

MEDICATION AND BREASTFEEDING

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It is well accepted that the best feeding method for infants is breastfeeding, due to its numerous biological and clinical effects on child and maternal health. The use of medication by the nursing mother and the physician's advice to stop nursing are the most common reasons for the cessation of breastfeeding. The physician plays an extremely delicate role and should be able to assess risks and benefits for both mother and child. The main factors that must be taken into account include pharmacokinetics, the duration of maternal therapy, the age of the infant and the general health of the infant. All physicians should have access to reliable and updated information on medication safety during breastfeeding (reference books, online medical literature). Few drugs have been demonstrated to be absolutely contraindicated during breastfeeding. Nevertheless clear, safe and reliable information is still lacking for most drugs and it would be desirable to improve the knowledge about mechanisms and consequences of infant exposure to drug present in milk.

CRITICAL APPRAISAL OF DIFFERENT ANTHROPOMETRIC CHARTS TO EVALUATE POST-NATAL GROWTH OF PRETERM INFANTS

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Preterm infants' survival has greatly increased in the last few decades thanks to the improvement in obstetrical and neonatal care. The correct evaluation of postnatal growth of these babies is nowadays of primary concern, although the definition of their optimal postnatal growth pattern is still controversial. Concerns have also been raised about the strategies to monitor their growth, specifically in relation to the charts used. At present, the charts available in clinical practice are fetal growth charts, neonatal anthropometric charts and postnatal growth charts for term infants. None of these, for different reasons, is suitable to correctly evaluate preterm infant growth. Recently, an international project has recently started aiming to create prescriptive standard for the evaluation of postnatal growth of preterm infants (INTERGROWTH-21st). Alternatively, at present, while specific charts for evaluating preterm infant postnatal growth are lacking, the best compromise is likely to be as follows: from birth to term neonatal anthropometric charts; International longitudinal charts WHO 2006 or CDC 2002 from term to childhood.

BIOLOGICAL, NUTRITIONAL AND CLINICAL ASPECTS OF FEEDING PRETERM INFANTS WITH HUMAN MILK

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Benefits of breastfeeding are widely recognized, during the last decades human milk has been identified as the normative standard for infant feeding and nutrition. Recent evidence focused on specific bioactive and immunomodulatory factors, such as oligosaccharides, lactose, glycosaminoglycans of human milk and the variability of their concentrations during lactation in both term and preterm milk. Human milk should be fortified with proteins, minerals and vitamins to ensure optimal nutrient intake for preterm VLBWI infants. Best fortification strategies as well as the “optimal” composition of fortifiers are still object of research. Short and long-term clinical, metabolic, immunologic and neurodevelopmental advantages of breastfeeding individualizes fortification - particularly adjustable fortification- has proven to be effective when compared to formula are well documented. Moreover several non-experimental studies observed that clinical feeding tolerance is improved and the attainment of full enteral feeding is quicker by a diet of human milk. In addition, benefits of breastfeeding on psychological and relational aspects have to be considered. Mother’s own milk remains the first choice for all neonates, when it is not available or not sufficient despite significant lactation support, donor milk represents the second best alternative and although some nutritional elements are inactivated by the pasteurization process, it still has documented advantages compared to formula.

AUXOLOGICAL EVALUATION OF NEWBORNS

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Auxological evaluation of the newborn should be based on accurate anthropometry at birth and a reliable estimate of gestational age (GA). However, a comprehensive evaluation of the neonate should consider not only anthropometric traits at birth, but also fetal ultrasound biometry and Doppler velocimetry. Many charts have been proposed, but they are hardly comparable with each other, due to numerous methodological problems. The Italian Societies of Neonatology, of Pediatric Endocrinology and Diabetology and the Italian Society of Medical Statistics and Clinical Epidemiology promoted a multicenter survey with the aim to produce an Italian neonatal anthropometric reference (Italian Neonatal Study [INeS] charts) fulfilling the set of the criteria that a reliable neonatal chart should possess. In order to construct an international standard, an international project (INTERGROWTH-21st) has started a study aiming to create a prescriptive standard. Until an international standard is developed, the use of national updated reference charts is recommended.

**DONOR HUMAN MILK VERSUS MOTHER'S OWN MILK IN PRETERM VLBWIS:
A CASE CONTROL STUDY**

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As for term infants, over the past decades there has been increasing evidence of the benefits of human milk in the feeding of Very Low Birth Weight Infants (VLBWI), influencing not only short-term health outcomes but also long-term neurodevelopmental, metabolic outcomes, and growth. Mother's own milk is the first choice for all neonates including preterm infants, when it is unavailable or in short supply, pasteurized donor breast milk offers a safe alternative and is considered the next best choice. The main aim of this case-control retrospective analysis was to evaluate short term advantages of mother's own milk as a sole diet compared to donor milk as a sole diet, in terms of growth, antiinfectious properties, feeding tolerance, NEC and ROP prevention in a population of VLBWI born in a tertiary center. We did not find significant differences in clinical outcome from mother's own milk compared with pasteurized donor milk. Only a slight and statistically not significant difference in growth could be observed, in favour of maternal milk. We conclude that the maximum effort should always be put in supporting and promoting breastfeeding and donor milk used not only as an alternative to mother's milk but also as a breastfeeding promotion and support strategy.

HYPERBILIRUBINEMIA AND MANAGEMENT OF BREASTFEEDING

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Hyperbilirubinemia and jaundice are natural, physiological phenomena which are only to be expected in the neonatal period, within certain limits. The highest percentage of jaundice in breastfed newborns should be evaluated in connection with inadequate management of breastfeeding rather than a direct effect of breast milk. Breastfeeding is also linked to visible jaundice persisting beyond the first two weeks of life (“breast milk jaundice”), but the appearance of skin jaundice is not a reason for interrupting breastfeeding which can and should continue without any interruption in most cases. There have been numerous contributions to the literature which have rescaled the direct role of breast milk both in early jaundice and in the more severe cases of late jaundice. The reviewed guidelines for detection and management of hyperbilirubinemia underline how prevention of badly managed breastfeeding and early support for the couple mother-child are effective prevention measures against severe early-onset jaundice; furthermore, the breastfeeding interruption is no longer recommended as a diagnostic procedure to identify breast milk jaundice because of its low specificity and the risk to disregarding the detection of a potentially dangerous disease.

COMMUNICATION IN NICUS

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In a Neonatal Intensive Care Unit (NICU) counseling should be a ‘shared culture’ for all the care givers: it should be developed by all the professionals, to face up to parents’ needs of information, explanations, facility of decisions, finding of resources, agreement, help, reassurance, attention. The first essential aspect is the training in counseling skills, by periodic courses for all professionals of the department (physicians, nurses, and physiotherapists). In our department, a professional counselor is present, assisting the medical staff in direct counseling. The counselor’s intervention allows a better parent orientation in the situation. A more effective sharing of these rules also facilitates the communication among parents and medical staff. Periodic meetings are established among the medical staff, in which the professional counselor discusses difficult situations to share possible communicative strategies. We wanted to have not only a common communicative style, but also common subjects, independent from the characteristics of each of us. Individuals are often faced with different situations. For every setting that we more frequently face in communication (for example the first interview with a parent of a very preterm infant) we have built an ‘algorithm’ that follows a pattern: (1) information always given; (2) frequent questions from parents; and (3) frequent difficulties in the communication. Counselling is also a tool to face some critical issue, such as the decision to open the department to parents 24 h on 24, or the promotion of mother’s milk use in Very Low Birth Weight Infants (VLBWI).

METABOLISM AND BIOLOGICAL FUNCTIONS OF HUMAN MILK OLIGOSACCHARIDES

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It is well known that breastfeeding is beneficial both for its nutritional properties and for the presence of biologically active compounds. Among these, human milk oligosaccharides (HMOs), representing the third largest fraction of human milk, have been assigned important biological functions, such as prebiotic and immunomodulatory and antimicrobial effects. HMOs are synthesized in the mammary gland by glycosyltransferase enzymes and can be divided in core-oligosaccharides, sialo-oligosaccharides, fucosyl-oligosaccharides and sialo-fucosyl-oligosaccharides on the basis of their chemical structure. Glycosyltransferases enzymes are partially regulated by genetic mechanisms; according to the expression of secretory and Lewis' genes, it is possible to classify human milk in 4 different secretory groups. We hereby present a review of the current knowledge concerning HMOs, their metabolism and main biological functions.

COW'S MILK PROTEINS IN HUMAN MILK

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Cow's milk proteins (CMPs) are among the best characterized food allergens. Cow's milk contains more than twenty five different proteins, but only whey proteins α -lactalbumin, β -lactoglobulin, bovine serum albumin (BSA), and lactoferrin, as well as the four caseins, have been identified as allergens. Aim of this study was to investigate by proteomics techniques cow's milk allergens in human colostrum of term and preterm newborns' mothers, not previously detected, in order to understand if such allergens could be cause of sensitization during lactation. Term colostrum samples from 62 healthy mothers and preterm colostrum samples from 11 healthy mothers were collected for this purpose. The most relevant finding was the detection of the intact bovine alpha-S1-casein in both term and preterm colostrum. Using this method, which allows direct proteins identification, β -lactoglobulin was not detected in any of colostrum samples. According to our results bovine alpha 1 casein that is considered a major cow's milk allergen is readily secreted in human milk: further investigations are needed in order to clarify if alpha-1-casein has a major role in sensitization or tolerance to cow's milk of exclusively breastfed predisposed infants.

**HIGHER PROTEIN INTAKE STRATEGIES IN HUMAN MILK FORTIFICATION FOR
PRETERMS INFANTS FEEDING.
AUXOLOGICAL AND NEURODEVELOPMENTAL OUTCOME.**

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Postnatal growth restriction and failure to thrive still remain a major problem in Extremely Low Birth Weight (ELBW) infants. The goal for the nutritional care of these infants is to achieve rate of growth similar to those of the fetus in utero at the equivalent gestational age. Human milk fortified remains the best food for all these preterms. Two groups of preterm of weight 580-1250 g and gestational age 23-32 wk, were fed with different protein intake in the human/maternal milk fortified (3,5 g Kg⁻¹ per day and 4,8 g Kg⁻¹ per day in the control and intervention group respectively). The feeding tolerance, intrahospital growth, neurological outcome and anthropometric data until 12 months of corrected age, were evaluated. The protein supplemented group (PSG) showed an intrahospital higher growth rate (mostly in head circumference, p 0,02, and length growth, p 0,04) only in the preterms with 580-980 g and 23-30 wk. In the same preterms, Griffith Development Mental Score at 3 and 12 months corrected age showed higher score than in the control group in the Performance (p 0,04) and Hearing/Language (p 0,03) items. The auxological evaluation in the postdischarge period showed in the PSG group mean z-score values for length higher than those in the control group at 9 (p 0,04) months of corrected age.

EARLY NEUTRAL PREBIOTIC OLIGOSACCHARIDE SUPPLEMENTATION REDUCES THE INCIDENCE OF SOME ALLERGIC MANIFESTATIONS IN THE FIRST 5 YEARS OF LIFE

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Background: A mixture of neutral prebiotic oligosaccharides has been shown to reduce the incidence of atopic dermatitis (AD) and allergy associated symptoms during the first 2 years of life. **Objective:** To evaluate if this protective effect against allergy lasted beyond the intervention period until 5 y of age. **Methods:** In a prospective, double blind, placebo-controlled fashion, healthy term infants at risk of atopy were fed either a prebiotic-supplemented (0.8 g/100 ml scGOS/lcFOS) or placebo-supplemented (0.8 g/100 ml maltodextrin) hypoallergenic formula during the first 6 mo of life. Following this intervention period, follow-up continued until 5 y of life. The present study evaluated (i) the cumulative incidence of allergic manifestations during 5 y, and (ii) the prevalence of allergic and persistent allergic manifestations at 5 y. Monitored allergic manifestations were AD, recurrent wheezing, allergic rhinoconjunctivitis and urticaria. **Results:** Ninety-two children (50 in placebo group, 42 in intervention group) completed the 5-y follow-up. The 5-y cumulative incidences of any allergic manifestation and atopic dermatitis were significantly lower in the scGOS/lcFOS group (30.9, 19.1 %, respectively) compared to placebo group (66, 38 %, respectively) ($p < 0.01$ and < 0.05). Children in the scGOS/lcFOS group tended to have a lower incidence of allergic rhinoconjunctivitis, and allergic urticaria (4.8 vs 16% for both manifestations, $p = 0.08$). There was no difference in the cumulative incidence of recurrent wheezing. With regard to the prevalences at 5 y, intervention group had significantly lower prevalence of any persistent allergic manifestation and rhinoconjunctivitis (4.8, 2.4 %, respectively) compared to placebo (26, 14 %, respectively) ($p < 0.01$ and $= 0.05$). Prevalence of persistent AD tended to be lower in the intervention group (2.4 vs 12 %, $p = 0.09$). Although intervention group had 75% reduction in the prevalence of persistent wheezing (4.8 vs 14 %), no significance was shown. **Conclusion:** Oligosaccharide prebiotics (scGOS/lcFOS), when started early in life have a protective effect against allergic manifestations in high risk infants. The protection lasts beyond infancy until 5 y of life, for AD and allergic rhinoconjunctivitis. Long-term follow-up studies in larger populations are warranted to evaluate the potential preventive effect of this mixture on asthma. **Abbreviations:** lcFOS: long chain fructo-oligosaccharides, scGOS: short chain galacto-oligosaccharides, HO: human milk oligosaccharides.

AMENDMENT TO 2010 ITALIAN GUIDELINES FOR THE ESTABLISHMENT AND OPERATION OF A DONOR HUMAN MILK BANK

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The present paper is an amendment to the recent Italian Guidelines of human milk banking published in 2010. Working Group on Guidelines (Panel) of the Italian Association of Human Milk Banks (AIBLUD) states, in accordance with the European Union Commission's Amending Directive of January 2011, that the hard plastic feeding bottles used in the collection, storage and pasteurization of the human milk should be Bisphenol A (BPA) free. Until new evidence are available polycarbonate feeding bottles should not be used for collection, storage and pasteurization of human milk. The paper summarizes the former and current European Commission Directives and shows the related amending changes to the 2010 Italian Human Milk Banking Guidelines.

UPDATE OF ADJUSTABLE FORTIFICATION REGIMEN FOR PRETERM INFANTS: A NEW PROTOCOL

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Preterm infants fed fortified human milk in standard fashion receive less protein than they need due to customary assumptions. Protein is limiting for growth and neurocognitive development, and shortfalls of protein are not acceptable. “Adjustable fortification” regimen has been proven as an effective way to provide adequate protein intakes and appropriate growth in this group of infants. Italian Association of Human Milk Banks (AIBLUD) has promoted and implemented this Adjustable fortification regimen in neonatal intensive care units (NICUs) with success. This paper presents an update of “Adjustable fortification” regimen; a new protocol already utilized in several Italian NICUs.

EARLY ENTERAL FEEDING WITH HUMAN MILK FOR VLBW INFANTS

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In a NICU early enteral feeding is usually possible only when the newborn clinical conditions permit it. Because of the frequent need of umbilical/central catheters, they usually start with parenteral feeding and/or with minimal enteral feeding (trophic feeding). This kind of management is even more frequent in VLBWIs, in which the risk of NEC is very high. In this work we describe a model of early enteral exclusive feeding (EEEF) based on the use of banking human milk followed by mother milk. In the Centre of Neonatology of Trento, as in other Centers, the newborns weighing less than 750g or with a GE <27 weeks, are treated with parenteral nutrition and minimal enteral feeding. The newborn weighing 750–1249g and with GE >26 weeks define a group in which we find critical neonates, who can not be treated with enteral feeding, and neonates whose clinical conditions permit EEEF. In particular, in a period of 16 years (1994-2009) in Trento, 308 newborns weighing 750-1249 g and GE >26 weeks were admitted. The 90,9% has been treated with prenatal steroids, the 91,9% was inborn, the 96,1% survived. In the 59,1% of the cases (175) we gave EEEF. We could continue with a complete EEEF in the 40,2% of the total (119 cases). The characteristics of these neonates and our centre management, based mainly on early use of banking human milk and mother milk, are detailed described.

TOLERABILITY OF DONKEYS' MILK IN 92 HIGHLY-PROBLEMATIC COWS' MILK ALLERGIC CHILDREN

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Objective: Not exclusively breastfed children with cows' milk allergy (CMA) require a formula or other alternative food, but past and present guidelines differ concerning the best choice. Our aim was to investigate the clinical tolerability, palatability and nutritional adequacy of donkeys' milk (DM) in children with proven CMA. It was important to identify a CM replacement for these children, highly problematic from the feeding standpoint, in spite of their age. **Study design:** A prospective study was conducted on 92 children with CMA, diagnosed through a CM elimination diet, followed by double-blind, placebo-controlled food challenge (DBPCFC) unless contraindicated. Maternal milk was unavailable and current CM substitutes could not be used. Moreover, 89% were affected by multiple FA, and subjected to very restricted diets. Within 3 months after the last CM challenge, DBPCFC for DM was performed. CM or DM skin prick test and sIgE determination preceded the CM or DM challenge, respectively. Native electrophoresis and immunoblotting were used to identify CM and DM cross-reactive proteins. Z-scores of weight and length/stature for age were calculated at DM food challenge (T_0) and during DM assumption. **Results:** 83 children (90.2%) liked and tolerated DM, at challenge and during follow-up, with increased Z-score for weight and length/stature and improved nutritional parameters. Bovine beta-lactoglobulin was identified as the cross-reacting protein among the DM allergic patients. **Conclusions:** DM was found to be a valid alternative foodstuff, in terms of clinical tolerability, palatability and nutritional adequacy, in subjects with CMA who were highly problematic from the feeding standpoint.

**RELATIONSHIP BETWEEN SLEEP/WAKEFULNESS
AND GASTROESOPHAGEAL REFLUX IN SYMPTOMATIC NEWBORNS.**

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The state of sleep/wakefulness is well known to influence esophageal acid exposure and the number of acid refluxes whereas it is uncertain whether the same is true of the non-acid refluxes that predominate in the newborns. To investigate the relationship between sleep/wakefulness and refluxes 45 newborns with gastroesophageal reflux symptoms were studied with combined multichannel intraluminal impedance and pH monitoring. We found that sleep/wakefulness influenced acid and weakly acidic reflux frequency (awake 2.6 ± 0.8 ; asleep 2.1 ± 1.1 ; $p=0.006$). A negative correlation was found between sleepness periods and the mean reflux duration for both acid ($R=0.55$; $p<0.001$) and weakly acidic ($R=0.51$; $p<0.001$) refluxes. This finding may raise some concerns about the over-prescription of antacid drugs in newborns.