

# Selected Abstracts of the 12<sup>th</sup> International Workshop on Neonatology

## 10 P PEDIATRICS: NOTES FOR THE FUTURE

### CAGLIARI (ITALY) • OCTOBER 19<sup>TH</sup>-22<sup>ND</sup>, 2016

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**ABS 1****ABNORMAL FETAL GROWTH ALTERS THE METABOLIC PROFILE OF EARLY HUMAN MILK**

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**BACKGROUND AND AIMS**

Maternal milk constitutes the optimal nutritional source for infants, especially during the first months after birth. Two pathological conditions deviate from the normal fetal growth (namely appropriate for gestational age, AGA): the large for gestational age (LGA, infants above the 90<sup>th</sup> percentile) and the intrauterine growth restriction (IUGR) newborns, characterized by failure of the fetus to reach its intrinsic growth potential. Both conditions are associated with nutrient and energy metabolism disorders in the short and long term. This study implemented NMR metabolomics in early maternal milk samples to investigate possible alterations in various metabolites, which may affect the nutritional value of maternal milk in relation to fetal growth. High resolution NMR spectroscopy elaborates minimally invasive procedures and yields high reproducibility unveiling markers that may correlate to each of the studied conditions.

**METHODS**

Milk samples, collected on the third or fourth day postpartum from 35 women living in Greece were examined by NMR spectroscopy (Varian 600 MHz). Multivariate data analysis elicited information from the NMR spectra and probed to metabolic signatures of the fetuses.

**RESULTS**

Spectroscopic data accomplished to classify the maternal milk samples in relation to fetal growth. Supervised analysis in terms of OPLS-

DA models discriminated the cases of LGA and IUGR, compared to the control samples (AGA). In particular, the LGA group presented with an increase of oligo-saccharides (fructose, lactose and galactose) compared to the AGA group. Moreover, an increase in the aminoacid content of IUGR samples compared to AGA samples pinpointed the metabolites isoleucine, leucine and valine. The extracted OPLS-DA models were validated with the use of ROC curves and permutation testing.

**CONCLUSIONS**

This holistic metabolomic study demonstrated an increase of oligosaccharides in the LGA, as well as an increase of the aminoacid content in the IUGR early milk samples, possibly pointing to an additional benefit of early breastfeeding in these two groups of infants, prone postpartum to hypoglycemia and hypoproteinemia, respectively. Furthermore, assessing the metabolic profile of maternal milk may enable the evaluation of its nutritional value adjusted to fetal growth, thus the introduction of appropriate dietary interventions.

**ABS 2****VENTED BASE FEEDING BOTTLE IN PRETERM INFANTS WITH GERD SYMPTOMS: EFFECTS ON RESPIRATION-DEGLUTITION PATTERNS AND REFLUX**

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**BACKGROUND**

In preterm infants a deficit of both coordination and gastro-intestinal motility is often the underpinning cause of oxygen desaturations and gastroesophageal reflux. Breastfeeding enhances this deglutition-respiration mechanism maturation. For this reason, a feeder that best recreates the physiological suction from the maternal breast is highly desirable in non-breastfed newborns.

**AIM**

The aim was to evaluate the effects of vented base bottles on the deglutition-respiration patterns and reflux in preterm infants with clinical suspect of gastroesophageal reflux disease (GERD).

## METHODS

In this prospective study, we compared the effects of classical feeders (A) versus vented base ones (B) on a group of patients with at least 2 clinical GERD symptoms. 24 hours of synchronized cardio-respiratory (CR) monitor and esophageal multichannel intraluminal impedance testing (MII-pH) were evaluated for each patient. During this period, patients were fed alternatively with feeder A and B.

## RESULTS

Data were collected from over 10 newborns during 56 periods of both CR and MII-pH monitoring: 28 (14 during feeding and 14 post-feeding) per type of feeder. Feeder A resulted to be associated to shorter feeding time ( $p = 0.04$ ) and less organized deglutition-respiration patterns. During post-prandial periods, feeder B was associated to a reduction of both oxygen desaturation ( $9.6 \pm 16.3$  vs.  $2.9 \pm 5.8$ ;  $p = 0.004$ ) and gastro-esophageal reflux ( $4.7 \pm 3.1$  vs.  $2.5 \pm 2.4$ ;  $p = 0.01$ ) episodes/hour.

## CONCLUSIONS

Vented base bottles are related with an improvement of deglutition-respiration patterns and gastro-esophageal reflux episodes. The use of such feeders may represent a new therapeutic option in order to treat preterm newborns with respiratory problems due to GERD and/or other alimentation deficits, when maternal breastfeeding is not available.

## ABS 3

### ANALYSIS OF CIRCULATING miRNAs IN OBESE CHILDREN BORN SMALL FOR GESTATIONAL AGE

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## BACKGROUND

Children born small for gestational age (SGA) are at increased risk of coronary heart disease and type 2 diabetes in adulthood, due to reprogramming of endocrine and metabolic functions. Dysregulation of specific miRNAs in response to genetic and environmental factors contribute to aberrant gene expression patterns underlying metabolic dysfunction.

## OBJECTIVE AND HYPOTHESES

We aimed to identify miRNAs associated with increased risk of obesity in SGA children. We hypothesized that circulating miRNA expression profiles vary according to differences in BMI and circulating miRNAs may reflect metabolic dysfunction.

## METHODS

We recruited 4 SGA obese children (BMI-SDS  $2.41 \pm 0.72$ ,  $11.96 \pm 1.76$  years) and 4 appropriate for gestational age (AGA) obese children (BMI SDS  $2.38 \pm 0.57$ ,  $13.61 \pm 0.5$  years), with their respective controls matched for sex and age. Small RNAs have been extracted by serum and sequenced by miSeq Illumina sequencer. miRNA-Seq data has been analyzed throughout a customized bioinformatics pipeline in order to detect and quantify miRNA profile in the groups analyzed. The results have been validated by RT-qPCR.

## RESULTS

We identified five down-regulated and eleven up-regulated miRNAs in the group of obese SGA; among the up-regulated miRNAs, four are shared with AGA obese children as controls (**Tab. 1** and **Tab. 2**). Specific miRNAs, such as miR-486-3p, miR-122-5p, miR-16-5p, miR-532-5p, miR-425-5p and miR-16-2-3p appeared specifically correlated with obesity in SGA children. We used mirTarBase (miRNA-target interactions database) to search experimentally validated mRNA targets. A functional analysis of these genes in the DAVID database showed a significant statistical enrichment in “regulation of cell proliferation” and “regulation of metabolic process”.

## CONCLUSIONS

We identified new serum molecular biomarkers, which may be useful for cardiometabolic risk prediction in SGA children.

**Table 1 (ABS 3).** Upregulated miRNAs in SGA and AGA obese children.

	SGA obese	Fold change	AGA obese	Fold change
<b>miR-423-5p</b>	↑	<b>2.4</b>	↑	<b>1.7</b>
<b>miR-92a-3p</b>	↑	<b>3.8</b>	↑	<b>2.6</b>
<b>miR-486-3p</b>	↑	<b>4.6</b>	↑	<b>2.3</b>
<i>miR-486-5p</i>	↑	4.3		
miR-451a			↑	2.8
miR-25-3p			↑	1.8
miR-15a-5p			↑	2.3
miR-30d-5p			↑	1.9
let-7b-5p			↑	1.8
<b>miR-484</b>	↑	<b>2.5</b>	↑	<b>3.4</b>
miR-660-5p			↑	2
miR-128-3p			↑	2.5
<i>miR-122-5p</i>	↑	4		
<i>miR-16-5p</i>	↑	1.8		
<i>miR-532-5p</i>	↑	2.3		
<i>miR-425-5p</i>	↑	1.9		
<i>miR-3615</i>	↑	3.4		
<i>miR-16-2-3p</i>	↑	3.2		

Eleven miRNAs are up-regulated in the group of SGA obese children: of these, four (in bold) are shared with AGA obese children.

**Table 2 (ABS 3).** Downregulated miRNAs in SGA and AGA obese children.

	SGA obese	Fold change	AGA obese	Fold change
<b>miR-181b-5p</b>	↓	<b>0.6</b>	↓	<b>0.6</b>
<i>miR-143-3p</i>	↓	0.3		
<i>miR-223-3p</i>	↓	0.2		
<i>miR-23a-3p</i>	↓	0.3		
<i>miR-28-5</i>	↓	0.3		

Five miRNAs are down-regulated in the group of SGA obese children: of these, one (in bold) is shared with AGA obese children.

## ABS 4

### CELOSOMY: OMPHALOCELE AND GASTROSCHISIS

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#### INTRODUCTION

Celosomy is a term used for a group of congenital anomalies characterized by opening of the somatic wall with evisceration. The most common types of celosomy are gastroschisis and omphalocele. Various maternal and environmental factors were also suggested in human and animal studies.

#### METHODS

We report 7 patients admitted to our ward for celosomy during the last years. This study aims to

reveal risk factors, treatment and outcome of this disease.

#### RESULTS

We gathered 7 patients. Two infants were born with gastroschisis while five presented omphaloceles. Two infants of the latter group were twins. The average maternal age was 35.5 years old. All mothers had no significant medical history. One of them had diabetes mellitus requiring insulin therapy. Prenatal diagnosis with obstetrical ultrasound was made for all patients before 32 weeks of gestational age. After delivery, the eviscerated intestine was wrapped in saline-soaked gauze and placed in a plastic bowel bag to protect against hypothermia and evaporative losses in all cases. The average birth weight was 2,760 g, with 3 infants weighing less than 2,500 g. Five patients were males and three were premature less than 34 weeks of GA. Physical examination revealed no gross dysmorphic features except for labio-palatal cleft. Large celosomy was noted in

three cases with exhibition of the intestines in all cases and the liver and the stomach in two cases. Operative management was undertaken quickly with a maximal delay of two days. The surgical management was different: the fascia and the skin were both closed in four cases (one gastroschisis and three omphaloceles). In two cases, only the skin could be closed because of considerable intra-abdominal pressure. However, little undermining of the skin was done in one case of a large omphalocele. Silastic silos were not employed. Four patients died at an average time of 11 days (two gastroschisis and two omphaloceles). One of these patients died secondary to peritonitis. The other deaths were attributable to respiratory distress due to increased intra-abdominal pressure.

#### CONCLUSIONS

Infants with omphalocele and gastroschisis represent a challenging group of patients. Antenatal diagnosis may affect immediate postnatal management. The goal of the surgeon is to accomplish abdominal wall closure in a single stage, but a tailored approach is needed. Long term outcome, in the absence of major chromosomal and structural anomalies, is excellent.

#### ABS 5

### BREAST MILK IN INTRAUTERINE GROWTH RESTRICTION: DIFFERENCES COMPARED TO ADEQUATE FOR GESTATIONAL AGE INFANTS

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#### BACKGROUND

Human milk is the best food for all neonates, especially for preterm and IUGR infants. However, breast milk without fortification does not cover the high nutritional needs of such patients. The condition of IUGR represents a risk category that can result in permanent changes in the physiology and the metabolism of the newborn, which can lead to an increased risk of disease in adulthood. The aim of the present study was to assess the role of individualized human milk fortification based on the analysis of maternal milk on the nutrition of preterm and IUGR infants hospitalized in the Neonatal Intensive Care Unit of Cagliari, and to evaluate the composition of breast milk in mothers of IUGR

infants compared to adequate for gestational age infants.

#### METHODS

We estimated the breast milk composition of 24 infants (12 IUGR, 12 AGA) with gestational ages between 27<sup>+5</sup> and 36<sup>+3</sup> weeks fed with human milk fortified in an individualized way. Small milk samples (~10 ml) taken from a pool collected from the mothers in the preceding 24-48 h were analyzed by Milko-scan 93/133 in the laboratory of the 3A Company in Arborea (Sardinia).

#### RESULTS

The qualitative and quantitative analysis of the breast milk samples showed differences in the principal macronutrients in the milk of mothers of IUGR infants compared to AGA. The concentration of lipid (p-value = 0.047) and protein was higher in IUGR infants; in contrast lactose was lower, in comparison with AGA.

#### CONCLUSIONS

The preliminary results of this study suggest that the composition of human milk seems to change according to birth weight and to reflect the different metabolic profiles of IUGR and AGA. Integration of breastfeeding should be specifically adapted to individual needs of IUGR infants, taking into account long-term consequences, such as the accumulation of inappropriate fat. Further studies are needed to improve growth during early critical phases of development, in order to prevent the onset of diseases in the adult age from the viewpoint of personalized, predictive and preventive medicine at the same time.

#### ABS 6

### A RATHER UNIQUE AND UNEXPECTED PEDIATRIC SURGICAL CASE

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#### INTRODUCTION

At Chaaria Mission Hospital we are used to perform almost daily a number of different surgeries, including minor and major ones, both in pediatric and adult patients, often under emergency circumstances. The case we are going to present here revealed quite an unexpected and rare finding. In fact, we present a surgical case of femoral hernia in an infant girl aged 3 months. We consider this

case of particular interest for two main reasons: the differential diagnosis of a groin mass in an infant, including a clinical suspicion of femoral hernia, which was confirmed during emergency open surgery. The second interesting finding is that we did not find the bowel or the bladder within the hernia sac, but to our surprise the uterus and a fallopian tube were contained in the hernia sac. Lastly, we comment on the importance to document similar cases by intra-operative imaging. In our case the camera facility was not available in the theatre and we could not document this interesting case by imaging. Certainly, this is a lesson learnt for the future.

#### CASE REPORT

A 3-month-infant girl was brought by her mother to our hospital. The mother had observed a groin lump in the last week, which was quite painful when pressure was applied, with the baby crying at palpation. There was no other complaint. On examination, we found the baby in good general health status, without signs of dehydration, no fever, nor inflammation; she was breastfed and appeared to grow normally for age. The only abnormal finding was the lump in her left groin, painful on palpation, of hard consistency, tender and firm, without signs of skin inflammation. A full blood count revealed mild leukocytosis and neutrophilia, with WBCs 18,000/microL, 80% neutrophils; ESR was 40 mm/h; HIV negative. No other recent medical history of note. We performed an ultrasound that revealed an open femoral canal, with apparent herniation through its ring: a picture that was suggestive of an irreducible femoral hernia. Since the lump could not be reduced, we were concerned about potential complications, such as strangulation of the hernia, perforation and peritonitis, with potentially life threatening consequences. Despite the very young age, and potential risks related to anesthesia, including lack in our facilities of a dedicated infant post-surgery intensive care unit, we considered the overall clinical picture in favor of performing an urgent surgical intervention, which the mother consented to. During open surgery, performed by Lockwood's infra-inguinal approach, it was clearly confirmed that the mass was due to a femoral hernia, however within the hernia sac we did not find the bowel, or part of the bowel wall, nor part of the urinary bladder, as often expected in similar cases. Indeed, to our surprise, we found in the herniated sac the uterus and the left fallopian tube. Although repair surgery was not a simple procedure due to the small hernia sac opening, we managed to successfully

reduce the uterus and fallopian tube in the abdomen. The infant tolerated well the general anesthesia and was awoken without any complications. The post-operative period was unremarkable, and the baby was discharged on day 5 after admission.

#### DISCUSSION

It is estimated that only 1 in 20 of groin hernia are femoral ones, with the majority being inguinal ones. Femoral herniae are uncommon in childhood, accounting for less than 1% of all groin herniae, and are often reported in infants below one year of age. Pre-operative misdiagnosis ranges from 35% to 75% [1, 2]. This case represents indeed an uncommon occurrence in our experience, and reflects the rarity of similar cases described sporadically in the literature.

#### CONCLUSIONS

Overall, this interesting case of femoral hernia in an infant girl was managed properly and with favorable outcome. The ironic remark is that unfortunately we did not have a camera in the theatre to document this quite unexpected finding, relating to the uterus and left fallopian tube being present in the hernia sac. Due to the emergency procedure, we could not focus on this during the intervention. However, for the future, this is a lesson learnt and we will consider keeping a camera in our theater, ready to document and share visual evidence, if any case of similar interest and rarity will present again.

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#### ABS 7

#### VATER SYNDROME

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#### INTRODUCTION

Vater Syndrome, also known as Vacterl association, is an acronym describing a range of interconnected congenital disorders, which are characterized by: V: abnormalities in the spine, A: anal atresia, C: cardiovascular anomalies, TE: tracheo-esophageal atresia or fistula, R: radius hypoplasia and kidney agenesis, L: alterations of the limbs (polydactyly, syndactyly, oligodactyly) and joint and rib defects. In

order to make a diagnosis, at least three of the above mentioned genetic defects have to be noted. No specific distribution or geographical predominance was noted. The etiology is not known; however, it was noted that some individuals have trisomy 12, or a deletion of the distal segment of chromosome 13q, and that the frequency is higher in children of diabetic or suffering from Fanconi anemia mothers and that there is a higher correlation, especially in the first trimester of pregnancy, with the use of estrogen



**Figure 1 (ABS 7).** X-ray in a case of Vater Syndrome. X-ray of vertebral column shows vertebral deformities, presence of supernumerary ribs, joint and kidney agenesis, rectal atresia.

and progestin medicines and benzodiazepine. The prevalence is about 1-9 per 100,000 live births; the incidence is 1/10,000-1/40,000 live births. The prognosis is generally good.

#### CASE REPORT

A baby girl was admitted to our department a few hours after birth for suspected solitary kidney; the X-ray of vertebral column showed vertebral deformities, presence of supernumerary ribs, joint and kidney agenesis, rectal atresia (**Fig. 1**).

#### ABS 8

#### SEVERE NECROTIZING ENTEROCOLITIS ASSOCIATED WITH GASTROSCHISIS: DIFFICULTIES OF CARE

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#### INTRODUCTION

Gastroschisis is a congenital malformation of the abdominal wall in which the intestinal loops pass through a defect in the abdominal wall. Its incidence is estimated at 1 birth/10,000. The etiology is unknown and associated malformations are exceptional. Prognosis mainly depends on the functional quality of the intestine and the speed of the surgical procedure. We present two cases observed at our centre to clarify the management difficulties of gastroschisis.

#### CASE REPORTS

We report the cases of two male newborns whose delivery was performed by cesarean section scheduled for gastroschisis a short time after antenatal ultrasound. Neonatologists were informed in advance. At birth, the first newborn had right gastroschisis with externalized intestines and abdomen flat. The rest of the examination was normal without respiratory distress or apparent malformations associated. The second newborn also had right gastroschisis with hail and colon outcome. Moreover, he presented respiratory distress requiring intubation in the delivery room. Both were entrusted to surgeons and were operated on the first day of life. The intervention consisted of a full reintegration of intestinal loops and closure of the abdominal wall in the same operation. The evolution was marked by the occurrence of necrotizing enterocolitis with bloated abdomen, greenish gastric residuals, marked biological

infectious syndrome and difficulties in introducing food. Broad-spectrum antibiotics administration and resuscitation could not avoid fatal outcome for both infants, who died at 7 and 14 days of life, respectively.

#### CONCLUSIONS

Necrotizing enterocolitis complicating the surgical repair of gastroschisis is an important prognostic factor, which depends on the functional quality of intestines attacked by amniotic fluid. This requires a careful and multidisciplinary management to improve survival.

#### ABS 9

##### RECURRENT ABDOMINAL PAIN AND JUVENILE SOLITARY POLYP (JSP): A CASE REPORT

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#### INTRODUCTION

Polyps are one of the most common causes of colorectal bleeding in children. The typical presentation of a colorectal polyp is painless rectal bleeding. We describe a case of a boy with recurrent abdominal pain and positive fecal occult blood test; colonoscopy and histology were consistent with juvenile solitary polyp (JSP).

#### CASE REPORT

A 13-year-old boy presented an 8-month history of abdominal pain, which started after gastroenteritis. Abdominal ultrasound (US) and anti transglutaminase antibodies were negative, fecal occult blood test was positive in 3 specimens and also after several months. Fecal calprotectin was slightly elevated and lactose breath test was negative. After having stopped milk assumption, pain improved. However, a colonoscopy was performed and showed a 12 mm pedunculated polyp in the proximal part of the descending colon. Endoscopic polypectomy was performed. Histology of the polyp was compatible with eroded JSP. The child recovered completely, and presented negative fecal occult blood test after a few months. No endoscopic follow-up was performed.

#### DISCUSSION

The prevalence of colorectal polyps in children was estimated 6% of all pediatric colonoscopies

and 12% of colonoscopies performed for lower gastrointestinal bleeding. Clinical presentation is hematochezia in the majority of cases but some patients can complain abdominal pain, diarrhea, prolapse of the polyp from the anus, anemia. Although recent studies reveal that JSP recur in approximately 17% of cases and that there is a 3-5% chance that a single JSP has adenomatous features, the debate is open on the best follow up for these children.

#### ABS 10

##### ULTRASOUND MONITORING OF LIVER ABSCESSSES IN NEWBORNS

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#### BACKGROUND

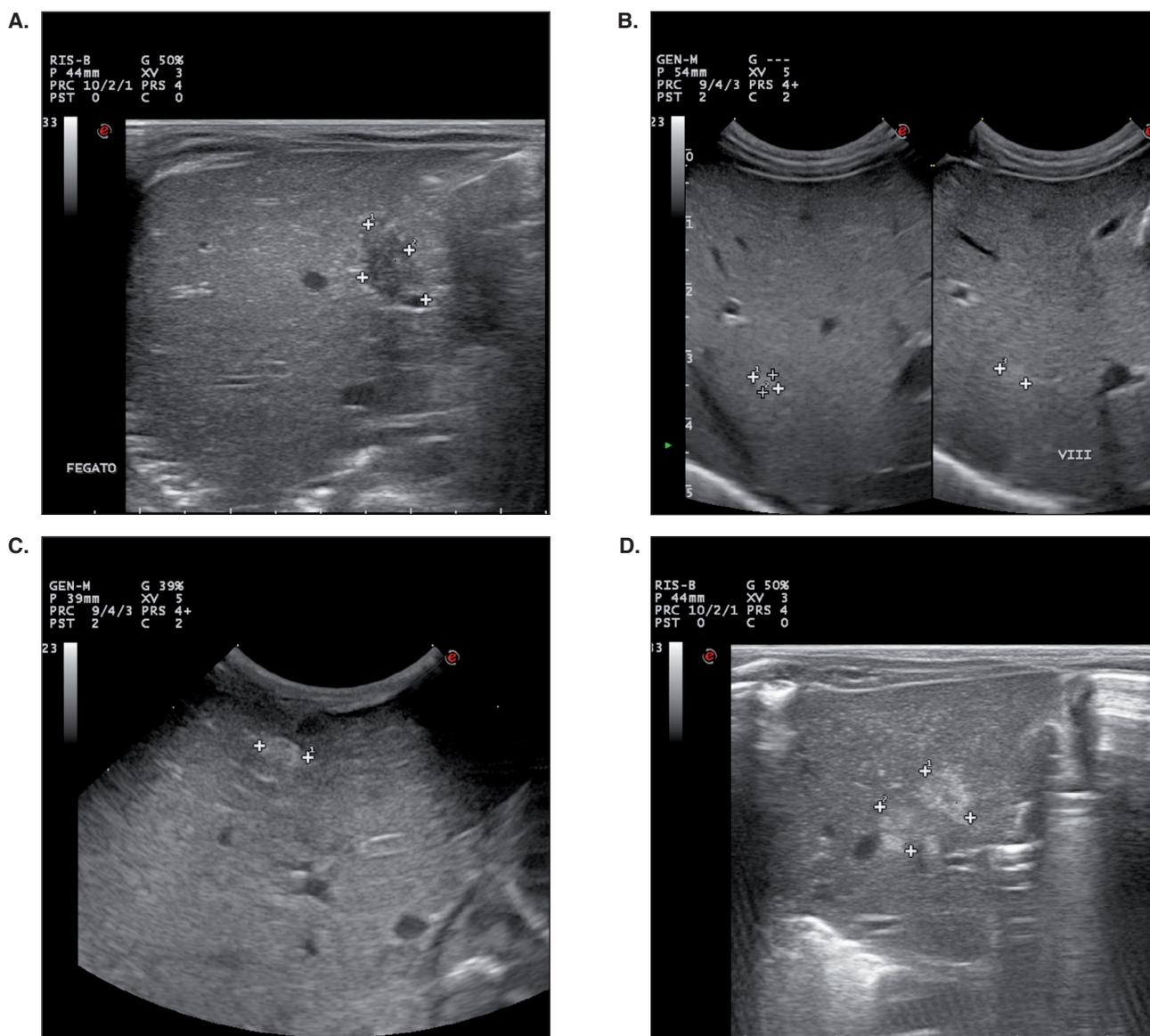
Liver abscesses are a rare but serious condition in newborns often associated with a high mortality rate. The main risk factors reported in literature for the development of this complication are sepsis, umbilical catheterization (UVC), central parenteral nutrition, NEC, surgery and prematurity. Treatment options depend on the diagnosis timing and include antibiotic therapy and surgical drainage. Early diagnosis is crucial, but it may be delayed because of the lack of specific signs and the subtle initial radiologic pattern that may be underestimated.

#### METHODS

We are presenting 4 cases of neonates diagnosed with liver abscess in our hospital unit. All of our patients were girls showing signs of inflammation, 5 to 72 days of age at the diagnosis. Observed risk factors were prematurity (3/4) and UVC (3/4). Diagnosis was made through an ultrasound (US) scan and all patients underwent ultrasonographic monitoring. The radiologic diagnosis was confirmed by the response to antibiotic therapy.

#### RESULTS

The radiologic pattern varied from indefinite hypoechoic areas, possibly containing an echoic core, to solid hyperechoic lesions. Different aspects may depend on the pathogen involved or on the different stages of the abscesses. In two patients, the main lesion was combined with satellite



**Figure 1 (ABS 10).** Different pattern of hepatic abscesses from our clinical record.

hyperechoic foci that gave the liver an irregular aspect. Furthermore, a hyperechoic septic embolus was recognized in two cases. All lesions responded to broad-spectrum antibiotic therapy, eventually disappearing or leaving a small hyperechoic area, probably due to fibrosis. No patients needed to undergo a surgical drainage.

#### CONCLUSIONS

Despite the severity of the condition, an early diagnosis based on recognition of the initial US pattern may prevent an invasive procedure such as surgical drainage. Abscesses should be investigated in newborns presenting risk factors, even in presence of vague signs, and an abdominal US scan should always be performed. In case of unknown pathogen, broad-spectrum antibiotics should be used and strict US monitoring must be planned in order to confirm

the efficacy of the therapy and promptly identify a possible progression of the disease (**Fig. 1**).

#### ABS 11

#### RESPIRATORY PROBLEMS IN CHILDREN WITH REPAIRED ESOPHAGEAL ATRESIA AND TRACHEOESOPHAGEAL FISTULA

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## INTRODUCTION

Children with congenital esophageal atresia (EA) and tracheoesophageal fistula (TEF) have chronic respiratory symptoms including recurrent pneumonia, wheezing and persistent cough.

## AIM

The aim of this study is to describe the clinical findings of surgically corrected patients with EA and TEF and the instrumental investigation to which they have undergone during follow-up evaluation, in order to better define a standardized algorithm for their long-term management.

## METHODS

A retrospective data collection was performed on 105 children with EA and TEF followed at Department of Pediatric Medicine of Bambino Gesù Children Hospital (Rome, Italy) between 2010 and 2015.

## RESULTS

64 (61%) children were treated at Bambino Gesù Children's Hospital for surgical repair of EA with TEF. 70 (66.6%) children reported lower respiratory symptoms with a mean age onset of  $2.2 \pm 2.5$  years and only 63 (60%) performed specialist assessment at Respiratory Unit. The first pneumological evaluation was performed at mean age of  $3.9 \pm 4.2$  years. 29 patients underwent chest CT with contrast enhancement detecting localized atelectasis (43%), residual tracheal diverticulum (35.7%), bronchiectasis (32.1%), tracheal vascular compression (21.4%) or without other causes (17.8%) and esophageal diverticulum (14.3%). 53 patients have undergone to airways endoscopic evaluation detecting tracheomalacia (74%), residual tracheal diverticulum (29.8%), tracheoesophageal fistula recurrence (21.2%) and vocal cord paralysis (12.7%). Of the remaining 35 patients, 13 (12.4%) referred only upper respiratory tract infections and 22 were asymptomatic for respiratory disturbances. None of them received pneumological assessment.

## CONCLUSIONS

Our study underlines that respiratory symptoms often complicate AE and TEF; their persistence despite surgical treatment of gastroesophageal reflux means that other etiological hypotheses must be examined. Associated cardiopathy and atopy may contribute to the early onset of symptoms. On the basis of the above considerations, due to

patients' complexity and comorbidity, a delayed pneumological assessment is unjustified.

## ABS 12

### FROM MAZARA DEL VALLO: PRAWNS IN CHILDREN'S DIET FOR THE ROOTS OF MEDITERRANEAN CULTURE

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*L.U.de.S. H.E.I., Malta*

The interdisciplinary scientific convention "The days of prawn" took place on July 21<sup>st</sup>, 2016, in Mazara del Vallo (TP, Italy). It was promoted by the "Innovation and Culture Association" under the patronage of the Municipality of the town. The meeting highlighted the advantages of the introduction of prawns in children's diet. A project was announced to be undertaken in Mazara del Vallo for the evaluation of children's appreciation of prawns. The project would involve schools, pupils and families.

#### PRAWNS IN CHILDREN'S DIET

The inclusion of prawns in children's diet promotes the consumption of fish, which is consumed in insufficient quantities in Italy. The consumption of fish is important because it guarantees the introduction of essential nutritional principles. On average, Italian children eat fish once a week at most, compared to the recommended intake of three times a week. The reasons for the low consumption of fish are various. For children, the lack of appreciation of fish is due to the presence of fish bones. For this reason, children prefer fillets or fish balls, shrimps, prawn or squids. Prawn is well accepted by children because the cartilages can be removed easily, totally isolating the meat. From the age of two to six years, children imitate the behavior of others, therefore the parents will have to make the cleaning operation slowly so that their child might repeat the operation. After six years the child is able to make autonomous mental operations based on what he observes, so it will be enough for parents to explain how to clean prawns, showing the most difficult phases. The red prawn Mazara offers an extra advantage, because it is known that the red color eases the acceptability of food, while the shrimp evokes pleasant memory of the sea in the child, increasing the appreciation of food. For parents, the scanty use of the fish is also determined by the long time to cook it, while cooking the red prawn is a quick process. Shrimps

can be cooked without shell. Prawns can be prepared by throwing them in a boiling pot of salted water and vinegar, removing them when the water starts to boil again and placing them in water and ice. As an alternative, they can be breaded without shell and baked in the oven at 250°C for 8 minutes. Cooked without shell, head and tail, they are even better accepted by the children. As an alternative, shrimps can be placed in a baking dish, sprinkled with coarse salt, then put in the oven, previously heated, at 180°C for 20 minutes.

#### THE ROOTS OF MEDITERRANEAN CULTURE

To use the prawn in the diet of children offers another advantage: it encourages the discovery of cultural roots. It is known that children and teenagers need “roots and wings” to grow. Roots are familiar, but there are also those represented by the area in which you live. The culture and life linked to the Mediterranean Sea are essential because they constitute the cultural and historical roots of Europe, which are present in the living and in the history of every family and community. This is also an important reason to promote the use of Mediterranean fish. In Mazara del Vallo, always point of union and integration of the Mediterranean people, the appreciation of red prawn will be evaluated with the involvement of students and families in a food education project. Red prawn will be offered in some schools to demonstrate the appreciation among children, while a cooking school will be created with the participation of parents and children together.

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#### ABS 13

#### THE METABOLIC FINGERPRINT OF TERM INFANTS WITH NORMAL AND INCREASED FETAL GROWTH

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#### INTRODUCTION

The intrinsic growth potential of a fetus is affected by maternal age, race, height and weight at the beginning of pregnancy, gestational age, parity as well as fetal gender and birth-weight. Under normal conditions, fetuses grow appropriately for gestational age (AGA), while infants with a larger than expected growth (above the 90<sup>th</sup> percentile) are referred as large for gestational age (LGA). A main cause of fetal macrosomia is maternal diabetes. High Resolution Nuclear Magnetic Resonance (HR-NMR) based metabolomics may provide information regarding the metabolic responses of living systems to disease and elucidate biomarkers of prenatal health. In this context, NMR metabolomics was employed to highlight metabolic changes underlying prenatal disorders and determine metabolites that could serve as potential markers related to LGA newborns.

#### METHODS

Diabetic mothers were followed by an Endocrinologist specialized in Gestational Diabetes and were treated according to the Guidelines on Hyperglycemia and Adverse Pregnancy Outcome. Blood was collected from full-term parturients being at the first stage of labor, as well as from the doubly clamped umbilical cords (UC-mixed arterio-venous blood) of their singleton infants at birth, representing the fetal state. NMR Spectroscopy (Varian 600 MHz) and Carr-Purcell-Meiboom-Gill (CPMG) pulse sequence was employed on maternal and umbilical cord (UC) serum. Multivariate data analysis elicited information from the NMR spectra and probed to metabolic signatures of macrosomic fetuses.

#### RESULTS

LGA fetuses presented with alterations in the amino acid profile, compared to AGA ones. Discrimination between LGA fetuses from mothers without Gestational Diabetes (LGA-NGDM) and LGA fetuses from mothers with Gestational Diabetes (LGA-GDM) was achieved both in maternal and in UC blood samples. The role of glutamine, alanine, valine, leucine isoleucine, threonine, glycerol and glucose is emphasized for maternal LGA samples differentiation. Glycine and histidine only contributed to the differentiation between UC samples, the former characterizing AGA controls,

while the latter ascribing to both LGA-GDM and LGA-NGDM cases.

#### CONCLUSIONS

This holistic metabolomics study provided validated statistical models separating LGA cases from AGA controls, as well as LGA-GDM from LGA-NGDM cases and unveiled secondary metabolites related to the LGA phenotype at the time of delivery.

#### ABS 14

### IN THEIR MOM THEY FIND THEIR ENTIRE WORLD, NOT JUST THE MILK: A REVIEW OF LITERATURE ABOUT SKIN-TO-SKIN

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The new mother and the family generally see the newborn as an individual with simple and basic needs, almost as if the motto “eat and sleep” could keep him completely satisfied. In 1954, the American psychologist Abraham Maslow developed the “Pyramid of human needs” model, which is a hierarchy of needs ranging from the lowest (primary, physiological needs) to the higher ones (the full achievement of human potential/self-actualization). Before birth, the child’s needs are entirely fulfilled by his mother’s body. Is it possible that just a few minutes after birth the hospital staff can take care of the same needs? If it is true that, in a partial way, the physiological needs can all be immediately met, all the other needs, the higher ones (physical and family security, protection and affection), remain unsatisfied. The “skin-to-skin”, or the mother-baby naked contact after birth, is nowadays seen as a real health care practice, aimed at moving from the most basic needs such as nutrition, homeostasis and sleep, to the highest ones. It is important to promote uninterrupted mother-baby contact for as long as possible, not only in the first moments of life of the newborn but also in the following days and weeks. At birth, the newborn is lying on the mother’s womb. Here, through touch and smell his needs are immediately satisfied. Studies show that holding a baby skin-to-skin stabilizes the little one’s heart, respiratory and oxygen saturation rates. It also regulates the baby’s body temperature and keeps blood sugar levels higher. There are several international studies that proved the effectiveness of skin-

to-skin as a first step in the path of a successful breastfeeding. In 2014, an Iranian team carried out a study on 92 mothers. 47 of them practiced skin-to-skin while the remaining 45 chose routine care. The differences between the groups became immediately evident: the first feed in newborns with skin-to-skin happened around the 21<sup>st</sup> minute; the other group was feeding around the 66<sup>th</sup> minute. The same study revealed that even during the first month of life there were substantial differences. In the first group an effective breastfeeding was recorded in around 56.6% of the mother-child pairs, while the percentage dropped to 35.6% in the second group. Another study carried out in 2014 in New Delhi provided even more striking data on the efficacy of skin-to-skin. 95% of the mothers who chose the skin-to-skin experienced exclusive breastfeeding within the first 48 hours after birth, while this amount was around 90% among those who did not. The first 6 weeks showed that 90% of the first group and only 28.6% of the second group then continued with exclusive breastfeeding. Skin-to-skin is the ideal condition for the establishment of a healthy microbiota. The microbial flora of the human body (or microbiota) should be considered as a real organ playing a vital role in human health: it promotes intestinal homeostasis, stimulates the development of the immune system, protects against pathogens and contributes both to processing nutrients and producing energy. Imbalances of the gut flora have been linked to an increasing number of diseases, including inflammatory bowel disease, necrotizing enterocolitis, diabetes, obesity, cancer, allergies and asthma. The two main determinants of the gut health in infants are the ways the baby is both delivered and fed. Cesarean delivery disrupts the normal gut microbiome of neonates, preventing them from encountering the bacteria of the birth canal and maternal rectum. Concerning feeding, it is well known that breastfeeding promotes a “healthy” gut providing selective metabolic substrates for beneficial bacteria. All these favorable attentions towards the child should not be confined to the delivery room and should continue throughout the entire hospitalization of the mother and child. The proximity throughout this time, called rooming-in, allows the continuation of the skin-to-skin and increases the opportunities to obtain an effective latching (basic need for feed). Several studies proved a significant increase in  $\beta$  endorphins that gratify and strengthen mother-child interaction, or what mothers perceive as a “desire for closeness”. From 1994 to 2003, Thailand conducted several

studies in “baby-friendly” hospitals showing a considerable increase in the duration of breastfeeding in the pairs practicing the rooming-in (from 22 to 31 weeks between 1993 and 2004). As a result, from birth to 5 months, there has been a successful improvement in exclusive breastfeeding rate going from 34% to 42%. What obstacles could stand in the way of promoting rooming-in? Most likely, the maternal fear of not being able to rest. However, the polls among mothers denied that the distance from the child allows them to rest better. Many mothers sleep more peacefully knowing they are able to breastfeed their baby on demand and comfort him if he or she cries (need for maternal rest and security for the child). It is crucial not to underestimate the role of the amount of suction at the breast when mother and child spend the night together. All professionals in maternity facilities should encourage an optimal relationship between mother and child; they should also promote skin-to-skin in the delivery room and the operating room in case of cesarean sections and provide strong support during the hospitalization if the woman chooses rooming-in. Consequences can only be favorable for the whole family: a more serene relationship with the newborn and higher chance of exclusive breastfeeding, with all its short and long-term benefits.

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## ABS 15

### UNEXPECTED PAINLESS DUODENAL ULCER IN A GIRL WITH REFRACTORY IRON DEFICIENCY ANEMIA (IDA) DUE TO *H. PYLORI* (HP) INFECTION

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Iron deficiency is the most common nutritional disorder in the world. In recent years, the asso-

ciation between *H. pylori* (HP) infection and iron deficiency anemia (IDA) has been confirmed with these possible mechanisms: increased iron loss due to micro hemorrhages secondary to gastritis, reduced iron absorption following chronic pan-gastritis and iron utilization by the bacterium. We report the case of a 12-year-old girl with refractory IDA secondary to HP infection associated with active painless hemorrhagic duodenal ulcer. She was admitted for severe anemia (Hb 4.8 g/dl, MCV 68.5 fl) requiring 2 blood transfusions. She was pale with asthenia and fatigue without gastrointestinal symptoms. Hb electrophoresis, hemocult (3 samples), hemolysis and malabsorption screening tests were negative. Iron intake was inadequate, without evidence of pica. Her periods were regular for frequency and quantity. Hematologic studies confirmed IDA. Oral iron bisglycinate chelate was started with progressive increase in Hb levels (Hb 11.5 g/dl). After having discontinued iron therapy Hb levels decreased. Therefore we started again oral iron therapy and we tested stools for HP, which were positive. After antibiotic treatment, stools became HP negative, but without increase of Hb level (Hb 8.6 g/dl). Therefore, to rule out gastrointestinal occult bleeding, abdominal scintigraphy and endoscopy were performed: the first one was negative for Meckel’s diverticulum, the second one showed gastric erosions and a painless hemorrhagic duodenal ulcer with size of a 1/3 of duodenal circumference. Therefore proton pump inhibitors were started. In case of refractory IDA secondary to HP infection, gastrointestinal ulcers should also be ruled out.

## ABS 16

### EARLY CLINICAL AND SEROLOGIC MARKERS OF BILIARY ATRESIA: ANALYSIS OF THREE CASES IN NORTH SARDINIA

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## INTRODUCTION

Biliary atresia (BA) is a rare but severe disease of infancy, characterized by progressive inflammation

and fibrosis targeting the extra- and intra-hepatic bile ducts. Early diagnosis allows the surgical intervention of “hepatic-portoenterostomy according to Kasai” avoiding or postponing later in life the need of liver transplantation in about half of cases. Unfortunately, delayed diagnosis is still common, significantly affecting the short and long-term prognosis.

#### AIM

The aim of the study was to identify clinical and biochemical markers for an early diagnosis of BA.

#### METHODS

The medical records of 3 BA infants diagnosed in 2011-2013 at 2 different Neonatology Units in North Sardinia were retrospectively analyzed.

#### RESULTS

Case 1 is a 29-day-old apparently healthy baby girl who presented with jaundice and acholic stools. Cholestasis was confirmed by increased serum total bilirubin (12.4 mg/dl), transaminases (AST 176 U/L: ALT 99 U/L) and  $\gamma$ -glutamyl transferases ( $\gamma$ GT 172 U/L) levels. BA diagnosis was highly suspected at the abdominal ultrasounds and promptly confirmed by liver biopsy, allowing a successful Kasai surgery at the 41<sup>st</sup> day of life. Case 2 is a 39-day-old baby girl with failure to thrive, jaundice, acholic stools, hyperchromic urine. In this case BA diagnosis was also suspected by clinical and serological evidence of cholestasis (Total Bil 10.9 mg/dl, Direct Bil 8.5 mg/dl, AST 123 U/L, ALT 63 U/L,  $\gamma$ GT 225 U/L) and by abdominal ultrasounds. Liver biopsy confirmed BA diagnosis. Kasai surgery was performed at the 44<sup>th</sup> day of life. Case 3 is a breastfed baby girl in apparently good health and growth, who came to our attention at 120-day-old because of prolonged jaundice. Cholestasis was revealed by increased serum levels of total and direct bilirubin (11.58 mg% and 4.6 mg%), transaminases (AST 234 U/L: ALT 145 U/L) and  $\gamma$ GT (237 U/L). Abdominal ultrasounds showed evidence of cirrhosis and portal hypertension. Liver biopsy confirmed a very advanced BA stage, precluding the Kasai surgery. The baby underwent a successful liver transplantation. Comparison and analysis of the 3 cases identified progressive serum  $\gamma$ GT increment as the most reliable and early BA marker.

#### CONCLUSIONS

The direct fraction of bilirubin and serum  $\gamma$ GT represent early biochemical BA markers that need close monitoring within the 1<sup>st</sup> month of life in all the newborns with prolonged jaundice with or without the clinical marker of acholic stools.

#### ABS 17

### GASTRIC PNEUMATOSIS IN AN EXTREMELY PRETERM INFANT: A CASE REPORT

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#### INTRODUCTION

Gastric pneumatosis is defined as gas within the wall of stomach. It is extremely rare in neonates and it is primarily a radiological diagnosis [1]. We report a case of gastric pneumatosis in an extremely preterm admitted to our service in the first hour of life.

#### CASE REPORT

A dichorionic, diamniotic pair of twins was born at a gestational age of 25 weeks by spontaneous vaginal delivery. Vaginal culture and urine screening were positive for Gram-Negative bacilli, which required peripartum antibiotic prophylaxis. Resuscitation in twin 2 included intubation at 15<sup>th</sup> minute with one dose of surfactant. Extubated after 10 hours, she required non-invasive ventilation for 5 days. Minimal enteral feeding was commenced 2 hours after delivery. Infection markers were negative in the first 12 hours. After 24 hours, therapy with hydrocortisone hemisuccinate was started for hypotension. Four days postpartum, blood transfusion was required for anemia and a treatment with intravenous sodium bicarbonate and phosphorus was started for metabolic acidosis with hypophosphatemia. Cerebral ultrasound showed right intraventricular hemorrhage (IVH) grade I. On day 5 of life, the neonate was noted to have abdominal distension, with bluish discoloration and absent peristalsis; the abdominal radiograph showed gastric pneumatosis without perforation. Classified as necrotizing enterocolitis (NEC) 2B stage, enteral feeding was stopped. Biochemical investigation showed increased PCT and pancytopenia, therefore antibiotics were started. Blood culture was positive for *E. cloacae*. For a progressive increase of oxygen needs associated to bradycardia, endotracheal intubation was performed and mechanical ventilation was started, followed by external cardiac massage and 8 doses of intravenous and endotracheal adrenaline, a dose of atropine, a solution of sodium bicarbonate and

calcium gluconate without any benefit. Ultrasound examination showed bilateral IVH grade III in the brain and impaired cardiac contractility with no free air in the abdomen. After more than 40 minutes, it was decided to stop resuscitation.

#### CONCLUSIONS

Gastric pneumatosis can be caused by several conditions, but its finding in neonates requires primarily the exclusion of NEC. It requires a rapid intervention through the establishment of an appropriate antibiotic therapy to reduce the risk of mortality [1, 2]. In our case, the uncontrolled septic shock and the subsequent death were not related to intestinal perforation, which represents the most frequent cause of mortality.

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#### ABS 18

##### RISK FACTORS OF FETAL ARRHYTHMIAS

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#### INTRODUCTION

Fetal arrhythmia (FA), according to different authors, is observed in 3-8%. It is associated with 58-60% of mortality among children. The reasons of FA are systemic and autoimmune diseases of the mother, diabetes, inflammatory diseases of the genitourinary system, hypothermia, hypoxia, hypokalemia, defects and tumors of the fetal heart, intrauterine infections. Currently no clear data about the etiology of FA are available; there is no uniform classification of the FA; no exhaustive clinical and laboratory diagnostic algorithm; there is no single approach to obstetric tactics for FA.

#### MATERIALS AND METHODS

We showed a serious gap in the knowledge of the nature of occurrence of the FA, paralleled by no universal classification dysrhythmia fetus without designated single optimal treatment strategy. The following analysis of clinical material includes the history of 255 women in childbirth, with urgently transabdominal delivery for acute fetal hypoxia.

#### RESULTS

We present a simple classification. It takes into account two groups dysrhythmia – “organic” and “functional”. We revealed leukocytosis (82%), colitis (41%) and preeclampsia (20%), burdened obstetric and gynecological history (68%), the threat termination of pregnancy (54.5%), of gestation toxicosis (27%) and infectious and inflammatory diseases of different localization during the current pregnancy (32%).

#### CONCLUSIONS

Our findings highlighted the important role of infectious factors in the development of the FA. This work discusses the optimal obstetric tactics, particularly when functional FA is present, focused to thereby reduce perinatal loss.

#### ABS 19

##### MALFORMATIVE PATHOLOGIES IN FETAL AUTOPSIES: A FOCUS ON CARDIOVASCULAR AND GENITOURINARY SYSTEMS. OUR DE-CENNIAL EXPERIENCE

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#### BACKGROUND

Fetal autopsies are increasing: the recognition of genetic syndromes and maternal diseases represents the cornerstones of future pregnancies programs. Cardiovascular and genitourinary systems require a special attention. An autopsy series of malformed fetuses in a regional reference center is reviewed.

#### METHODS

We reviewed all fetal autopsies for the period 2004-2014 of the Anatomic Pathology Unit of IRCCS San Martino-IST. All cases with an abnormal karyotype, with malformations or with karyotype-related placental abnormalities were included.

#### RESULTS

302 cases were considered; in 70% of cases karyotype analysis was available: Trisomy 21 (n = 78; 25.83%), Trisomy 18 (n = 25; 8.28%), Trisomy 13 (n = 19; 6.29%), and other. In most of the cases

a single body district resulted affected (n = 127; 42.05%). Cardiovascular (n = 55, 18.21%) and genitourinary malformations (n = 39, 12.91%) were uncommon, preceded by skeleton (n = 80, 26.49%), soft tissue and skin (n = 65, 21.52%), and digestive tract (n = 46, 15.23%) malformations. Septal defects resulted to be the most frequent malformation (interventricular n = 10, interatrial n = 8); aortic stenosis was the most observed malformation of large vessels (n = 10); valvular alterations were rarer but all valves were almost equally affected. Concerning the kidney, hydronephrosis was the most frequent defect of the renal pelvis (n = 11) while dysplasia was the most frequent defect of the parenchyma (n = 10). Ectopia was observed in a total of 8 cases.

#### CONCLUSIONS

Cardiovascular and genitourinary malformations are rare and only a handful of specific cases can be observed even in large series, requiring a specific expertise. The issuance of an effective autopsy report may represent the starting point of planning future pregnancies.

#### ABS 20

#### ROLE OF IMAGING IN NEONATAL ARTERIAL AND VENOUS STROKE

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#### INTRODUCTION

Neonatal arterial/venous cerebral stroke is diagnosed after birth, usually within the first 2-3 days of post-natal life, and in any event no later than 28 days, even in preterm childbirth. The arterial ischemic stroke is the most common form of cerebral infarct, with an incidence of 28 cases/100,000 year live births in US. Seizures are the most frequent symptom; the ischemic events should be differentiated from metabolic diseases and the infections of central nervous system. MRI is more sensitive and specific than US in the detection, diagnosis, prognosis of cerebral damage arterial and venous stroke; MRI defines the extent and vascular territory of the infarct, number of lesions and presence or absence of

hemorrhage. MRI is superior to CT in detecting small and early infarcts, without X-ray exposure. In early arterial ischemia diffusion weighted imaging (DWI) is positive before conventional MRI and CT; moreover, MRI combined with diffusion tensor imaging (DTI) is the study of choice for the evaluation of chronic damage.

#### AIMS

To define the role of ultrasound (US), magnetic resonance imaging (MRI) and computed tomography (CT) in diagnosis and follow-up in neonatal arterial and venous stroke.

#### DISCUSSION

The etiology of arterial cerebral ischemia remains mostly unknown; defects of coagulation are the most significant among the causes. MRI is the neuroradiological examination of choice as it is able to visualize lesions located to the convexity of the hemispheres, which are difficult to evaluate through US transfontanelar examination. Within 24 hours from the stroke event DWI allows detection of arterial ischemia damage. MRI angiography documents the arterial occlusion, congenital vascular anomalies, and carotid artery dissection. The cerebral venous infarcts (CVI) are mostly based on thromboembolism due to coagulation disorders or congenital heart disease, often due to unknown etiology. In the acute phase venous infarcts are characterized by an important hemorrhagic component; CVI can be studied with conventional MRI, MR angiography (MRA) and MR venography (MRV) to evaluate the occlusion point.

#### CONCLUSIONS

MRI, MRA, and MRV are techniques of choice in evaluation and diagnosis of acute stroke, with the documentation of extension of lesions and the location of occlusion. Conventional MRI and DTI have an important role in assessment of subacute-chronic damage, and in patient outcomes evaluation.

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## ABS 21

### UNEXPECTED ENDOCARDITIS IN A PRETERM INFANT

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#### INTRODUCTION

Neonates with congenital heart disease and percutaneous central catheters are at higher risk for endocarditis, which might also happen during septicemia.

#### CASE REPORT

We present the case of a preterm infant (32 weeks gestational age, birth weight 2,280 g) whose perinatal history was significant for preterm prelabour rupture of membranes (pPROM) at 26 weeks gestational age, oligohydramnios, Group B *Streptococcus* (GBS) negative maternal vaginal swab, and smelly amniotic fluid. At birth he was treated for infection (PCR 13 mg/L) with ampicillin and netilmicin for 10 days. Blood culture was negative. He was affected by respiratory distress syndrome (RDS), treated with one dose of surfactant and mechanical ventilation for 3 days, then extubated and treated with oxygen for 26 days. He received phototherapy for jaundice. Soon after birth two cardiac and head ultrasounds were negative. He received ultraviolet C (UVC) during the first 7 days and a peripheral inserted central catheter during the next 2 days.

The mother reported temperature instability during the first days. At 30 days, during a routine cardiac ultrasound (without a specific indication), a vegetation (2 mm diameter) on the tricuspid valve was detected. Laboratory tests, blood cultures (6 samples) and peripheral swabs were negative. He was treated with vancomycin (for 6 weeks) and gentamicin (for 2 weeks), and heparin for the first 11 days. No bacteria have ever been detected and cardiac function has always been within normal limits.

#### CONCLUSIONS

In preterm infants with risk factors, unexplained fever should always alert the physician to a possible endocarditis and a cardiac ultrasound should be performed during hospital admission to rule out possible vegetations.

## ABS 22

### SHOCK IN NEONATES: DON'T FORGET THE HEART!

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#### INTRODUCTION

Shock is not rare in neonatal age and it can be due to many causes. The goal of treatment is to ensure adequate perfusion of tissues, taking into account the underlying cause, therefore it is essential to perform an early correct diagnosis. Paroxysmal Supraventricular Tachycardia (PSVT) can produce cardiogenic shock related to a too high heart rate with almost absence of cardiac output; in children, it is the most common rhythm disturbance.

#### CASE REPORT

A 17-day-old full-term male neonate was admitted to our Neonatal Pathology because the parents reported poor feeding for 10 days and vomits in the last one. At observation, he presented poor general status, tachypnea, pale and cold skin; heart rate (HR) was 150 bpm in sinus rhythm, cardiac auscultation was normal and the oxygen saturation (SpO<sub>2</sub>) was normal at room air. After 2 hours, his clinical condition got worse, with mottled blue and white skin, irritability and SpO<sub>2</sub> of 76% despite

oxygen administration; his HR reached 320 bpm and blood pressure was not measurable. He was transferred to the Neonatal Intensive Care Unit (NICU) and visited by a pediatric cardiologist: at echocardiogram, the ejection fraction was 10% and the ECG revealed PSVT. He was supported with high-flow nasal cannula (HFNC) at 5 L/min with  $\text{FiO}_2 = 1$  to keep saturation about 83%. The vagal maneuvers did not work and after the positioning of an intraosseous access he started intravenous bolus of adenosine at crescent doses (from 0.1 to 0.25 mg/kg), with a reversion of PSVT to a sinus rhythm and progressive improvement of general status in the next hours. The exams showed metabolic acidosis, hyperlactacidemia, high values of liver enzymes, LDH, CK and CK-MB. He was progressively weaned off inotropic support and ventilation and oral administration of flecainide was started. Now the baby is followed by pediatric cardiologists and he is fine.

#### DISCUSSION

Cardiogenic shock in neonates is a rare medical emergency, but it should be kept in mind. Episodes of supraventricular tachycardia are usually paroxysmal, with rapid onset and termination; children may exhibit a range of clinical findings from no symptoms to cardiogenic shock, depending on the duration of PSVT. PSVT in early infancy can be fatal if not identified and treated early, also with electric cardioversion.

#### ABS 23

##### KAWASAKI DISEASE IN SARDINIA: A SINGLE-CENTER EXPERIENCE

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#### BACKGROUND

Kawasaki disease (KD) is an acute systemic vasculitis affecting young children, which is potentially fatal if not promptly diagnosed and treated. No study exists on KD in the island of Sardinia.

#### OBJECTIVE

To investigate the incidence and characteristics of KD in North Sardinia.

#### METHODS

We performed a 6-year (2009-2014) cross-sectional analysis of KD records at the Pediatric Clinic, University of Sassari, Sassari, Italy.

#### RESULTS

Seventeen children (mean age =  $28 \pm 26$  months;  $M = 9$ ) were identified, among whom 13 (76%) were aged below 5 years and the youngest was a 5-month-old baby. The overall incidence was 10/100,000, similarly to that reported in western countries, with no seasonality. The clinical records were available for 9 out of the 17 patients. Five of nine (56%) children (mean age 4.5 years; range 16 months-6 years) had complete KD at presentation, 3/9 (33%) had incomplete KD (23, 46 and 48 months; mean age 3.5 years) and only a 33-month-old boy had atypical KD (11%). Intravenous immunoglobulin (IVIG) therapy was given to all but one case, because of the delayed diagnosis. A high risk for coronary aneurisms was detected in 3/9 children (33%), two of them with complete and one with atypical KD; all responded to IVIG.

#### CONCLUSIONS

This is the first study on KD in a cohort of Sardinian children. An increased awareness among pediatricians that incomplete and atypical forms represent almost half of all forms of KD is essential to establish an early diagnosis and to prevent the worsening and cardiac complications of the disease.

#### ABS 24

##### COMPLETE ATRIOVENTRICULAR SEPTAL DEFECT (CAVSD) AND DOWN'S SYNDROME (DS): WHEN CARDIAC SURGERY IS NOT CORRECTIVE, BUT PALLIATIVE

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#### INTRODUCTION

CAVSD is a rare congenital heart disease (CHD) caused by the faulty development of the embryonic endocardial cushions; the consequence is a communication both in the

interatrial and the interventricular septum, with a common atrioventricular (AV) valve, generally insufficient. CHD are frequent in children with DS (40%), and ventricular septal defect (VSD) and AV septal defect are typical malformations.

#### CASE REPORT

S. is a preterm female neonate (34 weeks), born by urgent cesarean section for breech presentation and cardiocographic alterations. Prenatal echocardiogram found CAVSD without obstruction of the right outflow tract. Given the association between CAVSD and DS, amniocentesis was recommended, but it was not been performed for maternal choice. At birth the typical features of DS were present and the diagnosis was confirmed by karyotype. The ECG performed on the first day of life revealed signs of pressure overload on the right cardiac sections and the echocardiogram showed a severe insufficient common AV valve, a large ostium primum atrial septal defect, a large inlet VSD without obstruction of the right and left outflow tract and a large patent ductus arteriosus with bidirectional shunting because of systemic pressures in the pulmonary artery. The baby was diagnosed with unbalanced CAVSD, with hypoplastic left ventricle and severe AV valve insufficiency. The heart failure was medically managed with the use of furosemide (2 mg/kg/day in 2 doses) from 8 days of life. Thereafter, for the persistence of signs of pulmonary hyperflow, as respiratory distress with tachypnea, subcostal retractions, gallop rhythm (heart rate 170 bpm), palpable liver 3 cm below the costal margin, poor weight gain, the baby was entirely fed through a nasogastric tube with hypercaloric milk, and captopril (2 mg/kg/day in 3 doses) was added. During the last hospitalization, because of clinical deterioration, it was necessary to transfer the neonate to a cardiac surgery center, where she underwent palliative surgical therapy consisted of pulmonary artery banding in thoracotomy and ligation of the ductus arteriosus. Bilateral pulmonary atelectasis complicated the postoperative. Currently, S. is in labile hemodynamic compensation, waiting for two other surgeries that do not allow the resolution of her cardiopathy, but only its palliation.

#### DISCUSSION

Patients with DS have rarely unbalanced CAVSD that not permit complete biventricular repair; generally they have a decreased repair risk, lower mortality and morbidity.

#### ABS 25

### CONGENITAL ATRIOVENTRICULAR BLOCK: A CASE REPORT

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#### INTRODUCTION

Complete atrioventricular (AV) block is an uncommon congenital lesion, occurring in about 1 of 20,000 newborns. It is defined as the dissociation of atrial and ventricular contractions. This causes a significant drop in ventricular rate, which may cause fetal cardiac failure, including fetal hydrops.

#### CASE REPORT

Y., a 3,200 g female infant was delivered by a 30 year-old mother (gravida 1, para 2) at 37<sup>+5</sup> weeks of gestational age by cesarean section due to acute fetal distress. Family history was uneventful. Obstetrical ultrasound was normal. Before delivery, fetal heart rate monitoring showed extreme bradycardia. The baby cried immediately after birth with an Apgar score of 9/10 and 10/10 at 1 min and 5 min of birth, respectively. She didn't require resuscitation. Physical examination was normal except for bradycardia to 40 beats per minute without hemodynamic consequences. On electrocardiogram she had sinus rhythm with complete AV block. Echocardiography showed no structural heart disease. Her mother was examined for any feature of connective tissue disease, primarily lupus erythematosus (LE). However, there were no findings suggestive of any clinical and laboratory evidence of this disease (fluorescent antinuclear antibody, rheumatoid factor, and complement levels were normal). Echocardiogram at follow up showed the same findings. A permanent pacemaker was implanted on day 15. On follow up the infant had very good clinical conditions and was discharged to home on day 20.

#### CONCLUSIONS

Because fetal arrhythmias can now be evaluated prenatally by two-dimensional and M-mode echocardiographic and Doppler ultrasound techniques, complete AV block is more frequently identified during the fetal period. The prognosis of congenital complete atrioventricular block (CCHB) with no associated structural heart effects is usually favorable.

## ABS 26

**MISDIAGNOSED IDIOPATHIC SEVERE DILATED CARDIOMYOPATHY IN A 3-YEAR-OLD BOY**

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## INTRODUCTION

Heart failure as initial presenting symptom in cardiomyopathy is uncommon in pediatrics. The initial presenting symptoms in cardiomyopathies are often non-specific and may be confused with more common pediatric illnesses.

## CASE REPORT

We report the case of a misdiagnosed idiopathic severe dilated cardiomyopathy in a 3-year-old previously healthy boy. Three months before admission to hospital he started to suffer from a persistent cough; gastroenteritis, and fever with rhinitis occurred one week before admission. The day of admission to the hospital he was visited again for cough by a pediatrician who ordered a chest X-ray. It showed impressive cardiomegaly with interstitial pulmonary edema. The child was pale, anxious, and showed respiratory distress. Sinus tachycardias with a pansystolic murmur and gallop rhythm were recorded. His liver edge was palpable and he had distended jugular veins. An emergency echocardiogram revealed a massively dilated left ventricle, moderate mitral and tricuspid regurgitation with an ejection fraction < 3%. Because of congestive heart failure he was admitted to Intensive Care Unit. After elective intubation three cardiac arrests were documented, and inotropes (dopamine, dobutamine, adrenaline) were started. He was transferred to Cardiac Intensive Care Unit; head CT scan and MRI were negative, hypothermia was performed. Due to an unsuccessful pulmonary artery banding and worsening clinical condition a Berlin Heart was inserted, waiting for heart transplantation. Genetic, metabolic, and biopsy tests are pending.

## CONCLUSIONS

Heart failure in a young boy is rare and the initial symptoms are often non-specific. Cardiac ultrasound should not be delayed in order to start appropriate medical or surgical therapy.

## ABS 27

**DEVELOPING A TOOL FOR THE MANAGEMENT OF PEDIATRIC EMERGENCIES**

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## INTRODUCTION

Out-of-hospital pediatric emergencies are rare and stressful for medical teams, due to the limited experience and the high emotional involvement. Pediatric age includes patients of very different weight and size [1]. Thus, choosing adequate equipment and drug dosages is complex, making errors more likely [2]. The availability of easy-to-use tools could minimize such errors [2].

## AIM

To develop a tool for the quick identification of equipment and drug doses needed to manage out-of-hospital pediatric emergencies.

## METHODS

According to current literature, including international guidelines and studies focused on in- and out-of-hospital pediatric emergencies, metric reference tools based on anthropometric data, such as the Broselow® System, simplify the management of critically ill children. We used these data to produce a tool able to facilitate equipment and drug dosage choice during emergencies.

## RESULTS

We adapted the nine colors Broselow® System to the seven colors pediatric backpacks used by ambulance medical teams of ASL Cagliari Emergency Medical Services. Each backpack includes a tape divided in nine colored bands, corresponding to different ranges of weight, aimed at estimating child's weight according to his height. The same colors identify a bag inside the backpack, containing the equipment for a child of the corresponding weight, and nine plastic cards listing relevant equipment and pre-calculated drug dosages.

**CONCLUSIONS**

Tools that rationally organize equipment and free medical team from the need of calculating drug dosages may simplify the management of pediatric emergencies. The effectiveness of the tool will be evaluated in a second phase of the study, starting in September 2016.

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**ABS 28**

**TRAINING IN NEONATAL INTENSIVE CARE UNITS: A THREE-YEAR INNOVATIVE EXPERIENCE IN NEONATAL INTENSIVE CARE UNITS IN ROME (ITALY)**

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A training course in neonatology for the staff of neonatal intensive care units (NICUs) in Rome took place in Rome at the St. Camillo Hospital from 2009 to 2012. The course was promoted by the Italian Society of Neonatology, Lazio Region, and organized by the non-profit organization G.R.A.N.I.; it was entitled "Improving quality of care, supporting families, preventing burnout". It was attended by four Roman Hospitals: FBF St. Pietro, St. Filippo Neri, St. Camillo-Forlanini, St. Eugenio, with an annual average of 212 participants. The goal was to make the health professionals aware of relational aspects of neonatal care, in order to integrate a new empathic sensitivity to infant and parents with their professional skills. An original training methodology was employed, based on a participatory mode and individual involvement through thematic discussion groups beyond the traditional classroom teaching. In fact, the use of relational cases and problematic situations allowed to make tensions resurface through group discussion. Tensions were turned into resources for change and improvement. Sharing emotions helped to process such tensions and to support for example the emotional impact of prematurity.

**ABS 29**

**HEPATIC HEMATOPOIESIS: A COMPLEX STEM CELL NICHE AND A DYNAMIC PROCESS**

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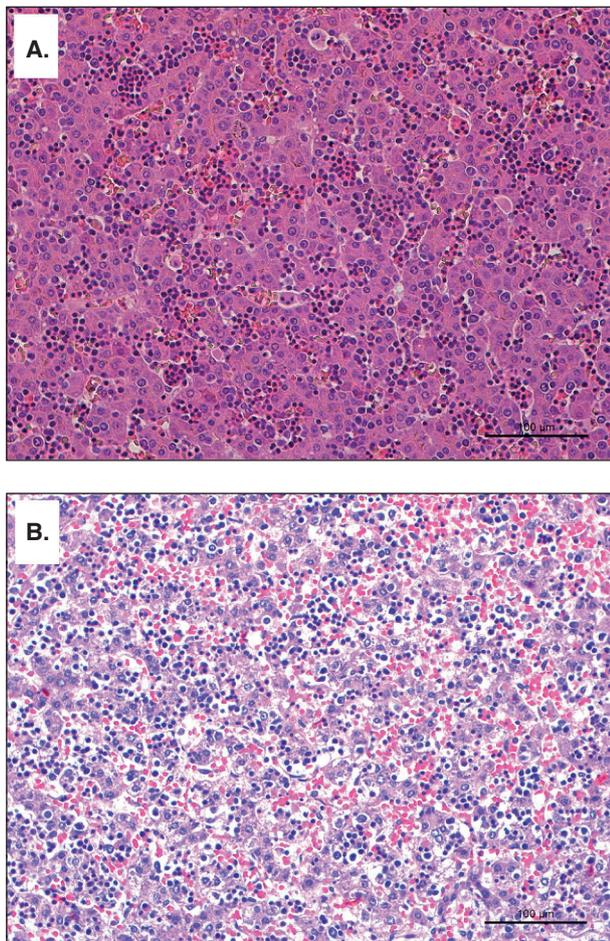
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After conception, the production of blood cells in the newly formed embryo starts extremely early in the Yolk Sac, where erythroid precursors begin producing nucleated red blood cells that fill the circulatory system. After hematopoiesis ceases in the yolk sac, the liver becomes the major hematopoietic organ. During gestation in the liver, a stem cell niche supports the maturation of hepatoblasts in hepatocytes and cholangiocytes. However, at the same time the liver becomes able to support hematopoiesis, thus constituting another niche for hematopoietic stem cells. Hematopoiesis in the fetal liver ceases right after birth, when the bone marrow becomes the only hematopoietic organ. The hematopoietic stem cell niche in the liver is not yet a completely characterized environment, and its regulatory processes are not yet completely clear. This niche is a likely to be a highly complex one and composed of numerous cells. Two cells have a clear role in supporting hematopoiesis: liver sinusoidal endothelial cells (LSECs) and hepatoblasts. Both these types of cells produce chemokines such as CXCL10 and CXCL12, the latter especially plays a major role in the migration of hematopoietic stem cells (HSCs). Indeed, C-kit<sup>+</sup> and IL-7R $\alpha$ <sup>+</sup> HSCs likely migrate from the sinusoids to the hepatic parenchyma, making contact with LSECs and then with hepatoblasts. After this, these cells differentiate into CD19<sup>+</sup> and SLC<sup>+</sup> preB cells [1]. Conditioned medium obtained from LSECs cultures has proven to stimulate HSCs migration; at the same time the activation of CXCR4, receptor for CXCL12, on LSECs promotes the adhesion between them and HSCs [2]. Simultaneously, hepatoblasts support hematopoiesis producing erythropoietin and stem cell factor; these cytokines are also produced by hepatic stellate cells, and evidence suggests that they even produce CXCL12 [3]. Cells residing in the vascular walls such as mesenchymal stromal cells (MSCs) could also be part of the niche, their

number increases during fetal hematopoiesis and they have shown the ability to produce regulatory factors for hematopoietic stem cells, however their real role in the niche is not yet clear [3]. Alongside the regulation of the niche, we believe that great attention should also be devoted to the morphology of the whole phenomenon of hepatic hematopoiesis. Simple observation of sections obtained from the livers of fetuses at different weeks of gestation could already give important insights on the morphology of this hematopoietic stem cell niche, on how different lineages of blood cells develop during gestation and on how the characteristics of hepatic hematopoiesis change depending on the gestational age. We believe, as our preliminary data suggest (**Fig. 1**), that this phenomenon is not a static one, where hematopoietic cells simply continuously develop until the liver can no longer



**Figure 1 (ABS 29).** Hepatic hematopoiesis at different times of gestation. **A.** Hematopoiesis at 12 weeks of gestation, primarily located at the interface between hepatoblast cords and the sinusoids. **B.** Hematopoiesis at 28 weeks of gestation, occupying a greater part of the parenchyma and with hematopoietic foci located among hepatoblast cords.

support hematopoiesis. On the contrary, this phenomenon seems rather a very dynamic one, where a complex set of regulatory factors governs the environment of the niche at different times, thus modifying the morphological characteristics of hepatic hematopoiesis at different gestational ages.

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#### ABS 30

#### INTRAOSSUEOUS LINE FOR ADENOSINE ADMINISTRATION IN THE NEWBORN: A CASE REPORT

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#### BACKGROUND

Adenosine, an ultra-short-acting AV nodal blocking agent, is the primary drug used in the treatment of supraventricular tachycardia (SVT) and it is indicated if vagal maneuvers are not effective. Adenosine is rapidly absorbed and metabolized and should be administered by rapid intravenous bolus to slow cardiac conduction through the AV node. In compromised neonates in whom intravenous access is impossible, immediate vascular access can be securely and rapidly established through intraosseous lines. There are no pharmacokinetic differences between intraosseous and intravenous lines. We have successfully used this route to administer the adenosine in a full-term infant with cardiogenic shock secondary to SVT.

#### CASE REPORT

M.L. a male full-term infant, on the 17<sup>th</sup> postnatal day was referred to our pediatric intensive care unit (PICU) because of the onset of SVT. On arrival he weighed 3,480 g and his conditions were severe: his skin was pale and mottled and he showed poor

perfusion and signs of respiratory distress, RR 80/min, increasing O<sub>2</sub> requirement, HR > 300/bpm, NiBP 65/24 mmHg (mean 39), SpO<sub>2</sub> 88%. CBG analysis revealed a metabolic acidosis. NIV was started (High-Flow Nasal Cannula, 7 lpm, FiO<sub>2</sub> 0.60) and he underwent an ECG + echocardiographic evaluation that confirmed the diagnosis and demonstrated a severe reduction of left ventricular function (EF about 10%). Vagal maneuvers were performed but without success. While preparing adenosine, several attempts to find a vascular access failed. Rapidly an I.O. access line was established (butterfly needle, 21 G) in the proximal extremity of the right tibia. Administration of three rapid boluses of adenosine (0.3 + 0.3 + 0.6 mg respectively) and flushes of NS (5 ml) allowed to restore at the third attempt the normal sinus rhythm. After achieving hemodynamic stability, the I.O. line was replaced with a 24 G peripheral one to continue the medical support.

#### DISCUSSION

In the primary resuscitation of neonates, drug treatment is rarely required. During resuscitation, it is generally impossible to administer drugs through a peripheral vein, because of a probable collapse due to insufficient perfusion. In critical neonates in whom intravenous access is not available, immediate vascular access can be safely and rapidly established through intraosseous lines. Different drugs can be infused, at varying flow rates, either continuously or as a bolus. However, they must be replaced with intravenous lines as soon as the infant stabilizes.

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#### ABS 31

#### CONGENITAL DACRYOCYSTOCELE: CASE REPORT

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#### INTRODUCTION

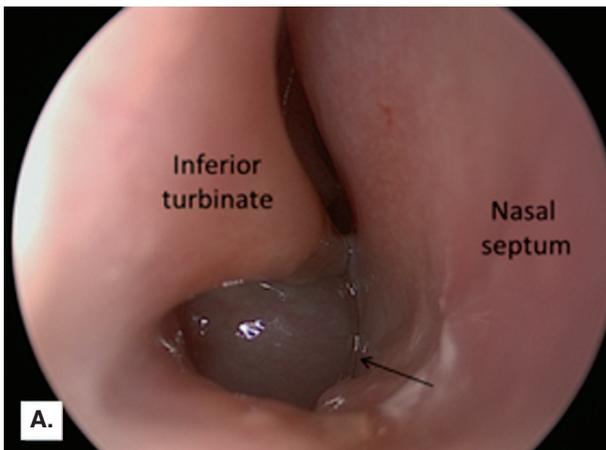
Congenital dacryocystocele is a rare anomaly, generally unilateral, characterized by difficulty in nasal breathing associated with bluish, cystic, and hard mass swelling at the inner side of the eye [1]. Congenital dacryocystocele has to be distinguished from all the nasal cavity anomalies causing nasal obstruction and/or facial swelling [1, 2]. Conservative treatment can be tried as first attempt, but timely surgical intervention may be mandatory [1]. Authors wish to make aware physicians among this rare pathology.

#### METHODS

The authors describe the clinical case of a 4-day-old girl with a unilateral (right) congenital dacryocystocele, treated at the Department of Otorhinolaryngology of the University of Cagliari (Italy) in February 2012.

#### CASE REPORT

Diagnosis was based on physical and endoscopic examination (**Fig. 1**) and tomography. The patient underwent endoscopic surgery under general anesthesia: the medial aspect of the mass was cauterized and removed under direct visualization

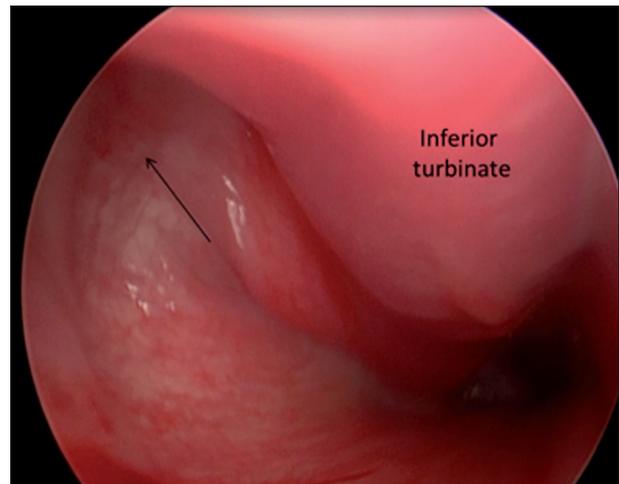


**Figure 1 (ABS 31).** Clinical presentation of the reported case. **A.** Endoscopic view of the congenital intranasal nasolacrimal duct cyst (arrow). **B.** Swelling of the inner side of the eye.

(pediatric 0° endoscopes), with the aid of a microdebrider. Postoperative nasal washing with saline solution was recommended. At 6 months no recurrence of the stenosis with optimal lacrimal drainage was observed (**Fig. 2**).

#### DISCUSSION

Canalization of the excretory lacrimal system is completed from the sixth fetal month to beyond term [2], but when the perforation fails, the obliteration of the nasolacrimal duct may cause a congenital dacryocystocele [2]. Characteristic symptoms are swelling of the lacrimal sac and epiphora, while the nasal obstruction occurs when the dilatation of the nasolacrimal duct expands distally into the nose to form an intranasal cyst [2]. The infection of this pathology causes the dacryocystitis [2], with pain, fever, purulent lacrimation, erythema, edema and increase of the swelling of the medial canthus. Differential diagnosis includes unilateral atresia or



**Figure 2 (ABS 31).** Endoscopic view of the orifice of the nasolacrimal duct (arrow) 6 months after the surgical procedure.

stenosis of the choanae, nasal mid-line masses, nasal pyriform aperture stenosis, meningoencephalocele, hemangioma and dermoid cysts [1-3]. Nasal endoscopic examination is essential for diagnosis [3], while imaging is helpful to differentiate a dacryocoele from an encephalocele or meningoencephalocele, to avoid unnecessary probing and possible violation of brain tissue [2]. Uncomplicated dacryocystocele may respond to medical management alone [3], but when the disorder persists or is associated with severe swelling of the face, dacryocystitis, cellulitis, breathing difficulty, or recurrent dacryocoele, surgical treatment is necessary to re-establish the nasolacrimal drainage.

#### CONCLUSIONS

A nasal duct cyst should be suspected in newborns with unilateral or bilateral nasal obstruction, especially when the nasal symptomatology is associated with swelling of the medial canthus. Surgical management is mandatory in case of severe symptomatology, complications or failure of a conservative management. When a surgical treatment is necessary, an endoscopic approach seems to be minimally invasive and effective.

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**ABS 32****HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS:  
THE GREAT DECEIVER**

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A 30-day-old female of African ethnicity arrived in Emergency Department for recent onset of fever, poor feeding and diarrhea. At evaluation she showed hyperpyrexia, hypertonia, abdomen distension, anemia (Hb 6.9 g/dl), neutropenia (680/mm<sup>3</sup>), thrombocytopenia (66,000/mm<sup>3</sup>), CRP 21 mg/L, PCT 9.45 ng/ml. Transferred to our Pediatric Intensive Care Unit (PICU), she developed tachypnea, hepatosplenomegaly, and metabolic acidosis (lactate 6.5 mmol/L); blood gases normalized after intubation and ventilation. Normal saline bolus was infused for persistent tachycardia, but soon the baby had oliguria and hypotension; inotropes and broad-spectrum antibiotics were started. Cardiogenic shock was ruled out by cardiac US. Lumbar puncture showed mild lymphocytosis. Microbiologic tests (CSF, blood) were negative. Abdominal US and CT demonstrated gas distension, air-fluid levels and splenomegaly. For worsening of anemia and acidosis, blood transfusion and IV bicarbonates were necessary. Subsequently cytopenias, hepatosplenomegaly worsened, and lymphocytosis emerged. Family history revealed a previous infant died at 40 days of life for suspected abdominal sepsis. In the hypothesis of hemophagocytic lymphohistiocytosis (HLH), second level tests showed ferritin > 20,000 mcg/L, increased LDH and TG, decreased D-dimer and fibrinogen, and prolonged PT and PTT. Bone marrow aspiration was negative. Genetic test was positive for type 2 familial HLH (perforin deficit), so the baby began immunosuppression with dexamethasone 10 mg/m<sup>2</sup>/day and cyclosporine. Due to high hemorrhagic risk for transfusion-dependency thrombocytopenia and severe dyscoagulation, the standard chemotherapy treatment based on etoposide was avoided and the baby was included in an experimental study with humanized anti-IFN $\gamma$  monoclonal antibody. Clinical conditions improved, with extubation on 15<sup>th</sup> day and transfer to the Oncologic Unit for continuation of care. In HLH excessive immune activation causes cytokine

overproduction leading to multiorgan failure. The familial type is autosomal recessive. The initial presentation mimics common infection, leading to a challenging diagnosis. Immunosuppression is the cornerstone of early treatment, but hematopoietic stem cell transplant is the only long-term cure in familial forms. In this case, the early onset is noteworthy, as it made nonspecific symptoms and signs more difficult to interpret and mimicked septic shock. Accurate familial history and aggressive support in PICU allowed proper diagnosis and effective clinical stabilization.

**ABS 33****SUBCLAVIAN VEIN CANNULATION IN NEO-  
NATES**

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**BACKGROUND**

Central venous catheter (CVC) insertion is often required in the management of critically ill neonates but remains challenging even in the most experienced hands. The subclavian vein (SCV) is a great alternative for CVC insertion, but cannulating SCV using landmarks is associated with a high rate of complications, especially in infants < 1 year of age. Ultrasound (US)-guided SCV catheterization via the supraclavicular approach yields higher success rates and lower complication rate, using the in-plane technique.

**AIMS**

1. To describe a 40-month experience with the US-guided SCV catheterization via the supraclavicular approach in neonates and infants weighing < 5 kg admitted to the NICU/PICU of the Pediatric and Neonatal Intensive Care Unit of the Paris South University Hospitals, Le Kremlin-Bicetre, France.
2. To evaluate the residents' learning curve of the US-guided SCV catheterization via the supraclavicular approach.

**METHODS**

Data were collected retrospectively by clinical records of neonates and infants weighing < 5 kg and admitted from January 2013 to April 2016

who received SCV catheterization. A written questionnaire was addressed to the residents to evaluate their competence on US-guided catheterization pre and post-stage.

## RESULTS

A total of 1,036 CVC were placed in neonates and infants weighing < 5 kg. 133 (12.8%) were supraclavicular US-guided SCV catheters. Gestational age: mean = 35<sup>+5</sup>, range = 25-41<sup>+5</sup>; birth weight: mean = 2,601 grams, range 590-4,170; weight at catheter placement: mean = 2,841 grams, range 705-4,960. 93% of the SCV-CVC was left-sided. The success rate was 97.6%. 1 case (0.8%) of accidental arterial puncture was registered. At the end of the stage (6 months), 45% of the residents were able to insert an US-guided SCV catheter after having placed a mean of 7.1 CVCs.

## CONCLUSIONS

The supraclavicular approach for SCV catheterization is a safe and feasible alternative for CVC insertion in neonates, and even premature infants. The learning curve is short when performed by operators with experience in US in-plane technique.

## ABS 34

### IS “NARRATIVOMICS” AN OMICS SCIENCE?

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The use of the suffix “omics” to describe the collective characterization and quantification of entire sets of biological information that translate into the structure, function and dynamics of an organism or organisms in physical and pathological conditions has become widespread in the last decades. Since the word “genomics” was first coined in 1986 to date, several hundred variants of this neologism have been coined, reflecting a shift in the conception of the body from a simple sum of its parts toward that of a highly interactive, interconnected and holistic complex. While traditionally applied to the physical substances (most often biomolecules) directly associated with molecular, cellular and organ systems, a broader interpretation of the concept can also be applied to the practice of narrative medicine, and what it reveals with regard to the totality of an

individual's biography, state of mind, inclinations and interpretation of their health or lack thereof [1]. This “narrativomics”, while difficult to quantify, is highly representative of the uniqueness of humans with regard to other organisms, and is complementary to the molecular messages of our genomes, proteomes, and metabolomes in obtaining a more holistic understanding of a patient. This paradigm, and the question of how a comprehension of these aspects can be more systematically integrated into the clinical process, effectively mining the richness of the relational aspects of the healthcare provider-patient interaction, is timely and fundamental for a more substantial implementation of the individualized medicine that the omics disciplines aim to deliver [2, 3]. This consideration finds a special space in perinatology, where the centrality of mother, fetus and newborn is essential for enabling care, research and training in an innovative “omics way”.

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## ABS 35

### ANCIENT ORAL MICROBIOTA IN CHILDREN SHEDS LIGHT ON THE MODERN STATUS OF HEALTH

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## BACKGROUND

The microorganisms of the human oral cavity include an extensive number of bacteria, more

than 700 species or phenotypes. Some of these bacteria have been linked to juvenile oral or systemic diseases, such as osteomyelitis infective endocarditis, preterm low birth weight, although little is known about the positive role of microflora in the healthy subject. Many articles indicate that some “diseases of civilization” are strictly correlated to changes in the microbiome following the food revolution that occurred after WWII. For that reason, a precise recognition of the microbiome profile before and after this period should be useful to determine the health-compatible model of microbiome. New research avenues should lead to a more individually oriented treatment, by providing the potential of manipulating the microbiome to optimize personal health. Recently, the use of dental tissues has been described as the most representative source of ancient DNA. The analysis of these samples with molecular biology tools may provide a powerful method of studying human habits, epidemiological diseases, human migrations and genetic drift. Subsequently, the aim of this study was to compare the microbiome profiles (numbers of total cells, and pathogen types) of dental samples obtained from two distinct groups of children, a 200-year-old retrieved one and a present one.

#### METHODS

Two different groups of samples have been studied: (i) a set of 50 recent subgingival plaque samples obtained from children of age 2-8 years, 14 males and 36 females. They were enrolled by the Department of Dental Disease Prevention (University of Cagliari) during standard dental care procedures. All parents signed an informed consent before the children took part in the microbiological analysis. None reported periodontal disease and none had been under antibiotic therapy during the previous 6 months. The health status was recorded and the subgingival plaque was immediately stored at  $-20^{\circ}\text{C}$ . (ii) an old retrieved group included 24 teeth from 6 different crania fragments; they were obtained from a 200 year-old charnel-house located in Villaputzu, a city close to Cagliari in Sardinia. The teeth were then extracted from the dental alveoli of the respective maxilla/jaws. Sample pretreatment and DNA extraction were performed following the procedures described by Bolnick and Orrù [1, 2]. Representative periodontal bacteria have been identified by a previously published real time PCR procedure [2] in which *P. gingivalis*, *T. forsythia*, *A. actinomycetemcomitans* and *F. nucleatum* were detected. In addition, the title of

each pathogen was expressed as a percentage of the total bacteria (biofilm) in the sample detected by a set of universal primers designed on *rrs* sequence of *E. coli* [2].

#### RESULTS AND DISCUSSION

The use of dental plaque (dp) has been identified as a relevant recovery source of ancient DNA (aDNA). Indeed, dp (subgingival and supragingival plaque) is rich in calcium phosphates and silicates; it calcifies *in situ* during the host life while forming layered fossilized concretions known as dental calculus and they remain intact for long periods of time, over millennia. The 200-year-old group displayed different dental/bone diseases, they were extensive caries (21.4%), tooth wear (21%) and dental calculus (7.1%). The profile of periodontal microbiome studied in these samples showed significant differences relative to the total number of bacteria and the title of each pathogen between recent and ancient samples; the total bacteria-genomes amount was  $5.10^9$  vs.  $1.10^8$ , respectively. Similarly, a 1 log difference has been observed for single periodontal species ( $p < 0.05$ ). In all analyzed series, the pathogenic *P. gingivalis* showed the highest title when compared to the other periodontal bacteria.

#### CONCLUSIONS

Our hypothesis is that the transfer of “commensal-pathogen” as an absolute number on the oral biofilm might be linked to the distinct alimentary habits of the two populations. Some diet rich in antioxidants, such as meat-based foods might be able to increase the average number of pathogen anaerobic bacteria in the oral microbiota. The outcome would be an increase of the oral systemic diseases reported with these pathogens. However, unexpectedly, the rate of pathogen/total bacteria remained constant. Our data suggest that the ancient Sardinian population was able to control the pathogen oral anaerobic biofilm by some diet rich in antioxidant compounds.

#### ACKNOWLEDGMENTS

The support of the administrative authorities of Villaputzu during samples collection is highly appreciated. We thank the Hygiene and Public Health Section of Cagliari for approving this study.

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## ABS 36

### IN SAN BENEDETTO DEL TRONTO THE “FIRST NATIONAL WEEK OF THE CHILD AT ‘KILOMETER ZERO’ SEA”

I. Farnetani

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The year 2017 will be the 10<sup>th</sup> anniversary of the institution of the Green Flag. The City of San Benedetto del Tronto (AP, Italy) was among the first to enter the top ten of the Italian child-friendly beaches. To celebrate the anniversary, the City Council of San Benedetto del Tronto will organize the “first national week of the child at ‘kilometer zero’ sea”, under the scientific Direction of Prof. Italo Farnetani. The celebration will take place from 17 to 24 June 2017, date suggested by Assoalbergatori Riviera.

#### OBJECTIVES

The research for the awarding of Green Flags indicated the priority to facilitate the life of children at the sea, providing opportunities for them to play with water and sand, while offering recreational opportunities for parents. The “first national week of the child at ‘kilometer zero’ sea” will test the possibility of building such a beach model. It will be an opportunity to study children holidays.

#### METHODS

The research will take place mainly among children under six years of age, who make up 65% of underage tourists visiting the beaches of San Benedetto del Tronto. Even if the majority of children (70%) comes from Lombardy, Triveneto and Emilia, the sample is heterogeneous and therefore indicative of the entire national territory behavior. When children are young, traveling by car can be difficult, therefore the project will promote partnerships with hotels, beaches, bars and shops. During the “first national week of the child at ‘kilometer zero’ sea”, mineral water will be offered free of charge to all children to get them used to drink before feeling thirsty, an early indicator of dehydration. During the day, activities for children will take place at the seashore. Entertainers will be present to organize and offer games with sea water to children 6-36 months, and games associated with sand for children 3-6 years old. Swimming lessons will be offered by experienced and qualified operators. In the evening, activities will move to the waterfront

and seaside establishments and will include games for children, films and recreational activities for parents, such as concerts, dances, fashion shows and conferences. Hotels will offer fish dishes free of fish bones to children, in order to survey their satisfaction with this food and their preferences over types of fish. Children’s preferences in terms of ice cream flavors and other food choices will also be evaluated.

#### RESULTS

This project will enable us to obtain useful information on food preferences of children. This will be helpful to organize effective preventive pediatric interventions on nutrition and lifestyle to raise nutritional awareness and fight obesity. This program will also confirm and promote the Green Flag model of beach, where parents and children spend together their vacations, both finding an answer to their different needs and an improved holiday experience in terms of relax and fun.

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## ABS 37

### URINARY NEUTROPHIL GELATINASE-ASSOCIATED LIPOCALIN LEVELS IN PREGNANCIES COMPLICATED BY INTRAUTERINE GROWTH RESTRICTION

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## BACKGROUND

NGAL (Neutrophil Gelatinase-Associated Lipocalin) is a glycoprotein expressed by neutrophils and various epithelial cells, with multiple functions, such as immune and transport. In literature, there are few articles about its role in presence of intrauterine growth restriction (IUGR) fetuses with Doppler alterations.

## METHODS

Singleton pregnancies were enrolled at a median of 30 weeks of gestation after a diagnosis of IUGR (defined as an estimated fetal weight [EFW] < 10<sup>th</sup> percentile) with umbilical artery (UA) Doppler alterations (pulsatility index [PI] above 2 standard deviations). There were two control groups: Group A (EFW between 10<sup>th</sup> and 90<sup>th</sup> percentile, Normal UA Doppler and a gestational week at delivery < 37 weeks) and Group B (EFW between 10<sup>th</sup> and 90<sup>th</sup> percentile, Normal UA Doppler and a gestational week at delivery > 37 weeks). Amniotic albumin and NGAL concentration were determined in an amniotic fluid sample.

## RESULTS

60 singleton fetuses were enrolled, of which 20 were classified as IUGR fetuses, 20 fetuses as control Group 1 and 20 as control Group 2. The median gestational age at delivery was 32 weeks. Median amniotic fluid albumin concentration was significantly higher in the IUGR Group (1.49 g/L) than in Group 1 and Group 2 (1.31 and 1.14 g/L;  $p = 0.01$ ). NGAL concentration was statistically different in the IUGR Group (170.1 ng/mL) compared to Group 1 and Group 2 (162.4 and 148 ng/mL,  $p < 0.05$ ).

## CONCLUSIONS

IUGR fetuses with Doppler alterations present higher albumin and NGAL levels in amniotic fluid, which could be possible markers *in utero* of early renal damage.

## ABS 38

### STEM/PROGENITOR CELLS IN THE DEVELOPING HUMAN LIVER: A PROPOSAL OF A PRACTICAL PANEL OF ANTIBODIES TO FIND THEM

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## INTRODUCTION

The identification and characterization of stem/progenitor cells represents a very important tool for the study of liver development, as well as for the interpretation of multiple pathological pictures in the adult liver. Even though it has been reported that stem/progenitors represent 2% of cells in the fetal liver, their identification on morphological bases is very difficult and, often, impossible. Their location in the developing human liver is controversial: according to some authors, liver stem cells might be located in the terminal branches of the intrahepatic biliary tree; others state that stem/progenitor properties could be exclusively attributed to periportal hepatocytes. Recently, a study from our group identified the stroma of the developing portal tracts as the preferential location of liver stem/progenitors, and this location was proposed as the stem cell niche of the human fetal liver [1]. On the basis of these data, the aim of the present work was to study the localization of stem/progenitor cells in 10 newborn livers, and to apply to the study of liver stem cells a panel of antibodies able to identify stem progenitors and to characterize their degree of differentiation toward the hepatocytic or the biliary lineage.

## METHODS

Liver samples were obtained at autopsy from ten human fetuses and newborns, ranging from 11 up to 32 weeks of gestation. Liver samples were formalin-fixed, routinely processed, and stained with H&E for histology. Section were also immunostained with the following antibodies: CD133, SOX9, Cytokeratin (CK) 7, 8, 18, 19, CD117 (c-kit), neural cell adhesion molecule (NCAM), epithelial cell adhesion molecule (EpcAM), alpha-fetoprotein and the placental form of glutathione-S-transferase (GST-P).

## RESULTS

Portal tracts appeared as the principal site of stem cell niche in the developing liver. Hepatic stem progenitors appeared as small spindle cells aggregated in small clusters inside the connective tissue of immature portal tracts. These multipotent cells appeared in close connection with the cells of the periportal lamina. At immunohistochemistry, CD133 and SOX9 were mainly expressed by small immature precursors located inside portal tracts, whereas CK 7, 8, 18 and 19 were detected in the multipotent cells of the periportal lamina.

## DISCUSSION

Our data confirm that developing portal tracts represent the principal localization of stem cell

niches in the fetal and neonatal human liver. The panel of antibodies here utilized appears very useful for the detection of liver stem/progenitors. Moreover, this panel allows the characterization of stem progenitors, allowing the identification of the different degrees of differentiation of hepatic progenitors. CD133 and SOX9 marked the less differentiated precursors, whereas CKs allowed the identification of the different steps of differentiation toward the hepatocytic (CK 8 and 18) and the biliary (CK 7 and 19) lineages.

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## ABS 39

### HUMAN MILK ADRENOMEDULLIN IS UNSTABLE DURING COLD STORAGE AT 4°C

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## BACKGROUND

Under some circumstances, mainly in Neonatal Intensive Care Units, human milk (HM) extraction and refrigerated storage may be necessary. Depending on the length and on the type of cold storage, milk may lose some important nutritional and functional properties, but current advices on safe human milk storage are discordant. Moreover until now no data in literature was present on the effect of prolonged cold storage on biological active components of the human milk such as adrenomedullin (AM). This important peptide is involved in response to hypoxia and inflammation and is associated with neovascularization in several tissues.

## AIM

The aim was to evaluate: (a) the presence of AM in preterm and term human milk; (b) the concentration of AM in refrigerated milk at 4°C at 24 h intervals, up to 96 hours of storage.

## METHODS

HM samples were collected from healthy mothers after term and preterm delivery, with standard extraction methods. The experiment was repeated 4 times to ensure reproducibility of the results. Immediately after collection, each HM sample deriving from each mother was divided into two parts: "Pool" line and "Unique Mother" line. One part (Pool line) was pooled in a sterile bottle and then divided into 5 aliquots. The other part (Unique Mother line) was immediately divided into 5 aliquots. From each line, one aliquot (0 h) was analyzed within 3 hours of collection, while the others (24 h, 48 h, 72 h, 96 h) were stored in the refrigerator at the NICU for 24, 48, 72 and 96 hours, respectively and then analyzed. AM levels were determined using a specific ELISA test.

## RESULTS

AM was detectable in all samples. Its concentration was significant higher in preterm milk with respect to term milk ( $p < 0.05$ ). Significant differences in AM levels were observed during the cold storage: data showed a significant reduction of 56% in concentrations in all samples at 24 hours ( $p < 0.05$ ). AM levels decreased steadily during the storage and the remaining concentration at 96 hours was approximately 2%.

## DISCUSSION

This study provides further evidences regarding the presence of AM in human milk, regardless of gestational age. In particular, the refrigeration of fresh human milk in controlled conditions significantly affected its bioactivity and nutritional quality related with AM, already at 24 hours.

## ABS 40

### STEM/PROGENITOR CELLS IN THE DEVELOPING HUMAN UTERUS

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## INTRODUCTION

In the human fetal endometrium, multipotent progenitor cells were identified in a distribution similar to that typical of basal/reserve cells. En-

ometrial stem cells were subsequently subdivided into three pools: mesenchymal stem-like cells, characterized by reactivity for CD146; epithelial endometrial progenitor cells, localized in the basalis of endometrial glands; endometrial endothelial progenitors, characterized by the ability to differentiate into the endometrial epithelium, the endometrial stroma and into endothelial cells [1]. A particular attention has been dedicated by some authors to the study of stem/progenitor cells involved in the development of the utero-vaginal anlagen, and in particular of the uterine cervix. Recently, a histological and immunohistochemical study carried out on 24 female fetuses and two newborns demonstrated that the cervical epithelium cranial to the squamocolumnar junction is of uterine Mullerian origin, and includes stem/progenitors with enough plasticity to differentiate also into squamous epithelium [2]. Insulin gene enhancer binding protein-1 (ISL1) is the protein encoded by the gene *ISL LIM Homeobox 1*. ISL1 is a transcription factor, which binds to the enhancer region of the insulin gene, regulating insulin gene expression [3]. ISL1 has been shown to play a major role during development in multiple organs, including heart, nervous system and pancreas [4]. Recently, ISL1 expression has been reported in the pericloacal mesenchyme and in the urorectal septum, suggesting a role for ISL1 in the etiology of bladder extrophy [5]. On the basis of these data, given the absence of any report of ISL1 expression in the genital system, this study was aimed at verifying ISL1 expression in the developing human uterus, at different gestational ages.

#### METHODS

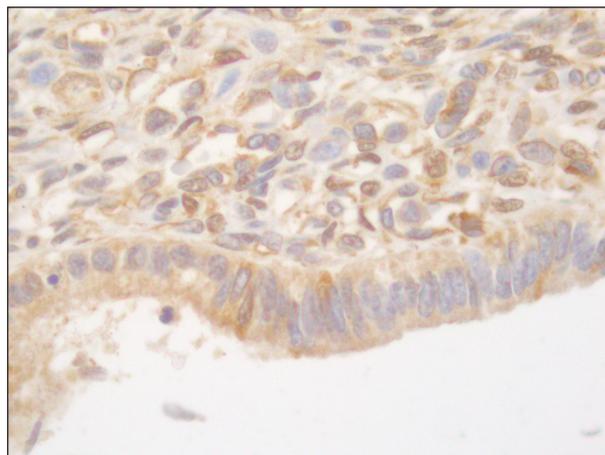
Uteri from 10 human fetuses ranging from 12<sup>th</sup> up to 40<sup>th</sup> week of gestation were formalin-fixed, routinely processed and stained with H&E. Tissue sections were also immunostained with ISL1.

#### RESULTS

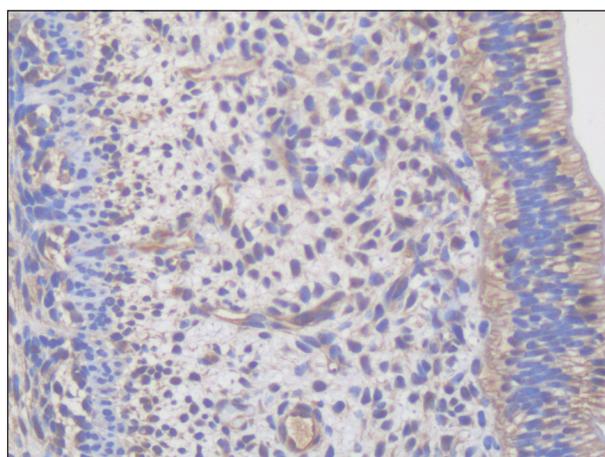
At histology, in all examined cases, stem cell niches were detected in close proximity to the superficial epithelium of the developing endometrium. Stem/progenitor uterine cells appeared as small-undifferentiated cells, with scant cytoplasm, arranged in rounded niches. ISL1-immunostaining expressed positive staining in the human fetuses. ISL1 was mainly observed in undifferentiated to the superficial epithelium of the developing endometrium cells and in stromal uterine cells (**Fig. 1** and **Fig. 2**).

#### CONCLUSIONS

Our preliminary data evidence the presence of stem cell niches in all the fetal uteri studied, and



**Figure 1 (ABS 40).** Fetal uterus: ISL1, 63X. Stem cell niches were detected in close proximity to the superficial epithelium.



**Figure 2 (ABS 40).** Fetal uterus: ISL1, 40X. Stem/progenitor uterine cells appeared as small-undifferentiated cells, with scant cytoplasm, arranged in rounded niches.

confirm previous data from our group regarding their preferential location in the superficial areas of the fetal endometrium. According to our data, ISL1 appears to be a very useful marker for the detection of endometrial stem cells. All these data taken together, the human uterus appears as a highly dynamic organ with a peculiar plasticity and a marked reproductive ability, due to the presence, in fetuses and in neonates, of a huge number of multiple stem/progenitor cell types, including endometrial, stromal and vascular progenitor cells. Further studies are needed in order to verify if this antibody might be useful for the identification of stem/progenitor cells even in the adult endometrium.

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## ABS 41

### CYSTIC LESIONS OF POSTERIOR CRANIAL FOSSA: IMAGING EXPLAINED THROUGH EMBRYOLOGY

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#### INTRODUCTION

The accidental discovery of a fluid collection within the posterior cranial fossa in a fetus or a newborn can be a tricky incidental finding during a routine scan. This review assesses the possible cystic lesions of posterior cranial fossa on the basis of embryological development, radiological findings and associated clinical aspects, in order to clarify the radiological differential diagnosis through embryology.

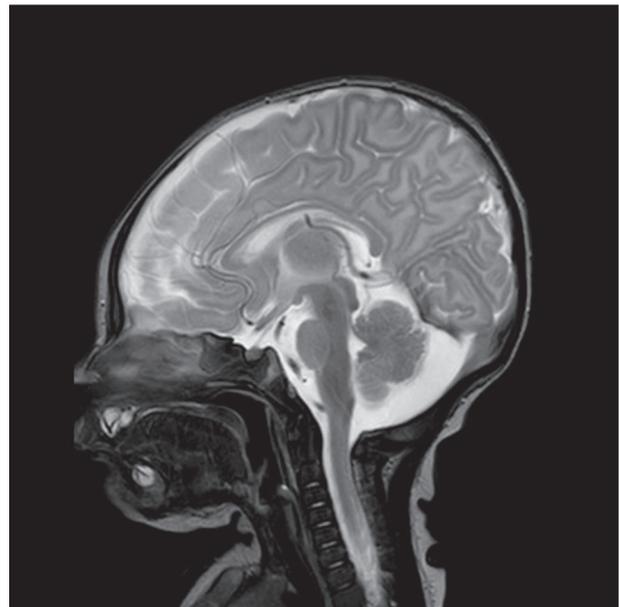
#### DIFFERENTIAL DIAGNOSIS

The main cystic lesions of the posterior cranial fossa are Dandy-Walker Malformation (DWM), Blake's Pouch Cyst (BPC), Arachnoid Cyst (AC) and Mega Cisterna Magna (MCM) (**Fig. 1**), although the latter is not a proper cyst. All of them seem to share a common embryological origin and differ in the severity of the insult and the anatomical predilection. The key event for the development of a DWM is a cerebellar vermis hypoplasia that causes the persistence of the superior membranous area, which expands into the posterior fossa forming a large cystic 4<sup>th</sup> ventricle. BPC is caused by the persistence and herniation of a different

membrane, the inferior membranous area that is supposed to disappear leaving a median opening that would become the foramen of Magendie. MCM originates if this membrane eventually disappears, leaving an enlarged posterior fossa cavity filled with cerebrospinal fluid physiologically connected with the subarachnoid fluid. Finally, arachnoid cysts are caused by a defined duplication of the arachnoid membrane that is subsequently filled with cerebrospinal fluid. Consequently, the radiological finding of a regular cerebellar vermis excludes the hypothesis of DWM and the position of the choroid plexus helps differentiate between DWM and BPC in controversial cases. Moreover, radiological findings in DWM include cystic dilatation of the 4<sup>th</sup> ventricle and enlargement of the posterior fossa. Absence of hydrocephalus comes out in favor of MCM. Absence of communication with surrounding cerebrospinal fluid defines an AC.

#### TREATMENT

While MCM is considered an anatomical variant that does not require any further investigation or treatment, the most severe complication of the cystic lesions is the development of hydrocephalus. This pathological condition is caused by mass effect in case of AC and lack of cerebrospinal fluid outflow in case of DWM and BPC and may require a shunt placement. Furthermore, in case of DWM associated central nervous system and peripheral abnormalities need investigation.



**Figure 1 (ABS 41).** Mega Cisterna Magna: enlarged posterior fossa in the presence of a regular cerebellar vermis and physiological fluid outflow.

**ABS 42****NORADRENERGIC REGULATION OF SPATIAL LEARNING AND MEMORY IN THE RAT: EFFECTS OF SELECTIVE LESIONS AND REPAIR BY TRANSPLANTED NORADRENERGIC NEUROBLASTS**

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*B.R.A.I.N. Lab for Neurogenesis and Repair, Dept. Life Sciences, University of Trieste, Trieste, Italy***INTRODUCTION**

Extensive degeneration of noradrenergic (NA) neurons in the Locus Coeruleus/SubCoeruleus (LC/SubC) and loss of fiber terminals in the neocortical and hippocampal target regions are nearly invariant features of Alzheimer's Disease (AD), and are believed to represent early neuropathological events prior to the appearance of overt dementia. However, it is still uncertain whether NA loss is causally linked to cognitive impairments in AD or simply reflects a non-specific response to other insults.

**METHODS**

In the present studies, the NA contribution to the regulation of spatial learning and memory was investigated following selective immunolesion of the developing LC/SubC system, followed by bilateral intrahippocampal implantation of a suspension rich in noradrenergic progenitors isolated from the embryonic (13-14 day gestational age) LC. Starting from 4-6 months and up to about 12 months post-lesion and transplant, the animals underwent sequential tests to evaluate sensory-motor, as well as spatial learning and memory abilities (Morris Water Maze, Radial Arm Water Maze tasks), followed by post-mortem immunohistochemical and stereological analyses.

**RESULTS**

In no case did the lesion produce sensory-motor changes that would account for performance in the Morris Water Maze task. When tested at about 6 months post-surgery, all animals in the Control, Lesion and Lesion + Transplant groups were equally efficient in the reference memory version of the test, whereas working memory abilities (as assessed by the Radial Arm Water Maze, RAWM, task) were seen consistently impaired in the Lesion-only rats. Interestingly, lesioned animals implanted with reinnervating NA-rich tissue grafts exhibited a fairly normal performance in the RAWM task which, however, became severely impaired following ab-

lation of the transplanted neuroblasts by a further dose of immunotoxin injected bilaterally into the site of implant. Morphological analyses confirmed the massive noradrenergic neuronal and terminal fiber loss induced by the lesion ( $\geq 90-95\%$ ), as well as the near-normal reinnervation of the hippocampus promoted by the transplanted neuroblasts, which, however, was completely abolished by the second lesion.

**CONCLUSIONS**

The results suggest that integrity of ascending noradrenergic inputs may be required for the regulation of specific aspects of learning and memory, namely those related to the rapid processing of cognitive information taking place in the hippocampus.

**ABS 43****HYPOTHERMIA TREATMENT IN ASPHYXIATED NEWBORNS, FOLLOW UP TO 6 MONTHS: A 5 YEARS CASE STUDY IN THE NEONATAL INTENSIVE CARE UNIT OF CAGLIARI**

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*Neonatal Intensive Care Unit, Neonatal Pathology and Neonatal Section, AOU and University of Cagliari, Cagliari, Italy***INTRODUCTION**

Asphyxia is one of the main problem faced by the neonatologists and responsible of about 1 million deaths/year worldwide.

**AIMS**

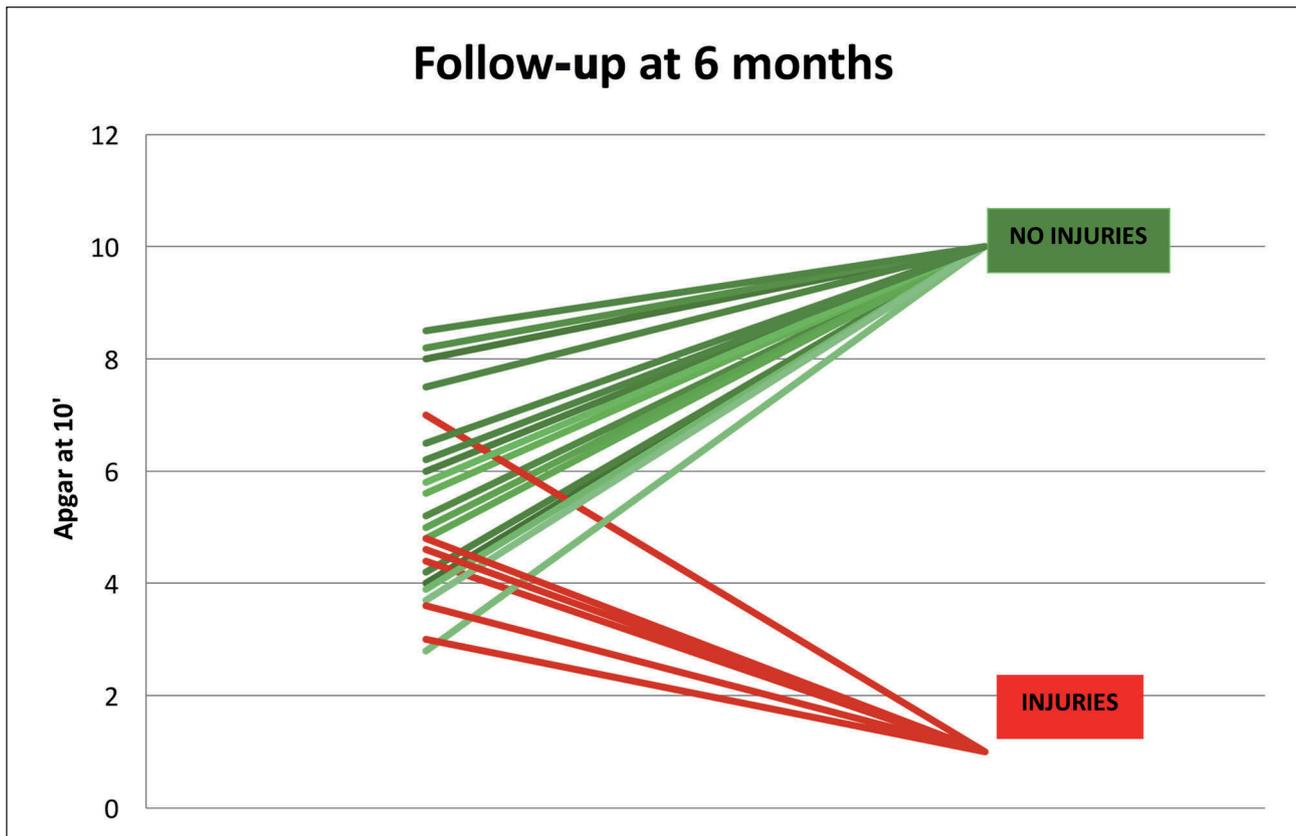
The aims of the study were the following: to assess the outcome of newborns treated with hypothermia in the NICU of Cagliari; to assess the reliability of Apgar score at 5' and 10' minute after birth, pH at birth and NMR at discharge as markers of long-term outcome.

**METHODS**

We describe 31 infants with gestational age of 39 weeks  $\pm$  2 days, weight 3,252  $\pm$  574 g, affected by moderate or severe hypoxic-ischemic encephalopathy who were treated with hypothermia before 6 hours after birth and continued for 72 hours, according to international and national guidelines. In a long term follow-up study, we present here the neurodevelopmental outcome assessed at 6 months of life.

**RESULTS**

Death occurred in 6 of these 31 infants (19%). At 6 months of life among the 25 survivors, 6 (23%) of



**Figure 1 (ABS 43).** Correlation between Apgar score at 10 minutes and follow-up at 6 months.

them had severe disability: 23% of cases presented tetraparesis and mental delay, associated with PEG in 12% and with blindness in 4% of these patients. 39% (12 infants) presented NMR negative for lesions at discharge, while 42% (13 infants) presented NMR positive for lesions at discharge and only 6 of them presented severe disability at follow-up at 6 months of life. The average Apgar score after 5 minutes was  $4.72 \pm 2.79$  while it was  $5.45 \pm 2.54$  after 10 minutes (**Fig. 1**). The average pH at birth was  $6.72 \pm 0.23$  but 19 of these 25 infants had a negative follow-up, while 6 of them had a positive follow-up at 6 months of life.

#### CONCLUSIONS

Hypothermia reduces the risk of death or disability in infants with moderate or severe hypoxic-ischemic encephalopathy. Apgar score at 5 or 10 minutes after birth, the pH at birth and NMR at discharge were unreliable as long-term outcome markers.

#### ABS 44

#### PSEUDO-PRECOCIOS PUBERTY IN INFANCY AS EXORDIOUS OF SECRETING GERM CELL TUMOR

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#### INTRODUCTION

Tumors of the central nervous system (CNS) represent the second most common pediatric cancer after leukemias, comprising approximately 25% of all childhood cancers [1]. Intracranial germ-cell tumors (GCTs) represent a rare and histologically heterogeneous group of predominantly midline neoplasms [2] and originate from totipotent primordial germ cells that have mislocated during their embryonic development [3]. Overall incidence is among 1.0 per million per year in Europe [4]. CNS germ cell tumors are most common in the second decade of life with a peak incidence between 10 and 14 years of age [5-7]. Teratomas, however, are more frequently diagnosed early in life, especially within 12 months. Males develop germ cell tumors more often than females, in a ratio of approximately 2:1. The WHO recognizes

multiple different types of germ cell tumors, ranging from mature teratomas to a variety of highly aggressive nongerminomatous germ cell tumors [6, 8] (**Tab. 1**). Precise diagnosis in secreting germ cell tumors is currently done through consistent radiological imaging and elevations of tumor markers such as  $\alpha$ -fetoprotein ( $\alpha$ FP) and/or human chorionic gonadotropin ( $\beta$ -HCG) in serum and/or cerebrospinal fluid (CSF), without attempting surgical biopsy. Treatment includes chemotherapy (CT) and radiotherapy (RT)  $\pm$  surgery, depending on the histological subtype, the tumor extension, the response to chemotherapy, the elevation of markers and the age of the patient [9]. Overall survival is excellent for patients with pure germinoma while it is inferior for those with secreting non-germinomatous germ cell tumors.

#### CASE REPORT

E.B. is a male infant of 22 months whose body weight and length progressively increased from age 12 months up to 90<sup>th</sup> percentile. At age of 18 months an increased volume of penis (7.5 x 2.5 cm) and testis (cc 4) appeared along with a hyperpigmentation of the scrotum, pubic hair and hoarse voice (G4P2 Tanner stages). Endocrine exams revealed a negativity of LHRH and ACTH test with an increase of plasmatic  $\alpha$ FP,  $\beta$ -HCG and testosterone (respectively 28.8 ng/ml, 215.9 U/l and 14.8 ng/ml). Hand and wrist X-ray showed a bone age of 3 years and 6 months (according to Greulich and Pyle) that was the double of the chronologic age. A pseudo-precocious puberty was suspected. Brain MRI showed a lesion of the pineal gland (15 x 11 x 16 mm).  $\alpha$ FP and  $\beta$ -HCG were increased in CSF as well. Thus CT with cisplatin, ifosfamide and etoposide was administered for 4 cycles with marker normalization and zeroing of markers and testosterone. Complete surgical resection was possible and histology showed a mature teratoma. During CT secondary sexual characteristics gradu-

ally regressed while  $\alpha$ FP and  $\beta$ -HCG values had an oscillating trend until normalization. Radiotherapy was omitted due to the biological complete response, the full resection and the patient age.

#### DISCUSSION

This case report describes an exceptional clinical presentation of a CNS germ cell tumor, which resulted in a complex therapeutic decision. Considering the precocious age of presentation and MRI aspect, a clinical diagnosis of teratoma was most predictable, but the elevation of serum and liquor  $\alpha$ FP and  $\beta$ -HCG suggested foci of malignant germ cell elements like yolk sac tumor and/or embryonic carcinoma and/or choriocarcinoma. Therefore, it was decided to start CT in the hope to omit RT because of the age of the patient, despite RT being a cornerstone in the management of intracranial GCTs. It can be hypothesized that malignant components responded to CT and this probably led to an evolution towards mature teratoma, clinically confirmed by normalization of phenotype and tumor markers. A major problem was the long total diagnostic interval (TDI, time between first symptom onset and diagnosis) of about 10 months, longer than an ideal median of 1.6 months as reported nowadays in the UK [10, 11], causing a not predictable endocrine and functional damage. This story also demonstrates the need to improve public and professional awareness of brain tumors in order to accelerate diagnosis and care of the patient.

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**Table 1 (ABS 44).** WHO classification of germ cell tumors.

Germ cell tumors
Germinoma
Embryonal carcinoma
Yolk sac tumor
Choriocarcinoma
Teratoma <ul style="list-style-type: none"> <li>• Mature teratoma</li> <li>• Immature teratoma</li> </ul>
Teratoma with malignant transformation
Mixed germ cell tumor

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## ABS 45

### HUMAN HERPESVIRUS 6 (HHV-6) ENCEPHALITIS IN TWO HEALTHY CHILDREN

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#### INTRODUCTION

HHV-6 is a frequent cause of exanthema subitum, a common benign febrile illness in infancy. However, HHV-6 rarely causes neurological complications. We describe two cases of HHV-6 encephalitis in healthy children.

#### CASE REPORTS

##### Case 1

A 19-month old male with fever (39°C), vomit, and otitis treated with amoxicillin/clavulanate. After 24 hours he showed drowsiness, gasping, ataxia. On admission to the hospital, blood tests, blood culture and head CT scan were negative. The EEG showed slow pattern without asymmetry. CSF examination: 45 leukocytes (neutrophil 70%), protein 24.2 mg/dl, glucose 61 mg/dl. CSF was negative for bacteria, PCR was positive for HHV-6, negative for other viruses. The baby received acyclovir for seven days. He quickly improved, and after seven days he showed no neurological deficits and normal EEG.

##### Case 2

A 20-month old SGA female baby was admitted to hospital for a two-day fever (40°C), vomit, pharyngitis, and drowsiness. CSF was normal. EEG showed bilateral slow pattern. On the 4<sup>th</sup> day, exanthema occurred, fever disappeared with-

out improvement of drowsiness, brain MRI was negative for acute encephalitis, and a second lumbar puncture was performed. CSF examination was normal. CSF culture was negative for bacteria. CSF PCR was HHV-6 positive, negative for other viruses. The baby received acyclovir for 7 days. She quickly improved and EEG became normal.

#### CONCLUSIONS

HHV-6 neurotropism is known. HHV-6 encephalitis should always be suspected in case of heralding symptoms, EEG abnormal findings, also in case of absence of exanthema, with negative MRI and negative CSF pleocytosis, which is unusual since viral DNA is not always detected. An immune pathogenetic mechanism has been proposed. HHV-6 encephalitis treatment still remains under investigation.

## ABS 46

### RETINOPATHY OF PREMATURITY: FROM DIAGNOSIS TO PREVENTION

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#### INTRODUCTION

Retinopathy of prematurity (ROP) is a maturation defect in retinal vasculature, which remains a major complication of prematurity, and affects the visual prognosis of former premature infants.

#### OBJECTIVES

The purpose of this study was to evaluate the incidence of retinopathy of prematurity in a medical department and neonatal resuscitation and identify different intervening risk factors in the onset of this disease.

#### METHODS

This is a retrospective study conducted at the neonatal intensive care medicine service Rabta Tunis over a period of 3 years 7 months (1 January 2012 to 31 July 2015) and covering all cases of ROP diagnosed with fundus oculi carried out at 28 days of life.

#### RESULTS

During the study period, retinopathy was detected in 21 neonates (NN) (11 boys and 10 girls). The average maternal age was 33 years. Pregnancy pathology was present in over half of pregnancies and pre-eclampsia was by far the most frequent complication. In 17 cases, corticosteroids were administered to the mother

before birth to a preterm labor. Five NN were from pregnancies complicated by chorioamnionitis. Labor was induced in 11 cases. The most common cause of induced preterm birth was preeclampsia. Most NN showed good adaptation to extra-uterine life. The mean birth weight was  $1,340 \pm 210$  g (range: 750-2,200 g). 80% of NN were eutrophic for the term. The mean gestational age of NN studied was  $29.8 \pm 2.2$  weeks (range: 27-33 weeks). Neonatal respiratory distress was the main pathology presented by NN on admission (17 cases). Late lung fluid reabsorption has been the most frequent cause. Artificial ventilation (invasive or noninvasive) has been used in 19 NN, both in the initial management of ROP and ventilatory support in case of hemodynamic disorders or secondary apnea with an average of 10.5 days. The use of surfactant in the case of hyaline membrane disease or secondary surfactant destruction was noted in 10 cases and nitrogen monoxide in 4 cases. A neonatal infection (perinatal infection, nosocomial infection) occurred in 21 cases. A profound anemia required transfusion of red blood cells in 18 premature infants. Hemodynamic instability, either present from birth or of secondary appearance, was noted in 18 NN requiring in 80% of cases the administration of vasoactive drugs. Nine NN developed a degree of intraventricular hemorrhage (grade I in the majority of cases). ROP was bilateral in 11 cases and control of fundus oculi (FO) returned normal in 8 cases. A newborn died before FO control.

#### CONCLUSIONS

Retinopathy of prematurity remains a topical problem in neonatal resuscitation. Apart from the usual screening criteria, it seems necessary to provide a systematic fundus to any premature who is transfused or has had unstable hemodynamic status.

#### ABS 47

##### ANALYSIS OF CRP AND PCT IN NEONATAL SEPSIS: A REPORT OF 81 CASES

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#### BACKGROUND

Neonatal sepsis is a clinical syndrome that accounts for 19% of overall neonatal deaths, in particular in preterms and in very low birth weight infants

(VLBW). According to the time of the occurrence it can be classified in two types: early-onset sepsis (EOS) and late-onset sepsis (LOS). Since symptoms and the signs of neonatal sepsis are aspecific, the diagnosis is based on clinical picture associated with the evaluation of markers, such as C-reactive protein (CRP) and procalcitonin (PCT).

#### METHODS

For this study 81 medical records collected from April 2015 to March 2016 were analyzed in our NICU, dividing the patients in 3 groups: group A, which were patients with risk factors for sepsis but who did not develop the pathology, group B1, corresponding to newborns with EOS, and group B2, corresponding to neonates with LOS. The markers levels (serum CPR and PCT) were evaluated in 3 times: T1, that for EOS coincides with the first 72 hours of life and for LOS coincides with the suspect of sepsis; T2, which corresponds with the beginning of antibiotic therapy; T3, which is the end of therapy.

#### RESULTS

CPR was elevated in 78 patients at T1, in 54 patients at T2 and in 44 patients at T3. CPR increased in time in 2 of 3 groups, despite the use of antibiotics. PCT was elevated in 67 patients at T1 (average PCT of 20.96 ng/ml in B1 and 36.11 ng/ml in B2), in 31 patients at T2 (average PCT of 7.56 ng/ml in B1 and 4.94 ng/ml in B2) and in 6 patients at T3 (average PCT of 1.39 ng/ml in B1 and 0.20 ng/ml in B2). PCT decreased in groups B1 and B2 thanks to the antibiotic therapy.

#### CONCLUSIONS

Serum PCT is a specific and sensitive marker of neonatal sepsis because it increases when septic symptoms or signs appear and decreases early with antibiotic treatment, whereas CRP remains high at the beginning despite antibiotic therapy.

#### ABS 48

##### DIAGNOSTIC AND PREDICTIVE VALUE OF SERUM CYSTATIN C IN CASE OF NEONATAL ACUTE KIDNEY INJURY IN CRITICALLY ILL FULL-TERM INFANTS

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#### INTRODUCTION

In most neonatal intensive care units, exam of renal functions is based on serum creatinine (SCr) level.

But using creatinine as a marker of renal dysfunction in neonates has some problems: SCr creatinine is not sensitive to small changes of glomerular filtration rate (GFR); SCr at birth reflects maternal serum creatinine; growth and changes in muscle mass influence SCr; neonates have passive reabsorption of filtrated creatinine across immature non-hermetic renal tubules [1, 2].

Several authors found that serum cystatin C (SCysC) is a better marker of GFR than creatinine, even in cases of sub-clinical renal dysfunction [3]. It is a proteinase inhibitor involved in intracellular catabolism of proteins, produced by all nucleated cells, freely filtrated across glomeruli, and completely catabolized and reabsorbed in the proximal tubule. There is no interference between SCysC and bilirubin, hemoglobin and ketone in laboratory findings. SCysC does not pass through the placenta and as a result, the values of SCysC reflect only neonatal GFR [4, 5]. However, there are limited studies available on reference values of SCysC in healthy and ill neonates.

#### AIM

The objective of the work was to determine diagnostic and predictive value of SCysC in case of acute kidney injury (AKI) in critically ill full-term newborns.

#### METHODS

A comprehensive paraclinical examination of 42 critically ill newborns including 20 infants

with disorders of the kidney function (group I), and 22 ones with diagnosed AKI (group II). AKI was detected by means of recommendations on kidney diseases according to Jetton and Askenazi [6]. The level of SCysC was measured by immunonephelometric methods on the basis of the laboratory Gemeinschaftslabor Cottbus (Germany).

#### RESULTS

Serum level of SCysC was  $1.55 \pm 0.04$  mg/l [1.21; 1.85] in newborns in the first group of observation, and  $1.77 \pm 0.02$  mg/l [1.61; 1.89] in the second group,  $p_{I-II} < 0.05$ . A high sensitivity (100%) and specificity (70.0%) of SCysC has been found during diagnostics of AKI in critically ill full-term newborns. High diagnostic value of this index is proved by diagnostic accuracy (85.7%) and high AUROC index (0.87); high predictive value by high readings of a positive predictive value (78.6%) and negative predictive value (100.0%). A threshold level of SCysC, which is indicative of the formation of AKI in full-term newborns with severe perinatal pathology, was detected to be higher than 1.61 mg/l.

#### CONCLUSIONS

Considering a high predictive and diagnostic value the authors recommend to measure SCysC level for identification of AKI in full-term infant into the practical work of neonatal intensive care units.

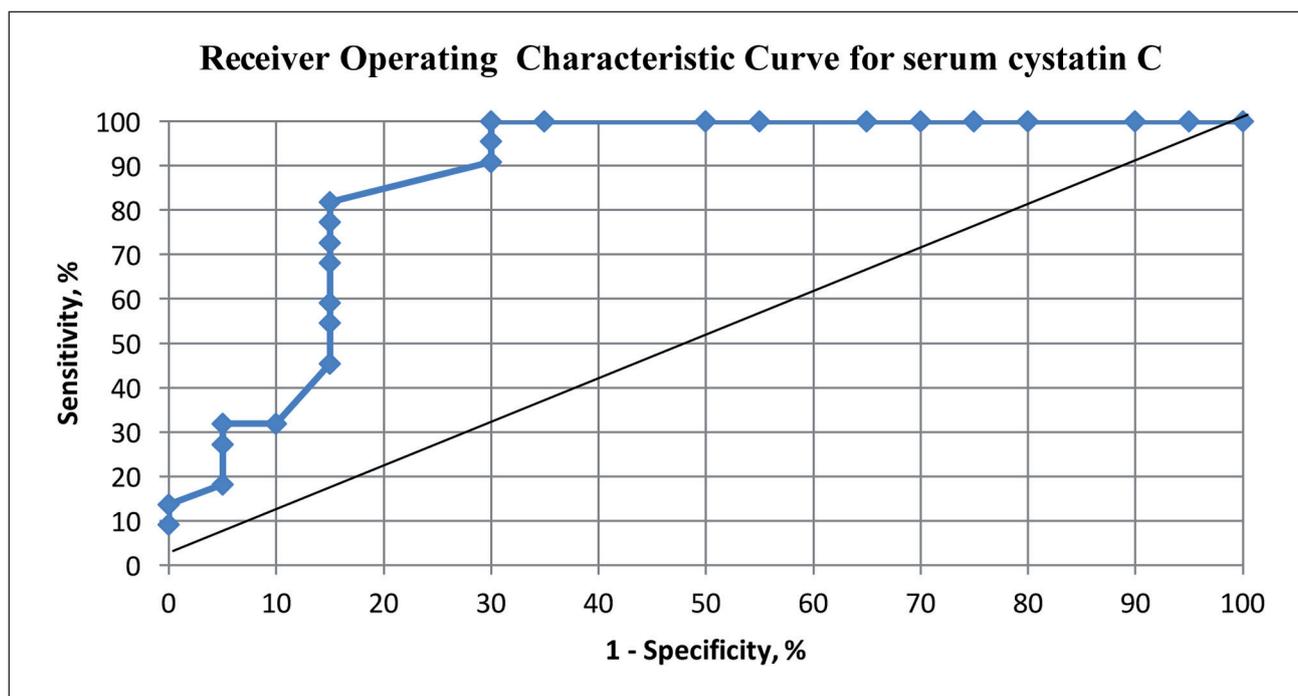


Figure 1 (ABS 48). Receiver operating characteristic (ROC) curve for serum cystatin C (SCysC).

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## ABS 49

### MENINGITIS AND MENINGOENCEPHALITIS IN YOUNG INFANTS. DESCRIPTION OF TWO CASES

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## INTRODUCTION

Meningitis and meningoencephalitis have high mortality and complication rate and diagnosis can be difficult in newborns and infants, because typical signs and focal symptoms could be absent. We report two cases of young infants with meningoencephalitis brought to our hospital with critical pathological EEG and MRI signs.

## CASE REPORTS

*Case 1*

The first patient, a 40 days-old male infant, was brought to the hospital with fever (39°C) and irritability. The day after he was lethargic and started hemiconvulsion. EEG showed focal seizures and MRI showed leptomeningeal hyper intensity. Lumbar puncture was performed and showed CSF leukocytes count > 5/mm<sup>3</sup>. Other laboratory results were negative except for a borderline blood cytomegalovirus IgM increase. Antibiotic, antiviral and chronic anti epileptic drug (AED) therapy was started. Development and neurological exam were normal. After 6 months the patient showed negative EEG and MRI; AED withdrawal was performed.

*Case 2*

The second patient, a 2-months-old baby with fever 40°C, poor feeding, and respiratory distress was hospitalized. Few hours after, the baby started repetitive seizures. EEG showed right temporal spike and MRI hyperflow in the right rolandic and left occipitoparietal region, multiple hemispheric layers with heterogeneous signal, and ventricular hyper intensity. Lumbar puncture showed *S. pneumoniae* infection. Antibiotic and AED therapy was started. Neurological, EEG and MRI follow up was performed. Last examinations were normal and AED was discontinued after 9 months.

## CONCLUSIONS

These two cases confirmed the important role of EEG and MRI and their relationship in diagnoses and follow-up of pediatric meningoencephalitis.

## ABS 50

### S. MARCESCENS INFECTION IN NICU: AGGRESSIVE EVOLUTION DESPITE APPROPRIATE ANTIBIOTIC THERAPY

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## INTRODUCTION

*S. marcescens* is a cause of sepsis in NICU. Preterm newborns are particularly at risk because of their immature immune systems, ineffective skin barrier and increased need of intensive care. *S. marcescens* sepsis is associated with high morbidity and mortality. We report 2 cases of neonatal sepsis due to *S. marcescens* with dramatic evolution in cerebral abscesses occurred in the same period.

## CASE REPORTS

*Case 1*

Gestational age (GA) 37 weeks, birth weight (BW) 2,010 g. Persistent and severe hypoglycemia in the first week. On 12<sup>th</sup> day: vomiting, diarrhea with malodorous stools, acidosis and fever. High values of CRP, PCT and WBC count were detected. Empiric IV antibiotics and Ig-IgM enriched were started. Blood and CSF cultures: *S. marcescens*. Antibiotics were modified to meropenem and gentamicin. Cerebral US: corpusculated material in cerebral ventricles and right parietal large (> 3 cm) cerebral abscess. General conditions improved, CRP and PCT drooped. Blood and CSF cultures

(day 7 of therapy): negative. US: another small left cerebral abscess was evident. NMR: multiple cerebral abscesses in frontal and temporo-parietal regions. Neurosurgical consultation indicated transfer for drainage.

#### Case 2

GA 26 weeks, BW 745 g. On the 18<sup>th</sup> day general conditions worsened: high values of CRP and PCT were detected. IV meropenem, gentamicin and Ig-IgM enriched were started. Blood culture: *S. marcescens*. CSF test: hyperproteinorrachia and hypoglycorrachia, negative culture. After 48 h CRP, PCT and blood culture were negative. General conditions rapidly improved. US (13<sup>th</sup> day of therapy): multiple small cerebral abscesses that became gradually larger with progressive ventricular dilatation at the subsequent controls. NMR (27<sup>th</sup> day): multiple cerebral abscesses in parietal regions and ventricular dilatation. Neurosurgical consultation indicated transfer for drainage.

#### DISCUSSION AND CONCLUSIONS

Cerebral abscesses are extremely rare in neonates. Clinical signs are usually non-specific, but the infant's clinical conditions could rapidly deteriorate; consequently, cerebral abscesses are frequently diagnosed only during autopsy. This condition is further aggravated when premature infants or non-usual pathogens are involved. Previous reports have documented an association between *S. marcescens* bacteremia, meningoencephalitis and brain abscesses. Central nervous system infection from *S. marcescens* is aggressive and may advance despite appropriate antibiotic therapy. It is very often associated with a poor neurological prognosis.

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#### ABS 51

#### THE USE OF METALLOME IN THE STUDY OF GESTATIONAL DIABETES MELLITUS

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#### INTRODUCTION

Gestational diabetes mellitus (GDM), when untreated, can be associated with maternal and neonatal morbidity. The use of metallomics of GDM appears to be a possible alternative in order to gain information about the molecular causes of this disease. Placenta was chosen as an alternative target organ for the analysis of the GDM metallome.

#### METHODS

This was a case-control study performed in the Department of Woman's and Child's Health of the University of Padua. Singleton pregnancies affected by GDM (median 30 weeks gestation) and controls were included. Placenta samples were collected in three specific points of the placenta (at the edge, near the cord insertion and in an intermediate position between the two points) after delivery and stored at -80°C until analysis. Each placenta sample was analyzed five times with ICP-MS. The detection limit (x<sub>D</sub>) for each element has been determined using the Voigtman procedure.

#### RESULTS

Thirty patients were healthy and 45 were affected by GDM. 180 placental samples were obtained. The comparison of the elemental concentrations in GDM and control patients evidenced that the patient's weight and ethnicity substantially influenced the placenta's composition (Fe, Co, Zn, Pb and Hg), superimposing to the effect of GDM itself. Cadmium had lower concentrations, and selenium had higher concentrations, in GDM placentas than in the control group.

#### CONCLUSIONS

ICP-MS confirms the picture of the elemental composition of healthy placentas available in the literature. The sampling site, the patient's weight and ethnicity should be considered in the approach to metallomics of GDM placenta.

#### ABS 52

#### MULTI-DRUG RESISTANT MYCOBACTERIAL CERVICAL LYMPHOADENITIS IN CHILDREN OF NORTH SARDINIA

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## INTRODUCTION

Mycobacteria are causative agents of cervical lymphadenitis (MCL) in young children, with an increasing frequency up to 3 cases per 100,000. The affected lymph nodes progressively and slowly enlarge and may suppurate, with the formation of a sinus tract. One-hundred-thirty species of mycobacteria have been isolated, including *Mycobacterium tuberculosis* (MT) and nontuberculous mycobacteria (NTM). The diagnostic approach includes the Mantoux skin test, interferon-gamma release assay (IGRA) and surgical excision. Medical therapy with at least 3 of the traditional anti-mycobacteria drugs is recommended, especially when surgical excision cannot be performed.

## CASE SERIES

This case series study was performed at the Pediatric Clinic, University of Sassari (Sassari, Italy) by reviewing the medical records of patients with MCL, over the period 2010-2015. Five cases of MCL, all girls with a single lesion, were identified: one was affected by MT, 3 by NTM, while in one case an etiology could not be determined. Detailed clinical data were available for 3 cases. The MT case was a 3-year-old child with right side MCL (4 x 3 cm), not painful and with intact skin. Among the patients affected by NTM, one was an 8-year-old child with right side MCL (2 x 2 cm), not painful and with intact skin, while another presented with right side MCL (> 2 cm), covered by violaceous skin and a visible suppurated sinus tract. All were Mantoux positives but IGRA negatives. The microbiological culture and/or molecular genetic analysis of the gastric aspirate confirmed the diagnosis of MT in one case, and of NMT in two cases (*M. scrofulaceum* and *M. avium*, respectively). Surgical excision was not possible both in the MT case, as the lesion was at high risk of facial nerve damage, and in the NTM case presenting with an advanced lesion. The MT case responded well to a standard, 9-month antituberculosis therapy. Both cases with NTM were found to be multi-drug resistant, including isoniazid, pyrazinamide and ethambutol; they responded to 3 months of therapy with clarithromycin combined with rifampicin, but recovery was faster after surgical excision of the lesion.

## CONCLUSIONS

Early diagnosis is essential for the best treatment and outcome of MCL in young children. Mantoux skin test was found to be a good screening test. Surgical excision of the lesion still represents the best

approach to treatment, especially in consideration of the increasing appearance of multi-drug resistant mycobacteria.

## ABS 53

### ADRENAL FAILURE IN A 20 DAY-OLD INFANT AFFECTED BY MULTIPLE ORGAN FAILURE

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## INTRODUCTION

The hypothalamic-pituitary-adrenal axis is critical in the response to stress in neonates. Cortisol is synthesized in the zona fasciculata of the adrenal cortex under stimulation from the adrenocorticotrophic hormone (ACTH) that is produced in the pituitary gland. Cortisol is involved in multiple biological functions including electrolyte balance, maintenance of appropriate blood glucose levels and endothelial integrity. Moreover, under physical stress, cortisol has a fundamental role in the suppression of inflammatory responses [1]. A proper synthesis of cortisol is particularly important in septic shock, in which the inflammatory response causes an excessive release of inflammatory mediators that adversely affect endothelial integrity, leading to capillary leak syndrome and multiple organ failure (MOF). The loss of the endothelial barrier represents the main pathological lesion of multiple organs in newborns affected by sepsis, being responsible for the evolution towards MOF [2]. In recent years, adrenal insufficiency has been reported more frequently in preterms and term infants, and the absence of an appropriate cortisol response to stress has been proposed as one of the principal factors leading to physiological instability and mortality [3]. The aim of this article is to report a case of a preterm newborn with bilateral adrenal failure in the setting of MOF.

## CASE REPORT

A female preterm, weighing 920 g, was born at 25 weeks + 3 days of gestation. Laboratory maternal tests evidenced increased levels of blood white cells (20,000/μl), suggesting the diagnosis of

maternal infection. The mother, 19 years old, was a frequent smoker (20 cigarettes/day). The amniotic liquid was green in color. Apgar index was 4 at birth. The newborn was admitted to the NICU Center of the University Hospital of Cagliari. Laboratory tests of the newborn evidenced increased levels of serum procalcitonin (13.50 ng/ml; N.V.: 0.5/ml). Blood culture tests were negative. The patient developed a respiratory distress syndrome and, at 20 days of age, the clinical status worsened till death. At autopsy, multiple organ failure was diagnosed. This pathological diagnosis was based on the finding on bilateral alveolar pneumonia, cerebral ventricular hemorrhage and acute kidney injury. The loss of the endothelial barrier was found in the vast majority of organs, mainly in the arteries. Multiple thrombi were detected in the pulmonary arteries. Moreover, a massive necrosis of both adrenal glands was detected, with areas of hemorrhage interesting both the cortical and the medullary zones (**Fig. 1**).

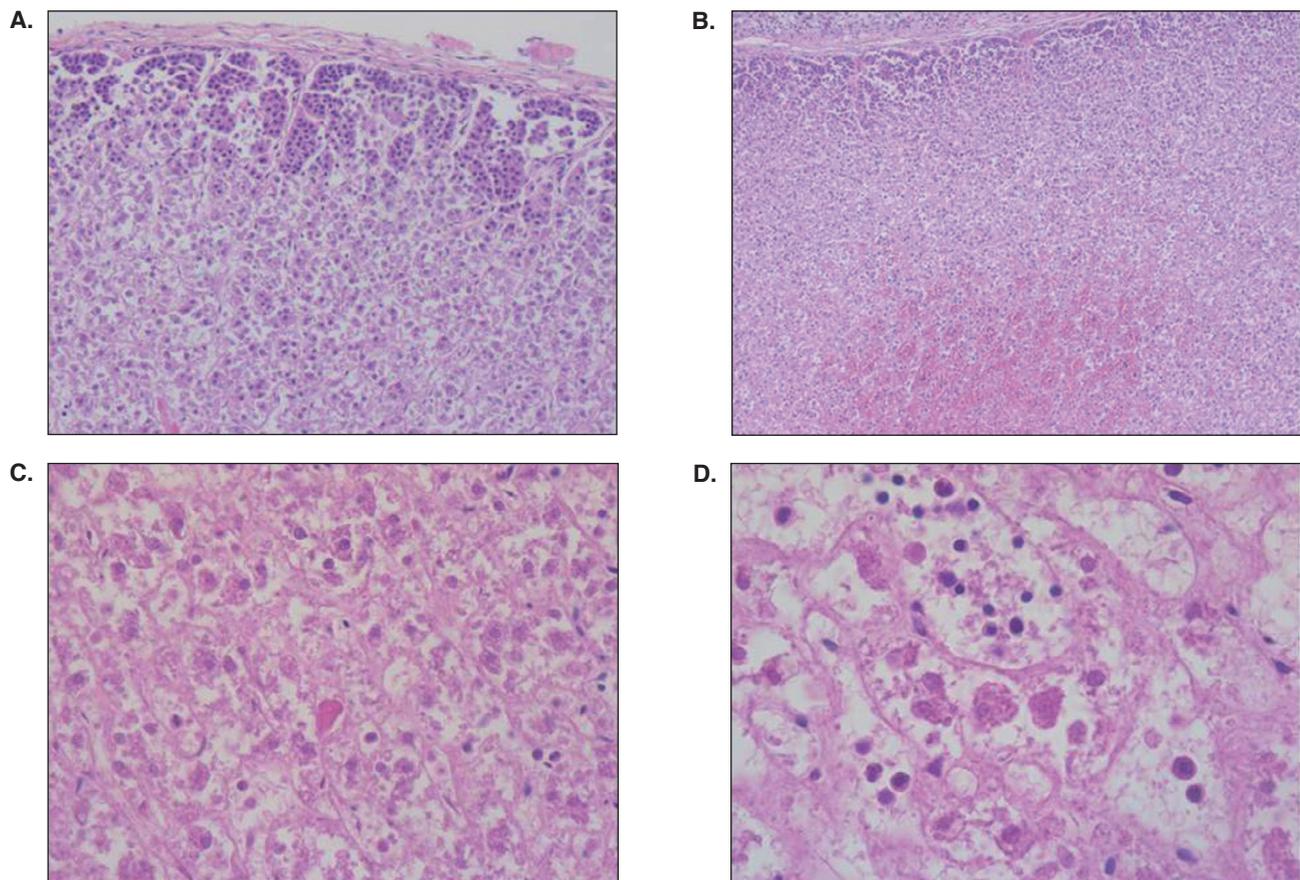
#### DISCUSSION

The case here reported underlines the fundamental role of adrenal glands integrity for the survival of

newborns and in particular of preterms undergoing septic shock. In our newborn, the clinical picture was characterized by a progressive improvement, followed by a dramatic worsening of the clinical status at the end of the third week of postnatal life, probably correlated with the adrenal insufficiency due to massive necrosis of both glands. The finding of a severe diffuse damage of the endothelium, detected in all organs, might be correlated to the loss of cortisol production by the affected adrenals, with loss of the protective function of cortisol against the excessive release of inflammatory cytokines. In conclusion, this case report represents increasing evidence that adrenal insufficiency may be at the basis of instability and hypotension in the critically ill preterm infant.

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**Figure 1 (ABS 53).** A massive necrosis of both adrenal glands was detected, with areas of hemorrhage interesting both the cortical and the medullary zones. **A.** Massive necrosis of adrenal glands. **B.** Massive necrosis with areas of hemorrhage in the adrenal cortical and medullary zones. **C, D.** Apoptosis and massive necrosis in the adrenal cortical zone.

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## ABS 54

### DUPLEX COLLECTING SYSTEM ASSOCIATED WITH URETEROCELE: A CASE REPORT

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#### INTRODUCTION

A duplex collecting system (DCS) is the most common congenital malformation of the urinary tract, occurring in around 1% of live births, with prevalence in females. The upper renal segment is involved in 85% of the cases and ureterocele occur between 24% and 47% of the cases [1]. Management of DCS depends on the severity of ureteral dilatation, voiding cystourethrography (VCUG) and renal scintigraphy (RS) results and severity and frequency of urinary tract infections (UTIs) [2].

#### CASE REPORT

We report the case of a female child born at term by vaginal delivery. Prenatal ultrasound at 22 weeks of gestational age showed a suspected DCS with an increased volume of the left kidney and a tortuous aspect of renal calyces with anteroposterior renal pelvis diameter of 13 mm. After birth, the diagnosis of left DCS associated with megaureter and ureterocele was confirmed and antibiotic prophylaxis was started. At two months of age, the child was admitted to our department for acute pyelonephritis positive to *P. aeruginosa*, treated with intravenous ceftazidime and tobramycin. After three further hospitalizations for recurrent UTIs, at 6 months old a sequential RS showed no sure signs of secretory activity of the higher part of the left kidney and a mild functional prevalence of the right kidney. Creatinine clearance according to Schwartz was 143 mL/min/1.73 m<sup>2</sup>. At 9 months old VCUG detected a vesicoureteral reflux in the distal tract of the megaureter. At 1 year and 6 months of age, the child was hospitalized two times for urinary tract infection treated with i.v. gentamicin. Abdominal CT was performed, showing a dysmorphic left kidney, markedly increased in size, with a polar multicystic and septate swelling. At 19 months of age, left upper pole nephroureterectomy was performed, and after one month she was admitted to our department for

a massive perirenal abscess, treated with drainage and intravenous antibiotics. Currently the child is 4 years old and the last ultrasound examination showed a right kidney increased in size, with absence of dilation and a left kidney of lower dimensions. RS shows functional exclusion of the left kidney and a mild excretory slowdown and a vicarious secretory activity of the right kidney.

#### CONCLUSIONS

Management of DCS is complex and requires special attention when associated with ureterocele and recurrent UTIs. A multidisciplinary follow-up is necessary, requiring a periodic ultrasound and renal function monitoring to prevent loss of kidney function.

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## ABS 55

### MATERNAL CARBAMAZEPINE THERAPY AND SHORT-TERM ADVERSE EFFECTS IN BREAST-FED INFANTS: A CASE REPORT

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#### INTRODUCTION

Usually, no adverse effects are observed in breast-fed infants whose mothers are treated with carbamazepine, although sedation, poor sucking, withdrawal reactions, hepatic dysfunction and cholestasis have been described. Some authors recommend monitoring infant serum carbamazepine levels, liver enzymes and complete blood cell count during mother's treatment with this medication.

#### CASE REPORT

A 40-day-old infant was admitted to the Pediatric Clinic at University of Sassari (Sassari, Italy) for recurrent regurgitations and vomiting. This infant female was born at term with a birth weight of 3,190 g, and was breastfed since birth. Her mother was under chronic anti-epileptic therapy with carbamazepine. History revealed that the baby exhibited poor sucking, vomiting and poor weight gain from the earliest days of life. Laboratory tests

and neurological assessment were normal. Initially, in the suspicion of gastroesophageal reflux, postural therapy and thickening of feeds were performed, with no benefits. Subsequently, carbamazepine levels in infant serum and in maternal breast milk were measured (Tab. 1). The presence of relevant levels of this medication in both biofluids suggested that infant's symptoms were secondary to carbamazepine ingestion through breast milk. The first therapeutic measure was to start mixed feeding (breastfeeding combined with formula feeding), but it was unsuccessful, therefore the use of exclusive formula feeding was needed. After this intervention, rapid resolution of symptoms and weight increase were observed. A short-term follow up confirmed a good weight gain and the absence of vomiting or regurgitation after discharge.

**Table 1 (ABS 55).** Carbamazepine levels in infant serum and maternal breast milk.

	Infant serum concentration	Breast milk concentration
08.00 am	1.3 mcg/dl	3.5 mcg/ml
11.00 am	-	4.4 mcg/ml
02.00 pm	-	3.1 mcg/ml

## CONCLUSIONS

The safety of maternal treatment with carbamazepine during breastfeeding, and particularly the potential adverse drug reactions in breastfed infants, raises several questions, even though the use of this drug is considered to be compatible with breastfeeding. When unexplained symptoms occur in breastfed infants whose mothers are treated with carbamazepine, it is mandatory to determine carbamazepine levels in infant serum. In our case, the discontinuation of breastfeeding with the use of exclusive formula feeding was sufficient to obtain the complete resolution of symptoms.

## ABS 56

### TUBULOINTERSTITIAL NEPHRITIS AND UVEITIS: A CASE REPORT OF A RARE SYNDROME

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Tubulointerstitial nephritis and uveitis (TINU) syndrome is a rare disorder characterized by idiopathic tubulointerstitial nephritis and generally bilateral, anterior uveitis. Most patients with TINU are adolescents and young women. We describe the case of a 15-year-old female who was referred to our hospital because of a 3-month history of a low grade fever with rapid spontaneous resolution in a few hours, accompanied by asthenia and 3 kg weight loss in the last month. In addition, she reported severe pain and photophobia at the right eye. Her physical examination showed discrete general conditions, 2/6 systolic murmur and intense conjunctival hyperemia, initially at the right eye that after a few days became bilateral. Her blood pressure was normal. The laboratory tests showed normocytic anemia (Hb 8.7 g/dl), increased inflammatory markers (ESR 77 mm/h, CRP 3.2 mg/dl), elevated blood urea nitrogen and serum creatinine (respectively 35 mg/dl and 2.4 mg/dl), mild hypokalemia (3.2 mEq/l). Liver function tests, total protein and albumin were normal. Urinalysis revealed proteinuria (30 mg/dl), normoglycemic glycosuria (280 mg/dl) and mild hematuria. Urinalysis in 24-hour samples detected a low creatinine clearance of 22 ml/min and proteinuria of 1.1 g.  $\beta_2$ -Microglobulin levels was elevated (0.6 mg/dl). Ophthalmology consultation showed bilateral anterior uveitis. HLA typing reported the presence of DQB1\*0201/\*0501 and DQA1\*0101/\*0501. HLA-DQB1\*05 and DQA1\*01 were reported to be strongly associated with TINU syndrome. The clinical summary and laboratory analysis were extremely suggestive of TINU. The patient started ocular therapy with tropicamide for 10 days with uveitis resolution, systemic prednisone at a daily dose of 1 mg/kg for 1 month and subsequent gradual dose reduction following normalization of renal function, glomerular filtration rate and urinalysis. However, during follow-up, there were 3 relapses of bilateral anterior uveitis. Therefore, it was necessary to add methotrexate (MTX), 15 mg/week a month, before the complete discontinuation of steroid therapy. From the start of MTX therapy the girl did not present further ocular or renal recurrences. TINU is generally a self-limiting disease with a good prognosis that rapidly responds to systemic steroid therapy. However, relapses of uveitis are common, which may require steroid-sparing immunosuppressive agents, such as MTX.

## ABS 57

### URETEROCELE: THE PROLAPSE IS A RARE COMPLICATION. A CASE REPORT

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## INTRODUCTION

Congenital anomalies of the kidney and urinary tract (CAKUT) are a group of heterogeneous disorders that affect kidneys, ureters and bladder. Ureterocele is an example of CAKUT; it is a cystic out-pouching of the distal ureter into the urinary bladder. According to its position, it can be intravesical or orthotopic, when the ureterocele is completely contained inside the bladder, and extravesical or ectopic, when part of the cyst extends to the urethra or bladder neck. Severe febrile urinary tract infection is the most common postnatal presentation of ureteroceles, but they, rarely in females, may prolapse and acutely obstruct the bladder outlet.

## CASE REPORT

We report the case of a female child who had an ureterocele prolapse when she was 6 months old. The child was born at term by spontaneous delivery (APGAR 9-10) with a prenatal diagnosis at 36 weeks and 3 days of bilateral hydronephrosis with right ureterocele. First ultrasound showed bilateral duplex collecting system (DCS), bilateral hydroureteronephrosis and two ureteroceles in the bladder (2.5 cm – 2.7 cm), therefore an antibiotic prophylaxis was started. At 50 days of age, the child was hospitalized for urosepsis, treated with gentamicin and ceftazidime. Renal function was preserved. At 3 months of age voiding cystourethrography showed 4-5° right vesicoureteral reflux (VUR); renal scintigraphy (RS) with MAG3 revealed a left ureteral transit delay, not obstructive and a right DCS, with reduced secretory function and retardation of lower renal segment drainage. When the child was 6 months old, she was admitted to our hospital with a large mass protruding from her vagina. In consideration of clinical history, the patient was transferred to a neonatal surgery, where the wall of the prolapsed ureterocele appeared necrotic in its middle and lower part, therefore it was resected and the remaining part was decompressed by endoscopy. A nephrostomy was performed. The endoscopic control identified right ureterocele dissected and left ectopic ureter on the neck of the bladder. After a month ureteroclectomy was performed.

## CONCLUSIONS

Prolapse is a rare ureterocele's complication. We must suspect this in presence of a vaginal mass or acute retention of urine, especially in female children with a history of ureterocele. Ureterocele is associated with DCS in 95% of females and with the presence of VUR, especially in extravesical forms. Clinical and ultrasound follow-up is important to establish a surgical treatment.

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## ABS 58

### NEONATAL LUPUS: A CASE REPORT

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## INTRODUCTION

Neonatal lupus is an uncommon autoimmune disease with varying degrees of skin, hematological and cardiac manifestation. Babies have maternal anti R-o/SSA, anti-La/SSB, or anti U1RNP auto-antibodies. We report a case of neonatal lupus manifestation exclusively on the skin.

## CASE REPORT

M., a Tunisian girl, was born at 38 weeks; her birth was uneventful. Her weight was 2,800 g, height 48 cm, head circumference 33 cm. Her mother (28 years old, primipara) was followed in internal medicine for a systemic lupus erythematosus discovered at the age of 20 on the occasion of diffuse arthralgia. From birth, M. presented erythematous and annular plaques on the face, scalp and an inflammatory periorbital erythema. The electrocardiogram and cardiac ultrasound were normal, but thrombocytopenia and hepatitis (AST/ALT = 94/100) were present. Speckled antinuclear antibodies were positive at 1/16,000, but no anti-SSA and SSB antibodies, anti-dsDNA, anti-Sm, anti-centromere, anti-nucleosome and anti-ribosomes were found. Sun avoidance was prescribed as well as a sunscreen cream with persistent scarring atrophic lesions and hyperpigmentation of the face and scalp. Now aged of 5 months, M. has good growth and shows no neurological, cardiac, hematologic

or kidney manifestations. A dosage of antibodies is planned at the age of 6 months.

#### CONCLUSIONS

Neonatal lupus is the perfect example of materno-fetal autoimmune disease, which is caused by placental transfer of SSA antibodies (52 and 60 KD), associated or not with anti SSB (48 KD).

The establishment of national registries and cohorts is necessary for proper epidemiological assessment of this rare entity. The prevalence of isolated skin involvement is underestimated compared with cardiac involvement, which remains the main obsession of every practitioner.

#### ABS 59

### HEME OXYGENASE-1 IN DONOR HUMAN MILK

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#### BACKGROUND

When the mother's own milk is not available, the best alternative is represented by donor milk (DM), i.e., human milk pasteurized with the Holder pasteurization (HoP) method in Human Milk Banks for safe storage. Advantages and disadvantages associated to this procedure have been widely discussed in Literature, but it currently represents the best compromise between microbiological safety and biological quality of DM.

#### OBJECTIVE

The aim of this study is to investigate the effects of HoP on Heme-oxygenase-1 (HO-1), an antioxidant protein involved in several cytoprotective actions that should play an important role in the development and protection of the gut.

#### METHODS

We performed a pretest-test study where the milk donors acted as their own controls in 14 mothers (who have delivered 7 at term and 7 preterm). Milk samples were divided into two parts: the first was frozen (-80°C); the second was Holder-pasteurized

before freezing (-80°C). HO-1 was quantified using an ELISA test.

#### RESULTS

HO-1 was detected in all samples. There were no significant differences in HO-1 concentrations between term and preterm milk samples and raw and pasteurized samples ( $p > 0.05$ ). There were no significant differences when results were adjusted for milk maturation degree ( $p > 0.05$ ).

#### CONCLUSIONS

The data suggest the efficacy of HoP procedure in DM storage and preparation regarding the HO-1 concentration.

#### ABS 60

### THE INTERSTITIAL CELLS OF CAJAL: WHAT IS THEIR ROLE IN HUMAN GUT DEVELOPMENT?

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The interstitial cells of Cajal (ICCs) are described as pleomorphic cells with large oval nuclei and several thin processes. They are of mesodermal origin. Located in the muscular layers of the gastrointestinal tract, ICCs are responsible for the generation of electric slow waves (pacemaker activity) through their nitregic and cholinergic activity and afferent neural signaling (stretch receptor). According to their specific topography and function, ICCs are classified in 5 subtypes (**Fig. 1**):

1. ICC of submucosa and submucosal plexus (ICC-SM in the stomach and ICC-SMP in the colon);
2. ICC of the circular muscle (ICC-CM), including ICC of the septa (ICC-SEP);
3. ICC of the deep muscular plexus (ICC-DMP in the small intestine);
4. ICC of the myenteric plexus (ICC-MP);
5. ICC of the longitudinal muscle (ICC-LM).

ICC-CM and ICC-LM are often collectively termed intramuscular ICC (ICC-IM). In the recent literature ICC located in the myenteric (Auerbach's) plexus are designated as ICC-MP instead of ICC-MY or ICC-AP. ICC of the subserosa (ICC-SS) were observed in the small intestine of mouse. In humans, ICCs are located from the esophagus to the inner sphincter region of the anus throughout the digestive tract [1]. ICCs express the receptor tyrosine kinase Kit encoded by a proto-oncogene. SCF (stem cell factor)

has been identified as a c-Kit ligand. The antibody anti-c-Kit is a useful immunohistochemical marker for the detection of the receptor tyrosine kinase Kit in ICCs. CD34 was utilized in development of ICCs in the human duodenum. Cells from the enteric plexuses and smooth muscle cells differentiation can be immunohistochemically ruled out respectively by using anti-neuron specific enolase and anti- $\alpha$  smooth muscle actin and anti-desmin antibodies [2]. The c-Kit positive cells can be observed for the first time at 7-8 weeks of gestational age around the inception of the myenteric plexus ganglia as a long wild belt around the foregut (esophagus, stomach and proximal duodenum) [2]. At 9 weeks, cells with the same c-Kit reactivity appear around the inception of the myenteric plexus ganglia as a thin row in the midgut (distal duodenum, jejunum and ileum in the proximal colon). These cells can be found after 9-10 weeks in the submucosal plexus and in the myenteric plexus forming two parallel belts [3]. In the hindgut or distal colon two parallel belts of densely packed c-Kit positive cells are present simultaneously in the submucosal plexus and myenteric plexus at 10-11 weeks [4]. ICCs play a central role in gastrointestinal contractions, being responsible of the etiology and pathogenesis in different motility disorders. Moreover, ICCs give rise to gastrointestinal stromal tumors (GISTs). The expression of c-Kit and CD34 are the

diagnostic tools for GISTs diagnosis especially in combination with DOG1 and PDGFR $\alpha$  antibodies [5]. Therefore, we would suggest adding even DOG1 and PDGFR $\alpha$  for better understanding the development of ICCs in the human gastrointestinal tract and the etiology and pathogenesis in different motility disorders.

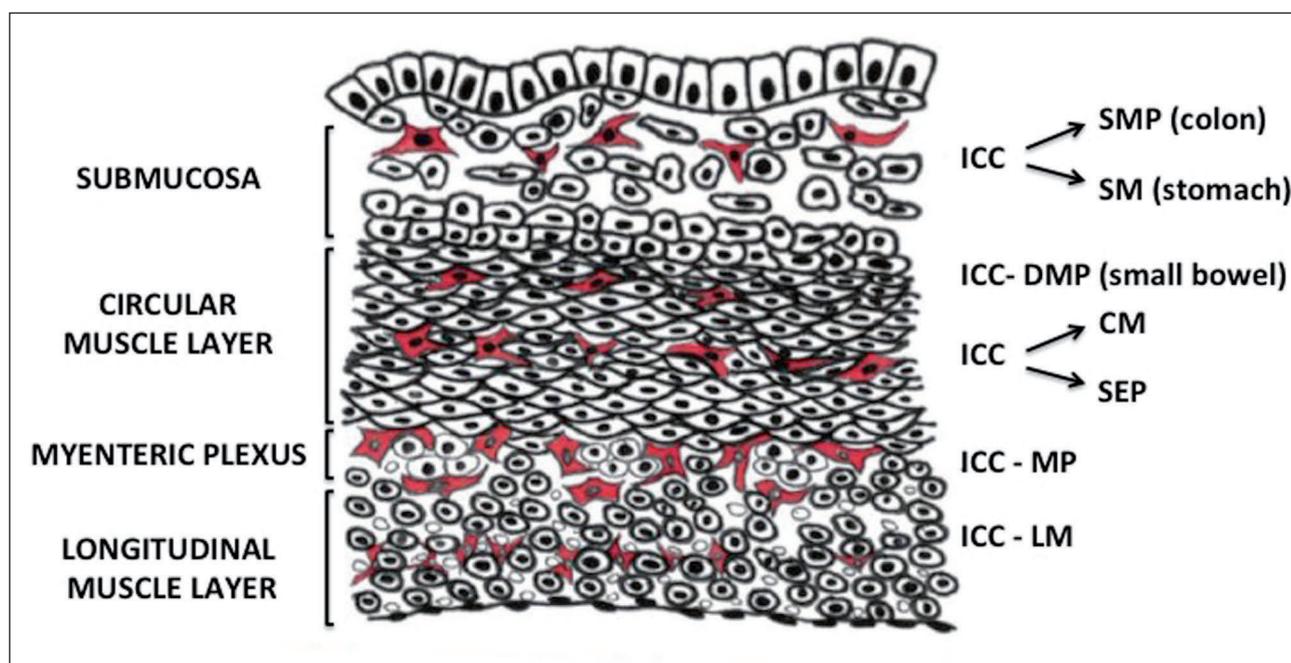
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#### ABS 61

#### BRONCHIAL SELECTIVE INTUBATION AND VOLUME GUARANTEE VENTILATION IN A PRETERM WITH LEFT LUNG INTERSTITIAL PULMONARY EMPHYSEMA

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**Figure 1 (ABS 60).** Distribution of c-Kit positive cells in the human developing gastrointestinal tract.

ICC: interstitial cells of Cajal; SMP: submucosal plexus; SM: submucosa; DMP: deep muscular plexus; CM: circular muscle; SEP: septa; MP: myenteric plexus; LM: longitudinal muscle.

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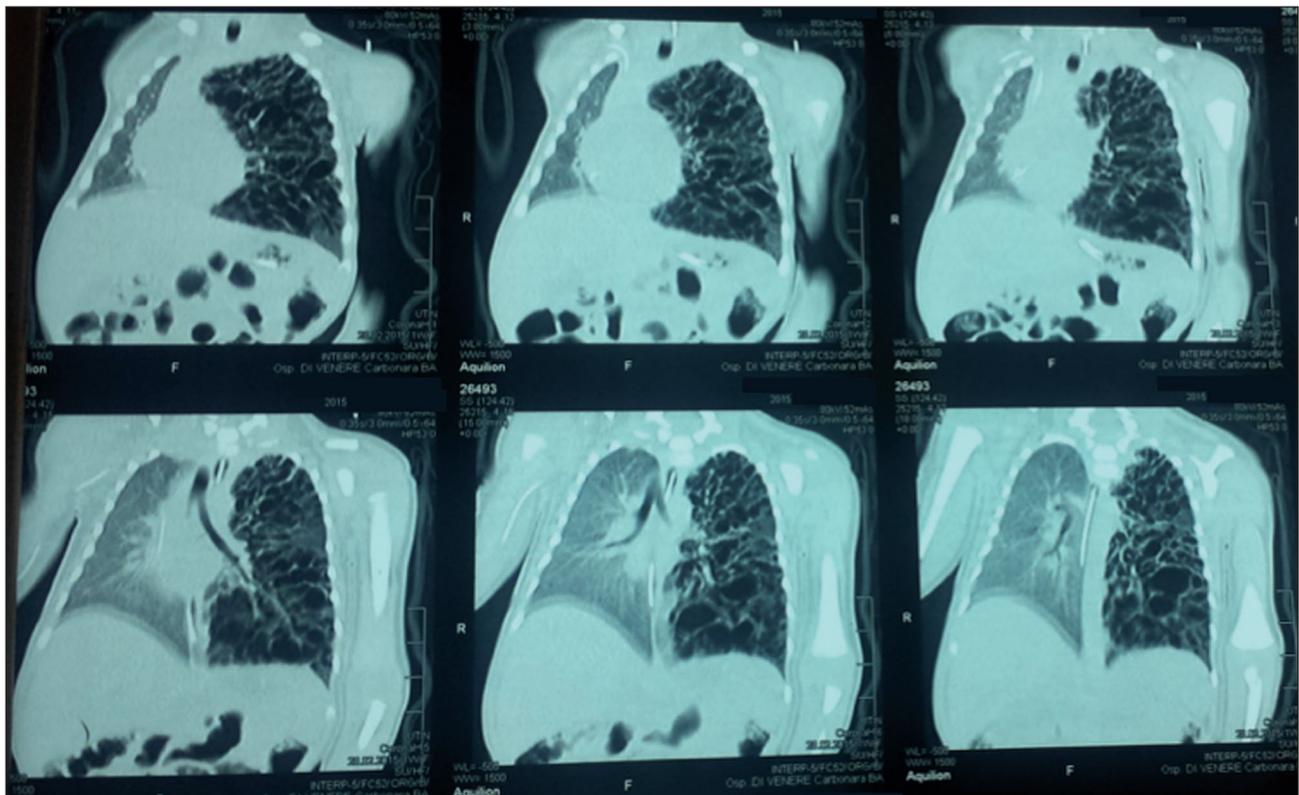
## INTRODUCTION

Persistent interstitial pulmonary emphysema (PIE) is a rare condition that occurs in preterm infants who are particularly disposed to overdistension from mechanical ventilation or continuous positive airway pressure. PIE is characterized by abnormal accumulation of air in the pulmonary interstitium, due to disruption of the basement membrane of the alveolar wall. PIE may be bilateral and diffuse or unilateral. In unilateral PIE, mediastinal shift causes compressive atelectasis of the opposite lung, which leads to an increased need for higher ventilatory pressures, progressive overdistension of the affected lung and worsening of clinical condition. The management of infants suffering from PIE varies according to the severity and stability of the patient, from conservative treatment to aggressive surgical treatment by pneumonectomy.

## CASE REPORT

We report a case of a female preterm neonate born at 32 weeks of GA by cesarean section for premature rupture of membranes. Even though Apgar score was 8 at the first minute and 9 after five minutes and she did not need resuscitation at

birth, she developed mild distress a few minutes after delivery. She was therefore treated with surfactant 200 mg/kg (INSURE technique) followed by nCPAP which was discontinued on the fourth day of life. After five days without any ventilator support, the patient showed dyspnea and required oxygen support. The chest X-ray showed a moderate alveolar hyperinflation of the left lung and we did not find any echocardiographic evidence of persistent pulmonary hypertension. Lung CT showed in more detail the hyperexpansion of the left lung with marked structural alteration of the lung parenchyma due to the presence of multiple bullous lesions and irregular interstitial thickening. The mediastinal structures were diverted to the right and the right lung appeared atelectatic (**Fig. 1**). Selective right bronchial intubation (**Fig. 2**) for treatment of left-sided PIE was performed and selective one-sided lung ventilation with SIPPV + volume guarantee was undertaken: PIP max 15, PEEP 4, Ti 0.30, RR 50, flow 8, TV 2.5 ml/kg and positioned in the left lateral decubitus to facilitate lung deflation. After 48 hours we observed the full resolution of the emphysema (**Fig. 3**) and the patient was extubated with no need of oxygen supplementation. The subsequent clinical course was normal and the neonate was discharged at

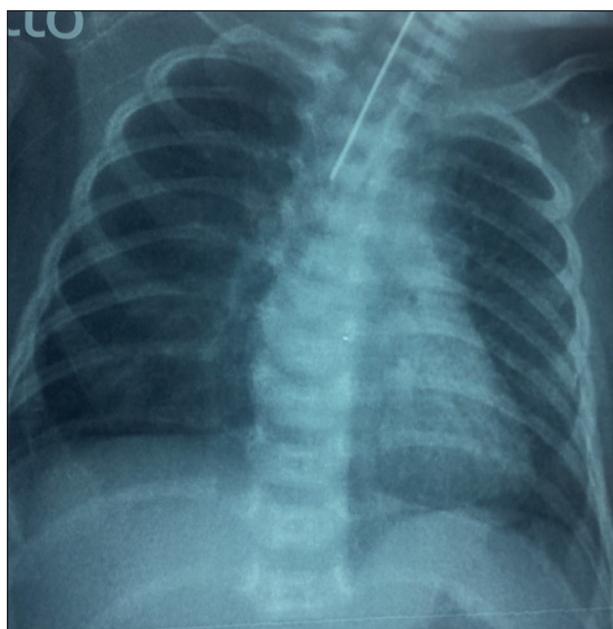


**Figure 1 (ABS 61).** Lung CT. The mediastinal structures are diverted to the right and the right lung appears atelectatic.

36 weeks of GA at 41 days of life. No respiratory problem was reported during the first year of life follow-up.



**Figure 2 (ABS 61).** Selective right bronchial intubation for treatment of left-sided persistent interstitial pulmonary emphysema (PIE) .



**Figure 3 (ABS 61).** Full resolution of the emphysema.

## CONCLUSIONS

Selective bronchial intubation and one-sided lung ventilation is accepted as effective therapy for neonates with unilateral PIE with severe hyperinflation. Subsequent deflation of hyperexpanded lung can restore pulmonary and cardiovascular function and result in resorption of interstitial air. Furthermore, the non-aggressive volume guarantee ventilation of the atelectatic lung with the halved TV provides the double benefit of favoring deflation of the lung affected by PIE and avoiding volutrauma for the normal lung.

## ABS 62

### EXTRALOBAR PULMONARY SEQUESTRATION: A PRENATAL AND POSTNATAL EVALUATION

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## INTRODUCTION

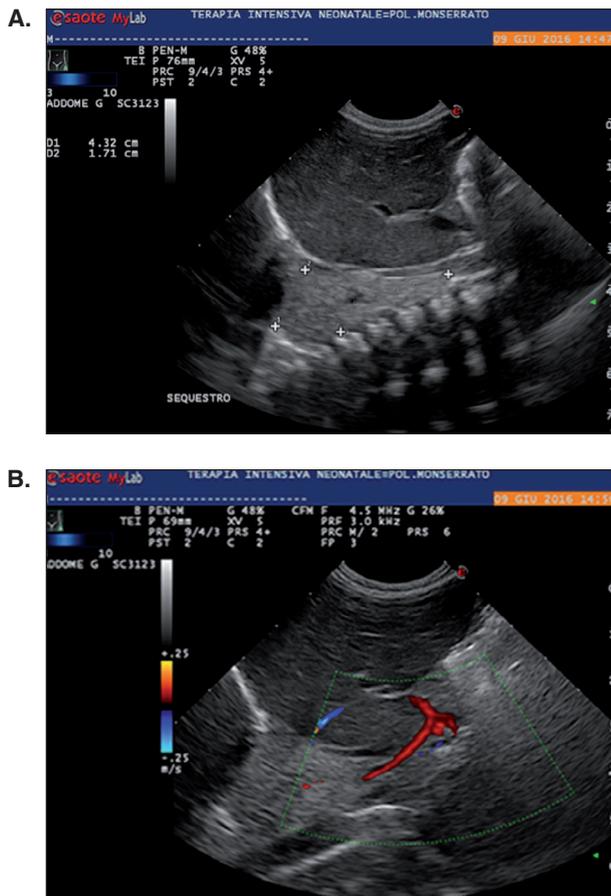
Pulmonary sequestrations (PSs) are the second most common congenital lung abnormalities diagnosed in antenatal and postnatal examinations with US and MRI imaging, after congenital pulmonary airway malformations. In this case report we present the radiological findings of a prenatal and postnatal diagnosis of an extralobar pulmonary sequestration (EPS).

## CASE REPORT

A 21-year-old primipara arrived to our attention after an US examination (19<sup>th</sup> weeks) and two fetal MRI (21<sup>st</sup> and 32<sup>nd</sup> weeks) carried out in another hospital. MRI (performed with a 1.5 T magnetic field and T2-SSFSE sequences) revealed a hyperintense, well-defined mass in the right prevertebral space and a feeding artery from the descending aorta, which was compatible with PS. This examination showed no other thoracic abnormalities. The female newborn was asymptomatic at birth. A postnatal US performed at our institution confirmed the supradiaphragmatic hyperechoic mass in the right lung; color Doppler sonography identified an anomalous feeding artery from the aorta (**Fig. 1**). The diagnosis of PS was confirmed.

## DISCUSSION

PS refers to an aberrant non-functioning portion of lung tissue separated from the thacheobronchial



**Figure 1 (ABS 62).** A. Postnatal US demonstrates the supra-diaphragmatic hyperechoic mass in the right lung. B. Color Doppler sonography identifies an anomalous feeding artery from aorta.

tree or pulmonary arteries; it receives arterial blood from the thoracic or abdominal aorta (from celiac or splenic artery, intercostal, subclavian and rarely from coronary arteries). In 1946 Pryce classified PSs in two distinct groups based on the relationship of the aberrant segmental lung tissue to the pleura and on the venous drainage. Intralobar pulmonary sequestration (IPS) does not have its own pleura, but it is closely connected to the surrounding normal lung; blood commonly drains into the pulmonary veins. EPS is separated by the surrounding lung by its own pleura and has a systemic venous drainage (most commonly through the azygos and hemiazygos system). While IPS is more frequent in childhood or adulthood and is associated with recurrent pulmonary infections, EPS is a congenital anomaly, typical of the neonatal period. Other congenital systemic anomalies (congenital diaphragmatic hernia, cardiac abnormalities, foregut duplication cyst) may be associated with EPS.

## CONCLUSIONS

The improvement of radiological techniques allows a better characterization of PS. An accurate analysis of the radiological findings allows a correct diagnosis that is necessary to guide the clinician in prenatal evaluation, appropriate peri-postnatal management and surgical treatment.

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## ABS 63

### RIGHT CARDIAC ISOMERISM: A SERIOUS HEART DEFECT. A CASE REPORT

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## INTRODUCTION

Right cardiac isomerism is a complex cardiac malformation often associated with asplenia syndrome. Among untreated patients, early occurrence of hypoxemia and cardiac failure accounts for a 79% mortality in the first year of life; one-third of the patients dies within the first week. We report the case of a newborn with right cardiac isomerism. Anatomical features, management and outcome are described referring to literature.

## CASE REPORT

A male infant of 3,400 g was born by vaginal delivery at 38 weeks gestational age to a G2P2 mother. The newborn's parents were in good health and first-degree consanguineous. No family history of congenital malformation was present. It was a poorly monitored pregnancy and antenatal ultrasound was not made. The Apgar score was 8, 8 and 10 at 1, 5 and 10 min respectively, requiring no resuscitation. The infant was transferred to our neonatology unit care at the fourth hour of life for respiratory distress. Physical

examination revealed cyanosis requiring oxygen supplementation and intense systolic murmur. The chest X-ray showed dextrocardia without cardiomegaly. Echocardiography was requested showing ambiguous situs with right isomerism and common atrioventricular valve with the appearance of common AV (atrioventricular). The pulmonary outflow tract was obstructed because of subvalvular pulmonary stenosis. Total anomalous pulmonary venous connection was present. The spleen was absent at the abdominal ultrasound. The diagnosis of Ivemark Syndrome was suspected. Urgent surgical palliation consisting of a systemic-pulmonary shunt was necessary but the infant died within few days of life due to refractory hypoxemia.

#### CONCLUSIONS

Despite advances in modern surgical techniques, the outcome of patients with right isomerism remains poor. The association of several cardiac defects, the complexity of their surgery related to their anomalous systemic and pulmonary venous connections, their disposition to suffer from dysrhythmias and the susceptibility of those born with asplenia to suffer from sepsis, all seem to contribute to a large mortality in infancy.

#### ABS 64

### TRIAGE AND SAFE MANAGEMENT OF THE PEDIATRIC PATIENT IN THE ACCIDENT AND EMERGENCY DEPARTMENT OF A GENERAL HOSPITAL

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#### INTRODUCTION

The majority of urgent pediatric cases are admitted to Accident and Emergency (A&E) Departments of General Hospitals, where setting and clinical evaluation are rarely tailored to children. Safe management since priority code assignment is of paramount importance, as under-triage is a major risk [1]. Therefore, nurses involved in triage need specific knowledge and adequate tools to safely identify critical children [2].

#### AIM

To evaluate the safety of pediatric triage in the A&E Department of a General Hospital.

#### METHODS

Descriptive study performed at the A&E Department of a General Hospital in Cagliari (Italy). Nurses working in the triage bay answered a questionnaire on pediatric triage at the arrival to the A&E, on specific training on pediatric triage, and on the perceived competence on attributing priority codes to children compared to adults.

#### RESULTS

All the nurses involved in triaging (n = 25) were enrolled. 23/25 nurses never worked in pediatric wards. None of them was specifically trained on pediatric triage, but all of them were trained in general triage, including topics on child's assessment. Only 32% was BLSD certified, whereas 8% participated to advanced courses. 96% (n = 17) considers complex the priority code attribution to children, but 68% (n = 16) states to have adequate knowledge to evaluate the child. 64% (n = 16) judged the instruments available in the triage bay insufficient (protocols, flow charts, medical devices dedicated to children).

#### CONCLUSIONS

This survey suggests that nurses working in the triage bay need further training to safely manage pediatric patients. Implementing the use of validated tools could allow risk reduction and better care in A&E Departments of General Hospitals.

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#### ABS 65

### NEONATAL ALLOIMMUNE THROMBOCYTOPENIA (NAIT): A RARE CASE DUE TO HLA CLASS I ANTIBODIES

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#### INTRODUCTION

Neonatal alloimmune thrombocytopenia (NAIT) is determined by fetomaternal incompatibility

for platelets antigens. Incompatibility causes transplacental passage of maternal anti-human platelet antigen (HPA) antibodies, including anti-human leukocyte antigen (HLA) antibodies in 31% of pregnant woman in Caucasian population, anti-HLA antibodies have been observed. However, few reports are available on NAIT resulting from anti-HLA antibodies.

#### CASE REPORT

A female, term baby with birth weight of 3,420 g was born from a woman at her second pregnancy without complications (no history of blood transfusions or autoimmune disease and negative tests for TORCH and vaginal Group B *Streptococcus* infections). In less than 12 hours of life the newborn presented petechiae and severe thrombocytopenia (platelets: 14,000/mmc) with normal hemoglobin and WBC counts and no signs of infections. Platelet transfusion was immediately performed (15 ml/kg) and IV immunoglobulin 1 g/kg was daily administered (3 doses). The platelets raised very slowly (28,000/mmc and 34,000/mmc respectively in II e III day of life) so therapy with metilprednisolone IV was started at the dosage of 3 mg/kg/die. After two weeks the platelets count raised above 100,000/mmc, thus cortisone therapy was reduced. The baby was discharged with oral prednisone and planned platelet monitoring in follow up. Hemorrhage or other abnormal findings such as hepatosplenomegaly were not present in an ultrasound scan of the brain and abdomen. Human platelet antigen genotyping showed that the mother was HPA 1a2a3b4a5a6a7a8a9a11a15ab positive and the ELISA on maternal serum showed only anti-HLA class I antibodies.

#### DISCUSSION AND CONCLUSION

Although one third of mother has HLA antibodies, the fetus is usually protected. The mechanism by which this occurs is not completely understood, with hypotheses including blocking antibodies and placental filtration. Neonatal thrombocytopenia is therefore rarely associated with this finding, generally in the second pregnancy and especially in SGA infants (damaged placenta may induce the leakage of maternal blood with anti-platelet antibodies to babies). Our case is a rare finding of severe symptomatic thrombocytopenia in newborn AGA from mother anti-HLA class I antibodies positive. We did not perform immunological analysis on neonatal serum because of prompt platelet transfusion and immunoglobulin and cortisone therapy.

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#### ABS 66

### ULTRASONOGRAPHIC HIP SCREENING OF 5914 NEONATES: A COMPARISON BETWEEN TERM AND PRETERM INFANTS

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#### BACKGROUND

Developmental Dysplasia of the Hip (DDH) is the most important skeletal pathology in pediatric age and it includes different anatomic-pathological and clinical pictures, from instability to dislocation. Ultrasound examination is the safest and most effective tool to precociously identify the dysplastic hip and is therefore used in different screening programs. Prematurity is often associated with DDH even if there is no consensus among the scientific community.

#### METHODS

5,914 infants, 2,845 males and 3,069 females were subjected to ultrasound hip examination. Neonates were divided in 2 groups based on the gestational age (GA) at birth: 422 preterm and 5,492 at term. Mean GA at birth was 39.5 weeks for term and 32.8 for preterm infants, respectively. Ultrasound examinations were performed following the Graft technique taking into consideration the patient's age, ultrasound examination results, type of the hip, diagnostic conclusions and therapeutic indications.

#### RESULTS

322 term infants showed hips above the 1b type, 425 pathological hips in total (3.87%), while only 6 preterm infants (0.71%) showed hips above 1b type and no bilateral.

#### CONCLUSIONS

Preterm birth is not a risk factor for DDH, thus these infants can follow the same indications

for screening, diagnosis, treatment and follow-up as term neonates, without the necessity of GA correction.

#### ABS 67

### GESTATIONAL DIABETES MELLITUS: FROM DIAGNOSIS TO MATERNAL-NEONATAL OUTCOME

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#### BACKGROUND

Gestational diabetes mellitus (GDM) is characterized by a variable degree of glucose intolerance, which begins or is diagnosed for the first time during pregnancy and, in most cases, resolves after delivery. The aim of this study was to evaluate the presence of a possible correlation between the metabolic status of the patient with gestational diabetes and fetal vascular function.

#### METHODS

This was a retrospective case-control study. 130 GDM patients and 130 healthy controls were enrolled. 55 patients with GDM performed ultrasound scan at the 30<sup>th</sup> gestational week, while 75 patients at 35 weeks of gestation. Clinical and medical history, glycemic and lipidic profile were evaluated in all patients. Moreover, the fetal aortic intima media thickness (aIMT) and the fetal aortic diameter were examined. Finally, we evaluated the area under the curve (AUC) for each glucose load curve performed at 24 weeks in all patients. Neonatal outcome was collected at delivery.

#### RESULTS

The aIMT of GDM fetuses was significantly higher than in controls at 30 and 35 weeks of gestation, respectively ( $p < 0.0001$ ). There was also a positive correlation between aIMT and area under the curve (AUC) of the OGTT of GDM patients (30 weeks  $p = 0.03$ ; 35 weeks  $p = 0.01$ ). The AUC also positively correlated with fetal weight at birth in GDM patients (30 weeks  $p < 0.0001$ ; 35 weeks  $p < 0.0001$ ,  $r^2 = 0.30$ ).

#### CONCLUSIONS

Maternal gestational diabetes correlates with fetal aIMT, known marker of endothelial remodeling.

#### ABS 68

### ISL-1 IS EXPRESSED BY A SUBSET OF HUMAN BREAST MILK STEM CELLS

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#### BACKGROUND

Human breast milk contains a heterogeneous population of cells, among which mesenchymal stem cells were confirmed by multiple immunohistochemical studies. For this reason, human breast milk is currently considered as a new potential source of stem/progenitor cells having the ability to self-renew and to develop into more differentiated cells. Several patterns of immunohistochemical markers have been studied; however, these results need to be completed using new stem cells mesenchymal markers [1]. In this study, for the first time to our knowledge, we investigated the expression of Islet 1 antibody (ISL-1) in cells isolated from fresh human milk. ISL-1 was considered an important transcription factor involved in the embryogenesis of pancreatic islets of Langerhans; furthermore, it was also studied as a marker of cardiac and neural progenitor cells [2].

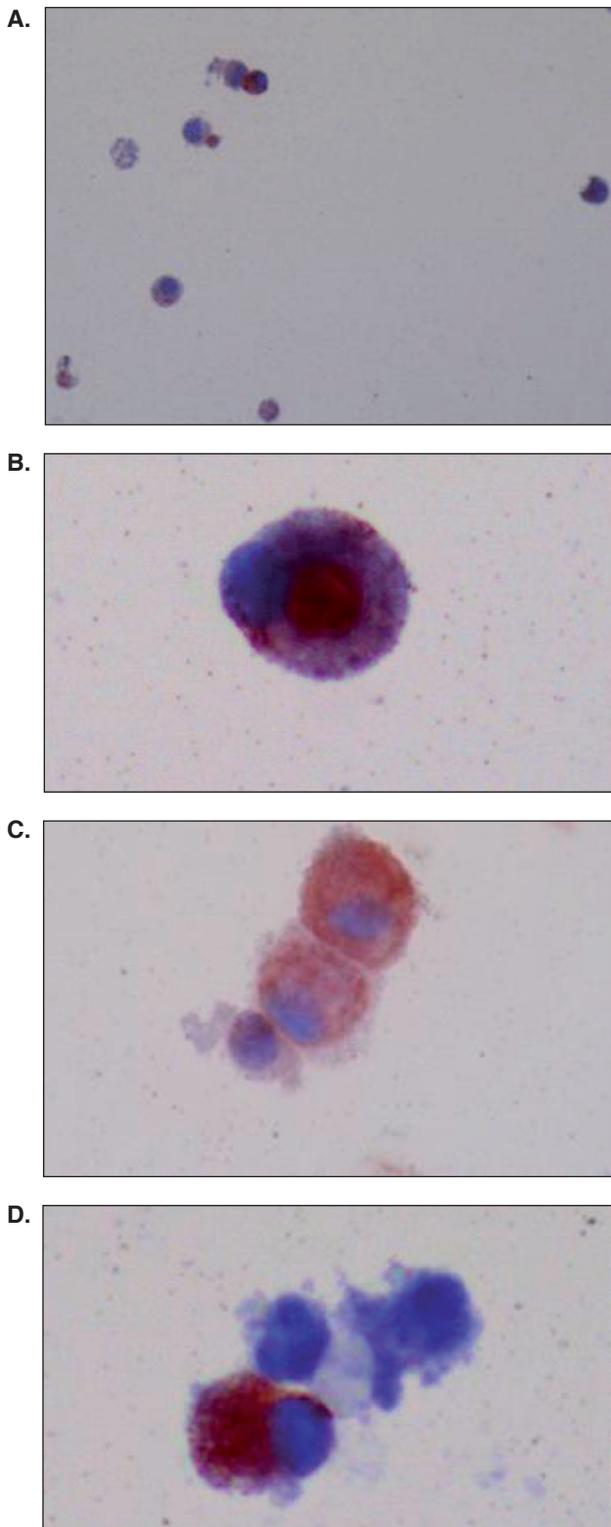
#### DESIGN

Fresh human milk was centrifuged and the pellet was stored in commercial Cytological ThinPrep solution (Hologic Inc.). Microscope cytological slides were obtained using the automatic ThinPrep processor (Hologic Inc.) and these slides were used for standard immunohistochemical reactions performed with an automated stainer (Dako), using a polyclonal anti-ISL-1 antibody (Bachem-Peninsula Lab, San Carlos, CA, USA).

#### RESULTS

An interesting ISL-1 positivity was constantly observed in a subset of some cells isolated from different samples of fresh human milk. ISL-1 positivity was frequently localized in the cytoplasm and only in few cases in the nucleus (**Fig. 1A**). Single cells (**Fig. 1B**) or two or more grouped cells

(Fig. 1C, Fig. 1D) showed ISL-1 positivity. In grouped cells, ISL-1 positivity was found either in one or in all cells (Fig. 1C, Fig. 1D).



**Figure 1 (ABS 68).** ISL-1 positivity was frequently localized in the cytoplasm and only in few cases in the nucleus (A). Single cells (B) or two or more grouped cells (C, D) showed ISL-1 positivity. In grouped cells, ISL-1 positivity was found either in one or in all cells (C, D).

## CONCLUSIONS

The presence of ISL-1 protein in mesenchymal stem cells, isolated from fresh human milk is a new important detail that could open new perspectives for these particular cells. In the samples studied, CD44 positive cells are in general more abundant than ISL-1 positive ones, suggesting that this new marker of progenitor cells may evidence a subgroup of stem cells with a possibly particular biological significance. Therefore, our results highlight the presence of a complex relationship between the mother and the lactating infant after birth, displayed in part by different subsets of milk stem cells.

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## ABS 69

### METABOLOMICS IN SCHIZOPHRENIA

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Schizophrenia (SCZ) is a severe, chronic psychiatric disorder with a prevalence of 1% in the general population. Twin studies estimated the heritability of SCZ at 80% [1], prompting the search for genetic determinants of risk. Only recently, non-hypothesis driven genome-wide association studies (GWAS) have reliably identified more than 128 significant association signals in 108 loci, increasing the knowledge of the genetic architecture of SCZ [2]. Importantly, GWAS-derived polygenic risk score profiling was able to explain roughly 7% of the variation on the liability scale to SCZ [2]. It is plausible that the remaining proportion of phenotypic variation could be partly explained by epigenetic determinants. Genetic and epigenetic determinants might act together in altering the neurobiological machinery up to the point where illness becomes phenotypically evident. In this

context, one key aspect is the identification of these neurobiological alterations before SCZ manifests, particularly in individuals at high genetic risk (i.e. with one or more first-degree relative affected). It is conceivable that signatures of these alterations might be detected through the analysis of peripheral sets of metabolites (metabolome). Here we review the recent literature on metabolomics of SCZ, focusing particularly on results obtained in drug-naïve first-episode psychotic patients, thus with minimal confounding from drug treatment. These evidences showed that metabolomics fingerprints specific to SCZ patients are able to: 1) discriminate between affected and unaffected individuals, and 2) identify stable metabolic markers associated with SCZ irrespective of drug treatment. In particular, first-episode patients had increased levels of N-Acetylserotonin, as well as increased ratio of N-Acetylserotonin to its precursor tryptophan, compared with healthy controls [3]. Another study showed specific metabolomic lipid signatures, lower plasmalogen levels compared to healthy controls, might be present at the onset of the illness in never-medicated SCZ patients [4]. This finding suggests that low plasmalogen levels might be a trait marker of SCZ that remains stable irrespective of drug treatment. Finally, decreased activity of sulfatase was found in plasma of 22 drug-naïve SCZ patients compared to healthy controls [5]. Taken together, these results indicate the potential of metabolomics as a practical method to detect specific biochemical fingerprints, not influenced by the effects of drugs, in SCZ individuals at the early stage of the illness. If validated in larger samples, these state-related biochemical alterations could be applied as illness biomarkers in large scale screening of at risk populations.

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## ABS 70

### MEDICAL IMAGING: HOW DO WE SEE AND WHAT DO WE SEE IN ULTRASOUND SCANS

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Neonatal ultrasound scans are images of great impact, capable of raising a great interest in both experts and common people. This is particularly due to the fact that ultrasound scans allow us to see something that we cannot normally see: the features and behavior of the fetus inside his mother's womb. One of the many interesting facts about these images is that some authors [1], discussing some ethical issues regarding the status and use of neonatal ultrasound scans, suggest to treat them straightforwardly as some kind of special photographs, whereas more is needed to be said about bridging the gap between photography and ultrasound technology. Therefore, the aim of my work has been to analyse the ontological and epistemic status of ultrasound images, trying to fill the said gap between mechanically produced images and representation. First of all, the dissertation inquires if a comparison between photographic and ultrasound technology is well-founded. Making the most of works by authors like Patrick Maynard and Kendall Walton, it is possible to argue that, at least at a structural level, photography is actually the technology that most resembles ultrasound technology. As a matter of fact, both technologies produce images that are "marks on special surfaces" [2], that are causally and counterfactually dependent on the subject they represent and they therefore maintain a direct interaction between the specimen and the mechanism used to produce the image (the light and sound waves involved in the production of the images both exploit the property of refraction to represent their subject). Ultrasound scans can therefore be addressed as Mechanically Produced Images (MPIs) [3], images that share a highly and widely acknowledged epistemic privilege with photography (a statement that is not shared by other means of medical imaging such as PET and fMRI). A problematic passage that the work examines is the attempt to define the status of 3-D ultrasound. 3-D ultrasound imaging is a hybrid between B-Mode

ultrasound and computer animation in which the representation of the subject is based on biometric indicators produced by the same waves of the B-mode, but the visual rendering of the image results from an intense mathematical processing. This process makes it very hard to characterize these images, causing their ontological and epistemic status to be uncertain. However, admitting the ability of ultrasound scans to convey objective information about their subjects is but a part of the characterization of ultrasound scans: it is thus necessary to investigate what kind of perceptual access both experts and novices have of the subject of these particular images. Taking advantage of some of the theories of pictorial representation and perception, it is possible to argue that the best way to define the perceptual experience of ultrasound images is according to Dominic Lopes' proposal. Drawing inspiration from the "seeing-in" and recognition theories of pictorial representation, he claims that an image is an object formed by a visible surface, capable of conveying information, inside of which the observer can recognize, hence see, the represented subject by means of his inborn cognitive and perceptual abilities [4, 5]. In conclusion, the proposal of the work is to consider ultrasound images as a particular kind of epistemically privileged natural representation of the fetus. The observation of these images results in a particular perceptual experience of "seeing-in": a double experience composed by the perception of the surface of the image (the screen or the photosensitive paper) and, together, the visual perception and recognition of the fetus inside the image.

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## ABS 71

### THE NEONATAL NEPHROLOGY GROUP OF THE ITALIAN SOCIETY OF NEONATOLOGY: THE FIRST 30 YEARS

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*The Italian Society of Neonatology, The Neonatal Nephrology Study Group*

## INTRODUCTION

The improvement in the care of prenatal, neonatal and pediatric age has increased the survival rate of newborn infants with severe medical conditions; these frequently concern not only brain, heart and lungs, but also kidneys, compromising their function. Moreover, a great contribution comes from the development of imaging, first of all ultrasounds, whereby the diagnosis of several pathology of neonatal and pediatric age has been made possible. We describe the development of Neonatal Nephrology in Italy starting from the foundation of the Neonatal Nephrology Study Group (NNSG) of the Italian Society of Pediatrics in 1986, followed by the evolution of programs of research and investigation on many different lines concerning clinical research on Acute Renal Failure (ARF), Urinary Tract Infection (UTI), ultrasound studies of the neonatal kidney and the publication of numerous papers on peer-reviewed journals.

## GOAL

To evaluate the research and educational activities of NNSG since its foundation (1986) in order to improve the care of newborns and children with kidney and urinary tract pathological conditions.

## METHODS

We considered the results of the Multicenter study programs performed and papers published from the investigators participating in the NNSG activities, from February 1986 until now (30 May 2016):

1. Multicenter Research Program on UTI of the newborn;
2. Multicenter Research Program on Polythelia and UTI in the newborn;
3. Multicenter Research Program on ARF in the newborn;
4. Multicenter Research Program on antenatal and postnatal Diagnosis of Urinary Tract Abnormalities (UTA) in the Newborn;
5. Multicenter Research Program on Kidney function in the newborn;
6. Research Program on Cystatin C in the perinatal period;
7. Multicenter Program on Kidney function in the newborn;

8. Multicenter Program on Dilated UTA in the newborn;
9. Multicenter Program on the Solitary Kidney;
10. Reviewing the UTI diagnosis and antimicrobial treatment as a tailored therapeutic treatment.

#### INVESTIGATIONS

Some results of the research programs are summarized as follows:

1. UTI investigation performed over twenty months, from January 1988 to August 1989. 2,342 at risk newborn infants were enrolled. 62/95 2<sup>nd</sup>-3<sup>rd</sup> level Italian Neonatal Unit were able to ultimate the research, so UTI was diagnosed in 428 at risk newborns (248 boys, 180 girls, 248 at term, 180 preterm newly born infant). Some data and results were presented at the “10<sup>èmes</sup> Journées Françaises de Néonatalogie”, and they were published in the French Journal of Congress Proceedings *Progrès en Néonatalogie* (1990).
2. Multicenter Research Program on Polythelia and UTI in the Newborn. As a close correlation between the presence of polythelia and presence of UTA has not been demonstrated for Italian babies. This study showed a significant malformation rate and a higher incidence of diseases affecting many organs and systems in subjects having not only supernumerary mammary areola and nipple, but also an accessory glandular tissue. This research showed the importance of the aberrant mammary glandular tissue in atopic supernumerary areolas.
3. Antenatal-neonatal screening of UTA diagnosis by Ultrasounds (1990-2000). The data collected in those years were presented at national and international meetings of Neonatology and Perinatal Medicine in Italy and abroad, and continue to represent the only point of reference for an objective evaluation of the phenomenon of ultrasound screening of malformative uropathies in Italy .
4. Italian Multicenter Study on Neonatal ARF (1990-1992) confirmed the importance of asphyxia and the important role of NAG as a marker of hypoxic tubular damage.
5. Multicenter Program on Kidney function in the premature babies. These results have been published on *Archives of Disease in Childhood* and *Pediatric Nephrology*.

#### TEACHING

Some books on the progresses of neonatal nephrology, kidney development and function, neonatal UTI, kidney and urinary tract ultrasound have been published from 1996 to 2012. Since 1988, NNSG has organized 25 national meetings, 20 Ultrasound

Postgraduate Courses, 18 Postgraduate courses of Advanced Neonatal and Pediatric Nephrology and 17 International Workshops on Neonatal Nephrology. International lecturers at these workshops were were K. Allegaert (Belgium), S. Andronikou (Greece), J.V. Aranda (USA), R.L. Chevalier (VA, USA), F. De Luca (RI, USA) V. Fanos (Italy), J.B. Gouyon (France), J.P. Guignard (Switzerland), G. Montini (Italy), A. Papageorgiou (Greece), Z. Papadopoulou Columbis (Greece), M.B. Pepys (UK), H. Rodriguez Soriano (Spain), S. Salcedo (Spain), U. Simeoni (France), M. Veleminsky (Czech Republic), R. Zetterström (Sweden) and many other Italian speakers (**Fig. 1**).

#### CONCLUSIONS

We outline the activity of each of the member of the group (NNSG) in improving the cure, the care, the teaching and the research programs for sick newborn infants with renal conditions.

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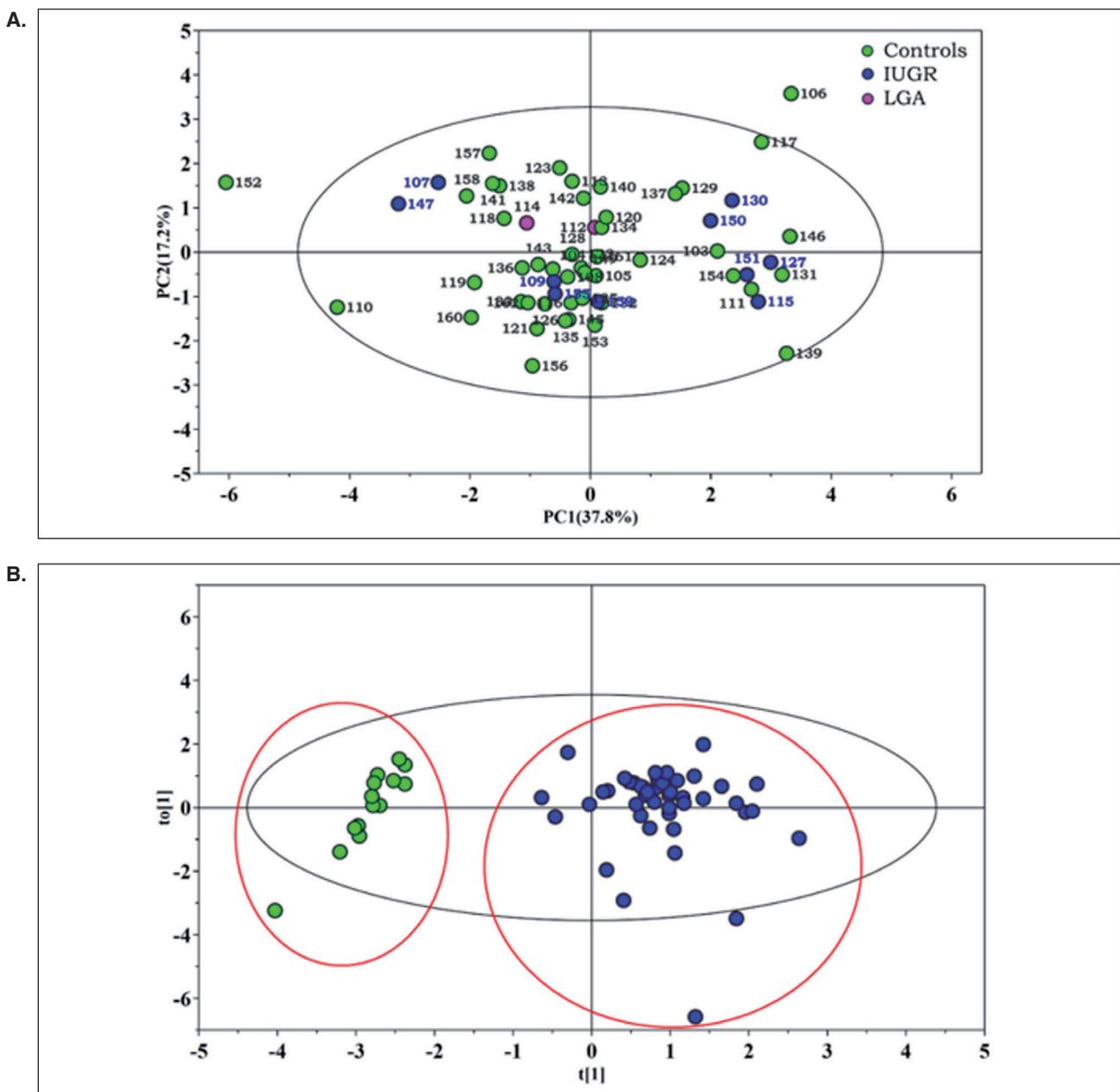


**Figure 1 (ABS 71).** Aversa 2008. The speakers of the XVI International Workshop on Neonatal Nephrology, during the annual International meeting, organized by Prof. Salvatore Vendemmia. From left to right: Prof. Luigi Cataldi (Rome, Italy), Prof. Robert L. Chevalier (Charlottesville, USA), Prof. Jack Aranda (New York, USA), Prof. Umberto Simeoni (Marseille, France), Prof. Vassilios Fanos (Cagliari, Italy).

ABS 72

<sup>3</sup>Department of Neonatology, National and Kapodistrian University of Athens, Athens, Greece**CHARACTERIZATION OF THE METABOLOME OF HUMAN MILK BY NMR METABOLOMICS**F. Cesare Marincola<sup>1</sup>, S. Corbu<sup>1</sup>, A. Dessì<sup>2</sup>, A. Noto<sup>2</sup>, T. Boutsikou<sup>3</sup>, D.D. Briana<sup>3</sup>, V. Fanos<sup>2</sup>, A. Malamitsi-Puchner<sup>3</sup><sup>1</sup>Department of Chemical and Geological Sciences, University of Cagliari, Cagliari, Italy<sup>2</sup>Neonatal Intensive Care Unit, Neonatal Pathology and Neonatal Section, AOU and University of Cagliari, Cagliari, Italy

Human milk is the first nutrient for the newborn and it is characterized by a peculiar composition that varies for each mother and it is designed to fulfill all the needs of the infant. Among its numerous components there are fat globule membranes, aqueous phase, colloidal dispersion of casein molecules, emulsion of fat globules and live cells. The quantity of each component is established during pregnancy thanks to hormonal interactions between mother and fetus and vice-versa, thus there is



**Figure 1 (ABS 72).** PCA (A) and OPLS-DA (B) scores plots of models from <sup>1</sup>H-NMR spectra of milk samples from mothers of AGA, IUGR and LGA infants.

a consistent literature concerning the difference in milk composition between mothers of term and preterm neonates. However, in the past 30 years, investigators have mostly taken into account the lipid phase, while there are fewer studies focusing on the aqueous phase. Metabolomics is a very recently developed technique that provides a complete and real-time picture of the metabolome of a human being through the analysis of biological samples such as urine, milk and blood. This technique has potentially infinite applications and today it is used as investigation tool in several research areas, including food science. The purpose of metabolomics in this field is to identify all the metabolites responsible for the features of a certain food. In the present study, we present the results of a preliminary investigation of the differences in the metabolome composition of milk from 58 mothers of term neonates (31 males and 27 females). Milk samples were collected after 3-4 days from delivery and analyzed by  $^1\text{H-NMR}$  spectroscopy. Comparison of the NMR spectral profiles by using unsupervised chemometrics techniques did not reveal significant differences in terms of infant status (**Fig. 1A**). Conversely, a class separation of samples according to maternal phenotypes was pointed out by supervised analysis (**Fig. 1B**): milk group 1 (green) completely lacked  $\alpha$ 1,2-fucosylated structures of human milk oligosaccharides (HMOs) and had a higher concentration of HMOs with ( $\alpha$ 1-3) and ( $\alpha$ 1-4)-linked fucose residue, thus indicating a  $Se^-/Le^+$  maternal phenotype; milk group 2 (blue) exhibited all fucosylated oligosaccharides and could be related to the  $Se^+/Le^+$  phenotype.

### ABS 73

#### DOWN SYNDROME ASSOCIATED TO DISORDER OF SEXUAL DIFFERENTIATION: A CASE REPORT

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#### INTRODUCTION

The disorder of sexual differentiation (DSD) is defined by a congenital discrepancy between external genitalia, gonadal and chromosomal sex. Its association to a trisomy 21 is not common. We report the case of a newborn that had both anomalies.

#### CASE REPORT

N.C. a 3,300 g newborn to a 33-year-old (gravida 1, para 1) mother at 37<sup>+5</sup> weeks gestational age was

delivered vaginally. The monitoring of the pregnancy was poor and only a single early fetal ultrasound at 12 weeks of GA was performed. At birth the baby was in very good conditions and did not need resuscitation. Physical examination revealed dysmorphic facial features characterizing Down syndrome. It also showed urogenital abnormalities with an enlarged phallus, a single urogenital sinus and a complete fusion of the labia with an empty scrotum (**Fig. 1**). The abdominal ultrasound showed a uterus and an intraperitoneal structure evoking a testicle. A karyotype was performed showing a trisomy 21 with a male genetic gender 47XY, +21. The newborn was therefore transferred to the pediatric surgery section and the external genitals were repaired to a male phenotype.



**Figure 1 (ABS 73).** Urogenital abnormalities in a newborn with Down syndrome.

#### CONCLUSIONS

Great advances have been made over recent years in the diagnosis and management of DSD. The management of these disorders requires multi-disciplinary experienced team, with the parents' and/or patients' approval, in order to make a well-judged decision. The association of this affection to a Down syndrome has rarely been reported and leads to a worse prognosis of the child.

### ABS 74

#### GC-MS METABOLOMICS IDENTIFICATION OF NEW BIOMARKERS OF CHORIOAMNIONITIS: A PILOT STUDY

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Chorioamnionitis is a bacterial infection that involves the amniotic cavity and the chorioamniotic membranes. It occurs in about 1% to 5% of all pregnancies and is associated with long-term unfavorable outcomes including sepsis, premature birth, brain injury and death. The diagnosis is based on symptoms such as maternal fever, leukocytosis, tachycardia, uterine tenderness, and preterm rupture of membranes; however, chorioamnionitis can also be subclinical, leading to poor outcomes [1, 2]. Therefore, the aim of this preliminary study was to characterize the pattern of the urine metabolites present in samples collected from mothers affected by chorioamnionitis (n = 5) compared with a control group (n = 10). To this aim, urine samples were thawed at room temperature and vortex mixed to homogenize. 150 µL of urine were transferred in a 2mL Eppendorf tube with 800 µL of urease solution, vortexed for 1', sonicated for 30'. 800 µL of cold methanol was added, vortexed for 1', centrifuged at 4°C, 14,000 rpm. 1,200 µL of supernatant were transferred in glass vials and evaporated to dryness overnight in an Eppendorf vacuum centrifuge. 30 µL of a 0.24 M solution of methoxylamine hydrochloride in pyridine is added to each vial, samples were vortex mixed 1' and left to react for 17 h at room temperature. 30 µL of MSTFA (N-Methyl-N-[trimethylsilyl]trifluoroacetamide) were added, vortex mixed 1' and left to react for 1 h at room temperature. The derivatized samples were diluted with hexane (600 µL) with tetracosane (0.01 mg/ml) as internal standard, just before GC-MS analysis. Samples were analyzed using an Agilent 5975C interfaced to the GC 7820 equipped with a DB-5ms column (J & W), injector temperature at 230°C, detector temperature at 280°C, helium carrier gas flow rate of 1 ml/min. The GC oven temperature program was 90°C initial temperature with 1 min hold time and ramping at 10°C/min to a final temperature of 270°C with 7 min hold time. 1 µL of the derivatized sample was injected in split (1:20) mode. After a solvent delay of 3 minutes, mass spectra were acquired in full scan mode using 2.28 scans/s with a mass range of 50-

700 Amu. A data matrix containing 150 metabolites was processed using the integrated web-based platform MetaboAnalyst 3.0 [3]. This tool allowed for partial least square discriminant analysis (PLS-DA) and its associated variables of importance (VIP) score determination. The PLS-DA model resulted statistically significant  $R^2 = 0.87357$ ,  $Q^2 = 0.87357$ ,  $p < 0.05$ . The differences found were related to compounds mainly belonging to the TCA cycle (citric acid, succinic acid, and malic acid), amino acids (glycine, and lysine). Metabolomics fingerprinting of urine enables the prediction of pregnancy-related disorders and the development of new diagnostics strategies.

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## ABS 75

### POLYCYSTIC OVARIAN SYNDROME, METABOLIC SYNDROME AND DYSBIOSIS OF GUT MICROBIOTA

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## INTRODUCTION

Polycystic ovarian syndrome (PCOS) is the most common cause of menstrual irregularity and anovulatory infertility and affects between 4% and 8% of reproductive-aged women. It is biochemically characterized by disordered gonadotropin secretion (Luteinizing hormone [LH]; Follicle stimulating hormone [FSH]) from the anterior pituitary. Clinically, this condition is characterized by free androgen levels, chronic low grade inflammation, and insulin resistance. Insulin resistance and inflammation are responsible for the increased risk of metabolic syndrome, cardiovascular diseases and

diabetes in this population. Most women suffering from PCOS are obese or overweight.

#### A NEW THEORY ABOUT POLYCYSTIC OVARIAN SYNDROME

We propose a new theory about the development of PCOS: the dysbiosis of gut microbiota (DOGMA). The DOGMA can result in the activation of the immune system of the host, triggering a chronic inflammatory response that impairs insulin receptor function and induces a state of insulin resistance. The resulting hyperinsulinemia interferes with follicular development (excess of androgen production by the ovarian theca cells).

#### THE PATHOPHYSIOLOGICAL KEY OF DOGMA

A diet high in saturated fats and refined sugars can favor the growth of “bad” Gram-negative bacteria reducing the growth of beneficial “good” bacteria (*B. lactis* BSO1, *L. acidophilus* LAO2, *L. paracasei* LPC00, *L. salivarius* LS03, *L. plantarum* LP02, *L. rhamnosus* LR06). The cell wall of Gram-negative bacteria contains a powerful immunomodulator called lipopolisaccharide (LPS). LPS can cause the activation of the innate immune system. Secondly, the diet high in saturated fats and sugar and low in fibers leads to an increase of the gut mucosal permeability, facilitating the transfer of LPS from the gut lumen into the circulatory system. This state of “metabolic endotoxemia” causes a chronic activation of hepatic and tissue macrophages and alters insulin receptor function and results in insulin-resistance. Hyperinsulinemia causes an increased production of androgens in the ovaries and slows down the normal ovulatory process. Follicle development stops and small-to-medium size antral follicles (2-10 mm) do not develop into mature “ovulatory” follicles.

#### CONCLUSIONS

The gut microbiota and lifestyle play an important role in the prevention of metabolic syndrome, PCOS and other metabolic diseases.

#### ABS 76

#### MATERNAL OBESITY: INFLAMMATORY AND ANTIOXIDANT MARKERS IN SALIVA

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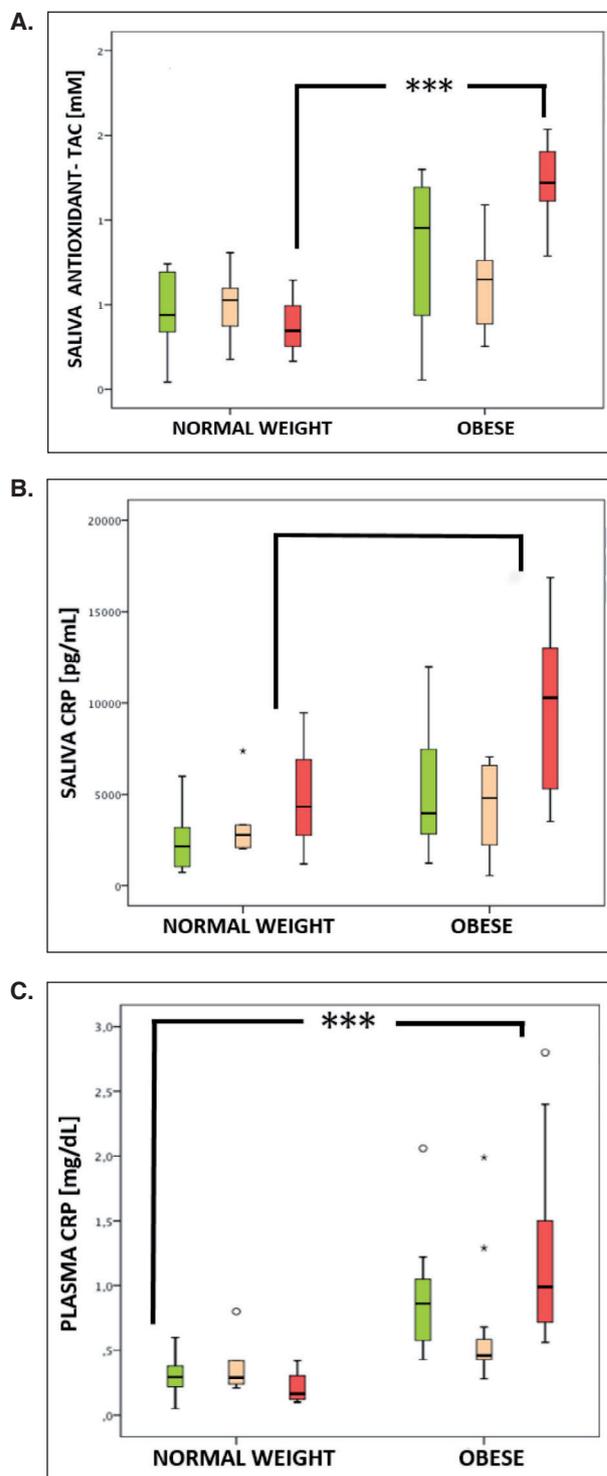
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#### INTRODUCTION

Maternal Obesity (MO) is due to calories imbalance and incorrect dietary intake. Obesity results in chronic mild inflammation and oxidative stress. Moreover, MO exerts its influence on perinatal and



**Figure 1 (ABS 76).** Saliva total antioxidant capacity (A), salivary C-reactive protein (B) and plasmatic C-reactive protein (C) in normal weight (NW) and obese women.

T-Test: \*\*\*  $p < 0.001$  vs NW.

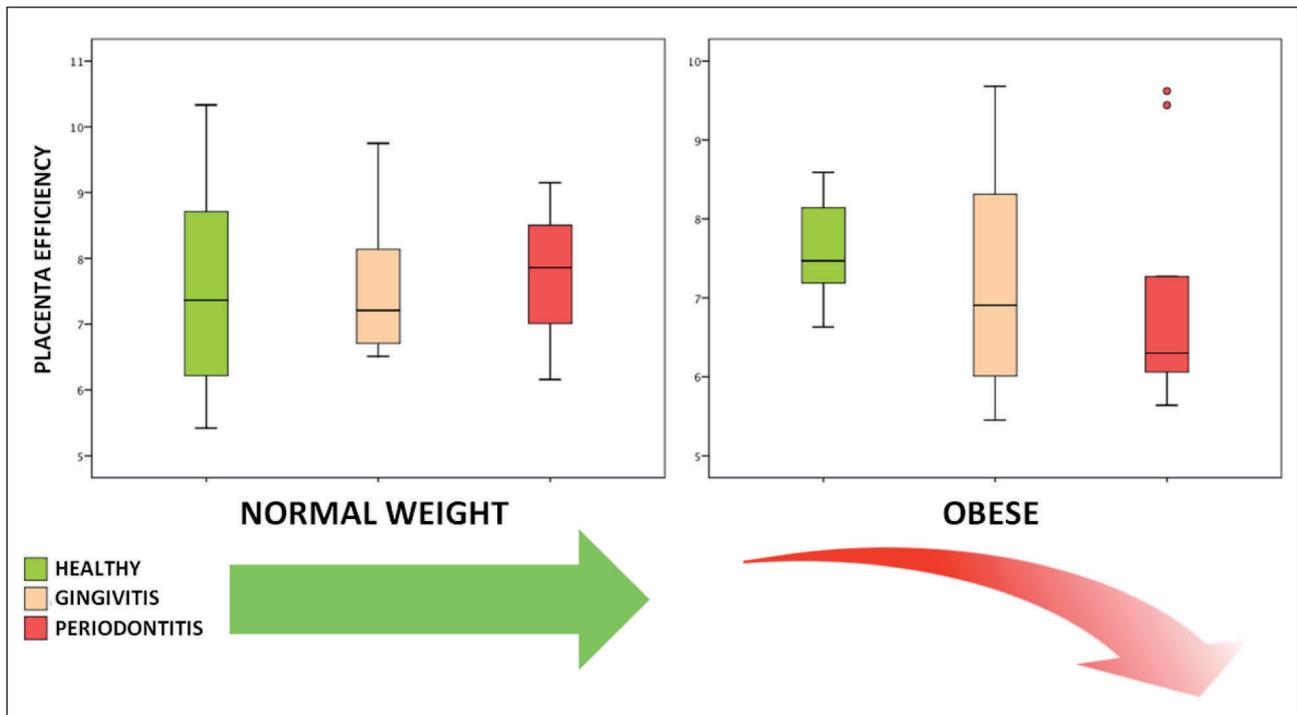


Figure 2 (ABS 76) Placental efficiency (fetal/placental weight).

childhood outcomes, related to maternal excessive Body Mass Index (BMI) and/or Gestational Weight Gain (GWG). Few studies investigated saliva biomarkers in pregnant women. Here we analyzed C-reactive protein (CRP) and total antioxidant capacity (TAC) in the saliva of pregnant women with pre-pregnancy obesity, extending our preliminary data [1].

#### METHODS

62 singleton-pregnant women (27 normal weight [NW] – BMI 18-24.9; 35 obese [OB] – BMI  $\geq$  30) were studied at 3<sup>rd</sup> trimester. Occurrence of periodontal disease – gingivitis or periodontitis – was assessed by an oral clinical exam [1]. Unstimulated saliva was analyzed to detect CRP (ELISA) and TAC (AntiOxidant Assay); CRP was also measured in plasma with an immunoturbidimetric assay. Clinical and molecular data were analyzed with T-test and Pearson Correlation ( $p < 0.05$ ).

#### RESULTS

Saliva TAC, saliva and plasma CRP were significantly higher in obese compared to normal weight women ( $p < 0.001$ ) and they correlated with each other ( $p < 0.001$ ;  $r > 0.60$ ) and with maternal pre-pregnancy BMI ( $p < 0.001$ ;  $r > 0.51$ ). Frequency of periodontal disease was significantly higher in OB (80%) compared to NW women (52%) [ $\chi^2 = 4.31$ ,  $\phi = 0.30$ ,  $p = 0.04$ ]. Periodontal disease in NW did not enhance molecular data, while

their levels were higher in OB with periodontitis (saliva TAC and plasma CRP:  $p = 0.001$ ) (Fig. 1). Placental efficiency (fetal/placental weight) showed a downward trend only in OB depending on periodontal disease severity (Fig. 2).

#### CONCLUSIONS

Mild inflammation is reported in tissues of OB subjects, but little is known about OB markers in saliva, an effective non-invasive diagnostic tool. The increase in CRP in OB plasma, as a marker of systemic inflammation, was confirmed in saliva. Higher saliva TAC suggests the induction of systemic antioxidant response, detectable in obese subjects. The higher periodontal disease frequency in OB might enhance CRP and compensatory TAC defenses, driven by both obesity and periodontal disease. These effects may also influence placenta efficiency.

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#### ABS 77

#### MONITORING AND SUPPORTING MATERNAL COMPETENCE IN PRETERM CONDITIONS: A LONGITUDINAL STUDY USING Q-SORT

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## INTRODUCTION

This contribution is a longitudinal study designed to explore parenting skills of mothers of preterm infants, conducted with a specific self-report tool, a Q-sort about maternal skills such as caregiving, scaffolding, cognitive and emotional coping. The possible modifications of these skills were monitored since the admission of the child to Neonatal Intensive Care Unit (NICU) (T1) until after the discharge (T2), since this could be a stressful condition for the infant and the mother and could affect the mother's perception of being a proper parent. Homecoming could generate apprehension over the ability to take care of the child and recognizing the evolutionary features of difficulties and resources that could degenerate into impairments of parenting capacity. This could therefore become a risk factor for the proper development of the infant. These considerations highlight the importance of monitoring and supporting maternal competences from the NICU admission of the neonate, in order to adequately prepare the mother for discharge and homecoming. The Q-sort used in the present study has the potential to be used in this scenario, not only as an assessment tool but also as a supporting-transformative intervention.

## AIMS

1. To verify possible differences among the scores obtained in different factors of maternal competence at T1 and T2.
2. To verify, for each considered time-point (T1 and T2), differences among scores obtained by the mothers in different factors of maternal competence, depending on the following variables: a) severity of preterm birth and b) socio-cultural level of the mothers.

## METHODS

The participants of the study were 36 mothers of preterm neonates admitted to the NICU of the University of Cagliari, including 4 ELBW (GA < 28 weeks), 14 VLBW (GA 32-28 weeks) and 18 LBW (GA > 32 weeks). The socio-cultural level was medium-low. The tool used to measure the maternal competence was a specific Q-sort, validated and in

the process of being standardized. The tool was used at two different times: T1, admission in the NICU in a non-critical phase or emergency; T2, 10 days after discharge. Data were analyzed with descriptive and parametric statistics: in particular, the paired sample-t test was used to verify differences in scores obtained by the mothers in the different maternal competence factors at the different time points (T1 and T2). Furthermore, a MANOVA for continue variables was performed, 3 (levels of severity of preterm birth) x 3 (socio-cultural levels) to verify scores variation in the different factors, for each of the considered time points, depending on the indicated independent variables (birth and socio-cultural level).

## RESULTS

Results concerning the differences among the scores of maternal competence in the two times (T1 and T2) highlighted statistically significant differences in: 'emotional coping' ( $t = -3.84$ ;  $p = .001$ ), that was increased at T2; 'cognitive coping' ( $t = 2.31$ ;  $p = .02$ ), that decreased at T2; 'relational scaffolding' ( $t = 2.76$ ;  $p = .009$ ), that increased at T2; 'compliance' ( $t = 3$ ;  $p = .005$ ), that decreased at T2. At T2, almost all factors tended to be lower than at T1, but this trend was not statistically significant. With reference to the MANOVA data, the significant differences highlighted at T1, adjusting for the severity of the preterm birth, are present only in the 'cognitive coping' ( $F = 5.6$ ,  $df = 2$ ,  $p = .008$ ), whereby this factor of maternal competence is less present in mothers of VLBW children. Taking into account the socio-cultural variable, there were significant differences in 'cognitive coping' ( $F = 4.2$ ,  $df = 2$ ,  $p = 0.2$ ), which is less present in mothers with a low socio-cultural level, and 'emotional scaffolding' ( $F = 9.1$ ,  $df = 2$ ,  $p = .001$ ), that is less present in mothers with high socio-cultural level. Taking into consideration, the crossed effect of the 2 variables at T1, significant differences emerged only in 'emotional scaffolding' ( $F = 4.5$ ,  $df = 2$ ,  $p = .02$ ); the highest scores were obtained by mothers of VLBW infants with medium socio-cultural level, while the lowest scores were obtained by mothers of VLBW with high socio-cultural level. Data of MANOVA at T2 did not show any significant difference associated with severity of the birth nor with socio-cultural level.

## CONCLUSIONS

Data obtained with the Q-sort showed a tendency of the mothers of preterm neonates, regardless of the severity of this birth, to improve at homecoming in certain areas only, mainly in the management of the self-relationship and (self emotional regulation)

and the relationship between the neonate and the family environment (rational scaffolding). On the contrary, it seems that homecoming affects the self perception of the mothers as adequately responsive to the needs of their infants, as capable to find their developmental resources and their difficulties. The study thus highlights the potentials of the Q-sort as a tool to monitor and support maternal competence, starting during the admission to NICU, and to facilitate the passage at discharge, moderating the impact that homecoming may have on the self representation as a competent mother and promoting the strengthening in a Positive Development pathway.

### ABS 78

#### APPENDICITIS IN NEWBORN: TWO CASE REPORTS

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#### BACKGROUND

Acute appendicitis is rare in newborns (incidence of 0.02-0.04%) and results from infective/inflammatory and obstructive injury.

#### CASE REPORTS

M. was born at 33 weeks of GA by cesarean section. At 7 days of life fever, abdominal distension, pain, tenderness and vomit occurred. Blood tests showed systemic infection, therefore we decided to start therapy with netilmicin and stop feeding. Abdominal and chest X-ray revealed free air in the abdomen. Exploratory laparotomy confirmed the suspect of acute appendicitis with peritonitis. Appendectomy without intestinal resection was performed.

C. was born at 35 weeks of GA by spontaneous delivery and he was affected by Down syndrome and Fallot Tetralogy. At 6 days of life he showed abdominal distension and biliary gastric retention. Antibiotic therapy with ampicillin, netilmicin and methronidazole was started. Abdominal X-ray revealed free air under the diaphragm. The exploratory laparotomy suggested the diagnosis of acute appendicitis and peritonitis. Appendectomy

without intestinal resection was performed. The post-operative course was complicated by sepsis.

#### CONCLUSIONS

Acute appendicitis in newborns is rare because of liquid feeding, appendix shape and narrow lumen. It is related to a large number of complications and high mortality. Clinic presentation includes fever, irritability, RDS, abdominal distension and vomit. Differential diagnosis consists of NEC and isolated intestinal perforation (IIP) with differences in etiology and GA of presentation. Acute appendicitis can be associated with other diseases, like Hirschsprung disease, cystic fibrosis and meconium plug syndrome. These cases highlight that abdominal pain and fever, rare in newborn, could be a sign of serious surgical disease.

### ABS 79

#### THE ROLE OF PEDIATRICIANS IN CORONARY ARTERY DISEASE PREVENTION: FAMILY HISTORY AS A POWERFUL SCREENING TOOL TO DETECT HYPERCHOLESTEROLEMIC CHILDREN

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#### BACKGROUND

Hypercholesterolemia is one of the main modifiable risk factors for atherosclerosis and coronary-artery disease (CAD). CAD is defined premature (pCAD) when it occurs before 55 years in males and before 65 years in females. Since atherosclerosis begins in childhood, lipid screening is an issue of utmost importance. Universal lipid screening is at present not advisable for cost-effectiveness reasons. A cascade screening based on the detection of an index case seems to be the best strategy, and the collection of family history is a powerful tool to detect high risk pCAD families.

#### METHODS

In a 2-month period (ongoing study), pCAD-oriented family history was collected for every child admitted to our Pediatric Department, investigating the presence of lipid disorders and pCAD in first and second degree relatives. The aim of this study was to identify high-risk pCAD families.

#### RESULTS

211 children were admitted to our Department. pCAD-oriented family history was collected for

158 children (53 were not included for emergency referral to other structures/non-Italian-speaking parents). 0/158 children (0%) had ever undergone lipid screening or had CAD-oriented family history collected by their family doctor. 4/158 children (2.5%) had a positive pCAD family history. Lipid screening was performed for these children testing total, LDL and HDL cholesterol and triglycerides. 4/4 children (100%) had hypercholesterolemia (LDL cholesterol above 95<sup>th</sup> centile for age and/or total cholesterol above 95<sup>th</sup> centile for age) and were referred to our Lipid Centers for further analysis and follow up.

#### CONCLUSIONS

Collecting pCAD-oriented family history is a powerful and inexpensive tool to detect families at high risk for pCAD and therefore to detect children with hypercholesterolemia. pCAD oriented family history is often not collected by family doctors nor by hospital's ones, showing a lack of awareness of the problem even among doctors. In this context, pediatricians should become more aware of pCAD risk and start screening and preventive actions in all their patients.

#### ABS 80

#### METABOLOMICS STUDY ON NEC OCCURRENCE BY GC-MS

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#### INTRODUCTION

Necrotizing enterocolitis (NEC) is one of the most devastating diseases in the preterm neonate [1]. The incidence varies depending on the series: between 1% and 8% in some Western countries, up to 20% in other South Asian case studies. There are several reasons that make the intestines of premature neonates susceptible to develop an inflammatory response: 1) an immature mucosal barrier, 2) an immune system more responsive to pro-inflammatory stimuli than anti-inflammatory, 3) an imbalance in the intestinal bacterial colonization,

4) the moment of transition from innate immunity to the adaptive, that seems to be the major risk for preterm infants. Metabolomics, the latest omics technology may help in the identification of novel biomarkers to formulate an early diagnosis and anticipate the outcome on the basis of the metabolic profile [2]. Therefore, the aim of this study was to test the hypothesis that specific biomarkers could be found in urine samples of preterm neonates that developed NEC.

#### METHODS

This study was carried out on urine samples of 14 neonates, admitted to the Neonatal Intensive Care Unit of "Hôpital de la Croix-Rousse (HCR) – Hospices Civils de Lyon" (Lyon, France). Each case of NEC was matched with a healthy control. The cases and controls were matched by sex, gestational age ( $\pm$  1 week), delivery type, and presence of intrauterine growth retardation. Study population was divided into two groups: Healthy infants (n = 7) and NEC infants (n = 7). Urine samples from neonates were collected at different time points from birth over an average period of two months of life. Samples were thawed at room temperature and vortex mixed to homogenize. 150  $\mu$ L of urine were transferred in glass vials and evaporated to dryness overnight. 30  $\mu$ L of a 0.24 M solution of methoxylamine hydrochloride in pyridine was added to each vial, samples were vortex mixed and left to react for 17 h at room temperature. Then 30  $\mu$ L of MSTFA (N-Methyl-N-[trimethylsilyl]trifluoroacetamide) were added and left to react for 1 h at room temperature. The derivatized samples were diluted with hexane (600  $\mu$ L) and analyzed on an Agilent 5975C interfaced to the GC 7820. All chromatograms were analysed with the free software AMDIS (automated mass spectral deconvolution and identification system) [3], and a data matrix containing 176 metabolites was obtained. Multivariate model based on Partial Least Square-Discriminant Analysis (PLS-DA) was performed in Simca 13.0 (Umetrics, Umeå, Sweden) and used to overview the data variance structure in supervised mode.

#### RESULTS

PLS-DA model showed separation between the two groups ( $R^2X = 0.422$ ,  $R^2Y = 0.552$ ,  $Q^2 = 0.282$ ) with a statistical significance ( $p = 0.003$ ). Among the metabolites, gluconic acid, sedoheptulose, taurine, quinolinic acid, cysteine, stearic acid, oxalic acid, and ethanamine were up regulated in the NEC group while creatine, galactose, sucrose, lactose and few unknown molecules were down regulated.

## CONCLUSIONS

GC-MS-based metabolomics analysis of the urinary metabolome seems to have the requested sensibility and specificity to get more insights on the NEC condition and to investigate about the inner mechanism of its activation.

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## ABS 81

### A CASE REPORT OF INTESTINAL INTUSSUSCEPTION

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#### INTRODUCTION

Intussusception is one of the most frequent causes of acute abdomen in infancy. It affects more frequently patients from 2 months to 2 years old. It is characterized by an intestinal intussusception in the immediately following section.

#### CASE REPORT

A 9-month-old baby girl presented to our facility; she had undergone surgery, approximately two months before, due to a rectal prolapse with Fischer's cerclage. Another team of surgeons had performed the surgery. The little patient was brought to our hospital since she was crying and she was vomiting and showing abdominal pain and constipation. The clinical conditions were not great; she had dry skin, coated tongue, acetone odor of breath, she was underweight and malnourished. Everything seemed to suggest a hypovolemic shock. An abdominal physical examination shows bulbous abdomen, with diffuse sensitivity to palpation and increased tympany and increased peristalsis. At rectal exploration a rectal prolapse of about 2 cm was immediately visible. Blood tests showed the presence of low levels of hemoglobin (3 g) and hypokalemia, hyponatremia and leukocytosis. We proceeded with an abdominal ultrasound study, which was quite difficult to perform due to the poor collaboration of

the patient and an accentuated intestinal bloating. The images showed anyway evidence of a mass at the level of the right hip and a neoformation like pseudo-kidney with thickened walls, hyperechoic in the middle. After some effort it was possible to get the IV access and immediately start a resuscitation, infusion therapy to rehydrate the little patient and allow an explorative laparotomy. Exploration of the abdominal cavity shows the presence of jejunal and ileal loops dilated and the last ileal loop seems to be engaged to the descending colon, and the latter turns by the transverse colon, forming a three-cylinder intussusception with advanced signs of vascular pain. Carefully, we tried to reduce the intussusception, but unfortunately it was not possible to reduce the whole intussusception given the poor clinical condition of the patient and the extended vascular disorders of the intestinal tract affected. We therefore decided to opt for a bowel resection. We resected the last section of the ileum and the descending colon with the creation of a transverse ileo-colon anastomosis. In the post-operative period the patient underwent a resuscitation infusional therapy and a blood transfusion. She was discharged in good clinical condition after 15 day without significant post-operative complications.

#### DISCUSSION

The types of possible invagination are usually 4: ileum-ileal; ileocolic with involvement of the ileocecal valve; ileocolic without involvement of the ileocecal valve; colo-colic. It may be idiopathic or due to the presence of intestinal duplication, Meckel's diverticulum, tumors, intestinal parasites, bacterial or viral gastrointestinal infections, in particular rotavirus and adenovirus. In most cases, the classic symptoms of onset are the following: sudden cramping pain, palpable abdominal mass, stools like currant jelly. If the diagnosis appears precocious, the patient's conditions are not yet critical, and there is no sign of vascular changes, conservative treatment of intussusception can be opted for, attempting to reduce it with enemas containing low pressure air, saline or barium. If the clinical conditions appear precarious or the intussusception is not resolved, then it is necessary to proceed with an exploratory laparotomy in order to reduce the intussusception or if not possible, to perform a resection of the intestinal tract affected.

## ABS 82

### DETECTION OF FAMILIES AT HIGH RISK FOR CARDIOVASCULAR DISEASE: THE PEDIATRIC POINT OF VIEW

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## BACKGROUND

Lipid screening in childhood is an issue of utmost importance for cardiovascular disease prevention, since hypercholesterolemia is one of the main modifiable risk factors for atherosclerosis and cardiovascular disease. The aim of this study was to find an effective screening strategy to detect families at high risk for cardiovascular disease.

## METHODS

A questionnaire investigating the knowledge of lipid and cardiovascular disease issues was distributed to the parents of the newborns at Neonatology of Piacenza Hospital over a 6-month period. Eligibility criteria were: term birth, Apgar score above 7 at 5 minutes, Italian-speaking parents, no neonatal abnormalities. 600 newborns were assessed for eligibility, 290 did not meet eligibility criteria. 244 completed the study (Tab. 1).

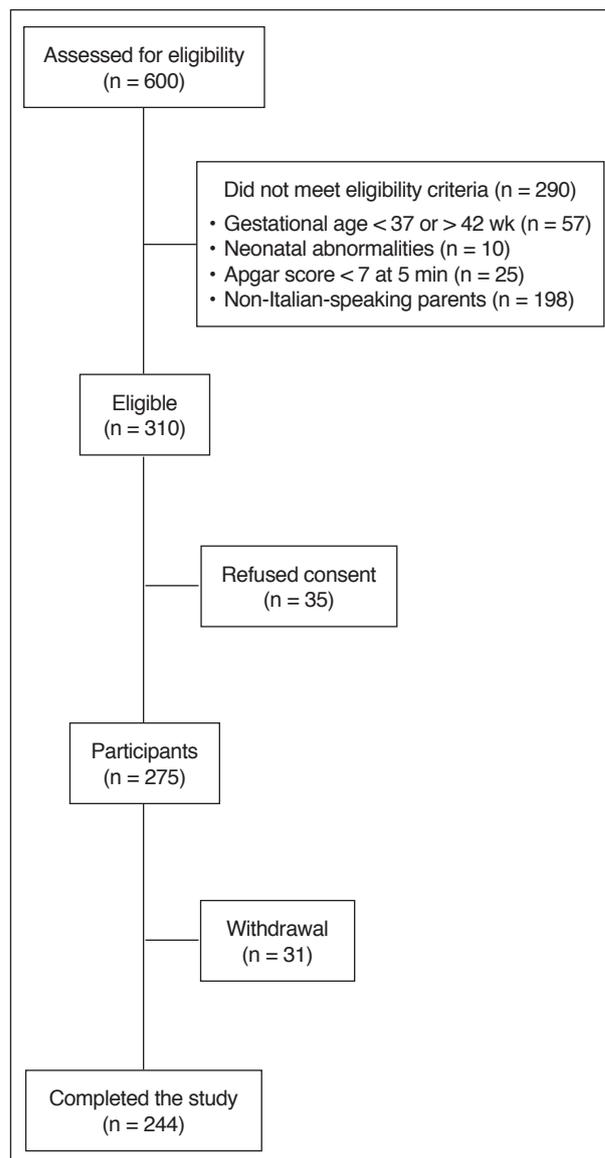
## RESULTS

244 questionnaires have been collected so far (ongoing study). 61 couples of parents (25%) knew their own lipid profile. 61 couples of parents (25%) knew the correct normal values of total cholesterol. 88 couples of parents (36%) had first or second degree relatives with lipid disorders. 73 couples of parents (29%) had first or second degree relatives with premature cardiovascular disease. Considering the couples with positive family history for premature cardiovascular disease, only 33 out of 88 (37%) were aware of their own lipid profile. Considering the couples with positive family history for both premature cardiovascular disease and lipid disorders, 21 out of 35 (60%) had never had blood lipid screening done.

## CONCLUSIONS

Collecting a problem-tailored and accurate family history seems to be a good strategy to detect high-risk families, but the parents' poor awareness of the problem puts some limits to it. These preliminary data suggest that the percentage of adults with a positive family history for cardiovascular disease and/or lipid disorders and who are unaware of their own lipid profile is higher than expected. This implies that the number of undetected pediatric patients at high cardiovascular risk might also be higher than expected. In this context, the identification of an effective and reliable screening strategy for cardiovascular disease in childhood is highly advisable.

**Table 1 (ABS 82).** Flow diagram of subject progress throughout the study.



## ABS 83

### PLACENTAL CALCIFICATIONS: OCCURRENCE AND CLINICAL RELEVANCE

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## INTRODUCTION

The human placenta probably represents the “flight recorder” of gestation and, when accurately studied and interpreted, it may be the source of a huge amount of data for neonatologists for a better interpretation of

the health status of the newborn. Calcium deposits represent one of the most intriguing features that may be encountered in the analysis of placenta. Placenta calcifications have been for a long time considered a sign of placenta ageing. Placenta calcium deposits from the 37<sup>th</sup> week of gestation have been considered physiological. In recent years, due to the progress of 3D sonar graphics, placenta calcifications have been identified before birth, even in early pregnancy, suggesting the hypothesis that a precocious placenta ageing might be associated with intrauterine growth restriction or, in general, with adverse maternal and fetal outcome [1, 2]. The aim of this study was to analyze the presence of calcifications in human placenta at different gestational ages.

#### METHODS

In this retrospective study, 20 consecutive placentas were selected from the files of the department of pathology of the University Hospital of Cagliari. All placentas were selected due to the presence of placental calcifications (**Fig. 1** and **Fig. 2**). Women were classified into three groups: group 1, the early

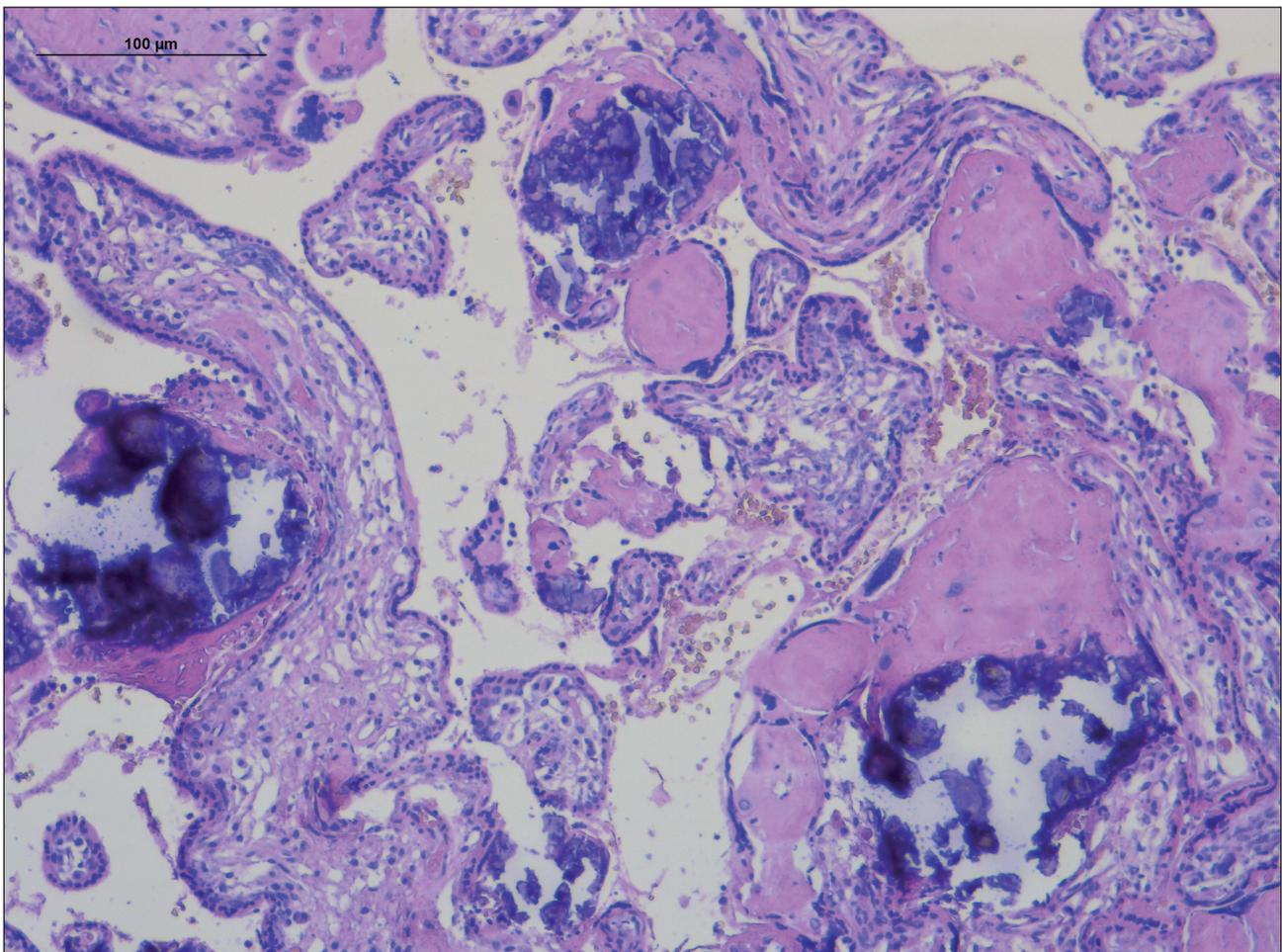
preterm group (< 32 w); group 2, the late preterm group (32-36 w); group 3, the term group (> 36 w).

#### RESULTS

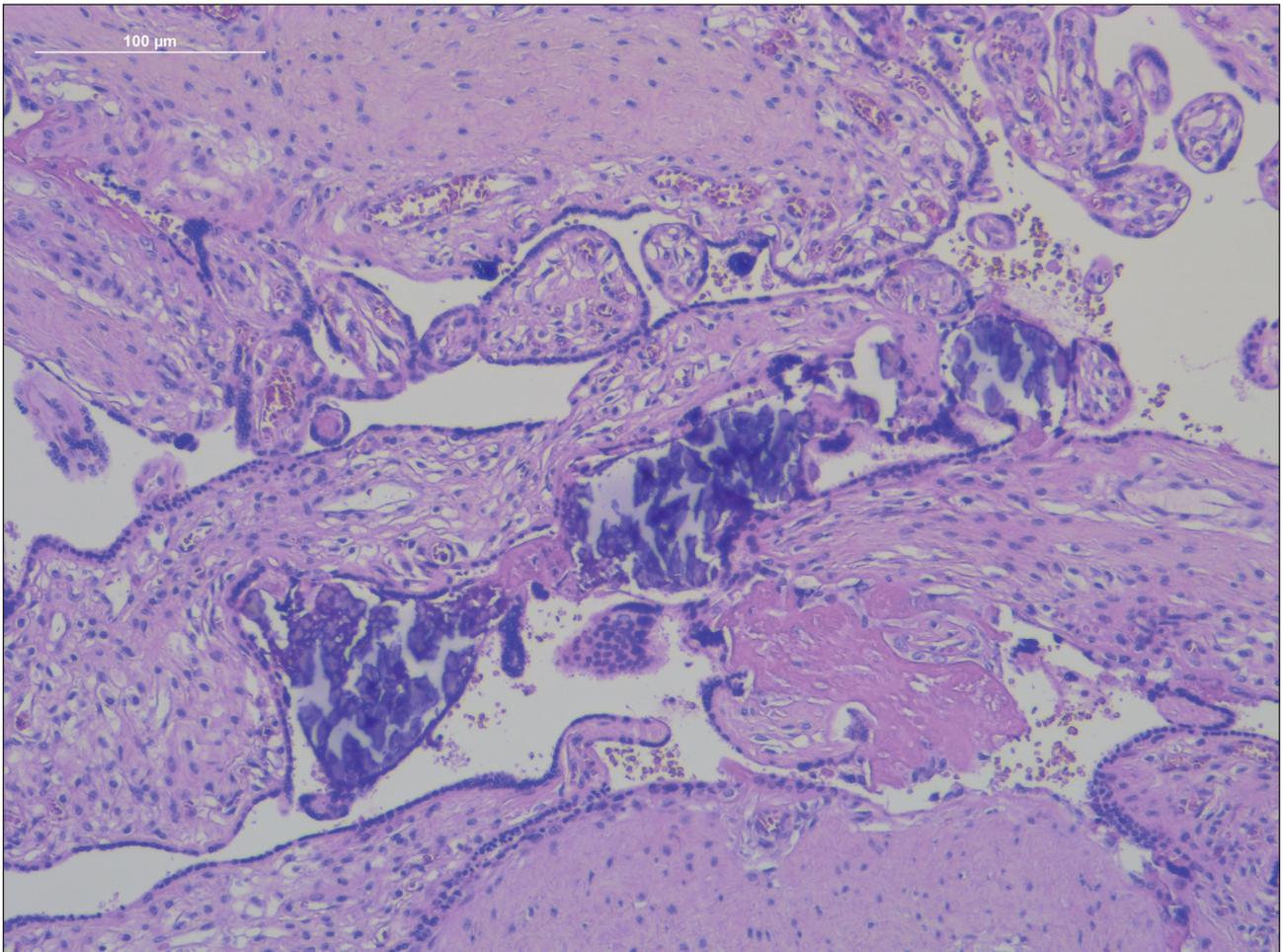
In all women of group 1, the presence of placental calcifications was constantly associated with other placental pathological changes, including hemorrhage and multiple infarcts. Moreover, placental classifications in early and very early preterms were frequently associated with adverse pregnancy outcome and adverse fetal outcome, including low birth weight, low Apgar score and perinatal death. In women of group 1 and 3, the presence of placental classification was occasionally associated with a precocious aging of placenta, in the absence of any sign of adverse pregnancy outcome. In group 2, placental calcifications were associated with adverse pregnancy outcome only in a minority of cases, always in association with high-risk pregnancy.

#### CONCLUSIONS

Our data show that placental calcifications have a completely different clinical significance at different



**Figure 1 (ABS 83).** Placental calcifications at 22 weeks of gestation



**Figure 2 (ABS 83).** Placental calcifications at 31 weeks of gestation

gestational ages and in different clinical settings. In at term pregnancy (> 36 weeks of gestation), they should be simply considered a sign of aging [1]. Moreover, no significant clinical significance should be assigned to placental calcifications in late preterm infants (> 32 weeks of gestation) in the absence of high-risk pregnancy factors. On the contrary, their finding in high-risk pregnant women affected by hypertension, placenta previa, diabetes or severe anemia [3], should be considered a predictor of adverse outcome.

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#### ABS 84

#### METABOLOMICS DIFFERENCES IN PATIENTS WITH BICUSPID AORTIC VALVE WITH AND WITHOUT ASCENDING AORTA DILATATION: A COMPARATIVE PROSPECTIVE STUDY

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#### BACKGROUND

Bicuspid aortic valve (BAV) is the most common congenital heart disease, which natural history is characterized by the incidence of clinically relevant valvular and vascular complications regarding the

thoracic aorta (dilation, aneurysm, dissection). BAV may be heritable, with an autosomal dominant pattern of inheritance with reduced penetrance; some data suggest that BAV and thoracic aorta aneurysm are independent manifestations of a single gene defect. Metabolomics analysis is able to detect the medium-low molecular weight analytes (up to 1,000 Da), including amino acids, oligopeptides, sugars, steroids, bile acids, simple fatty acids and intermediate compounds of many biochemical pathways. Preliminary data indicate that, in preterm infants, a “metabolic signature” of the PDA can be identified through the use of metabolomics analysis on urine samples collected shortly after birth.

#### AIM

The aim of this protocol is to collect after informed consent human urine samples from pediatric and adult patients, to be destined to metabolomics analysis <sup>1</sup>H-NMR-based in order to identify some metabolites as “metabolic signature” of two different group of patients: patients with BAV and patients with BAV associated to dilatation of ascending aorta.

#### METHODS

A total of 150 patients will be evaluated: 50 “control subjects” without cardiovascular diseases, 50 patients with only a bicuspid aortic valve, 50 patients with a BAV associated with ascending aorta aneurysm. The “control subjects” are patients that after the echocardiographic examination can be considered free from cardiovascular anomalies.

#### EXPECTED RESULTS

Until now we recruited a total of 75 patients in 10 months: 30 patients with BAV, 30 patients with BAV associated to dilatation of ascending aorta and 15 “control subjects”. The mean age is 20 years old for each group. The prevalence of BAV and its susceptibility to aortic complications during the whole life result into the need of strict clinical follow-up and appropriate therapies to be addressed according to guidelines specifically designed for these patients. In this contest, we hope that this metabolomics analysis could become helpful as an indicator tool to assess the presence of bicuspid aortic valve, and as an early predictive tool of ascending aorta aneurysm in patients with bicuspid aortic valve.

#### ABS 85

### THE GREIG CEPHALOPOLYSYNDACTYLY SYNDROME: A SUSPECTED CASE REPORT

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#### INTRODUCTION

The Greig cephalopolysyndactyly syndrome (GCPS) is a rare, multiple congenital anomaly autosomal dominant syndrome characterized by the clinical triad of polysyndactyly, macrocephaly and hypertelorism. The incidence is 1-9/1,000,000. The syndrome is determined by loss of function mutations in the GLI3 transcription factor gene. The treatment of the form is symptomatic with plastic or orthopedic surgery. The prognosis is excellent. We report a suspected case of this rare disorder.

#### CASE REPORT

A one-day-old baby girl, born of non-consanguineous Sardinian marriage, was admitted with complaint of bilateral hands and feet polysyndactyly. She was born at full term with Apgar Score 8 (1') and 9 (5') by normal vaginal delivery with an uneventful neonatal course. Birth weight was 3.960 kg (92<sup>nd</sup> percentile) and birth length was 53.0 cm (96<sup>th</sup> percentile). There was no family history of polysyndactyly. On examination, the child was found to be dysmorphic: she had broad forehead with frontal bossing, broad nasal root, ocular hypertelorism, bilateral blepharophimosis, low-set ears, macrocephaly (head circumference 37.1 cm) which was at 99<sup>th</sup> percentile for age, hoarse cry. Blood tests, urinalysis, echocardiography and ultrasound of abdomen were normal. Ultrasound of cranium detected frontoparietal prenatal cysts and subependymal cysts. ABR and otolaryngologist visit were normal, while fibroscopy detected posterior laryngomalacia during crying. Column X-ray was normal. Left and right hands X-ray showed doubling of the distal phalanx of first finger and total membranous syndactyly of the third and fourth finger. Left foot X-ray showed doubling of distal phalanx of the first and second finger. Right foot X-ray showed preaxial polydactyly with doubling of the distal phalanx of first finger. Consulting orthopedic suggested new hands and feet X-ray after 6 months, before planning corrective surgery when the child will be about 1 years old. Mutated gene research is currently in progress.

#### CONCLUSIONS

GCPS diagnosis is clinical and molecular. A suspect of diagnosis of GCPS must arise visiting

patients with the classic triad of polysyndactyly, hypertelorism and macrocephaly. Patients with a phenotype consistent with GCPS and GLI3 mutation may be diagnosed definitively with GCPS. In addition, patients with GCPS phenotype who have in the family a diagnosed member in a pattern autosomal dominant inheritance may be diagnosed definitively as well.

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#### ABS 86

### A NEW APPROACH TO THE DIAGNOSIS OF CONGENITAL TOXOPLASMOSIS IN NEWBORNS

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#### INTRODUCTION

Diagnosis of congenital toxoplasmosis at birth, even with the most sensitive serological test, is only possible for 70-80% of newborns whose mothers were treated during pregnancy. They must be followed until 1 year of age; furthermore, treated infants could be serologically negative if they are under treatment. In order to improve and shorten diagnosis we set up a serological and immunological diagnostic protocol.

#### METHODS

From January to December 2014, 132 newborns born from mothers with certain (seroconversion) or suspected (not high avidity) Toxoplasmosis in pregnancy and treated with spiramycin were serologically and immunologically tested. All the mother-newborn paired samples were tested at birth with LIAISON® Toxo IgG/IgM CLIA, ELISAToxoIgA (Diasorin Saluggia Italy) ISAGA Toxo IgM (Biomérieux Marcy l'Etoile France), Interferon Gamma Release Assay (IGRA – Quantiferon – ELISA Cellestis Australia) and ImmunoblotToxo IgG/IgM. A 1mL blood sample in Lithium Heparine to perform Interferon Gamma Release Assay (IGRA) with Toxoplasma antigen kindly provided by DiaSorin was also required. The

follow-up was continued monthly for the first three months and then every two months until one year of age.

#### RESULTS

At the end of one year follow up, 10 newborns were found congenitally infected. IGRA test was performed in 74 newborns and in 9 out of the ten congenitally infected babies. Only 4 of the congenitally infected newborns were positive at birth for IgM and/or IgA antibodies, 9 were positive in WB and all of them were positive in IGRA test during the first three months of life. No congenitally infected baby resulted negative at IGRA test when serologically negative under treatment. In two cases diagnosis was made because of a positive PCR on amniotic fluid and confirmed by IGRA in the first three months.

#### CONCLUSIONS

Following this diagnostic protocol, it was possible to make the diagnosis of congenital toxoplasmosis in almost all the infected newborns during the first three months of life. All the congenitally infected babies were immediately treated and clinically followed. This protocol avoids mother anxiety and unnecessary therapy in the newborn.

#### ABS 87

### A RARE CASE OF NEONATAL INTUSSUSCEPTION

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#### INTRODUCTION

Intussusceptions occurring in neonatal period are very rare, accounting for only 3% of all the cases of neonatal intestinal obstruction and 0.3% of all the cases of childhood intussusceptions [1-5]. Clinical features are vague and include abdominal distension, bilious vomiting and bloody stools. This condition when presenting in neonatal period is also mistaken for necrotizing enterocolitis (NEC) [1]. It is most commonly ileoileal than ileocolic compared to the older age groups [1]. The etiology of neonatal intussusceptions is mostly unknown. Here, we present a rare case of intussusception in a newborn.

## CASE REPORT

A 10-day-old boy was brought to casualty with a one-day history of fever, irritability and vomiting. The perinatal history was unremarkable: he was delivered at term by spontaneous vaginal delivery with good Apgar score and a birth weight of 3.25 kg. Clinical examination revealed an irritable infant, sometimes lethargic and well perfused. He was pyrexial (37.7°C) and tachycardic but normotensive with normal respiratory rate and oxygen saturations. Chest and heart examination were normal. Abdominal examination showed no organomegaly. He had a soft fontanelle, normal pupillary responses and no meningism was evident. He presented some episodes of apneas with crying; vomiting was not present in every feeding. The level of irritability and lethargy prompted the clinicians into performing a lumbar puncture. On investigation, Hb was 13.8 g/dl, WBC 9,500/mL, with 32% neutrophils and platelets of 180. Inflammatory markers were unremarkable. A capillary gas, electrolytes, liver transaminases and a coagulation screen were normal for his age. A chest and abdominal X-ray, ECG and an abdominal ultrasound were all within normal ranges. Intravenous fluids, gentamicin and ampicillin were administered. On the following day the newborn showed a transient rash. The cerebrospinal fluid was normal and blood culture resulted negative. In the suspicion of allergy to cow's milk proteins, he began feeding with hydrolyzed formula. Abdominal distension was noted on day 13 of life. An abdominal ultrasound was repeated which revealed the "doughnut" sign and the baby underwent laparotomy. Intraoperatively, an ileoileal intussusceptions was found and was resected. The rest of the viscera was found to be normal. The baby has been followed up on a regular basis and is currently well and free from any symptoms.

## DISCUSSION

Intussusception is most common in infants between 5 and 18 months of age [6, 7]. It is an extremely rare clinical entity in the newborns, with less than 1% of all cases happening in the neonatal period, resulting in less than 3% of neonatal bowel obstructions [1-5]. The etiology of neonatal intussusceptions is mostly unknown with some evidence in literature suggesting a link with different viral infections [8]. Neonatal intussusception is often difficult to diagnose as the cardinal symptoms of paroxysmal colicky abdominal pain, palpable mass, and recurrent jelly stools are usually not present. These

neonates often present with abdominal distension, bilious vomiting, and bloody stools, signs that are often mistaken for NEC [9]. Vomiting during the neonatal period is frequent and can mimic so many conditions, leading to delay in diagnosis. Instead lethargy can be the sole presenting symptom of intussusception, which makes the condition's diagnosis challenging, as in our case. Early diagnosis improves prognosis and may be achieved with use of ultrasound scan. Intussusception can be treated successfully with resection and primary anastomosis, achieving good results. The differential diagnosis of an intussusception should be considered in neonates with acute abdominal distension and lethargy, as it happened in our case.

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## ABS 88

### URINARY GC/MS METABOLOMICS IN ASPHYXIATED NEWBORNS UNDERGOING HYPOTHERMIA: FROM BIRTH TO 72 HOURS OF LIFE

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## BACKGROUND

The aim is to explore urine patterns of small metabolites that are associated with the perinatal asphyxia event using four collection time points: at birth and at 72 hours (at the end of hypothermia process).

## METHODS

Twelve cases of asphyxiated newborns were included in this study. Urine metabolites were measured by gas chromatography mass spectrometry. One-way Anova, principal component analysis, and orthogonal partial least square discriminant analysis (OPLS-DA) were applied to investigate the association between metabolites and asphyxia.

## RESULTS

Among the metabolites identified in this study, twenty-nine metabolites were significantly different using univariate statistical analysis. After performing multivariate statistical analysis, the most important metabolites were identified related to the single collection time points. These analyses indicated energy and homeostasis as the most affected by the perinatal asphyxia event. The metabolomic analysis also showed a correlation between the basal metabolism at T0 and the mortality in the first week of life.

## CONCLUSIONS

Our study identified multiple metabolites associated with perinatal asphyxia event. These findings implied that metabolomics is a useful method to study the metabolic changes in asphyxiated newborns after hypothermia treatment.

## ABS 89

### PRENATAL SUBSTANCE USE: THE EXPERIENCE LIVED BY THE NEWBORN

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## INTRODUCTION

Prenatal substance use has maternal and fetal consequences. The most commonly used substance is tobacco, followed by alcohol, cannabis and other illicit substances. In particular, opioid use in pregnancy is associated with an increased risk of neonatal abstinence syndrome (NAS). The most important symptoms are hyperirritability, tremors, sleep disturbance, hyperthermia, tachypnea, jitteriness, hypertonia and poor sucking. We report 2 clinical cases of maternal drug addiction with neonatal effects.

## CASE REPORTS

### Case 1

G., a one-day-old baby girl born to a smoking mother (6-7 cigarettes/die) addicted to heroin on therapy with methadone (35 mg/die) for 10 months, was admitted with complaints of generalized hypertonia and sub-pyrexia (T = 37.3°C). She was born at full term with Apgar Score 9 (1') and 10 (5') by caesarian section. Birth weight was 2.900 kg (35<sup>th</sup> percentile). On examination, the baby had fair general conditions with drowsiness, frantic hands sucking and urinary positivity to methadone. Finnegan Score was 0 at hospitalization and 7 after eight hours.

### Case 2

M., a IUGR two-day-old baby girl born to a smoking mother (3-4 cigarettes/die) addicted to occasional use of cannabis and with cytomegalovirus IgM seroconversion during first pregnancy trimester, was admitted with complaints of suspected NAS. She was born at full term with Apgar Score 9 (1') and 9 (5') by normal vaginal delivery. Birth weight was 2.070 kg (1<sup>st</sup> percentile). On examination, the baby had fair general conditions without neurological signs and urinary positivity to cannabis. Finnegan Score was 8.

## DISCUSSION

NAS therapy with phenobarbital is needed when Finnegan Score > 12 or when it is > 8 in subsequent determinations every 4 hours. Both babies did not need pharmacological therapy but only cardiorespiratory monitoring, early enteral feeding and reduction of environmental stimuli.

## CONCLUSIONS

The effects of drugs on the neonate is influenced by the type of drug, the combination of drugs, the amount and frequency of use, the trimester in which they are used, the timing of withdrawal and the genetic susceptibility of the fetus. That is why accurate maternal history is essential for the discrimination of NAS. Mothers often do not admit drug addiction and neonatal symptoms can therefore be misleading.

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## ABS 90

### A RARE CASE OF CONGENITAL EPICRANIAL pPNET: THE IMPORTANCE OF ULTRASOUND FOLLOW-UP

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## BACKGROUND

Primitive neuroectodermal tumors (PNET) are rare malignant neoplasms that occur mostly in childhood and early adulthood [1]. The peripheral one (pPNET) is due to chromosomal translocations, the same found in Ewing Sarcoma [2, 3]. pPNET can be found in different districts of the body, in the soft tissues, and it is generally aggressive, possibly damaging the bone [3]. We report a rare case of congenital epicranial pPNET in a newborn, analyzing the clinical and imaging findings, focusing on the importance of ultrasound in the suspicion of diagnosis.

## CASE REPORT

We present the case of a newborn girl, born at 40 weeks of gestational age by caesarean section for fetal bradycardia and oligohydramnios. At birth the baby presented a swelling of soft consistency in the left part of brow, covered by intact skin. At the first ultrasound the lesion had hypo-anechoic appearance, with well-defined margins, with no vascular elements that, also considering the clinical history, were not compatible with a certain diagnosis of cephalohematoma. MRI performed one week after birth showed an expansive extracranial formation in the context of soft tissues, with different signals and with modest pathological enhancement after contrast, compatible with cephalohematoma. Ultrasound follow-up after 10 and 20 days showed an increasing size of the lesion; the internal structure was not homogeneous with granulations and hyperechoic shoots, surrounded by a well-defined hyperechoic membrane (**Fig. 1**). The TC scan pointed out a massive new formation, with different densities, an irregular post-contrast enhancement and intralesional



**Figure 1 (ABS 90).** Ultrasound follow-up after 10 and 20 days showed an increasing size of the lesion; the internal structure was unequal with granulations and hyperechoic shoots, surrounded by a well-defined hyperechoic membrane.

calcifications. These features allowed to exclude the hypothesis of cephalohematoma, rather suggesting a neoplastic aggressive lesion. After excluding bleeding events predisposition (including the XIII and von Willebrand factor), the tumor was removed *en bloc*. The lesion showed macroscopic characteristics of a solid encapsulated neoplasm. The histopathologic diagnosis was pPNET, immunohistochemistry studies excluded differential diagnosis with Ewing sarcoma and rhabdomyosarcoma [3].

## CONCLUSIONS

The rarity of this case is the unusual epicranial location associated with the very young age of the patient. It is important to consider the diagnosis of pPNET in children and adolescent with an apparent soft-tissue mass. Radiographic findings vary and are not helpful in differentiating PNET from other tumors [1]. In this case the follow-up with ultrasound had a crucial role in monitoring the characteristics and evolution of the lesion, directing towards more imaging studies and an early diagnosis of the tumor.

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