Crisis: antimicrobial agent resistance

Novel forms of antimicrobial resistance to various classes of therapeutic agents have appeared at a frenzied pace recently. A global public health emergency has materialized as fewer agents have maintained efficacy against a growing number of microorganisms. Clinical microbiologists, at the vanguard of this confrontation with antimicrobial resistance, find themselves in sentinel positions, because their labs are the first to identify and confirm detection of microorganisms unlikely to respond to treatment with particular antimicrobial agents. Theirs is an ideal position to spot population trends toward increased resistance within a geographical region. They also provide information to clinicians regarding substitute agents likely to be effective when the primary choice is not.

The microbiology lab’s ability to recognize resistance has been compromised by the phenotypic invisibility of some newer forms of resistance. Detecting oxacillin, clindamycin, and vancomycin resistance in staphylococci, vancomycin resistance in enterococci, penicillin and third-generation cephalosporin resistance in pneumococci, and third-generation cephalosporin resistance in enteric Gram-negative bacilli offers significant challenges. Modifications of existing test procedures in each of these instances enhance the likelihood that labs will recognize these resistant forms. Some modifications alter growth media used during testing, some lengthen incubation periods for tests, and others define screening and confirmatory tests that can be employed to document the specific resistances.

The NCCLS has kept member labs apprised of optimal methods for detecting antimicrobial resistance via annual updates to its antimicrobial resistance testing standards; the CDC complemented that effort by authoring and distributing a free educational testing CD to U.S. labs. Biennial CLIA surveys conducted under the auspices of the CMS ensure that labs performing antimicrobial resistance testing follow proper procedures.

Microbiology lab med techs performing antimicrobial resistance testing can no longer rely exclusively on the results obtained after testing is completed. Their increasingly complex responsibilities require that they ask whether the microorganism and antimicrobial agent test result in question falls into a category requiring technologist intervention and manual modification of the result.

Modern laboratory information systems include provisions for creating logic-based rules that can alert med techs to situations in which a manual override of test results is indicated. Clinical microbiologists need to understand how information technology can be leveraged to eliminate reporting incorrect results.

Molecular techniques now used to recognize some antimicrobial resistances undoubtedly will be used to recognize more in the future. The limitation of the molecular approach, however, is that only known mutations can be sought. Recently emerged forms of resistance must be detected phenotypically until DNA sequence changes responsible for conferring resistance have been characterized.

Even under ideal circumstances, antimicrobial resistance testing may not accurately predict the outcome of antimicrobial therapy. Influences of pharmacokinetic (PK) properties of antimicrobial agents and pharmacodynamic (PD) effects specific to the host all contribute to the complex interactions of systems that determine success of antimicrobial treatment, and that cannot be replicated in an in vitro test system. Clinical microbiologists should become conversant with antimicrobial PK/PD principles, so they can participate with members of the patient care team in evaluating antimicrobial agent choices for a particular patient.

Most alarming perhaps in the present antimicrobial resistance crisis is the meager number of new antimicrobial agents currently in the development pipeline. If the practice of reserving particularly effective antimicrobial agents for treating resistant microorganisms only continues, few, if any, alternatives will be available once resistance develops against the reserved agents. Yet, the pharmaceutical industry allocates the bulk of its resources to developing drugs for treatment of chronic conditions rather than brief episodes of infectious disease—understandable in our capitalistic, free market economy. An incentive must be found (or created) to persuade companies to renew their interest and reallocate their resources toward new antimicrobial agent discovery and development. Anything short of this will lead to an inability for clinicians to successfully manage patients with antimicrobial resistant infections.

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