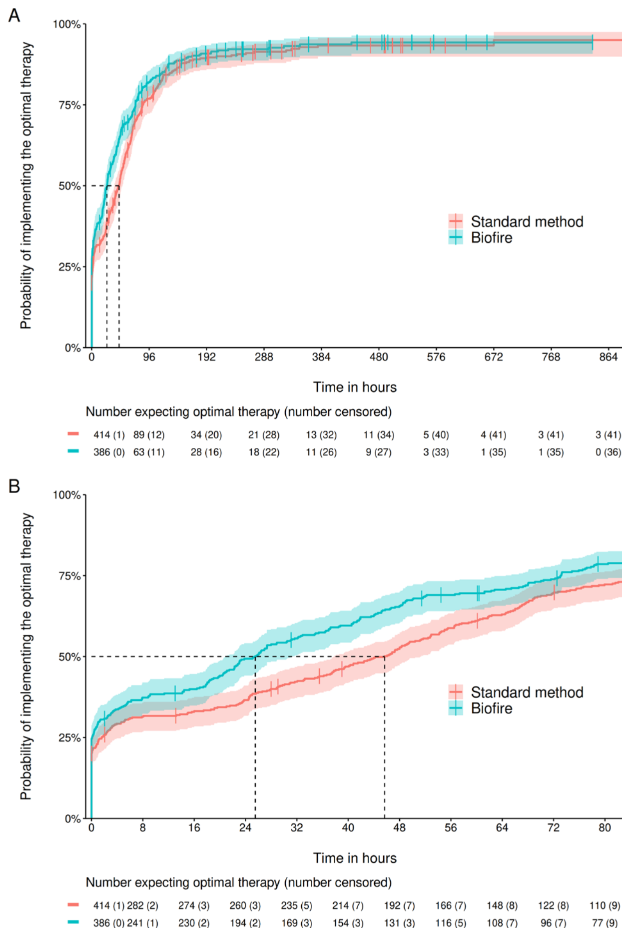
and 44.3 hours by the conventional method. Patients with BF-FA-BCIP received the optimal therapy after a median of 25.5 hours (95%CI 21.0 - 31.2) as compared to 45.7 hours (95%CI 37.7 - 51.2) in the control group (Figure 1). We found no effect of the identification method on secondary outcomes.

Kaplan-Meier curve representing the probability of implementing the optimal therapy at any given time according to the identification method (Standard vs. BF-FA-BCIP).



Shaded ribbons represent the 95 % confidence interval (CI). The vertical dashes represent censored data. The vertical dotted lines represent the median time, i.e. the time at which 50 % of the patients obtained the optimal therapy, for the two methods. Median (95 % CI) time to optimal therapy is 45.7 (37.7 - 51.4) hours with the Standard method and 25.5 (21.0- 31.2) hours with Biofire. The tables below the curves present the numbers expecting optimal therapy according to the bacteria identification method, as well as the number of censored data in parenthesis. Panel A shows data from 0 to 900 hours. Panel B shows the data from 0 to 90 hours to better visualize how the probability to implement optimal therapy varies in the first 72 hours.

Conclusion. In conclusion, rapid pathogen identification by BF-FA-BCIP was associated with an almost 24h earlier initiation of the optimal antibiotic therapy in BSI. However, the overall benefit for individual patients seems to be limited. Future studies should assess the cost-effectiveness and impact on the prevention of antibiotic resistance using this diagnostic approach.

Disclosures. **All Authors**: No reported disclosures

654. Performance of the T2Resistance Panel in Detecting Antibiotic Resistant Bacteria Directly in Whole Blood, and Implications for Improving Appropriate Therapy of Bloodstream Infections

Abigail Skeel, n/a[1,2]; Cornelius J. Clancy, MD[1]; Aaron Lucas, MD[2];
Kailey L. Hughes, MPH[2]; Ryan K. Shields, PharmD, MS[1]; Minh-Hong Nguyen, MD[1];
[1]University of Pittsburgh, Pittsburgh, PA; [2]University of Pittsburgh Medical Center, Pittsburgh, PA

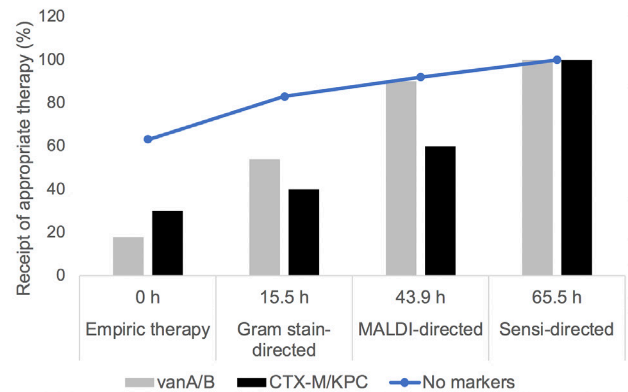
Session: P-29. Diagnostics: Bacteriology/mycobacteriology

Background. Appropriate antibiotic (Ab) therapy of bloodstream infections (BSI) is often delayed by time to blood culture (BC) positivity, species (sp) identification and Ab sensitivity (sensi). The T2Resistance (T2R) Panel is a direct-from-blood (culture-independent) diagnostic that detects 13 genetic markers associated with methicillin-resistant *S. aureus* (MRSA), vancomycin-resistant Enterococcus (VRE), ESBL- and carbapenemase-producing Enterobacteriaceae (E). We assessed T2R performance in detecting these resistant bacteria in whole blood (WB) and analyzed possible impact on time to appropriate Ab.

Methods. We performed T2R using WB samples obtained from patients (pts) on the same day as BCs from July 2019-2020. Receipt of appropriate Ab was assessed at time of empiric, Gram stain-directed, MALDI-directed (sp identification) and sensi-directed therapy. T2R results were not available to care teams. Teams were notified of positive BCs. Stewardship optimized Abs based on sensi.

Results. BC from 103 pts grew 114 bacterial sp: E (n=54; 16 ESBL-, 1 KPC-producer), *S. aureus* (n=29, 22 MRSA), Enterococcus (n=21, 16 VRE), *P. aeruginosa* and others (n=10). 12 ESBL-E produced CTX-M 14/15. T2R sensitivity and specificity was 78% and 99%, respectively, compared to sequencing of resistance markers. Sensitivity was excellent for vanA/B, KPC (100% each), and CTX-M14/15 (92%); sensitivity was 58% for mecA/C. T2R detected resistance determinants in 3-7h. Median time to appropriate Ab was 16.3h, which was significantly longer for VRE (25.6h) and ESBL- or KPC-E (50.9h) BSIs than for T2R marker-negative bacteria (6.7h; p=0.04). Pts with VRE or ESBL-/KPC-E BSI were less likely to received appropriate empiric Ab (18% and 30%, respectively) than pts with T2R marker-negative BSI (63%; p=0.02; Fig.1). Median times to achieve ≥80% appropriate Ab therapy of marker-negative, VRE and CTX-M/KPC-E BSIs were 15.5h (after Gram stain), 43.9h (after MALDI) and 63.5h (after sensi), respectively.

Antibiotic Therapy



Conclusion. There was a significant delay in appropriate Ab therapy of BSIs, especially in pts infected with VRE and ESBL/KPC-E. T2R rapidly and accurately detected BSI caused by VRE and ESBL/KPC-E, and has the potential to significantly shorten time to appropriate Ab.

Disclosures. **Cornelius J. Clancy, MD**, **Merck** (Grant/Research Support) **Ryan K. Shields, PharmD, MS**, **Shionogi** (Consultant, Research Grant or Support) **Minh-Hong Nguyen, MD**, **Merck** (Grant/Research Support)

655. Patterns of Interferon-Gamma Release Assay (IGRA) Testing for Tuberculosis in Patients Less Than 2 Years Old

Mary Tabatneck, MD[1]; Jeffrey Campbell, MD[1]; Mingwei Sun, BA[1]; Wei He, M.S.[2]; Gabriella S. Lamb, MD, MPH[1]; Gabriella S. Lamb, MD, MPH[1]; Don Goldmann, MD[3]; Vishakha Sabharwal, MD[4]; Thomas Sandora, MD MPH[1]; Jessica Haberer, MD, MSc[2];
[1]Boston Children's Hospital, Boston, MA; [2]Massachusetts General Hospital, Boston, MA; [3]Boston Children's Hospital, Harvard Medical School, Washington, DC; [4]MD, Boston, MA

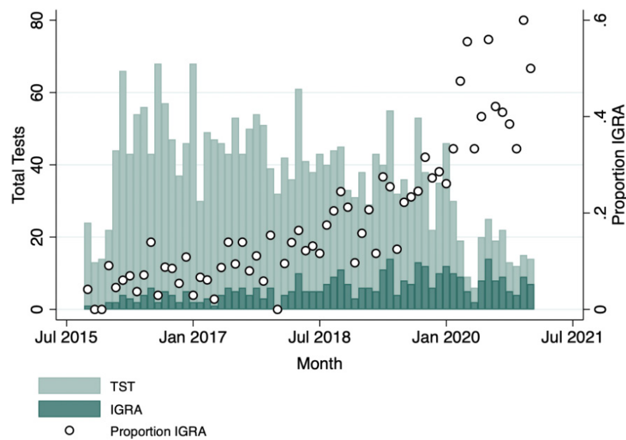
Session: P-29. Diagnostics: Bacteriology/mycobacteriology

Background. The American Academy of Pediatrics recommends use of Interferon-Gamma Release Assays (IGRAs) to diagnose tuberculosis (TB) infection in patients ≥2 years old. However, IGRAs are not currently recommended in younger patients due to limited data and concerns of invalid/indeterminate test results, which occur if there is a positive or negative control failure. We sought to characterize the patterns of IGRA use in clinical practice and results of IGRAs in patients < 2 years old.

Methods. We conducted a retrospective cohort study of children < 2 years old at two large health systems in the Boston area who had IGRA and/or tuberculin skin test (TST) performed from October 1, 2015 – January 31, 2021. We reviewed medical records to determine IGRA test type, IGRA result (positive, negative, invalid/indeterminate) and location of testing (outpatient primary care, outpatient subspecialty, inpatient). We summarized test interpretability, location, and changes in proportion of IGRA vs. TST.

Results. We identified 330 IGRA (268 T-SPOT.TB, 62 QuantiFERON Gold) and 2029 TST results among 1982 patients who were < 2 years old (range: 11 days – 1.9 years). Monthly proportion of IGRAs among all TB tests ordered increased from 2015 to 2021 (Figure 1) (Pearson correlation coefficient 0.85, P < 0.001). Among IGRA results, 314 (95%) were negative, 3 (1%) were positive, and 13 (4%) were invalid/indeterminate (11 T-SPOT.TB, 2 QuantiFERON Gold). Of 324 IGRA tests for which testing location was known, 233 (72%) and 91 (28%) were ordered in outpatient and inpatient settings, respectively. Of tests in outpatient settings, 132 (57%) were ordered in primary care offices, 53 (23%) were ordered in subspecialist offices, and 48 (21%) were obtained in outpatient labs of unidentified clinics.

Tuberculosis infection tests and proportion IGRA.



Total number of tests and proportion of IGRA:TST obtained by month, from October 2015-January 2021.

Conclusion. While most TB infection tests in this age group were TSTs, the monthly proportion of tests that were IGRAs increased over time between 2015-2021. IGRAs were obtained in varied clinical settings. In this low-burden setting, rates of invalid/indeterminate IGRAs were low among children < 2 years old, which suggests that IGRAs are reasonable TB testing options for patients < 2 years old, and may be preferred given limitations of TSTs.

Disclosures. **Gabriella S. Lamb, MD, MPH**, Nothing to disclose

656. Sulbactam-Durlobactam MIC Determination: Comparative Evaluation of the New ETEST® SUD to the CLSI 2021 Broth Microdilution Method

Veronique Sauvonnet; Elodie Escoffier, n/a; Christine Franceschi, n/a; Diane Halimi, MA; Roland Martelin, MS; Laetitia Pellet, n/a; Gilles Zambardi; Biomerieux SA, La Balme Les Grottes, Rhone-Alpes, France

Session: P-29. Diagnostics: Bacteriology/mycobacteriology

Background. Species belonging to the *Acinetobacter baumannii-calcoaceticus* (ABC) complex, such as *A. baumannii, A. pittii* and *A. nosocomialis,* are a major cause of hospital acquired infections and outbreaks with increasing occurrence of multidrug-resistance. Sulbactam-durlobactam (SUD), a combination of one active β-lactam antibiotic (sulbactam) with a new β-lactamase inhibitor (durlobactam), is currently being tested in a phase 3 clinical trial by Entasis Therapeutics for the treatment of serious infections caused by ABC, including multidrug-resistant strains. At the same time, an ETEST® SUD (sulbactam-durlobactam - MIC range 0.004/4-64/4 µg/mL) has been developed and calibrated versus the broth microdilution reference method (BMD) as described by the Clinical and Laboratory Standards Institute (CLSI). This test is intended to determine the MIC of sulbactam-durlobactam for species of the ABC complex. The aim of this study was to perform a first comparative study of ETEST SUD with the CLSI BMD method on a panel of 263 isolates.

Methods. The panel consisted of 204 *A. baumannii*, 29 *A. pittii,* 30 *A. nosocomialis*, including 24 SUD-resistant strains, and one CLSI QC strain. BMD was performed using the 2021 CLSI guidelines. ETEST SUD was evaluated using the standard ETEST procedure for *Acinetobacter* spp. (inoculum 0.5 McFarland, Mueller Hinton medium, incubation at 35°C for 20-24h). For each method, the MIC was read at complete inhibition of visible growth. To determine category agreement (CA) and error rates, the sulbactam-durlobactam provisional breakpoint of 4 µg/mL was applied.

Results. The QC strain MICs were in the expected range with reproducible results. The essential MIC agreement [EA, ±1 dilution] was 97.7% without any tendency to over- or underestimate the MIC when compared to BMD. The CA was 98.5%. Two Very Major Errors, both within the EA, and two Major Errors, one within the EA, were observed.

Conclusion. In this study, the ETEST SUD was found to be equivalent to the CLSI reference method. MIC end points were easy to read. With a 15-dilution range and simplicity of use, ETEST SUD could represent a valuable tool for MIC determination and could be an alternative to BMD.

For Research Use Only. The performance characteristics of this product have not been established yet.

Disclosures. **All Authors**: No reported disclosures

657. Genomic Insights into Virulence Factors Affecting a Tissue-invasive *Klebsiella pneumoniae* Infection

Takashi Matono, MD, PhD[1]; Masatomo Morita, PhD[2]; Nodoka Nakao, MT[1]; Yuji Teshima, MT[1]; Ryosuke Yamate, MD[1]; Takamichi Hijikata, MD[1]; Kosuke Hoashi, MD[1]; Yusuke Ohashi, MD[1]; Yuichi Hasegawa, MD[1]; Tomohide Okinaka, MD[1]; Makoto Ohnishi, MD, PhD,[2]; [1]Aso Iizuka Hospital, Iizuka, Fukuoka, Japan; [2]National Institute of Infectious Diseases, Shinjyuku, Tokyo, Japan

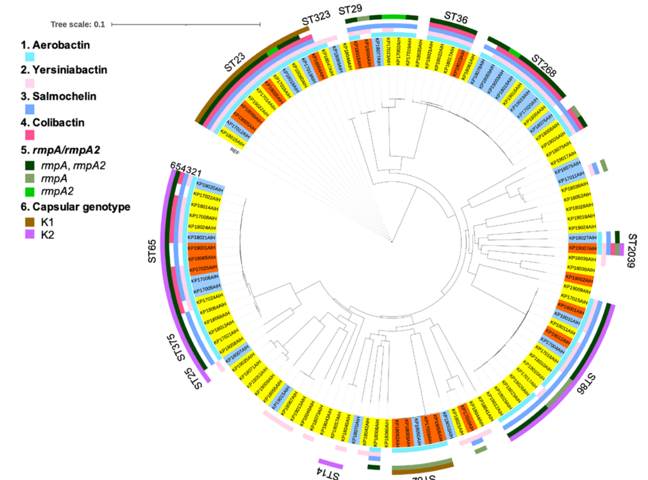
Session: P-29. Diagnostics: Bacteriology/mycobacteriology

Background. Japan is one of the hypervirulent *Klebsiella pneumoniae* (hvKp) endemic areas, resulting in an alarming issue in actual clinical settings. However, little is known regarding key virulence factors responsible for hvKp infection.

Methods. We analyzed *K. pneumoniae* isolates collected between 2017 and 2019, and defined hvKp as a pyogenic infection. Classical *K. pneumoniae* (cKp) involved a non-invasive infection or uncomplicated bacteremia. Isolates belonging to the *K. pneumoniae* species complex were excluded.

Results. We analyzed 112 isolates, including 19 hvKp, 67 cKp, and 26 colonizers, by whole-genome sequencing. Population genomics revealed that the K1-sequence type (ST) 82 clade was distinct from that of K1-ST23 clone (Figure 1). The virulence-gene profiles also differed between K1-ST82 (aerobactin and *rmpA*) and K1-ST23 (aerobactin, yersiniabactin, salmochelin, colibactin, and *rmpA*/*rmpA2*). The K2 genotype was more diverse than that of K1. A neighboring subclade of K1-ST23 (comprising ST29, ST412, ST36, and ST268) showed multidrug-resistance and hypervirulence potentials. Logistic-regression analysis revealed that diabetes mellitus was associated with *K. pneumoniae* infection (odds ratio [OR]: 4.11; 95% confidence interval [CI]: 1.14–14.8). No significant association was found between hvKp diagnosis and clinical characteristics, such as diabetes mellitus or community acquisition (Table 1). The K1 genotype (OR: 9.02; 95% CI: 2.49–32.7; positive-likelihood ratio [LR]: 4.08), *rmpA* (OR: 8.26; 95% CI: 1.77–38.5; positive LR: 5.83), and aerobactin (OR: 4.59; 95% CI: 1.22–17.2; positive LR: 3.49) were substantial diagnostic predictors of hvKp (Table 2).

Figure 1. Phylogenetic distribution of genetic virulence factors in 112 *K. pneumoniae* isolates



The highlighted strains are clinically pathogenic (orange, hypervirulent *K. pneumoniae*; yellow, classical *K. pneumoniae*; sky blue, colonization). The non-highlighted strain (NTUH-K2044) is a reference *K. pneumoniae* strain.

Table 1. Variables analyzed for predicting hvKp infection

Variables	OR (95% CI)	p value
Diabetes mellitus	1.49 (0.52–4.23)	0.46
Liver cirrhosis	12.4 (1.21–127)	0.034
Community-acquired	1.34 (0.48–3.73)	0.58
Positive string test	4.07 (1.08–15.3)	0.038
K1	9.02 (2.49–32.7)	0.001
K2	0.94 (0.32–2.82)	0.92
Aerobactin	4.59 (1.22–17.2)	0.024
Yersiniabactin	2.11 (0.74–6.04)	0.16
Salmochelin	2.56 (0.83–7.91)	0.11
Colibactin	1.86 (0.63–5.52)	0.26
rmpA	8.26 (1.77–38.5)	0.007
rmpA2	1.26 (0.44–3.37)	0.71

hvKp, hypervirulent *K. pneumoniae*; OR, odds ratio; CI, confidence interval

Table 2. Microbiological diagnostic predictive values for hvKp

Characteristics	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	LR+	LR–
Positive string test	84.2	43.3	29.6	90.6	1.49	0.37
K1 genotype	61.5	84.9	42.1	92.5	4.08	0.45
Aerobactin	30.8	91.2	84.2	46.3	3.49	0.76
rmpA	33.3	94.3	89.5	49.3	5.83	0.71

hvKp, hypervirulent *K. pneumoniae*; PPV, positive predictive value; NPV, negative predictive value; LR, likelihood ratio