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Lectures

Selected Lectures of the Round Table on "Antibiotic Resistance and Endocrine Disruptors"

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The Round Table on "Antibiotic Resistance and Endocrine Disruptors" is a Satellite Meeting of the 21st International Workshop on Neonatology and Pediatrics, Cagliari (Italy), October 22nd-25th, 2025.

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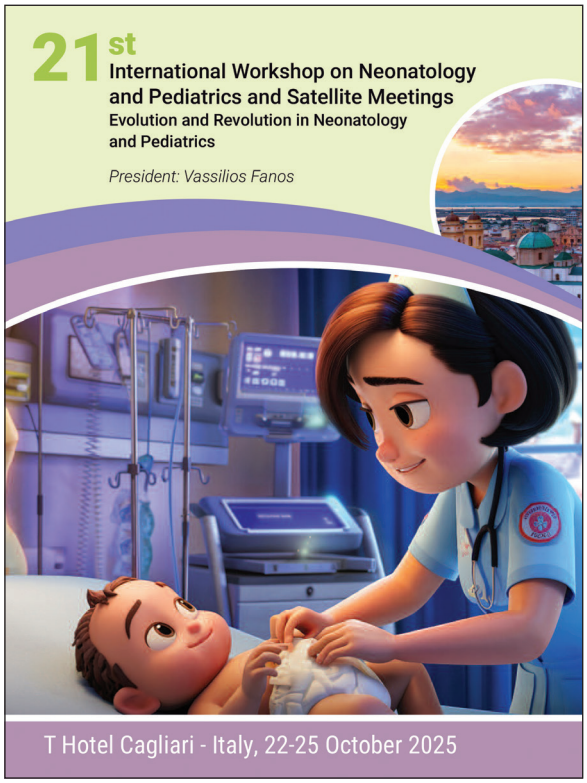

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LECT 1

ANTIMICROBIAL RESISTANCE AND ENDOCRINE-DISRUPTING CHEMICALS (EDCs)

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Currently, it is recognized that over 350,000 human-made chemicals have been synthesized. Among these, some have adverse effects on health through endocrine-disrupting mechanisms, including an impact on the increase in non-communicable diseases and on the immune system [1].

Antimicrobial resistance is a global concern that has been at the forefront, primarily attributed to the incorrect use of antibiotics, and involves various mechanisms. In recent years, it has been shown that exposure to specific endocrine-disrupting chemicals (EDCs) is associated with proven mechanisms leading to antimicrobial resistance.

Both antibiotics and EDCs are found in receiving waters. EDCs can interfere with bacterial metabolism and resistance mechanisms in various ways [2].

Antibiotic resistance genes (ARGs) present in bacteria protect them from the effects of antibiotics. These bacteria and genes are present in the environment, and through inhalation, ingestion, or contact, polluted air, food, or water can contaminate humans by transporting mechanisms of antimicrobial resistance. Antimicrobial chemicals such as triclosan, triclocarban, and methyl-, ethyl-, propyl-, and butylparaben are found in the dust microbiome and increase the number of ARGs. These latter are, by definition, also emerging contaminants and represent a critical focal point in public health and environmental safety.

Bisphenols (BP A, S, F, and AF) are common plasticizers that have been shown to interfere with bacterial metabolism as they upregulate capsule polysaccharide biosynthesis and metabolic enzymes within *Acinetobacter baylyi ADP1*, enabling the formation of thicker capsules for capturing free plasmids. At the same time, genes encoding DNA uptake and translocation machinery become incorporated to enhance the natural evolution of antibiotic resistance. Another mechanism that has been proven for BPS involves its hydroxyl group combining with biofilms through a hydrogen bond force, which leads to several changes that, in turn, favor an increase in ARGs [3]. Furthermore, BPS increases oxidative stress, disrupts membrane homeostasis, and increases expression of conjugation-related genes. In *Enterococcus faecalis*, BPA can also mimic a pheromone.

Phthalates are also implicated and, at concentrations commonly found in the environment, they enhance plasmid-mediated conjugation transfer of ARGs among intrageneric, intergeneric, and wastewater microbiota.

Interestingly, metal resistance genes are linked to antibiotic resistance genes and heavy metal contamination, and antibiotic resistance and heavy metal contamination overlap, suggesting an interwoven evolutionary history.

Finally, per- and polyfluoroalkyl substances accumulate in the human gut microbiota, as demonstrated in 38 different strains, indicating potential further risks.

The effects of mixtures of chemicals and interactions with other contaminants, such as mycotoxins, as well as the effects of climate change and microplastics, remain unknown. EDC removal methods from wastewater are under study.

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LECT 2

NEW ANTIMICROBIALS FOR EMERGING AND RE-EMERGING PATHOGENS

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Antimicrobial resistance (AMR) has emerged as a critical threat to global public health. As conventional antibiotics progressively lose their efficacy, the development of novel antimicrobial agents has become not only urgent but essential. The WHO has classified AMR as a global health emergency, with profound implications across medical, veterinary, and economic fields. This scenario presents an increasingly complex challenge to healthcare systems worldwide, as it severely limits therapeutic options, prolongs hospital stays, increases treatment costs, and contributes to rising morbidity and mortality rates. Despite the increasing request for new antimicrobials, investment in their discovery and development, particularly in small molecules of natural or synthetic origin, remains insufficient. New compounds with innovative chemical structures and mechanisms of action are critically needed to combat multidrug-resistant (MDR) pathogens that have evolved resistance to existing antibiotic classes. Such innovation is essential for restoring the efficacy of antimicrobial therapies and ensuring the long-term sustainability of infection control strategies. Multidisciplinary research has identified promising candidates, including synthetic compounds such as coordination complexes based on noble metals. These compounds have garnered increasing attention due to their unique physicochemical properties and biological versatility. Metal ions play either structural or functional roles, stabilizing biomolecular architectures, particularly proteins, or participating directly in catalytic and bioactive processes. These dual functionalities make metal-containing compounds highly attractive scaffolds for designing novel antimicrobial agents. In this context, gold-based coordination complexes, such as ethylbenzylpyridines, have demonstrated significant antimicrobial activity, particularly against MDR strains commonly associated with nosocomial infections, including *K. pneumoniae* and methicillin-resistant *S. aureus*. Although these compounds are not yet approved for clinical use, they represent a field with substantial potential for the development of a new class of functional antimicrobials. Notably, their multi-target mode of action, often involving mechanisms distinct from those exploited by conventional antibiotics, significantly reduces the likelihood of resistance development. As such, gold-based compounds emerge as compelling candidates in the fight against antimicrobial resistance, warranting continued investigation and translational research toward clinical application.

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LECT 3

ANTIBIOTIC RESISTANCE IN INTENSIVE CARE

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Antibiotic resistance represents one of the major threats to global public health, with a particularly significant impact in Intensive Care Units (ICUs), where critically ill patients are exposed to invasive treatments and intensive use of antibiotics. In this context, the emergence of multidrug-resistant bacterial strains compromises the effectiveness of antimicrobial therapies, increasing morbidity, mortality, and healthcare costs. The primary causes include the empirical and sometimes inappropriate use of antibiotics, selective pressure from prolonged treatments, and the transmission of nosocomial infections.

In ICUs, the microorganisms most frequently associated with antibiotic resistance are:

- *Klebsiella pneumoniae* (often producing carbapenemases, such as KPC);
- *Acinetobacter baumannii* (resistant to carbapenems and other antibiotics);
- *Pseudomonas aeruginosa* (with multiple resistances, including carbapenems);
- methicillin-resistant *Staphylococcus aureus* (MRSA);
- vancomycin-resistant *Enterococcus faecium* (VRE);
- *Escherichia coli* producing extended-spectrum beta-lactamases (ESBL).

These microorganisms are responsible for severe infections, including ventilator-associated pneumonia, sepsis, and urinary tract infections, which carry high mortality rates and pose significant therapeutic challenges. Prolonged use of broad-spectrum antibiotics and the presence of invasive devices (catheters, ventilators) are key risk factors.

Effective management of antibiotic resistance in ICUs requires a multidisciplinary approach integrating rapid microbiological diagnostics, antibiotic stewardship, epidemiological surveillance, and continuous training of healthcare personnel. In particular, the active involvement of nurses in antibiotic stewardship has proven crucial to improving clinical outcomes and reducing the incidence of healthcare-associated infections. It is essential to promote evidence-based organizational models and "One Health" strategies to address this health emergency systematically and sustainably.

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LECT 4

ANTIBIOTIC RESISTANCE IN NEONATAL INTENSIVE CARE

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Antibiotic resistance is the ability of a bacterium to survive and multiply even in the presence of antibiotics, and it is a global health problem, particularly in Neonatal Intensive Care Units (NICUs) [1-3]. Newborns, especially premature babies, are very vulnerable because they have immature immune systems, receive antibiotics early in life, and can acquire resistance genes from their mother or the hospital environment [1-3]. Birth represents newborns' first exposure to antibiotic-resistant microorganisms that could colonize their gut [3]. Several factors, including delivery mode, the mother's previous exposure to antibiotics, gestational age, breastfeeding and antibiotic use in early childhood, have been described as modulators of the newborn's microbiota and, consequently, the resistome [3]. In the NICU, factors related to the newborn are compounded by those associated with the specific environment, including the succession of procedures and the use of intravascular devices, endotracheal tubes, on which a biofilm characterized by multidrug-resistant polymicrobial flora can develop [1, 2]. Prompt diagnosis and the shortest possible duration of empiric antibiotic therapy, followed by a switch to targeted therapy, are essential in managing neonatal infections [2]. Furthermore, good clinical practice guidelines should be combined, including monitoring the development of biofilm-mediated infections by removing or exchanging invasive devices as soon as possible and, if necessary, combining them with short-term antibiotic therapy to combat any bacteria that may have been released into the bloodstream [2]. To help evaluate the impact of neonatal sepsis and antibiotic resistance in the NICU, a retrospective observational study was initiated at our center. It considered the number of sepsis cases before hospitalizations between January 1, 2024, and March 31, 2025, analyzing in particular the association with central vascular access (umbilical venous catheter and central venous catheter) and paying attention to the presence or absence of antibiotic-resistant germs in positive blood cultures, identifying a prevalence of *Staphylococcus epidermidis* with the detection of mecA and mecC resistance genes. The result highlights the need to further study the topic of antibiotic resistance in the NICU to seek new preventive and therapeutic strategies and reduce the morbidity and mortality of neonatal sepsis.

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LECT 5

UNDERSTAFFING AND OVERCROWDING IN NEONATAL INTENSIVE CARE UNITS

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Neonatal Intensive Care Units (NICUs) represent the only care setting capable of ensuring adequate treatment and favorable outcomes for critically ill newborns. The high clinical and organizational complexity of these Units is often burdened by risk factors that significantly impact the well-being of neonates. Among these, patient overcrowding and staff shortages (or understaffing) are two interrelated variables that have a profound impact on the quality of neonatal care, the effectiveness of infection prevention and control strategies, and, consequently, the growing issue of antimicrobial resistance.

This lecture aims to analyze the interconnection between overcrowding and understaffing in NICUs, with a particular focus on nursing care delivery. Existing literature highlights how an inadequate nurse-to-patient ratio is consistently associated with increased individual workload, reduced adherence to key infection prevention practices (including hand hygiene), decreased compliance with sepsis prevention bundles, and a higher incidence of errors and adverse events.

Similarly, persistent overcrowding in NICUs poses a substantial risk to optimal care provision and Unit management, as it reduces the amount of dedicated care time per infant and increases the likelihood of procedural mistakes. In overcrowded settings, healthcare professionals work under considerable pressure and stress, which can compromise their ability to deliver high-quality, individualized care, respond promptly and effectively to emergencies, and prevent the spread of cross-infections.

A critical aspect to consider is the relationship between understaffing/overcrowding and the emergence of neonatal infections caused by antibiotic-resistant or multidrug-resistant organisms. In this context, care overload – whether due to an excessive number of patients or insufficient staffing – can lead to ineffective or delayed clinical and microbiological monitoring (e.g., delayed execution of culture tests with antibiograms). In a high-risk, infection-prone environment such as the NICU, this may result in poor adherence to infection management protocols, excessive or inappropriate use of empirical antibiotic therapy, and ultimately the selection of resistant bacterial strains.

Addressing antimicrobial resistance in the NICU setting requires a re-evaluation of organizational models that recognize both physicians and nurses as key players in neonatal safety. Therefore, adequate workforce planning based on patient care complexity indicators must be viewed as an essential investment to curb the rise of antibiotic resistance and improve clinical outcomes.

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LECT 6

ANTIBIOTIC RESISTANCE IN PEDIATRIC SURGICAL CARE: A NARRATIVE REVIEW INVESTIGATING AN EMERGING INVISIBLE SURGICAL CHALLENGE

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BACKGROUND

Antibiotic resistance has represented an increasingly worrisome global health concern in modern medicine, including the surgical fields. In pediatric surgery, this issue remains critical and needs to be addressed to improve the prevention and treatment of multidrug-resistant (MDR) pathogen infections.

AIMS

Our work aimed to synthesize the current literature on the prevalence and clinical implications of antibiotic resistance in pediatric

surgery practice, to identify risk factors, and thus implement antibiotic stewardship to improve patient outcomes.

METHODS

For this narrative review, a PubMed search was conducted to identify articles on antibiotic resistance in pediatric surgery, yielding a total of 395 results that were initially analyzed as potentially relevant. A total of 13 articles met the inclusion criteria.

CONCLUSIONS

In recent years, scientific literature has drawn attention to the increasing rates of MDR organisms among common pathogens responsible for pediatric infections. The inadequate use of broad-spectrum antibiotics has undoubtedly played a significant role in the emergence of antibiotic resistance. In surgical settings, the challenge lies in balancing the risk of infection, which is managed through perioperative prophylaxis and postoperative treatment, with the need to avoid unnecessary antibiotic exposure in children. Current literature highlights the issue of MDR pathogens, even in community-acquired infections requiring surgical therapy. The findings we analyzed in the articles included in our review underscore the necessity of revising prophylactic and therapeutic protocols to develop more efficient prevention and control strategies for MDR infections. Nonetheless, further studies are needed to establish the true extent of the problem. Interdisciplinary collaboration among surgeons, pediatricians, and infectious disease specialists is key to developing standardized measures to minimize antibiotic resistance. Pediatric-specific clinical trials are required to establish optimal antibiotic use, thereby safeguarding the efficacy of current therapies and improving surgical outcomes.

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LECT 7

ANTIBIOTIC RESISTANCE IN ANIMAL FARMING: THE ADVANTAGES OF ORGANIC FARMING

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The increase in antibiotic-resistant infections, both in animals and humans, is closely linked to the use and abuse of antimicrobials in animal farming. Today, it is well understood that human health, animal health, and environmental health are closely interconnected, and that it is necessary to approach health issues with a new, global, multidisciplinary, and holistic perspective, capable of integrating resources and expertise across the human, veterinary, and environmental fields. In this context, food quality and production methods play a crucial role in determining the standards of human, animal, and environmental health, as outlined in the "One Health" concept. In particular, the organic production method is an approach to agriculture and livestock farming that excludes synthetic chemical products, favors natural substances, respects the rhythms of nature and biodiversity, and reduces the use of antibiotic therapy compared to conventional production methods, which are instead focused on increasing productivity through the use of modern feeding techniques and synthetic chemical products. More specifically, the organic method does not use antibiotics for preventive purposes in livestock farming, regulates the use of antibiotics for curative purposes, and promotes practices that increase animal welfare, thus reducing the need to resort to these drugs. For this reason, organic farming represents an opportunity to reduce the prevalence of antibiotic resistance as it limits the selection and spread of resistant bacteria, which can then spread and pose a risk to human health.

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