Conclusion. Despite appropriate treatment with IV acyclovir, HSE survivors frequently experienced severe morbidities after initial hospitalization, including HSE relapse, discharge to long-term care facilities, and neurocognitive impairment. Risk of death was highest within one month of admission. Further investigation is needed to optimize treatment of HSE to improve mortality and to reduce permanent neurologic deficits.

Disclosures. All Authors: No reported Disclosures.

Table 1.†

| Demographics |   |
|--------------|---|
| Number of confirmed HSE cases | 32 |
| Age at diagnosis (years) | 62 (45-72) |
| Male | 16 (50%) |

**Treatment**

| Received intravenous acyclovir | 32 (100%) |
| Time from symptom onset to IV acyclovir treatment (days) | 5 (3-8) |
| Duration of IV acyclovir (days) | 24 (19-30) |
| Length of admission (days) | 12 (7-20) |

**Readmission**

| All-cause 3-month readmission | 15 (47%) |
| Patients readmitted with HSE relapse | 6 (19%) |

**Discharge disposition after initial admission**

| Home | 11 (35%) |
| Acute care facility | 2 (6%) |
| Long-term care facility | 16 (50%) |
| Death during hospitalization | 3 (9%) |

**Discharged patients with lasting neurologic deficits**

| Cognitive | 19 (66%) |
| Motor | 9 (31%) |
| Sensory | 2 (7%) |

†Continuous variables presented as median and interquartile range.

**Characteristics**

| Characteristic | Median (IQR) or n (%) |
|----------------|-----------------------|
| Age, years | 55 (40-69) |
| Male | 83 (65%) |
| Weight, kg | 83 (66-108) |
| CrCl, ml/min | 87 (44-132) |
| APACHE II | 18 (12-22) |
| Sources of infection, n | |
| Abdominal | 34 |
| Lung | 50 |
| Wound | 24 |
| Duration of therapy, days | 12 (7-17) |

**Drug**

| Drug | N | Daily dose, grams | Infusion time, hr | Cmin, mg/L | MIC, mg/L |
|------|---|------------------|------------------|------------|----------|
| Cefepime | 87 | 6 (4-6) | 0.5 (0.4-2.0) | 18.3 (11.4-34.3) | 1 (0.1-4) |
| Meropenem | 20 | 3 (2-4) | 0.5 (0.5-0.6) | 13.5 (8.9-16.9) | 0.75 (0.25-4) |
| Piperacillin | 18 | 3.5 (2.5-7.5) | 1.75 (0.5-4.5) | 31.6 (7.4-61.6) | 12 (4.2-32) |

**Drug Exposure**

| Drug | AUC<sub>0-tau</sub> (mg·h/L) | Creatinine Increase (mg/dL) | p-value |
|------|------------------------------|-----------------------------|---------|
| Cefepime | 3.01 (2.01-4.01) | 3.01 (2.01-4.01) | 0.001 |

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1826. Impact of Rapid Diagnostics and Cezafamidine–Avibactam on Mortality on Mortality on Bacteremia Caused by Carbapenem-Resistant Enterobacteriaceae
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Background. Patients with bloodstream infections (BSIs) due to carbapenem-resistant Enterobacteriaceae (CRE) have long delays until receipt of appropriate antimicrobial therapy and high mortality rates. Rapid molecular diagnostics and novel therapies, such as cezafamidine–avibactam (CAZ-AVI), offer promise to improve outcomes, but their clinical impact is unclear.

Methods. We studied an observational study of patients with CRE BSI from January 2016 to June 2018 in New York and New Jersey medical centers. Patient demographics, comorbidities, clinical presentations, diagnostic methods, and treatments were compared between patients who died within 30 days of BSI onset and survivors. Multivariable Cox proportional hazards regression for mortality was identified using univariate analysis. We then compared time to receipt of active antimicrobial therapy between patients whose positive blood culture bottles underwent testing for the Klebsiella pneumoniae carbapenemase gene (blaKPC PCR) and patients where this test was not used.

Results. 178 patients with CRE were identified. (K. pneumoniae: n = 26, 15%; Entrobacter cloacae: n = 26, 15%; Escherichia coli: n = 26, 15%). The 30-day mortality rate was 38%. An increasing Acute Physiology and Chronic Health Evaluation II score (adjusted odds ratio [aOR] 1.06; P = 0.005) was independently associated with increased 30-day mortality. Time to receipt of active antimicrobial therapy (aOR 0.3; P = 0.001), and source control (aOR 0.25; P = 0.001), and their clinical impact is unclear.

Conclusion. The use of PCR to rapidly identify blood culture bottles with blaKPC and definitive therapy with appropriate antimicrobials or aminoglycosides were associated with decreased mortality after CRE bacteremia.

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1827. Genetic Characterization of Methicillin-Resistant Staphylococcus aureus (MRSA) Isolates Associated with the Development of Reduced Susceptibility to Vancomycin from Latin America
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Background. Vancomycin (VAN) is a first-line therapeutic option for severe MRSA infections, especially in Latin America where other options are limited. However, reduced susceptibility to VAN may lead to therapeutic failures. The molecular mechanisms leading the development of VAN-intermediate S. aureus (VISA) and heterogeneous-VISA (hVISA) phenotypes are still unclear. We explored genetic signatures associated with hVISA phenotype in MRSA isolates recovered from bacteremic patients in 9 Latin American countries (2011–2014) in order to develop a genomic platform to identify these isolates.

Methods. From 538 VAN-susceptible MRSA (MICVAN = 1 µg/mL) we identified 30 hVISA isolates using GRD and macrometh F-tests; from these, we were confirmed with PAP-AUC. Whole-genome sequencing was performed in all 30 isolates using Illumina platform. Based on previous studies, we selected 64 genes in vitals development. Multiple Blast alignments were performed using genomes of ATCC29213 and N315 (VAN-susceptible), Mu3 (hVISA) and Mu50 (VISA) as references.

Results. A total of 130 changes in 46 predicted proteins belonging to 8 functional categories were determined: 48 changes related to cell wall biosynthesis, 22 to DNA/RNA processing, 17 to regulatory systems, 12 to cofactors and enzymes, 11 to membrane biosynthesis, 9 to virulence, 6 to amino acid metabolism, and 5 to transport of nitrogen and putrescine/putrescine. The most common changes identified in all the hVISA were Y38H in Atl, N16S in PBP4, S160A in RpoB, L14I in WalK and E156G in VraS, compared with VISA strains. The proteins with the highest number of changes detected in the isolates confirmed by PAP-AUC were: CapD, DhpA, Phtp4, TacA, LytM (Cell wall biosynthesis); MuL, Rp08 (DNA/RNA processing); GraS (Regulatory systems).

Conclusion. Changes in genes associated with cell wall biosynthesis, DNA/RNA processing, regulatory systems, and membrane biosynthesis were the most prevalent in Latin American hVISA strains. Genetic signatures in genes encoding GraR (N197S), Rp08 (H481Y, H481N), VraS (TNS), WalR (L14, R87, R97K) and MsoR (E146K) are potentially associated with this phenotype. These changes could be used to develop a platform for possible identification of hVISA isolates.

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1828. Bedaquiline Resistance in Mycobacterium intracellulare Is Mediated by the Transcriptional Repressor MmpT4
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Background. Bedaquiline (BDQ) is an FDA approved antibiotic with antimycobacterial activity. BDQ resistance has been observed in several Mycobacterium species. High-level resistance is due to mutations in ATP synthase. Low-level resistance is attributed to drug efflux. Previously, we suggested that the MmpS5L efflux system mediates BDQ resistance in M. intracellulare. Here, we examine the role of MmpT5 in transcriptional regulation of mmpS5L and BDQ resistance.

Methods. In this study, mmpS5L-mmpT5 genes were cloned from 2 pre-treatment (wild-type mmpT5) and 2 relapse (mutant mmpT5) isolates of M. intracellulare and transformed into M. smegmatis. BDQ MICs were determined as well as other antimicrobials after 24 hours of BDQ (3 µg/mL) exposure. MICs were determined by broth dilution. Transcription of the M. intracellulare mmpS5L and mmpT5 promoters was monitored with luciferase reporter gene fusions in the presence of wild-type and mutant alleles of mmpT5. Single and multigene constructs were created using the MoClo system, and transformed into E. coli DH5α. Constructs containing the M. tuberculosis rv0678 gene, which mediates low-level BDQ resistance in M. tuberculosis, were also examined.

Results. The BDQ MIC for the M. smegmatis control strain, and all strains containing a wild-type mmpT5 showed an MIC of 0.007 µg/mL. Even so, strains containing mutant mmpT5 alleles showed enhanced survival after 24 hours exposure to 0.007 µg/mL BDQ. Bacillary colonies associated with mutant mmpT5 alleles exhibited altered morphology relative to wild-type strains. Transcription of mmpS5L was repressed by wild-type mmpT5, but neither mutant mmpT5 nor rv0678 repressed transcription. The mmpT5 luciferase reporter was not active.

Conclusion. MmpT5 represses transcription of mmpS5L whereas the operon is dysregulated by mmpT5 mutations. Although rv0678 regulates mmpS5L expression in M. smegmatis, it cannot repress the BDQ efflux. BDQ and aminoglycosides are two treatments that may have potential for use in treating BDQ-resistant strains of M. tuberculosis.

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1829. The Paradox of KPC Bearing Strains of Klebsiella pneumoniae with the D179Y Substitution: Resistance to Ceftazidime/Avibactam (CZA) and Susceptibility to Meropenem (MEM)
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References.
(Full reference page is available on request.)