The Opening and Closing of Empiric Windows: The Impact of Rapid Microbiologic Diagnostics

TO THE EDITOR—With the advent of rapid diagnostic techniques for pathogen identification, clinicians are encountering increasing windows of time when they are aware of an infecting organism’s species without yet knowing its susceptibilities [1, 2]. We believe that it is worthwhile to formally recognize these empiric windows in the management of infectious diseases (Figure 1). These windows include infectious syndrome–guided therapy (empiric window 1), Gram stain morphology–guided therapy (empiric window 2), and pathogen-guided therapy (empiric window 3), before, finally, susceptibility-guided therapy.

Rapid speciation methods including matrix-assisted laser desorption/ionization–time of flight, and, potentially, polymerase chain reaction–based methods, could close the empiric window 2 by half (from 54 to 24 hours), while opening empiric window 3 much more widely (from 3 hours up to 21 hours) [1, 2, 4]. The alteration of these empiric windows can have significant impact on patient outcomes and may pose new challenges for treating physicians.

Empiric window 2 has historically been a critical time period where clinicians may adapt their treatment approach based on Gram staining. Having less time between the Gram stain and pathogen identification may lead clinicians to wait for speciation results rather than having to make more frequent antimicrobial changes.

Empiric window 3, traditionally a small window between speciation and susceptibility results, will be increased with rapid speciation techniques, and this means that clinicians have time to adapt their empiric therapy accordingly. This will suddenly make institutional species-specific antibiograms much more clinically useful. Moreover, clinicians may be able to more quickly discontinue therapy following identification of obvious culture contaminants (eg, Corynebacterium species), or more rapidly de-escalate therapy after identification of organisms with predictable susceptibilities (eg, Listeria monocytogenes). In some instances, empiric window 3 will cause pathogen-guided escalation prior to susceptibility-guided de-escalation of empiric therapy (eg, Enterococcus species or Pseudomonas species) [1].
Effective and timely empiric antimicrobial therapy is an important determinant of patient outcomes [3], and with the advent of rapid speciation techniques there is an opportunity to improve this coverage, with the added possibility of decreasing unnecessary antimicrobial usage [1, 2]. However, clinicians will need to be comfortable with the possibility of multiple, rapid antimicrobial changes in short windows of time, the possibility of escalating prior to de-escalating empiric therapy, and the uncertainty of whether these rapid changes in antimicrobials could contribute to drug resistance or increased drug-related adverse effects. Local antimicrobial susceptibility data can be employed to improve empiricism at all window points, but will be particularly useful in empiric window 3 when speciation is known but susceptibility results are pending. In the coming years, advances such as rapid detection of antimicrobial resistance will continue to shift these empiric windows. Further research on how to best utilize local susceptibility data, patient-specific risk factors, and prior isolate results will help inform each empiric antibiotic selection.

**Note**

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