

Atsushi Matsui, MD²; Hideki Niimi, MD, PhD³; Isao Kitajima, MD, PhD³; ¹Hitachi, Ltd., Kokubunji-shi, Tokyo, Japan; ²Toyama University Hospital, Toyama-shi, Toyama, Japan; ³University of Toyama, Toyama-shi, Toyama, Japan

Session: 243. Bacterial Diagnostics
Saturday, October 5, 2019: 12:15 PM

Background. To prevent the spread of drug-resistant bacteria, a rapid and accurate antimicrobial susceptibility test (AST) is necessary. Recently, morphokinetic microscopy approaches have been reported as a rapid AST method. However, these still require several hours to obtain a minimum inhibitory concentration (MIC). Adenosine triphosphate (ATP) luminescence has also been reported as a rapid AST method that can detect bacterial growth more rapidly than morphokinetic approaches, since ATP in bacteria increases prior to bacterial division. In this study, we designed a new machine learning-based algorithm that predicts MIC rapidly, using a dataset that contains ATP luminescence patterns and conventional MICs determined by turbidity. Essential agreement (EA) rates between rapid and conventional MIC were then evaluated.

Methods. Sixty-three strains of *E. coli* (ATCC 25922 and clinical isolates from Toyama University Hospital) were tested. Bacterial suspensions were diluted 500-fold in Mueller-Hinton broth from 0.5 McF solutions, and the final concentration of bacteria was 3×10^5 CFU/mL. The suspensions were dispensed into a 96-well microplate, which had 12 antimicrobials in two-fold dilution series, and the microplate was incubated at 35°C. At each measurement time point, the amount of ATP in a 10 µL aliquot from each well was evaluated by our original measurement system, which can sensitively detect ATP luminescence equivalent to a single bacterium. After 22 hours, MIC was determined conventionally by measuring turbidity. A rapid MIC for each bacterium was estimated by the algorithm based on the dataset consisting of the rest of the 62 strains (leave-one-out cross validation).

Results. Table 1 shows the EA rate for the 12 antimicrobials; EA rates > 90% were achieved for 7 antimicrobials in 2 hours and for 12 antimicrobials in 3 hours. In 6 hours, an average EA rate > 97% was achieved.

Conclusion. Using the dataset, our new machine learning-based algorithm predicted MIC rapidly within 2 hours with an EA rate > 90% for 7 antimicrobials. The rapid AST detected by the ATP luminescence method will contribute toward both appropriate antimicrobial treatment and reduction in medication and admission charges. In the future, other species of bacteria will be evaluated by our ATP method.

Table 1 EA* rate (%) by ATP luminescence and machine learning

| | ABPC | P/T | CAZ | CTX | CFPM | CPFX | LVFX | MINO | AMK | AZT | MEPM | IPM | Average |
|---------|------|------|------|------|------|------|------|------|------|------|------|------|---------|
| 6 Hours | 100 | 95.2 | 100 | 96.8 | 95.2 | 95.2 | 100 | 96.8 | 93.7 | 100 | 100 | 98.4 | 97.9 |
| 4 Hours | 100 | 95.2 | 96.8 | 96.8 | 95.2 | 95.2 | 100 | 96.8 | 93.7 | 98.4 | 100 | 98.4 | 97.2 |
| 3 Hours | 100 | 92.1 | 95.2 | 98.4 | 95.2 | 98.4 | 93.7 | 95.2 | 95.2 | 100 | 98.4 | 96.4 | 96.4 |
| 2 Hours | 95.2 | 79.4 | 87.3 | 77.8 | 95.2 | 98.4 | 84.1 | 95.2 | 76.2 | 100 | 96.8 | 90.1 | 90.1 |

Abbreviations: ABPC: Ampicillin, P/T: Piperacillin/Tazobactam, CAZ: Ceftazidime, CTX: Cefotaxime, CFPM: Cefepime, CPFX: Ciprofloxacin, LVFX: Levofloxacin, MINO: Minocefline, AMK: Amikacin, AZT: Aztreonam, MEPM: Meropenem, IPM: Imipenem
*EA (Essential Agreement): Agreement within ± 1 two-fold dilution of conventional MIC

Disclosures. All authors: No reported disclosures.

2137. Impact of Accelerate Pheno™ Rapid Blood Culture Detection System with Real-time Notification vs. Standard Antibiotic Stewardship on Clinical Outcomes in Bacteremic Patients

Courtney Pearson, MD¹; Katherine Lusardi, PharmD, BCPS-AQ ID²; Kelsey McCain, PharmD³; Jacob Painter, PharmD, MBA, PhD⁴; Mrinmayee Lakkad, MS⁵; Eric R. Rosenbaum, MD, MPH¹; Kay Daniels, PharmD⁵; Serena Van, BA⁵; J Ryan. Bariola, MD⁶; Ryan K. Dare, MD, MS¹; ¹University of Arkansas for Medical Sciences, Little Rock, Arkansas; ²Hospital Pharmacy, University of Arkansas for Medical Sciences, Little Rock, Arkansas; ³St. Vincent Infirmary Medical Center, Little Rock, Arkansas; ⁴Division of Pharmaceutical Evaluation & Policy, University of Arkansas for Medical Sciences, Little Rock, Arkansas; ⁵College of Pharmacy, University of Arkansas for Medical Sciences, Little Rock, Arkansas; ⁶University of Pittsburgh Medical Center, Pittsburgh, Pennsylvania

Session: 243. Bacterial Diagnostics
Saturday, October 5, 2019: 12:15 PM

Background. Accelerate Pheno™ blood culture detection system (AXDX) provides identification (ID) and antimicrobial susceptibility testing (AST) within 8 hours of growth in blood culture. We previously reported length of stay (LOS), time to optimal therapy (TTOT), and antibiotic days of therapy (DOT) decrease following AXDX implementation alongside an active antimicrobial stewardship program (ASP). It is unclear whether real-time notification (RTN) of results further improves these variables.

Methods. A single-center, quasi-experimental before/after study of adult bacteremic inpatients was performed after implementation of AXDX. A 2017 historical cohort was compared with two 2018 intervention cohorts. Intervention-1: AXDX performed 24/7 with results reviewed by providers or ASP as part of their normal workflow. Intervention 2: AXDX performed 24/7 with RTN to ASP 7 days per week 9a-5p and overnight results called to ASP at 9a. Interventions 1 and 2 were utilized on an alternating weekly basis during the study (February 2018–September 2018). Historical ID/AST were performed using VITEK® MS and VITEK®2. Exclusion criteria included polymicrobial or off-panel isolates, prior positive culture, and patients not admitted at the time of AST. Clinical outcomes were compared with Wilcoxon rank-sum and χ^2 analysis.

Results. 540 (83%) of 650 positive cultures performed on AXDX had on-panel organisms. 308 (57%) of these cultures and 188 (77%) of 244 reviewed historical

cultures met inclusion criteria. Baseline illness severity and identified pathogens were similar between cohorts. Clinical outcomes and antimicrobial DOT are reported in Tables 1 and 2.

Conclusion. Following our implementation of AXDX, clinical outcomes including LOS, TTOT, total DOT, BGN DOT, and frequency of achieving optimal therapy were significantly improved compared with a historical cohort. Addition of RTN for AXDX results in the setting of an already active ASP did not further improve these metrics. However, compared with historical arm, AXDX with RTN did significantly impact specific subsets of antibiotic use while AXDX alone did not. This may be due to earlier vancomycin de-escalation. These results support the benefit of integration of AXDX into healthcare systems with an active ASP even without the resources to include real-time notification.

Table 1: Clinical Outcomes comparing historical, intervention-1, and intervention-2 arms

| Clinical Outcomes | Historical N = 188 | Intervention-1 N = 155 | Intervention-2 N = 153 | Historical vs Intervention-1 P value | Historical vs Intervention-2 P value | Intervention-1 vs Intervention-2 P value |
|----------------------------|-----------------------|---------------------------|---------------------------|--|--|--|
| LOS, days; mean (±SD) | 11.89 (11.0) | 9.54 (9.8) | 10.08 (11.0) | <0.01* | <0.01* | 0.68 |
| ICU LOS, days; mean (±SD) | 5.17 (6.2) | 5.20 (5.9) | 5.55 (8.82) | 0.79 | 0.99 | 0.79 |
| TTOT, days; mean (±SD) | 2.69 (1.8) | 1.58 (1.5) | 1.48 (1.3) | <0.01* | <0.01* | 0.51 |
| Optimal Tx Achieved, n (%) | 159 (84.6) | 145 (93.6) | 146 (95.4) | <0.01* | <0.01* | 0.47 |

LOS: length of stay; ICU LOS: intensive care unit length of stay; TTOT: time to optimal therapy; Tx: treatment; Optimal Tx Achieved: directed therapy based on organism ID and AST; SD: standard deviation; *statistical significance (p value ≤0.05)

Table 2: Antimicrobial use comparing historical, intervention-1, and intervention-2 arms

| Antimicrobial Use | Historical N = 188 | Intervention-1 N = 155 | Intervention-2 N = 153 | Historical vs Intervention-1 P value | Historical vs Intervention-2 P value | Intervention-1 vs Intervention-2 P value |
|-----------------------------|-----------------------|---------------------------|---------------------------|--|--|--|
| Total DOT, days; mean (±SD) | 8.83 (6.8) | 7.23 (5.6) | 7.90 (6.6) | <0.01* | 0.04* | 0.47 |
| BGP DOT, days; mean (±SD) | 4.85 (5.1) | 4.22 (4.6) | 3.88 (4.7) | 0.12 | 0.02* | 0.80 |
| BGN DOT, days; mean (±SD) | 6.15 (7.6) | 4.54 (5.1) | 4.69 (6.8) | 0.01* | <0.01* | 0.83 |
| NBL DOT, days; mean (±SD) | 2.05 (3.3) | 2.23 (3.8) | 2.99 (4.6) | 0.57 | 0.02* | 0.07 |

DOT: days of therapy; BGP: broad gram-positive (vancomycin, daptomycin, linezolid); BGN: broad gram-negative (cefepime, piperacillin/tazobactam, levofloxacin, meropenem, ertapenem, amikacin, tobramycin, gentamicin); NBL: narrow beta lactams (ampicillin, ampicillin/sulbactam, ceftazidime, ceftriaxone); SD: standard deviation; *statistical significance (p value ≤0.05)

Disclosures. All authors: No reported disclosures.

2138. Follow-up Investigation of Antibody Titers and Diagnostic Antibody Cut-Off Values in Scrub Typhus Patients in Korea

Dong-Min Kim, MD Degree¹; Choon-Mee Kim, Doctor's Degree²; Na Ra Yun, MD, PhD³; ¹Chosun University Hospital, Gwangju, Kwangju-jikhalsi, Republic of Korea; ²Chosun University, Gwangju, Kwangju-jikhalsi, Republic of Korea; ³Chosun University Hospital, Gwanjugwangyeoksi, Kwangju-jikhalsi, Republic of Korea

Session: 243. Bacterial Diagnostics
Saturday, October 5, 2019: 12:15 PM

Background. Scrub typhus is a mite-borne infectious disease caused by *Orientia tsutsugamushi*. There have been few follow-up studies assessing antibody titers using serologic tests from various commercial labs.

Methods. A prospective investigation to assess antibody titers of scrub typhus patients and seroprevalence for health checkup individuals were evaluated. The antibody titers of former patients diagnosed with scrub typhus at least 1 year and a maximum of 13 years were also investigated. The following tests were performed simultaneously: (i) immunofluorescence antibody assays (IFAs) that detect immunoglobulin (Ig) M and IgG, (ii) IFA that detects total Ig by a commercial lab, (iii) antibody tests using two commercially available kits.

Results. In prospective analyses with cutoff values set to $\geq 1:16$ for IgM, $\geq 1:256$ for IgG based on the KCDC's criteria, and $\geq 1:40$ for total Ig. The antibody positive rates of 102 confirmed scrub typhus patients were 44%, 35.3%, and 57.6%, respectively, in the first week after symptom onset. Among 91 former patients recovered, the follow-up IgM, IgG, and total Ig positivity rates were 38.5% (35/91), 22% (20/91), and 76.9% (70/91), respectively. In overall cohort of 216 health checkup subjects, 4.2% (9/216) IgM and 0% (0/216) IgG seroprevalence was observed.

Conclusion. The IFA from KCDC and commercial lab, and rapid commercial kits cannot differentiate between former patients recovered from scrub typhus and current scrub typhus. In Korea and other countries where low antibody cut-off titer values have been used as criteria for diagnosing and reporting scrub typhus, upward adjustments of cut-off values may be necessary.

