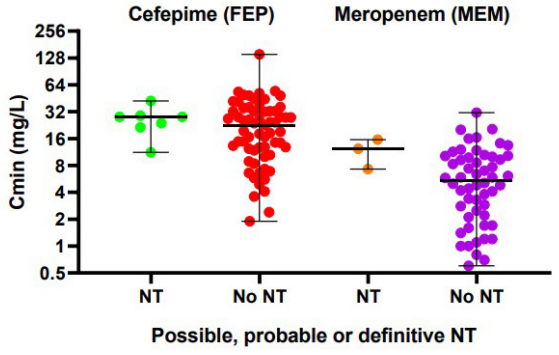
Figure 2. Patient Demographics and Treatment Characteristics

Patient Demographics	Cefepime N= 70 (%)	Meropenem N = 57 (%)
Sex (female)	26 (37.1%)	19 (33.3%)
Median Age (Range)	61 (23-87)	59 (18-85)
ICU Admission	42 (60.0%)	38 (66.6%)
ID Consult	47 (67.1%)	45 (78.9%)
Treatment Indication	Bacteremia: 20 (28.6%) Pneumonia: 28 (40.0%) Empiric: 5 (7.1%) Other: 17 (24.3%)	Bacteremia: 19 (33.3%) Pneumonia: 19 (33.3%) Empiric: 6 (10.5%) Other: 13 (22.8%)
Selected Comorbidities	**Cefepime N= 70 (%)**	**Meropenem N = 57 (%)**
Chronic Kidney Disease	15 (21.4%)	11 (19.3%)
End Stage Renal Disease (dialysis)	4 (5.7%)	3 (5.3%)
Seizure Disorder	5 (7.1%)	5 (8.8%)
Prior Adverse Neurologic Reaction to β-lactam	0 (0.0%)	3 (5.3%)
Stroke Hemorrhagic Ischemic	5 (7.1%) 2 (2.9%) 3 (4.3%)	1 (1.8%) 1 (1.8%) 0 (0.0%)
Alcohol Use Disorder	7 (10.0%)	3 (5.3%)
Treatment Characteristics	**Cefepime N= 70 (%)**	**Meropenem N = 57 (%)**
Median duration of treatment (Range)	8 (3 – 53)	11 (2 – 118)
Median time to PK sampling, hours (Range)	60.1 (24 - 293)	63.6 (13 - 325)
Trough concentration range	1.9 – 140.5	0.6 – 31.3
Median trough concentration CrCl > 60 mL/ min CrCl < 60 mL/ min	 12.7 mg/L 28.1 mg/L	 4.1 mg/L 9.3 mg/L
Sampled dosing regimen **2g q 8h** **2g q 12h** 1g q 6h 1g q 8h 1g q 12h Other	 **26 (37%)** **22 (31%)** 3 (4.3%) 8 (11.4%) 5 (7.1%) 6 (8.6%)	 **23 (40.4%)** **7 (12.3%)** 2 (3.5%) 15 (26.3%) 6 (10.5%) 4 (7.0%)
Receipt of prolonged infusion (defined as ≥3 hours)	57 (81.4%)	49 (85.9%)
Receipt of renal replacement therapy	6 (8.6%)	8 (14.0%)
Dose appropriate for renal function	**63 (90%)**	**51 (89.5%)**
Median # of Concomitant NT Rx/patient NT No NT	 **4** **4**	 **5** **6**

Figure 3. Adverse Neurologic Events and Attributable Neurotoxicity

Neurotoxicity	Cefepime N= 70 (%)	Meropenem N = 57 (%)
Any Adverse Neurologic Events	29 (41.4%)	30 (52.6%)
Attributable Rate of Neurotoxicity	**7 (10%)**	**3 (5.3%)**
NTAB review not indicated	42	27
Neurotoxicity Unlikely	21	27
Neurotoxicity Possible	3	2
Neurotoxicity Probable	**3**	**1**
Neurotoxicity Definitive	1	0
Description of Neurotoxicity Altered Mental Status Myoclonus	 6/7 (85.7%) 1/7 (14.3%)	 3/3 (100%) 0 (0.0%)

Figure 4. β-Lactam Exposures in Relationship to Attributable Neurotoxicity



Conclusion. Our study is the first to evaluate FEP NT prospectively and compare rates of NT to pts receiving MEM. We established criteria that were applied by a blinded NTAB. In doing so we found rates of NT to be lower than previously reported and not statistically different between FEP and MEM. Cmin values were highly variable and associated with numerically, but not statistically higher rates of NT for both agents. These findings serve as the basis for larger, multicenter studies and justify use of routine TDM to limit NT among high-risk pts.

Disclosures. **Brandon Smith, MD, PharmD**, **Shionogi** (Consultant, Advisor or Review Panel member) **Alexandra Urban, MD**, **Neuropace** (Consultant) **Ryan K. Shields, PharmD, MS**, **Shionogi** (Consultant, Research Grant or Support)

1101. Implementing a Beta-Lactam Therapeutic Drug Monitoring Program: Experience from a Large Academic Medical Center

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Session: P-62. PK/PD Studies

Background. Beta-lactams (BL) are the cornerstone of antimicrobial treatment for infections. Beta-lactam therapeutic drug monitoring (BL-TDM) optimizes drug concentrations to ensure maximal efficacy and minimal toxicity. The goals of this study were to describe the implementation process of a BL-TDM program and to further describe our experience using BL-TDM in clinical practice.

Methods. This was a retrospective review of adult patients with available BL-TDM between January 2016 and November 2019 at the University of Florida (UF) Health Shands Hospital. Total serum concentrations of BL were measured in the Infectious Diseases Pharmacokinetics Lab (IDPL) at UF, using a validated ultrahigh pressure liquid chromatography assay with triple quadrupole mass spectroscopy (LC-MS-MS). At our institution, TDM is available for 11 BLs and in-house assays are performed from Mon-Fri for most BLs.

Results. A total of 3,030 BL concentrations were obtained. An analysis was performed on the first BL-TDM encounter in 1,438 patients. The median age was 57 years (IQR, 41-69) and the median BMI was 27.5 kg/m^2 (IQR, 22.5-34.5). On the day of BL-TDM, the median serum creatinine was 0.83 (IQR, 0.59-1.30). Fifty-one percent of patients (n=735) were in an ICU at the time of BL-TDM with a median SOFA score of 6 (IQR, 3-9). BL-TDM was most frequently performed on cefepime (61%, n=882), piperacillin (15%, n=218), and meropenem (11%, n=151). The BL was administered as a continuous infusion in 211 (15%) patients. An interim analysis of 548 patients showed that BL-TDM was performed a median of 2 days (IQR, 1-4) from the start of BL therapy and resulted in a dosage adjustment in 26% (n=145).

Conclusion. BL-TDM was performed in older, non-obese patients with normal renal function. Over half of the evaluated patients were in an ICU at the time of TDM. This finding emphasizes the value of BL-TDM in the ICU setting because altered pharmacokinetics during critical illness has been linked to enhanced BL clearance. Interestingly, BL-TDM resulted in dosage adjustment in 1 in 4 patients who were receiving licensed BL dosing regimens, thus highlighting the role of TDM in dose individualization. BL-TDM was performed most commonly within the 72-hours of therapy initiation. Early BL-TDM has been shown to improve patient outcomes and should be promoted.

Disclosures. **Venugopalan Veena, PharmD**, **Melinta** (Other Financial or Material Support, Received a stipend for participation in a drug registry)**Merck** (Other Financial or Material Support, Received a stipend for participation in a drug registry) **Charles A. Peloquin, Pharm.D.**, Nothing to disclose

1102. Evaluation of Vancomycin Accumulation in Patients with Obesity

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Session: P-62. PK/PD Studies

Background. Current vancomycin guidelines recommend using actual body weight for dosing. However, in patients with obesity, this may result in lower initial vancomycin concentrations that can accumulate with continued doses due to differences in volume of distribution. The objective of this study is to evaluate the incidence of vancomycin accumulation in patients with obesity and identify potential factors associated with accumulation.

Methods. This is a single-center, retrospective, observational study at a tertiary academic medical center. Adult patients with a BMI ≥ 30 kg/m^2 and with ≥ 2 vancomycin serum trough concentrations within the same encounter in 2019 were screened. Patients were excluded if they were pregnant, had unstable renal function or severe renal impairment, received < 3 doses before a concentration was drawn, or had inconsistent dosing prior to a concentration draw. Linear kinetics were used to correct for differences in timing of concentration or dose changes. The major endpoint was the incidence of vancomycin accumulation, defined as a 20% increase in trough concentration between the first and any subsequent trough concentrations within the first 10 days of therapy. Minor endpoints included the percentage of supratherapeutic concentrations and the incidence of acute kidney injury (AKI). Descriptive statistics were used to evaluate endpoints and multivariable logistic regression was used to evaluate factors associated with accumulation.

Results. We screened 543 patients, and 162 were included in our analysis. The median age was 56.5 years (interquartile range [IQR] 43 - 65.3), and 62.3% were male. The

median weight was 112.7 kg (IQR 99.8 - 122.6) and the median BMI was 36.8 kg/m^2 (IQR 33.1 - 41). The median total daily vancomycin dose at initiation was 28.7 mg/kg/day (IQR 25.4 - 31.2). Vancomycin accumulation occurred in 99 patients (61.1%) within the first 10 days of therapy and AKI occurred in 21 patients (14.9%). No factors studied, including age, gender, obesity class, initial dose, SCr, or frequency were associated with accumulation.

Conclusion. Most patients with obesity experienced vancomycin accumulation within the first 10 days of therapy. Providers should be cautious when assessing a vancomycin concentration early in the treatment course.

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

1103. Minocycline (MIN) Pharmacodynamics (PD) against *Stenotrophomonas maltophilia* (STM) in a Neutropenic Murine Thigh Infection Model

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Session: P-62. PK/PD Studies

Background. Antibiotic treatment options for serious STM infections are limited. MIN displays in vitro activity against STM; however, limited data supports optimal dosing for STM. Herein, we employed the murine neutropenic thigh infection model to assess MIN PD against STM.

Methods. Four clinical STM isolates with MIN MICs 0.25 – 1 mg/L were included. Both thighs of neutropenic ICR mice were inoculated with bacterial suspensions of 10^7 colony forming units (CFU)/mL. Mice received uranyl nitrate on Day -3 to provide predictable renal impairment. Two hours after inoculation, MIN or control was administered subcutaneously. Pharmacokinetic (PK) studies of 2.5, 25, 50, and 100 mg/kg were conducted. Previously reported protein binding of 78.1% was used to define free exposure. Dose ranging studies were conducted on all STM to assess in vivo activity over a range of MIN exposures. MIN total daily doses (TDD) of 10, 20, and 50 mg/kg were fractionated q24h, q12h, and q6h against a single STM to determine the PD index best correlated with reductions in CFU/mL. Efficacy was measured in $\log_{10}$CFU/thigh at 24h compared with 0h controls. Composite CFU data were fitted to an E_{max} model to determine the *f*AUC/MIC exposure for stasis and 1 $\log_{10}$ reduction.

Results. MIN PK was linear up to 50 mg/kg and well described by a 1 compartment model with first order absorption and elimination. Mean PK parameters across the linear range were: Vd, 2.97 L/kg; K01, 10.62 1/h; and K10, 0.35 1/h. Mean ± SD bacterial burden at 0h across all isolates was 6.17±0.20 $\log_{10}$CFU/thigh. In 24h controls, bacterial growth was 7.90±0.85 $\log_{10}$CFU/thigh. A dose response was observed across all isolates using TDD of 2-300 mg/kg. PD indices correlated with CFU reductions as follows: *f*AUC/MIC (R^2=0.613), *f*Cmax/MIC (R^2=0.590), and %*f*T >MIC (R^2=0.504). The *f*AUC/MIC needed for stasis and 1 $\log_{10}$ reduction at 24h was 9.6 and 23.6, respectively.

Conclusion. These are the first data describing MIN PD against STM. Against these STM, MIN *f*AUC/MIC was the PD index best correlated with CFU reductions. The exposure thresholds defined in this study will be useful in designing optimal MIN dosing regimens for treating STM infections and re-assessment of the current susceptibility breakpoint.

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1104. Comparison of Antibiotic Sampling Techniques: Predicting Plasma Vancomycin Concentrations Using Volumetric Absorptive Microsampling (VAMS) from Capillary and Venous/Arterial Whole Blood

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Session: P-62. PK/PD Studies

Background. Therapeutic drug monitoring (TDM) is paramount to optimize the safety and efficacy of vancomycin (VAN). In children, TDM is challenged by difficulty in obtaining venous samples, impeding timely sampling. We assessed the ability of volumetric absorptive microsampling (VAMS) as a novel, whole blood sampling technique to predict plasma VAN concentrations in plasma.

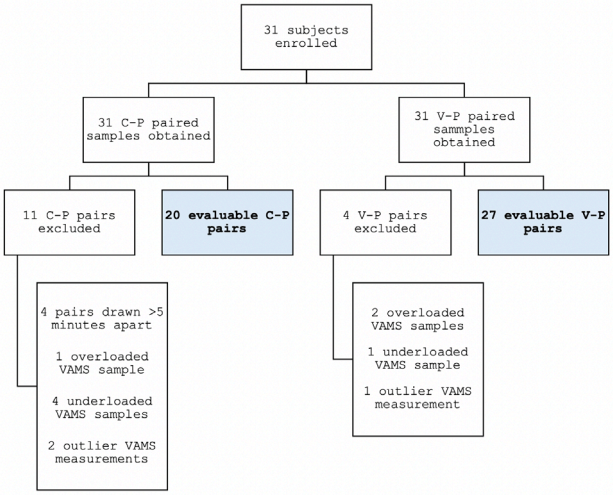
Methods. We conducted a prospective pilot study among critically ill children prescribed VAN for clinical care. Coincident with VAN TDM in plasma (P), we collected 20 µL of capillary whole blood (C) and venous/arterial whole blood (V) using VAMS. Paired VAMS-P samples drawn >5 mins apart and VAMS samples with over- or under-loaded filter tip on visual inspection were excluded. Plasma concentrations were measured via chemiluminescent immunoassay in the Chemistry Laboratory. VAMS C and V concentrations were measured using LC/MS in the Bioanalytic Core Laboratory. Plasma concentrations were predicted from whole blood VAMS with Passing-Bablok regression using 3 methods: 1) uncorrected VAMS measures, 2) hematocrit-corrected VAMS, and 3) lab-corrected VAMS (Figure 1). We then assessed bias, imprecision, and accuracy of plasma predictions from VAMS (C and V) as compared to coincident P concentrations for each technique (Figure 1).

Figure 1. Methods for relating whole blood vancomycin concentrations collected via VAMS to plasma concentrations and measure to evaluate predictive performance.

Method	Technique for predicting plasma from VAMS
Uncorrected VAMS	1. Predicted plasma calculated from Passing-Bablok regression of measured plasma on uncorrected VAMS
Hematocrit-corrected VAMS	1. Hct-corrected VAMS = VAMS / 1-(Hct / 100) 2. Predicted plasma calculated from Passing-Bablok regression of measured plasma on HCT-corrected VAMS
Lab-corrected VAMS	1. Lab-corrected VAMS = VAMS / 0.718[a] 2. Predicted plasma calculated from Passing-Bablok regression of measured plasma on lab-corrected VAMS
Predictive performance measure	**Equation**
Bias, calculated as median percentage predictive error (MPPE)	Median of ([VAMS] – [plasma] / [plasma]) x 100%
Imprecision, calculated as median absolute percentage predictive error (MAPE)	Median of (|[VAMS] – [plasma] / [plasma]|) x 100%
Accuracy, calculated as proportion of samples with MAPE within 20%	Number of pairs with MAPE <20% / evaluable pairs
[a] Correction factor derived from lab validation study in CHOP Bioanalytic Core.	

Results. Paired samples were collected from 31 enrolled subjects (Figure 2), with a median age of 3.3 years (range 0.1-17.9). Measured P concentrations ranged from 4.6 - 54.9 mg/L. 11 C samples (29%) and 3 V samples (10%) were excluded due to collection issues. Prediction results are shown in Figure 3. The 3 prediction techniques had similar performance characteristics, with each method displaying minimal bias (-0.4-2.0%) and reasonable imprecision (13.7-20.2%). The accuracy of prediction of P concentrations using VAMS was better for V than C samples.

Figure 2. Flow diagram from sample collection to evaluation.



Abbreviations: C-P, capillary VAMS-plasma; V-P, venous/arterial VAMS-plasma; VAMS, volumetric absorptive microsampling.

Figure 3. Performance of 3 techniques to predict plasma vancomycin concentrations using whole blood collected via VAMS.

Capillary VAMS-plasma (n = 20 paired samples)			
	Method 1 Uncorrected VAMS	**Method 2 Hematocrit-corrected VAMS**	**Method 3 Lab-corrected VAMS**
Regression equation[a]	P = 1.32 * C – 1.37	P = 0.90 * C – 0.34	P = 0.95*C – 1.38
Pearson correlation	.939	.926	.938
Bias[b]	0.3%	-0.4%	1.7%
Imprecision[c]	14.7%	20.2%	19.1%
Accuracy[d]	60%	50%	55%
Venous/Arterial VAMS-plasma (n = 27 paired samples)			
	Method 1 Uncorrected VAMS	**Method 2 Hematocrit-corrected VAMS**	**Method 3 Lab-corrected VAMS**
Regression equation[a]	P = 1.17 * V + 1.05	P = 0.79 * V + 1.36	P = 0.82 * V + 1.28
Pearson correlation	.941	.941	.941
Bias[b]	0.0%	0.0%	2.0%
Imprecision[c]	15.9%	13.7%	16.0%
Accuracy[d]	67%	70%	70%

[a] Equations derived from Passing-Bablok regression of plasma concentrations on predicted plasma concentrations from VAMS.
[b] Bias calculated as median percentage predictive error (MPPE).
[c] Imprecision calculated as median absolute percentage predictive error (MAPE).
[d] Accuracy defined as proportion of samples with MAPE <20%.
Abbreviations: C, capillary whole blood concentration via VAMS; P, plasma concentration; V, venous/arterial whole blood concentration via VAMS.