www.jpnim.com Open Access eISSN: 2281-0692
Journal of Pediatric and Neonatal Individualized Medicine 2024;13(2):e130206
doi: 10.7363/130206
Published online: 2024 Oct 24

Lectures

Selected Lectures of the 20th International Workshop on Neonatology and Pediatrics

CHILDREN'S HEALTH: MESSAGES FROM THE FUTURE

CAGLIARI (ITALY) • OCTOBER 23RD-26TH, 2024

The Workshop has been organized with the patronage of Autonomous Region of Sardinia, City of Cagliari, Azienda Ospedaliera di Cagliari, University of Cagliari, Board of Physicians of the Province of Cagliari, Italian-Albanian Pediatric Society, AMBO (Alleanza per un Ambiente a misura di Bambino: alliance for a child-friendly environment), European Project Better4u, Eropean Project Life Milch, National Confederation of Pediatrics Heads (CONAPP), Italian Federation of Family Pediatricians (FIMP), Italian-Arabian Pediatric Society (IAPS), Italian-Romanian Pediatric Society (IRPS), Norman Group of Neonatal and Pediatric Nephrology, International Academy of Perinatal Medicine, Italian Society of Pediatric Allergology and Immunology (SIAIP), Italian Society of Clinical Biochemistry (SIBioC), Italian Society of Gynecology of Infancy and Adolescence (SIGIA), Italian Society of Neonatology (SIN), Italian Society of Hospital Pediatricians (SIPO), Association SIPO in the World, Italian Society of Pediatric Psichology (S.I.P.Ped.), Romanian Society of Pediatrics, Italian Society for Research on Essential Oils (SIROE), Italian Society of Neonatal Nursing (SIN INF), Union of European Neonatal and Perinatal Societies (UENPS).

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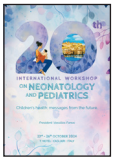

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How to cite

[Lecture's authors]. [Lecture's title]. In: Selected Lectures of the 20th International Workshop on Neonatology and Pediatrics; Cagliari (Italy); October 23-26, 2024. J Pediatr Neonat Individual Med. 2024;13(2):e130206. doi: 10.7363/130206.

LECT 1

NEONATOLOGY FROM THE PAST TO THE FUTURE

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Throughout history, neonatology has evolved remarkably, reflecting advances in medical knowledge, technology, and our understanding of infant care. This evolution is a testament to the dedication of medical professionals and researchers in improving the survival and health of newborns. In Biblical times, women were assisted during childbirth by other women using "birthing bricks" placed underneath their feet. These stones provided midwives or assistants extra room to catch the baby. During the Middle Ages, births were exclusively assisted by midwives, as men, including doctors, considered it inappropriate to enter the delivery room. In the 19th century, physicians, particularly obstetricians, began to show interest in newborn care.

In 1923, J.W. Ballantyne noted, "There is need for specialization in neonatal medicine. This applies to doctors and nurses as well as teaching and construction of hospitals. The specialist in neonatal diseases and the nurse intensively trained and expert in the management of delicate newborns will be commonplace ere long". In 1939, C.G. Grulee observed, "In previous times the problems of the newborn child have been the province of the obstetrician, a field in which he has taken comparatively little interest and to which he has contributed little. As pediatricians, we have but scratched the surface".

The treatment of premature infants likely began in the latter half of the 19th century. In the early 1950s, Virginia Apgar proposed a standardized assessment at birth, known as the Apgar score, which remains a valuable predictor of which babies will need ongoing support and those at higher risk of mortality. The inability of preterm infants to maintain their body temperature was recognized in the late 19th century, leading to the development of incubators.

In the mid-1950s, preterm infants who died after several days were found to have histologic evidence of hyaline membranes in their lungs, a condition termed hyaline membrane disease (HMD). In 1959, Mary Ellen Avery, inspired by John Clements and Jere Mead, demonstrated that HMD was linked to a deficiency of surfactant in lung fluid.

A significant leap in neonatology is closely connected to the tragic death of President John F. Kennedy's son, Patrick Bouvier Kennedy, who was born prematurely and died after 39 hours of life on August 7, 1963. Patrick was born at about 37 weeks, weighing 4 pounds, 10 ½ ounces (2,100 g). As his respiratory distress worsened, he was airlifted to Children's Hospital in Boston and placed in a hyperbaric chamber. HMD was the apparent cause of death, prompting President Kennedy to invest significantly in neonatal research, investigating the cause and management of the disorder.

One of the doctors contacted by Patrick Kennedy's physicians was Dr. Maria Delivoria-Papadopoulos, a young pediatrician from Toronto Children's Hospital, who is now considered the "mother of neonatology".

The discovery and application of prenatal corticosteroids were concurrent with the assessment of fetal lung maturity. This began in 1972 with the publication on the use of betamethasone to prevent or minimize the severity of respiratory distress syndrome (RDS).

The start of the antibiotic era and neonatal screening programs coincided with the beginning of modern neonatology. The trajectory of neonatology continues to advance, guided by historical insights and modern innovations.

WHAT THE FUTURE HOLDS FOR US?

In the Present

- Learning with high-fidelity simulation: training healthcare professionals using advanced simulation techniques to improve neonatal outcomes.
- Standardizing and unifying care: ensuring consistent and high-quality care across different healthcare settings.
- Gene therapy: exploring genetic interventions to treat congenital disorders early.
- Rapid identification of infectious diseases: utilizing advanced techniques (e.g., polymerase chain reaction – PCR) for quick and accurate diagnosis of infections.

- Multicenter and multidisciplinary trials: collaborating across disciplines and centers to improve neonatal care practices.
- Use of biomarkers: identifying at-risk infants through advanced biomarkers.
- New vaccines: developing vaccines to protect newborns from emerging infectious diseases.
- Blood substitutes: creating alternatives to blood transfusions for infants.

In the Next Decade

- Precision medicine: tailoring medical treatments to individual genetic profiles.
- Routine use of omics techniques: applying genomics, proteomics, and other omics technologies in neonatal care.
- Development of an artificial placenta: supporting preterm infants' development outside the womb.
- Fetal gene sequencing: sequencing fetal genomes to identify and address genetic conditions early.
- Artificial intelligence (AI): leveraging AI to predict, diagnose, and treat neonatal conditions with unprecedented accuracy.

The journey from birthing bricks to AI in neonatology illustrates a continuous quest to improve infant care. Each historical milestone laid the groundwork for modern advancements, demonstrating the importance of building on past knowledge to innovate and enhance future care. The future of neonatology, inspired by historical progress, promises to bring even greater precision, efficacy, and compassion to the care of our most vulnerable patients.

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LECT 2

HUMAN BREAST MILK MICROBIOTA AND CHILDREN'S HEALTH

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Although both WHO and UNICEF recommend excusive breastfeeding until 6 months of age in all newborns and children, only 41% of children arrive at 6 months with breast milk all over the world.

Breast milk is unique and complete from a nutritional and biological point of view and is also recommended for preterm babies. It is highly sustainable also from a social and economic point of view. In addition, breast milk promotes mother-child interaction (bonding) and is recognized as a vital ecosystem. It is not sterile and contains bacteria, viruses and other microorganisms. The composition of the human milk microbiota may be influenced by several factors, including the stage of lactation, maternal body mass index, age and diet, parity, geographical location, socioeconomic status, use of antibiotics or probiotics during pregnancy, and mode and time of delivery. Nine different bacteria give origin to the so called "core" of bacteriome and represent about half of the overall microbial community. The absence or the marked reduction of these bacteria, due to a small amount of milk or short duration of breastfeeding, is related to a greater risk of chronic diseases during life, like asthma and obesity.

Obesity depends on an altered *Firmicutes*/*Bacteroidetes* ratio, with reduction of *Bacteroidetes*. A greater prevalence of *Actinobacteria* and *Bifidobacteria* may be associated to a lower risk of food allergies. Some metabolites produced by *Prevotella spp.* (short chain fatty acids) are related to a minor incidence of allergic diseases; on the other hand, *Proteobacteria* (for example *Pseudomonas spp.* and *Acinetobacter spp.*) are associated to a greater prevalence and risk of food allergy in the pediatric population.

Fetal growth restriction is one of the greater epigenetic stress on many metabolic pathways. It is responsible for a variation in fetal programming, with many adverse effects, leading to an early development of chronic non transmissible diseases, such as cardiovascular pathologies, hypertension, diabetes, overweight and obesity, metabolic syndrome, often evident later during childhood or adolescence, as well as in adulthood. Similar effects may be also seen in macrosomic newborns, in relation to an epigenetic effect.

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LECT 3

DEVELOPMENTAL NEUROBIOLOGY: THE EVOLUTION OF NEONATAL BRAIN

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3 million 300,000 years ago, a child of about 2 or 3 years of age (the so called DIK-1 child), belonging to the species of our oldest ancestor, *Australopithecus afarensis* (a pre-human hominin) [1], had a cerebral volume of about 275-340 cm^3; after about 2 million years, the archaic human forms of *Homo* (e.g., *H. naledi*, *abilis*, *erectus*) and then, later in time, those of *Homo sapiens* had an encephalic volume, at the same age, of about 900 cm^3. How did this come about? The evolution, growth and reorganization of the brain and, specifically, of some of brain areas (encephalization), made it so that, from the archaic monkeys and australopithecines, it could reach our kind of *Homo sapiens sapiens* and his refined motor, sensitive, linguistic, thinking and social skills. The brains of our first ancestors, as demonstrated by an elegant experiment recently conducted on brain organoids (mini-brains) modified with genes of archaic (NOVA-Ar/Ar) vs. modern man (NOVA-Hu/Hu), were simple, roundish, with a wider occipital lobe and greater extension of the limbic and the frontal olfactory regions, and largely populated by excitatory glutamatergic neurons. The slow process of evolution has then shaped and reorganized the brain areas as we know them today: increasing the size of what was most needed by our species (e.g., parietal visual-spatial areas; temporal hearing and language areas; and frontal thought and abstract areas), at the expense of what was progressively less needed (e.g., occipital visual and olfactory sensitive areas). This process of encephalization [2] occurred, in the human evolutionary line, at simultaneous phases of growth and reorganization according to a mosaic mechanism. The brain volume has grown and, as it grew, the relationships between some of its areas changed. With the archaic human forms of *Homo erectus* (about 1.5 million years ago) the brain clearly begins to grow, but also to modify the relationships between its areas. Similar changes have also occurred at the cellular and molecular level: man, who is "neotenic", continues to organize the cerebral cortex and to modulate the axon and dendritic fibers until the age of 25, with a resulting time gain in the processes of storage and learning, still however depending on parental care for a longer period [3]. At the same time, different synaptic receptor systems appear in time sequence in the various developmental periods of the child: the newborn/infant is richer in excitatory neurons (glutamatergic) (as it occurred in our antecessors' brains) [3], the child and toddlers increase their inhibitory receptors (i.e., GABAergic), whilst adolescents express more modulatory receptors (i.e., serotoninergic and dopaminergic). The gradual morphological and receptor change, in the evolutionary arc of a child's life, reflects the change occurring in the brain throughout the human evolutionary line.

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LECT 4

FETAL PROGRAMMING OF ADULT DISEASES

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The theory of fetal and perinatal programming of adult diseases was first proposed by David J.P. Barker and C. Osmond in the eighties of the previous century. In their pivotal articles, these authors correlated maternal and fetal malnutrition during gestation with the susceptibility to develop ischemic heart disease in adulthood. According with the Barker hypothesis, poor maternal living conditions during gestation should represent an important risk factor for the onset of severe atherosclerotic cardiac disease later in life. In further studies, Barker hypothesized that low body weight at birth should be considered a sign of a deficient development during gestation, resulting in immaturity of fetal organs, followed by the susceptibility to develop multiple diseases in adulthood. Following contributions evidenced the association of low birth weight with an increased risk to develop insulin resistance, changes in cholesterol metabolism, metabolic syndrome,

kidney failure and neuropsychiatric disorders, such as Alzheimer's and Parkinson's diseases, later in life. In more recent years, the fetal programming hypothesis has been associated with susceptibility to the insurgence of different cancer types and to the development of a very severe type of COVID-19. Since body weight at birth is generally considered as a practical indicator of the fetal nutritional status during gestation, every subject with a low, or very low birth weight, should be considered a "at risk" subject for the development of multiple acute and chronic diseases in their adult life. Moreover, according with the Barker hypothesis, every patient presenting with renal insufficiency, particularly young subjects, should be asked about their body weight at birth, in order to potentially correlate fetal conditions during gestation with a susceptibility to develop kidney failure. The linkage between susceptibility to undergo kidney failure and a low weight at birth should be identified in a low nephron number related to a decreased development of the fetal kidney, due to maternal bad conditions during pregnancy. A similar linkage could be identified for neuropsychiatric disorders: a low number of dopaminergic neurons in the substantia nigra (first hit, during gestation) could represent a risk factor for the insurgence of Parkinson's disease, following the exposition to neurotoxic agents such as paraquat (second hit, in adulthood). Similarly, a low neuron burden in the cerebral cortex might represent the risk factor for the insurgence of Alzheimer's disease later in life. Regarding susceptibility of infants with low birth weight to develop diabetes in childhood, the fetal programming theory underlines a low number of Langerhans islets at birth as the risk factor for the insurgence of endocrine pancreatic insufficiency later in life. From a practical point of view, the Barker hypothesis clearly evidences that the prevention of multiple "adult onset" diseases should start from the intrauterine life, encouraging a healthy maternal lifestyle, discouraging maternal smoking and alcohol use during all phases of gestation. Neonatologists are asked to act immediately after birth in any case of intrauterine growth restriction, given that the first weeks after birth may represent a "window" in which regeneration remains active at least in some organs. A new fascinating theory, defined "physiological regenerative medicine", based on the administration in the perinatal period of natural substances able to stimulate organ development in the neonate, could increase his/her resistance to develop multiple diseases later in life.

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LECT 5

SKIN MICROBIOTA IN ATOPIC DERMATITIS: IS IT POSSIBLE AN INTERVENTION?

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Atopic dermatitis (AD) is a chronic inflammatory skin condition characterized by itchy, red, and swollen skin. The skin microbiota, particularly the presence and balance of various bacterial species, plays a significant role in the pathogenesis and exacerbation of AD. Here, we explore the potential interventions targeting skin microbiota to manage and treat AD.

PROBIOTICS AND PREBIOTICS

Probiotics are beneficial bacteria that can be applied topically or taken orally to improve the balance of the skin microbiota. Prebiotics are substances that promote the growth of beneficial bacteria.

- Topical probiotics: these are applied directly to the skin to restore the natural balance of bacteria. Studies have shown that certain probiotics, such as *Lactobacillus* species, can improve skin barrier function and reduce inflammation.
- Oral probiotics: taken as supplements, they can modulate the immune system and have shown potential in reducing the severity and frequency of AD flare-ups.
- Prebiotics: substances like oligosaccharides can be included in skincare products to encourage the growth of beneficial bacteria on the skin.

ANTIMICROBIAL PEPTIDES

Antimicrobial peptides (AMPs) are part of the skin's natural defense system and can be used to target harmful bacteria without affecting beneficial bacteria.

- Synthetic AMPs: these can be designed to specifically target *Staphylococcus aureus*, a bacterium commonly found in higher numbers on the skin of AD patients.

BACTERIOPHAGE THERAPY

Bacteriophages are viruses that specifically infect bacteria. Phage therapy can be used to target and reduce pathogenic bacteria such as *Staphylococcus aureus*.

- Phage-based topicals: these can be formulated to reduce harmful bacterial load without disturbing the overall microbiota balance.

MICROBIOTA TRANSPLANTATION

Transplantation of healthy microbiota from a donor to the patient's skin can help restore a balanced microbial environment.

- Skin microbiota transplants: though still in the experimental stages, this approach involves transferring skin microbiota from healthy individuals to patients with AD.

SKINCARE PRODUCTS WITH MICROBIOME-FRIENDLY INGREDIENTS

Products formulated to maintain and support the natural skin microbiome are becoming more popular. These include cleansers and moisturizers that avoid harsh chemicals which can disrupt the microbiota.

- Gentle cleansers: these avoid stripping the skin of its natural oils and beneficial bacteria.
- Barrier repair moisturizers: formulated with ingredients like ceramides, these can help restore and maintain the skin's barrier function.

ANTI-INFLAMMATORY AND IMMUNOMODULATORY THERAPIES

Certain treatments can help modulate the immune response and reduce inflammation, indirectly supporting a healthy skin microbiota.

- Topical corticosteroids and calcineurin inhibitors: these are commonly used to reduce inflammation and manage symptoms.
- Biologics: targeted therapies like dupilumab can help manage severe cases of AD by modulating immune pathways involved in inflammation.

DIETARY INTERVENTIONS.

Diet can influence the skin microbiota and overall skin health.

- Anti-inflammatory diets: diets rich in omega-3 fatty acids, antioxidants, and vitamins can support skin health and potentially improve AD symptoms.

RESEARCH AND CLINICAL TRIALS

Ongoing research and clinical trials are essential to better understand the interactions between skin microbiota and AD, and to develop effective microbiome-based therapies.

CONCLUSION

Intervening in the skin microbiota offers a promising approach to managing and treating AD. While many of these interventions are still under research, the potential benefits highlight the importance of the skin microbiome in maintaining skin health and preventing AD flare-ups. As our understanding of the skin microbiome grows, more targeted and effective treatments are likely to emerge.

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LECT 6

SKINOMICS: SKIN METABOLOMICS AND MICROBIOMICS

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In the present era, technological and bioinformatic innovation has conquered dermatology, a discipline that is now moving towards precision medicine. The objective is not limited to improving current therapies for skin diseases but extends to perfecting the function of healthy skin. This approach encompasses not only prevention but also progress in the cosmetic field. This has been made possible by the recent advances in "omics" technologies, which have enabled the transition from one-way studies to integrated analyses using high-throughput technologies. These technologies facilitate the validation of the biological functions of differential substances, including not only genes, proteins, metabolites and the microbiome, but also the resulting interactions between them. The integration of different multi-omics data is crucial for this process. Consequently, an innovative field of dermatological research, skinomics, was established, encompassing genomics, proteomics, transcriptomics, lipidomics, microbiomics and metabolomics of the skin [1, 2]. This approach is well-suited to the high complexity of the skin system, which relies on a delicate balance between the genetics of the host, the interaction of the host with resident microbes, and between microbes and microbes, as well as the influence of the environment. Consequently, it will be possible to obtain a comprehensive overview of the metabolic states of different skin types under different conditions in order to validate skin type-specific biomarkers in an attempt to predict individual response to pharmacological treatments and the efficacy of different cosmetic products on individual subjects. This will also be facilitated by the creation of extensive multi-omics data archives [2, 3]. According to the systems biology paradigm, within the skin ecosystem, it is of paramount importance to integrate metabolomics, a relatively recent omics science, which provides a snapshot of gene expression during its interaction with the environment, with microbiomics, which is the detection of the genotype and characterization of a microbial community of a given environment. This could facilitate the development of simple and rapid non-invasive tests capable of identifying numerous diseases and skin conditions [2].

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LECT 7

PULMONARY HYPERTENSION IN THE NEWBORN

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Persistent pulmonary hypertension of the newborn (PPHN), also called persistence of foetal circulation (1:1,500 newborns), is a clinical condition characterised by pulmonary hypertension manifesting even over days and weeks after birth with patency of ductus arteriosus and foramen ovale with right-to-left blood shunt across them [1]. Generally speaking, PPHN occurs in born at term and with normal birth weight newborns with a background of perinatal asphyxia. Predisposing factors are often acute hypoxia at birth, intrauterine chronic hypoxia, and maternal acetylsalicylic acid or indomethacin (e.g. inhibitors of prostaglandin E1) intake during the third trimester of pregnancy. In about half of the cases, no clear origin of PPHN can be identified [2]. Newborns with PPHN are tachypneic and cyanotic. Arterial desaturation is higher in lower limbs that in the upper. On cardiac auscultation a pansystolic murmur is heard due to tricuspid valve insufficiency. A loud second component of S2 is noted as well. On electrocardiography there is right ventricular overload. Echocardiography plays a pivotal role in making PPHN diagnosis. In fact, the main pulmonary artery with its branches and right chambers are dilated. A right-to-left shunt at the interatrial septum and/or ductus arteriosus is detected. Right ventricular systolic pressure and/or pulmonary vascular pressure is calculated from tricuspid valve regurgitation. PPHN severity varies a lot. Management of PPHN encompasses many things, including maintaining temperature, glucose, cardiovascular support, and intravascular volume.

Ionotropic drugs are often administered in PPHN, mostly dopamine and milrinone. The mainstay of PPHN therapy is improving oxygenation by using mechanical ventilatory support. Adequate ventilation and maintaining appropriate lung volume is pivotal in PPHN. Studies display conflicting results regarding surfactant use in PPHN. In newborns with parenchymal lung disease, surfactant administration is linked with improved oxygenation in mild PPHN. Inhaled nitric oxide is the only FDA approved pulmonary vasodilator therapy in newborns with PPHN causing selective pulmonary vasodilation. Its action is quick and potent. Inhaled nitric oxide treatment should always start at 20 ppm to evaluate for a clinical response. Large studies demonstrated the efficacy of inhaled nitric oxide in decreasing the need for extracorporeal membrane oxygenation (ECMO). Unfortunately inhaled nitric oxide did not decrease mortality, hospital stay, or risk of neurologic impairment. Milrinone is an inotropic vasodilator inhibiting phosphodiesterase III. It ameliorates right and left ventricular functions and can improve oxygenation in infants with severe PPHN. Milrinone decreases systemic vascular and pulmonary venous pressure, thus improving left ventricular performance. It is used in combination with nitric oxide. Sildenafil is a phosphodiesterase V inhibitor. Although it has not been approved by the FDA yet for the therapy of PPHN, clinical data suggest its beneficial effects in newborns not responding to nitric oxide. Agitation can impair pulmonary vascular resistance and further worsen PPHN. As such sedatives and anxiolytic are given to infants with PPHN as adjunctive therapy to reduce wide swings in saturations. ECMO, by bypassing the heart and lungs, provides the needed time for resolving lung pathology. In severe respiratory failure, ECMO use was associated with improved survival. The results of ECMO use in PPHN depend on the underlying aetiology [3].

In mild PPHN prognosis is usually good. In approximately two weeks high pulmonary pressures return to a normal condition and a clinical improvement is seen. In severe PPHN mortality is up to 25-35%. As such, a prompt diagnosis is crucial [2].

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LECT 8

LOOKING FOR A VEIN? THERE IS A LIGHT AT THE END OF THE TUNNEL

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Newborns and children undergoing intensive care, surgery or intravenous therapy require peripherally inserted venous catheters (PIVC). Intravenous access can be difficult, time-consuming and challenging for healthcare providers and painful for patients because their veins are frequently thin, deep or may have been exhausted in previous attempts. Venous prominence and visibility can be increased with simple measures such as active warming or hydrating the infant. If these methods are unsuccessful, alternative sites can be considered, assistance from a more experienced colleague may be sought, and additional tools such as near infrared (NIR) vein detectors or ultrasound-guided catheterization can be used; however, these options are costly and not always readily available. In emergency situations, difficult venous cannulation can delay life-saving treatment. For this reason, venous access algorithms have been proposed for children: after two unsuccessful attempts on each side, intraosseous or central venous access should be pursued. However, these techniques are difficult to perform and any system that can facilitate peripheral cannulation should be utilized. Transillumination facilitates the visualization of peripheral veins in infants and children and this technique can be achieved by using a high power, cold-light LED source. Various transillumination devices have been used in our hospital which have not fully met our expectations because, despite their low price, a single source of not dimmable red light (the ON-OFF effect) has made the technique useful but not always effective. Since several years we have introduced the use of a new device (ASTODIA®, Stihler Electronic GmbH, Stuttgart, Germany), equipped with two independent yellow and red LED lights. Yellow light, especially useful in preterm and newborns, is used to visualize the thinner veins closest to the surface of the skin, while red light, useful in older children, allows you to visualize the deeper veins. Furthermore, transillumination may be used to identify the radial and ulnar arteries in premature infants or newborns and guide arterial access. The LEDs are adjustable with different brightness gradients, and, in our experience, it

allows to adequately visualize even the veins of children up to 4-6 years of age. The wand is small and lightweight, can be covered with a sterile sheath to ensure asepsis and can be held under the patient's extremities without needing to move the patient out of the incubator. Automatic safety features ensure that the patient is never exposed to the risk of burns. In conclusion, transillumination may be a useful technique to improve the success rate of difficult venous cannulation in infants and young children. The use of an adjustable powerful red-yellow LED transilluminator significantly increases the success rate of first attempts at insertion of PIVC in small infants and in older children in different hospital environments such as Intensive Care Units, Operating Rooms and Emergency Rooms.

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LECT 9

NEONATAL TRANSPORT BY HELICOPTER

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Available transport vehicles for neonates are the following: ground ambulance (GA), fixed-wing aircraft (FWA), rotary-wing aircraft (RWA) and hydro-ambulance. GA is the commonest vehicle, while RWA covers 2% of Newborn Emergency Transports (NETs) only. If we compare the main vehicles we find the following results [1]:

1. safety – fair for RWA, good for FWA, excellent for GA;
2. noise – poor for RWA, poor for FWA, good for GA;
3. vibration – poor for RWA, good for FWA, and GA;
4. reliability – fair for RWA and FWA, good for GA;
5. costs – poor for RWA, fair for FWA, good for GA;
6. divertibility during transport – fair for RWA, poor for FWA, good for GA;
7. availability – fair for RWA and FWA, good for GA;
8. transit time – excellent for RWA and FWA, fair for GA;
9. space – poor-fair for RWA, poor for FWA, good for GA.

Versus GA, RWA has a higher-level of noise, body vibration, and acceleration, whereas GA has more dynamic effects on braking, shock, impulsive noise [2]. Also, the accident rate for helicopter is higher than GA or aircraft and specific safety protocols should be applied to reduce it. As we may see, RWA is not the preferred vehicle, however in some situations it must be chosen, for example when we need a long-distance coverage with a short transit time, and FWA is not available (e.g. due to landing problems or aircraft models). This happens for example in some Italian regions due to orographic conformation. That's why, even though RWA is not recommended for transports over 100 miles, helicopter is used to avoid longer transport time by GA. Adverse weather and poor landing helipads close to the referring hospital sometimes may hinder RWA transport. When RWA is activated, we have also to keep in mind how far is the helipad, and if the neonatal transport crib is suitable to the helicopter model available. If the helipad is far, a GA has to be used first to transport the neonate to the helicopter surface; if the neonatal crib for helicopter is different, a switch of neonatal crib has to be done. Differently from adult or pediatric Helicopter Emergency Medical Services, crew members for a neonatal RWA transport are: a neonatologist, and a neonatal nurse of the referral Neonatal Intensive Care Unit (NICU), a pilot and a co-pilot; all the transport equipment is of the referral NICU as well. Training for helicopter transportation must include knowledge of altitude physiology, in particular for transportation of air leak syndromes and congenital diaphragmatic hernia. We have also to consider that its costs are always very high. For example, in Veneto Region the cost is 20 euro/min, but if it is requested by private is 90 euro/min (up to a maximum of 7,500 euro); the cost of the ambulance with nurse is 80 euro (+80 euro for MD) per transport. Therefore the "Golden Hour" should be one of the guiding criteria to activate helicopter transport, also because RWA is a standard in NETs for which specific training is needed [3].

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LECT 10

THE NUTRIENT CYCLE: FROM MATERNAL NUTRITION TO HUMAN MILK COMPOSITION VIA PLACENTA-FETAL EXCHANGES

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INTRODUCTION

Maternal nutrition during pregnancy and lactation is a key determinant of infant development and long-term health outcomes for both mother and child. The quantitative assessment of the nutrient cycle from mother's diet to the fetus and the newborn remains extremely complex to determine. The challenge begins with a reliable collection of the mother's nutrient intake with conventional dietary assessment methods like food frequency questionnaires (FFQ) and 24-hour recalls (R24h) that are prone to errors. Bioanalytically determined food intake biomarkers (BFI) using urinary metabolomics offer a promising approach for more accurate dietary assessment.

MATERIALS AND METHODS

Diet (FFQ and R24h), urinary BFI and human milk (HM) vitamins were measured in a longitudinal mother-infant birth cohort in the Spanish-Mediterranean area.

RESULTS

We herein report on vitamin data. Dietary analysis shows that around 60% of vitamins (A, D, E, B5, B7, B9, B12, C) are below the dietary recommended values (DRV) and that dietary supplements couldn't reach DRV levels for all vitamins, and vitamin D in particular. Hierarchical clustering analysis of BFI profiles revealed three distinct dietary patterns among the study population. Significant correlations were found between specific urinary biomarkers and their corresponding food groups from R24h including proline betaine, anserine and trimethylamine-N-oxide for fruits, meat and fish, respectively. Neither dietary intake data or urinary BFI were reflected in HM vitamins based on multivariate statistical analysis. However, some mild correlations could be observed (Pearson's $R > 0.3$). Several vitamins (A, B1, B6) show time-dependent variations from birth throughout the first 6 months of lactation. Furthermore, we noticed that HM pasteurization that is required for donor milk fed infants associates with a significant loss of almost all vitamins. In an independent cohort of infants, we investigated the putative variations of vitamin levels between venous and arterial blood samples collected from the umbilical cord. Results didn't show any clear clustering of vitamin levels at time of birth between venous and arterial blood samples. However, vitamin levels in umbilical cord samples do not systematically reach levels of adequate status despite the reported consumption of vitamin supplements during pregnancy.

CONCLUSIONS

This work highlights the complexity of tracking vitamin cycle from mother's diet to HM. It calls for the improvement of dietary assessment tools to quantitatively measure the impact of nutrition on HM vitamin composition. It also opens questions about the efficacy of dietary supplements on achieving adequate vitamin status of HM and ultimately of the infant. Maternal and infant vitamin metabolism is far from being completely understood, with key questions remaining about the accuracy of vitamin reference values in diet, milk, and blood for both the mother and the infant.

LECT 11

IS IT STILL TIME FOR SUSTAINED INFLATION IN THE DELIVERY ROOM?

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Mechanically ventilated preterm infants are at risk both for bronchopulmonary dysplasia (BPD) and brain injury. On the contrary, by using non-invasive respiratory support, it is possible to prevent BPD and death, without increasing brain damage. The recent European respiratory distress syndrome (RDS) guidelines [1] suggest to stabilize spontaneously breathing preterm infants using continuous positive airway pressure (CPAP) and

to intubate only babies not responding to CPAP or positive pressure ventilation (PPV). Anyway 40-50% of very low birth weight infants initially in nasal CPAP (nCPAP), show an nCPAP failure and need for mechanical ventilation (MV), because these babies are not able to reach an adequate functional residual capacity (FRC) at birth and to maintain lung volume only by nCPAP. How can we try to guarantee an adequate FRC at birth and to improve nCPAP success? Sustained inflation (SI) (i.e., a peak pressure of 20-25 cmH_2O maintained for a prolonged time, e.g. for 10-15 second, associated to an adequate positive end-expiratory pressure [PEEP], e.g. 5 cmH_2O) applied at birth in the Delivery Room (DR) has been demonstrated to clear the lung fluid and to achieve a precocious and efficacious FRC with an uniformity of lung volume in animal studies. Therefore, SI was investigated in the neonatal transition of preterm infants in the DR. In 2014, Schmölzer et al. in a systematic review and meta-analysis concluded that infants initially treated with a SI had improved short respiratory outcomes (i.e., reduced need of MV in the first 72 hours); however, BPD and/or death occurrence were not improved. Unfortunately, the results of the large multicenter study (SAIL trial) [2] that wanted to explore the effect of SI in very preterm infants (23-25 weeks' GA) in term of reduction of BPD or death occurrence at 36 weeks' GA did not confirm the potential role of SI. A recent *Cochrane* review [3] concluded that there is no evidence to support the use of SI. Also the European Resuscitation Council (ERC) and American Academy of Pediatrics (AAP) in 2021 did not support the use of SI (more than 2-3 seconds, by ERC) and any SI (between 1 and 10 seconds, by AAP) for the management of preterm infants in the DR. Many are the ongoing questions about SI: the exact definition (in term of peak pressure, duration and number); if SI has to be used as a rescue or prophylactic approach; which is the role of spontaneous breathing on the efficacy of SI (e.g., do we have to use a respiratory function monitor [RFM] when we use SI, to detect the interaction with infant's breath?); how to monitor the efficacy of SI during its use (e.g., with electrical impedance tomography [EIT] and/or forced oscillation technique [FOT]?); which is the real impact of SI on relevant clinical outcomes (e.g., air leaks, death, BPD); which could be the best target population of SI (e.g., asphyxiated term infants? preterm infants only at specific gestational age?). Probably only when further research will be able to answer these specific questions, we will understand if SI is really a "good thing" and its potential role in clinical practice.

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LECT 12

INFECTIONS AND ANTIMICROBIAL USE

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Infections are a significant cause of neonatal morbidity and mortality, resulting in over 550,000 neonatal deaths every year. Most of these deaths can be averted by preventive measures, early diagnosis, timely care-seeking, and treatment with appropriate antibiotics.

Neonatal infections are primarily bacterial, including sepsis and meningitis. Sepsis is a significant cause of neonatal morbidity and mortality, with an incidence from 1 to 4 per 1,000 live births in the USA, with significant variability worldwide. It is a clinical syndrome potentially leading to multiorgan dysfunction and even death. Isolating a pathogen from a symptomatic patient's blood or cerebrospinal fluid indicates a bloodstream infection. Meningitis in neonates is usually hematogenous. Neonatal sepsis is classified, depending on the age of onset, as early-onset sepsis (EOS), late-onset sepsis (LOS), and very late-onset sepsis. EOS is defined as an infection occurring in the first 7 days, whereas, for infants hospitalized, in the first 72 hours of age. The most common pathogens, typically maternal genitourinary tract colonizers, are Group B *Streptococcus* (GBS),

Escherichia coli, and *Listeria monocytogenes*. LOS presents beyond 3 to 7 days of age mainly due to organisms acquired from interacting with the hospital environment or the community, most commonly *Staphylococcus aureus*, *Enterococcus spp.*, GBS, *Escherichia coli*, *Klebsiella spp.*, *Enterobacter spp.*, *Citrobacter spp.*, *Serratia spp.*, *Acinetobacter spp.*, and *Pseudomonas aeruginosa*. Most often, meningitis is a late-onset infection resulting from the hematogenous spread of a microorganism into the central nervous system and less frequently results from a contiguous spread. Initial empiric treatment for suspected EOS typically combines ampicillin and an aminoglycoside, such as gentamycin. Third-generation cephalosporins should be avoided due to their association with increased risk for antibiotic resistance and invasive fungal infections. Although there is no consensus upon the ideal empiric antibiotic regimen for LOS, initial treatment for community-acquired sepsis typically includes a beta-lactam (usually ampicillin) with an aminoglycoside (usually gentamycin), while in nosocomial sepsis, vancomycin (or an antistaphylococcal beta-lactam antibiotic) combined with an aminoglycoside (gentamycin or amikacin). Clindamycin or metronidazole may be added for anaerobic coverage in necrotizing enterocolitis cases. Cefotaxime is added when there is a concern for meningitis.

Neonatal infections, a significant contributor to neonatal morbidity and mortality worldwide, demand an early diagnosis and treatment and effective preventive strategies from prenatal care to infection control in healthcare settings.

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LECT 13

NEUROPROTECTIVE STRATEGIES FOR ASPHYXIATED NEWBORNS IN THE EARLY NEONATAL PERIOD: A FOCUS ON BRAIN-ORIENTED INTERVENTIONS

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Perinatal asphyxia is the main trigger of significant neurological impairments and the second responsible factor of neonatal death among term infants. At present, instant apoptosis due to necrosis cannot be prevented by any treatment. However, certain medical strategies, for instance therapeutic hypothermia (TH), have proven ability in reducing delayed programmed cell death. This procedure has been demonstrated to significantly improve overall outcomes by lowering the rates of mortality and major neurodevelopmental disabilities. During the latent period and subsequent energy shortage periods following hypoxia-ischemia, hypothermia helps by reducing cerebral energy expenditure, apoptosis, and the discharge of excitatory neurotransmitters, reactive species, and cytokines. Despite its benefits, approximately only 50% of patients undergoing TH experience positive outcomes, plus it must be initiated as soon as possible after the hypoxic-ischemic event to be most effective [1].

This presentation will delve into what could be optimized to improve brain health in children with hypoxic-ischemic encephalopathy (HIE). Strategies such as managing low carbon dioxide levels [2], preventing low blood sugar [3], ensuring effective pain relief [4], and monitoring brain activity [5] are considered beneficial approaches for improving outcomes in critically ill infants with HIE. Pharmacological interventions aimed at protecting the brain are currently under investigation. Promising emerging drugs include allopurinol, erythropoietin, and melatonin, but more rigorous randomized controlled trials are necessary to confirm their effectiveness and identify the most effective treatment strategies. While TH is a pivotal intervention for patients with HIE, it is not sufficient on its own. To maximize outcomes, it is essential to simultaneously address the underlying respiratory, metabolic, and cardiovascular impairments. This may involve ensuring adequate oxygenation and ventilation, correcting electrolyte imbalances, and maintaining hemodynamic stability. By providing comprehensive support in these areas, healthcare providers can enhance the effectiveness of TH and improve the overall prognosis for newborns with this condition.

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LECT 14

METABOLOMICS IN NECROTIZING ENTEROCOLITIS

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Necrotizing enterocolitis (NEC), a lethal acute gastrointestinal complication of premature newborns, has an incidence range from 2% to 13%. It is estimated that the mortality rate is approximately 25% and, furthermore, this pathology is associated with a high risk of long-term complications in survivors, including an increased likelihood of impaired physiological and neurodevelopment growth [1, 2]. However, it can also affect term babies with other comorbidities, including perinatal asphyxia, polycythemic/thrombotic conditions, endocrine diseases, perinatal sepsis and congenital heart disease [1]. The multifactorial pathogenesis and complex clinical picture, which presents with mild, non-specific symptoms, as well as the poor diagnostic value of existing tests, collectively contribute to the significant challenge of early diagnosis of NEC. In order to achieve timely identification of severely ill patients, research has focused on the application of modern omics sciences, especially metabolomics, with the aim of identifying reliable and early biomarkers of NEC through minimally invasive methods [2]. The metabolomic approach is based on the quantitative analysis of a large number of low-molecular-weight metabolites, i.e., by-products of all metabolic pathways in an organism, useful for identifying possible telltale changes of disease. In fact, each metabolomic profile provides a snapshot resulting from the interaction between gene expression and the environment [3]. Beyond the identification of specific and timely disease biomarkers, metabolomics in the context of NEC can enhance our comprehension of the microbiota-host cross-talk, thereby facilitating the identification of metabolic pathways that may be implicated in the disease. This, in turn, enables the formulation of efficacious preventive strategies, particularly for children at elevated risk [2].

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LECT 15

LEVERAGING PREDICTIVE ANALYTICS FOR MATERNAL IMMUNIZATION

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Neonatal and infant diseases have undeniably reduced due to maternal immunization (MI). However, its exact role in determining the infant's immune system remains an important research area. Several studies have studied how maternal antibodies transferred to the fetus can influence the change of the infant's immune system, modeling its future reactions to infections and vaccines. The current research focuses on the effect of MI on infant immune development, the bearing on specific diseases, and the likely long-term advantages. The availability of large datasets on MI has prompted the extensive adoption of information technology tools like machine learning, predictive analytics (PA), and artificial intelligence (AI). This research focuses on using PA as a possible tool in MI.

PA can be an effective tool in studying the long-term influences of MI and its effect on specific diseases. Predicting disease occurrences helps detect areas that may require better intervention. Using statistical modeling, data science AI, and predictive models can help forecast potential occurrences by analyzing historical data on disease outbreaks,

immunization rates, and connected factors. PA can assess the effectiveness of MI programs over time. Researchers can compare disease incidence rates in vaccinated and unvaccinated populations to decide the long-term advantages of these programs. Though very rare, PA can identify risk factors for side effects and develop strategies to lessen their occurrence.

PA is a key component of precision medicine [1]. PA would help identify high-risk populations by analyzing maternal age, medical history, and geographic location to identify women at higher risk for specific diseases or complications during pregnancy. Based on these risk assessments, healthcare providers can tailor vaccine recommendations to individual women, ensuring that they receive the most appropriate and effective immunizations. PA models can help assess MI programs' effectiveness by analyzing vaccination rates, disease incidence, and maternal and infant outcomes data to improve vaccine coverage. Healthcare providers can implement targeted interventions to increase vaccine coverage and reduce disease burden by identifying women at higher risk. Furthermore, by analyzing data on disease trends, vaccine efficacy, and the timing of maternal infections, PA can help optimize immunization schedules to maximize protection for both mothers and infants.

A study from Pakistan proposed a defaulter prediction model for accurately identifying defaulters [2]. A feasibility study proved that PA can accurately identify children at higher risk for defaulting on routine immunization visits [3]

PA can help improve the effectiveness and efficiency of MI programs by providing personalized recommendations and educating our understanding of vaccine impact.

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LECT 16

RESPIRATORY SYNCYTIAL VIRUS (RSV) PREVENTION: MESSAGES FROM THE PRESENT

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Respiratory syncytial virus (RSV) remains a leading cause of respiratory infections in pediatric populations, significantly contributing to the global burden of acute lower respiratory tract infections (LRTIs). Among infants, RSV is the predominant pathogen responsible for bronchiolitis and pneumonia, with approximately 80% of bronchiolitis cases and 40% of pneumonia cases in the first year of life attributable to RSV. The economic implications are considerable, with the annual direct healthcare costs in children under 5 years of age amounting to approximately £80 million [1].

Traditional prevention methods have primarily relied on palivizumab, a monoclonal antibody targeting high-risk infants such as preterm newborns and those with chronic lung or congenital heart disease. Despite its efficacy, palivizumab is limited by its requirement for multiple doses and its applicability to a narrow patient group, leaving a significant proportion of infants vulnerable to severe RSV disease. Recent advancements have introduced nirsevimab, a long-acting monoclonal antibody that provides broad protection across diverse infant populations, including healthy full-term infants. Nirsevimab has demonstrated robust efficacy in preventing RSV-related hospitalizations, as confirmed by both clinical trials and real-world studies conducted in various world regions [2].

Moreover, maternal immunization has emerged as a promising strategy to confer passive immunity to newborns. The bivalent RSV prefusion F protein-based (RSVpreF) vaccine, administered during pregnancy, has shown effectiveness in reducing severe LRTIs associated with RSV during the critical early months of life. Clinical trials have highlighted its safety profile and its potential to significantly decrease the incidence of RSV-related hospitalizations when administered between the 24th and 36th week of gestation [3].

In Italy, public health authorities have recognized the importance of integrating RSV prevention into national immunization schedules, advocating for the inclusion of monoclonal antibodies like nirsevimab. The proposed strategy includes a paradigm shift from traditional vaccination schedules to comprehensive immunization plans that encompass both active and passive immunoprophylaxis. The adoption of such

measures is expected to provide equitable protection to all infants, particularly during their first RSV season, thereby reducing the disease burden and associated healthcare costs.

The ongoing evolution of RSV prevention strategies, by adopting a multi-faceted approach, promises to enhance the effectiveness of public health interventions, ultimately leading to improved outcomes for infants at risk of severe RSV infections. As countries like Italy begin to implement these recommendations, the global effort to combat RSV will likely see significant advancements, reducing the overall incidence and severity of RSV-related diseases in early childhood.

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LECT 17

GENETICS AND EPIGENETICS OF THE FUTURE

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Great interest has been devoted in the last years to the field of studies named "Epigenetics", that is the science investigating the effect of environment on gene expression. Epigenetic modifications are able to affect gene function without any change in the DNA sequence, thus representing a mechanism of gene regulation not detectable by using the typical tools of genetic investigations, such as gene sequencing.

DNA methylation, chromatin organization and miRNA expression are the main mechanism of epigenetic modification of gene expression, which can be affected by several environmental factors, represented by four classes: lifestyle, chemical and physical exposure, social-economic status and ecosystem. The quick changes of our lifestyle, mainly in our diet, and of the environment, mostly due to the massive presence of endocrine disruptors, have been demonstrated to be involved in the dramatic increase of the prevalence of non-communicable diseases (NCDs). Moreover, the ability of epigenetic modifications to be transmitted to the offspring via a transgenerational model likely represent the main cause of the increased prevalence of NCDs among children, at present a worldwide emergency. Since epigenetic modifications are reversible, a correct strategy of prevention and restoration of a correct epigenetic arrangement of our genes will likely represent the most useful strategy to fight against the progressive diffusion of NCDs in our countries.

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LECT 18

MENINGITIS TODAY

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BACKGROUND

Meningitis is one of the most important pediatric infections caused by bacteria, viruses or other infectious and non-infectious agents. A high morbidity and mortality are associated with bacterial etiology of meningeal inflammation. Considering the importance of the infection and the impact that it has in children health, we analyzed the children with meningitis hospitalized in our hospital, which is the only tertiary medical center of Albania. With a population of 2,829,109 inhabitants, 374,800 of which live in the urban area of Tirana city, pediatric age (0-14 years) accounts for 16.3% of total

population [1]. Vaccines against *H. influenzae* and *Str. pneumoniae* (PCV13), and measles, mumps and rubella (MMR) are included in the mandatory national schedule of immunization.

AIM

Aim of this study was to analyze epidemiological and etiological data of acute meningitis of pediatric age, admitted to the Pediatric Infectious Diseases Service of the University Hospital Center "Mother Teresa" during the last decade, to evaluate the natural trend of this infection and factors that influenced its natural course. Aim of this study was also to find out the impact of the COVID-19 pandemic (if any) in the prevalence of this important invasive infection.

MATERIAL AND METHODS

This retrospective cohort study analyzed a 10-year period (2014-2023) and included children aged 1 month - 14 years diagnosed with meningitis. The diagnosis was established on: bacteria isolated from the cerebrospinal fluid (CSF) obtained via lumbar puncture, CSF bacterial culture, CSF molecular assays (polymerase chain reaction [PCR] or other nucleic acid amplification tests (NAAT]). Meningeal inflammation was demonstrated by increased pleocytosis, elevated protein level, and low glucose level in the CSF. Bacterial meningitis (BM) score [2-4] was used, when bacteriological signs were not available.

We reviewed the medical records, and obtained CSF data, analyzed by biochemical methods and microbiological studies. Epidemiological characteristics, such as age, gender, chronology of infections and incidence, were analyzed. Etiological data were provided by the Central Laboratory of the University Hospital Center "Mother Teresa" and the National Laboratory of Microbiology and Investigations of the National Institute of Public Health in Tirana. The diagnosis of viral meningitis (VM) was based on: negative CSF culture, slight pleocytosis with normal protein, normal glucose values, confirmation of the virus by PCR, serology, or underlying viral disease (varicella, measles, etc.). Data were analyzed using SPSS®, and X^2 and Mann-Whitney test were applied. $P < 0.05$ was considered significant.

RESULTS

186 children with meningitis were identified. 105 cases were with BM, 54 with VM, and the remaining patients (with negative microbiology and ambiguous CSF data) were with unconfirmed etiology. The age distribution was as follows: 37 patients (19.9%) were younger than 12 months of age, 43 patients (23.1%) were 1-4 years of age, 106 patients (57.0%) were 4-14 of age, with a significant predomination of cases above 4 years of age. BM was the most common etiological factor for children younger less than 4 years, while VM was found more above this age.

The majority of cases was recorded in autumn, with 56 patients (30.1%), followed by summer, with 44 patients (23.7%); an equal number of cases was recorded in winter and spring, with 43 patients (23.1%) in each season.

There was a significant decrease during the pandemic years, with an increase in number of cases during 2023, reaching a number higher than mean values of pre-COVID-19 period ($p < 0.02$).

The main agents were *N. meningitidis* and *Str. pneumoniae* (and, to a lesser degree, *H. influenzae*), despite a good coverage of immunization. Our cases had a benign course without permanent sequelae. Usually, opportunistic microorganism are the main causes of BM in infants younger than 3 months. Among viral agents causing meningitis, we found in more than 60% enterovirus, followed by varicella zoster virus, measles, herpes virus 6, West Nile virus and SARS-CoV-2. Important complications were found in 18% of children with BM, subdural empyema, brain abscess, hydrocephaly, persistence of seizures, some extra neurological complications such as Schoenlein-Henoch purpura, pericarditis, erythema nodoses. The most severe cases were those associated with sepsis, multiorgan failure, severe hyponatremia, mainly caused by *N. meningitidis* and *Str. pneumonia*, and those with very young age, who developed different sequelae. The overall case fatality rate was 1%.

CONCLUSIONS

BM is still an important invasive infection among young children despite improvement in the immunization schedule and very good coverage (98%) for Albanian children. The determination of causative agents and their serotypes remain a challenge for our pediatricians. COVID-19 pandemic has modified the natural course of meningitis in children, as in other infections. The main focus are the 3 major causative agents (*N. meningitidis*, *Str. pneumoniae* and *H. influenzae*), without neglecting other etiological agents depending on age, predisposing factors and underlying diseases.

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LECT 19

BODY DYSMORPHIC DISORDER

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Since 2010, the non-fatal self-harm attempt rate in female teens showed in the USA a vertical increase by 311%. The mental well-being of teens is under stress, in many countries and at the same time. Apparently hyperconnected, their one-to-many broadcasted communication lacks real social attunement and conceals a disembodying asynchronous social-validation feedback loop. In the lack of a definitive cross-cultural accepted interpretation, a temporal coincidence with the widespread availability of technologically advanced, portable internet connecting apparatuses is evident. One should admit that teens from Gen Z are the first generation to experience a smartphone-based childhood.

Social media Super-Users, from Gen Z on, appear more prone to experience anxiety, depression, low self-esteem, social deprivation, increased attempts of self-harm and suicide. They are tormented by obsessive thoughts associated with a part or parts of their physical appearance being flawed in some way; yet, these flaws tend not to be noticeable to anyone but themselves. One master key is self-oriented perfectionism. They believe their life satisfaction hinges on their looking hench, and desperately attempt to pursue ways to achieve that. In the DSM 5, the American Psychiatric Association has categorized this condition as body dysmorphic disorder (BDD), one of the obsessive-compulsive related disorders.

The most damaging part of living with this disorder is the toll it takes on someone's self-worth.

Today, social media, interactively compelling in the definition of "universal beauty standards", is one of the most important factors contributing to the mental, emotional, physical and spiritual health of an individual. With the media constantly portraying ideal beauty and body image comparisons, men's and women's beauty choices are globally affected.

Images on social media are user-generated and posted to receive the most likes and comments. Although the universally spread use of cosmetics has democratized the right to personal beauty and, most of all, the right to be beautiful, youngsters use retouching filters on their selfies posted on the social threads. They struggle to achieve the targeted beauty standards, keenly aware that they may not even get any better. They perceive the communicated beauty ideals as unrealistic and unattainable, regarding their image on social media as biased and not corresponding with their appearance in reality. They ponder distrustfully before showing off their filter-free face because it just doesn't look as good as it would once beautified. They end up surrending, preferring to look like their retouched-self instead of their real-self. As a matter of fact, social media contributes to the development of body dissatisfaction and body image disturbances, both directly and indirectly, through peers, acquaintances, buddies and partners.

The "Imperfect Beauty" project aims to support self-esteem in the hyperconnected teens, promoting a wider concept of "Beauty" that includes the option of being imperfect.

LECT 20

DECODING THE MIND: GENETIC INNOVATIONS IN PSYCHIATRIC RESEARCH AND TREATMENT

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INTRODUCTION

The field of psychiatry is experiencing a paradigm shift with the advent of genetic research, offering novel insights into the etiology and treatment of mental disorders. Advances in genome sequencing, polygenic risk assessment, and gene-editing technologies, such as clustered regularly interspaced short palindromic repeats (CRISPR), are poised to revolutionize psychiatric research and clinical practice.

OBJECTIVE

This study aims to explore the implications of recent genetic discoveries on tailored therapy in psychiatry, focusing on developments since 2015.

The review also addresses the ethical considerations that arise from these advancements.

METHODS

A systematic review of literature was conducted using databases such as PubMed, Google Scholar, and NCBI, focusing on recent studies related to genetic findings in psychiatry. The review encompassed genome-wide association studies (GWAS), next-generation sequencing (NGS) studies, and studies on epigenetic modifications, among others.

RESULTS

The review highlights significant findings in the genetic basis of psychiatric disorders, including heritability estimates and the identification of specific genetic risk factors. Key advancements include the discovery of over 270 genetic loci associated with schizophrenia and 30 loci linked to bipolar disorder. Additionally, epigenetic studies have revealed the impact of environmental factors on gene expression, furthering our understanding of psychiatric conditions.

CONCLUSION

Genetic innovations are set to transform psychiatric diagnosis and treatment, moving towards a precision medicine approach. However, these advancements bring ethical challenges, including issues of genetic privacy, informed consent, and potential stigmatization. Addressing these concerns is essential as psychiatry advances into this genetically informed era.