VIEWPOINT

Diagnostic Stewardship—Leveraging the Laboratory to Improve Antimicrobial Use

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Antimicrobial stewardship programs have emerged as a means to address inappropriate antimicrobial use, manage costs, decrease drug resistance, and prevent medication-related adverse events. The traditional stewardship model relies on pharmacists, infectious disease physicians, or both, providing feedback to clinicians.

Culture-based and non–culture-based diagnostic tests help establish the presence or absence of infection. Although routine, the process of ordering and interpreting diagnostic tests is complex and frequently results in diagnostic error.[1] The decision to order a test should be guided by careful clinical evaluation, recognition of a clinical syndrome, and estimation of the pretest likelihood of the condition for which the test is obtained. Tests are ordered, specimens collected and processed, and results reported. Clinicians then interpret these results and decide whether to initiate or continue treatment.[1]

However, clinicians often order common tests for patients without symptoms specific for the disease process (ie, those with a very low pretest likelihood of infection), eg, *Clostridium difficile* stool testing among patients without diarrhea, or urine cultures among patients without symptoms referable to the urinary tract. When positive test results are obtained in these and other scenarios, unnecessary therapy is often prescribed, even though the results represent false-positive findings or colonization rather than true infection.[1,2]

The problem with ordering tests in the setting of low pretest likelihood of disease is magnified by the availability of increasingly sensitive molecular tests, many of which are combined into "syndromic" testing panels.[3] Some panels detect more than 2 dozen targets simultaneously, and future next-generation sequencing tests will detect the presence of any microbial genetic material.[3] The pretest likelihoods of infection attributable to each target in these assays vary substantially, further complicating the interpretation of positive test results and potentially contributing to overtreatment.[3]

Diagnostic Stewardship

Diagnostic stewardship involves modifying the process of ordering, performing, and reporting diagnostic tests to improve the treatment of infections and other conditions. Within the laboratory community, these steps are referred to as preanalytic, analytic, and postanalytic interventions.[3] With growing recognition of false-positive results and inability of most tests to distinguish colonization from infection, some hospitals have launched efforts to improve diagnostic stewardship. Implementation of diagnostic stewardship has varied from laboratory policies that include refusing to process specimens that are collected or handled inappropriately to using multiple tests in a cascading fashion—for example, performing urinalysis but proceeding to urine culture only if pyuria is present.

Some hospitals have gone further, engaging in educational campaigns to teach clinicians appropriate indications and sampling for tests. One program reported a 46% reduction in blood cultures among critically ill children.[4] Diagnostic stewardship has been operationalized in the electronic health record through removal of specific tests, clinical decision support to guide appropriate testing, or allowing the option to order testing if results of initial tests are positive, eg, "urine culture if pyuria present," which reflexively orders a urine culture if pyuria is present on urinalysis. Some of the most common infectious disease tests and potential diagnostic stewardship interventions are described in the **Table**.

Potential Benefits

Diagnostic stewardship emerged from the desire to improve clinical care, with fewer false-positive test results and less overdiagnosis while identifying true-positive cases. Accurate diagnosis is also closely associated with more appropriate antibiotic use, resulting in fewer adverse effects and shorter hospital stays. Decreasing false-positive test results can also improve patient care by allowing clinicians to avoid a prolonged workup of false-positive results or being falsely reassured by an incorrect diagnosis, eg, a diagnosis of urinary tract infection when a patient has delirium due to a medication adverse effect. Although most diagnostic stewardship is focused on decreasing inappropriate testing, other aspects such as rapid identification of bacteria in blood cultures emphasize the overall goal of more appropriate and timely therapy.

Given that a laboratory generally serves a large population of patients and that diagnostic stewardship would apply every time a target test is performed by that laboratory, the potential benefits of diagnostic stewardship may be broader than traditional antimicrobial stewardship, which focuses on target medications. Ideally, diagnostic stewardship is developed under the larger umbrella of a comprehensive antimicrobial stewardship program.

Potential Harms

As with any change in care delivery, a potential for unintended consequences and harm exists. The most immediate concern is that by improving the positive predictive value of testing, some diagnoses may be missed.[1] Thoughtful application of diagnostic stewardship principles can avoid this,[4] but close monitoring should be ongoing as diagnostic stewardship is expanded. Other potential harms relate to clinician frustration with restrictions or limitations on testing, because such guidance could seem like a reduction in clinician autonomy. As such, transparency is essential in the education of all health care workers involved when a testing process is being changed.

Table. Steps at Which Diagnostic Stewardship May Improve Testing for Common Infectious Disease Tests

	Ordering (Preanalytic)	Collection (Preanalytic)	Processing (Analytic)	Reporting (Postanalytic)
General principles	Test only if clinical presentation is consistent with the infectious etiology (high pretest probability)	Pay attention to sample collection and transport, to optimize yield and reduce contamination	Use adjunctive laboratory tests to distinguish colonization from infection	Report results in a format that guides appropriate practice
Urine cultures	Test only when symptoms suggest urinary tract infection or, if asymptomatic, concordant with guidelines (eg, urologic surgery, pregnancy)	Use aseptic technique—midstream clean catch after periurethral cleansing Obtain catheter sample from collection port (not bag), prefer newly inserted catheter	Only perform urine culture if pyuria present	Text interpreting result, eg, "multiple organisms indicating likely contamination"; "no pyuria, culture not performed" Selective reporting of antibiotic susceptibilities—display preferred antibiotics only
Blood cultures	Test only when symptoms of infection present (fever) Avoid repeat cultures unless concern for persistent or endovascular infection	Use aseptic technique—prefer peripheral samples obtained by trained phlebotomists Avoid catheter draws	Consider rapid testing on initial positive results, eg, polymerase chain reaction, PNA-FISH, MALDI-TOF	Text interpreting result, eg, "likely skin contaminant"; "*Staphylococcus aureus*, likely pathogen consider infectious diseases consult" Selective reporting of antibiotic susceptibilities
Clostridium difficile testing	Test only when disease likely (eg, recent antibiotic exposure, ≥3 loose stools/d, duration >24 h, and no recent laxative use) Avoid tests of cure	Only collect and send loose stool (ie, that conforms to the container)	Consider use of a testing algorithm that includes toxin immunoassay	Text interpreting result, eg, "toxin−/PCR+ indicating possible colonization rather than disease"
Molecular detection panels (ie, "syndromic testing")	Test only when pretest probability moderate to high for ≥2 targets on the panel, and when results will influence management	Use recommended collection and transport conditions to reduce contamination and optimize yield	Follow stringent contamination prevention guidance in the laboratory to avoid false-positive results	Selective suppression of results for tests on panel if other testing approach used in the laboratory (eg, *C difficile* testing on stool pathogen panel) Text interpreting results discussing colonization
Forms of automation	Clinical decision support requiring documentation of symptoms Hard stops for contraindications—eg, laxative use within 48 h of *C difficile* test)	Recording site and method of collection Orders requiring supplementary tests—eg, urinalysis before urine culture	Laboratory support systems performing cascades of tests	Prepopulated reports that can be reviewed and modified by laboratory personnel
Clinician education	Yes	No	No	Yes

Abbreviations: PNA-FISH, peptide nucleic acid–fluorescence in situ hybridization; MALDI-TOF, matrix-assisted laser desorption/ionization time-of-flight.

Caveats and Unknowns

Diagnostic stewardship should facilitate appropriate clinical decision making but should not be absolute or impede a nuanced approach to patient care. Tests targeted by stewardship should also be available by special request or in certain circumstances. For example, urine cultures should be available without urinalysis demonstrating pyuria in pregnant women or patients undergoing urologic surgery, because treatment of asymptomatic bacteriuria is appropriate in these situations. The criteria for diagnostic stewardship should be monitored and revised if potential harms are observed or gains are not as large as expected.

The most beneficial form of diagnostic stewardship has not been defined. Ideally, tests and methods of testing are evaluated in clinical studies with patient outcomes. For example, use of different cutoffs for pyuria (>10 vs >50 white blood cells per high-power field) to trigger reflex urine cultures could be studied by examining outcomes among patients tested for potential urinary tract infection.

Application to Future Tests

Many new tests for infectious disease rely on detection of very small amounts of genetic material from many potential pathogens. There is significant potential for confusion between colonization and infection, with overdiagnosis leading to overtreatment of disease. The most appropriate use of such tests requires the perspective of diagnostic stewardship and research on the effects of tests on clinical outcomes rather than comparison with other tests.

Conclusions

Diagnostic stewardship is increasingly used as a way to guide appropriate clinical behavior to reduce unnecessary testing and false-positive results and to more quickly identify pathogens and target therapy. Diagnostic stewardship has evolved in relation to bacterial cultures and *C difficile* testing but will be even more important for the expanding array of molecular tests. A laboratory working with a stewardship team can best implement diagnostic stewardship to reduce unnecessary testing and improve patient care.

ARTICLE INFORMATION

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REFERENCES

1. McGlynn EA, McDonald KM, Cassel CK. Measurement is essential for improving diagnosis and reducing diagnostic error: a report from the Institute of Medicine. *JAMA*. 2015;314(23):2501-2502.

2. Polage CR, Gyorke CE, Kennedy MA, et al. Overdiagnosis of *Clostridium difficile* infection in the molecular test era. *JAMA Intern Med*. 2015;175(11):1792-1801.

3. Messacar K, Parker SK, Todd JK, Dominguez SR. Implementation of rapid molecular infectious disease diagnostics. *J Clin Microbiol*. 2017;55(3):715-723.

4. Woods-Hill CZ, Fackler J, Nelson McMillan K, et al. Association of a clinical practice guideline with blood culture use in critically ill children. *JAMA Pediatr*. 2017;171(2):157-164.