Audiologists, Neonatologists and Paediatricians.

ABS 64

USE OF UMBILICAL CORD BLOOD (UCB) FOR NEONATAL EARLY ONSET SEPSIS SCREENING

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BACKGROUND

Early neonatal sepsis detection requires phlebotomies at admission in order to perform blood culture (BC), complete blood count (CBC), procalcitonin (PCT) and C-reactive protein (CRP). UCB drawn has been proposed to prevent acute anemia. Concordance between UCB and infant CBC has already been confirmed.

AIM

To assess the concordance between PCT, CRP and BC values obtained from UCB and infant blood.

METHODS

A prospective bicentric cohort study comparing paired samples of UCB and infant blood. Intraclass Correlation Coefficient (ICC) and % of agreement in terms of in/out reference intervals assessed the concordance between CRP and PCT. Difference between BCs in terms of specificity was assessed by McNemar test.

RESULTS

We enrolled 52 infants (GA 34.8 ± 3.4 wks – BW 2,245 ± 805 g). CRP showed a ICC >= 0.99, while PCT showed a ICC = 0.75 with a $p < 0.000$, indicating a significant concordance. The % of agreement was 100% for both. One BC was positive on infants, but not on the corresponding UCB (specificity = 98%), while 6 BCs were positive on UCB, but not on the corresponding infants (specificity = 89%). False positive rate was not significant ($p = 0.125$). No infant had sepsis confirmed by CRP and PCT. No correlation between BC results and prolonged rupture of membranes, vaginal cultures, antibiotic prophylaxis and type of delivery was detected.

CONCLUSIONS

UCB can safely substitute infant blood in sepsis evaluations at birth. Practice and improved asepsis in sampling blood culture may increase the concordance between the results. Due to the lack of septic infants, we couldn't compare the BCs false negative incidence on UCB.

ABS 65

SEVERE HYPOGLYCAEMIA ASSOCIATED WITH CHOLESTATIC JAUNDICE IN THE NEWBORN: A POSSIBLE MARKER OF CONGENITAL HYPOPITUITARISM

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BACKGROUND

Neonatal hypoglycaemia is a common clinical sign for many diseases. Therefore, to understand its aetiology is not an easy task. Moreover, if the diagnosis and the treatment are delayed, severe and permanent neurological damages may occur as a result.

CLINICAL HISTORY

In our NICU, 2 African newborns, a male and a female, with normal auxological parameters, had been recently hospitalized. Between the 1st and 3rd day of life they presented severe hypoglycaemia, which persisted in spite of elevated enteral and intravenously glucose administrations. Neither of them showed evident dysmorphic features, with the exception of a micropenis in the male

patient. Female presented a septic shock, which at first misled the clinical about aetiology of hypoglycaemia. Both developed cholestatic jaundice with increasing hepatic cytolysis indices. The diagnosis was established after brain MRI, which was performed respectively at 33 and 32 days of life. Evidence of pituitary abnormality allowed to define the diagnosis of congenital hypopituitarism. In particular, in female MRI showed agenesis of the anterior pituitary, in the male adenohypophysis hypoplasia with absence of the pituitary stalk. In both the neurohypophysis was ectopic. Hydrocortisone supplementation was started in both, respectively at 30 and 24 days of life. While in the female blood glucose values were immediately normalized thanks to the treatment, in the male the hypoglycaemia was definitely corrected only after the beginning of GH therapy. Moreover, in the male, cholestatic jaundice did not regress after hydrocortisone treatment, while it was complicated with the appearance of a severe and progressive liver failure. Only more detailed investigations permitted to identify a concomitant congenital CMV infection, which delayed the achievement of clinical stability.

CONCLUSIONS

Neonatal hypoglycaemia is a medical urgency and its aetiology must be identified as soon as possible in order to begin an appropriate treatment. In particular, the association of severe hypoglycaemia and cholestatic jaundice should suggest the suspicion of congenital hypopituitarism to the neonatologist.

ABS 66

CAESAREAN SECTION AND ASTHMA IN CHILDREN: A CASE-CONTROL STUDY

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BACKGROUND

The type of delivery and the composition of the intestinal flora in children may increase the possibility of asthma or more generally of allergic diseases.

OBJECTIVE

We tested the hypothesis that the risk of asthma is higher for children born after caesarean sections rather than vaginal delivery.

METHODS

We examined 205 asthma cases (mean age 10.4) and 212 controls (mean age 8.24). Asthma was defined as physician-diagnosed asthma and wheeze in the previous year.

RESULTS

Of the 205 subjects with asthma, 139 (67.8%) were born by vaginal delivery, and 66 (32.2%) were born by caesarean section. Of the 212 controls 167 (78.8%) were born by vaginal delivery, and 45 (21.2%) by caesarean section.

The children born by caesarean section had a higher odds of asthma than those born by vaginal delivery (odds ratio 1.76; 95% C.I. 1.13-2.73).

CONCLUSIONS

Our findings suggest that caesarean delivery is associated with asthma. This could be explained by reduced or absent labor during caesarean delivery.

ABS 67

PAX-2 IMMUNOREACTIVITY IN HUMAN DEVELOPING KIDNEY

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INTRODUCTION

Pax-2 (Paired homeobox 2) is one of the main trascription factors involved in nervous and urogenital development. The gene pax2 encodes a highly conserved paired box domain which binds target DNA sequences driving transcription of other genes [1]. Heterozygous deletion or mutation cause a severe condition called RCS (renal coloboma syndrome) clinically seen as optic nerve colobomas and renal hypoplasia, while homozygous loss of function leads to death due to kidney agenesis. Kidney formation needs the Wolffian duct to branch, forming the ureteric bud, whose interaction with the metanephric mesenchyme (MM) will lead to nephron genesis. Pax-2 is a master regulator of this process, cooperating with other trascription factors to drive the ureteric bud branching: in fact it forces GDNF production by the MM [2], activation of Ret signaling cascade in the nephric duct's epithelial cells (**Fig. 1**). This is the first step of the mesenchymal-epithelial transition (MET)

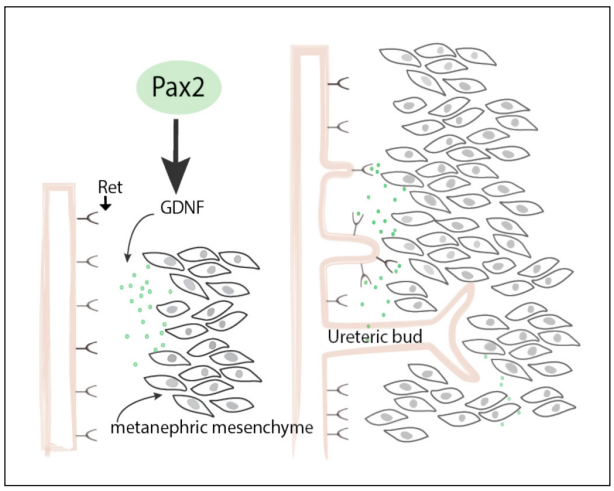

Figure 1.

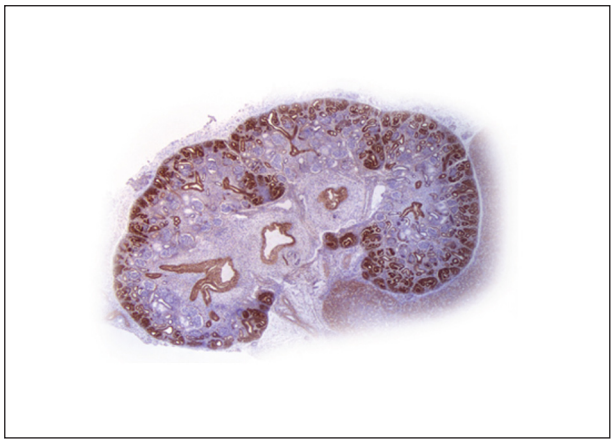

Figure 2.

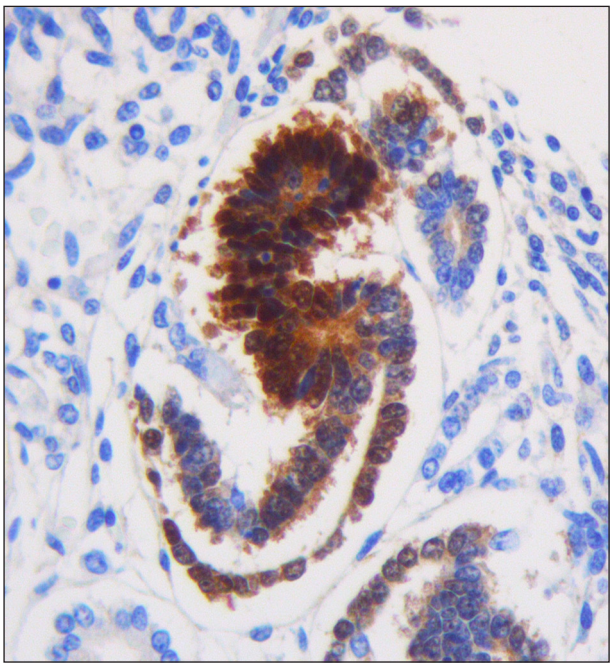

Figure 3.

required for glomerular and tubular development [3]. Despite its relevance, the molecular pathway of Pax-2 and its expression during renal development are still unclear. In this study we investigated the spatial and temporal localization of Pax-2 during human nephrogenesis.

MATERIALS AND METHODS

Our study was carried out on 50 fetuses and newborns of gestational age ranging from 10 weeks up to newborns. Kidney samples were formalin-fixed, routinely-processed and paraffin-embedded. 3-4 µm-thick sections were immunostained for Pax-2 (Abnova monoclonal mouse Ab M01 dilution 1:300). Deparaffinizing, antigen retrieval and imunostaining were carried out according to standard procedures.

RESULTS

Immunoreactivity for Pax-2 was detected in all kidney samples analyzed. At low power, reactivity for Pax-2 was mainly observed in the subcapsular kidney regions, being strictly associated with the nephrogenic zone (**Fig. 2**). Moreover, Pax-2 was strongly expressed in collecting ducts emerging from the renal hilum and extending towards the renal capsule. At higher power, a preferential expression of Pax-2 was observed in renal vescicles, in comma-shaped and in S-shaped bodies (**Fig. 3**). In these developing structures, immunoreactivity for Pax-2 was not homogeneous: the highest level of Pax-2 immunostaining were detected in the medial and distal part of the S-shaped body, programmed to originate the proximal and the distal tubule, respectively (**Fig. 3**). Intermediate levels of Pax-2 expression were found in the proximal part of the S-shaped body, in the parietal epithelial cells (PECs) of the developing Bowman's capsule, whereas reactivity for Pax-2 in podocyte precursors was patchy and weak (**Fig. 3**).

CONCLUSIONS

Our preliminary data show, at immunohistochemical level, that Pax-2 plays a major role in human nephrogenesis, being expressed at high levels during nephrogenesis. Immunostaining for Pax-2 appeared higher in the nephrogenic zones, S-shaped bodies expressing the highest levels of the protein. The uneven Pax-2 expression in the S-bodies suggests a preferential role of the protein in tubular development than in glomerular morphogenesis, confirmed by the absence of significant reactivity for Pax-2 in mature glomeruli. Further studies are needed for a better understanding of the modulation

of Pax-2 expression at different gestational ages during pregnancy [4].

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ABS 68

EFFECT OF SURFACTANT THERAPY ON CARDIAC ENZYME LEVELS IN VERY LOW BIRTH WEIGHT INFANTS WITH RESPIRATORY DISTRESS SYNDROME: A PRELIMINARY STUDY

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BACKROUND

Cardiac troponin T (cTnT) and creatine kinase isoenzyme MB (CK-MB) are considered useful markers in detecting myocardial ischemic damage in adults and infants. It is known that respiratory distress syndrome (RDS) could influence cardiac functions.

OBJECTIVES

The aim of this study is to determine the effect of surfactant therapy on myocardial dysfunction in infants with RDS.

METHODS

Concentrations of cTnT and CK-MB were compared between VLBW infants with and without RDS. Cardiac enzymes were measured before and six hours after surfactant treatment in infants with RDS and six hours interval in control group within 24 hours of birth. Samples were collected from 36 VLBW infants (25 RDS and 11 controls).

RESULTS

Gestational age and birthweight of RDS and non-RDS group were similar. The median (interquartile range) concentration of cTnT and CK-MB were significiantly high in infants with RDS than non-RDS [0.144 (0.105-0.189) μg/l vs 0.068 (0.047-0.082) μg/l in cTnT and 5.97 (3.54-9.68) ng/ml vs 4.20 (2.50-5.72) ng/ml in CK-MB respectively, $p < 0.05$]. The concentrations of both enzymes were significantly higher 6 hours later of the first sample taken in both groups. However the percentage of increase in cTnT and CK-MB were similar between RDS and non-RDS group (24.8% vs 15.5% in cTnT and 55% vs 50% in CK-MB respectively, $p > 0.05$).

CONCLUSION

Infants with RDS have significantly higher concentrations of cTnT and CK-MB than non-RDS group. These enzymes tended to rise similarly in first 24 hours of life in both groups. There is no favorable influence of surfactant treatment on cardiac morbidity in infants with RDS according to our preliminary results.

ABS 69

COMBINED EFFECTS OF GESTATIONAL AGE AND LACTATION STAGE ON THE METABOLITE PROFILE OF HUMAN BREAST MILK: A ^{1}H-NMR INVESTIGATION

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BACKGROUND

Human milk (HM) is the optimal food for infants, both in its nutritional composition and in the nonnutritive bioactive factors that promote survival and healthy development. HM composition is dynamic and varies within a feeding, diurnally, over lactation, and between mothers and populations. Understanding HM composition provides an important tool for the management of infant feeding, particularly of fragile, high-risk infants, such preterm (less than 37 completed weeks of gestation) of low birth weight (less than 2,500 g).

OBJECTIVES

The aim of this article was to apply a NMR-based metabolomics approach to compare the low molecular weight metabolic profile of human breast milk (HBM) from mothers of preterm infants at different gestational age (GA) and lactation stages.

DESIGN

Complete 24-hour expressions of milk were obtained at specific postpartum weeks (from 1 to 12) from 8

mothers giving birth at 26 to 29 weeks of gestation and from one mother who had delivered term infant (GA = 42 week). GA to the nearest completed week was determined from menstrual data. At the completion of each 24-hr period, the total daily volume of milk was well mixed and an aliquot was removed and stored at -80°C for analysis. Modified method of Bligh-Dyer [1] was used to extract the water-soluble fraction. ^{1}H-NMR experiments on the aqueous extracts of milk were carried out at 300 K on a Varian Unity 500 spectrometer operating at 499.83 MHz. The middle field portion of the ^{1}H-NMR spectra (3-5.4 ppm) was reduced into consecutive integrated spectral regions (bins) of width 0.01 ppm. The region δ 4.60 4.90 was excluded from the analysis in order to remove the effects of variations in the suppression of the water resonance. Subsequently, the final spectral data set sized sized 64x176 (samples x bins) was normalized to the total area to minimize the differences due to the sample extract dilutions and, then, Pareto scaled prior to Principal Components Analysis (PCA).

RESULTS

The PCA model showed a clear relationship of the metabolite profile of HBM both with the gestational age and the lactation time, pointing out, in particular, the approach of the metabolite profile of preterm mother's milk to those of term mother's milk as the lactation stage increases. Our data confirmed lower lactose concentrations and higher level of oligosaccharides in preterm milk compared to term milk.

CONCLUSIONS

Our results demonstrated a promising potential of NMR-based metabolomics for a rapid analysis of HMB useful in strategies for improving infant feeding.

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ABS 70

IDENTIFICATION OF CELL-MEDIATED IMMUNITY REFERENCE VALUES FOR A POPULATION OF PRETERM INFANTS USING THE CYLEX™ IMMUKNOW® ASSAY

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BACKGROUND

Cylex™ ImmuKnow® is a functional FDA-approved assay routinely used in adult transplant recipients to assess cell-mediated response by quantifying the APT produced by CD4+ lymphocytes after stimulation. The test identifies the immunocompromised patients who are at high risk of infection. Reference values for the pediatric population have been established in 2005 but currently there are no published data regarding the newborns and in particular the preterm infants.

AIM

To identify Cylex™ references values at birth and at 1 months of age in a population of preterm newborns; to correlate the Cylex™ results with birth weight (BW), gestational age (GA) and the risk of infection during the first month of life.

METHODS

All infants with BW ≤ 1,500 g and GA ≤ 32 weeks were included in a prospective study started in January 2013. A blood sample to perform the Cylex™ test was taken from each patient at birth and repeated at one months of age.

RESULTS

28 infants were enrolled in the study (GA 28 weeks ± 2.3 days; BW 1,043 ± 296 g). Median Cylex™ values were 89.5 ng/ml [mean: 133.5 ± 132.8; range: 5-588] at birth and 163 ng/ml [mean: 179.2 ± 106.2; range:19-365] at one month respectively. Cylex™ values at birth significantly correlated both with BW ($p < 0.05$; $r = 0.4$) and GA ($p < 0.05$; $r = 0.37$). Data at one month of age showed and increase in Cylex™ values compared to values at birth. Five subjects developed an infection between the third and the fourth week of age (1 NEC, 1 *E. Coli* sepsis, 3 postnatali CMV infections). These infants showed an opposite trend of Cylex™ values ($\Delta C = Cylex^{TM}_{1\ month} - Cylex^{TM}_{birth}$) compared to the subjects who did not develop infection (68.9 ± 30.8 vs 105.5 ± 30.5; $p < 0.01$).

CONCLUSIONS

Cylex™ values at birth and at one month of age are lower than the reference values published for the pediatric population. The values at birth strictly correlate with both BW and GA.

The subjects who did not show a maturation in the cell-mediated immune response are at markedly increased risk of both viral and bacterial infections. Although larger sample sizes are needed to confirm the present data, Cylex™ ImmuKnow® is likely

to become a useful tool to identify those preterm subjects with increased risk of infection who might benefit from specific prophylactic strategies.

ABS 71

THE EFFECT OF SERUM IGF-1, IGFBP-3 AND ERYTHROCYTE TRANSFUSIONS ON DEVELOPMENT OF MILD RETINOPATHY OF PREMATURITY

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INTRODUCTION

The most important factors in retinopathy of prematurity (ROP) are prematurity and oxygen toxicity although blood transfusions, insulin like growth factor-1 (IGF-1), insulin like growth factor binding protein 3 (IGFBP-3) and vascular endothelial growth factor (VEGF) also have important roles.

The objectives of this study were: a) to measure IGF-1 and IGFBP-3 levels in preterm newborns before and after blood transfusion; b) to assess if the effect of transfusion in development of ROP is mediated by these mediators; c) to investigate whether IGF-1 and IGFBP-3 levels measured at 32 and 33 gestational age (GA) were different in preterm newborns with and without ROP.

MATERIAL AND METHODS

Preterm newborns with gestational age ≤ 34 weeks were included and blood samples were obtained before and after red blood cell (RBC) transfusion.

RESULTS

Thirty newborns were included, 17 of whom had ROP (stage 1: n = 11, stage 2: n = 5, stage 3: n = 1). IGF-1 and IGFBP-3 levels did not change after RBC tranfusion. Excluding the patient with stage 3 ROP, all ROP patients were referred as mild ROP. No difference was observed between IGF-1 and IGFBP-3 levels of the patients with and without mild ROP. Patients with mild ROP had a significantly higher number of transfusions.

CONCLUSIONS

RBC transfusions did not affect serum IGF-1 and IGFBP-3 levels; however, they were associated with increased risk of mild ROP.

ABS 72

IS IT POSSIBLE TO SAVE CENTRAL VENOUS CATHETER (CVC) IN CRITICALLY ILL NEWBORNS WITH INVASIVE FUNGAL INFECTION?

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BACKGROUND AND AIMS

Fungi are able to adhere to the internal catheters biofilm in case of bloodstream fungal infection. Failure to promptly remove or replace central venous catheter (CVC) in infants with invasive fungal infections places them at higher risk of prolonged infection, mortality, and long-term neuro-developmental impairment, because. In vitro studies support the efficacy of ethanol solutions and echinocandins lock therapy to eliminate fungal biofilms; therefore lock therapy with ethanol can be proposed in life threatening conditions, when catheter removal involves high risks for the instable patient. Systemic echinocandins are increasingly used as antifungal agents due to their property to destroy the biofilm. As micafungin has an enhanced clearance in neonates, especially in preterm infants, the dose to administer to neonates is still uncertain. We therefore developed a micromethod with EDTA for the measurement of plasmatic micafungin levels even in neonates, with the goal of withdrawing only small amounts of blood.

METHODS

We describe three neonates with fungal catheter associated bloodstream infection successfully treated with systemic micafungin combined with lock therapy for catheter salvage. We also describe the validity of the micromethod to assess plasmatic levels of micafungin. Having the aim to perform a combined lock therapy with micafungin and ethanol to increase lock therapy effectiveness, micafungin stability test in ethanol 70% was performed by serial dosages carried out at the beginning of the test and then after 2, 6, 12, and 24 hours.

RESULTS

Systemic therapy with liposomal amphotericin-B (5 mg/kg) and micafungin (10 mg/kg) was started as soon as candidemia was detected. As these neonates were critically ill, catheter removal was

strongly contraindicated; therefore lock therapy was performed to save the catheter. A solution containing ethanol 70% and mycamine 5 mg/L was instilled and the catheter was closed for 4 to 12 hours. 2 locks were performed in each patient with a distance varying from 24 to 48 hours. Sterilization was obtained in all patients allowing catheter salvage. Drug concentration, analyzed by high performance liquid cromatography (HPLC), was unchanged at all timepoints.

CONCLUSIONS

Neonatologists should attempt to remove a CVC as soon as candidemia is detected unless it cannot be removed or replaced because of severe generalized or unstable critical conditions. Our experience suggests that the ethanol-micafungin lock therapy associated with systemic treatment may allows salvage of the catheter. Nevertheless further experience is needed to determine the appropriate length of duration of the lock and the number of locks necessary for catheter sterilization.

ABS 73

ANTONIO CAO, AN UNFORGETTABLE MASTER

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There are men whose demise makes us feel like orphans.

Rev. Andrea Gallo on the death of Paride Batini

INTRODUCTION

Having had the honour of knowing Professor Antonio Cao personally, the authors wanted to arrive at deeper insights into his scientific and human personality as a physician and untiring researcher.

OBJECTIVES

To describe the figure of Antonio Cao, emphasizing the characteristics of this distinguished researcher from different viewpoints in the hope of handing down to the next generations the priceless content of his professional work as a scientist, a human being and his social commitment, to bear witness to his activities, his ideas, his love for children and the people of his native land.

METHODS

Consultation of documents, publications and writings of different kinds, also including those produced by others; collection of numerous direct testimonials of persons who knew him.

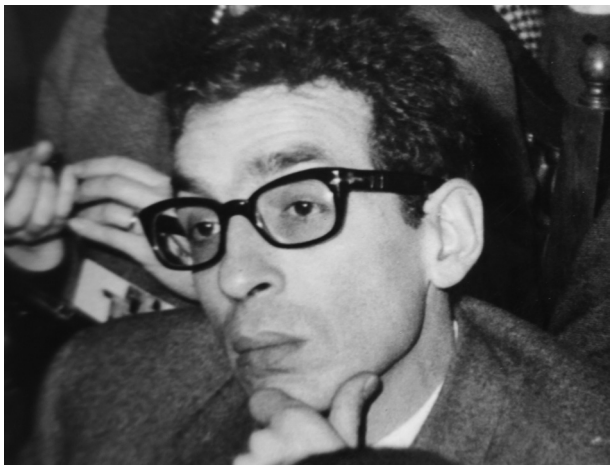

Figure 1. Prof. Antonio Cao when he was 38 years old.

RESULTS AND CONCLUSIONS

Antonio Cao devoted much attention and importance to his studies, nurturing his curiosity and intelligence, with attention to his personal history, that of his family and paediatrics in Cagliari.

He has left his mark in the the history of Sardinia starting from the 1950s and 60s: at that time the healthy carriers of thalassemia major represented about 13% of the population: one couple out of seventy was at risk of giving birth to an affected child. Every year a hundred and fifty children were born with thalassemia major: the disease was considered incurable so that the parents in their profound distress could do nothing but await the death of their child.

Young Doctor Cao (**Fig. 1**) sensed the importance of a global approach to the disease: he promoted assistance, transfusion therapy and sequestrants, but he also searched for a solution at the origin through prevention. With his trustworthiness and the esteem he enjoyed he was able to perform the first prenatal diagnoses on Sardinian women, first on foetal blood and later by means of DNA. The Sardinian model for the control of thalassemia, and later that of other genetic diseases created by Doctor Cao, was adopted in other countries as well. This led to recognition by the World Health Organisation of his "Ospedale Microcitemico", for which he fought throughout his entire life, as a Centre of Reference for haemoglobin disorders and other hereditary diseases.

Cao was the paediatrician of thousands of Sardinian and mainland Italian children and he trained diverse generations of paediatricians. He received important awards, among which the Allan Award

of the American Society of Human Genetics, the M. Philipson prize of the Academy of Scandinavian Paediatricians and the prestigious titles of Master of Paediatrics of the Italian Society of Paediatrics and the "Sardus Pater" award of the Presidency of the Sardinian Region, of which Antonio Cao was especially proud.

The *Maestro* left us on a muggy day in July of 2012 at the age of 83, but perhaps many years will go by before we realise the extent of the loss suffered by the people of his land, Sardinia, and not only them, with his passing away.

ABS 74

LONG TERM EFFECTS OF ADENOSINE (Ad) AND HYPOTERMIA (HT) ON THE KIDNEYS OF ASPHYXIATED NEONATAL RATS

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BACKGROUND

The availability of HT therapy has changed the prognosis of asphyxiated infants. Little is known about renal changes in asphyxiated infants who underwent HT. In the kidney Ad mediates heterogeneous effects and has potential role in preventing and treating renal injury.

OBJECTIVE

To test the hypothesis that HT and Ad cause chronic renal changes in neonatal rats exposed to hypoxic-ischemic brain injury (HIE).

DESIGN

HIE was produced in 7 day old (P7), newborn Sprague Dawley (SD) rats using the Vanucci-Rice Model (carotid artery ligation and hypoxia). Following HIE the pups received a single IP injection of: 1) Sal (0.02 ml) without (controls) or with HT; 2) Ad (0.4 mg/kg) with HT (34°C for 24-hr post HIE). At P36 renal mitotic and apoptotic indexes were calculated as numbers of mitotic figures and apoptotic globules in 5 fields at x 400.

RESULTS

The proximal tubules of renal cortex were mainly involved (**Fig. 1** and **Fig. 2**). Especially in juvenile male HT group, the mitotic index was slightly higher than the apoptotic index (**Fig. 3** and **Fig. 4**), in contrast with HT group at P8 (**Fig. 5**). At P36 no critical differences in Ad + HT groups were found compared to HIE control (**Fig. 3**).

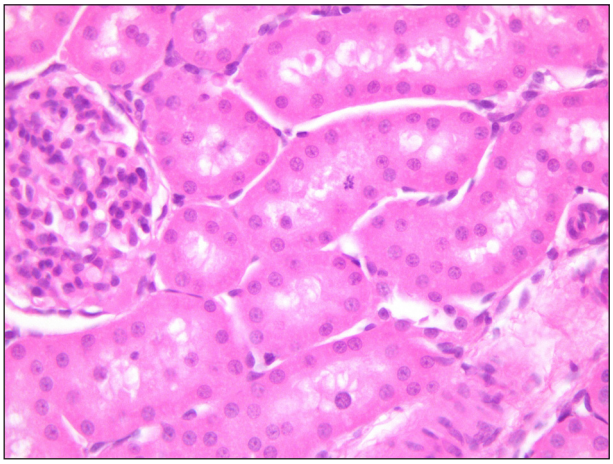

Figure 1. Mitoses in the proximal tubules of the renal cortex.

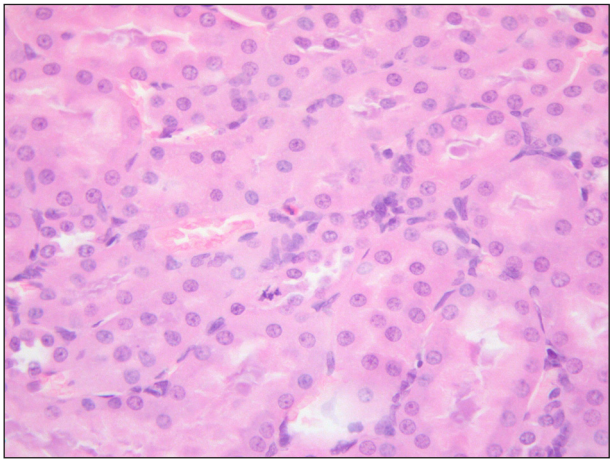

Figure 2. Mitoses and apoptosis in the proximal tubules of the renal cortex.

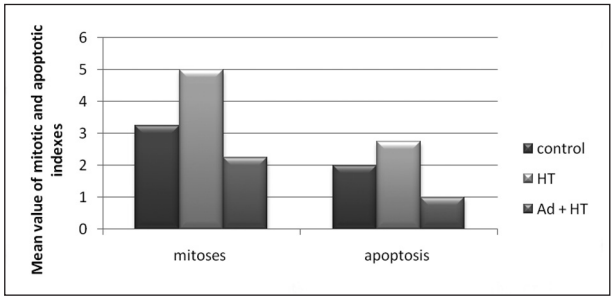

Figure 3. Mean value of mitotic and apoptotic indexes on the renal cortex in HT and Ad + HT groups compared to HIE control at P36.

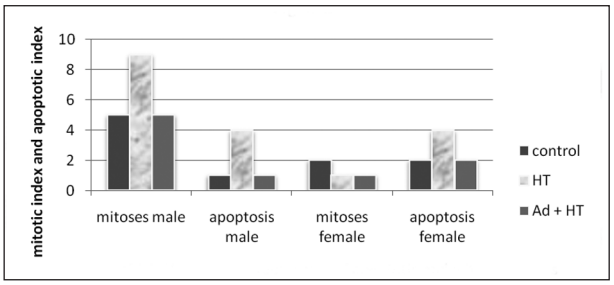

Figure 4. Difference between sexes of apoptotic and mitotic indexes on the renal cortex in HT and Ad + HT groups compared to HIE control at P36.

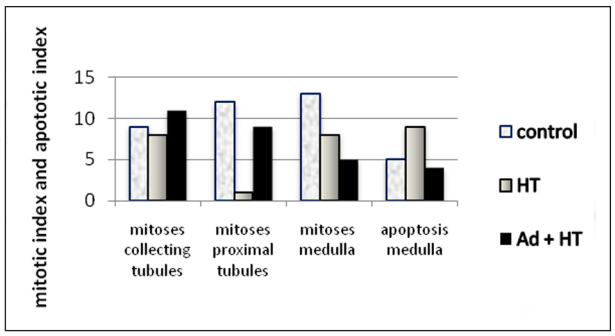

Figure 5. Apoptotic and mitotic indexes in HT and Ad + HT groups compared to HIE control at P8.

CONCLUSION

HT does not cause critical chronic renal pathological changes. Ad + HT treatment does not seem to have long term effects even though Ad may balance the apoptotic and mitotic changes suggesting a protective effect against hypoxia-ischemia damage. The long term effects of HT and Ad may differ between sexes. These promising preliminary results need confirmation through larger studies.

ABS 75

NUTRIMETABONOMICS IN PEDIATRIC RESEARCH

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INTRODUCTION

Human fetal and post-natal life faces a continuum of physiological and metabolic adaptations to environmental factors with nutrition owning a pivotal role in providing the necessary nutrients to ensure proper growth and functions from cells to organs. Gestational and extra uterine nutrition is identified as a key biological determinant that extends its role to meet immediate energy and nutrient requirements to possibly program the metabolism to future health outcomes [1]. Among the environmental factors that trigger the biology of the newly born infant, the colonization of the gastrointestinal tract by microorganisms (i.e. the gut microbiota) and its potential modulation by nutrition is increasingly being considered for its role not only on the functional maturation of the gut and the immune system, but also on the dietary uptake of nutrients and their subsequent metabolism. Metabonomics is becoming a popular approach to revisit neonatal metabolism through the analysis of metabolic variations in biological samples [2]. In particular, the study of urine metabolic variance provides a non invasive approach to inspect high density metabolic profiles that represent an average of recent homeostatic regulations. Of particular interest is the ability of the metabolic profiling to deliver molecular information not only on the host physiology but also on the functional interactions with the gut microbiota [3]. Nutritional metabonomics, or nutrimetabonomics, ambitions to decipher the complex interplay between nutrients and the metabolism of the host and microbiota complex system [4]. We herein provide a brief overview of the main analytical approaches and clinical applications of metabonomics in the neonatology area. A particular emphasis is given to nutrimetabonomics, a new complementary approach based on comprehensive nutrient profiling that is foreseen to provide a link between physiological regulatory processes and nutritional metabolic phenotypes.

METABONOMIC ANALYTICAL APPROACHES

Metabonomics consists in acquiring metabolic profiles from intact or extracts of biological samples such as biofluids (mostly blood plasma/serum and urine), cells, or tissues [2]. The obtained profiles are subsequently processed using statistical techniques in order to extract the relevant metabolic information depending on the scope of the study. These last can be classified into either unsupervised, i.e. no a priori observation is used during data processing (i.e. principal component analysis), supervised (i.e. partial least square analysis, partial least square discriminant analysis) approaches. Nowadays, nuclear magnetic resonance (NMR) spectroscopy and mass spectrometry (MS) have become routinely used for metabolic profiling. Proton NMR based metabonomics is particularly well suited to measure a broad set of metabolites including amino acids, carboxylic acids, carbohydrates, lipids,

methylamines among others [5]. The relative sensitivity of proton enables rapid acquisition of quantitative information on many metabolites in a holistic and highly robust way. A proton NMR spectra of human newborn urine samples collected during the first and second days of life are displayed on **Fig. 1**.

Metabonomic investigations also benefit from advances of MS techniques that can be deployed both in untargeted and targeted ways (i.e. quantification of a predetermined set of metabolites) [6]. MS can be associated with chromatography, either in gas or liquid phases, to perform separation, identification and quantitation of metabolites from complex biological samples. Although generally requiring more elaborated sample preparation steps relatively to NMR, MS provides low detection limits and high resolution capabilities for the analysis of metabolites.

RECENT APPLICATIONS OF METABONOMICS AND NUTRIMETABONOMICS IN NEONATOLOGY AND PEDIATRIC RESEARCH

Metabonomics is becoming a very popular approach in neonatology and pediatric research as early life metabolic regulations can be revisited in a holistic manner [7]. Within less than ten years, many investigations have used Metabonomics to study the rate of poor pregnancy outcomes [8], risk of early onset of preeclampsia [9], intrauterine growth retardation [10], signature of small-for-

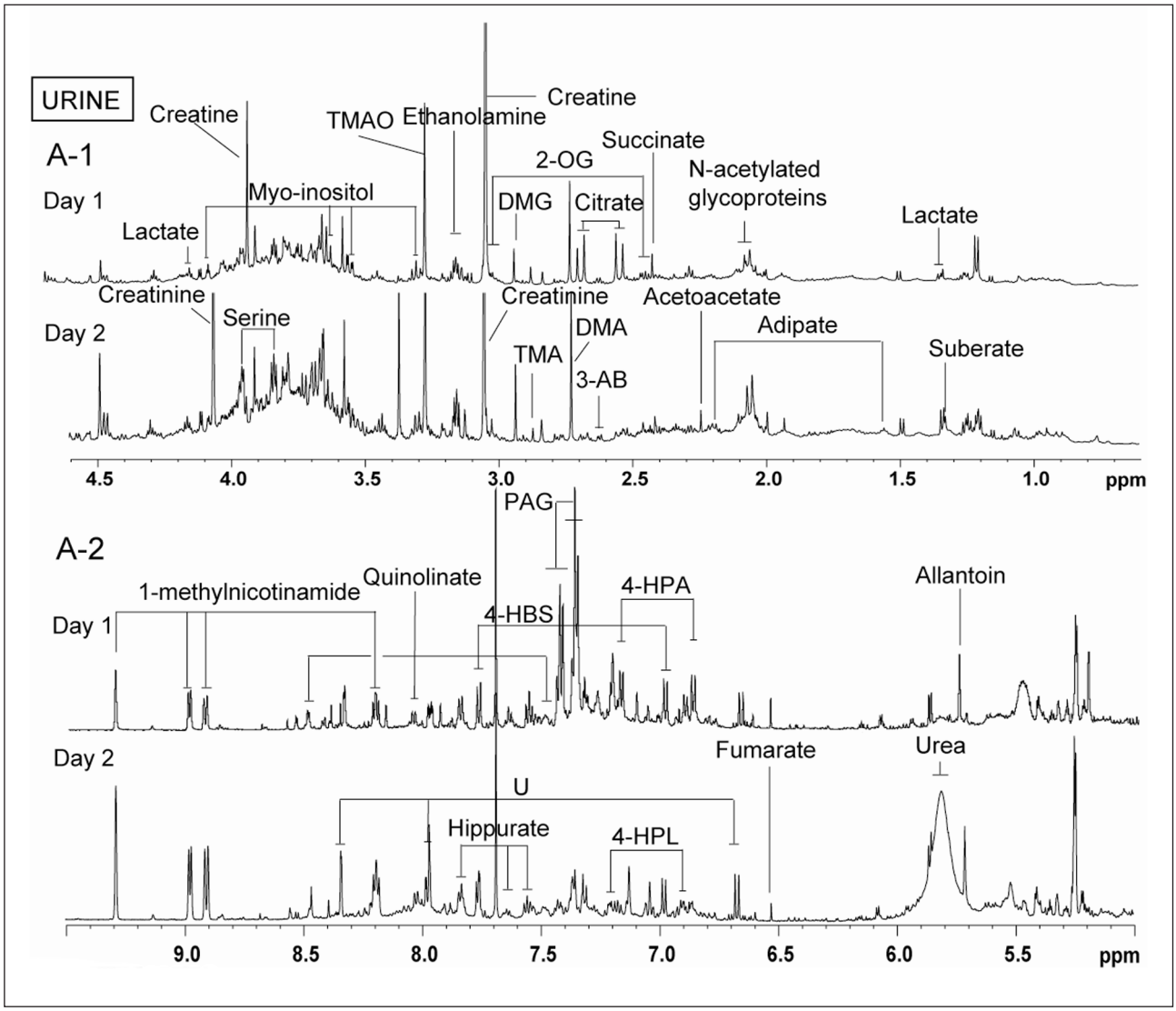

Figure 1. Typical aliphatic (A-1) and aromatic (A-2) regions of 600 MHz 1H-NMR spectra of urine obtained from a baby on the first and second days of life.
3-AB: 3-aminoisobutyrate; 4-HBS: 4-hydroxybenzoate; 4-HPA: 4-hydroxyphenylacetate; 4-HPL: 4-hydroxyphenylactate; 2-OG: 2-oxoglutarate; DMA: dimethylamine; DMG: dimethylglycine, PAG: phenylacetylglutamine; TMA: trimethylamine; TMAO: trimethylamine-N-oxide.

gestational-age in early pregnancy [11], neonate prematurity [12], prematurity associated respiratory distress syndrome [13], cystic fibrosis [14], nephrouropathies [15], prenatal disorders [16], markers of fetal malformations [17] and inborn error of metabolism [18]. Yet, if nutrition is known to be a key determinant on neonate's health status and possibly on perinatal programming as well, nutrimetabonomic investigations on neonate or pediatric populations remain largely unexplored. Recently, Marincola et al. have conducted a metabolomic study of human breast milk and preterm formula milk using NMR spectroscopy and MS coupled to gas chromatography [19]. The authors emphasized the usefulness of such an approach to delineate the role of nutrition on neonatal metabolism.

However, Nutrimetabonomics has been well deployed on adult populations with various attempts to elucidate metabolic signature associated with dietary patterns [20], particular nutritional interventions [21, 22], and longitudinal monitoring of the metabolic effects of diet [23]. All these studies have contributed to shed new light on the modulations of metabolic dynamics by nutrition and associations could even be made on the molecular interplay between the host and gut microbiota. Nevertheless, it also appeared that linking nutrient intake to specific metabolic regulation of a complex biological system such as a mammalian organism would require a new approach to integrate nutrient intake and metabolism and metabolic phenotype at the system level.

MOVING TOWARDS NEXT GENERATION OF NUTRIMETABONOMICS

As we made considerable progress on our ability to measure metabolic regulations through metabonomic approaches, the ambition to delineate the functional role of dietary nutrients on the modulation of specific metabolic networks of the host-microbiota symbiotic system requires to build a novel metabonomic-like approach to comprehensively measure the fate of nutrient patterns in biological fluids. In particular, it is foreseen that such an approach would enable to revisit the role of micronutrients as per their actual metabolic fate in neonatal and pediatric populations considering the genetic polymorphism of the host and the role of gut microbiota functional ecology on the metabolism of nutrients. For instance, the relationship between the polymorphism of the gene encoding for the methylene tetrahydrofolate reductase enzyme, folate status and homeocysteine metabolism, exemplifies how important could be to consider the actual nutrient requirement of an individual as a function of his genetic background [24]. Other studies have associated genetics with nutrient metabolism such as the effect of apolipoprotein E genotype on fat-soluble plasma antioxidants [25], the role of vitamin D binding protein genotype on circulating 25-hydroxyvitamin D levels [26] or newly identified variants associated with serologic response to vitamin E supplementation [27]. A key success driver of such a nutrient profiling approach would be to develop the next generation of analytical assays that would be able to capture both native and metabolized forms of nutrients. This is indeed foreseen to generate a nutrient data dimensionality that would be compatible with modern genetic, metagenetic and metabolic profiling capabilities. Nutrient profiling would thus help revisiting the interindividual variability on nutrient metabolism via its integration with metabonomic profiles. Alike the many foreseen applications to enable future targeted nutrition in health and disease conditions in adulthood, integration of system nutrient profiling with genomics and metabonomics approaches may help to revisit nutrient requirements and status in neonatology and pediatrics populations.

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ABS 76

POSTPARTUM DEPRESSION AND PUERPERAL PSYCHOSIS IN THE ANCIENT WORLD

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In books XVI and XLVIII of the *Dionysiaca* by Nonnus of Panopolis (5th century AD) we find the story of two nymphs, Nicaea and Aura, seduced by Dionysus and forced to come to grips with unwanted pregnancies followed by the distress of childbirth. By means of images and symbols belonging to the ethnobiology of reproduction in the ancient world, the author describes a series of symptoms compatible with postpartum depression in the first episode and a puerperal psychosis in the second. Nicaea's weeping, manifestations of anger, sleep disorders, obsessive ideas and suicidal tendencies are the onset of a difficult and painful transition to maternity. And if Nicaea arrives at a resigned and sad acceptance of her change in status from girl to mother, Aura rejects this to the end, negating and rejecting pregnancy, childbirth and breastfeeding in a psychotic delirium that leads her first to infanticide and then to suicide. The description of puerperal psychosis offered by Nonnus is surprising since it was a condition not knowingly recognized at that time: we find its first reliable nosographic descriptions only in the 19th century. All the same, Nonnus of Panopolis offers a plausible description of both depressive and psychotic symptoms, probably on the basis of personal experience or reports by others, handing down anamnestic data coherent with the clinical pictures of puerperal psychosis and postpartum depression in current medical literature. On this basis it does not appear unjustified to conclude

that what we find in Nonnus corresponds to a detailed description that allows us to suppose that in the 5th century AD, in a social and cultural milieu different and far removed from ours, there were psychic disorders superimposable on those which today we identify as cases of postpartum depression and puerperal psychosis.

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ABS 77

EFFECTS OF INTRAPERITONEAL MELATONIN INJECTION ON AUTOPHAGY AND ENDOPLASMIC RETICULUM (ER) STRESS IN A PRETERM RAT MODEL OF LPS-INDUCED LEUKOENCEPHALOPATHY

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Epidemiologic studies, as animal models, revealed that infection/inflammation associated with prematurity are related to white matter injury. Melatonin (Mel), a hormone physiologically secreted by pineal gland regulating circadian clock has neuroprotective effect in hypoxia-ischemia models linked to anti-oxidative, anti-inflammatory and anti-apoptotic properties. Autophagy, a process by which mammalian cells regulate the turnover of long-lived proteins by lysosomal system, was found to have both neuro-protective and neuro-lesive effects. The endoplasmic reticulum (ER), specific protein-degrading apparatus halts the build up of proteins induced by excessive protein traffic (ER stress) usually caused by infections. However, if the stress cannot be resolved, the cell dies by apoptosis. Aim: to analyze the effects of intraperitoneal (IP) Mel on autophagy and on ER stress in a rat model of preterm leukoencephalopathy produced by IP LPS injections on the 19th and 20th day of gestation. Methods: Western blot analysis was performed on brain samples of P1 pup rats, separated onto SDS-polyacrylamide gels and probed with antibodies anti-LC3 and anti-Beclin 1 (two authophagic markers), anti phospho(p)-eIF2α: a downstream target of the PERK pathway activated after endoplasmic reticulum (ER) stress and anti-GRP78: an ER chaperon that is upregulated during ER stress. Monoclonal antibody against β-actin was used as a control. Blots were analyzed using the J-Image software. Data were normalized to β-actin and expressed as % of control. Results: Immunoblot analysis showed that prenatal LPS injections induced a significant reduction of both lipidated LC3 (a microtubule-associated protein that is lipidated upon activation of autophagy) and beclin 1 (a component of the PI3K complex that is required for autophagy) expression in comparison with control group. In the LPS+Mel group, the autophagy inactivation was not observed (**Fig. 1**). The expression of p-eIF2α significantly increased after maternal LPS injections (**Fig. 2A**). This effect was completely reverted by the prenatal Mel exposure. However, after maternal LPS injections and prenatal Mel administration no changes in GRP78 expression were observed (**Fig. 2**).

CONCLUSIONS

Autophagy process is reduced in P1 pup rats by maternal LPS injection when compared to

control. The neonatal reduction is prevented by prenatal melatonin exposure. The increase in eIF2α phosphorylation (ER stress) observed after maternal LPS injection is prevented by prenatal Mel exposure. These very encouraging results strongly support the anti-inflammatory and antiapoptotic effect of Mel and pave the way for randomized clinical trials in newborns.

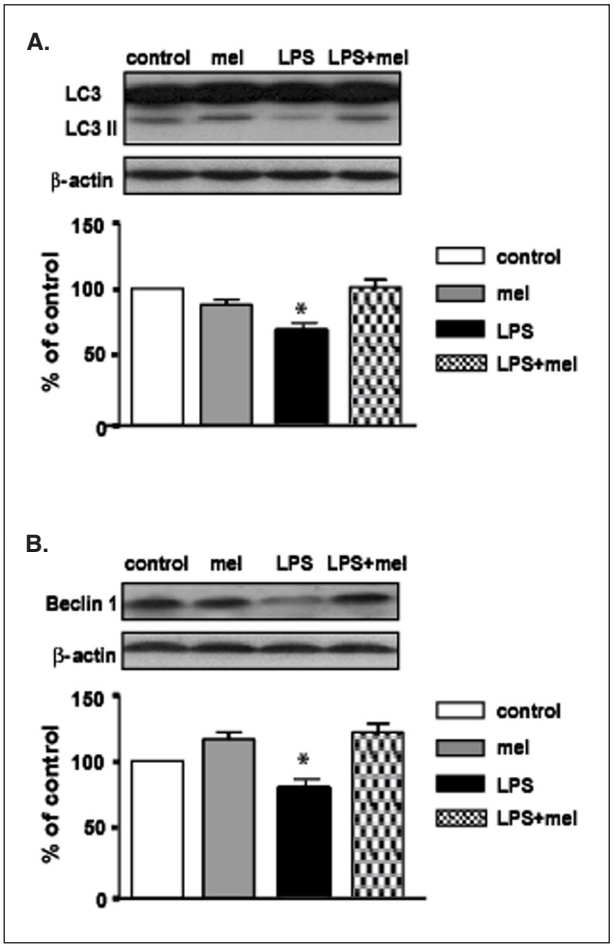

Figure 1.

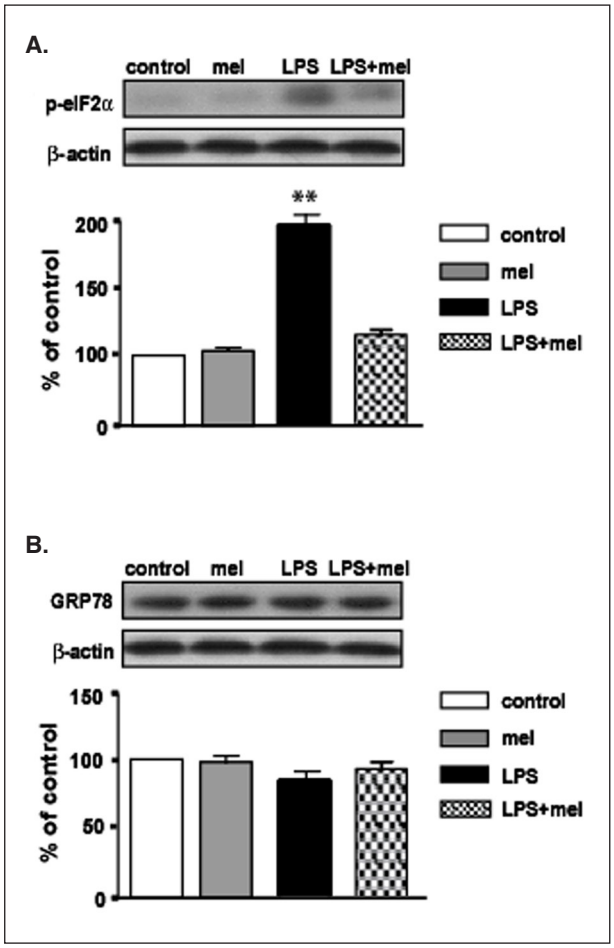

Figure 2.