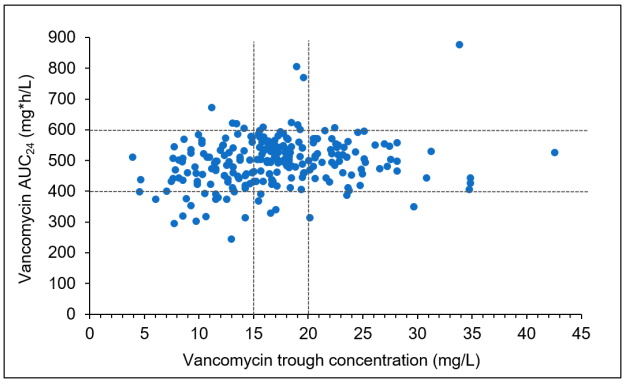
Session: P-59. PK/PD studies

Background. New vancomycin (VAN) guidelines have been published, with recommendations that dosing in patients (pts) with methicillin-resistant *S. aureus* (MRSA) infections be guided by VAN area under the concentration-time curve from 0 to 24 h to MIC ratio (AUC_{24}). The guidelines emphasize daily AUC_{24} values should be between 400-600 mg*h/L to maximize efficacy and minimize likelihood of acute kidney injury (AKI). Our physicians and clinical pharmacists currently use trough levels to manage outpatient VAN dosing with a general target of 15-20 mg/L. The current pharmacokinetic (PK) model provides an option for dosing using trough or calculated AUC_{24}.

Methods. We identified pts receiving VAN for *S. aureus* infections (default MIC of 1 mg/mL) from 2018-2020. We conducted a PK evaluation of pts with ≥1 trough level and compared it to model predicted AUC_{24}. Data collected included pt characteristics, VAN regimen, trough concentrations, PK evaluation, and AKI, defined as a 50% decrease in CrCL from baseline. A Bayesian PK model was used to calculate predicted dosing based upon trough concentrations (DoseMeRx®, Moorestown, NJ).

Results. 100 pts (mean age: 61±15 yrs, 62% male) from 6 OICs were included, with 82% treated for MRSA and 18% for methicillin-sensitive *S. aureus* infection. Mean initial dose of VAN in the OIC was 2.6±1 g/d in divided doses, most frequently every 12 hrs (68%). Median duration of outpatient therapy was 28 days [IQR, 16-36]. 69% received VAN in the hospital prior to the OIC. 100 pts had 239 trough levels with a corresponding PK analysis. Mean trough levels were 17.1±6.4 mg/L. Mean corresponding AUC_{24} was 498±98 mg*h/L. The relationship between trough and AUC_{24} is shown in Fig 1. 25 evaluations indicated an AUC_{24} < 400, with 8 (32%) resulting in a dose increase. 13 evaluations indicated AUC_{24} > 600, with 6 (46%) resulting in a subsequent dose decrease. 4 pts developed reversible AKI, all with AUC_{24} > 540. Use of AUC_{24} for dosing provided opportunities to adjust dosing in 38/239 evaluations (16%).

Figure 1. Relationship between Trough and AUC24 (n=239)



Conclusion: This PK evaluation showed a correlation between trough levels and AUC_{24} with opportunities for VAN dose adjustment using AUC_{24}, and to identify pts at risk for developing AKI. Dosing with AUC_{24} is particularly useful in the outpatient setting in which true trough evaluations can be difficult to obtain.

Disclosures. **Brian S. Metzger, MD, MPH**, **Allergan** (Speaker's Bureau)**Cumberland** (Speaker's Bureau)**Melinta** (Speaker's Bureau) **Richard L. Hengel, MD**, **Merck & Co.** (Other Financial or Material Support, Grant Steering Committee Member) **Kimberly A. Couch, PharmD, MA, FIDSA, FASHP**, **Allergan** (Speaker's Bureau) **Lucinda J. Van Anglen, PharmD**, **Merck & Co.** (Grant/Research Support)

1328. Vancomycin exposure and utilization following implementation of an AUC-guided monitoring guideline in children

Ruquaya Quraishi, PharmD[1]; Negar Ashouri, MD[1]; Richard Beuttler, PsyD, MS[2]; Martin T. Tran, PharmD[3]; [1]CHOC Children's, Orange, California; [2]Chapman University, Irvine, California; [3]CHOC Children's Hospital, Orange, California

Session: P-59. PK/PD studies

Background. The 2009 guideline for vancomycin (VAN) monitoring recommended trough (TR) of 15-20 mg/L to correlate with AUC/MIC ≥ 400. Studies have suggested attainment of target AUC/MIC ratio with TR 7-11 mg/L in most children. Prior to 2018, TR 15-20 mg/L was the primary target for VAN therapeutic monitoring at CHOC Children's. Beginning in 2018, a clinical guideline was implemented which recommend targeting AUC/MIC of 400-600 or TR of 7-15 mg/L. Our objectives are to evaluate differences in VAN utilization, exposure, nephrotoxicity and cost savings between pre (Pre-guideline, pG) and post implementation (Post-guideline, PG) of a VAN monitoring guideline at CHOC Children's.

Methods. Retrospective chart review of patients prescribed VAN between Jan 2016 – Jun 2017 (pG) and Jan 2018 – Jun 2019 (PG). Primary objectives evaluated differences in pharmacokinetic (PK), AUC and rate of nephrotoxicity in patients 3 months to < 18 years who received VAN ≥ 24 hour with ≥ 1 TR. Secondary objectives assessed differences in overall VAN utilization following guideline implementation.

Results. Seventy patients were included in the PK analysis, 35 in pG and 35 in the PG group. Median age, weight, gender, baseline creatinine, concurrent nephrotoxic agents were similar. There were no differences in duration of therapy or starting doses (mg/kg/day) between the two groups. The highest daily dose (mg/kg) and AUC (mg*h/L) attained was significantly higher in pG compared to PG group (74.9 vs. 59.9, p = 0.002 and 647 vs. 469, p < 0.0001), respectively. Changes in AUC from the initial regimen to the highest adjusted regimen was also higher in pG group (532 vs. 647, p = 0.0008) while there was no difference in PG group (459 vs. 469, p = 0.647). More patients experienced nephrotoxicity in pG compared to PG (11.4% (4/35) vs. 0 (0/35), p = 0.039). Logistic regression analysis identified AUC 800-900 as a significant risk for nephrotoxicity. Compared to pG, PG resulted in a net reduction in VAN utilization of 19.7 DOT per 1000 patient days, savings of $100,150 and 738 fewer levels drawn.

Conclusion. In line with the 2020 consensus guideline recommendation for AUC-based VAN monitoring, our study found AUC-guided VAN monitoring in children resulted in less exposure, utilization, and nephrotoxicity.

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

1329. Vancomycin Therapeutic Drug Monitoring: How to hit the Curve

Michael Vala, n/a[1]; Ryan Chapin, PharmD[1]; Nicholas J. Mercuro, PharmD[1]; Christopher McCoy, PharmD, BCIDP[1]; [1]Beth Israel Deaconess Medical Center, Boston, Massachusetts

Session: P-59. PK/PD studies

Background. For the management of serious *S. aureus* infections, area-under-the curve to minimum inhibitory concentration (AUC/MIC) applied dosing is recommended as the preferred method to goal trough-based monitoring. This pharmacodynamic dosing demonstrates efficacy with optimized exposure and decreased nephrotoxicity. While two levels are ideal for estimating AUC/MIC mathematically, the logistics and costs may outweigh the benefits of this approach. This study will compare AUC/MIC estimates using two single-level pharmacokinetic calculators (C2 and C3) and a Bayesian dosing calculator (C1) versus steady-state troughs.

Methods. A retrospective cohort study using a data repository to identify patients from 2019 included patients on intravenous vancomycin for greater than 48 hours with a steady state trough. Patients on dialysis or with unstable renal function were excluded. Vancomycin AUC/MIC and peak levels were estimated using C1, C2, and C3. The objective was to assess correlation of trough levels of 10-20mcg/ml to an AUC/MIC of 400-600 mg·h/L. Secondary outcomes included examining the difference in R-squared values of the three calculators, and the percentage of patients with dose adjustments.

Results. 55 patients met inclusion criteria. Of 55 troughs, 78% were 10-20mcg/ml and 5% were >20mcg/ml. On average, the three calculators found 85% of all initial troughs and 93% of therapeutic troughs correlated to an AUC >400. However, less than half of therapeutic troughs corresponded to an AUC of 400-600 mg·h/L. Nearly 70% of patients had one or more dose adjustments often for unclear reasons as the AUC/MIC target of 400-600 mg·h/L was met in 29-63% of initial adjustments. The three different calculators showed noticeable variability in calculating AUC/MIC.

Figure 1

Figure 1

Baseline Characteristics: (N=55)

Characteristic	N (%)
Age – yr	
Mean	62.9
Median	64
Range	28-92
Male sex	27 (49)
CrCl-mL/min	
25th Percentile	76.64
Median	33
75th Percentile	114
Weight (kg)	
25th Percentile	67.09
Median	81.85
75th Percentile	96.63
IBW:ABW ratio	
>1.5	11 (20)
1-1.5	34 (62)
<1	9 (16)

Figure 2

Figure 2

True Trough (mcg/ml)	
0-5	0
5-10	9 (16)
10-15	24 (44)
15-20	19 (35)
20-25	3 (5)
Trough Timing	
>3 hours early	6 (11)
2-3 hours early	5 (9)
1-2 hours early	17 (31)
<1 hour early	17 (31)
<1 hour late	5 (9)
1-2 hours late	2 (4)
2-3 hours late	3 (5)
Number of dose adjustments	
0	*17 (31)*
1	31 (56)
2	3 (5)
3	1 (2)
4	3 (5)
One or more	**38 (69)**
Number of dose adjustments when AUC/MIC target of 400-600 mg-h/L had already been met	
C1	*11 (29)*
C2	15 39)
C3	24 (63)

Figure 3

Figure 3

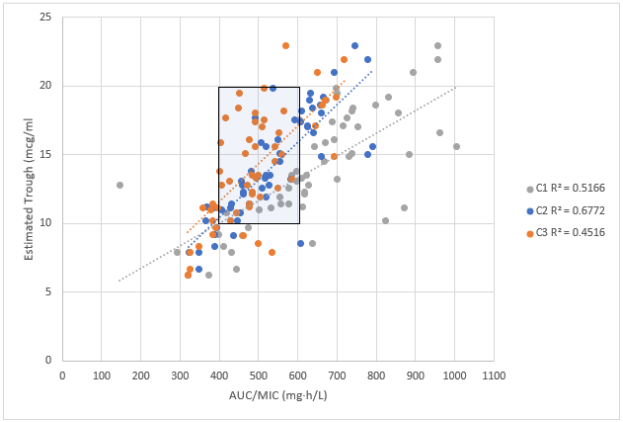
	Subtherapeutic trough			Therapeutic trough			Therapeutic trough			Supratherapeutic trough		
	(<10 mcg/mL)			(10-15 mcg/mL)			(15-20 mcg/mL)			(>20 mcg/mL)		
	N=9			N=24			N=19			N=3		
AUC/MIC Estimate (mg·h/L)*	<400	400-600	>600	<400	400-600	>600	<400	400-600	>600	<400	400-600	>600
Calculator												
C1	3 (33)	5 (56)	1 (11)	1 (4)	11 (46)	12 (50)	0	0	19 (100)	0	0	3 (100)
C2	7 (78)	1 (11)	1 (11)	3 (13)	20 (83)	1 (4)	0	6 (32)	13 (68)	0	0	3 (100)
C3	6 (67)	3 (33)	0	5 (21)	18 (75)	1 (4)	0	15 (79)	4(21)	0	1(33)	2 (66)

*A vancomycin MIC of 1 mcg/mL was assumed for all calculations. No patients had a culture growing *Staphylococcus aureus* with a vancomycin MIC >1 mcg/mL

Conclusion. A weak relationship between AUC/MIC and steady state troughs was found. Excess vancomycin exposure was demonstrated in 39% of therapeutic troughs. Over 25% of dose adjustments were deemed unnecessary. Utilizing AUC/MIC estimates for vancomycin may limit excess exposure while reducing the overall number of drug levels. Selecting a single-level calculator is problematic with the high degree of variation between calculators.

Figure 4

Figure 4



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

1330. Development of a Pediatric Emergency Department (ED) Uropathogen Antibiogram and Empiric Urinary Tract Infection (UTI) Treatment Algorithm

Akshith M. Dass, PharmD[1]; Eleanor K. Broadbent, PharmD[2]; Caitlin Schanz, n/a[3]; Nicole Louden, PharmD[4]; Lizbeth Hansen, PharmD[5]; Elizabeth B. Hirsch, PharmD[6]; Kimberly D. Boeser, PharmD, MPH, BCIDP[1]; Laura E. Norton, MD, MS[7]; [1]M Health Fairview, University of Minnesota Medical Center, Minneapolis, Minnesota; [2]M Health Fairview, University of Minnesota Medical Center; Boston Medical Center, Brookline, Massachusetts; [3]University of Minnesota Medical Center, Randolph, Minnesota; [4]M Health Fairview University of Minnesota Masonic Children's Hospital, Minneapolis, Minnesota; [5]M Health Fairview, Minneapolis, Minnesota; [6]University of Minnesota, Minneapolis, MN; [7]M Health Fairview, University of Minnesota Masonic Children's Hospital, MINNEAPOLIS, Minnesota

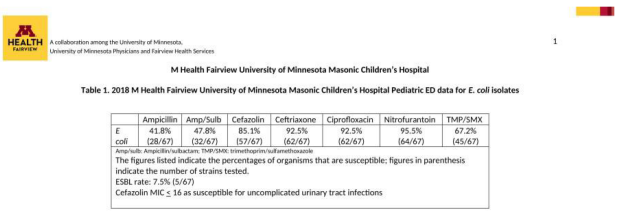
Session: P-60. Pediatric Antimicrobial Stewardship (inpatient/outpatient pediatric focused)

Background. Antimicrobial Stewardship efforts in adult ED settings lead to improved patient outcomes and fewer adverse events. However, there are limited data on incorporation of multiple interventions to assist with empiric and definitive antibiotic therapy selection, particularly in the pediatric ED setting. The purpose of this project was to create an antibiogram and empiric UTI treatment algorithm for use in a pediatric ED.

Methods. This is a multi-phase program implementation in a pediatric ED. Patients aged 2 months -18 years presenting to the ED between January to December 2018 with an ICD10 code for cystitis or pyelonephritis and collection of urine culture were included. Patients were excluded if they were admitted to an inpatient unit or they had a polymicrobial urine culture result. The antibiogram was prepared by including the first isolate of a species from each patient in the given time frame using Clinical and Laboratory Standards Institute recommendations.

Results. A total of 145 unique patients with 160 ED encounters were included in phase I of the project. Median patient age was 5 years (IQR 1.4-8). Discharge diagnosis for 75% of the 160 ED encounters was pyelonephritis. Urogenital flora was cultured from 19.4% of cultures and 21.2% of cultures were without any growth. The most common pathogen isolated was *E. coli* (39.4%). For ages 2 months – 18 years, susceptibility of urinary *E. coli* isolates was 95.5% for nitrofurantoin, 92.5% each for ceftriaxone and ciprofloxacin, and 85.1% for cefazolin. Cefdinir and cephalexin were the empiric antibiotics prescribed on discharge 76.3% of the time. After consideration of factors such as antimicrobial stewardship and spectrum of activity, cephalexin was chosen as the treatment of choice for the 2 months – 11 years age group. For children ≥ 12 years, nitrofurantoin was selected as preferred treatment for uncomplicated cystitis while cephalexin was selected as preferred treatment for pyelonephritis.

M Health Fairview University of Minnesota Masonic Childrens ED 2018 E coli isolate antibiogram


A collaboration among the University of Minnesota, University of Minnesota Physicians and Fairview Health Services

1

M Health Fairview University of Minnesota Masonic Children's Hospital

Table 1. 2018 M Health Fairview University of Minnesota Masonic Children's Hospital Pediatric ED data for *E. coli* isolates

	Ampicillin	Amp/Sulb	Cefazolin	Ceftriaxone	Ciprofloxacin	Nitrofurantoin	TMP/SMX
E coli	41.8% (28/67)	47.8% (32/67)	85.1% (57/67)	92.5% (62/67)	92.5% (62/67)	95.5% (64/67)	67.2% (45/67)

Amp/sulb: Ampicillin/sulbactam; TMP/SMX: trimethoprim/sulfamethoxazole

The figures listed indicate the percentages of organisms that are susceptible; figures in parenthesis indicate the number of strains tested.

ESBL rate: 7.5% (5/67)

Cefazolin MIC ≤ 16 as susceptible for uncomplicated urinary tract infections

Conclusion: An empiric UTI treatment algorithm incorporating local antimicrobial susceptibility pattern alongside recommendations from national organizations was created. Phase II of the project will evaluate the implementation of the algorithm to determine its impact on readmission rates and antibiotic/pathogen mismatch.

Disclosures. **Elizabeth B. Hirsch, PharmD**, **Merck** (Grant/Research Support)**Nabriva Therapeutics** (Advisor or Review Panel member)

1331. Reducing Inpatient Antimicrobial Treatment Duration for Febrile Infants through Implementation of Rapid Diagnostic Testing and Clinical Risk Definition

Guliz Erdem, MD[1]; Joshua Watson, MD[2]; Don Buckingham, N/a[3]; Octavio Ramilo, MD[1]; William J. Barson, MD[4]; [1]Nationwide Children's Hospital, columbus, Ohio; [2]Nationwide Children's Hospital and The Ohio State University College of Medicine, Columbus, OH; [3]NCH, Columbus, Ohio; [4]Ohio State University College of Medicine and Public Health and Nationwide Children's Hospital, Columbus, Ohio

Session: P-60. Pediatric Antimicrobial Stewardship (inpatient/outpatient pediatric focused)

Background. The management approach to febrile infants remain challenging. Despite new advances in rapid diagnostic testing, febrile infants with a viral infection could receive prolonged antimicrobial treatment due to concerns for co-existing serious bacterial infection (SBI). We sought to decrease the duration of antibiotic treatment in febrile infants less than 8 weeks of age hospitalized on inpatient infectious disease service following sepsis evaluation, who have enterovirus, parechovirus, or respiratory viruses detected, from average 30 hours to 24 hours and sustain for six months.

Figure 1. Antibiotic Treatment Duration of Infants Underfoing Evaluation for Sepsis