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Rapid diagnostic tests for detecting emerging antibiotic resistance are mostly available and should be used now.

Clinically-significant multidrug-resistant bacteria are increasingly reported within enterobacterial species (e.g., *Escherichia coli, Klebsiella pneumoniae, Enterobacter* spp) and also within the two nosocomial Gram-negative pathogens, namely *Pseudomonas aeruginosa* and *Acinetobacter baumannii* [1].

The antibiotic resistance traits that are currently widespread in these Gram-negatives are mostly extended-spectrum ß-lactamases (ESBL) and carbapanemases producers [2, 3]. The ESBLs confer resistance to all b-lactams, with the exception of cephamycins and carbapenems, while carbapenemases confer resistance to virtually all b-lactams including carbapenems [2, 3]. In addition, ESBL and carbapenemase-producers are often resistant to non-related broad-spectrum antibiotics such as aminoglycosides and fluoroquinolones. Among the latest emerging antibiotic resistance traits, polymyxin resistance and pandrug resistance to aminoglycosides are also of concern [4, 5].

Historically, diagnosis and evaluation of antimicrobial resistance has been based on the culture of microorganisms. This 'old-fashioned' way of testing antibiotic susceptibility has proven to be quite accurate; however, it is time consuming, especially for slow-growing organisms (from 24 hour rapid-growth bacteria to several days), and it is neither adapted to adequate antibiotic stewardship nor to epidemiological purposes including the identification of the resistance mechanism(s).

As an example, bloodstream infections have the highest impact in term of morbidity, mortality and health care costs [6]. Empirical antibiotic therapy is the rule for treating severe sepsis and a timely and adequate treatment has been demonstrated to significantly reduce infection-related mortality [7, 8].

Detection and resultant control of antimicrobial resistance has therefore become a major issue in clinical microbiology. In the field of infectious diseases, we are currently witnessing a revolution in the development of diagnostic techniques for diseases and their resistance traits. The rapid diagnostic techniques available for detection of antibiotic resistance are based on molecular biology, biochemistry, physics, immunology and rapid culture techniques. We believe use of those techniques now may contribute to an optimal therapeutic choice of antibiotics for treating infections due to ESBL, carbapenemase producers, polymyxins and pan aminoglycoside resistant Gram-negatives as well as controlling their spread in nosocomial settings.

Use of molecular biology and in particular PCR-based techniques is nowadays the key approach for rapid and accurate identification of many etiological agents, including those considered to be difficult, or even impossible, to cultivate [9].

The main advantages of molecular techniques are sensitivity, specificity and rapidity. Among the currently used molecular-based techniques there are real-time PCR protocols that may target clinically-relevant antibiotic resistance genes. Such PCR-based detection methods of antimicrobial resistance are now commercially available and provided by many companies. Many of them are easy to implement and do not require outstanding expertise.

However, the main caveat of these tests is that they remain relatively expensive, making them affordable only for certain countries, but unaffordable for many others where the problem of resistance is extremely high.

Furthermore, it is very important to highlight that these tests cannot fully substitute the antibiogram since they only target some given resistance determinants and do not evaluate the real susceptibility of the isolate to a large variety of drugs. Indeed, a good correlation between the gene identification on one hand, and the resistance phenotype on the other hand, is not always observed (gene expression and modulation). In addition, the same resistance phenotype may result from several mechanisms that can be combined and therefore is difficult to predict through molecular approaches.

Moreover, as soon as a novel resistance gene emerges that is not included in the screening then antibiotic susceptibility testing based only on gene identification is obviously no longer reliable. Finally, it is worth highlighting that molecular methods are overall efficient genetic tools for the prediction of resistance, but are conversely not adapted to the prediction of susceptibility, with is a major drawback when considering antibiotic stewardship.

New tests based on biochemistry, immunology and rapid cultures have now been developed. This is the case with biochemical detection of carbapenemase activity (Rapid Carba NP test; bioMérieux, La Balme-Les-Grottes, France) and the detection of the ESBL activity (Rapid ESBL NP test) [10–12]. The main advantages of these tests are their speed (30 minutes) and low cost, in contrast to most other known techniques.

In addition, a significant advantage is that they can be used not only for bacterial cultures but also directly for blood and urine [13–15]. Consequently, they can now be used to optimize the stewardship of carbapenems considering that those molecules hydrolyzed by carbapenemases are spared by ESBLs. As an example, in a context of increased prevalence of ESBL producers, rapidly confirming the lack of such determinant in a given isolate means that broad-spectrum cephalosporins can be safely used, and that the last-resort carbapenems can be spared.

MALDI-TOF – a technology based on mass spectrometry coupled with a light analyzer – is now widely used for identification of microorganisms at the species level. Recent studies have shown that MALDI-TOF can also be used for the purpose of detecting resistance to antibiotics based on the detection of enzymatic activity, such as that of carbapenemases usually correlating with resistance to carbapenems [16]. This is an interesting use of this technique; however, it still needs to be precisely tuned in a lab and currently requires 30 minutes to 3 hours to get the results.

Immunological lateral flow techniques have recently been successfully implemented to detect carbapenemase producers (those producing enzymes such as KPC and OXA-48) from bacterial cultures within 15 minutes [17].

Rapid culture techniques have been recently developed for detection of polymyin and pan-aminoglycoside resistance in *Enterobacteriaceae*. The Rapid Polymyxin NP test (Rapid Polymyxin NP; ELITech Microbiology, Puteaux, France) may detect any polymyxin-resistant isolate, the corresponding resistance mechanisms being either chromosome- or plasmid-encoded (*mcr-1, mcr-2*) [18]. The Rapid Aminoglycoside NP test detects pandrug resistance to aminoglycosides resulting from the expression of 16S rRNA methylases [19]. Results of both rapid tests are obtained within 1–2 hours, either using bacterial cultures or blood cultures as samples [20].

Advances in high-throughput sequencing technologies, often named next-generation sequencing, recently opened significant research pathways, particularly in the field of molecular diagnostics of antimicrobial resistance [9]. The latest development of next-generation sequencing will be (or is) high-resolution epidemiology that will replace conventional epidemiological tools such as pulsed-field gel electrophoresis and multi-locus sequence typing.

Since very few novel antibiotic molecules will be marketed in the near future, control of antimicrobial resistance spread is primarily based on their rapid diagnosis. Actually, an early detection of the major resistance traits as described above is absolutely crucial for controlling spread. In addition, we believe that many of the rapid diagnostic techniques that are available may be used as companion diagnostics (precise medicine) to optimize the use of novel molecules such as the combinations of ß-lactams and ß-lactamase inhibitors. Use of those novel and rapid diagnostic techniques may contribute to preventing antibiotic overuse or misuse.

The revolution we are currently facing in rapid diagnostic techniques may allow us to optimize the management of treatments for infections caused by multidrug resistant bacteria and also contribute to controlling their spread. Rapid diagnostics contribute to the overall reduction of broad-spectrum antibiotic use and consequently could slow down the rise of resistant bacteria. This means we could expect to deal with such diagnostics either in primary care and hospital setting situations.

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