using the BioFire FilmArray meningitis/encephalitis (BFME) panel for cerebrospinal fluid (CSF) specimen analysis. We hypothesized that the diagnosis of VZV CNS infection increased at our institution with the implementation of this diagnostic panel.

Methods. We conducted chart reviews of patients from 2 time periods. In the first period, April 2013–March 2016, BFME was not available for CSF analysis (pre-BFME period). We reviewed all positive CSF VZV PCR results during this period. Medical charts of these patients were reviewed for epidemiology, clinical presentation, treatment course, and outcome. In the second period, April 2016–March 2018, BFME was performed on all CSF specimens obtained by lumbar puncture (BFME period). Patients with a positive VZV result on BFME underwent similar chart review.

Results. In the 3-year pre-BFME period, 292 VZV PCR tests were performed. Six patients were diagnosed with VZV CNS infection; median age 61 years. Five of the 6 patients (83%) had cutaneous zoster. All 6 patients received antiviral therapy. Five of the 6 patients clinically improved; 1 patient with VZV encephalitis died. In the 2-year BFME period, 1,113 CSF samples were evaluated, and 18 of these were positive for VZV (1.6%); median age 55 years. Only 7 of the 18 (39%) had cutaneous zoster at the time of hospitalization. All 18 received antiviral therapy with clinical improvement.

Conclusion. Prior to implementation of the BFME panel at our institution, VZV CNS infection was rarely diagnosed. Diagnosis at that time relied on physicians' requests for a targeted CSF VZV PCR. The majority of the patients during that period had a concurrent zoster rash. In a shorter period utilizing syndromic testing (BFME) on CSF specimens, we diagnosed 3 times as many cases of VZV CNS disease. Only a minority of these patients presented with a concurrent zoster rash. The use of syndromic testing of CSF will likely identify more cases of VZV CNS disease.

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

867. Upregulated Matrix Metalloproteinase-2 Relates to Milder Hearing Impairment in Bacterial Meningitis

Okko Savonius, MD[1]; Irmeli Roine, MD, PhD[2]; Saeed Alassiri, DDS[3]; Taina Tervahartiala, DDS, PhD[3]; Otto Helve, MD, PhD[1]; Josefina Fernandez, MD[4]; Heikki Peltola, MD, PhD, Professor[1]; Timo Sorsa, DDS, PhD[3] and Tuula Pelkonen, MD, PhD[1], [1]Children's Hospital, Helsinki University Hospital, and the University of Helsinki, Helsinki, Finland, [2]Faculty of Medicine, University Diego Portales, Santiago, Chile, [3]Department of Oral and Maxillofacial Diseases, Institute of Dentistry, Helsinki University Hospital and the University of Helsinki, Helsinki, Finland and [4]Infectious Diseases Department, Robert Reid Cabral Children's Hospital, Santo Domingo, Dominican Republic

Session: 86. Pushing the Envelope in CNS Infections
Thursday, October 4, 2018: 2:00 PM

Background. Hearing impairment is a well-recognized sequela caused by bacterial meningitis, but the underlying pathophysiology remains largely unknown. Matrix metalloproteinase-2 (MMP-2) is known to affect neuronal cell damage and survival in different diseases of the brain. We investigated whether levels of MMP-2 in the cerebrospinal fluid (CSF) relate to the extent of hearing impairment in children with bacterial meningitis.

Methods. Clinical data of 179 children were obtained from a previous clinical trial examining the adjuvant treatment of bacterial meningitis in Latin America in 1996–2003. At discharge or shortly thereafter, the ability to hear was measured with brain stem evoked response audiometry or traditional pure tone audiometry. Levels of CSF MMP-2 on admission (CSF1, $n = 161$) and 12–24 hours later (CSF2, $n = 133$) were assessed by zymography. The combined results for the detected pro-form and active MMP-2 were compared with the audiological outcome of the patients.

Results. MMP-2 was detected in half of both the CSF1 and CSF2 samples. The median densitometric values with interquartile ranges (IQRs) were 0.04 (IQR 0.00–0.29) for CSF1 and 0.00 (IQR 0.00–0.33) for CSF2. Detectable MMP-2 associated with milder hearing impairment in CSF1 ($P = 0.05$), but not in CSF2 ($P = 0.1$). Patients who were deaf at discharge had lower levels of MMP-2 in both samples (CSF1, $P = 0.05$; CSF2, $P = 0.04$), compared with patients who were not deaf. A MMP-2 level over the 75th percentile in CSF1 predicted lower odds of any audiological sequelae (odds ratio 0.30, 95% confidence interval 0.14–0.68, $P = 0.004$).

Conclusion. The upregulation of MMP-2 in the CSF associated with a better audiological outcome in children with bacterial meningitis. The results suggest that MMP-2 might play a protective role in the development of hearing sequelae due to bacterial meningitis.

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

868. Prospective Pathogen Detection in Patients With Central Nervous System Inflammation Using Metagenomic Sequencing

Anne Piantadosi, MD, PhD[1]; Shibani Mukerji, MD, PhD[2]; Simon Ye, BA[3]; Michael Leone, MS[2]; Lisa Freimark, MS[3]; Jacob Lemieux, MD, PhD[1]; Isaac Solomon, MD, PhD[4]; Asim Ahmed, MD[5]; Sanjat Kanjilal, MD, MPH[1]; Robert Goldstein, MD, PhD[1]; Vijay Ganesh, MD, PhD[2]; Bridget Ostrem, MD, PhD[2]; Jesse Thon, MD[2]; Cormac Kinsella, MS[6]; Gordon Adams, BA[1]; Eric Rosenberg, M.D.[1]; Marcia Goldberg, MD, FIDSA[1]; Pardis Sabeti, MD, DPhil[7] and Tracey Cho, MD[2], [1]Department of Medicine, Division of Infectious Diseases, Massachusetts General Hospital, Boston, Massachusetts, [2]Department of Neurology, Massachusetts General Hospital, Boston, Massachusetts, [3]Broad Institute, Cambridge, Massachusetts, [4]Pathology, Brigham and Women's Hospital, Boston, Massachusetts, [5]Boston Children's Hospital, Boston, Massachusetts, [6]University of Amsterdam, Amsterdam, Netherlands, and [7]Organismic and Evolutionary Biology, Harvard University, Cambridge, Massachusetts

Session: 86. Pushing the Envelope in CNS Infections
Thursday, October 4, 2018: 2:00 PM

Background. Metagenomic sequencing can identify pathogens in patients with central nervous system (CNS) inflammation, who often have no diagnosis achieved despite extensive clinical testing.

Methods. This prospective study enrolled patients with CNS inflammation at a tertiary hospital from 2016 to 2017. Total nucleic acid was extracted from cerebrospinal fluid (CSF). Libraries were constructed by random primer cDNA synthesis from RNA, and Nextera XT preparation from both cDNA and DNA. Sequencing was performed on an Illumina platform. Reads from human and environmental contaminants were removed. Metagenomic analysis was performed with Kraken and confirmed with viral-ngs. The Institutional Review Board approved the study, and informed consent was obtained.

Results. Of 68 subjects enrolled, 63% were men and 84% were white. The median age was 58 years. The median CSF pleocytosis was 80 cells/mm^3 [IQR 17–132]. A median of 2.4 million RNA and 6.8 million DNA sequencing reads were generated per sample. Twenty-five subjects had no diagnosis achieved by routine clinical testing; metagenomic sequencing identified enterovirus in 2 of these subjects, and no pathogen in 23. Thirty-six subjects were clinically diagnosed with an infection. In 12 of these, pathogen nucleic acid was detected in CSF by clinical polymerase chain reaction (PCR); metagenomic sequencing detected the expected pathogen in 10 subjects (83%). The other 24 subjects were clinically diagnosed with infection by serology or PCR from blood. Among these, metagenomic sequencing detected the CSF presence of HIV and locally important tick-borne pathogens Powassan virus, *Borrelia burgdorferi,* and *Anaplasma phagocytophilum*. Four subjects with West Nile Virus (WNV) infection did not have WNV RNA detected in CSF by sequencing or clinical PCR testing. Among 7 subjects diagnosed with malignancy or autoimmune disease, no pathogens were detected by metagenomic sequencing.

Conclusion. When applied broadly to patients with CNS inflammation, metagenomic sequencing identified known and unexpected pathogens in CSF, including emerging tick-borne pathogens, highlighting its potential as a diagnostic tool. Patients in whom no pathogen nucleic acid was detected could have had an infection with low pathogen burden or short duration in CSF, or a noninfectious syndrome.

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

869. Evaluation of Broad-Spectrum Antibiotic De-Escalation in Patients with Health-Care Associated Pneumonia (HCAP) and No Microbiological Diagnosis

Twisha S. Patel, PharmD, BCPS[1]; Lindsay Petty, MD[2]; Anna Conlon, PhD[3]; Gregory Eschenauer, PharmD, BCPS[1]; Daniel Nielsen, MS[3]; Valerie Vaughn, MD, MSc[4]; Keith S. Kaye, MD, MPH[2]; Anurag Malani, MD, FIDSA[5]; Danielle Osterholzer, MD[6]; Rama Thyagarajan, MD[7]; Scott Flanders, MD[8] and Tejal N. Gandhi, MD[2], [1]Michigan Medicine, Ann Arbor, Michigan, [2]Internal Medicine, Division of Infectious Diseases, Michigan Medicine, Ann Arbor, Michigan, [3]University of Michigan Health System, Ann Arbor, Michigan, [4]Internal Medicine, University of Michigan, Ann Arbor, Michigan, [5]St. Joseph Mercy Health System, Ypsilanti, Michigan, [6]Hurley Medical Center, Flint, Michigan, [7]Internal Medicine/Infectious Disease, Beaumont Health- Dearborn, Dearborn, Michigan, and [8]University of Michigan, Ann Arbor, Michigan

Session: 87. Respiratory Infections: An Update
Thursday, October 4, 2018: 2:00 PM

Background. Broad-spectrum (BS) antibiotics directed against *Pseudomonas aeruginosa* and methicillin-resistant *Staphylococcus aureus* (MRSA) are commonly used for health-care associated pneumonia (HCAP) treatment. Many patients with HCAP do not have a microbiologically confirmed diagnosis. The goal of this study was to evaluate the impact of antibiotic de-escalation on clinical outcomes in patients with HCAP without a microbiological diagnosis.

Methods. This is a retrospective cohort study of adult, non-ICU, medical patients hospitalized with HCAP between January 2016 and February 2018 at 46 Michigan hospitals. Exclusions included extrapulmonary infection, severe immune suppression, or clinical instability on day 4. Included patients: (1) lacked any positive culture (blood/sputum); (2) started on empiric anti-*P. aeruginosa* and anti-MRSA therapy by hospital day 2; (3) switched to a narrow-spectrum (NS) regimen (no anti-*P. aeruginosa* or anti-MRSA coverage) or maintained on BS antibiotics (anti-*P. aeruginosa* ± anti-MRSA) by therapy day 4 (Figure 1). Mortality, readmission, *Clostridium difficile* infection, and adverse events from antibiotics were compared between the BS and NS groups. Data were analyzed using logistic generalized estimating equation models and inverse probability of treatment weighting.

Results. Of 363 patients with HCAP included, 73 (20%) were switched to an NS regimen. Of 290 patients maintained on anti-PSA BS regimens, 47.6% also continued anti-MRSA therapy. The median age was 72 (IQR, 61–81) and Charlson comorbidity index was 4 (IQR, 2–6) of the entire cohort. Baseline characteristics were similar between BS and NS groups, except more patients had chronic kidney disease in the BS group. On multivariable analysis, no other baseline factors were