IS THE JUICE WORTH THE SQUEEZE?
RAPID IDENTIFICATION AND ANTIMICROBIAL SUSCEPTIBILITY TESTING USING THE ACCELERATE PHENO™ SYSTEM

K Chapin¹,², R Rogers², A Zaninni¹, M Kearney¹, A Bobenchik¹, C Cunha²,
Departments of Pathology¹ and Medicine², Alpert Brown Medical School and Lifespan Hospitals
DISCLOSURES

- K Chapin Clinical Advisory/Consulting for Accelerate
- All other authors no conflicts
Rapid identification (ID) and antimicrobial susceptibility testing (AST) have the power to appropriately guide antibiotic therapy and optimize healthcare outcomes.

The Microbiology lab at Rhode Island Hospital performs:
- 50,000-60,000 blood cultures/year
- 700,000 tests/year
- 24h/7d

High volume and varied tech capabilities (55) does not favor methods with multiple hands-on manipulations for rapid ID and AST.
The purpose of this study was to prospectively evaluate the Accelerate Pheno™ system (Pheno) for blood cultures positive for Gram negative rods (GNR) in the context of:

- routine laboratory workflow
- accuracy with current identification and AST methods
- identify medically actionable benefits as part of:
  - business plan for the lab
  - stewardship plan for implementation
ACCELERATE PHENO™ SYSTEM

- FDA cleared Feb 2017
- Direct from positive blood culture
- ID in 90 minutes
- AST in ~ 7 hrs
  - GN 15 antibiotics
  - GP 8 antibiotics
- Entire process contained in 1 kit

www.acceleratediagnostics.com

3 feet/ 32 cm
20”/43 cm
Automated sample prep and bacterial immobilization to enable microscopy-based, single-cell analysis for ID and AST

ID performed using fluorescence in situ hybridization (FISH)
- target organism specific rRNA sequences with several mono-labeled DNA probes

Colocalization of target probe with universal probe signal confirms the presence/identity of target while differentiating non-specific staining
The MIC and categorical interpretation are generated using morphokinetic cellular analysis by dark-field microscopy of individual, live, growing, immobilized bacterial cells:

- in near real-time (q 10 min)
- in presence (test) and absence (control) of a single concentration of antimicrobial agent

Data analysis: billions of data points per run and growth curve algorithm analysis used to predict susceptibility.
**AST- Morphokentic Cellular Analysis**

- Bacteria are grown up to 4 hrs in presence of single concentration of antibiotic.
- Growth response is measured using time-lapse imaging.
- MICs determined by matching growth patterns to reference growth profiles that correlate to MICs.

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4/23/2019
From January to August 2018, Pheno was prospectively evaluated from 100 blood cultures determined as GNR based on Gram stain.

Per protocol:

- Positive bottles are stained, read and subbed to media for next day bench reading.
- During the study period, technologists (1\textsuperscript{st} and 2\textsuperscript{nd} shifts) were trained and Pheno performed as part of the routine workflow.
- After gram stain return to bottle and withdraw specimen for plate subbing and pheno inoculation.
# ACCELERATE PHENO™ SYSTEM

<table>
<thead>
<tr>
<th>Identification</th>
<th>SAM</th>
<th>TZP</th>
<th>CPM</th>
<th>CAZ</th>
<th>CRO</th>
<th>ETP</th>
<th>MEM</th>
<th>AMIK</th>
<th>GEN</th>
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<td>A. baumannii</td>
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</table>

**Klebsiella spp.**
- K. oxytoca, K. pneumoniae

**Enterobacter spp.**
- E. cloacae, E. aerogenes

**Proteus spp.**
- P. mirabilis, P. vulgaris

**Citrobacter spp.**
- C. freundii, C. koseri
Pheno provided automated ID/AST results, which were recorded and compared to laboratory standard of care:

- MALDI-TOF ID and VITEK® 2 AST

Tabulated:
- Time points for all ID/AST results
- Accuracy of ID/AST comparisons
- Chart review was performed to assess underlying:
  - Diagnosis
  - Antibiotic use and assessment
  - Length of stay (LOS)
  - Mortality
Jan – May 2018 had **585** Positive Blood cultures at RIH

65 (11%) Pheno tests on Blood Cultures with Single morphology of GNRs on GS

Single organism = 56 (86%) ; > 1 organism = 9 (14%) → 70% with an ID/AST

- **E.coli** 58%
- **Klebsiella spp** 9%
- **Proteus spp** 22%
- **S. marcescens** 5%
- **Citrobacter spp.** 2%
- **Enterobacter spp** 2%
- **Ps. Aeruginosa** 2%

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Was there a change in atbx after Vitek AST reported?

- Yes 77%
- No 23%

Where was change NOT happening?

- Surgical Service
- Those already on appropriate antibiotics

YES!!

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Pheno gave interpretable ID/AST results for 76% of specimens.

Identification
- 81 specimens monomicrobial/ID sensitivity 100% and specificity 100%
- 19 polymicrobial/ID sensitivity 83.3% and specificity 100%

Susceptibility
- 96.7% Essential Agreement and 96.3% Categorical Agreement

Results 100: Pheno Data

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## 100 PROSPECTIVE GNR RESULTS
### 76% CORRECT ID/AST

### TABLE 1

<table>
<thead>
<tr>
<th>PH MALDI/VITEK</th>
<th>Pheno</th>
<th>PH MALDI/VITEK</th>
<th>Pheno</th>
<th>PH MALDI/VITEK</th>
<th>Pheno</th>
<th>PH MALDI/VITEK</th>
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<td>1 BURK</td>
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<td>26 PR</td>
<td>PR</td>
<td>51 ENT, ECOC</td>
<td>ENT</td>
<td>76 BACT</td>
<td>Strep - no AST</td>
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<td>2 PR</td>
<td>PR</td>
<td>27 KL</td>
<td>KL</td>
<td>52 EC</td>
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<td>53 HAF</td>
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<tr>
<td>5 KL, ECOC</td>
<td>EC, KL - no AST</td>
<td>30 CIT</td>
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<td>6 KL</td>
<td>KL</td>
<td>31 SER</td>
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<tr>
<td>7 HFLU</td>
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<td>8 PR</td>
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<td>EC</td>
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<tr>
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<tr>
<td>10 BACT</td>
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<td>60 ENT, PANT, SPHING</td>
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<td>85 EC</td>
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<tr>
<td>11 EC</td>
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<td>67 CIT</td>
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<td>75 PA</td>
<td>PA</td>
<td>100 EC, CONS</td>
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</tbody>
</table>


Assessment of timing distribution of positive blood cultures/gram stains and Pheno AST allowed assessment of instrument needs.

**TIMING OF NEW GNR+ GRAM STAINS**

- Only 12 new GNR+ stains within 6 hours of the prior.
Comparison of average time from Gram stain to final AST:
- Pheno was 8.4 hours and
- VITEK 48.3 hours ($p<0.0001$)

Easily incorporated into routine workflow
Time distribution of Pheno results would allow 2/3 of patients to have same day AST intervention.
Mortality due to GNR sepsis was 17%
RESULTS
CHART REVIEW AND STEWARDSHIP OPPORTUNITIES

- 17% mortality
- LOS 9.1 days
- Over 50% of GNR infections were due to:
  - UTI or uncomplicated sepsis and
  - 20% were polymicrobial
- De-escalation from broad-spectrum antibiotics:
  - could have occurred in 79% of patients
  - Antibiotic changes were delayed in 40% and
  - Discharge was delayed in 11% because of pending standard protocol AST results
- Cost of one septic patient RI $28,000

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CONCLUSIONS

➢ Diagnostic management including microbiology and antimicrobial stewardship programs (ASPs) providing rapid ID/AST and active consultation respectively, could have major impact on this GNR septic patient population with high mortality

➢ Pheno was easily incorporated into routine micro workflow and gave results for almost 80% of all GNR

➢ Stewardship currently reviews all GNR blood cultures and agreed that they could incorporate Pheno results into daily consults
BUSINESS PLAN SUPPORT

Support data for Accelerate Pheno testing Implementation  K. Chapin MD

11/2018

Sepsis Background:
Over 60,000 bloodstream infections/year US
Blood stream infections are the leading cause of mortality due to infection in US,
resulting in increased length of stay (LOS), and increased expenditures
in conjunction with antimicrobial stewardship programs (ASP) has shown improved outcomes for
patients in terms of:
Mortality*
LOS*
Readmissions*
Adverse drug reactions
Overall hospital costs

*Lifespan quality measures
Increasing bacterial resistance for the most common blood stream infections meant
New Technology — rapid identication (ID) and susceptibility platform, Accelerate Pheno,
targeted antimicrobial therapy is even more critical.

SUSCEPTIBILITY TESTING (AST)
A recently FDA-cleared rapid ID/AST and susceptibility platform, Accelerate Pheno,
currently available and 2 instruments exist at Lifespan.
The Microbiology Laboratory prospectively evaluated 100 patients with various
negative bacteraemia. Data was compared to current ID/Susceptibility methods,
to final ID and full susceptibility result was calculated, and retrospective chart review
was performed to assess diagnosis, antibiotic use and LOS to identify ASP
opportunities.

Time difference between current methods vs. Pheno was 48.3 hours versus 8.4 hour
(p < 0.0001)
Mortality in this population was 17%
79% could have had antibiotics de-escalated with reduction of adverse events
40% had delayed appropriate antibiotic changes due to TAT of current methods
11% of patients had delayed discharge due to pending standard antibiotic
susceptibility results

Current data shows that the best combination for cost expenditures, quality of life/mortality is
the combination of rapid microbiology results in conjunction with ASP
Costs testing (based on current contracts provided) and Sepsis Patients (based on data
generated from Mylonakis 2018)

Lifespan Labs currently perform approximately 50,000 blood cultures for potential
sepsis per year.
Approximately 250 – 300 are Gram negative rod(GNR) bacteraemias
Cost for 1 Pheno test $250
Cost to run 300 patients @ $250 = $75,000/year

Hospital Costs for 1 septic patient $28,000

Hospital improved patient outcomes based on Quality score and most savings in hospital costs was
in the use of a rapid ID/AST and Susceptibility methods with Antimicrobial stewardship program
in 2018. Lifespan Lab ID and Susceptibility study 77%

Conclusions:
This patient population exhibits a very high mortality (sepsis from GNR bacteraemia)
This patient population has high hospital expenditures (Average LOS 9.1 days)
Benefits of implementing a Pheno system in conjunction with antimicrobial stewardship for
antibiotic therapy, decrease LOS, and reduce overall costs. Mortality can only be assessed based
on prospective implementation.

References
The Cost-Effectiveness of Rapid Diagnostic Testing for the Diagnosis of Bloodstream Infections
with or without Antimicrobial Stewardship. Clinical Microbiology Reviews
E. Pikasoti, A. Andreatos, F. Sheehan, A. Ziafas, E Mylonakis
Decreased Mortality Associated With Prompt Gram Staining of Blood Cultures J Barrenfanger et al,
AICP 2003.
Goto M, Al-Hasan MN. 2013. Overall burden of bloodstream infection and
nosocomial bloodstream infection in North America and Europe. Clin Microbiol
Infect 19

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Both acute care hospitals will use Pheno for GNR
Retrain and train our remaining micro staff
AMS interventions tracking planned

- AMS Interventions
  - Intervention made: yes/no
  - Intervention type: de-escalation, escalation, initiation, etc
  - Intervention outcomes: accepted/rejected
  - Date/Time intervention

- Process Measures
  - Time to effective therapy
  - Time to de-escalation

- Other Metrics
  - Source of BSI
  - LOS
| Accelerate PhenoTest™ BC kit, Accelerate Diagnostics, Inc | 00X XU | Infectious disease (bacterial and fungal), organism identification, blood culture, using rRNA FISH, 6 or more organism targets, reported as positive or negative with phenotypic minimum inhibitory concentration (MIC)-based antimicrobial susceptibility | April 1, 2019 | July 1, 2019 | CPT 2020 |

Will help with cost justification and comparisons to current methods

ID 87077 and AST 87186 reimbursement from CMS = $20.64

4/23/2019

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THANK YOU