**[A New Practice to Promote Antimicrobial Stewardship]**

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One of the most urgent and pressing global health issues is antibiotic resistance. Antibiotics are misused and overused both in agriculture and in human clinical settings. Combatting this issue begins with the crucial responsibility of physicians and other health professionals to prescribe the correct antibiotic therapy. Since resistance has become such an important issue, many hospitals have implemented antimicrobial stewardship programs to promote the optimal use of antibiotics. A key test that these programs rely on is antimicrobial susceptibility testing (AST) that identifies the pathogen and its susceptibility. The main issue with these tests is that they typically take over 24 hours to yield accurate results. This amount of time is not optimal for patients; in reality, many patients cannot and do not want to wait that long for a treatment. A study by Flentie et al. (2019) revealed a novel rapid susceptibility test by measuring bacterial surface areas through a cationic probe. The test takes only around five hours and could largely advance stewardship programs and the way antibiotics are prescribed.

**Introduction**

The effects of antibiotic resistance are incredibly far-reaching. Today, many antibiotics that were once known as “cure-alls” have become increasingly ineffective at treating infections. Bacteria have the ability to change in a way that makes them difficult to target and resistant to antimicrobial drugs. Although resistance occurs naturally anywhere both bacteria and an antibiotic are present, the continual misuse and overuse of antibiotics in clinical settings escalates the issue. It is disturbing but not inaccurate to say that we could globally head in a direction in which everyday infections are deadly if serious action is not taken to combat resistance.

 In 2018, the World Health Organization released five objectives to the “Global action plan on antimicrobial resistance.” One of the objectives, “To optimize the use of antimicrobial medicines,” is extremely relevant in healthcare facilities. Administration of the wrong antibiotic therapies to patients not only lengthens their recovery time but also contributes to antibiotic resistance. Hospitals and other healthcare facilities have recently begun implementing antimicrobial stewardship programs in which infectious disease specialists, pharmacists, and other health professionals work together to promote the optimal use of antibiotics. A key way in which these stewardship programs aim to prescribe the correct antibiotic therapies is through antimicrobial susceptibility testing (AST). AST is a procedure that uses bacterial samples from patients and then tests which antibiotics the pathogen or pathogens are susceptible to. Much of the current AST takes over 24 hours to allow growth and bacterial identification, and the rapid tests that are available are unable to test a wide range of antibiotics (Maurer et al. 2017). Researchers are currently looking for ways to improve this kind of testing to advance antimicrobial stewardship.

**Recent Progress**

Over the past few years, medical laboratories have welcomed several new approaches to bacterial identification and antibiotic susceptibility testing. One approach in particular, phenotypic susceptibility testing, shows to be promising and advantageous (Maurer et al. 2017). The main issue these tests face is the time it takes to receive an accurate response. The traditional “gold standard” for phenotypic susceptibility testing by the Clinical and Laboratory Standards Institute (2012) is the broth microdilution assay (BMD). This assay is highly accurate and determines the minimum inhibitory concentration for a given pathogen – simply, the smallest amount of antibiotic it takes to effectively kill or inhibit bacterial growth. The problem with BMD is the incubation time; by following the BMD procedure, this assay often takes place overnight in a medical laboratory. The longer it takes for physicians and other health professionals to receive the results, the longer the patient has to stay, and the chances of mortality increase. Flentie et al. (2019) revealed a new susceptibility test that is rapid, accurate, and able to test a wide range of antibiotics. The test is a surface area assay that could potentially transform the way antibiotics are prescribed in a clinical setting. An issue faced by current AST that measures concentration is the way in which some antibiotics, particularly beta-lactam antibiotics, kill bacteria. Beta-lactam antibiotics can induce a change in bacterial cell morphology that elongates or swells the cell temporarily before lysing (Walsh and Wencewicz 2016). Under standard testing, the antibiotic-susceptible cells that undergo these morphological changes cannot be distinguished from resistant cells that grow and divide; for example, one elongated cell could be the same size as four daughter cells. This can lead to inaccuracies in the readings. This new surface area assay, however, is a method that can account for bacterial morphological changes, and thus solve this issue (Flentie et al. 2019). By measuring surface area, it can be seen that the elongated cells have a reduced surface area as compared to the dividing cells, which add surface area after each division (Flentie et al. 2019). To determine the viability of this type of test, the researchers initially used immunoglobulin G (IgG) antibodies to serve as binding probes for bacterial surfaces. The antibodies were introduced to the bacteria after 3.5 hours of incubation and following another short incubation time, the unbound probes were washed away. The resulting concentration of antibody probes is proportional to the concentration of bacteria present (Flentie et al. 2019). Their results revealed matching MICs to those determined by the CLSI, and the procedure only took around five hours to complete. After addressing the obvious issues of using IgGs as binding probes, like the large amounts it would require, the researchers switched to a different surface-binding agent (Flentie et al. 2019). Because bacterial membranes are highly anionic, a cationic probe – europium-cryptate-diamine chelate – was chosen. After testing, it was found that the probe could successfully bind several non-fastidious bacteria. The MIC values again agreed with those of the CLSI and took about five hours to complete. Ceftazadime, a beta-lactam antibiotic, was one of the antibiotics used in the study to determine whether or not the test could account for morphological changes in the bacterial cell – the matching MIC values reveal that the test can account for these morphological changes.

**Discussion**

The surface area assay appears promising for the direction toward rapid AST. While much of the current AST takes over 24 hours to complete, this microplate-based surface area assay takes only around five hours to yield accurate results. As noted by Flentie et al. (2019), the current AST that tests concentration cannot account for morphological changes in the bacterial cell. The most profound result in this study was the ability of the surface area assay to account for these morphological changes through the use of a cationic probe. The implications of this kind of testing could largely advance stewardship in the clinical setting; however, there are a few questions that need to be addressed. To begin, Flentie et al. (2019) did not test any fastidious species; the introduction of a nutritional requirement could possibly affect the binding. Another obvious question that is not addressed is the cost of this type of testing and whether or not it is completely practical. Hospitals and clinics that have not yet implemented antimicrobial stewardship programs may argue that if expensive, these tests are not worth it when other accurate susceptibility tests are already in place. The most important factor, however, is that the study did not test a wide range of pathogens. Many more species will need to be tested in further research.

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