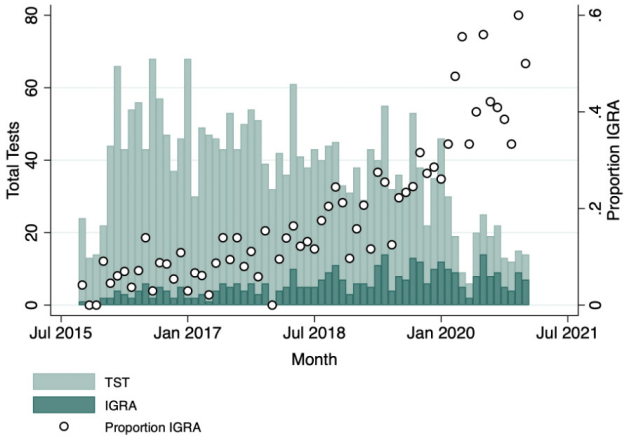

Total number of tests and proportion of IGRA:TST obtained by month, from October 2015-January 2021.

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

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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

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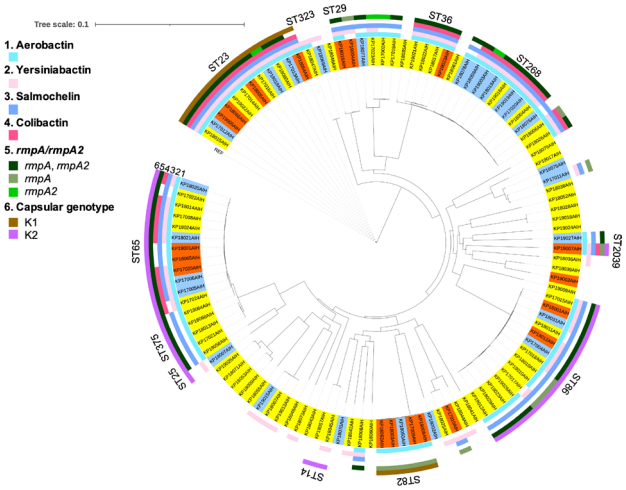
Session: P-29. Diagnostics: Bacteriology/mycobacteriology

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

Conclusion. In hvKp-rich settings, diabetes mellitus, community-acquisition, and siderophores other than aerobactin were not remarkable predictors of hvKp infection. However, the K1 genotype, *rmpA*, and aerobactin were found to be substantial predictors, warranting clinical assessment of any possible/further pyogenic (metastatic) infection. We believe that these findings shed light on key hvKp virulence factors.

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

658. Diagnostic Testing Among Patients with Suspected Recurrent *Clostridioides difficile* Infection (rCDI) in ECOSPOR III a Phase 3 Clinical Trial: Implications for Clinical Practice vs Clinical Trials

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Session: P-29. Diagnostics: Bacteriology/mycobacteriology

Background. Accurate diagnosis of rCDI is challenging because of limitations in test performance and alternative causes of recurrent diarrhea, such as post-infectious irritable bowel syndrome (IBS). Stool enzyme immunoassay (EIA) toxin testing (TOX) is the best predictor of active disease, but may miss cases of CDI when toxins are below the limit of detection. In contrast, glutamate dehydrogenase (GDH) or PCR have high sensitivity but cannot differentiate colonization from infection, leading to possible overdiagnosis due to low specificity. In ECOSPOR III, SER-109, an investigational purified microbiome therapeutic, was superior to placebo in reducing rCDI (12.4% vs 39.8%, respectively; p-value < 0.001). We examined diagnostic testing patterns among screened subjects.

Methods. Patients with ≥2 prior episodes and ≥3 unformed bowel movements over 48 hours were screened. To ensure enrollment of patients with active CDI, toxin testing was required at entry via a local certified or central lab (Eurofins; Framingham, MA). Subjects with discordant GDH+/TOX- tests at the central lab had reflex confirmatory testing with a cell cytotoxicity neutralization assay (CCNA), considered the "gold standard" for toxin testing.

Results. The leading reason for screen failure among 281 subjects screened was a negative toxin test (50/99; 50.5%). Of 182 patients enrolled, 59 (32.4%) qualified with EIA TOX+ at the local lab (33 TOX+; 25 GDH+/TOX+) and 122 (67.0%) qualified by the central lab (Table 1). Of these 122 subjects, 87 qualified by GDH+/TOX+ but 35 required additional reflex testing by CCNA due to discordant GDH+/TOX-results; all 35 were positive.

Diagnostic Testing for Qualifying C. difficile Episode in ITT Population

Test for qualifying episode	SER-109 N=89 n (%)	Placebo N=93 n (%)
LOCAL LAB	24 (26.9)	35 (37.6) *
TOX+ alone	14	19
TOX+ GDH+	10	15
CENTRAL LAB	64 (71.9)	58 (62.4)
GDH+ TOX+	44 (49.4)	43 (46.2)
GDH+ TOX- CCNA+	20 (22.5)	15 (16.1)
MISSING	1 (1.1)	0

*includes 1 patient enrolled with PCR+ test

Conclusion. These diagnostic testing patterns suggest a subset of patients with suspected rCDI have toxin concentrations below the EIA threshold for detection or may have an alternative cause of diarrhea, such as post-infectious IBS. Thus, the limitations of EIA toxin testing need to be considered in clinical practice when evaluating patients with compatible symptoms of rCDI and a high prior probability of infection. In contrast, in trials of investigational agents, toxin testing assures enrollment of patients with active disease and accurate estimates of efficacy.

Disclosures. **Matthew Sims, MD, PhD, FACP, FIDSA**, **Astra Zeneca** (Independent Contractor)**Diasorin Molecular** (Independent Contractor)**Epigenomics Inc** (Independent Contractor)**Finch** (Independent Contractor)**Genentech** (Independent Contractor)**Janssen Pharmaceuticals NV** (Independent Contractor)**Kinevant Sciences gmBH** (Independent Contractor)**Leonard-Meron Biosciences** (Independent Contractor)**Merck and Co** (Independent Contractor)**OpGen** (Independent Contractor)**Prenosis** (Independent Contractor)**Regeneron Pharmaceuticals Inc** (Independent Contractor)**Seres Therapeutics Inc** (Independent Contractor)**Shire** (Independent Contractor)**Summit Therapeutics** (Independent Contractor) **Sahil Khanna, MBBS, MS**, **Seres** (Grant/Research Support) **Darrell Pardi, MD**, **seres** (Consultant)**Vedanta** (Consultant) **Paul Feuerstadt, MD, FACG**, **Ferring/Rebiotix Pharmaceuticals** (Consultant, Scientific Research Study Investigator, Speaker's Bureau)**Finch Pharmaceuticals** (Scientific Research Study Investigator)**Merck and Co** (Speaker's Bureau)**SERES Therapeutics** (Consultant, Scientific Research Study Investigator)**Takeda Pharmaceuticals** (Consultant) **Elaine E. Wang, MD**, **Seres Therapeutics** (Employee) **Elaine E. Wang, MD**, **Seres Therapeutics** (Employee, Shareholder) **Barbara McGovern, MD**, **Seres Therapeutics** (Employee, Shareholder) **Lisa von Moltke, MD**, **Seres Therapeutics** (Employee, Shareholder)

659. Correlate Clinically and More-Use of Interpretative Comments in Clinical Microbiology Reporting

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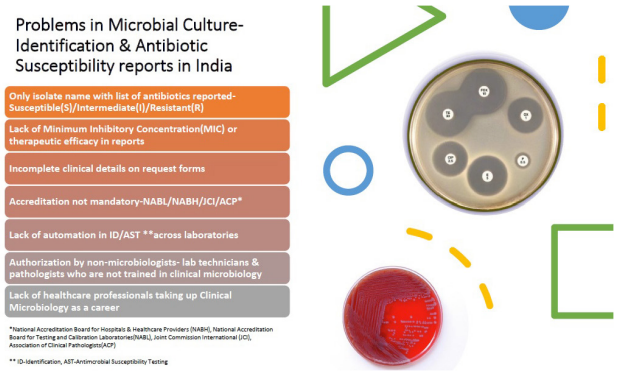
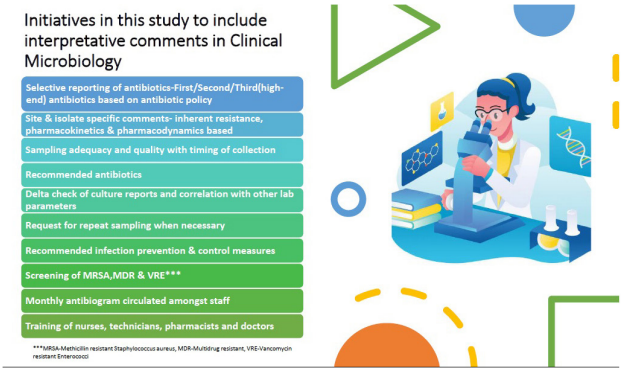
Session: P-29. Diagnostics: Bacteriology/mycobacteriology

Background. Microbial identification & antibiotic susceptibility testing is an important investigation in clinical microbiology laboratory. In many centres in India the report has only the isolate and antibiotics tested. The additional comments if added give guidance to the clinicians to utilize the results. Pre-analytical issues of adequate & relevant clinical history, appropriate sampling techniques, timely transport & storage, history of antibiotic usage along with post analytical issues of recommended line of antibiotic therapy and infection control practices are better addressed with this practice.



Methods. This was a prospective qualitative study from the period of January 2017-March 2021 where in the standard operating protocol of Clinical Microbiology was reviewed and appropriate comments were included in the Laboratory Information System once the isolate was identified using VITEK 2, automated ID/AST instrument and interfaced. The Clinical Microbiologist would then review the comments upon discussion with the clinicians and then authorize reports. The reports included sample & isolate specific details , recommended antibiotic therapy and infection control related comments. This was based on standard international and national guidelines (CLSI, EUCAST, IDSA, IAP, and National Treatment Guidelines of India).



Results. There was a gradual improvement in completion of request forms with clinical history, sample site and antibiotic history being mentioned. This was assessed through periodic audits conducted every quarter from 36% in March 2017 to 95% in March 2021. Clinical communication with the microbiology laboratory also showed improvement with documentation. Feedback from clinicians was also taken on the utility of these comments, (87/120)72.5% of the clinicians found them useful(Grade 5). (32/120) 26 %(Grade 3) of the clinicians had concerns about the turnaround time and requested for provisional reports.