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# Modeled Impact of Rapid Diagnostics on the Treatment of Gram-negative Bacteremia at a Tertiary-Care VA Medical Center

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## ABSTRACT

**Background:** Gram-negative pathogens take 24-72 hours to be identified (ID) and for antimicrobial susceptibilities (AS) to be obtained from blood cultures. Rapid molecular diagnostic tests (RDT) can shorten time to pathogen identification and antibiotic optimization. We compared our current processes with the predicted impact of an RDT system, to assist with an institutional decision to invest in RDT. The Accelerate PhenoTest™ BC Kit, which provides pathogen ID within 90 minutes of positive growth and AS within 7 hours, was selected as an example of a commercially available system for study purposes.

**Methodology:** A retrospective review of adult patients between January 2016 and September 2017 with ≥ 1 positive blood culture with a Gram-negative organism detectable by the RDT system was conducted. Subject characteristics and organisms identified were recorded. Primary endpoints of the study were potential change in times to ID and AS with use of RDT. Standard laboratory procedures were used for ID and AS (pre-intervention period). The same subject population was used to calculate a theoretical time to ID and AS if RDT were used (modeled post-intervention). Patients were excluded if they expired or were discharged prior to culture results, on hemodialysis, were an outpatient at the time of + culture, or if time of ID or AS was not reported in the electronic record.

**Results:** 156 subjects met inclusion criteria. The most common organisms isolated were *E. coli* (45%) and *K. pneumoniae* (22%). The pre-intervention mean time to ID and AS in the medical record were identical at 56 hours (using VITEK®). The mean times to effective (covering) and optimal (targeted/consolidated) therapy for the pre-intervention group were 8 hours and 75 hours, respectively. For the modeled post-intervention period, RDT could decrease time to ID by 54 hours (95% CI: 50.5-59.1, $p < .001$) and AS by 49 hours (95% CI: 45.1-53.5, $p < .001$).

**Conclusion:** Time to optimal therapy of gram-negative bloodstream infections at our facility was ~ 3 days (within a day of final organism ID and AS). This demonstrates excellent communication protocols between our microbiology and clinical departments, suggesting that our modeled benefit to RDT for organism ID and AS has good potential to be translated into clinical benefits.

## INTRODUCTION

- Mortality rates up to 35% may be seen with Gram-negative bacteremia
- Mortality is increased in patients receiving inappropriate or delayed antimicrobials
- Conventional microbiology laboratory testing methods may take up to 72 hours for organism ID and AS after a blood culture is reported positive
- Rapid molecular diagnostic tests may assist to earlier optimize antimicrobial therapy
- At our institution, a particular RDT system (Accelerate PhenoTest™) is being considered for implementation
- Pre-acquisition investigations can assist with institutional decision-making as well as enhance technology implementation

## HYPOTHESIS

**We hypothesized that future implementation of a molecular diagnostic technology for identification of Gram-negative pathogens in blood has potential to shorten time to pathogen identification and antibiotic optimization.**

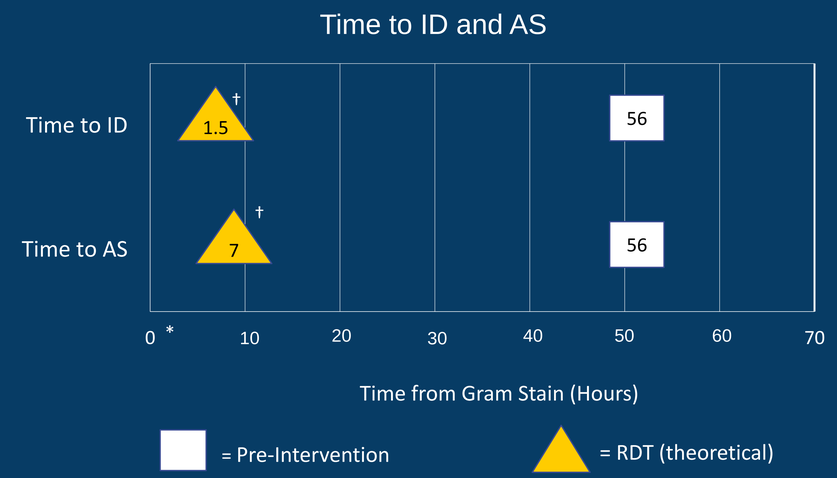
## METHODS

- Design: Retrospective review of all Gram-negative bacteremias from 01/16 – 10/17
- Primary Objective: Evaluate the *potential* impact of an RDT on time to organism ID and AS in patients with Gram-negative bacteremia
- Secondary Objectives: Measure current time to therapy, length of stay, mortality
- Definitions:
  - Time to *optimal* therapy: time from blood culture draw to de-escalation or escalation of therapy
  - Time to *effective* therapy: time from blood culture draw to administration of antimicrobial therapy that is active against the organism based on antimicrobial susceptibility results
- Inclusion Criteria: >18 years of age, blood culture positive for Gram-negative organism, and organism detectable by RDT (selected RDT was Accelerate PhenoTest™)
- Exclusion Criteria: Expired/discharged before culture results, transfer from outside facility, dialysis outpatient at time of positive culture

## RESULTS

| Pre-intervention Demographics | n=156 |
|---|---|
| Average age ± SD (years) | 70 ± 12.1 |
| Male, % | 95.5 |
| Caucasian, n (%) | 89 (57.1) |
| Comorbidities, n (%) | |
| Diabetes Mellitus | 52 (33.3) |
| Hematology/Oncology Malignancy | 52 (33.3) |
| Chronic Kidney Disease | 31 (19.9) |
| Cerebrovascular Accident | 19 (12.2) |
| Congestive Heart Failure | 18 (11.5) |
| Organism, n (%) | |
| *Escherichia coli* | 70 (44.8) |
| *Klebsiella pneumoniae* | 34 (21.8) |
| *Enterobacter cloacae* | 14 (9.0) |
| *Pseudomonas aeruginosa* | 13 (8.3) |
| *Proteus mirabilis* | 11 (7.1) |
| Effective therapy at time of gram stain (n=156), n (%) | 151 (96.8) |

## RESULTS




*Time Gram stain performed; median 21 hours after blood culture collection (range, 4-129 hours)

† *P*-value <0.001; RDT (theoretical) vs. Pre-Intervention

| Pre-Intervention Clinical Parameters Potentially Impactable by RDT | |
|---|---|
| Time to effective therapy, hours, median (range) | 2 (-51-91)* |
| Time to optimal therapy, hours, median (range) | 74 (-30-252)* |
| Length of stay, days, mean ± SD | 53 ± 164.5 |
| ICU length of stay, days, mean ± SD | 2 ± 22.7 |
| 30-day mortality (n=156), n (%) | 12 (7.7) |

* Negative numerical value indicates therapy was started prior to blood culture draw

## CONCLUSIONS

- Optimal therapy for Gram-negative bacteremia at our institution currently occurs within 24 hours of conventional ID/AS results
- This indicates excellent communication between our laboratory and clinical services and timely action by clinicians in response to microbiologic results
- Implementation of RDT therefore has good potential to positively impact not only early organism identification, but also clinical outcomes at our facility
- Once RDT is implemented however, ongoing process analysis will be necessary to account for unexpected contributors to variability in actionable results

**References**
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