Kentucky Antimicrobial Stewardship Innovation Consortium

Educational Pearl

Cultures and Next-Generation Sequencing

Cultures have been a staple for organism identification for decades while next-generation sequencing (NGS) represents an emerging diagnostic modality. Although platforms vary, NGS generally identifies microbial genetic material by comparing sequenced DNA fragments from clinical samples against databases of organisms, often with very high sensitivity.[1] Despite growing curiosity for these assays, the clinical role of NGS remains uncertain and with limitation. When should NGS be considered instead of conventional cultures alone?

Limitations of Cultures and NGS

Conventional cultures are imperfect and may be affected by prior antimicrobial exposure while requiring viable organisms for growth.[1] In contrast, NGS can detect microbial genetic fragments without requiring living organisms. Although potentially advantageous, this sensitivity may also detect colonization, contamination, or organisms of unclear clinical significance. Additionally, NGS platforms differ substantially in methodology and specimen requirements, with some assays requiring tissue or site-specific samples rather than blood alone.

The Infectious Diseases Society of America (IDSA) has previously highlighted several concerns regarding the clinical use of NGS assays, including uncertainty surrounding the relationship between detected genomic fragments and a patient's clinical syndrome, inability to reliably determine phenotypic antimicrobial resistance, and overall cost/access.[2] In its 2024 microbiology utilization guide, the IDSA further emphasized operational limitations of these platforms, including prolonged turnaround times related to reliance on specialized reference laboratories, as many commercially available assays must be performed at manufacturer-designated facilities.[3]

Possible Role of NGS

In practice, NGS platforms are expensive and may provide diagnostically redundant information when conventional microbiology is adequate. For most patients, particularly during the initial infectious work-up, routine use should generally be avoided. "Potential clinical scenarios in which patient outcomes data would be most valuable, and where NGS may be reasonably considered, include:

- High suspicion for infection despite exhaustive conventional diagnostics
- Difficult-to-culture microbes
- Situations where prolonged antimicrobial therapy is anticipated

High quality data evaluating the clinical utility of NGS are limited. There is interest in NGS particularly for infections with low culture yields such as prosthetic joint infections (PJI). One systematic review identified 6 of 9 studies reported a >50% organism detection rate using NGS in patients with culture-negative PJI.[4] A direct comparison of management strategies with NGS and cultures versus cultures alone is needed.

Key Takeaway: Cultures are reliable for detection of typical bacterial growth. Next-generation sequencing should not be routinely employed for most patients, particularly in the initial work-up.

References:

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Created 5.20.26