Assess the risk/benefit ratio for indications for late preterm delivery, or weeks gestation). Age implies that the delivery was necessary for surgical changes in respiratory and The transition from the intra, to the extrauterine environment is an important priority for obstetric practitioners. During the past 15 years in the United States the percentage of infants born before 40 weeks’ gestation has dramatically increased and the percentage of infants born after 40 weeks’ gestation has decreased. In this shift several factors have been implicated: increased medical surveillance and interventions, increased multifetal pregnancies, maternal obesity (risk for preeclampsia, diabetes and other complications), maternal autonomy, route and timing of delivery. Birth before fetal maturity contributes to short-term and long-term morbidity and mortality in late preterm (34+0 to 36+6 weeks’ gestation). Age stratified cohort studies confirms that adverse neonatal outcome decrease with increasing gestational age independent of delivery mode. Because of the known morbidity and mortality associated with late preterm birth, iatrogenic delivery in this period has become a major concern. Preterm birth has been characterized as either “spontaneous” or “indicated.” For the most part, spontaneous late preterm births are difficult to avoid, whereas the term “indicated” implies that the delivery was necessary for maternal or fetal benefit. Gyamfi-Bannerman and colleagues found that 56.7% of late preterm non spontaneous deliveries were non-evidence based, concluding that more data were needed to justify many indications. A recent workshop by the Society for Maternal-Fetal Medicine developed consensus recommendations regarding the gestational age for delivery. These recommendations and those of the American College of Obstetricians and Gynecologists (ACOG) are based on the balance between maternal and newborn risks of early delivery with the risk of further continuation of pregnancy. To decrease the mortality and morbidity associated with late preterm births, prevention is one of the key components. The ACOG does not recommend induced vaginal or planned cesarean delivery prior to 39 weeks gestation unless medically indicate. If elective induction is undertaken for nonmedical reasons, it should only take place if the preinduction assessment ensures the gestational age is at least 39 weeks. In addition, further research is needed to refine the management of late preterm gestation (such as better identification of pregnancies that require early delivery for medical conditions).  

- Identify management strategies to improve outcomes in late preterm infant (antenatal steroids)
- Improve the precision of determining gestational age.

A1

Delivery and late preterm birth
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Delivery of infants who are physiologically mature and capable of successful transition to the extraterine environment is an important priority for obstetric practitioners. During the past 15 years in the United States the percentage of infants born before 40 weeks’ gestation has dramatically increased and the percentage of infants born after 40 weeks’ gestation has decreased. In this shift several factors have been implicated: increased medical surveillance and interventions, increased multifetal pregnancies, maternal obesity (risk for preeclampsia, diabetes and other complications), maternal autonomy, route and timing of delivery. Birth before fetal maturity contributes to short-term and long-term morbidity and mortality in late preterm (34+0 to 36+6 weeks’ gestation). Age stratified cohort studies confirms that adverse neonatal outcome decrease with increasing gestational age independent of delivery mode. Because of the known morbidity and mortality associated with late preterm birth, iatrogenic delivery in this period has become a major concern. Preterm birth has been characterized as either “spontaneous” or “indicated.” For the most part, spontaneous late preterm births are difficult to avoid, whereas the term “indicated” implies that the delivery was necessary for maternal or fetal benefit. Gyamfi-Bannerman and colleagues found that 56.7% of late preterm non spontaneous deliveries were non-evidence based, concluding that more data were needed to justify many indications. A recent workshop by the Society for Maternal-Fetal Medicine developed consensus recommendations regarding the gestational age for delivery. These recommendations and those of the American College of Obstetricians and Gynecologists (ACOG) are based on the balance between maternal and newborn risks of early delivery with the risk of further continuation of pregnancy. To decrease the mortality and morbidity associated with late preterm births, prevention is one of the key components. The ACOG does not recommend induced vaginal or planned cesarean delivery prior to 39 weeks gestation unless medically indicate. If elective induction is undertaken for nonmedical reasons, it should only take place if the preinduction assessment ensures the gestational age is at least 39 weeks. In addition, further research is needed to refine the management of late preterm gestation (such as better identification of pregnancies that require early delivery for medical conditions).

- Assess the risk/benefit ratio for indications for late preterm delivery, such as more accurate estimation of fetal outcome in presence of maternal diseases.

A2

The transition of late preterm
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Background: The transition from the intra- to the extra-uterine life is characterized by major physiological changes in respiratory and hemodynamic functions [1]; moreover, the intrauterine thermostability has to been replaced by the neonatal termoregulation [2]. Many of the antepartum and intrapartum risk factors associated with the need of resuscitation may be present in late-preterm neonates (34+0/7 to 36+6/7 weeks) [3]. It is also reported a double risk of Caesarean Section (CS) in case of late-preterm compared to term deliveries [4]. Our objective was to evaluate the transition period in late-preterm infants in particular considering the need for resuscitation and the incidence of hypothermia.

Materials and methods: This was a retrospective study of all late preterm neonates during a 1-year period from January 2013. Gestational Age (GA) was calculated as a function of the date of last menstrual period and/or biometrics assigned from the ultrasound measurement of the first trimester. Type of pregnancy (singleton or multiple), use of antepartum steroid therapy, maternal medical disorders, obstetric and/or fetal complications, intrapartum fetal distress, birth weight (BW), gender, Apgar score, need for resuscitation were collected from medical records Rectal temperature was measured in all neonates at birth and at admission to nursery.

Results: During the study period there were a total of 3354 births. The number of preterm neonates was 478 (14.2%), of these 279 (58%) were late-preterm (249 singleton pregnancy and 30 multiple pregnancy). Three neonates were excluded due to in utero fetal death. Table 1 summarizes the characteristics of the population according to GA: 34 weeks of gestation (Group I), 35 weeks (Group II) and 36 weeks (Group III). The twins rate was significantly higher (p<0.001) in Group I than the others. The CS rate was similar among the groups and increased in comparison to that reported in our Department for term deliveries (44%). A higher number of neonates with Apgar score <7 was present in Group I in comparison to the others, as well as a higher number of neonates requiring resuscitation, independently of the mode of delivery. In Group II and III, all neonates requiring resuscitation were born by CS. Higher number of neonates with mild hypothermia at admission was detected in Group I. Considerable variations occur in the temperature values in all infants in DR as well as during the transport to the nursery.
Conclusion: Late-preterm birth by CS is associated with significant GA-dependent neonatal depression. Additional close monitoring and timely intervention are necessary in the management of these infants in DR.

References

A4

Roaming in organization to prevent neonatal mortality and morbidity in late preterm infants

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Despite most infants born at 34+0 through 36+7 weeks’ gestation are thought to be at low risk during the birth hospitalization and have a neonatal course with no significant complications, they are physiologically and metabolically immature with a higher rates of morbidity and mortality than term infants [1]. Most common medical condition associated with late-preterm births are respiratory distress, apneic, temperature instability, hypoglycemia, hypocalcemia, jaundice, poor feeding, sepsis and finally an higher rates of mortality and the morbidity are higher than in term neonates. The rate of complications decreases with the progression of gestational age through the late preterm period [1]. Intrauterine growth restriction (IUGR) is one of the cause for the late preterm delivery and it occurs more often in late preterm infants than term ones. Itself constitutes a risk factor for morbidity and mortality [2,3]. IUGR, as well as associated peri-natal morbidities, contributes to increase the risk, in these infants, of postnatal growth impairment, metabolic diseases and poor neuro-developmental outcome [1,4]. Late preterm small for gestational age (SGA) infants were 44 times more likely to die in the first month and 22 times more likely to die in their first year than term adequate for gestational age (AGA) newborns. This increased risk cannot be fully explained by an increasing prevalence of lethal congenital conditions among SGA late preterm newborns [5]. The ability to recognize abnormal growth at birth and or a intrauterine malnutrition is of great importance for the care and the prognosis of these neonates. Neonatal anthropometric charts are commonly used for the diagnosis at birth of SGA newborns [6]. The terms SGA and IUGR are often used as synonyms, however they reflect two different concepts. SGA refers to a statistical definition, based on an auxological cross-sectional evaluation (prenatal or neonatal), and denotes a fetus or a neonate whose anthropometric variables (usually weight) are lower than a given threshold value computed on a set of infants having the same gestational age. IUGR instead refers to a clinical and functional condition and denotes fetuses unable to achieve their own growth potential. Such a condition can be assessed by ultrasonography during pregnancy by a longitudinal evaluation of fetal growth rate. The current gold standard in neonatal auxological evaluation is based on informations obtained from both neonatal anthropometric charts and intrauterine growth charts [7]. At present specific growth charts to monitor postnatal growth of late preterm infants are not available. In the next future the late preterm postnatal longitudinal growth standards will be available as a result of “Intergrowth21st Project”.

References

Table 1(abstract A4) Assessment and care of the late preterm infant [3]

<table>
<thead>
<tr>
<th>Assessment and care of the late preterm infant</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Assess gestational age of neonate</td>
<td>Assess and monitor respiratory status</td>
</tr>
<tr>
<td>Assess for risk factors</td>
<td>Appropriate respiratory interventions</td>
</tr>
<tr>
<td>Assess for heat loss and cold stress</td>
<td>Assess for risk factors and symptoms of heat loss and/or cold stress</td>
</tr>
<tr>
<td>Interventions to maintain a neutral thermal environment</td>
<td>Interventions and assessment of hypoglycemia including transfer to higher acuity unit or facility if indicated</td>
</tr>
<tr>
<td>Phototherapy as indicated</td>
<td>Assess for maternal and neonatal risk factors for sepsis</td>
</tr>
<tr>
<td>Parent education regarding signs and symptoms of jaundice and hyperbilirubinemia</td>
<td>Antibiotic therapy and diagnostic evaluation if sepsis is suspected</td>
</tr>
<tr>
<td>Breastfeeding, and support for breastfeeding mothers</td>
<td>Assess for presence of jaundice and hyperbilirubinemia</td>
</tr>
</tbody>
</table>

Discharge planning including parent education, counseling, and validation of knowledge about recognizing and acting on risk factors.
the hospital readmissions during the neonatal period. These morbilities result in workup for sepsis evaluations, antibiotic therapy, intravenous fluid administration, ventilatory support and increased length of stay with higher hospital costs [2].

Rooming-in organization of late preterm births aims to assess and identify risk factors, prevent and manage potential medical complications during hospitalization. Interventions and practices recommended are illustrated in table 1. Evidence of physiologic maturity, feeding competency, thermoregulation and absence of medical of medical illness are minimum discharge criteria for late-preterm newborns. Furthermore it's of great importance to assess educational programs with special instruction and guidance to parents, engaging families in providing appropriate home care after hospital discharge. A long term follow-up arrangements is also recommended to assess and plan early interventions in case of neurodevelopment delay [4].

We conclude that, based on the significant morbidity and mortality of late preterm births, the health care focus on prematurity should be expanded to include the late preterm period.

References


A5 Preventing sudden unexpected postnatal collapse in term and late preterm newborn infants: a surveillance protocol

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Early and prolonged skin-to-skin contact (SSC) after birth between a mother and her newborn has been shown to generate beneficial effects on mother-infant relationship and breastfeeding. SSC may ease the infant’s transition to extra uterine life and helps to regulate the infant’s body temperature and nursing behavior. However, reports of sudden unexpected postnatal collapse (SUPC) soon after birth, in healthy term and late preterm neonates, in association with skin-to-skin contact, have raised concerns about the safety of this practice.

Based on the available evidence, the working group on breastfeeding of the Maternal and Child Health Institute of Trieste (Italy) developed a surveillance protocol to be implemented in the Delivery Room and Postnatal Ward. The aim of our protocol is: 1) promoting safe mother-infant bonding 2) establishing successful early breastfeeding and 3) correcting the risk factors for sudden unexpected postnatal collapse (SUPC). This protocol is especially focused on the first 2 hours of life, when about 1/3 of SUPC occur, but extends to the whole duration of the infant stay in the maternity ward.

The following interventions will be undertaken: 1. antenatal and early postnatal oral and written information to parents about: a) the risk of bed-sharing b) avoidance potentially suffocating infant positions (i.e. mouth/nose obstruction) c) the need of an adequate supervision of the infant in the first hours/days after birth. 2. periodical assessment (position, colour, breathing) of the infant (at 10, 30, 60, 90 and 120 minutes of life) by midwives in the delivery room. 3. discourage bed-sharing 4. encouragement of skin-to-skin contact only when mothers are fully awake 5. avoidance of mothers left alone with the baby in the first hours after birth particularly during skin-to-skin contact and first breastfeeding attempts.

As there is no evidence of effective interventions to prevent SUPC, our protocol has been written as a potential best practice. Evidence of its clinical effectiveness is obviously needed.

A6 Psychological distress in postpartum: influence of late preterm delivery

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Background: Psychological distress in women during the postpartum period has been for a while an issue of great concern. There is substantial evidence that maternal psychological distress after pregnancy is associated with an adverse cognitive and behavioural consequence in the offspring [1]. There are also severe implications during the perinatal period for the mother’s long term mental health [2,3], her partner’s mental health [4,5], and for the parental relationship [6]. The growing trend in late preterm deliveries suggests research on postpartum psychological distress risk in this group of vulnerable women.

Materials and methods: This prospective case control study was performed with the approval of the ethics committee, in accordance with the Declaration of Helsinki. Women who gave birth from 34/0 to 36/6 weeks and the next women who gave birth from 37º to 40/6 weeks able to give informed consent were eligible. Three days after childbirth, mothers of late preterm infants (n=42) and the next mother of at term infant, matched for parity and delivery route (n=42) completed medical history that covered key demographic and social information and the following questionnaires: State-Trait Anxiety Inventory questionnaire (STAI-Y) [7], Edinburgh Postnatal Depression Scale (EPDS) [8], and Psychological Stress Measure (PSM) [9].

Results: Findings show that mothers of late preterm infants, presenting with comparable key demographic and social antenatal risk factors, have more stress, anxiety, and depression than mothers of at term infants (State Anxiety-state 42.6±5.3 vs 49.5±9, p<0.002; Anxiety-trait 39.6±1 vs 45.8±10.1, p<0.02; EPDS 6.3±3.9 vs 9.5±4.5, p<0.008; PSM 38.9±4.5 vs 46±5.9, p<0.001). In addition, Anxiety-state levels were associated with longer time to stay in hospital (days 6.1±1.8 vs 4.7±1.2: p<0.01).

Conclusions: These data indicate that late preterm delivered mothers are at increased psychological risk in a critical period for establish a correct mother infant relationship. This can happen in two ways: first of all perhaps, by averting preterms’ delivery and secondly by working through the distress. Moreover, what should be consider of great importance during the postpartum period is the presence of an entourage that can help relieve the mother from psychological distress and to support her and her child in case of acute symptoms [10]. Taking into account all these consideration it would be great to be able to arrange a psychological treatment for these mothers n terms of their immediate and future well-being, and must therefore be targeted for intervention.

References

Late-preterm newborns accounted for 8.7% of all US births in 2009, while in Italy, according to Euro-Peristat Report 2010, rate of preterm live births between 32 and 36 weeks accounts for 6.4%: therefore late-preterm incidence is around 5% [1]. In the literature it is reported that late preterm infants are at increased risk of neonatal mortality and morbidity, including feeding problems, hyperbilirubinemia, hypoglycemia, and respiratory problems. So, in recent years, research has focused on hospital care, with little known about the real needs of care after discharge and in the home. However, it’s known that early discharge places these infants at greater risk of complications such as rehospitalization, particularly in breastfed infants [2]. Therefore in this population it’s fundamental to plan an “appropriate” discharge. What does “appropriateness” mean? In health care the appropriateness has two aspects: 1) the “clinical” appropriateness that refers to the criteria of efficacy and safety; 2) the so-called “administrative” appropriateness that indicates the extent of provision of health according to the criterion of efficiency, that is the best use of available resources, with respect to the clinical case to be treated. Because the resources available vary by context, administrative appropriateness is a very dynamic concept.

In the discharge of late-preterm baby, clinical appropriateness requires individualization and involvement of family. Discharge criteria are substantially similar to those of full-term [3] but include longer observation times, more attention to the real understanding and involvement of the family in the scheme of nutrition and follow-up, and an increased need for planning follow-up and integration with local services. Although discharge criteria for late preterm infants are quite precise, however there is a large inter-center heterogeneity regarding the timing of discharge. It’s clear that the choices on the discharge of late preterm newborns are strongly influenced by the organizational context. It should be essential to have accurate population-based surveillance data and organizational data, as well as clinical ones. Only in this way it is possible to evaluate the efficacy (and on which outcomes) of programs of protected discharge, and their compatibility with the available resources. For example, some studies suggest that home visiting promotes improved parent-infant interaction; however further studies are needed to demonstrate whether such interventions in at-risk populations may strengthen their impact and cost benefits [4].

References

A7
Discharge of late preterm newborn: appropriated, controlled...namely safe
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In order to improve perinatal outcomes, national guidelines proposed by the National Committee for Mother and Child Health, were promulgated by the Ministry of Health in 1990. A Child and Maternal Hospital Healthcare Referral Network was created. This document advised for some innovating and frontal aspects: 1. Maternities with less than 1500 deliveries per year should be closed; 2. Hospitals were classified as Perinatal Care Hospitals (Level II-able to provide care to pregnant women and normal newborns, and should include a Neonatal Intermediate Care Unit) and Differentiated Perinatal Care Hospitals (Level III-to provide care to high risk pregnant newborns, and should include a Neonatal Intensive Care Unit). Functional According Units were created to connect the Hospitals to the Primary Healthcare Centres; 4. Cycles of Special Studies on Neonatology were created to graduate Paediatricians in Neonatology; 5. The recognition that the best transport for the newborn is the mother’s womb; however, in 1987, a Neonatal Transport was created to unavailable situations. Both pregnant women and newborns are transferred according to the following priority: pathology, geographical referral and available vacancy.

Another important aspect was the organization of paediatricians and neonatologists (1985) as scientific societies and the publication of national protocols as an attempt to standardize methodologies. The National Registry of VLBWinfants, inspired on Vermont-Oxford Network, was an initiative started in 1994 with a voluntary participation of the NICU’s. All these aspects had clinical implications, namely in decreasing mortality rates, as shown in table 1.

In conclusion, the reform of perinatal care in Portugal is an example of how a good diagnosis and adequate proposals combined with a strong political will are crucial for changing.

A9
Are all Italian newborns equal?
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The debate on the restructuring of Chapter Five (Titolio Quinto) of the Italian Constitution has brought once again the issue of the allocation of powers between the State and its regions under the spotlight. According to Article 117 of the Italian Constitution, as reformed in 2001, the State and its regions share normative competences in regulating certain matters. In the field of core civil and social rights, including health care, it is the responsibility of the State to identify fundamental levels of services and assistance that have to be guaranteed to everyone across the nation. The aim of this provision was to prevent unacceptable disparities in the enjoyment of the right to health. In practice, however, this has not been the case. On the one hand, Italian regions have disciplined certain matters in fairly different ways, forcing the Ministry of Health to exercise its role of warrantor of fairness more than expected. On the other hand, the quality of services has been greatly affected by a “geographical” factor, depending on availability of resources, different organization of health system and bureaucracy at regional level.

Health care services for newborns are a case in point. Two examples — among others — are worth exploring further. The neonatal screening programmes for cystic fibrosis and inherited metabolic diseases are a lot different among different regions and sometimes even among different towns or hospitals in the same town. Some legislative measures have been taken to overcome this situation, but the implementation of the national regulation remains difficult to attain. Should the responsibilities and
decisions involved depend on the place a baby is born? As a matter of fact, this observation keeps playing an important role as to the possibility of addressing the most critical situations in a successful way. Even though the neonatal mortality rate in Italy is nowadays among the lowest in the world, infants born in Southern Italy still run a higher risk of dying in the neonatal period. Against this background, the situation of neonatal intensive care units points to inequalities that are not new for the country and yet hard to reconcile with the idea of sharing the same fundamental constitutional rights. Starting with everyone’s birth.

A10 Neonatal hyperbilirubinemia
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Unconjugated hyperbilirubinemia is a common condition in the first week of postnatal life. Low levels of bilirubin exert antioxidant effects, but some neonates may develop very high levels of unconjugated bilirubin (UCB), with an increase of the unbound free fraction (βbil), able to diffuse through the blood brain barrier. Amount and duration of hyperbilirubinemia and the neurodevelopmental age (preterm neonates) at the time of insult exposition is supposed to influence the location of selective brain damage, as well as the severity of consequences [1]. The clinical manifestations range from the less severe Bilirubin-Induced Neurological Damage (BIND) to a more severe chronic kernicterus, while the regional selectivity of damage may elicit to motor disorders and athetosis (basal ganglia and cerebellum), auditory dysfunction (inferior colliculus), memory and leaning impairment (hippocampus) [2]. To avoid neurological consequences, the Clinical Practice Guideline of the American Academy of Pediatrics recommend total bilirubin determination (TSB) on every jaundice infant, both during hospital stay and post discharge follow-up. To this goal, Bilistik [3], a new minimally invasive method for measuring TSB, may improve substantially the triage of jaundice newborns with potential risk of brain damage and kernicterus to be addressed to phototherapy. Moreover, recent studies have raised concerns about the potential toxicity of intensive phototherapy in preterm neonates, and no information about its effectiveness in quickly reducing brain bilirubin concentration are yet available [4].

Early neuronal accumulation of bilirubin in damaged regions and its brain metabolism may have a role in the marked regional differences observed in kernicterus impairment. This hypothesis is supported by the role of brain cytochrome P-450 (Cyp), known to oxidize UCB. In the brain of Gunn rats, an early upregulation of Cyp mRNAs was observed in the unaffected brain regions, cortex and superior colliculus, in contrast to the delayed and slight upregulation observed in the affected regions, inferior colliculus and cerebellum [6], where UCB alters the cell cycle inducing apoptosis [7]. Clarification of pathophysiology of UCB neurotoxicity, that continues to be a relevant issue among newborns worldwide, may open new perspectives for therapeutic approaches, focused in protecting directly the brain, the final target of bilirubin toxicity. To this aim the development of new research models, appear of particular relevance. Among them the organtopic brain cultures, living slices of the CNS that can be cultured in vitro and challenged with bilirubin in controlled (concentration/timing) manner, strictly modelling different histopathological aspects of neurological conditions.

References

A11 Risk of BIND and kernicterus in late preterm
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Severe hyperbilirubinemia can induce devastating and permanent neurodevelopmental handicaps in infants. The occurrence of hyperbilirubinemia is higher in late preterm than in term infants, ranging from 8 to 40% of the former according to different definitions of hyperbilirubinemia. The mechanisms by which this occurs is not completely understood, however an increased bilirubin load on hepatocytes, as result of decreased erythrocyte survival and increased erythrocyte volume, increased enterohepatic circulation of bilirubin, decreased hepatic uptake of bilirubin from plasma, defective bilirubin conjugation, and diminished serum bilirubin binding capacity play a relevant role.

Hyperbilirubinemia in late preterm infants is not only more prevalent than in term neonates, but also it occurs later and is more severe and protracted. In fact, Maisels et al. (Pediatrics 2006;117:1169) demonstrated that at 72 hours of life the value of 50 percentile of total conjugate bilirubin (TcB) is 9 mg/dl in 35-37 wks infants, while is <6 mg/dl in >40 wks infants. Moreover, they found that the decrease of TcB is slower in 35-37 wks infants than in >40 wks infants, since at 96 hours of life the value of 50 percentile of TcB is 9 mg/dl in 35-37 wks infants, while is <3 mg/dl in >40 wks infants.

Late preterm infants are at higher risk of bilirubin induced neurological dysfunction (BIND) and kernicterus than term infants. The mechanisms that potentially could explain the high susceptibility of central nervous system to bilirubin-induced damage in late preterm neonates have not been well defined. However, some of the factors that can potentially contribute are the diminished serum bilirubin binding capacity due to the lower serum albumin levels, an enhanced permeability of the blood–brain barrier to unconjugated bilirubin influx, and an immaturity of neuronal protective mechanisms. This is probably the reason why late preterm neonates are at an increased risk to develop acute bilirubin encephalopathy and or kernicterus as demonstrated in the USA pilot kernicterus registry (Semin Perinatol 2006;30:89) in which this category of infants is over-represented compared to term neonates. Thus, clinicians need to be more concerned and conscientious to identify late preterm’s risk for severe hyperbilirubinemia in view of their increased susceptibility to BIND. This can allow of planning a prevention program including nursing and parental education, screening for jaundice in the nursery, the provision of lactation support, timely post discharge follow-up, and appropriate treatment when clinically indicated.

A12 Cholestasis in preterm infants: when is a yellow alert?
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Besides the transient bilirubin transport immaturity, preterm infants are particularly at risk for different forms and degrees of bile formation impairment because of metabolic demands that are not matched by functional maturation in the first weeks of life.
Cholestasis, affecting approximately 1 of 2 500 infants, is more commonly reported in preterm infants with an incidence varying between 10 and 20%, and it is mainly due to a combination of factors including delayed enteral nutrition, low birth weight, prolonged parenteral nutrition, hypoxia, infection, liver ischemia, immaturity of bile acid metabolism, surgical procedures and multiple drug treatments [1]. This reality of the setting is defined as transient or multifactorial cholestasis [2], which is the most frequent form of cholestasis in neonatal intensive care unit, usually transient and followed by a gradual full recovery [3]. Cholestasis in preterm infants may however also be indicative of a severe liver disease such as biliary atresia (BA) or other biliary tract disorders. The development of a persistent cholestatic jaundice, even in presence of colored stools, incentives to conduct a thorough investigation [4]. Abdominal ultrasonography may support the diagnosis of BA showing: absence of gallbladder, the “triangular cord” sign or a cyst located at porta hepatitis. Transient multifactorial cholestasis is a diagnosis of exclusion and a definitive diagnosis can be made only after the complete resolution of the clinical picture. Moreover, diagnosis of biliary atresia in preterm jaundiced neonates is difficult since discoloration of stools can occur several weeks after birth [4].

Besides specific cholestatic disorders for which specific medical and surgical treatment are available, there is no unequivocal evidence that any medical treatment alters the natural history of multifactorial cholestasis. Treatment with ursodeoxycholic acid may indeed be useful, although there is no evidence of effectiveness. Every effort must be made to remove all risk factors for liver injury. Consequences of cholestasis also need to be managed by administering fat -soluble vitamins, especially vitamin K and nutritional formulas containing medium-chain fatty acids. Although multifactorial transient cholestasis is the most common cause of prolonged jaundice in preterm infants, neonatologists need to be aware that premature infants can also present with signs of severe liver disease. To avoid any diagnostic delay it is mandatory to promptly identify all the conditions suitable for an early and specific treatment with a structured approach to the investigation of cholestasis tailored to the preterm infant [5].

References

A13
Hypoglycaemia and neonatal brain injury
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The spectrum of cerebral injury associated with hypoglycaemia is wide and includes: white matter injury including parenchymal haemorrhage and ischaemic stroke, cortical neuronal injury, and sometimes signal change in the basal ganglia (mainly the globus pallidus) and thalamus. Vulnerability of the white matter cortex of the posterior parietal and occipital lobes has been well reported in human imaging studies, but the site of injury is more widespread in pathological and experimental studies of neonatal hypoglycaemia. In the largest series of infants with isolated neonatal hypoglycaemia and acute neurological dysfunction, there was an association with a predominantly posterior pattern of injury in one third of the cohort, and a more extensive distribution of lesions was common. Safe clinical management relies on the identification of infants at risk of neurological sequelae from hypoglycaemia, adequate energy provision after birth, monitoring of blood glucose, and prompt intervention to raise the BG at specified thresholds, with the caveat that acute neurological dysfunction in association with low BG at any level should prompt urgent investigation and treatment. The optimal target blood glucose level for ensuring adequate energy provision in health and in HIE remains unknown. However, recent data support guidance to maintain blood glucose concentration ≥2.5mmol/L in neonates with signs of acute neurological dysfunction, which includes those with HIE, and is higher than the accepted threshold of ≥2mmol/L in infants without abnormal signs or hyperinsulinism.

A14
The kidney of late preterm infants
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Introduction: The risk of morbidity in late preterm neonates varies greatly depending on gestational age: it is 1 out of 2 at 34 weeks, 1 out of 4 at 35 weeks and 1 out of 10 at 36 weeks. Very little is known about the renal pathology of these infants.

Nephrogenesis in the late preterm: The process of nephron formation ceases between 34 and 36 weeks of gestation [1], the limit within which the term late preterm is applied.

Figure 1(abstract A14) Zones where stem cells were found in the kidney of the late preterm infant (from Faa G et al. JPNIM 2014 in press, with permission)
In 1943, Potter and Thierstein examined the autopsies of 1000 fetuses and neonates and found the presence of the nephrogenic zone in 100% of 30-week fetuses, in about 80% of 34-week cases and in 30% of 36-week cases. They stated that in most of these neonates nephrogenesis had ceased at 35 weeks [2].

In 2008, Ferraz et al., on applying immunohistochemistry to the kidneys of 86 fetuses of different gestational ages, observed the disappearance of the nephrogenic zone in all fetuses above 35 weeks of gestational age [3]. On the contrary, Faa et al. found the presence of active nephogenesis up to the 38th week [4]. It appears that in agreement with the data of Rodriguez et al. [5], the nephrogenic process continues after preterm birth for a period of at least 6 weeks; this window decreases further if the neonate develops acute renal injury or if he/she presents a intratuerine growth retardation. Stem cells are present in different parts of the neonatal kidney (Figure 1) [6]. A marked interindvidual variability in the number of nephrons has been observed: 6 to 8 glomerular columns were present in late preterm infants (8 columns in Rodriguez’ cases), but also in a large number of those up to 23 weeks.

Renal function and pathology in the late preterm: Cuzzolin et al. studied 246 preterms divided into 4 groups based on gestational age (one of late preterms): the creatinine values at birth were similar in the groups, with differences appearing from the 3rd and up to the 21st day of postnatal life [7,8]. No correlation between late preterm birth and the onset of renal pathologies was found shortly after or some time after delivery. This was confirmed by Pinece’s wide ranging study on 417 late-preterm infants [9].

References

A16
The role of probiotics in nosocomial infections
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Italian Journal of Pediatrics 2014, 40(Suppl 2)A16

Background: Nosocomial infections are among the leading causes of mortality and morbidity especially in neonatal intensive care unit (NICU) [1]. The intestinal microbiota of the gut is nowadays considered to play an important functional role in the host’s health through nutritional, physiological and immunological processes. For these reasons, probiotics may exert actions of prevention and therapy of infectious diseases.

Results: The mechanisms of action of probiotics are strain specific but can be summarized mainly in three areas: changes of gut ecology, modulation of gut mucosal barrier and regulation of the immune response through interaction with gut-associated immune system [2]. Several studies regarding the supplementation of probiotics in nosocomial infections have been conducted mainly in adult population. Among pediatric studies major findings have been observed in treatment of acute gastroenteritis, primarily caused by Rotavirus [3,4], and in the prevention of antibiotic associated diarrhea (AAD) [5]. Supplementation with probiotics has proven useful even in the treatment of Clostridium difficile disease (CDD), the most common pathogen involved in AAD [6]. Data from meta-analysis and cochrane review on the prevention of necrotizing enterocolitis (NEC) show an overall benefit of probiotic supplementation [7]. The limitations of the above cited studies are mainly related to heterogeneity in terms of strain, dosage and duration of treatment and the lack of studies on extremely low birth weight preterm infants. Data on nosocomial pneumonia and ventilator-associated pneumonia in neonatal and pediatric age is scanty. In a large randomized, double-blind placebo controlled study, Hojsak et al demonstrated that supplementation with Lactobacillus GG significantly decreased the risk of nosocomial respiratory tract infections [8]. On the other hand, the data from adult studies have been conflicting, with a tendency towards the demonstration of probiotic efficacy in reducing the incidence of ventilator-associated pneumonia [9]. Meticillin-resistant Staphylococcus aureus (MRSA) is a multidrug-resistant nosocomial pathogen and a recent review of literature [10] showed that many probiotic strains inhibit MRSA growth in vitro. Furthermore, this review describes that there is little published clinical data on the use of probiotics in prophylaxis or treatment of MRSA-mediated infections.

Conclusions: Due to the significant heterogeneity between the studies in literature it is not possible to draw consistent conclusions on extensive

A15
Mineral homeostasis in late preterm infants
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80% of mineral accretion take place in the third trimester of gestation with a fetal accretion rates of 100-150 mg/kg/day for calcium, 50-70 mg/kg/day for phosphate and 3 mg/kg/day for magnesium. During the third trimester of gestation fetal weight triples but Ca content quadruples with a faster increase in fetal body Ca accretion from 32 to 40 weeks of gestation [1]. As a result, late preterm infants will be deprived of the intrauterine supply of calcium and phosphorus during a period of rapid skeletal growth affecting bone mineral mass. Late preterm infants have a higher incidence of hypocalcaemia [2] and represent an intermediate risk category as compared with term and very preterm infants. AGA late-preterm infants have a higher bone turn-over than term infants, but smaller than very preterm newborns rates [3]. During the third trimester of gestation, bone mineral density (BMD) increases at a faster rate in uterus (term infants) than ex utero (preterm infant) according to gestational age. At term newborns have a physiological reduction in BMD in the first 2-3 months of life with a recovery during the first year of life. Preterm newborns present a similar event with a higher reduction of mineral retention from birth to term in the presence of high skeletal growth. Inadequate supply of calcium and phosphate to newborns requiring parental nutrition and several drugs (steroids, methylxanthines, diuretics) may increase the risk of osteopenia. Drugs affect bone metabolism decreasing calcium absorption and osteoblasts proliferation and increasing calcium renal excretion and osteoclasts activation. How do we best support the rapid skeletal growth of late preterm infants? Have early nutrition during the first weeks of life been adequate? Enriched formulas for preterm newborns have a positive and probably long-term effect on bone mineralization [4,5]. In late preterm infants the goal should be to provide nutrients based on gestational age instead of relying on birthweight. However there are no specific recommendation and further studies are warranted to determine the best care for late preterm infants.

References
use of probiotics in prevention and treatment of nosocomial infections, except for acute gastroenteritis, AAD, CDD and NEC.

References


A17

Mode of delivery and gut microbiota

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In 1985 the World Health Organization (WHO) stated: “There is no justification for any region to have Caesarean Section (CS) rates higher than 10-15%” [1]. During the last decades the percentage of births managed by CS has increased beyond the recommended level, especially in high income areas such as Italy, Germany, France, United Kingdom, and North America [2,3]. Emerging evidences indicate that the early composition of neonatal gut microbiota is responsible for shaping of immune response since there is a complex interaction between the intestinal microbiome and the immune system (Gut-Associated Lymphoid Tissue) and this cross-talk is involved in maintaining normal immune homeostasis [4]. The microbiome promotes human health, but can also drive disease. The potential disadvantages of caesarean delivery include altered bacterial profile known as dysbiosis of the gut microbiota which in turn leads to immune dysfunction and increased tendency for immune-mediated diseases such as allergies [5,6] and autoimmunity [7].

Upon delivery, the neonate is exposed to a wide variety of microbes, many of which are provided by the mother during and after the passage through the birth canal, a heavily colonized ecosystem. The neonatal colonization pattern is further influenced by several post-natal environmental factors such as the place and mode of delivery, the level of affluence, the number of siblings, the use of antibiotics and infant feeding.

The reduced microbial exposure and delayed colonization occurring in caesarean born infants have been associated with the development of allergic disease. CS delivered infants, deprived of contact with the maternal vaginal microbiota, experience a deficiency of strict anaerobes such as Bacteroides, E. coli, and bifidobacteria and a higher presence of facultative anaerobes such as Clostridium species, compared with vaginally born infants [8].

It is debated whether a low total diversity of the gut microbiota during infancy is more important than an altered prevalence of particular bacterial species (Clostridia) for the increasing incidence of allergic disease [5,6]. Recently Bisgaard et al. demonstrated that reduced diversity of intestinal microbiota during infancy is associated with increased risk of allergic disease during childhood [9]. The concept of probiotics has attracted increasing attention in recent years since several clinical studies have been published suggesting that probiotics may convert a dysbiosis to a symbiosis in infants with inadequate intestinal colonization (premature delivery, delivery by CS and excessive use of perinatal antibiotics) [10-15]. Clinical evidences suggest that probiotics could substantially affect metabolic and immunomodulatory functions [16].

References


A18

New trends on childhood nutrition

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Background: An optimal growth is the first objective of feeding during infancy. Recent trials demonstrated that environmental and nutritional influences during critical periods in development, can have permanent effects on an individual’s predisposition to diseases in adulthood.

Materials and methods: This review summarises the studies on the association between nutrition during pregnancy and infancy with illnesses later in life.

Results: Maternal nutrition during gestation is important for metabolic programming. Individuals born small for gestational age or prematurely have higher rates of insulin resistance, confirming an association between birth weight and later diabetes, heart disease and obesity [1-3]. High-protein intake during early childhood is associated with obesity, while breastfeeding and timely introduction of complementary foods were shown to protect against obesity in adulthood. Direct benefits of exclusive breastfeeding to the infant’s nutrition, gastrointestinal function, host defence and psychological well-being are known in literature. Although evidence is often inconclusive, breastfeeding may be associated with long term benefits such as lower risk of acute illnesses, obesity, cancer, adult coronary heart disease, allergic conditions, type 1 diabetes and inflammatory bowel disease [4]. The ESPGHAN recommends complementary foods introduction between 17 and 26 weeks of age [5,6].

Early introduction has been associated with an increased risk of obesity [7,8]; feeding cereals to infants at high risk for type 1 diabetes or celiac disease before 3 months of age may increase the risk of autoimmunity. Later introduction of complementary foods may be associated with adverse effects: decreased growth, iron deficiency, development of atopy and celiac disease or type 1 diabetes. Primary prevention of allergic disease through nutritional interventions has changed [9]. Avoidance diets during pregnancy and lactation are not recommended. Exclusive breast-feeding for at least 4 up to 6 months is endorsed. Hydrolyzed formula prevents allergic disease and cow’s milk allergy in high-risk infants who cannot be exclusively breast-fed. Complementary foods can be introduced between 4 and 6 months of age even for high risk infants. The important role of Vitamin D during pregnancy and infancy is still supported by literature [10,11]. Several recent clinical trials have been conducted to evaluate the effect of supplementation of Docosahexaenoic acid (DHA) in infants and children and its management: review of current evidence to support clinical efforts to optimize nutrition during gestation, infancy, and early childhood.

Conclusions: Controlled trials of early nutritional interventions with long-term outcomes are still lacking. Nonetheless, there is ample circumstantial evidence to support clinical efforts to optimize nutrition during gestation, infancy, and early childhood.

References
8. Huh SY, A20
9. Huh SY, A20

A19
Fluoride therapy in the prevention of dental caries
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The document “National Guidelines for the prevention and oral health promotion in childhood”, 2013, is an act of address for those involved in the management of oral health and in particular to the pediatrician, because the figure of the pediatrician in the prevention of oral health is absolutely critical, as confirmed by the entire international literature in recent years. Correct attitudes and behaviors adopted since childhood will allow the child to protect his health. The fluoride is the cornerstone of prevention of tooth decay and is required for all individuals.

Over the years, have been developed different means of administration of fluoride, each with different strengths, dosages and frequency of use. Fluoride supplements should be prescribed by the pediatrician in cases of real difficulty for topical administration of fluoride through toothpaste or fluoride added as a method of in subjects at risk of tooth decay. The decline of caries in our country it is highly likely also due to the pediatrician who, using the national guidelines, can inform parents and families induce the acquisition of preventive behaviors currently defined by scientific research.

To this end, again, the ministerial guidelines on the subject that were reviewed by a team of experts representative of the Italian research in this area.

References

A20
Cranial ultrasound screening in late preterm infants
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Late preterm births have enormously increased in the last decades and there is mounting evidence showing that infants born late preterm are less healthy than infants born at term [1] and they are more likely to develop neonatal morbidities (temperature instability, respiratory distress syndrome, excessive weight loss and dehydration requiring intravenous infusion, sepsis, hypoglycemia and jaundice requiring phototherapy) [2].

More recently, an increased neuromorbidity has been documented and long-term neurodevelopmental impairments (poor school performance, early intervention services, special education needs) have been reported in this population [3,4]. The neuromorbidity of the late preterm infants has been attributed to both the potential detrimental neurological effects (extrinsic vulnerability) of the morbidities these babies experience in the neonatal period, and to the intrinsic brain vulnerability. Advances in neuroimaging techniques have highlighted a higher intrinsic vulnerability of the late preterm brain due to the structural and molecular immaturity of the developing brain at specific gestational ages [5,6].

Therefore, late preterm infants have a risk to develop brain lesions which is lower than more premature babies but higher than term newborns and they can be affected by brain lesions common to both preterm and term infants [7]. However, the incidence of brain abnormalities in this specific population has never been investigated as late preterm infants have long been considered a low-risk and low-risk population.

Considering that most of the brain lesions are clinically subtle or silent during the neonatal period, a cranial ultrasound screening may play a role in: 1. detecting babies at risk of impaired neurodevelopment later in childhood and who may benefit from early intervention programs; 2. identifying the most significant perinatal risk factors associated with brain abnormalities in such a large low-risk population in order to target the potential need for cranial ultrasound at birth. Based on these assumptions we performed a cranial ultrasound screening project on late preterm infants. Our preliminary data (unpublished data) suggest that lower gestational age, within the late preterm period, and early neonatal morbidities, can provide an indication at birth to undergo a cranial ultrasound scan as they are associated with a higher risk to develop brain abnormalities. Late preterm infants represent a vulnerable population and investigation and follow-up program should be modulated according to the prenatal, perinatal and postnatal characteristics.

Follow-up studies are needed to correlate cranial ultrasound findings with long-term neurobehavioral outcomes in late preterm infants.

References

A22
Chorioamnionitis and neonatal outcome: early vs late preterm infants
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Chorioamnionitis (CA) describes an intrauterine status of inflammation and/or infection of placental membranes, referring to both histological and clinical CA [1]. It is considered the major risk of spontaneous preterm delivery, especially at earlier gestational age. The intrauterine exposure to infection/inflammation leads to the fetal inflammatory syndrome (FIS) that together with CA is responsible for multiple organ injury, neonatal morbidity and mortality [2]. Strong evidences support that neonates exposed to CA are sicker at birth, have a higher rates of early-onset sepsis, respiratory distress syndrome (RDS), bronchopulmonary dysplasia (BPD), intraventricular hemorrhage (IVH), retinopathy of prematurity (ROP), patent ductus arteriosus (PDA) and surgical necrotizing enterocolitis (NEC) as compared with unexposed neonates [3-6]. Neonates with ≤ 28 weeks of gestational age (GA) have a significantly higher mortality than neonates with a longer gestation period [7]. Recently Pappas et al reported an increased odds of cognitive impairment and death/neurodevelopmental impairment in extremely low birth weight (ELBW) exposed to CA [8]. In infants born at 36 weeks or later in gestation CA has been indentified as an independent risk factor of CP [9]. Lee et al. [10] highlighted that acute histologic CA is a risk factor for adverse neonatal outcome in late preterm birth after preterm premature rupture of membranes (PPROM) [10]. Nevertheless, the effects of CA on the neonatal outcome remain under debate, because gestation-independent effects of CA on neonatal outcomes are difficult to assess. Thus in some studies at adjusted analyses for GA, the adverse impact of CA on neonatal outcome is not confirmed [11]. Additionally in many study groups

A21

Vulnerability and “minor” developmental disorders in late preterm infants
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The National Institute of Child Health and Human Development panel reviewed the evidence of increased risk of infants with a gestational age of 34-36 weeks and, in 2006, changed the earlier definition of "near term" to "late preterm (LPT)". LPT infants represent 70% of all the whole population of preterm but while it is known that they are at major risk of mortality and morbidity than term infants, less is known about their development outcome. Samra et al. [1] in 2011 published a review about this topic based on 817 articles but their conclusion was that, due to paucity and heterogeneity of the existing data, there was no clear characterization of the long-term risks. Since then some other interesting papers have been published, quite all in the direction that LPT children have some “minor” problems. In 2013, for example, Vohr B. [2] suggested that LPT infants are at increased risk of neurologic impairments, developmental disabilities, school failure, and behavior and psychiatric problems suggesting also that for each 1 week decrease in gestational age below 39 weeks, there are stepwise increases in adverse outcomes after adjusting for confounders. In 2014, Chan et al. [3] described the negative impact of LPT birth on academic outcomes at 7 years and Brumbaugh et al. [4] the negative impact on executive function at preschool age.

A possible explanation of these results is i) the demonstrated major vulnerability to the brain injury in the late preterm infant respect to the term infant, particularly involving the white matter [5] since that at 34 weeks the late preterm brain weights only 65% of the term brain and ii) the possible role of the extraterine life compared with the intratherine life during the last weeks of gestation.

References
discrimination between ELBW and late preterm infants is not considered. In the future, sufficiently powered cohort studies and well-matched case-control studies will be able to provide useful informations regarding the different outcome between extremely and late preterm infants. An dequate antenatal screening and treatment for CA will improve the prognosis for infants at risk of multiple organ disease as a result of exposure to infection/inflammation before birth [12-14].

References

A23 Early and late onset sepsis in late preterm infants
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Late preterm infants are inherently prone to develop sepsis: 1) Preterm labor and preterm premature rupture of membranes, together accounting for the 80% of the causes of preterm delivery [2], are well known risk factor for early onset sepsis (EOS); in fact, intrapartum antibiotic prophylaxis is widely recommended to prevent group B streptococcal EOS in women undergoing preterm delivery (risk factors approach), and sepsis work-up is frequently performed in late preterm infants [1]. 2) Some degree of immaturity of both innate and adaptive immunity makes late preterm infants at increased risk to develop sepsis [3]. 3) Increase rate of morbidity (respiratory problems, needs for reanimation in delivery room, hyperbilirubinemia, hypoglycemia, and feeding problems) exposes these infants to prolonged hospitalization and invasive procedures favouring nosocomial infections to occur [1].

References

A24 Lung development in the late preterm
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An increasing incidence of moderate-to-late prematurity is observed worldwide (6-7% of all births). Moderate-to-late prematurity is a cause of important mortality and morbidity, even when it is just a few weeks before term gestation [1]. Respiratory distress related to moderate prematurity include delayed neonatal transition to air breathing, respiratory distress resulting from delayed fluid clearance, surfactant deficiency, and pulmonary hypertension. There is increasing evidence to support the hypothesis that preterm delivery, even in the absence of any neonatal respiratory disease, may have adverse effects on subsequent lung growth and development, and that these alterations may persist during the early
years of life. Premature birth interrupts normal utero lung development and results in an early transition from the hypoxic intrauterine environment to a comparatively hyperoxic atmospheric environment [2]. Alveolar walls may be thicker, impairing optimal gas exchange. Colin et al. proposed that preterm birth leads to decreased parenchyma elasticity and subsequent airway tethering, a mechanism by which airway wall compliance keeps surrounding alveoli well opened [3]. The long-term significance of reduced airway function early in life has been emphasized in a longitudinal study involving a large group of non-selected infants who had participated in the Tucson Children’s Respiratory study [4]. In this study, Stein et al. showed that infants whose pulmonary function was in the lowest quintile also had pulmonary function in the lowest quintile throughout the years of follow-up until early adulthood. These findings in a normal unselected population suggest that the level of pulmonary function in early life tracks and changes little with growth. Several authors suggest that deficits in lung function during early life, especially if associated with lower respiratory illnesses, increase the risk of chronic obstructive pulmonary disease in late adult life [5-7]. Of particular importance in this context may be the role played by RSV, which affects most children during their first year of life. The risk of life-threatening RSV infection appears relevant up to a post-conceptional age of 44 weeks. Stein et al. reported that RSV lower respiratory tract illness during the first 3 years of life in a healthy birth cohort was associated with recurrent wheeze up to age 11 [8].

In conclusion altered lung development is a characteristic feature of the late preterm infants and its impact on neonatal and postnatal morbidity needs to be considered.

References


Point-of care lung ultrasound in the NICU: uses and limitations of a new tool

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Pulmonary imaging in the neonatal intensive care unit (NICU) relies traditionally on the conventional chest radiogram. Translating evidences from adult emergency medicine, pediatricians and neonatologists have recently started to apply lung ultrasonography to the critical infant and child with respiratory problems [1]. Because of the high impedance of a normally aerated lung, an ultrasound scan does not render an anatomical image of the organ. However, ultrasounds clearly define the pleural surface with the normal sliding movement. Pleural effusions and lung consolidations can also be reliably diagnosed with ultrasonography. However, ultrasounds penetrating the lung will also generate artifacts (i.e. structures not naturally present in the living that appear as authentic images). These imagery anomalies come from the machine acquisition of the ultrasound beam path through means with markedly different acoustic impedance in close proximity. The horizontal reverberations of the pleural line (aka the A lines - see Figure 1A) and the vertical hyperechoic image departing from the pleura (aka the B lines- see Figure 1B) are commonly seen artifacts.

Real and artefactual images have been combined in disease specific ultrason profiles. Using these profiles, adult emergency physicians have shown that lung ultrasound outperforms conventional radiology in relevant diagnoses such as pleural effusion, pneumonia or pneumothorax. Pediatricians have started to use lung ultrasound with success to their patients affected by pneumonia but also by bronchiolitis [2]. In the NICU, lung ultrasound has found its specific applications, not without controversies [3]. Transient Tachypnea of the Newborn and Respiratory Distress Syndrome have been described with ultrasound profiles that are both highly sensitive and specific [4]. A relevant limitation of chest ultrasound is that surfactant administration gives a persistent white lung image rendering any follow-up essentially unfeasible. Ultrasounds can, however, accurately describe the fluid to air transition after birth and identify those neonates who will fail to adapt to extrauterine life needing respiratory support [5]. In a series of preterm neonates with moderate respiratory distress, recent work by our group shows that chest ultrasound is significantly more accurate than conventional radiograph in predicting the failure of non invasive ventilation [6].

Lung ultrasound is a very promising clinical tool in the NICU whose potential applications are well worth future multicenter trials.

Figure 1(abstract A25) 1A: reverberations of the pleural image (aka A-lines) in the normally aerated lung. 1B: the prevalence of vertical B-lines (in between arrows) has been linked to the interstitial syndrome in the adult and to a progressive aeration of the neonatal lung after birth.
Follow-up of late preterm infants: why, what and who? 
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Late preterm infants (LPI) represent a growing population with own peculiar vulnerabilities; only recently attention has been focused on the impact of late preterm birth on child health, in order to define short and long-term outcomes [1,2]. LPI are physiologically and metabolically immature; they are at higher risk than term infants of developing medical complications, resulting in greater rate of mortality and morbidity not only in the neonatal period, but also during infancy, childhood, adolescence, and through adulthood [2,3]. Increasing evidence shows the association between late-preterm birth and various long-term medical and behavioral morbidities, including cerebral palsy, attention problems and antisocial behavior, as well as lower IQ, impaired cognitive and academic performance at school age. Fetal brain undergoes a dramatic growth and maturation during last four weeks of gestation, and this is probably the most important reason of LPI worse neurodevelopmental outcomes compared to full-term infants [3-5]. Physical development is an other important outcome for LPI; in addition to intraterine growth restriction, LPI may be susceptible to feeding difficulty resulting in poor weight gain and underweight. Since failure to thrive in early infancy may also be associated with adverse cognitive and developmental outcomes, close monitoring of LPI growth pattern is needed [6]. Moreover, late-preterm birth has a negative effect also on maturation of the lungs, interrupting evolution from alveolar saccules to mature alveoli. LPI have been shown to develop early respiratory morbidities more frequently than infants born at term. However, the risk for long-term respiratory problems, such as asthma, has not yet been established in this group of patients [3,7]. Therefore LPI need a multidisciplinary, personalized and effective follow-up care that begins at birth and continues, with varying degrees of surveillance and reflecting individual needs, throughout the lifespan. Pediatricians must play a crucial role by ensuring that appropriate screening and assessments are completed, referrals are made and continuity of care is coordinated. They have to be aware of the major problems that LPI may encounter, providing anticipatory guidance when needed. Pediatricians together with parents, child development specialists, and professionals need to know the possible school underachievement and behavioral problems so that prompt referrals to early intervention services are made [8,9].

Up to now, standardized short and long term follow-up schedule for LPI has not been developed yet; therefore, further research should focus on systematic evaluation of outcomes of LPI, in order to optimize follow-up monitoring of this population of children.

References
Table 1 (abstract A27) Basal characteristics and anthropometric and body composition parameters at term and at 3 months of corrected age of the study population

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Full term infants</th>
<th>Late preterm infants</th>
<th>Very preterm infants</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gestational age (wks)</td>
<td>388 ± 1.4</td>
<td>353 ± 0.75</td>
<td>291.1 ± 2.1</td>
</tr>
<tr>
<td>Birth Weight (g)</td>
<td>3074 ± 409</td>
<td>2946 ± 330</td>
<td>1202 ± 238</td>
</tr>
<tr>
<td>Birth length (cm)</td>
<td>493 ± 2</td>
<td>448 ± 1.7</td>
<td>372.2 ± 3.5</td>
</tr>
<tr>
<td>Birth head circumference (cm)</td>
<td>342.1 ± 1.17</td>
<td>316 ± 1.2</td>
<td>29.07 ± 2.1</td>
</tr>
<tr>
<td>Weight 40 wks (g)</td>
<td>3074 ± 409</td>
<td>3396* ± 390</td>
<td>3015 ± 403</td>
</tr>
<tr>
<td>Fat free mass 40 wks (g)</td>
<td>2794 ± 358</td>
<td>2837° ± 255</td>
<td>2459 ± 320</td>
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<tr>
<td>Fat mass 40 wks (g)</td>
<td>280 ± 106</td>
<td>559# ± 196</td>
<td>565 ± 168</td>
</tr>
<tr>
<td>Weight 3 mo (g)</td>
<td>5978 ± 722</td>
<td>6197° ± 589</td>
<td>5557 ± 669</td>
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<tr>
<td>Fat free mass 3 mo (g)</td>
<td>4345 ± 484</td>
<td>4500° ± 390</td>
<td>4157 ± 461</td>
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<tr>
<td>Fat mass 3 mo (g)</td>
<td>1632 ± 355</td>
<td>1672° ± 348</td>
<td>1405 ± 362</td>
</tr>
</tbody>
</table>

*late preterm vs full term p=0.001
*late preterm vs very preterm p<0.001
#late preterm vs full term p<0.001


A28

The late preterm in low income

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References

Neonatologists generally recognize that late preterm infants face more problems in the immediate newborn period compared with their full-term counterparts. [1,2]. This excess morbidity extends beyond the initial birth hospitalization [3] and the literature recognizes that readmission rates of late preterm infants are 1.5 to 3 times that of term infants [4-7]. In this group of infants, the overwhelming reasons for rehospitalisation are jaundice and feeding problems.

The most widely studied metric of health care utilization in late preterm infants is short-term readmission (the first two weeks) after birth hospitalization. Escober [8] found that late preterm babies with short NICU stays had the highest rehospitalisation rates and in a follow-up study they found that rehospitalisation rates within 2 weeks were higher among late preterm infants who were never admitted to the NICU [4]. Shapiro-Mendoza [7] found that late preterm babies discharged early were at greater risk of neonatal morbidity. They also found that risk factors for subsequent readmissions were birth hospital stay less than 4 days, breastfeeding, Asian/Pacific Islanders, first born infants, and public payers at the time of delivery.

In the United Kingdom, Oddie [9] also noted that late preterm infants had the highest rate of readmission but infectious disease and not jaundice was the leading factor for readmission, which the investigators attributed to a differing approach to management of jaundice in the United Kingdom. Escober [10] examined late rehospitalisation (after the first two weeks) and found 36 week gestation newborns at higher risk for readmission. Paradoxically, babies of 34 and 35 weeks were not at higher risk and this may be explained by more frequently delayed discharge of infants of shorter gestational age. McLaurin [5] also demonstrated increased late rehospitalisation rates in late preterm infants and found that the subset with prolonged birth hospitalizations (≥4 days) had the highest rates of rehospitalisation. Respiratory disease (bronchiolitis and pneumonia) was the most common cause of readmission. The late preterm infant is particularly responsive to the benefits but vulnerable to the risks of early discharge home. Longer length of stay before discharge is protective against readmission but it is not reasonable to prolong the birth hospitalization of newborns who meet criteria for discharge. Care efforts need to be placed to reduce the risk of jaundice and feeding problems in these patients: to avoid mother and infant separation during birth hospitalization, to arrange a follow-up appointment within 48 hours of discharge, to promote and support lactation before and after discharge.

**Conflict of interest:** The author has no conflict of interest to declare.

**References**


Figure 1(abstract A30) Simulation-based training of an ultrasound-guided central venous catheterization. The figure illustrates the ultrasound-guided vessel puncture technique by using phantoms. The trainee visualizes the simulated vessel in transverse scans (short axis) and advances the needle tip (red circle) towards the vessel (green square bracket) during the procedure.

Immunity and nutrition: from research to clinical practice
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Human immune system is a complex and efficient defence system, consisting of an integrated set of cells and chemical mediators, which protects from external insults (chemical, traumatic or infectious), in addition to a series of defensive “modular” responses to protect and modulate immune response inside our body. It is extremely difficult to determine what might be the influence of diet on this system. This is true not only for adults, but can be extended also to every phase of life. To express the correlation between nutrition and immunity in the early stages of an individual’s life it is absolutely essential the knowledge of both subjects, immunity and nutrition, to justify any intervention carried out in this early stage of development. It assumes even a greater value if we talk about newborn infants –preterms especially– maximum expression of an immature system, conditioned in all its forms by any external intervention. Theoretically, the limited opportunities in neonatal nutrition (breast milk or formula) make easier to report specific nutritional effects on any of its functions although in reality it is much more complex.
In newborn a nutritional “programming” can already be affected by prenatal interferences. In order to characterize the correlation between nutritional interventions and development of immunity some interesting clinical trials in developing countries are in progress (eg, ENID: Early Nutrition and Immune Development, The Gambian): this study wants to investigate if some interventions, conducted in pregnant woman and in the early stages of childhood, can modify parameters such as anthropometry at birth and during the first months of life, morbidity, thymus dimension and some biochemical immune responses [1].

About newborn infants, other defence mechanism must be considered: 1) the system of maternal IgG antibodies that fetus receives via the placenta; 2) the system of breast-milk proteins: secretory IgA antibodies which bind the microbes on the infant’s mucosal membranes; lactoferrin which destroy microbes and reduce inflammatory responses, non-absorbed milk oligosaccharides which block attachment of microbes to the infant’s mucosa; other numerous additional proteins in the milk as the anti-secretory factor, which is anti-inflammatory, preventing diarrhoea in infants; 4) the system of micronutrients as zinc, vitamin A, B, C, iron and cytokines [2,3].

In any case breastfeeding and a good nutritional status are essential to give a functionally correct amount of these nutrients. Even the development of adapted formulas is directed to clarify functional actions of nutrients, including the improvement of immune response [4].

References

A32 Probiotics for prevention of necrotizing enterocolitis: a systematic review of current evidences

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Background: The use of probiotics has been proposed to reduce the incidence of necrotizing enterocolitis (NEC) in preterm neonates.

Aims: To systematically review the evidences regarding the use of probiotics in preterm neonates to prevent NEC.

Methods: We revised studies with high level of evidence (randomized clinical trials and meta-analysis). Database: MEDLINE and Pubmed. Search term: Probiotic (AND) Very Low Birth Weight (AND) necrotizing enterocolitis. Limits: Randomized clinical trial (AND) Meta-analysis.

Results: We analyzed 20 manuscripts (13 Randomized clinical trial and 7 Meta-analysis) that were published from 2005 to 2014 and that analyze 3025 neonates. Analysis of the best evidences revealed that probiotics may have beneficial effects in the prevention of NEC, however current studies have failed to control for numerous confounding variables such as breast feeding rates, antibiotic exposure, feeding practices, and environmental cross-contamination. The incidence of NEC (stage > 2) was significantly lowered only in infants weighing 1001 to 1500 g. Thus, there is not enough evidence to support the efficacy of probiotics in extremely low birth-weight infants, and future well-designed studies are needed. Trials performed at institutions with high NEC rates have shown significant benefit from probiotics, while those institutions with low NEC rates have shown limited effects. Multistrain probiotics may be more effective than single-strain products. Currently, data from about 3000 neonates indicates that significant adverse effects of probiotics are rare.

Conclusions: Probiotics appear to be effective in preventing NEC only in specific setting. Although reports of probiotic-related sepsis are limited, caution should be used when considering probiotic supplementation in infants at greatest risk for an impaired mucosal barrier. Policies regarding storage, preparation, distribution, administration and documentation of probiotics to ensure patient safety should be adopted.

A33 Control of breathing

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Late preterm infants have been called “great imposters” [1] because they often appear to be and are therefore treated as term infants, however their brainstem development and neural control of respiration are less mature than in full-term infants. During late gestation there are dramatic developmental changes in the brainstem and forebrain: at 34 gestational weeks the total brain weight is 65% of that at term [2]. The control of lung volume, laryngeal reflexes, upper airways, chemoreceptor activity, coordination of sucking, swallowing, breathing, the incidence of apnea and periodic breathing and the control of heart rate are still developing during late gestation and the degree of maturity of these mechanisms appears to lie on a continuum that extends from more immature infants to after term. Also, these reflexes are influenced by sleep-wake states whose neurobiological development is still evolving. The brainstem is not completely mature even at term, as confirmed by the fact that it’s myelination, the marker of completed neuronal/axonal maturation, is still incomplete at that time. This protracted maturation is not surprising, considering that the neuro-development of the respiratory control and sleep-wake cycle continues into infancy. The few data on control of breathing in late preterm infants indicate that ventilatory responses to CO2 and hypoxia as well as autonomic control of heart rate are not yet mature at 36 weeks PMA. Clinically, late preterm infants have more apnea and periodic breathing than term infants and immature coordination of sucking, swallowing and breathing often delay their ability to feed without episodes of bradycardia, desaturation and even apnea [3]. The incidence of apparent life-threatening events is more common in preterm infants (8-10%) than full-term infants (1% or less). In the Collaborative Home Infant Monitoring Evaluation studies the frequency of conventional and extreme (clinically relevant) events in near term infants is intermediate between preterm infants <34 weeks at birth and full-term infants [4]. Clinical data indicate that late preterm are also predisposed to wheezing in infancy and early childhood although not exposed to excessive supplemental oxygen or ventilator support [5]. Exposure to 21% oxygen could represent premature exposure to hyperoxic environment compared to that in utero, with long-term effects on the still immature conducting airways. Recent data demonstrate that immature human airway smooth muscle are highly sensitive to even short durations of hypoxia, with increased proliferation at moderate levels of oxygen (<60%) but apoptosis at higher levels [6].

References
A34

Acute respiratory morbidity in late preterm infants
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Background: Late preterm (LP) infants (gestational age (GA): 34-36 weeks) are at increased risk of neonatal acute respiratory morbidity compared with term infants (GA: 37-41)[1,2]. The observed rate of acute respiratory morbidity, in a population of about 20,000 LP infants, was 10-12% vs 1.4% of term infants [1]. Transient tachypnea of the newborn (TTN) and respiratory distress syndrome (RDS) are the most common diagnosis, with RDS rate reaching 10.5% in infants born at 34 weeks of GA [1,2]. Major causes of respiratory morbidity in LP are: prematurity and birth by Cesarean Section (CS) [1,3].

Material and methods: We retrospectively studied 830 LP and moderate preterm (MP) infants (GA: 33-36 weeks) admitted to our unit from June 2009 to December 2013. Infants were classified according to GA: 33 weeks (n=129), 34 weeks (n=176), 35 weeks (n=225), 36 weeks (n=300). Clinical charts for each patient were reviewed and main diagnosis recorded.

Results: Twenty-six percent of LP/MP infants (214/830) had an acute respiratory disorder. The most frequent causes were: TTN (n=75; 9.0%); respiratory failure (RF) (n=65; 7.8%) and RDS (n=62; 7.5%); pneumothorax / pneumomediastinum (n=16; 1.9%); pneumonia (n=13; 1.6%); apnea of prematurity (n=5; 0.6%); persistent pulmonary hypertension (n=2; 0.2%). All the 62 infants with RDS were intubated, required mechanical ventilation (1-4 days) and surfactant administration (1-4 doses). The forty-three percent of infants with RDS also had a concomitant diagnosis of infections. The infection rate in infants with RDS was significantly higher than that in other respiratory morbidities (p<0.05). Complete results are reported in Table 1. Of the 62 cases of RDS reported: 60 resolved and 2 deceased (one patient with necrotizing enterocolitis, one patient with disseminated intravascular coagulation).

Conclusions: Acute respiratory morbidity in our unit affects a quarter of LP/MP infants. An important percentage (7.5%) is represented by RDS, that is often associated with infection. Infants born at 34 weeks of GA are the population at higher risk of RDS. Even if rate and severity of acute respiratory morbidity in LP are already described by a number of epidemiological studies, further investigation is needed to better clarify the optimal timing and dose of surfactant administration and to correlate different strategies of respiratory management with long-term respiratory and neurological outcomes. The high infection rate found among infants with RDS and acute respiratory morbidity, emphasizes the importance of a prompt diagnosis and treatment of chorioamnionitis and perinatal infections.

References

Table 1 (abstract A34) Acute respiratory morbidity in LP/MP infants (n= 830)

<table>
<thead>
<tr>
<th>GA* (weeks)</th>
<th>33</th>
<th>34</th>
<th>35</th>
<th>36</th>
<th>TOT</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>129</td>
<td>176</td>
<td>225</td>
<td>300</td>
<td>830</td>
</tr>
<tr>
<td>Respiratory morbidity</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n (%)</td>
<td>60 (46.5)</td>
<td>53 (30.1)</td>
<td>42 (18.7)</td>
<td>59 (19.7)</td>
<td>214 (25.8)</td>
</tr>
<tr>
<td>TTN* b n (%)</td>
<td>14 (10.9)</td>
<td>15 (8.5)</td>
<td>16 (7.1)</td>
<td>30 (10.0)</td>
<td>75 (9.0)</td>
</tr>
<tr>
<td>RF* c n (%)</td>
<td>31 (24.0)</td>
<td>14 (8.0)</td>
<td>12 (5.3)</td>
<td>8 (2.7)</td>
<td>65 (7.8)</td>
</tr>
<tr>
<td>RDS* d n (%)</td>
<td>12 (9.3)</td>
<td>24 (13.6)</td>
<td>12 (5.3)</td>
<td>14 (4.7)</td>
<td>62 (7.5)</td>
</tr>
<tr>
<td>PNX* e n (%)</td>
<td>1 (0.8)</td>
<td>-</td>
<td>8 (3.5)</td>
<td>7 (2.3)</td>
<td>16 (1.9)</td>
</tr>
<tr>
<td>Pneumonia n (%)</td>
<td>1 (0.8)</td>
<td>3 (1.7)</td>
<td>1 (0.4)</td>
<td>8 (2.7)</td>
<td>13 (1.6)</td>
</tr>
<tr>
<td>AOP* f n (%)</td>
<td>3 (2.3)</td>
<td>-</td>
<td>-</td>
<td>2 (0.7)</td>
<td>5 (0.6)</td>
</tr>
<tr>
<td>PPH* g n (%)</td>
<td>-</td>
<td>1 (0.6)</td>
<td>1 (0.4)</td>
<td>-</td>
<td>2 (0.2)</td>
</tr>
<tr>
<td>MAS* h n (%)</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Infection in infants with RDS n (%)</td>
<td>3 (25.0)</td>
<td>9 (37.5)</td>
<td>6 (50.0)</td>
<td>9* (64.3)</td>
<td>27* (43.5)</td>
</tr>
<tr>
<td>Infection in infants with other respiratory morbidity n (%)</td>
<td>8 (16.7)</td>
<td>10 (34.5)</td>
<td>11 (39.7)</td>
<td>14* (31.1)</td>
<td>43* (28.3)</td>
</tr>
</tbody>
</table>

* p<0.05
a gestational age. b transient tachypnea of newborn. c respiratory failure. d respiratory distress syndrome. e pneumothorax / pneumomediastinum. f apnea of prematurity. g persistent pulmonary hypertension. h meconium aspiration syndrome.
The children with the above mentioned clinical conditions, particularly in cases of hospitalization, are more likely to require admission to an intensive care unit and need mechanical ventilation. In addition they have high rates of re-hospitalization for lower respiratory tract infections [5,6]. Therefore, all these categories of infants are likely to benefit from prophylaxis, and have been included in the recommendations. Specific recommendations are provided according to gestational age at birth.

RSV infections occur most frequently during the period between October-March. According to this observation, prophylaxis with Palivizumab is indicated in this 5-6 month long seasonal window of RSV infection. The duration of prophylaxis (up to one year or up to two years of life during the seasonal period) depends on the underlying condition.

Palivizumab is clinically effective; however, the cost is very high. In our opinion strict criteria for patient selection and reduced drug costs would work to improve the cost-effectiveness of the prophylaxis [7].

References

A36 Management of breastfeeding for late preterm infants
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Breast milk is the preferred feeding for all infants. Unfortunately, late preterm infants (LPIs) have a lower rate of feeding at breast and lower expressed breast milk intake than other infants [1]. In fact, literature documents an increased risk of morbidity and even mortality of LPIs, often related to feeding problems, possibly due to an inadequate support of the breastfeeding [2].

Born with low energy stores and high energy demands, LPIs may be sleepier and have more difficulty with latch, suck, and swallow. They are at risk for hypothermia, hypoglycemia, excessive weight loss, dehydration, failure to thrive, kernicterus, and breastfeeding failure. Establishing breastfeeding in LPIs is problematic, due to neonatal physiologic and psychological immaturity and due to maternal risk factors leading to delayed lactogenesis II. Mothers may be obese, experienced a cesarean delivery, have pregnancy induced hypertension, diabetes, or been treated for preterm labor. They easily experience anxiety about milk insufficiency and about separation from their babies for medical problems. Sanitary staff has to encourage the immediate and extended skin-to-skin contact to improve postpartum stabilization of heart rate, respiratory effort, temperature control, metabolic stability, and early breastfeeding, possibly within 1 hour after birth. If the infant is healthy, it’s important to allow rooming in and free access to the breast.

It may be necessary to wake the baby up if he/she does not indicate hunger cues, which is not unusual in LPIs. The infant should be breastfed (even with expressed milk) 8 to 12 times/day. It is important observing the baby feeding at breast and showing the mother techniques to facilitate effective latch and adequate support of the neonate’s head. A nipple shield could be recommended. Pre- post-feeding weight may be helpful to assess milk transfer, because a supplementation with small quantities of maternal expressed milk, donor human milk, or formula may be necessary. If supplementing, the mother should pump milk after breastfeeding, 6 to 8 times/day to establish and maintain milk supply [3].

LPIs developing complications are often discharged early, after successful transition to extra-uterine environment, but before lactogenesis II is fully established. Before discharge, adequate milk intake should be documented by feeding volume or by thriving. One or two days after discharge, a follow up to check weight, feeding ability and jaundice is recommended.

In conclusion we may say that breastfeeding LPIs is possible, but to achieve this target, an adequate maternal support and a regular neonatal monitoring is required [4].

Competing interests: The authors declare that they have no competing interests.

References

A37 Formula feeding for late-preterm infants
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Preterm birth interrupts physiological foetal development, leading to various degrees of immaturity according to the gestational age at which the infant is born [1]. Since 2005, the precise definition of “near-term” infants has been replaced with “late-preterm”, which includes infants born between 34/0/7 and 36/6/7 weeks of gestation [2]. Late-preterm infants are at higher risk than term infants of developing medical complications that result in higher rates of mortality and morbidity [3], including thermal instability, respiratory problems, hypoglycaemia, jaundice, and feeding problems. Breastfeeding is the first nutritional choice for all infants, especially for those born preterm. The establishment of successful breastfeeding in late-preterm infants is usually problematic, as late-preterm infants can be sleepier, have less muscular strength and more difficulty with latch, suck and swallow than term infants [4]. For this reason, health-care providers should implement specific strategies aimed at anticipate, identify promptly, and manage breastfeeding problems that the late-preterm infant and mother can experience. However, when exclusive breastfeeding does not guarantee adequate nutrition, supplements might be advisable. Nutritional requirements of late-preterm infants are currently derived from speculations on foetal growth and requirements of preterm and term infants, while specific data on nutritional needs of this population are scarce. There is currently no consensus on nutritional feeding of late-preterm infants who would benefit most of a high-protein diet, such as that proposed for “micropreterm” infants [5], or of a low-protein diet, such as that recommended for full-term infants. Some studies suggest that the provision of extra protein and energy could reduce weight loss and increase growth velocity [6], thus decreasing the risk for dehydration and hospital readmission. However, it is important to note that growth rate during late gestation decreases dramatically, and it is likely that protein and energy...
requirements for infants born during this period wouldn't be as high as those of very preterm infants [7].

Current guidelines recommend the supplementation with essential nutrients also for late-preterm infants. Actually, it has been shown that supplementation with LC-PUFAs improves visual acuity and cognitive development in infants 30-37 weeks gestation [8].

The best nutritional approach to late-preterm infants still needs to be determined. Human milk's benefits are undoubted; however, caregivers have to adequately support the establishment of successful breastfeeding and also identify those cases where some supplementation is needed.

Further studies will have to clarify whether all late-preterm infants, or only a subgroup such as small-for-gestational-age infants, could benefit from formulas with high energy and protein content.

References


A38

Developmental haemostasis in moderate and late preterm infants

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Introduction: The term "developmental haemostasis" was first coined by Maureen Andrews to describe the age-related physiological changes of the coagulation system during childhood.[1] Given the age-dependent specificity of haemostasis, the evaluation and the interpretation of coagulation assays in newborns may present diagnostic difficulties and appropriate reference ranges for the diagnosis and management of coagulopathies in moderate and late preterm infants are needed.

Age-related changes in the coagulation plasma proteins: The haemostatic system is a dynamic evolving process that is age-dependent. At birth, plasma concentrations of vitamin K-dependent and contact factors (F) are decreased if compared with adult levels [2]. During the first 6 months of life, they gradually increase to values approaching adult levels. [2] These changes in protein levels lead to corresponding changes in global tests of coagulation such as the Prothrombin Time and the Activated Partial Thromboplastin Time. Plasma concentrations of fibrinogen, FV, FVIII, FXIII and von Willebrand are not decreased at birth [2]. In addition, plasma concentrations of antithrombin, protein C and protein S are low at birth, and they reach adult levels at about 6-12 months of life. [2] In the fibrinolytic system, plasma concentrations of plasminogen are decreased at birth, whereas tissue plasminogen activator and plasminogen activator inhibitor are increased [2]. These postnatal changes in the coagulation system, observed both in term and preterm neonates, are functionally balanced, suggesting a normal haemostasis during early infancy in healthy conditions.

Reference ranges of coagulation tests in moderate and late preterm infants: Considering the developmental changes of coagulation proteins in term and preterm neonates, specific age-related reference ranges are necessary for an accurate diagnosis and management of neonatal coagulation disorders. In table 1 reference ranges for coagulation assays obtained in moderate and late preterm neonates are summarized [3]. Since coagulation assays are analyzer and reagent dependent, laboratories should develop specific reference ranges to their own testing systems [4].

New diagnostic assays: Thromboelastography and the measurement of thrombin generation are methods that provide a global assessment of hemostasis. Recently, the use of these assays has been reported in neonates and the results suggest that these methods may offer advantages for the evaluation of developmental hemostasis. Thrombo- elastography, in particular, may be less sensitive to age-related changes of coagulation protein [5,6] However, the introduction of these methods into clinical practice of neonatal medicine should be based on larger studies confirming the predictive value of the assays.

References


Table 1 (abstract A38) Reference values for coagulation tests in healthy moderate and late preterm neonates (30 to 36 weeks gestation) during the first 6 months of life

<table>
<thead>
<tr>
<th>Postnatal Age</th>
<th>PT (s)</th>
<th>APTT (s)</th>
<th>Fibrinogen (g/L)</th>
<th>AT-III (U/mL)</th>
<th>Protein C (U/mL)</th>
<th>Protein S (U/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 1</td>
<td>130</td>
<td>53.6</td>
<td>2.43</td>
<td>0.38</td>
<td>0.28</td>
<td>0.26</td>
</tr>
<tr>
<td>(10.6-16.2)</td>
<td>(27.5-79.4)</td>
<td>(1.50-3.73)</td>
<td>(0.14-0.62)</td>
<td>(0.12-0.44)</td>
<td>(0.14-0.38)</td>
<td></td>
</tr>
<tr>
<td>Day 5</td>
<td>125</td>
<td>50.5</td>
<td>2.80</td>
<td>0.56</td>
<td>0.31</td>
<td>0.37</td>
</tr>
<tr>
<td>(10.0-15.3)</td>
<td>(296-741)</td>
<td>(1.60-4.18)</td>
<td>(0.30-0.82)</td>
<td>(0.11-0.51)</td>
<td>(0.13-0.61)</td>
<td></td>
</tr>
<tr>
<td>Day 30</td>
<td>118</td>
<td>44.7</td>
<td>2.54</td>
<td>0.59</td>
<td>0.37</td>
<td>0.37</td>
</tr>
<tr>
<td>(10.0-13.6)</td>
<td>(269-625)</td>
<td>(1.50-4.14)</td>
<td>(0.37-0.81)</td>
<td>(0.15-0.59)</td>
<td>(0.22-0.90)</td>
<td></td>
</tr>
<tr>
<td>Day 90</td>
<td>123</td>
<td>39.5</td>
<td>2.46</td>
<td>0.83</td>
<td>0.45</td>
<td>0.76</td>
</tr>
<tr>
<td>(10.0-14.6)</td>
<td>(283-50.7)</td>
<td>(1.50-3.52)</td>
<td>(0.45-1.21)</td>
<td>(0.23-0.67)</td>
<td>(0.40-1.12)</td>
<td></td>
</tr>
<tr>
<td>Day 180</td>
<td>125</td>
<td>37.5</td>
<td>2.28</td>
<td>0.90</td>
<td>0.57</td>
<td>0.82</td>
</tr>
<tr>
<td>(10.0-15.0)</td>
<td>(217-53.3)</td>
<td>(1.50-3.60)</td>
<td>(0.52-1.28)</td>
<td>(0.31-0.83)</td>
<td>(0.44-1.20)</td>
<td></td>
</tr>
</tbody>
</table>

All values are given as a mean followed by lower and upper limit (95% of confidence interval). From Andrew M et al., modified [3].
Iron is essential for the Central Nervous System development, i.e. mielination process and cellular differentiation as well as correct functioning of neurotransmitters [1]. Preterm infants show an increased risk of iron deficiency (ID) since 80% of the iron storage at birth is accumulated during the third trimester of pregnancy. Rapid child growth and elevated red cell turn over in the neonatal period may exhaust iron storage after two months of age [2]. ID risk is greater in the breast-fed babies, since maternal milk does not contain an amount of iron sufficient to demands. However, ID prevalence equal to 14%, between the fourth and the eighth month of age [3], is also reported in the preterm infants who are nourished with milk formulas enriched with iron. Referred long-lasting effects of ID in infancy include reduced cognitive functions, motor performances and social-emotional development, as well as persisting neurophysiologic abnormalities [1]. As a consequence early iron supplementation is recommended for preterm and very-low-birth-weight infants [3]. Healthy late-preterm infants are often treated with the same modalities that term neonates. For these infants we lack strong evidence based recommendations about supplementation of iron, doses, time of beginning as well as duration of treatment. The RCT evidence to date does not suggest a definite threshold of birth-weight or gestational age at which iron supplementation becomes beneficial. Two methodologically sound trials suggest a benefit even for marginally low-birth-weight infants, whether term or preterm [4]. As recently reported, marginally low-birth-weight neonates showed a high prevalence of ID and Iron Deficiency Anemia (IDA) when evaluated at the age of six months, especially in the case of exclusive breast feeding to age six weeks [5]. Maternal supplementation lowered ID and IDA prevalence without adverse effects. In conclusion, despite the amount of studies concerning ID in infancy, there is still a paucity of evidence about the effects of iron deficiency/overload with respect to growth, morbidity and neurodevelopmental outcomes in the different categories of neonates, as well as about the reliability of the presently available iron metabolism markers.

References

Immune development in late preterm neonates
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Several recent studies have underlined that late preterm infants have a significantly increased risk of infection and sepsis, (1-3) mainly related to problems of adaptation from intra- to extra-uterine life of the immune defense mechanisms. Indeed, both the innate (natural, non specific) and the adaptive (acquired, specific) immune systems are incompletely developed at birth, the more preterm the neonate, the more severe and prolonged the immunodeficiency [4,5]. T lymphocytes response to mitogens is poor, and T and B lymphocytes are immature: higher percentage of CD4+ T lymphocytes and lower of CD8+ cells, with a gradual decline with age of the CD4+/CD8+ ratio, and predominant naive phenotype with elevated percentages of CD4+/CD45RA+ T cells; in addition, cytokine production is reduced and Th1-like response inadequate. The immaturity of lymphocytes and of antigen presenting cells are responsible for the marked deficiency of antibody production; also, levels of IgG are low in late preterm infants because transplacental passage from the mother mostly occurs during the last trimester of gestation; therefore, these neonates may lack the protection ensured by maternal derived pathogen-specific IgG. The inability to produce adequate amounts of hematopoietic growth factors, particularly G- and GM-CSF, and the reduced neutrophil, complement and natural killer cell activity, may further amplify the neonatal impairment of immune defenses. The combined neonatal deficiency of immunoglobulin, complement and neutrophil activity results in increased susceptibility to systemic infections from encapsulated pathogens, such as Group B Streptococcus, Staphylococci and Klebsiella, that require opsonization for efficient phagocytosis and killing. The immaturity of pattern recognition receptors (PRR) response to pathogen-associated molecular patterns (PAMP), in particular the impaired TLR4 (Toll Like Receptor) signaling, [1] may contribute to the late preterm vulnerability to Gram-negative bacteria [6].

It should be noted, however, that neonatal T cells are capable to raise type 1 and 2 immune responses upon appropriate stimulus. Neonatal immunization does not generally lead to rapid antibody responses, however, it may result in an efficient immunologic priming which can act as a basis for future responses. It is therefore possible to induce early protection by immunization at birth [7]. Finally, to mitigate detrimental consequences of immunodeficiency in late preterm infants, it is of paramount importance to maintain the mother-newborn protective immunological link by ensuring the host of protective components provided by human milk [8].

References

Erythropoietin use in the newborn
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The first descriptions of blood transfusion in neonates date back to the nineteenth century. Time is past but uncertainties still remain considerable on optimal red blood cell (RBC) transfusion use in an era of evidence-based medicine. The need for RBC transfusion in critically ill neonates is differently judged among clinicians due to a lack of an agreement on measures of the need for transfusion. However some studies have shown an association between preterm infant morbidities, such as necrotizing enterocolitis and significant intracranial hemorrhage, with transfusions. The erythropoietin (EPO) use might prove clinically important. Physiologically in all newborns there is a progressive fall in hemoglobin concentrations to the nadir at about 8–12 weeks of life. The nadir is even lower and sooner in preterm
neonates. This anemia of prematurity is the consequence of multiple factors, some are physiological processes as vulnerability of red cells to oxidative damage, reduced red cell lifespan when compared to the adult, lower erythropoietin (EPO) response to anemia than in older ages, increased requirements due to the postnatal growth; some are non-physiological processes as iatrogenic blood sampling, inter-current illnesses and sepsis. All these factors are responsible for low plasma EPO concentration in preterm newborns. This provides a rationale for the use of EPO in prophylaxis or treatment of the anemia. EPO has been used clinically for more than 20 years and many randomized clinical trials demonstrated that EPO successfully stimulates erythropoiesis and decrease the need of transfusion in anemic adults and children with end-stage renal disease or cancer. Differently in preterm newborns, the EPO treatment has demonstrated varied success in decreasing the total number and volume of transfusions. There are not clear evidences from high quality trials to define the absolute requirement and benefit for neonatal RBC transfusion. A recent Cochrane metaanalysis performed by Ohlsson A and Aher S.M. (1) to assess the effectiveness and safety of early initiation of EPO or darbepoetin in reducing RBC transfusions in preterm and/or low birth weight infants, concludes that the small reductions in RBC transfusion observed after EPO treatment are of limited clinical importance. In contrast the possibly increased risk of ROP, does not recommend the administration of EPO. Darbepoetin requires further study for definitive conclusions.

Reference

### A42

"Crack babies": the management protocol

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**Italian Journal of Pediatrics** 2014, 40(Suppl 2):A42

**Introduction:** During the pregnancy maternal drugs use represent an important socio medical issue for their children. In the USA, 10% of women takes drugs during pregnancy: 1-2% use heroin, 3-4% cocaine and less than 1% cannabinoids [1]. The phenomenon is increasing and the country and the neonatal divisions need new management protocols. In Italy children of a mother drug addict born as late preterm are the 17 - 29%. The “crack babies” are children exposed to drugs during the pregnancy; we can already define them drug addicts. They may show intrauterine (choking, infection, malformations), neonatal (withdrawal symptoms, prematurity, respiratory distress syndrome, growth restriction neonatal hyperbilirubinemia), and postnatal complications (delay in psychomotor, deficit in language, SIDS, learning disabilities, difficulties in concentration, instability etc)[2].

In some countries several projects about essential care have been elaborated and realized. In Campania people involved in this field are pediatricians, child psychiatrists, psychologists, teachers judges, social assistants, without a real defined cooperation.

**Network:** Protocol provides hospital stay of drug addict woman during the labour to guarantee assistance and monitoring of the mother and the child [3]. For this reason it has been created a sociology service to coordinate the network. System facilities are: the Ser.T (services for drug addicts) to help the mother, a territorial social office which provides to the child, the Minor’s court, the hospital for the psychological and physiological children development (if he was born with Newborn Abstinence Syndrome) and the obstetrical service.

**Conclusion:** Our protocol has two main targets:

- Safe the health, the security and the wellness of the child even after the discharge trough periodical check-up of follow-up (DH);
- Facilitate the development of relationship between mother and child to reduce the necessity of Minor’s court interventions.

Only in this way it will be possible to realize a real and integrated takeover of the mother-child entity.

**References**

### A43

"A hug of cuddles"

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**Italian Journal of Pediatrics** 2014, 40(Suppl 2):A43

**Venue:** 1st level Nursery, LUIGI SACCO HOSPITAL MILAN, 1250 births per year.

**Late Preterm (LP) : 8%**

**Target:** Create procedures cannot break the creation of bonding: the process that contribute to form the bond between parents and children necessary to reach a mutual harmony. In the LP this interactive dance where you learn to recognize, is less rigidly determined and you have to start it with a well-defined Care program.

**Participants:** Late preterm infants, parents, and professionals who are trained with periodic refresher course.

**Project:** Smooth approach with new parents that are made immediately present to the new born babies. They are supported and accompanied in this path that leads to the creation of a unique and indissoluble bond like that with their children.

**Introduction**

Presentation of the structure, the incubator and equipment that monitor the baby. Support in the first contact between parents and child. Kangaroo therapy at different times and different way depending on the clinical condition of the child.

**Ad hoc preparation of the room in order to involve all the senses of the newborn.**

Involvement of parents in the care of the newborn LP: postural care, nest, wrapping, holding, hygiene care, serving meals, breast feeding, even if the baby is in the incubator. Course with parents, aimed to autonomy.

**Planned Hospital discharge**

**Massage Course**

**Results:** The impressions collected at discharge and beyond, demonstrate how this project is hugely important, not only for children but also for the well-being and balance of the newly couples, who often find themselves terrified and frightened by their child premature birth and they just need to be supported and accompanied in this path that leads to the creation of a unique and indissoluble bond like that with their children.

### A44

Clinical care issues between safety and quality of care for the late preterm: “The Future of Nursing in Neonatology”

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**Italian Journal of Pediatrics** 2014, 40(Suppl 2):A44

**Neonatology and pediatric nursing in the world and in Europe:**

Professional standards of the American and Canadian companies stress the importance of a minimum number of “experts” nurses of neonatology or pediatrics in the reality where infants and children are assisted.

Also the document about PNAE of Education stresses how training programs for the general nursing in many countries don’t give the necessary preparation to nurses in this area.

**The professional practice of neonatology and pediatric area in Italy:**

The Pediatric Nurse in Italy is the figure that the DM 70/1997 has identified as the one responsible of the nursing care to individuals in growth.

These are flanked by the generalist nurses with specialized annual training.

But also the general nurse according to DM 793/1994 can assist babies and children, as he’s generally enabled to the nursing care of individuals of all ages.

Even the Midwife is enabled to care babies and also in delivery room.
The collaboration between different professionals, from obstetric to neonatal care area, is necessary in order to ensure an interdisciplinary and highly specialized standard of care.

**Materials and methods:** After approbation of the Hospital Committee we planned a scheduled care process that provides:

- Early stage of training: acquisition of care pathways encoded for every professional involved, including participation in training specialized courses and simulation cases;
- The establishment of a multidisciplinary study group that defines the indicators and the standard of result to be achieved, including the emotional and psychological aspect of the new mother and the identification of the role of the various members of the team;
- Strict planning and management of human resources and equipment available, listed in detail and sequence of use, updated with the latest national legislative directives;
- Estimates of possible variables and complications; identification of properly safety systems and alternative recommendations to be observed, not covered by the standard procedure;
- Insertion of a self-assessment system in order to check the feasibility and the adherence to the protocol.

**Results:** We performed a procedural planning that ensures the standardization and uniformity of the nursing of the multiple late preterm newborn, managing the collaboration between several professionals in order to minimize adverse and unexpected events.

**Conclusions:** The quality of the health care level provided depends on the cooperation of the professionals. The management of the team work allows to ensure an optimal and personalized care level from the medically assisted reproduction center to the neonatal intensive care unit, following the updated scientific evidence and the humanization of birth route.

**References**


**A46**

Nursing surgery in late preterm
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Nursing surgery born for an organizational and strategic choice which allowed us to create a link whist hospital and territorial children’s doctor, going to fill the lack of assistance during the period of hospital discharge and first visit of specialist for children’s. Our aims are essentially two: see to peaceful back home baby and their family, insure a continuity of care, continuing the technical educational intervention started during hospitalization, increasing the confidence in themselves in this new role. This anamnestic assessment carried out together with the parents enables us to empathize with the parent to allow itself to expose their doubts and questions. The cases to which addressed a nurse’s control are: weight loss >10%, maternal-fetal incompatibility group, deficit of G6PDH (Glucose-6-phosphate dehydrogenase), values predischarge of bilirubins in the intermediate zone of risk such as describe of AAP guidelines, baby with perinatal risk factors of infection, preterm infants, SGA (Small for Gestational Age) infants, infants from families at risk (drug addiction, alcoholism, poor socio-economic conditions, migrant families without residence permits) , red highlights not executed due to technical problems at birth (eyelids tightened; doubt audiological screening at birth, any other baby who, for whatever reason, the physician who performs the discharge decides to revalue in post discharge. Access to the surgery is by reservation CUP that takes place directly at the discharge of the baby and is closely related to the hospital stay and do not in any way replace the first visit to the pediatrician to be made within 7° to 10° days after discharge.

**A47**

Implementing the family-centered care model, parents’ satisfaction and experiences in neonatology
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**Background:** The quality of family-centered care (FCC) in Neonatal Intensive Care Unit (NICU) is often assessed through Parental satisfaction (PS). Empathic-N, a validated questionnaire to evaluate PS in NICU, was recently developed in the Netherlands [1].To our knowledge similar instruments have not yet been used in Italy. The aim of this project is to translate the 57-item Empathic-N questionnaire and to develop and adapted Italian version for post-NICU (Empathic-SN) taking the Italian cultural adaptation into account, and to test their psychometric validity.

**Materials and methods:** The translation process followed a structured method including forward and backward translation [2]. The psychometric validation of both the Empathic-N and the Empathic-SN questionnaires is being performed by administering the questionnaires...
to parents of newborns discharged from 9 NICUs and post-NICUs across Italy. Ethical approval is granted by the Bambino Gesù Children’s Hospital. Written informed consent forms are collected.

Results: 150 questionnaires from NICU and 150 from post-NICU are being collected. Preliminary analyses showed a positive correlation between the questionnaire items and the overall satisfaction indicators. Reaches scores ranged from 4.1 to 5.9 for the Empathic-N and from 4.2 to 5.7 for the Empathic-SN, on a 1-to-6 Likert scale. Results from Cronbach’s alpha coefficients attested the reliability of the scale. Thematic analysis of the open answers identified 385 quotations, coded into seven major themes, expressing parents’ experiences. Generally, a good overall parents’ satisfaction is showed. Further descriptive statistical analysis will be performed on the complete sample.

Conclusion: Validity and reliability of the Italian version of the questionnaires assessed by psychometric testing is expected. The Empathic-N and Empathic-SN questionnaires, or their further versions, would constitute important tools to assess the actual quality of FCC in Italian NICUs and post-NICUs and to set the baseline for improvement interventions.

Acknowledgements: The Italian Empathic-N Study Group, was as follows: Luca Di Sarra, Catholic University of Rome; Gina Ancora, Sandra Lazzari, Hospital of Rimini; Marilena Galeazzo, Elisabetta Lolli, University Hospital of Padova; Enrica Luca, Buzzi Children’s Hospital, Milan; Silvia Prunecchi, Meyer Children’s Hospital of Florence; Angela Ragni, Bambino Gesù Children’s Hospital IRCCS Rome, Rosanna Bruno, Antonella Raimondi, San Carlo Hospital, Potenza; Liliana Vagliano, Serena Rovei, Sant’Anna University Hospital, Turin; Loredana Bonafede, Anna Marotta, San Eugenio Hospital, Rome.

The contribution of the Centre of Excellence for Nursing Scholarship for the funding to this project is acknowledged.

References

A48

The primary nursing implementation in late preterm R Oringaretto, F Villardino, F Faggion, S Tossatti, A Croso
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Background: The Primary Nursing is a nursing care policy based upon an individualized patient-nurse relationship, with a particular attention to the communication and the continuity of the health care. This model has been implemented in all the structures of the ASL of Biella in 2013. The nurse becomes the coordinator of the patient’s assistance. The Primary Nursing objective is to develop the principles of self-care and empowerment through taking care of the person and the continuity of care. The patient care is committed to a specific nurse (primary nurse) who is responsible for him during the hospitalisation.

The primary nurse, planning a personalized and continuous assistance in cooperation with the patient, the family and the health staff, is the point of reference, not only for the patient and the family, but also for the health team.

Objective: The introduction of the Primary Nursing policy in the Neonatal Intensive Care Unit aimed at:

1) increasing the satisfaction:
   - of patients and families who are better informed and supported by an individualized and qualified assistance
   - of nurses because the increase responsibility raises their competence and the ability to cooperate in the health staff

2) developing the continuity of the health care by increasing the parent’s self government in the late preterm care and the quality of nursing management

Material and methods: The method chosen for the care policy trial can be divided in two parts: the general area; the paediatric nurses take part to the different steps of the hospital health care strategy defined by the guidelines of the literature (FAD residential practical training)

the specific area with the achievement of nursing plans, tools and monitoring systems for the application and the evaluation of the policy in the specific area

Results: We analysed 79 medical records, that is all the newborns discharged from 1st September 2013 to 31st March 2014. Outcomes highlight that 64.6% of the patients have been taken in care by a PN; that 39.2% of prescriptions have been planned; the 53% of the latter has been followed by the associated nurses. Conflicts between nurses have been observed in only 3.9% of the cases.

Conclusions: In the analysis of data, we notice a constant improvement of outcomes in the nursing care plan compiling. We intend to propose a new period of data collection in 2015.
Data on outcomes of CCHD specifically in late preterm infants are exceedingly scarce.

The preterm newborn with associated complex CHD presents many intricate problems to clinicians who take care (neonatologist, cardiologist, cardiothoracic surgeon). Therapies used for the preterm neonate without heart disease frequently need to be altered in the presence of heart disease and those needed for management of heart disease may need to be altered because of prematurity.

The population of newborn born preterm is at higher risk for postoperative death and short and long term complications than term newborn with the same CHD and the causes of this are multifactorial. Technical issues related to small cardiac structure, immaturity of other organ systems, decreased nutritional and cardiac reserve, increased risks of bleeding, abnormal chest wall mechanics after sternotomy can all together account for this epidemiologic data. In past years these findings were related in particular to low-birth weight infants and conventional management was oriented to await a threshold weight in order to reduce bypass-related morbidities. From 1990 rates of LPB have risen and now account for 75% of all preterm births. Whether late preterm infants with CHD, who may be only marginally more immature than their term counterparts, remain at risk for adverse outcome is unclear. Some recent papers do demonstrate the independent effect of LBW on mortality and morbidity if a CHD is present and this issue emerge as an important factor for a correct counseling. Natarajan have observed that the weight at surgical intervention was significantly lower and age higher in the late preterm infants compared to those delivered at term. Late preterm infants had significantly higher rates of NEC and seizures, with a greater risk of supplemental oxygen and tube feeding at discharge. Costello have examined mortality and morbidity stratified by gestational age, reporting for LBW group with CHD an hospital mortality rate of 16.4% compared to 2.6-8% in the term group. The exact mechanism of this vulnerability remains unclear although functional immaturity of the lung and the brain are plausible aetiologies. Altered intrinsic cardiac mechanism could play a role in adverse outcome of late preterm with CHD. Gestational age at delivery can be a risk factor over which clinicians might have some control. Before birth the challenge is planning the time and the place for the delivery of a foetus with CHD. After birth the challenge is not waiting for obtain an arbitrary correct weight for surgery but working in a complex team to discuss each case in order to maximize outcome.

Domande inerenti la relazione del Dott. Stefano Fiocchi a complex team to discuss each case in order to maximize outcome.

Domande inerenti la relazione del Dott. Stefano Fiocchi a complex team to discuss each case in order to maximize outcome.

Considerations in the late-preterm newborn with cardiac problems: Una cardiopatia congenita critica è:

- a) Quasi sempre mortale
- b) se esiste una osturazione “critica” agli eflussi ventricolari
c) se richiede l’uso delle prostaglandine
d) se richiede intervento chirurgico nel primo mese di vita

Qual’è il peso ottimale per la correzione chirurgica di una cardiopatia congenita critica?

- a) Non esiste un peso “ottimale”
- b) > 2000 gr
- c) > 2500 gr
d) > 3000 gr

Il rischio di mortalità neonatale nel late preterm affetto da cardiopatia congenita critica è:

- a) 8%
- b) < 5%
c) 25-30%
d) 15-20%

La aumentata vulnerabilità del late preterm con cardiopatia congenita si associa a:

- a) Ventilazione prolungata
- b) Prolungato uso delle prostaglandine
c) Presenza di altre malformazioni associate
d) Tutte le precedenti

### A51

**Treatment of pulmonary hypertension**

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The therapeutic approach to the management of pulmonary hypertension (PH) is based on strategies to decrease pulmonary vascular resistance (PVR) whilst ensuring optimal cardiorespiratory support to improve oxygenation. Inhaled nitric oxide (INO) remains the mainstay of treatment for this condition. As an inhaled agent it reaches the alveolar space and diffuses into the vascular smooth muscle of the adjacent pulmonary arteries where it causes vasodilation by increasing guanosine monophosphate (cGMP) levels without affecting systemic vascular tone. Although INO significantly reduces the need for extracorporeal membrane oxygenation, almost 25-40% of INO-treated infants are considered INO non-responders.

A complementary vasodilatory pathway in the lung is mediated by cyclic adenosine monophosphate (cAMP); prostacyclin stimulates adenyl cyclase in vascular smooth muscle cells and causes an increase in intracellular cAMP and vasodilation of the systemic and pulmonary circulatory systems. If given as an inhaled drug the vasodilatory effects of prostacyclin tend to be limited to the pulmonary circulation, making this strategy appealing when acute pulmonary vasodilation is needed [1]. Inhibition of the cGMP-degrading phosphodiesterase (PDE5) and inhibition of the cAMP-degrading phosphodiesterase (PDE3) are two other promising therapies. Sildenafil is a PDE5 inhibitor, the predominant PDE isoform in the lung responsible for the breakdown of cGMP. It acts by enhancing NO-mediated vasodilation and may facilitate INO discontinuation in infants with critical illness[2]. Milrinone is a PDE3 inhibitor with inotrophic and vasodilatory effects; it improves the left ventricular cardiac function both directly and by reducing systemic afterload and exerts also important effects on the pulmonary vasculature by reducing PVR. It may be a plausible agent for treating patients with PH and impaired myocardial function [3].

One of the most potent vasoconstrictors described in the pulmonary vasculature is Endothelin-1 (ET-1). Inhibition of ET-1 mediated vasoconstriction could be achieved by administration of an endothelin receptor antagonist (Bosentan). Bosentan lowers pulmonary artery pressure and PVR in children with diverse causes of PH and may improve oxygenation in neonates with persistent pulmonary hypertension; it has also been successfully used as an adjunctive treatment for children receiving long-term prostacyclin therapy.

**Conclusion:** Although a great deal of progress has been made in recent decades in PH treatment, it remains a devastating illness that requires further studies to adapt the therapy to pediatric lung and its peculiar vasculature.

**References**


### A52

**Non-pharmacological intervention for neonatal pain control**

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Italian Journal of Pediatrics 2014, 40(Suppl 2)A52
Background: Acute pain and distress during medical procedures are commonplace in newborn admitted to Intensive Care Unit and can have detrimental effects, if uncontrolled. Accumulating evidence suggests that neonates, as older children, could benefit of non pharmacological interventions (NPIs) to relieve mild to moderate pain, anxiety and discomfort from minor invasive procedures [1]. These therapies include non nutritive sucking (NNS) both with and without sucrose, swaddling, positioning, facilitated tucking (FT), kangaroo care or skin to skin contact (KMC), multi-sensorial stimulation (SS) and music therapy.

Material and methods: To assess efficacy of NPIs for acute procedural pain in neonate, a literature search covered the period 2000-2014 via Medline and Cochrane Library database, was undertaken. Inclusion criteria were preterm and newborn, involved in randomized controlled or crossover trial. Pain reactivity was described in term of physiological parameters (heart rate, oxygen saturation) behavioral indicators (duration of first cry and total crying time) and validated unidimensional, multidimensional and/or composite pain scores such as PIPP, NIPS, DAN, NFCS etc. Two independent reviewers extracted data and methodological quality was assessed, according with GRADE system.

Results: Nineteen Randomized Controlled Trials and twelve meta-analysis and systematic reviews were taken in consideration. The efficacy of NPIs in relieving pain and distress from skin-breaking procedures has been demonstrated mostly in heel prick and venipuncture (Table 1). There are sufficient evidence that supports efficacy in reducing pain-relating behaviors for NNS, swaddling and FT in preterm and term neonates. [1] KMC appears to be effective, as measured by composite pain score including physiological and behavioral indicators and safe for single painful procedures, alone or combined with other NPIs [2]. Small volumes of 24% sucrose with or without NNS reduced efficiently behavioral expressions of pain and crying time, as well as PIPP scores [3]. Also expressed human milk or breastfeeding, if available, should be used to alleviate procedural pain [4], as well as 20-30% glucose [5]. SS is more effective than glucose and sucking, but there are no studies comparing SS and standard sucrose 24% and NNS with pacifier, which actually is the standard of care for heel lance [6]. Limited evidence suggests that Music Therapy may be beneficial primarily for measures of behavior and pain, however the heterogeneity of the study preclude definitive conclusions [7].

Conclusions: As the efficacy of the majority of NPIs is clearly demonstrated in preterm and neonate, they should be considered for inclusion in a graduated multidisciplinary algorithm for neonatal pain management.

References

Table 1 (abstract A52) Efficacy of environmental, behavioral and non-pharmacological strategies on pain reactivity in newborn

<table>
<thead>
<tr>
<th>Behavioral, cognitive and contextual interventions</th>
<th>Level of evidence</th>
<th>Grade of Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-nutritive sucking (NNS): placing a pacifier or non-lactating nipple in an infant’s mouth to promote sucking behavior with no breast or formula milk to provide nourishment.</td>
<td>1 1</td>
<td>Strong</td>
</tr>
<tr>
<td>Facilitated tucking: holding the arms and legs in a flexed position</td>
<td>1 1</td>
<td>3 ET Suctioning</td>
</tr>
<tr>
<td>Swaddling: wrapping securely the neonate in a sheet/blanket</td>
<td>1 1</td>
<td>-</td>
</tr>
<tr>
<td>Positioning: laying the neonate supine</td>
<td>3 3</td>
<td>-</td>
</tr>
<tr>
<td>Maternal touching and holding: cradling the baby in the mother’s arms</td>
<td>3 3</td>
<td>-</td>
</tr>
<tr>
<td>Environmental care controlling/ reducing light and noise, clustering care etc.</td>
<td>3 3</td>
<td>-</td>
</tr>
<tr>
<td>Individualized developmental care e.g. limiting environmental stimuli, lateral positioning, using supportive bedding, monitoring behavioural clues, respecting circadian rhythms</td>
<td>- -</td>
<td>3 ROP screening</td>
</tr>
<tr>
<td>Skin to skin or Kangaroo Mother Care an infants is placed on their care-giver’s bare chest during a painful procedure or for soothing after a painful procedure</td>
<td>1 2</td>
<td>2 IM</td>
</tr>
<tr>
<td>Sensory saturation: multiple sensorial stimulation at gustatory, auditory, olfactory and tactile level</td>
<td>1 -</td>
<td>-</td>
</tr>
<tr>
<td>Music therapy: music with intrauterine sounds or instrumental music in association with NNS</td>
<td>3 3</td>
<td>-</td>
</tr>
<tr>
<td>Sucrose 24%: in dose of 1-0.3 ml orally 2 minutes before the procedure in preterm infants and 1-2 ml in term infants</td>
<td>1 1</td>
<td>-</td>
</tr>
<tr>
<td>Breastfeeding or expressed human milk</td>
<td>1 1</td>
<td>-</td>
</tr>
<tr>
<td>Glucose solutions 20-30% in dose of 1-2ml orally 2 minutes before the procedure.</td>
<td>1 1</td>
<td>-</td>
</tr>
</tbody>
</table>

ET suctioning= endotracheal suctioning, ROP= retinopathy of prematurity IM= intramuscular injection

Legend
1. Sufficient evidence supports efficacy for reducing pain-related behaviors (support of two or more trials)
2. Limited evidence suggests efficacy for reducing pain-related behaviors (e.g. support of 1 trial or heterogeneity among trial)
3. Limited evidence suggests inefficacy for reducing pain-related behaviors (e.g. support of 1 trial or heterogeneity among trial)
4. Sufficient evidence supports inefficacy for reducing pain-related behaviors (support of two or more trial)
Pharmacological errors in NICU
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Background: Medical errors are particularly frequent in Neonatal Intensive Care Units (NICUs) [1], increasing morbidity and mortality of newborns [2]. This category of patients requires the application of high technology and needs individualized medical prescription mainly based on body weight and gestational age [3]. The most frequent event categories are wrong medication, dose, schedule, or infusion rate; error in administration or method of using a specific treatment; patient misidentification; error or delay in diagnosis and in the performance of an operation, procedure, or test [2]. The staff inexperience and intensity of workload are indicated as risk factors [4]. Most vulnerable newborns are those with indwelling infusion lines and long length of stay [1]. Common errors are due to the dose because of the lack of reference standards and of awareness of pharmacokinetics and pharmacodynamics drug [1]. The Joint Commission for Accreditation of Health Care Organization (JCHAO) estimates as many as 95% of adverse drug reactions (ADRs) in children remain unreported each year [5]. Frequent analysis of reporting data, training and meeting of all participating NICUs, implementation of computerized physician order entry (CPOE), and improve the staff with supervisor pharmacist might be help to detect errors and to learn about these [1,4].

Materials and methods: We carried out our study from 2011 and 2012 in Department of Medical and Surgical Neonatology of Bambino Gesù Children’s Hospital. We recorded throughout retrospective methods nursing reports to detect an error or incidents. We used voluntary reporting, non punitive, of medical errors by health care providers.

Results: From 2011 and 2012 we detected 29 adverse events in Neonatal Department; 15 (58%) of whom were therapeutic errors concerning of drug process: 2 (13%) order, 1 (7%) preparation, 7 (46%) prescription, 5 (33%) administration (Figure 1). While in the Bambino Gesù Children’s Hospital the adverse events related to pharmacological errors were only 20%.

Conclusions: The voluntary reporting system represents the best option to detect the human errors. In our experienced the introduction of shared protocols, of the nurse staff training, and the following of the JCHAO directives have been achieved to identify all procedures performed for patient care. To reduce the ADRs the Paediatric Investigation Plans should be required by the Paediatric Committed to guarantee safer and tolerated drugs, especially for newborns.

References

Figure 1 (abstract A53) Adverse events at the Bambino Gesù Children’s Hospital from 2011 to 2012. Distribution of adverse events at the Bambino Gesù Children’s Hospital (BGCH), at the Department of Medical and Surgical Neonatology (DMSN) and the percentage of different stages of the drug within the DMSN.


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