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Lectures

Selected Lectures of the Congress of Pediatrics

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The Congress of Pediatrics is a Satellite Meeting of the 21st International Workshop on Neonatology and Pediatrics, Cagliari (Italy), October 22nd-25th, 2025.

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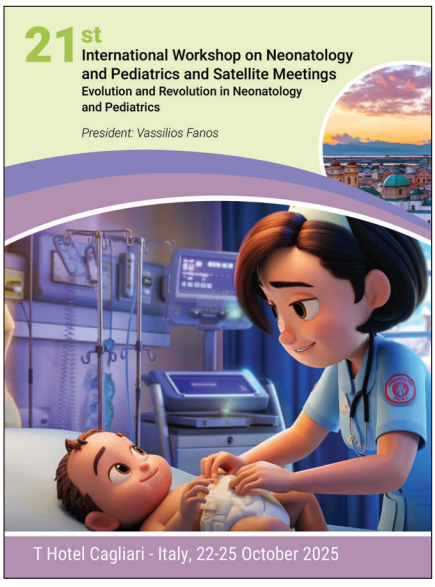

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LECT 1

POLLUTION AND NEONATAL INTENSIVE CARE

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The Neonatal Intensive Care Unit (NICU) is a highly technological environment, essential for the survival of premature babies. However, it can also expose them, albeit unintentionally, to potentially harmful chemical and physical factors that can interfere with their development. The high level of care provided also involves significant energy consumption and greenhouse gas emissions, contributing to the environmental footprint of the wards. It is well known that the healthcare sector contributes 4-5% of total greenhouse gas emissions, so much so that if it were a country, it would rank 5th (after the United States, China, Russia, and India) in the world ranking for the amount of CO_2 released into the environment. The environmental impact of the healthcare sector has indirect yet concrete consequences for the future of newborns, as it damages the planet they will inhabit after discharge. From a One Health perspective, the report provides a comprehensive and up-to-date summary of the available evidence to date. It translates it into operational guidelines for combining clinical safety and sustainability in NICUs.

Particular attention is paid to chemicals released by medical devices (phthalates, such as di-[2-ethyl hexyl] phthalate [DEHP], per- and polyfluoroalkyl substances [PFAS], bisphenol A [BPA], and related substitutes, whose safety profiles are still to be defined), micro- and nanoplastics, already detected in the prenatal period, as well as indoor air pollutants (particulate matter, volatile organic compounds [VOCs]), which can penetrate from outside or be produced in the ward. Even within a constantly evolving research context, exposure to these factors in early life is associated with alterations in respiratory, neurobehavioral, endocrine-metabolic, and immune systems, which necessitate the adoption of precautionary strategies proportionate to the risk. Noise and light pollution are other aspects to consider in NICUs. Excessive auditory stimulation caused by high background noise and poorly managed alarms has been associated with cardiorespiratory instability in newborns. At the same time, light pollution, in terms of quantity, spectrum, and timing of exposure, can interfere with the maturation of circadian rhythms and the neurological development of newborns.

These findings give rise to operational priorities: promoting procurement criteria that favor the purchase of medical devices with low or zero content of potentially hazardous chemicals, without compromising clinical efficacy and safety; conscious use of such devices, aimed at limiting the release of potentially dangerous substances; improving air quality through adequate ventilation and filtration systems; management of light and noise consistent with the physiology of the newborn, through the use of sound-absorbing materials and indirect and cyclical lighting; selective use of disposable items (where possible, in compliance with hygiene standards and sterility protocols) and promotion of energy efficiency in NICUs. These actions must necessarily be part of a periodic monitoring system that includes, where possible, biomarkers of exposure, to assess both the environmental and clinical impact of the choices made. Through indispensable multidisciplinary collaboration between neonatologists, clinical engineers, environmental experts, architects, and caregivers, the goal is to achieve a safe and sustainable NICU that can protect neonatal health in both the short and long term, while also contributing to the protection of the planet in which newborns will grow up.

LECT 2

ARTIFICIAL INTELLIGENCE IN PEDIATRIC PNEUMO-ALLERGOLOGY

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Artificial intelligence (AI) is rapidly reshaping the landscape of modern medicine, and its applications in pediatric pneumo-allergology are increasingly promising. From decision support systems to multi-

omics data integration, AI tools can enhance both clinical diagnostics and research, contributing to more precise, personalized approaches to allergic and respiratory diseases in children.

In clinical contexts, chatbot technologies such as ChatGPT exemplify how natural language processing can facilitate communication between patients, families, and healthcare providers. However, their use in pediatrics must be tempered by the need for accuracy, mainly when used for patient education or triage. AI systems can provide plausible responses, but their outputs require careful human oversight to avoid misinformation or diagnostic errors. The need for human oversight highlights the indispensable role of clinicians in verifying AI-generated content and maintaining a human-centered approach to care.

In the research domain, AI methodologies, such as Random Forest analysis, have already demonstrated potential in identifying key biomarkers in pediatric conditions, including COVID-19 and multisystem inflammatory syndrome in children (MIS-C). Similarly, in allergology and immunology, machine learning can process complex datasets to uncover disease patterns and predict treatment responses. Despite these advances, AI adoption remains limited by challenges such as data quality, model interpretability, and the need for cross-disciplinary collaboration.

Ultimately, AI should not be viewed as a replacement for clinical judgment but rather as a supportive tool that complements the intuition and expertise developed through years of practice. Ensuring that AI tools are developed and implemented in partnership with pediatric specialists will be crucial to maximizing their benefit and minimizing risks. Ongoing dialogue between developers, clinicians, and researchers will be essential to drive meaningful progress.

As pediatric pneumo-allergology moves toward precision medicine, the integration of AI holds transformative potential, provided its limitations are acknowledged and its use remains grounded in clinical reality.

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LECT 3

HIGH BLOOD PRESSURE IS NOT JUST AN ADULT PROBLEM

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Pediatric hypertension (PH) is an emerging public health challenge, with an estimated prevalence of between 2% and 5% and rapidly increasing in parallel with the obesity epidemic. Once dominated by secondary forms, primary PH is now the most common form in older children and adolescents. Despite its growing clinical relevance, the condition often remains underdiagnosed, partly due to the complexity of percentile charts based on age, sex, and height, which hinder early recognition.

Early identification is crucial: high blood pressure in childhood tends to persist into adulthood and is associated with subclinical organ damage, including left ventricular hypertrophy, arterial stiffness, and early atherosclerotic changes. Longitudinal evidence also shows an increased risk of cardiovascular events in adulthood. Differences in risk between subtypes (isolated systolic, isolated diastolic, or combined) underscore the need for precise stratification.

The biological mechanisms are multifactorial and closely linked to obesity, endothelial dysfunction, and chronic inflammation. Elevated biomarkers, such as C-reactive protein and interleukin-6, suggest a shared pathogenetic pathway with adult cardiovascular disease, linking excess adiposity, low-grade chronic inflammation, and increased blood pressure. Appropriate dietary interventions have been shown to counteract these processes by reducing inflammation, improving endothelial

function, and lowering blood pressure and LDL cholesterol levels.

Simplifying diagnosis remains a challenge. Alternative tools, such as the blood pressure/height ratio or fixed thresholds (120/80 mmHg between 6 and 12 years; 130/80 mmHg between 13 and 17 years), offer pragmatic solutions for pediatric practice. Ambulatory and home blood pressure monitoring is essential for confirming the diagnosis, recognizing white coat hypertension, and guiding treatment decisions.

Prevention through the promotion of healthy habits is essential. Once PH is confirmed, treatment begins with lifestyle changes and, if necessary, progresses to drug therapy. To monitor clinical evolution and therapeutic response, periodic reassessments of blood pressure, monitoring of inflammatory and metabolic markers, and cardiac evaluations are recommended. Follow-up ensures adherence to dietary guidelines and allows for timely adjustment of therapy.

In conclusion, PH is often underestimated, yet it has a significant impact on long-term cardiovascular health. Integrating early diagnosis, understanding of pathogenic mechanisms, simplified diagnostic strategies, and structured follow-up is essential to reduce the future burden of adult cardiovascular disease originating in childhood.

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LECT 4

THE FAMILY PEDIATRICIAN AND THE FUTURE

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The Italian pediatric population is in steady decline, particularly since 2016, when the number of children under the age of one fell below 500,000 for the first time.

In 2023, the number of children in their first year of life fell below 400,000.

In 2024, the number was approximately 372,000.

In the current context, it is essential to reorient the organizational models of pediatric care to respond to a declining population, which is burdened by an increase in neurodevelopmental disorders and adolescent distress.

The implementation of the National Plan for Chronic Conditions in Children must be defined at the national level and implemented at the regional level (*Accordi Integrativi Regionali* – AAIIRR [i.e., Regional Supplementary Agreements]) through the activation of early recognition and/or screening strategies, the planning of structured primary and secondary prevention activities, and the activation of coordinated care systems with multidisciplinary teams (*Unità Complesse di Cure Primarie* – UCCPs [i.e., Complex Primary Care Units], Community Houses).

To achieve the health objectives associated with public health activities and projects (national, regional, and corporate), the participation of Family Pediatricians is essential.

Functional Territorial Aggregations (FTAs) must be established and strengthened in all Italian regions, which should maintain a strong territorial identity, serving as a proper place of care where proactive "proximity" medicine will be implemented.

All FTAs, as well as the less widespread UCCPs, must be functionally linked to Community Houses (Ministerial Decree 77/2022, Art. 5), rather than being physically included in the Houses themselves.

Access to healthcare services must be improved through the use of telemedicine, IT networks, and greater integration between services. In particular, these tools will be used primarily in sparsely populated areas where we currently encounter the most critical issues in the allocation of the underserved regions.

For "ethical" reasons, too, the unique experience of Family Pediatrics must be maintained, as it is essential to defend the category and support the many young people who will want to pursue this professional career in the future.

Family Pediatrics will be able to modify its organizational structure in part, preserving what really matters, the continuity of the relationship of trust and proximity to the needs of families, which have always been the pride of the profession, while shifting the bulk of care to where it should be, i.e., in the community.

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• DM 77/2022 – Regolamento recante la definizione di modelli e standard per lo sviluppo dell'assistenza territoriale nel Servizio Sanitario Nazionale.

LECT 5

NEW FRONTIERS IN GENETICS

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The transition from targeted testing to whole-exome/whole-genome sequencing (WES/WGS) has demonstrated higher diagnostic yield, the potential for repeated re-analysis over time, and possible cost savings compared to phenotype-guided tests. In paediatrics, where phenotypes often change, and timely treatment is crucial, current guidelines recommend WES/WGS as a first-line investigation for various indications; rapid WGS has also become standard in intensive care settings. Practical implementation, however, remains limited by hospitals' IT capabilities, workforce shortages, and cultural resistance in some laboratories. Accurate phenotyping is indispensable to narrow down thousands of variants to a truly diagnostic subset. Gaps in expertise make it necessary to embed decision-support tools, such as artificial intelligence (AI), large language models (LLMs, e.g., ChatGPT), targeted training, and human phenotype ontology (HPO)-driven deep phenotyping. As the use of WES/WGS expands beyond syndromic presentations, organ-specific specialists can enhance phenotyping and integrate findings into management; for example, an epileptologist can relate a genetic profile to the indications and contraindications of anti-seizure medicines, alongside other factors guiding therapy choices. Continuous access to clinical geneticists – via telephone, email, or telegenetics – remains essential for test selection and interpretation of results. Meanwhile, interest in genomic newborn screening is growing. Current programmes, based mainly on mass spectrometry, restrict the number and types of conditions that can be screened; spinal muscular atrophy is currently the only disorder for which genetic testing is routinely used as a first-line test in most European countries, whereas for other conditions, genetic testing is employed as a confirmatory second-tier screen. A WGS-based newborn screening has significant potential to expand diagnosis but requires appropriate technological, interpretative, and ethical readiness. Pilot trials have shown promising technical results and have addressed psychosocial effects; in Italy, the adoption of next-generation sequencing (NGS) for screening is already progressing. However, interpretative barriers remain across all conditions due to the under-representation of many populations in global databases.

In this context, Sardinia, a genetic isolate with founder effects and a distinctive haplotypic architecture, offers a unique opportunity to improve variant interpretation. We propose a WGS-first approach alongside developing a Sardinian Reference Genome (SRG), providing population-specific allele frequencies and linkage disequilibrium patterns. The SRG will enhance the interpretative power of WES/WGS in rare and complex paediatric diseases, reducing variants of uncertain significance (VUS) (with the consequent interpretative difficulties), increasing the identification of founder variants, and enabling more timely access to time-sensitive therapies (including gene therapies). The integration of AI/LLM with clinical data is starting to support standardised workflows for both clinical geneticists and other specialists, preserving the expert perspective valuable for true precision medicine. The combined WGS-first and SRG approach presents a new, practical, and scalable frontier in clinical genetics: it accelerates diagnosis and decision-making, improves appropriateness and equity, and offers a model that can be adapted for use with other European populations, not just underrepresented ones.

LECT 6

DIABETES SCREENING

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Type 1 diabetes is an autoimmune disease caused by the destruction of insulin-producing beta cells. The disease is preceded by a long presymptomatic phase that can be identified by testing for autoantibodies against beta cells. Presymptomatic type 1 diabetes comprises 3 stages: stage 1, characterized by the presence of 2 or more autoantibodies and normal blood glucose; stage 2, marked by 2 or more autoantibodies and dysglycemia; and stage 3, characterized by hyperglycemia and clinical signs of diabetes.

Italy is the first country in the world to establish a national screening program for type 1 diabetes and celiac disease. The goals are to prevent diabetic ketoacidosis (DKA) at the onset of type 1 diabetes, identify individuals with presymptomatic type 1 diabetes, and diagnose celiac disease early.

Approximately one-third of children with type 1 diabetes have DKA at onset. In industrialized countries, the risk of morbidity and mortality associated with DKA is approximately 1%. Even a single episode of moderate or severe DKA can cause central nervous system damage, resulting in permanent cognitive deficits. DKA at the onset of diabetes is associated with prolonged hospitalization, worsening metabolic control for many years after the onset of diabetes, and increased healthcare costs. Finally, it is essential to remember the devastating psychological impact on the child and family when type 1 diabetes begins with DKA.

To implement Law 130/2023, the Italian National Institute of Health (*Istituto Superiore di Sanità* – ISS) coordinated a preliminary feasibility study, designated as D1Ce. This pilot project, which began in March 2024, enrolled over 5,000 children from 4 Italian regions: Campania, Lombardy, Marche, and Sardinia. Screening for autoantibodies using fingerstick capillary blood sampling, performed by pediatricians, is aimed at children in 3 age groups: 2, 6, and 10 years old. The study involved the ISS, pediatricians, clinical centers specializing in type 1 diabetes and celiac disease, and centralized laboratories. The study results confirmed the feasibility of the screening process. They identified 0.5% of children with the presence of at least 1 autoantibody and 0.2% of children with 2 or more autoantibodies (stage 1 type 1 diabetes). All these subjects will be enrolled in follow-up programs at Pediatric Diabetes Centers.

LECT 7

RARE DISEASES: ALPHA-MANNOSIDOSIS AND MORE

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Rare diseases constitute a complex, broad, and heterogeneous group of pathological conditions. They are morbid conditions, often chronic and/or disabling, or cause premature mortality. In the European Union, rare diseases are defined as those with a prevalence of no more than 5 in 10,000 inhabitants. The rarity of these diseases partly determines the difficulty for patients in obtaining an appropriate and timely diagnosis for adequate treatment. The latency period between disease onset and diagnosis is often long, negatively impacting prognosis. Among these, lysosomal diseases are multisystemic disorders characterized by a broad spectrum of visceral, skeletal, and hematological manifestations, sensory deficits, and frequent involvement of the central nervous system. The age of onset and clinical course are variable, with rapidly worsening neonatal-onset forms and late-onset forms with attenuated phenotypes. The cumulative incidence is approximately 1 in 5,000 to 7,500 births. These figures are expected to change in the near future thanks to the spread of neonatal screening programs. A rare example of this is alpha-mannosidosis, an autosomal recessive disease caused by mutations in the *MAN2B1* gene, which encodes the alpha-mannosidase enzyme, which degrades complex glycoproteins. The enzyme deficiency leads to the accumulation of mannose-rich oligosaccharides in lysosomes, which is responsible for the clinical manifestations of this disease. It has been highlighted in recent years that the pathogenesis is not solely linked to substrate accumulation, but to a cascade of cellular reactions triggered by the accumulation itself, including dysregulation of autophagy, mitochondrial function, calcium homeostasis, and cellular vesicular trafficking. Alpha-mannosidosis can manifest with a broad clinical spectrum and significant individual variability, even among siblings with the same genotype. Children may present with typical facial features: prominent frontal bossing, a wide nasal bridge, and prognathism. Furthermore, mild-to-moderate intellectual disability, both conductive and sensorineural deafness, and ocular abnormalities complete the phenotype. Respiratory infections and recurrent ear infections are frequent in the first decade of life, while myopathy and ataxia become prominent in the second decade. Acute hydrocephalus can complicate the disease course. Diagnosis is based on the detection of elevated urinary oligosaccharide levels and the determination of deficient enzyme activity in leukocytes. Molecular genetic testing confirms the diagnosis. Enzyme replacement therapy with velmanase alfa is now available. Enzyme replacement therapy is

available not only for alpha-mannosidosis, but also for other lysosomal diseases, which are now treated with significant benefits for patients.

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LECT 8

CONGENITAL HEART DISEASE

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Congenital heart defects are structural anomalies of the heart and great vessels; they are the most common neonatal malformations, occurring in nearly 1% of live births [1], and are the most frequent cause of infant mortality. All heart defects arise from an alteration in the development of the heart during embryonic and fetal life. These defects are well tolerated during intrauterine life and become fully serious only after birth, sometimes resulting in true neonatal emergencies [2]. There are multiple risk factors associated with the onset of heart disease, and they are often linked to maternal, familial, and fetal conditions.

The need for early diagnosis, even during the fetal period, stems from the increased survival rate of newborns when delivery is scheduled in Level III Centers equipped with neonatal cardiac surgery [3]. Some heart conditions must be diagnosed, treated, and operated on immediately in the neonatal period because they are incompatible with life; others, however, allow a waiting period of a few months, and the symptoms of heart failure can be reduced by resorting to medical therapy based on diuretics and ACE inhibitors while awaiting corrective surgery. The point of delaying surgery as long as possible lies in the possibility of achieving better results, a lower incidence of complications related to anesthesia and surgery, and a quicker and less insidious postoperative recovery.

If a prenatal diagnosis is not made, however, specific symptoms in the newborn should raise suspicion and warrant further diagnostic investigation. The symptom that most often raises suspicion is a heart murmur, which is distinct from the innocent murmur frequently detected by pediatricians. When present in the first few days of life, it should prompt a referral to a pediatric cardiologist. Other significant symptoms include cyanosis, sweating, fatigue during meals, and difficulty gaining weight. If such a clinical picture is present, the child should be referred to a Pediatric Cardiology Clinic for a cardiac examination, an ECG, and an echocardiogram.

The vast majority of congenital heart defects can be treated with a high probability of success through conventional surgery and/or hemodynamic interventions, allowing for the correction of the defect, restoration of normal cardiac function, and a return to a normal life. In more complex cases, surgery often cannot recreate normal anatomy; in these instances, palliative surgical interventions are employed, with the ultimate goal of making the heart defect compatible with life, although they cannot guarantee a quality of life perfectly comparable to that of their healthy peers. It is essential that parents, and subsequently patients, understand the importance of adhering to any prescribed pharmacological therapy and undergoing periodic check-ups at the Pediatric Cardiology Center of reference. The purpose of these periodic check-ups is to evaluate the evolution of congenital heart defects over time, whether natural or surgical, to detect any recent complications, such as arrhythmias, and, above all, to plan the most effective therapeutic path.

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LECT 9

DO NEWBORNS FLY? FROM THE WINGS OF A STORK TO THE WINGS OF AN AIRPLANE

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Neonatal transport is a key element in ensuring survival and appropriate care for critically ill newborns, particularly in island regions where access to specialized centers is limited. Sardinia represents a peculiar case in the Italian context: its insularity, population decline, progressive reduction of birth centers, and the absence of advanced neonatal surgery services (especially cardiac and neurosurgery) make extraregional transfers unavoidable. These are carried out by the Italian Air Force, specifically the 31st Wing, through life-saving flights that are indispensable but also demanding in terms of organization and costs.

Our work analyzes air neonatal transfers from the University Hospital of Monserrato (Cagliari) to mainland referral centers over the period 2014-2024. Despite a marked decline in births, the number of transfers remained stable, leading to a proportional increase in the share of critical newborns. The primary indications for transfer were surgical conditions that could not be managed within the region. The analysis of territorial origins highlighted inequalities related to inadequate pregnancy monitoring, particularly in inland areas. Comparison with the Azores experience revealed alternative organizational models, such as the implementation of *in-utero* transfer and the deployment of specialized surgical teams on-site.

The findings confirm the strategic role of the Italian Air Force in guaranteeing access to high-specialty care but also highlight the urgent need to reorganize the regional system, including the possible implementation of a neonatal transport network in Sardinia.

LECT 10

SOCIAL MEDIA AND NUTRITION EDUCATION

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The most recent scientific research has demonstrated that the use of social media can be a risk factor for the development of eating disorders and the increase in overweight and obesity [1]. In the case of the former, the predominant mechanisms include social comparison, internalization of the ideal of thinness or fitness, and self-objectification, which is defined as perceiving oneself as an object subjected to aesthetic judgment. Conversely, an association has been observed between the early and daily use of digital platforms, beginning as early as elementary school, and weight gain, as these platforms have been implicated in promoting sedentary behaviors and increasing exposure to unhealthy food advertisements [1]. This phenomenon is evidenced by an escalating consumption of snacks and energy-dense foods, which fosters a high-calorie dietary pattern, particularly in the absence of adequate early nutrition education [2, 3]. Indeed, repeated exposure to fruits and vegetables has been demonstrated to play a pivotal role in fostering the development of healthy dietary habits, a critical component in environments characterized by the pervasive presence of ultra-processed foods (UPFs) [2, 3]. This exposure is particularly significant in light of the evidence suggesting that highly palatable foods, such as UPFs, can modify taste sensitivity, thereby enhancing the perceived unpleasantness of more natural flavors. This phenomenon can be attributed to the fact that frequent exposure to highly palatable foods, such as those with high sugar, fat, and salt content, can cause the brain's reward circuits to become more attuned to these stimuli. The exposure to highly palatable foods, in turn, can lead to a state of sensory adaptation, resulting in a diminished responsiveness of the reward system to weaker stimuli, such as those derived from fresh, unprocessed foods [3]. Consequently, there is an imperative to adapt scientific communication strategies, promoting increased active engagement on social media by healthcare professionals and researchers. This initiative aims to counteract the dissemination of misinformation and to disseminate educational content and high-quality research. Indeed, prominent scientific societies, including the North American Society of Pediatric Gastroenterology, Hepatology, and Nutrition (NASPGHAN), have advocated for the recognition of substantial social media engagement as an official component of academic promotion and career advancement evaluations [4, 5].

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LECT 11

NEONATAL SEIZURES

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Seizures are the most common neurological emergency in the neonatal period, and in contrast to those in infancy and childhood, are often provoked seizures. Acute provoked seizures cause most neonatal seizures (85%). The most common cause in term infants is hypoxic-ischemic encephalopathy. Neonatal-onset epilepsy syndromes also exist but are less common. In 2021, the International League Against Epilepsy (ILAE) introduced a new classification and framework for seizures in the neonatal period, emphasizing the crucial role of electroencephalography (EEG) in diagnosing seizures in this age group [1]. The ILAE neonatal seizure classification divides EEG-defined seizures into those with clinical signs and those without clinical signs. Clinical seizure types with motor manifestations include automatisms, clonic, epileptic spasms, myoclonic, and tonic. Non-motor seizures include autonomic and behavioral arrest. Sequential seizures can be both motor and non-motor [2]. Phenobarbital is a first-line treatment for neonatal seizures, but recent studies evidence that sodium channel blockers are more effective than other anti-seizure medications in treating acute provoked seizures associated with arterial ischemic stroke in term neonates [3]. Despite advancements, challenges persist, including the need for accurate diagnosis and the limited availability of evidence-based treatment protocols, which emphasize the importance of global efforts to standardize care.

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LECT 12

SLEEP AND EPILEPSY

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Sleep problems are markedly more frequent in children with epilepsy than in the general pediatric population. Insomnia, fragmented sleep, circadian misalignment, parasomnias, and excessive daytime sleepiness are common and often under-recognized. Disturbed sleep can lower seizure thresholds, increase interictal epileptiform discharges, and degrade daytime behavior and cognition, creating a self-reinforcing loop between poor sleep and worse epilepsy.

Beyond symptoms, sleep microstructure links directly to learning and brain plasticity. During non-rapid eyes movements (REM) sleep, slow-wave activity (SWA) supports synaptic renormalization, and spindles, generated by thalamo-cortical networks, coordinate hippocampal-cortical communication for memory consolidation. Epileptic activity can blunt the overnight decline of SWA, fragment spindles, and disrupt slow-wave-spindle coupling, thereby impairing attention, memory, and academic learning. REM sleep exerts an "antiepileptic" effect, and it is typically reduced in pediatric epilepsies; its loss may further increase nocturnal spikes and seizures.

In clinical practice, differential diagnosis can be challenging because sleep-related seizures may mimic non-rapid eyes movements (NREM) parasomnias (confusional arousals, sleep terrors). Clues favoring epilepsy include stereotypy, very brief or clustered events, abrupt onset and offset, and prominent dystonic or hyperkinetic movements. Conversely, variable semiology, clear precipitating

factors such as sleep deprivation, and occurrence in the first third of the night favor parasomnias. A correct diagnosis is crucial for preventing overtreatment of benign disorders and avoiding missed epilepsy.

Sleep should be screened systematically; contributors to poor sleep should be assessed (nocturnal epileptic activity, anti-seizure medication effects, comorbid sleep disorders); and care should be personalized (anti-seizure medication dose/timing should be optimized, sleep hygiene and psychoeducation should be provided, and comorbidities should be treated) with referral to specialized sleep-epilepsy services for refractory cases.

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LECT 13

DEVELOPMENTAL AND EPILEPTIC ENCEPHALOPATHIES: AN OVERVIEW

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Developmental and epileptic encephalopathies (DEEs) are a group of disorders characterized by severe, continuing seizures, refractory to antiepileptic drugs, associated with electroencephalographic anomalies, and behavioral impairment of varying degrees. In particular, the severity of epileptiform activity may result in developmental slowing or regression. When we consider the DEEs, it should be emphasized that seizures are part of the disorder, often the presenting feature, but many other findings, such as developmental behavioral disorders, feeding issues, musculoskeletal issues, and sleep problems, are part of the clinical picture. Parallel to pharmacological innovation, standards for supportive care should also be considered. A multidisciplinary approach, which includes neurodevelopmental alertness, physiotherapy, speech therapy, and behavioral interventions, is mandatory to alleviate comorbidities and improve quality of life.

From a pathophysiological perspective, the majority of DEEs are related to pathogenic variants in genes mainly coding for ion channels. That finding gives rise to genetically distinct DEEs with specific pathophysiological mechanisms. From a therapeutic point of view, the management has traditionally aimed at obtaining seizures reduction. In this perspective, broad-spectrum antiseizure medications (ASMs), such as valproate, benzodiazepines, topiramate, and levetiracetam, have been widely used in combination with the ketogenic diet and vagus nerve stimulation. However, this traditional approach is of limited efficacy and is often complicated by the occurrence of severe adverse events. Recent advances in molecular genetics have allowed for significant conceptual changes in the standard of care for DEEs. Indeed, early targeted interventions, within the context of precision medicine, may significantly alter the clinical trajectory of these severe disorders. Concrete examples of genotype-guided therapy in DEEs include the introduction of stiripentol, cannabidiol, and fenfluramine, or sodium channel blockers in gain-of-function *SCN2A/SCN8A* mutations, m-Tor inhibitors in tuberous sclerosis complex, as well as the avoidance of sodium channel blockers in Dravet syndrome. Moreover, antisense oligonucleotides, gene replacement therapies, and RNA-modifying therapeutics are entering clinical pipelines, offering the prospect of disease-modifying strategies. In other words, many ASMs currently available have not been designed to address individual genetic abnormalities, but rather to reduce neuronal excitation. Understanding the relative pathways involved and the different proteins for which the involved genes code may enable a more targeted approach in treating DEEs.

LECT 14

SYNDROMES WITH EPILEPSY

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Genetic syndromes encompass a wide range of genotypic and phenotypic spectra, characterized by neurocognitive and motor delays, dysmorphic features and/or malformations, and multisystem involvement [1, 2]. Among the most frequent clinical manifestations, after intellectual disability,

epilepsy plays a particularly relevant role. An increased risk of developing epilepsy or presenting with electroencephalographic (EEG) abnormalities, even in the absence of overt epileptic seizures, has been reported.

In many genetic syndromes, epilepsy has polymorphic and nonspecific features, with age of onset and sex prevalence varying across syndromic conditions. In specific genetic syndromes, a strong correlation with the development of epilepsy can be identified. This association may be either specific and consistent or simply frequent. A consistent association is defined as a correlation between the genetic syndrome and epilepsy in more than 70% of cases, and in some instances approaching 90%. In recent years, several dysmorphic syndromes have been associated with specific electroclinical patterns. In such cases, seizure onset often occurs early, typically within the first year of life. These include Angelman syndrome, Wolf-Hirschhorn syndrome, Rett syndrome, and ring chromosome syndromes such as Ring 14 and Ring 20. In contrast, in other syndromes, EEG patterns are heterogeneous and nonspecific. Therefore, in genetic syndromes with epilepsy, electroclinical correspondence is not always univocal [2].

However, it remains uncertain whether identifying the type of epilepsy and its EEG pattern significantly contributes to the syndromic diagnosis. While specific syndromes are indeed associated with distinctive EEG features that may suggest a particular epilepsy type, the reverse is not always true: a given epilepsy phenotype is not necessarily linked to a specific syndrome. The predisposition to seizures may result from neurotransmitter dysfunctions (involving GABA or glutamate), ion channelopathies (e.g., potassium channels), or structural abnormalities of the central nervous system, all of which may be caused by the same chromosomal aberrations, either separately or in combination.

In conclusion, although genetic syndromes associated with epilepsy are rare pathological conditions, it is essential to identify and recognize them to implement long-term follow-up and provide comprehensive family support, aimed at assessing familial risk and developing a preventive program through prenatal screening [1].

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LECT 15

LONGITUDINAL ASSESSMENT OF NEURODEVELOPMENT

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A snapshot of children's health today highlights the increasing incidence of chronic degenerative diseases, metabolic and cancerous diseases, and neurodevelopmental disorders (NDDs). NDDs are a group of complex conditions that onset early in childhood and typically manifest themselves in preschool age. Such disorders can be considered chronic, heterogeneous conditions that cause difficulties in various aspects of a child's life as they interfere with personal, social, and academic functioning [1].

The scientific literature provides few studies measuring the prevalence of NDDs in the population under the age of 18 according to the DSM-5 (2013) criteria. The following rates have been reported in the most common neurodevelopmental disorders: intellectual disability, 0.63%; attention deficit/hyperactivity disorder, 5-11%; autism spectrum disorder, 0.70-3%; specific learning disorder, 3-10%; communication disorders, 1-3.42%; and motor disorders, 0.76-17%. Many studies support the idea that such disorders may be underdiagnosed and that comorbidity of multiple NDDs is the norm [1].

The experience of Family Pediatricians suggests a significant increase in prevalence even in the absence of reliable epidemiological data, with 4% to 12% of patients affected by NDDs with diagnoses confirmed by Child and Adolescent Neuropsychiatry Centers. These figures are likely to be underestimated, given the significant number of patients awaiting diagnosis.

Early diagnosis is crucial, given that this complex of disorders entails a high health, social, and economic burden, but above all, in light of scientific evidence indicating that early interventions are more effective and allow for the development of personalized rehabilitation and therapies aimed at enhancing the child's cognitive, social, and emotional outcomes. This proactive care can significantly improve quality of life and offer adequate support to the family, thus helping to reduce the impact of the disorder on development.

The Italian National Institute of Health (*Istituto Superiore di Sanità*) has developed neurodevel-

opmental assessment forms, endorsed by Scientific Societies representing pediatrics, neonatology, and child neuropsychiatry, to facilitate the early identification of children with symptoms of NDDs. Each development observation and promotion form includes the 6 main behaviors to be assessed to ensure effective neurodevelopmental monitoring of the child in the 3 neurofunctional areas (domains): motor, socio-communicative, and regulatory [2].
Active surveillance by Family Pediatricians and their coordination with specialist Child Neuropsychiatry Units is essential for early recognition, care, and timely intervention, which are strategic actions for improving the quality of life of people with neurodevelopmental disorders.

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LECT 16

SKIN, SUN EXPOSURE, PHOTOPROTECTION, AND RELATED DISEASES

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All current guidelines on sun exposure and photoprotection recommend that everyone – adults and children alike – protect their skin from solar ultraviolet (UV) radiation by seeking shade, wearing sun-protective clothing, and using sunscreen containing photoprotective agents. These measures aim to reduce the incidence of skin cancers, particularly cutaneous melanoma, in both adults and children.
A recent study [1] conducted in the United States revealed a general decline in the incidence of cutaneous melanoma diagnoses among both youth and older populations. This trend may be attributed to increased efforts to shield the skin from excessive UV exposure during childhood, compared to previous generations, along with a reduced use of tanning beds and a more widespread adoption of sunscreens.
Nonetheless, the skin possesses its own defense mechanisms that activate upon sun exposure, including epidermal hyperplasia, thickening of the stratum corneum, hyperpigmentation, and continuous DNA damage repair. Therefore, gradual sun exposure that allows the skin to develop these protective responses is crucial. With proper precautions, moderate sun exposure can be beneficial for the skin and may help alleviate conditions such as atopic dermatitis or psoriasis.
A recent Expert Panel [2] on pediatric photoprotection aimed to:

a. assess sun exposure habits and sunscreen use among Italian families based on data from a questionnaire distributed to parents;
b. define practical guidelines for safe sun exposure using an Italian mnemonic acronym easily understood and remembered by parents (C.O.C.C.O. – *Camicia, Ombra, Cappello, Crema, Occhiali*, i.e., shirt, shade, hat, cream, glasses);
c. promote the use of sunscreens containing inorganic filters such as zinc oxide, with features including water resistance, fragrance-free formulas, biodegradability, and eco-friendly packaging.

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LECT 17

PARENTAL STRESS IN NEONATAL INTENSIVE CARE

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The hospitalization of an infant in the Neonatal Intensive Care Unit (NICU) represents a profoundly traumatic event for parents, with repercussions not only on their psychological and physical well-being

but also on the child's cognitive development, social relationships, and physical health, both in the short and long term. Separation from the infant, the underlying condition leading to NICU admission, the inability to provide care, and the presence of intrusive medical equipment that limits physical contact all contribute to undermining the parental role as caregiver. These circumstances often generate a profound sense of helplessness and intensify the emotional burden associated with hospitalization.

Anxiety disorders and post-traumatic stress disorder (PTSD) are the most common psychopathological conditions affecting parents of NICU infants. It is estimated that approximately 41% of mothers and 21% of fathers experience high levels of psychological stress during their child's hospitalization, and that nearly one-quarter of parents continue to report anxiety and PTSD symptoms up to 12 months after birth.

Identifying risk factors and the most vulnerable groups for the development of anxiety and PTSD, as well as recognizing symptoms at an early stage, is essential for healthcare professionals to implement supportive practices that can alleviate parental emotional distress during and after the infant's hospitalization. In recent years, several supportive strategies for parents have been developed.

One is Family-Centered Care (FCC), grounded in the principle that the family plays a central role in the child's care process, with parents being actively involved in both caregiving and decision-making. Reported benefits of FCC include improved parental mental health, enhanced neonatal weight gain, and reduced length of hospital stay. Another one is Kangaroo Mother Care (skin-to-skin contact): widely recognized for its benefits to infants, it has also proven effective in reducing parental stress while improving mood and sleep quality. More recently, the Single-Family Room model has emerged, allowing parents to spend more time with their infant and to be more engaged in routine care.

In addition, the importance of routine screening for anxiety, PTSD, and depression among parents, as well as the presence of a psychologist within NICU settings, is now well established. Psychological intervention serves as a protective factor, enhancing parental mental well-being and the quality of parent-infant interactions. Furthermore, such supportive interventions foster parental empowerment and promote the development of emotional competencies that may be temporarily inhibited by physical or psychological stress.

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LECT 18

COAGULATION DISORDERS IN THE NEWBORN

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Abnormalities of the hemostatic system during the neonatal period can pose a diagnostic and therapeutic challenge for healthcare professionals working in Neonatal and Pediatric Wards, particularly.

Deficiencies and/or elevations of specific coagulation proteins, combined with acquired or genetic risk factors, can lead to hemorrhagic or thromboembolic emergencies. Prompt diagnosis of congenital or acquired hemorrhagic or thrombotic disorders can prevent significant long-term sequelae. This presentation reviews current knowledge of neonatal hemostatic balance, as well as the etiology and management of neonatal coagulopathies.

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LECT 19

STREPTOCOCCAL PHARYNGITIS AND ITS RELATED ISSUES: WHAT'S NEW?

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Recurrent respiratory infections are defined by a specific number of respiratory infections based

on age, excluding secondary causes. Risk factors include immunological inexperience, exposure to secondhand smoke, pollutants, prematurity, and inadequate vaccination. Prevention is based on vaccinations, limiting exposure to environmental factors, and vitamin D supplementation; the use of prophylactic antibiotics is discouraged. Waldeyer's ring includes the adenoid, tubal, palatine, and lingual tonsils, with tonsillar hypertrophy assessed on a scale of 0 to 4 based on age and the percentage of space occupied between the tonsillar pillars.

The etiological diagnosis of tonsillopharyngitis cannot be based solely on clinical findings; scores such as the McIsaac score help assess the likelihood of GABA infection, but rapid testing is indicated in all cases except those with very low scores. Italian guidelines recommend the rational use of antibiotics with appropriate dosages and duration to prevent complications. The treatment of choice for streptococcal pharyngitis is penicillin V or, in its absence, amoxicillin administered at 50 mg/kg/day in 2-3 oral doses daily for 10 days.

Although not routinely indicated due to their high cost and broad spectrum of activity, second-generation cephalosporins (cefaclor 40-50 mg/kg/day in 2 doses or cefuroxime axetil 20-30 mg/kg/day in 2 doses; cefprozil 15-30 mg/kg in 2 doses) for 5 days could be used in cases of questionable compliance with amoxicillin treatment for 10 days.

Rheumatic disease is a multisystem autoimmune disease resulting from untreated GABA infection. Its pathogenesis is not fully understood but is linked to an autoimmune reaction (molecular mimicry). Diagnosis is based on the Jones criteria (1992 and AHA 2015 revision), with differentiation between low- and high-risk areas; Italy is considered a high-risk area. Manifestations include carditis, migratory arthritis, chorea, erythema marginatum, and subcutaneous nodules. Carditis is present in 50-60% of cases, with pathological murmur and possible valvular insufficiency; the arthritis is migratory and asymmetric, affecting large joints and regressing spontaneously. Chorea occurs in 10-30% of cases, particularly in females, characterized by involuntary movements and a fluctuating course. Treatment includes antibiotics, non steroidal anti-inflammatory drugs (NSAIDs), corticosteroids, and specific drugs for chorea, with periodic antibiotic prophylaxis to prevent relapses.

PFAPA (Periodic Fever, Aphthous stomatitis, Pharyngitis and Adenitis) syndrome presents with periodic fever, pharyngitis, and lymphadenitis, accompanied by regular growth and the absence of interictal symptoms. The recommended treatment is betamethasone during febrile episodes, with close monitoring and a gradual resolution expected within 5 years. It is essential to distinguish PFAPA from recurrent respiratory infections and other immune-mediated disorders.

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LECT 20

BIOACTIVE NUTRITIONAL COMPONENTS IN PEDIATRICS

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Bioactive nutritional components represent an emerging and strategic area in pediatric nutrition and in the primary prevention of chronic diseases with early onset. These molecules, naturally present in foods or derived from them, exhibit positive physiological activity in addition to their simple nutritional value. In pediatrics, interest is primarily focused on long-chain polyunsaturated fatty acids (LC-PUFAs), probiotics and prebiotics, polyphenols, beta-glucans, lactoferrin, lutein, zeaxanthin, melatonin, and bioactive peptides, whose actions are expressed in various biological functions, ranging from supporting neurocognitive development to immune modulation. LC-PUFAs, particularly docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA), are crucial for neurogenesis and retinal development in the first 1,000 days of life [1]. Probiotics and prebiotics

contribute to the formation and maintenance of a eubiotic intestinal microbiota, positively influencing the immune response and reducing the risk of infections and allergies [2]. Polyphenols and beta-glucans, thanks to their antioxidant and anti-inflammatory activity, could play a role not only in counteracting the early stages of metabolic syndrome and low-grade chronic inflammation, but also in supporting the immune defenses during infectious diseases in children [3]. Lactoferrin is effective in reducing the frequency and duration of recurrent respiratory infections in preschool children [4]. Lutein and zeaxanthin, antioxidant carotenoids, have a protective effect on the retina and central nervous system, with potential benefits for children exposed to digital screens. Melatonin, in low doses, is used to regulate sleep disorders related to circadian rhythm disorders or hyperarousal. However, the use of nutraceuticals in children still raises questions regarding safety, dosage standardization, and the quality of products available on the market. Pediatric nutraceuticals should be considered an integral part of a multidisciplinary approach to health promotion, supported by solid scientific evidence and careful medical evaluation, to avoid improper medicalization or uncontrolled consumption. Clinical studies on pediatric populations are still needed to consolidate indications for use and define targeted and personalized supplementation protocols.

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LECT 21

SPORTOMICS: METABOLOMICS AND SPORT

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Sportomics is the application of metabolomics science to sport. Metabolomics is the individual fingerprint that is key to personalized medicine, and in our case, it is also key to personalized sports science. Metabolomics analyzes the metabolites produced by the body, i.e., small molecular-weight substances present in all biofluids, providing a detailed map of the biochemical and metabolic processes occurring. Metabolomics is the secret language of the body, which can now be deciphered, a language used by cells to communicate with each other, as well as with microorganisms and organs. Metabolomics is considered the "Rosetta Stone" of microbiomics. Microbiomics studies the microbiota, the set of microorganisms that populate our body, with particular attention to those in the intestine. A cutting-edge topic is the intersection between "omic" disciplines (metabolomics, microbiomics) and sport, a constantly evolving field that promises to revolutionize the way we think about athletic training, nutrition, and the health of athletes. The main objectives of this work are multiple: to provide a clear and accessible overview of the scientific basis of these disciplines, to explore their practical applications in sport, and to stimulate new perspectives for research and innovation. In recent years, the integration of metabolomics and microbiomics has opened up new perspectives in the study of human physiology, particularly in enhancing athletic performance. These two emerging fields of science offer innovative tools for better understanding how the body works, personalizing nutritional interventions, and optimizing training strategies.

How can athletes' health be improved? How can injuries be prevented? How can personalized nutritional strategies be used? Is it possible to optimize recovery from fatigue? Sportomics can provide the most advanced scientific answers available today, which are of extraordinary importance for athletes, not only elite ones. A closely related topic is that of biotics (prebiotics, postbiotics, synbiotics, and above all, probiotics) as supplements that can enhance athletic performance by strengthening the individual's immune system.

Sportomics is crucial for all those who participate in sports, especially at a high level, and for the staff who support them (doctors, nutritionists, physiatrists, specialists, coaches, athletic trainers, etc.), to enable them to perform at their best while ensuring maximum safety.

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LECT 22

EUROPEAN PROJECT "BETTER4U": WHERE ARE WE NOW?

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Obesity remains a public health priority, and "one-size-fits-all" approaches have limited effectiveness because they do not consider people's biological, behavioral, and social heterogeneity. BETTER4U (https://better4u.eu/) was created to bridge this gap by developing and validating truly personalized interventions guided by artificial intelligence models throughout the entire lifespan. The project integrates large European databases, combining genetic, metabolome, and microbiome analyses with diet, physical activity, sleep, and socioeconomic and environmental determinants to identify the causal determinants of weight gain and stratify individuals and contexts at different risk. Based on this evidence, BETTER4U is developing targeted intervention packages (including nutritional, behavioral, and digital support) to be evaluated in a multicenter randomized trial across several European countries, with real-time monitoring to support adherence and provide continuous feedback. The UNICA team (of the University of Cagliari, Italy) is a partner in the project and is responsible for evaluating the correlations between metabolic profiles, analyzed with the Nightingale Health, Metaboneer, and Biocrates metabolomics platforms, and high body mass index values in different European cohorts. It will also conduct metabolomic analysis of 2,000 samples from obese individuals enrolled in various European countries.

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