Survival at 240 days after transplant was 62% often with long-term neurologic sequelae. CSF tended to have lymphocyte predominance and nearly all patients had peripheral lymphopenia. Other at risk populations identified included 2/19 (11%) patients who received chimeric antigen receptor (CAR) T-cell therapy, 2/19 (11%) who received biologic immunotherapy, and 2/19 (11%) who had non-HSCT hematologic malignancy. Notable discordance among testing platforms was found in 5/9 (55%) of patients receiving both testing platforms.

CSF and Laboratory Analytes

Median Values of CSF Analytes and Laboratory Findings

	HSCT Cohort (n=12)*	CART Cohort (n=2)	Non HSCT, CART Cohort (n=4)	Total Cohort (n=19)
LP Timing (Days)	4 (0-21)	3 (1-5)	4.5 (4-6)	4
CSF Protein mg/dL	68 (35-158)	106 (92-120)	49 (25-68)	68
CSF Glucose mg/dL	62.0 (44-115)	50.5 (32-69)	54.0 (45-73)	59.0
CSF WBC cells/μL	4.0 (0-58)	35.0 (25-45)	11.5 (0-24)	7.5
CSF % Lymph	67 (20-100)	75.5 (70-81)	77.5 (0-90)	72
CSF RBC cells/μL	3.5 (0-8800)	2.0 (2)	2.0 (0-25)	2.0
Peripheral WBC 1000 cells/μ	3.95 (0.1-10.7)	3.4 (3.3-3.5)	2.75 (0-6.9)	3.40
Peripheral ANC 1000 cells/μL	3.36 (1.39-9.84)	2.18 (1.92-2.45)	1.84 (0-3.74)	3.40
Peripheral ALC 1000 cells/μL	0.360 (0.09-1.180)	0.68 (0.66-0.70)	0.56 (0-1.40)	0.36

*Patient 13 excluded as LP was prior to symptom onset
*Patient 4 did not have a differential on CSF WBC analysis
*Patient 12 did not have glucose or protein analysis sent on initial LP

Findings and Outcomes in HSCT Patients

Findings and Outcomes

Patient	Days from HSCT to CNS dysfunction	Initial Symptoms	Electroencephalogram (EEG)	MRI foci of T2/FLAIR/DWI hyperintensity	Plasma HHV-6 DNA copies/mL*	CSF HHV6 Test	CSF HHV-6 DNA Peak copies/mL	CSF HHV-6 Testing Discordant	Etiology	Prophylactic Antivirals	Antiviral Treatment	Outcome
1	28	Confusion Mutism Nausea/Vomiting	Multifocal intermittent epileptiform discharges, bitemporal region dysfunction	Bilateral posterior occipitoparietal regions	600	Viracor HHV-6 PCR	106	N/A	HHV-6 PALE	Valacyclovir -> Foscarnet day 20 (HHV-6 viremia)	Foscarnet 21d -> Cidofovir Brincidofovir	Died day 85 from disseminated adenovirus
2	25	Anterograde amnesia Retrograde amnesia	Diffuse disturbance of cerebral activity with theta wave bursts	Medial temporal lobe	Detected <188	Viracor HHV-6 PCR	143	N/A	HHV-6 PALE	Valacyclovir	Foscarnet 21d	Alive day 1148, moderate cognitive recovery, but persistent memory dysfunction. Remains no evidence of malignant disease
3	31	Anterograde amnesia Retrograde amnesia Non-sensical Speech	Diffuse disturbance of cerebral activity with epileptiform waveforms	Bilateral hippocampi	29500	Viracor HHV-6 PCR	211000	N/A	HHV-6 PALE	Valacyclovir	Foscarnet 34d	Died day 68 from respiratory failure, no microbiologic diagnosis, HHV-6 DNA 1700 copies/mL in bronchoalveolar lavage
4	10	Confusion Fever Rash	Mild generalized slowing	Known myelomic disease without new findings	1000	Viracor HHV-6 PCR	Detected <81	N/A	Confirmed HHV-6 Encephalitis	Valacyclovir	None	Died day 491 from retropharyngeal abscess and diskitis, encephalitis resolved after engraftment before HHV-6 testing resulted. Relapsed malignant disease
5	19	Headache Fever	ND	None	5500	Viracor HHV-6 PCR	59400	N/A	HHV-6 Aseptic Meningitis	Valacyclovir	Foscarnet 14d	Alive day 905, remains in clinical remission
6	32	Anterograde amnesia Retrograde amnesia Non-sensical Speech	Normal, repeat EEG day 4 with diffuse disturbance of cerebral activity and left temporal lobe epileptogenicity	Bilateral hippocampi, parietal cortices	15500	Viracor HHV-6 PCR	135000	N/A	HHV-6 PALE	Valacyclovir	Foscarnet 15d IVIG (1 dose)	Alive day 908, persistent memory and neurocognitive deficits up to 12 months but returned to normal function, remains no evidence of malignant disease
7	1265	Headache Fever Nausea/Vomiting Photophobia Syncope	ND	6mm right frontal subdural hematoma without other foci	600	Viracor HHV-6 PCR Biofire® MEP	1100	No	HHV-6 Aseptic Meningitis	Valacyclovir	Foscarnet 43d IVIG (6 doses) Valganciclovir 23d	Died day 1830 from *Escherichia coli* bacteremia, relapsed malignant disease
8	711	Episodic confusion Impaired hand-eye coordination Word finding difficulty	Diffuse disturbance of cerebral activity	Punctate right clivus	2900	Viracor HHV-6 PCR	Detected <81	N/A	Possible HHV-6 Encephalitis	Valacyclovir	None	Died day 737 from relapsed and progressive extramedullary disease, encephalitis resolved prior to HHV-6 testing resulted
9	43	Fever Lethargy Rash	ND	ND	Detected <188 ++	Viracor HHV-6 PCR Biofire® MEP	Not Detected	Yes, only MEP positive	Possible HHV-6 Encephalitis	Valacyclovir	Foscarnet 14d	Alive day 850, no residual neurocognitive deficits, relapsed malignant disease, repeat HSCT 12/2019.
10	19	Episodic somnolence Slowed speech	Diffuse disturbance of cerebral activity	Right cerebellum	Not Detected	Viracor HHV-6 PCR Biofire® MEP	Detected <81	No	Confirmed HHV-6 Encephalitis	Valacyclovir -> Acyclovir -> Foscarnet day 15 for presumed resistant oral HSV lesion	Foscarnet 38d	Died day 110 from multiorgan failure due to disseminated adenovirus, RSV pneumonia and steroid refractory GVHD
11	24	Headache Rash Seizure	Diffuse disturbance of cerebral activity	Bilateral supratentorial, cerebellum and right splenium of corpus callosum	12700	Viracor HHV-6 PCR Biofire® MEP	4700	No	HHV-6 PALE	Valacyclovir -> Foscarnet day 19 for HHV-6 viremia	Foscarnet 21d	Alive day 717, moderate cognitive recovery, some difficulty with concentration and writing 1 month after discharge but returned to normal function
12	43	Headache Nausea/Vomiting Exacerbated facial nerve palsy	ND	None	Detected <188 +++	Viracor HHV-6 PCR Biofire® MEP	Not Detected	Yes, only MEP positive	HHV-6 Aseptic Meningitis	Valacyclovir, Letermovir -> Foscarnet day 11 for 14d for HHV-6 viremia -> cidofovir day 25 for adenovirus viremia -> Valacyclovir	Foscarnet 15d	Died day 188 from *Staphylococcus aureus* bacteremia. Meningitis resolved but developed BK viuria and adenovirus viremia with seizures. Treated with cidofovir
13	185	Fever Headache Nausea/Vomiting	Diffuse disturbance of cerebral activity with epileptigenic potential	ND	5700	Viracor HHV-6 PCR Biofire® MEP	4200	No	HHV-6 PALE	Valacyclovir -> Valganciclovir day 174 for 4d for CMV reactivation -> Foscarnet day 178 for 14d for detected HHV-6 in CSF -> Valacyclovir	Foscarnet 14d	Died day 200 from *Streptococcus viridans* and *Enterococcus* bacteremia and sepsis. HHV-6 detected initially in CSF when taken prior to intrathecal chemotherapy before symptoms developed

ND = not done; RSV = respiratory syncytial virus; GVHD = graft versus host disease
*Peak plasma level within 7 days before or after dysfunction onset
++ Was 23900 26 days prior to presentation
+++ Was 27400 35 days prior to presentation

Findings and Outcomes in Non-HSCT Patients

Findings and Outcomes

Patient	Initial Presentation	Electroencephalogram (EEG)	MRI foci of T2/FLAIR/DWI hyperintensity	Plasma HHV-6 DNA copies/mL	CSF HHV-6 Test	CSF HHV-6 DNA Peak copies/mL	CSF HHV-6 Testing Discordant	Etiology	Prophylactic Antivirals	Antiviral Treatment	Outcome
14	Confusion Disorientation Hallucinations	Mild diffuse generalized slowing	Periventricular and subcortical white matter	Not Detected	Viracor HHV-6 PCR	Detected <81	N/A	Confirmed HHV-6 Encephalitis	Valacyclovir	None	Alive day 1028 after presentation, improved before testing resulted. Remains no evidence of malignant disease
15	Fever Seizure	Left temporal and frontal region dysfunction with epileptiform discharges	Right hippocampus/parahippocampal gyrus, right putamen, bilateral posterior medial thalami and right middle frontal gyrus	2100	Viracor HHV-6 PCR Biofire® MEP	Detected <81	Yes, only Viracor positive	HHV-6 Limbic Encephalitis	Valacyclovir	Foscarnet 7d	Died day 80 after presentation from *Enterobacter*, *Staphylococcus aureus*, rhinovirus, enterovirus pneumonia. After foscarnet, did not recover neurologically, repeat lumbar puncture for fever and CSF HHV-6 DNA up to 241 copies/mL, foscarnet restarted until death
16	Headache Neck Stiffness Nausea/Vomiting	ND	Left suprasellar cistern	Not Detected	Viracor HHV-6 PCR Biofire® MEP	Not Detected	Yes, only MEP positive	HHV-6 Aseptic Meningitis	Valacyclovir	Foscarnet 7d	Alive day 495 after presentation, symptoms improved after foscarnet. HHV-6 DNA in plasma rose to 32,100 copies/mL and repeat CSF check day 314 without symptoms with 1000 copies/mL of HHV-6 DNA. Underwent HSCT day 243 after presentation
17	Fever Seizure Left Eye Deviation	Mild diffuse generalized slowing	Bilateral cerebral hemisphere white matter	60900	Viracor HHV-6 PCR Biofire® MEP	Not Detected	Yes, only MEP positive	HHV-6 Limbic Encephalitis	Valacyclovir	Foscarnet 11d -> Ganciclovir/ Valganciclovir 15d -> Foscarnet 7d -> discontinued at discharge	Unknown, discharged to hospice day 47 after presentation due to progressive HLH refractory to ruxolitinib, rituximab, clofarabine
18	Fall Lethargy Mutism	Mild diffuse generalized slowing	Bilateral periventricular and deep white matter	24200	Viracor HHV-6 PCR	20600	N/A	Confirmed HHV-6 Encephalitis	N/A	Foscarnet 14d	Alive day 783 after presentation, moderate neurologic recovery but continued memory difficulty. Nivolumab stopped after HHV-6 episode and remains on clinical surveillance
19	Anterograde Amnesia Retrograde Amnesia Fever Headache Non-sensical Speech Hyponatremia	Mild diffuse generalized slowing	ND	7800	Viracor HHV-6 PCR	22300	N/A	Confirmed HHV-6 Encephalitis	N/A	Foscarnet 11d -> Valganiclovir for planned 28d	Unknown, discharged with significant neurologic recovery but lost to follow-up

ND = Not done; MEP = Meningitis Encephalits Panel

Conclusion: In addition to HSCT patients, HHV-6 reactivation leading to CNS disease also occurs in settings such as following adoptive T cell therapy or biologic immunotherapy. Significant diagnostic discordance exists between testing platforms.

Disclosures: Rodrigo Hasbun, MD, MPH, Biofire (Consultant)

52. A Nationwide Analysis of the Trends and Outcomes of Cryptococcal Meningitis in the United States

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Session: O-10. CNS Infections

Background: Cryptococcal Meningitis (CM) is the most common presentation of invasive cryptococcosis. Seen in patients with and without HIV, CM is associated with significant morbidity and mortality. We present findings from a nationwide analysis of patients admitted with CM in the United States between 2007 and 2016.

Methods: The national inpatient sample (NIS) database was queried for all inpatient visits for Cryptococcal Meningitis between January 2007 and December 2016. Logistic regression models were used to determine risk factors for mortality, prolonged admissions, and delays in obtaining an initial lumbar puncture.

Results: The number of admissions for CM decreased during the study interval, from 3590 in 2007 to 2830 in 2016. Mortality did not change over this period (9.9%), however length of stay and inpatient cost significantly increased ($P = 0.003$ and $P < 0.001$ respectively). The proportion of patients with HIV declined from 70.7% to 54.0% ($P < 0.001$). HIV patients had a lower risk of mortality (OR = 0.77, CI 0.68–0.86, $P < 0.001$), whereas Africa-American, Hispanic and Native American ethnicities had a significantly increased association with mortality. Delay in lumbar puncture beyond the first 24 hours was independently associated with mortality, with an OR of 1.55 (CI 1.31–1.82, $P < 0.001$). . Patients admitted on a weekend, those of African-American ethnicity, and those without a known history of HIV were more likely to have delays in obtaining an early LP.

Conclusion: Inpatient mortality for patients with CM continues to remain high, with an increasing proportion of patients without underlying HIV infection. We found significant deviations in management of CM from IDSA guidelines, and an independent association of delay in early lumbar puncture with worsened patient outcomes.

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

53. Incidence of Bloodstream Infections and Outcomes in Patients with Severe COVID-19 Pneumonia

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Session: O-11. COVID-19 Clinical Calls and Indicators 1

Background: Coronavirus disease 19 (COVID-19) leading to acute respiratory distress syndrome is associated with need for intensive care (IC), mechanical ventilation (MV), and prolonged recovery. These patients are thus predisposed to blood stream infections which can worsen outcomes. This risk may be aggravated by adjunctive therapies.

Methods: We reviewed the medical records of all adults admitted to Stony Brook University Hospital, NY, from March 1 to April 15, 2020 with severe COVID-19 pneumonia (requiring high-flow O_2). Patients who received MV or died within 24h were excluded. Patients were followed until death or hospital discharge. We reviewed positive blood cultures (PBC) for pathogenic microorganisms, and calculated the incidence of bacteremia, rates of infective endocarditis (IE), and impact on mortality. Microbes isolated only once and belonging to groups defined as commensal skin microbiota were labelled as contaminants. We also examined the impact of adjunctive therapies with immunosuppressive potential (steroids and tocilizumab), on bacteremia.

Results: A total of 469 patients with severe COVID-19 pneumonia were included (**Table 1**). Of these, 199 (42.4%) required IC and 172 (36.7%) MV. Median length of stay was 13 days (8–22) and 94 (20.0%) had PBC. Of these, 43 were considered true pathogens (bacteremia), with predominance of *E. faecalis* and *S. epidermidis,* and 51 were considered contaminants (**Table 2**). The incidence of bacteremia (43/469, 9.2%) was 5.1 per 1000 patient-days (95%CI 3.8–6.4). An echocardiogram was performed in 21 patients, 1 had an aortic valve vegetation (IE) by methicillin sensitive *S. aureus*. Bacteremia rates were nonsignificantly higher with steroids (5.9 vs 3.7 per 1000 patient-days; P=0.057). Use of tocilizumab was not associated with bacteremia (5.8 vs 4.8 per 1000 patient-days;

P=0.28). Mortality was nonsignificantly higher in patients with (15/43, 34.9%) vs. without (108/426, 25.4%) bacteremia (P=0.20). Length of stay was the strongest predictor of bacteremia, with risk increasing by 7% (95%CI 6%-9%, P< 0.001) per additional day.

Cohort Characteristics of Patients with Severe COVID-19 Pneumonia on High-Flow O2 (N= 469)

Table 1: Patient Characteristics (N=469)

Characteristic	Value
Age, years	61 (50-73)
Female	166 (35.4%)
White	249 (53.1%)
Black	31 (6.6%)
Asian	29 (6.2%)
Hispanic	158 (33.7%)
Body mass index, kg/m^2	29.3 (26.1, 33.9)
Duration of symptoms, days	7.0 (3.5, 9.0)
O_2 saturation, %	91 (87, 93)
Temperature, °C	38.1 (37.5, 39.0)
Hypertension	265 (56.5%)
Diabetes	155 (33.1%)
Coronary artery disease	71 (15.1%)
Atrial fibrillation	58 (12.4%)
Chronic lung disease	49 (10.4%)
Chronic kidney disease	48 (10.2%)
Congestive heart failure	45 (9.6%)
Asthma	36 (7.7%)
Immunocompromised	35 (7.5%)
Statins	180 (38.4%)
Angiotensin-converting enzyme inhibitors	74 (15.8%)
Angiotensin receptor blockers	73 (15.6%)
NT-proBNP pg/mL	205 (56, 991)
Troponin, ng/mL	0.01 (0.01, 0.01)
Creatine phosphokinase, IU/L	163 (80, 375)
Erythrocyte sedimentation rate, mm/h	54 (31, 80)
C-reactive protein, mg/dL	11.9 (6.4, 19.3)
D-Dimer, ng/mL	362 (241, 747)
Procalcitonin, ng/mL	0.21 (0.13, 0.49)
Ferritin, ng/ml	919 (489, 1534)
Lactate dehydrogenase, IU/L	407 (305, 538)
Interleukin-6, pg/mL	63 (30, 112)
Lymphocyte count, K/uL	0.8 (0.6, 1.1)
Creatinine, mg/dL	1.0 (0.8, 1.3)
Alanine transaminase, IU/L	34 (21, 55)
Aspartate aminotransferase, IU/L	46 (32, 70)
International normalized ratio	1.2 (1.1, 1.3)
Corrected QT interval on ECG, ms	437 (418, 460)

Values are N (%) or median (25th, 75th percentile)

All Microorganisms Isolated from Blood Cultures

Table 2. Distribution of Microorganisms in Positive Blood Cultures

True pathogens		Possible contaminants	
Enterococcus faecalis	8	*Coagulase negative Staphylococci*	
Moraxella osloensis	1	*Staphylococcus epidermidis*	40
Escherichia coli MDR	1	*Staphylococcus hominis*	19
Candida albicans	3	*Staphylococcus pettenkoferi*	3
Staphylococcus aureus (MSSA)	2	*Staphylococcus simulans*	1
Candida parapsilosis	2	*Staphylococcus warneri*	1
Candida tropicalis	1	*Staphylococcus caprae*	1
Klebsiella pneumoniae MDR	2	*Staphylococcus cohnii*	1
Staph lugdunensis	2	*Staphylococcus haemolyticus*	1
Strep pneumoniae	1	*Staphylococcus capitis*	3
Klebsiella (enterobacter) aerogenes	1	*Corynobacterium spp*	2
Pseudomonas oryzihabitans	1	*Dermabacter hominis*	1
Eggerthella lenta *	1	*Actinomyces oris*	1
Peptoniphilus harei *	1	*Bacillus spp, not anthracis*	2
*Bacteroides vulgatus group**	1	*Micrococcus*	1

* All isolated from an 81-year old female with intrabdominal abscess

Conclusion: The incidence of bacteremia was relatively low and IE was uncommon in this study of severe COVID-19 patients. Risk of bacteremia increased with longer hospital stay and with steroids use, but not with tocilizumab.

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

54. Microbiologic Characterization and Antibacterial Use in Hospitalized Adults with covid-19 Infection

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Session: O-11. COVID-19 Clinical Calls and Indicators 1

Background: Coronavirus disease 2019 (CoVID-19) admissions, oft complicated by an uncertain trajectory, lent to treatment influenced by supposition. Respiratory bacterial co-infection frequently was invoked. The purpose of this study was to determine the respiratory pathogen distribution and antibiotic prescribing patterns in hospitalized patients with CoVID-19.

Methods: Patients with a severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) ICD-10 code and/or positive polymerase chain reaction (PCR) hospitalized between March 1 and May 31, 2020 were included. Antibiotic utilization (patient days of therapy-pDOT) was collected for the institution during this period and two years prior. Respiratory microbiologic cultures were reviewed to examine the frequency of co-infection on presentation, categorized as within 3 calendar days from admission or afterward. The relationship of antibiotic utilization to positive cultures was also categorized.

Results: Of the 7,969 encounters, 829 were ICD-10 coded and/or confirmed SARS-CoV-2 PCR positive and 196 (23.6%) had positive respiratory cultures. 89.8% of patients had endotracheal samples, the rest were isolated from sputum or bronchoalveolar lavage (17.4% and 6.6%, respectively). Patients were more likely to isolate commensal respiratory flora (108 versus 78 patients within the first 3 days of presentation. Notable isolates such as *Staphylococcus aureus* and *Pseudomonas aeruginosa*, were more often isolated after 3 days of hospitalization. While the CoVID-19 average hospital census was only 14.7% of the total, antibiotic utilization, (pDOT/1000) was 2.3 times higher, 831.9 versus 368.3 across the institution. During similar periods in 2018 and 2019, days of therapy overall were lower. For CoVID-19 infected patients, the frequency of antibiotic initiation was 73.2%. The length of therapy was on average 8 days with a high rate of observed restarts.

Table 1: Patient characteristics for CoVID-19 infected patients admitted during March 1 to May 31, 2020

	N=829
Sex, male n (%)	410 (49.5)
Age, years (SD)	64.9 (17.9)
PCR positive, n (%)	819 (98.8)
Race	
• White	314 (37.9)
• Black	208 (25.1)
• Hispanic	151 (18.2)
• Asian/Pacific Islander	41 (4.9)
• Other	38 (4.6)
• Unknown	77 (9.3)
Hospital admission in last 90 days, n (%)	112 (13.5)
Comorbid conditions, n (%)	
• Hypertension	330 (39.8)
• Diabetes Mellitus	341 (41.1)
• Congestive Heart Failure	159 (19.2)
• Chronic Obstructive Pulmonary Disorder	84 (10.1)
• Obese	161 (19.4)
• End Stage Renal Disease	54 (6.5)
• HIV	2 (0.2)
Events after admission	
Length of stay, days median (IQR)	6 (2-13)
C diff PCR + during hospital stay	29 (3.5)
Inpatient mortality/discharge to hospice	171 (20.6)

Figure 1: Positive respiratory pathogen culture results for CoVID-19 encounters (March 1-May 31, 2020)