

Handling the challenge of antimicrobial resistant superbugs in the clinical setting: nursing staff as a pivotal player

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Abstract: Bacterial resistance to antibiotics (antimicrobial resistance, AMR) is rapidly spreading globally among major Gram-positive and Gram-negative bacterial pathogens (including staphylococci, enterococci, *Enterobacterales*, *Pseudomonas aeruginosa*, and *Acinetobacter baumannii*); this phenomenon has a remarkable impact on morbidity, mortality and healthcare-associated costs. Evolution and dissemination of AMR can be counteracted with a combined strategy based on I) antimicrobial stewardship programs aimed at a prudent and appropriate use of antibiotics to improve clinical outcomes and reduce the selective pressure for resistance; and II) infection prevention and control (IPC) practices, to limit the spread of resistant pathogens within the healthcare settings. In this scenario, the nursing staff plays a pivotal role, since these figures are involved in the enforcement and supervision of IPC bundles (e.g., contact precautions, hand, and environmental hygiene, active surveillance, patient isolation, or cohorting), which are essential to limit the spread of resistant pathogens among different patients.

Keywords: Antimicrobial Resistance, Infection Prevention and Control, Nursing Staff.

The increasing burden of antimicrobial resistance

Since their introduction in clinical practice, antibiotics have provided an outstanding contribution to decrease morbidity and mortality by bacterial infections; they have also been instrumental to the success of medical practices associated with a high risk of secondary infections such as contaminated surgery,

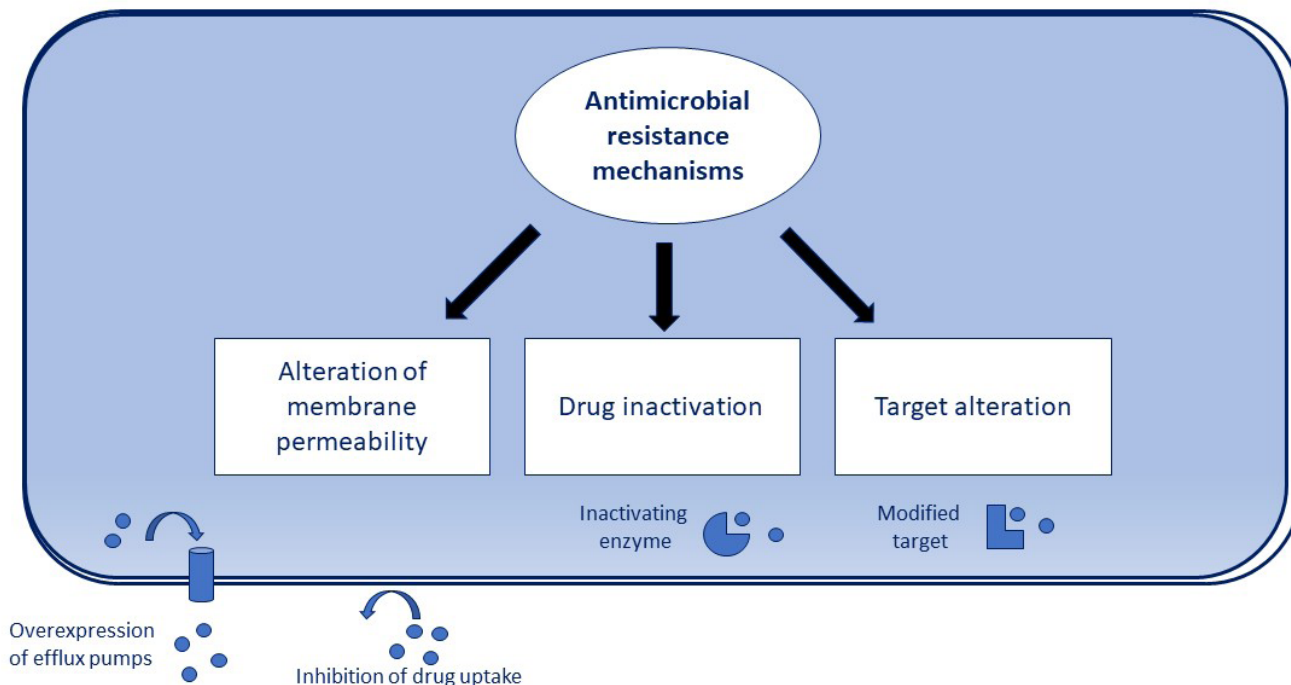
organ and tissue transplantation, implantation of devices, and other invasive procedures.¹

However, the efficacy of antibiotics has been impaired by the phenomenon of antimicrobial resistance (AMR), which is mediated by several mechanisms that bacteria have evolved to defend themselves, such as antibiotic-degrading enzymes,

antibiotic target modification, or reduced drug uptake (Figure 1).² Accretion of several resistance mechanisms may also occur in bacterial strains, with

ultimate conferral of complex multidrug-resistant (MDR) phenotypes that leave limited treatment options.

Figure 1. Main antimicrobial resistance mechanisms.



During the past decades, AMR has spread globally among many bacterial pathogens, and the simultaneous lagging of antimicrobial discovery and development programs has magnified the impact of this phenomenon. This conjuncture, also indicated as AMR crisis, has led to the emergence of bacterial strains which are resistant to most or even all available agents; such a mechanism carries a substantial risk of moving back to the pre-antibiotic era, with dramatic consequences in terms of morbidity, mortality and healthcare-associated costs.³ In 2016, the number of deaths associated with AMR infections was estimated at around 700,000, with an increasing trend,⁴ and in 2019, a total of 1.27 million deaths related to AMR infections per year have been estimated globally based on statistical models with data for 23 pathogens and 88 pathogen–drug combinations in 204 countries and territories.⁵

The recent revamping of specific antimicrobial development programs in response to this AMR crisis has led to the introduction of some new antibiotics that are active against MDR pathogens^{6,7}. Still, more is needed to cover all unmet needs, while a substantial effort is warranted to minimize the emergence of resistance against these new antibiotics.

The major antimicrobial resistant superbugs in the clinical setting

AMR affects most bacterial pathogens, but it has become especially problematic with some of them, often referred to as antimicrobial-resistant superbugs. These include methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant enterococci (VRE) among Gram-positive cocci, and carbapenem-resistant *Enterobacterales* (CRE), carbapenem-resistant *Acinetobacter baumannii* (CRAB), and extensively drug-resistant *Pseudomonas aeruginosa* (XDR-PA) among Gram-negative bacilli.⁸ The repertoire of drugs exhibiting activity against these pathogens is overall limited and, in some cases, seriously limited. In fact, the WHO has listed some of these resistant superbugs among those with the highest priority to target, with the final aim of developing new antibiotics.⁹

Strategies to mitigate the phenomenon of antimicrobial resistance

The phenomenon of AMR is virtually unavoidable after the introduction of therapeutic and prophylactic use of antibiotics. Still, two major factors can modulate its evolution: I) the policies of antibiotic prescription and II) the efficacy of infection prevention and control (IPC) practices. Indeed, robust antimicrobial stewardship,

promoting the prudent and appropriate antimicrobial use, minimizes the selective pressure for resistance and maximizes favorable clinical outcomes. At the same time, efficient IPC practices can control the spread of already selected resistant superbugs within the hospital settings.¹⁰ In fact, variable compliance with antimicrobial stewardship and IPC practices are among the major causes of different AMR prevalence in other countries. In Europe, where the rate of AMR among the most important pathogens are overall high, remarkable differences are apparent across different countries, with higher rates being observed in Eastern Europe and the Mediterranean Area,¹¹ where problems of poorer compliance with these practices and understaffing tend to be more common.

Since antibiotics are also used outside the clinical sector (e.g., in veterinary medicine and agriculture), AMR can also emerge in those settings, and the importance of the transference of AMR among different sectors has been increasingly acknowledged from a so-called "one-health" perspective. has been increasingly acknowledged from a so-called "one-health" perspective¹².

In hospital settings, the risk for AMR selection and spread is higher due to the frequent use of antibiotics and the higher likelihood of cross-transmission of resistant bacteria among inpatients. This is true both for acute-care hospitals and long-term-care facilities, where the prevalence of AMR may be similar to or even higher than that observed in acute-care hospitals.¹³

Specific bundles have been designed to limit the dissemination of AMR superbugs in healthcare settings based on IPC interventions; these activities include passive and active surveillance, isolation precautions, patient and staff cohorting, personal and environmental sanitation, and staff education, combined with antimicrobial stewardship programs aimed at optimizing antimicrobial prescriptions. In this context, all healthcare professionals are involved, with nursing staff representing crucial players.

The crucial role of nursing staff in curbing antimicrobial resistance

Nurses involved in clinical settings play a pivotal role in correctly deploying infection prevention and control (IPC) practices; these are essentially aimed at limiting the spread of resistant superbugs among different patients within healthcare environments, thereby limiting the phenomenon of AMR.

In this perspective, it should be noted that while

basic IPC measures (e.g., contact precautions, hand and environmental hygiene) should be adopted in all settings, other measures such as active surveillance of multi-drug resistance organisms (MDRO), patient isolation or cohorting, and staff cohorting, could be dependent on the type of patients and wards, and the local MDRO epidemiology. Colonization and cross-transmission pathways can differ for resistant superbugs.¹⁴ For instance, the main reservoir of CRE and VRE is represented by intestinal colonization of carriers. At the same time, MRSA, CRAB, and XDR-PA are commonly isolated from the skin or upper respiratory tract. Moreover, when different resistance mechanisms are present among the same category of resistant superbugs (e. g. serine- or metallo-beta-lactamases in CRE), it may be necessary to modulate cohorting accordingly, in order to avoid the emergence of strains with multiple resistance mechanisms that are resistant to new antibiotics. with multiple resistance mechanisms that are resistant to new antibiotics.

It should also be underscored that the presence, in each hospital, of experienced infection control nurses, who are able to supervise IPC protocols and provide continuous training to other healthcare workers, is essential for the success of antimicrobial resistance control measures.

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