Goodbye Troughs, Hello AUC?
A new vancomycin dosing paradigm

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Objectives

• Describe the pharmacokinetic and pharmacodynamic properties of vancomycin
• Review recent literature on vancomycin dosing and clinical outcomes in patients
• Given a patient case, apply pharmacokinetic principles to dose individualization in patients prescribed vancomycin therapy targeting AUC
Have your calculators ready!
VANCOMYCIN

History Lesson

• Missionary from Borneo sent a sample of dirt to a friend at Eli Lilly
• An organism from the dirt sample was isolated that was active against most gram positive organisms
• Named vancomycin from the word ‘vanquish’
• Required significant purification before human clinical trials due to its brown color – dubbed “Mississippi Mud” by scientists at Eli Lilly
• FDA approved in 1958

Levine DP. Clin Infect Dis 2006;42:S5
REASSESSMENTS OF VANCOMYCIN—A POTENTIALLY USEFUL ANTIBIOTIC

Based on Symposia Held in
Atlanta, Georgia, November 1–2, 1978;
San Francisco, California, November 16–17, 1978; and

Guest Editors: Robert I. Wise and Mitchell Kory
### VANCOMYCIN

#### Definitions

<table>
<thead>
<tr>
<th></th>
<th>MIC (mcg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vancomycin Susceptible <em>S. aureus</em></td>
<td>≤ 2*</td>
</tr>
<tr>
<td>Heteroresistant Vancomycin Intermediate <em>S. aureus</em> (hVISA)</td>
<td>1 - 4</td>
</tr>
<tr>
<td>Vancomycin Intermediate <em>S. aureus</em> (VISA)</td>
<td>4 - 8</td>
</tr>
<tr>
<td>Vancomycin Resistant <em>S. aureus</em> (VRSA)</td>
<td>≥ 16</td>
</tr>
</tbody>
</table>

*decreased from ≤ 4 in 2007

- hVISA – Contain subpopulation of cells that exhibit higher MIC values when plated onto agar plates with vancomycin
  - Difficult to detect in the laboratory
  - Prevalence likely underreported
  - In vitro data demonstrates relationship between low vancomycin concentrations and development of hVISA

VANCOMYCIN
Pharmacokinetics & Pharmacodynamics

• Large glycopeptide (MW ~1450 Da)
• A – Oral vancomycin not absorbed in GI tract
• D – Widely distributed in body tissue and fluid
  – ~50% protein bound
  – Low CSF penetration – increased with higher doses and inflamed meninges
  – Relatively poor, highly variable lung tissue penetration
• M & E – Minimal metabolism, primarily excreted unchanged in the urine via glomerular filtration
  – Half-life in adults without renal insufficiency 6-8 hours

VANCOMYCIN
Pharmacokinetics & Pharmacodynamics

Bactericidal, time-dependent action
Kills bacteria most effectively when drug concentrations are 3-5x the MIC for the bacteria
2009 Vancomycin Therapeutic Guidelines

• Dosage
  – Initial doses should be calculated on total body weight
  – Loading doses (25-30 mg/kg) can be considered

• Concentrations
  – An AUC/MIC ratio of $\geq 400$ is a target to achieve clinical effectiveness with vancomycin
  – Trough serum concentrations are the most practical/accurate method of monitoring
  – Troughs should be obtained before the 4th dose
  – Troughs should always be maintained $>10$ mg/L to avoid development of resistance

Rybak MJ. AJHP 2009;66:82
2009 Vancomycin Therapeutic Guidelines

• Concentrations (cont’d)
  – Goal trough 15-20 mg/L recommended for bacteremia, endocarditis, osteomyelitis, meningitis, and pneumonia

• Toxicity
  – Vancomycin-induced nephrotoxicity if multiple (>3 consecutive) high serum creatinine concentrations (increase of 0.5 mg/dL or >50% from baseline) are documented after several days of vancomycin in the absence of alternative explanation

Rybak MJ. AJHP 2009;66:82
Origin of the AUC goal

• Retrospective evaluation of all patients with *S. aureus* lower respiratory tract infection at a 300-bed teaching hospital over one year

• An AUC/MIC value of $\geq 400$ was associated with a successful outcome, whereas an AUC/MIC $<400$ was associated with a lower eradication rate and higher mortality rate ($P = 0.005$)

• AUC calculation was done with a simple formula based on daily vancomycin dose and estimated renal function

VANCOMYCIN CHALLENGES

We can’t get there from here.

• Series of Monte Carlo simulations performed for vancomycin regimens ranging from 0.5 g IV every 12 hours to 2g IV every 12 hours

• Probability of achieving an AUC/MIC ratio ≥400 for each dosing regimen was calculated for MICs ranging from 0.5 to 2 mg/L

VANCOMYCIN CHALLENGES

We can’t get there from here.

Probability of achieving AUC/MIC ratio ≥400 for vancomycin with $C_{\text{min}}$ values 15-20 mg/L

We can’t get there from here.

Table 4. Overall Probability of Achieving an AUC/MIC Ratio of 400, by MIC Value, Versus the Probability of a Nephrotoxic Event

<table>
<thead>
<tr>
<th>MIC value</th>
<th>AUC/MIC ratio ≥400 (%)</th>
<th>Nephrotoxic event (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0.5mg/L</td>
<td>1.0mg/L</td>
</tr>
<tr>
<td>500 mg IV Q12H</td>
<td>57</td>
<td>15</td>
</tr>
<tr>
<td>1000 mg IV Q12H</td>
<td>90</td>
<td>57</td>
</tr>
<tr>
<td>1500 mg IV Q12H</td>
<td>97</td>
<td>79</td>
</tr>
<tr>
<td>2000 mg IV Q12H</td>
<td>98</td>
<td>90</td>
</tr>
</tbody>
</table>

VANCOMYCIN CHALLENGES

We can’t get there from here.

- High degree of variability between the AUC\textsubscript{72-96h} and C\textsubscript{min} at 96h values
  - AUC was highly dependent on daily dose and CrCL
- C\textsubscript{min} of 15-20 mg/L do not consistently result in AUC/MIC $\geq 400$ when MIC is 2 mg/L
- Conversely, troughs of 15-20 mg/L not always needed to achieve AUC/MIC $\geq 400$ when MIC is 1 mg/L

VANCOMYCIN CHALLENGES

Targeting Higher Troughs

• Retrospective, single-center study of clinical outcomes and costs pre- and post-aggressive dosing implementation

• Patients in the pre-period group had significantly lower success rates with vancomycin than the post-period group (45% vs 60%; p = 0.034)

• Patients in the pre-period group had lower rates of nephrotoxicity (15% vs 18%; p = 0.85)

• Total hospital costs not significantly different between the groups, but drug and monitoring costs higher in the post-period

VANCOMYCIN CHALLENGES

Targeting Higher Troughs

• Single center retrospective analysis of 320 patients with MRSA bacteremia
• Troughs of 15-20 mg/L associated with significantly lower failure rates compared to troughs of <10 mg/L or 10-14.9 mg/L

Vancomycin nephrotoxicity

- **Mechanism:** can be at least partially attributable to an increased production of reactive oxygen species and oxidative stress on proximal renal tubule

- **Risk factors**
  - high trough vancomycin level (especially >20 mg/L) or doses (>4 g/day)
  - AUC/MIC >600 (especially >1300)
  - concomitant treatment with nephrotoxic agents
  - prolonged therapy (more than 7 days)
  - admittance to an intensive care unit
  - History of kidney disease
  - Total body weight >101.4 kg

Vancomycin nephrotoxicity

- More-intensive vancomycin dosing regimens = increase in vancomycin-induced nephrotoxicity
- Troughs \( \geq 15 \) associated with increased odds of nephrotoxicity relative to troughs <15 (OR 2.67; 95% CI, 1.95-3.65)
  - Risk persists after adjustment for covariates known to independently increase the risk of a nephrotoxicity event

Historically, trough values drawn as surrogate markers for AUC. Majority of studies shown no link between clinical success and vancomycin trough levels.
VANCOMYCIN CHALLENGES

Adequacy of Troughs

• Pharmacokinetic model of adult patients with normal renal function and therapeutic AUC of $\geq 400$

• For an organism with a vancomycin MIC is 1 mg/L, approximately 60% of patients were expected to have a trough <15 mg/L

• Targeting a minimum of 15 mg/L can result in unnecessarily high doses therefore increasing risk of toxicity

Vancomycin dosing strategies

• Nomograms

• Pharmacokinetic calculations using population pharmacokinetic parameters targeting goal troughs
  – Current guideline recommended method

• Pharmacokinetic calculations using population pharmacokinetic parameters targeting goal AUC/MIC
  – Future guideline recommended method
AUC Based Dosing Strategy

• Exclusions to the calculations that follow
  – Patients with (suspected) meningitis or CNS infection
  – Surgical prophylaxis
  – Skin and soft tissue infection
  – Patients receiving renal replacement therapy (e.g., intermittent hemodialysis, continuous renal replacement therapy, peritoneal dialysis)
Patient Case

- 58 year old female with a history of diabetes and COPD ordered vancomycin (pharmacy to dose per protocol) and piperacillin/tazobactam in the ICU for hospital acquired pneumonia
- Weight = 56 kg, height 164 cm, BP 85/60, HR 96, RR 22, Tmax 39.1°C

What should the patient’s loading dose be?
A. 1000 mg
B. 1500 mg
C. 2000 mg
D. She doesn’t qualify for a loading dose
Determine if a loading dose is needed

• Loading dose is designed to shorten the time to therapeutic trough concentrations and should be used for critically ill patients and for severe infections

• Consider a loading dose for the treatment of suspected or documented meningitis, and in patients meeting 2 or more of the following:
  – Temp >38°C or <36°C
  – HR >90 beats per min
  – RR >20 breaths per minute
  – WBC >12,000 mm³, <4,000 mm³, or >10% bands
  – Hypotension (SBP <90 mmHg, MAP <60 mmHg, or requiring vasopressors)
Loading Dose Calculation

• Based on PK principles using the following equation:
  – LD = Cmax desired x Volume of distribution
• For simplicity, a weight based calculation is advocated
  – LD = 25-30 mg/kg assuming normal renal function and volume of distribution (~0.65 L/kg) to target a Cmax of 35-45 mcg/mL
• LDs should be calculated based on total body weight but due to safety concerns and lack of literature supporting higher doses, should be capped at 2,500 mg (some institutions choose to cap at 2,000 mg)
• In patients with decreased and/or fluctuating renal function, consider lower LD of 20 mg/kg
Patient Case

- 58 year old female with a history of diabetes and COPD ordered vancomycin (pharmacy to dose per protocol) and piperacillin/tazobactam for hospital acquired pneumonia
- Weight = 56 kg, height 164 cm, BP 85/60, HR 96, RR 22, Tmax 39.1°C

What should the patient’s loading dose be?
A. 1000 mg
B. 1500 mg 25 mg/kg
C. 2000 mg
D. She doesn’t qualify for a loading dose

This patient’s criteria for a loading dose:
- Temp >38°C
- RR > 20 bpm
- HR >90
- SBP <90
Maintenance Dose Calculations

Estimate Volume of Distribution (Vd) based on total body weight:

<table>
<thead>
<tr>
<th>Population</th>
<th>Vd (L/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>0.7</td>
</tr>
<tr>
<td>Dehydrated</td>
<td>0.5-0.6</td>
</tr>
<tr>
<td>Obese</td>
<td>0.4-0.6</td>
</tr>
<tr>
<td>Overhydrated</td>
<td>0.7-0.85</td>
</tr>
<tr>
<td>Septic Shock ICU Trauma ESRD</td>
<td>0.7-0.75</td>
</tr>
</tbody>
</table>
58 year old female with a history of diabetes and COPD ordered vancomycin (pharmacy to dose per protocol) and piperacillin/tazobactam in the ICU for hospital acquired pneumonia

Weight = 56 kg, height 164 cm, BP 85/60, HR 96, RR 22, Tmax 39.1°C

What is the patient’s volume of distribution (Vd)?

Vd = 0.7 x 56 kg = 39.2 L
Maintenance Dose Calculations

C-G Equation to estimate renal function:

\[
\text{CrCl}_{(\text{ml/min})} = \frac{(140-\text{age})(\text{ABW})}{(72)(\text{Scr})}
\]

Multiply by 0.85 (Female)

Estimate Elimination Rate Constant \((k_e)\)

Ducharme Equation: \(k_e = 0.0016 \times \text{CrCl}\)

- Most aggressive
- Consider in younger, previously healthy patients without significant comorbidities

Matzke Equation: \(k_e = (0.00083 \times \text{CrCl}) + 0.0044\)

- Least aggressive
- Consider in older patients and/or patients with significant comorbidities (diabetes, CKD, etc)

58 year old female with a history of diabetes and COPD ordered vancomycin (pharmacy to dose per protocol) and piperacillin/tazobactam in the ICU for hospital acquired pneumonia

Weight = 56 kg, height 164 cm, BP 85/60, HR 96, RR 22, Tmax 39.1°C

Calculate the patient’s CrCl and Ke

CrCl: 77.4 mL/min

\[ k_e = (0.00083 \times \text{CrCl}) + 0.0044 = (0.00083 \times 77.4 \text{ mL/min}) + 0.0044 = 0.069 \text{ hr}^{-1} \]
Maintenance Dose Calculation

Estimate Half-life ($t_{1/2}$)

$$t_{1/2} = 0.693/k_e$$

1. Calculate a Dosing Interval

$$T = \frac{\ln\left(\frac{\text{Peak}}{\text{Trough}}\right)}{k_e} + t$$

$T = \text{tau} = \text{dosing interval}$

$t = \text{infusion time}$
Patient Case

• 58 year old female with a history of diabetes and COPD ordered vancomycin (pharmacy to dose per protocol) and piperacillin/tazobactam in the ICU for hospital acquired pneumonia

• Weight = 56 kg, height 164 cm, BP 85/60, HR 96, RR 22, Tmax 39.1°C
• Vd = 39.2 L
• CrCl: 77.4 mL/min
• \( k_e = (0.00083 \times CrCl) + 0.0044 = (0.00083 \times 77.4 \text{ mL/min}) + 0.0044 = 0.069 \text{ hr}^{-1} \)

Calculate the patient’s estimated half-life and dosing interval

\( T_{1/2} = 10 \text{ hours} \)
Dosing interval = \( \ln (\text{desired peak/desired trough})/ke + t = \ln (35/17)/0.069 + 1 = 11.5 \text{ hours} \)
\( \rightarrow \) round to 12 hours
Maintenance Dose Equations – when targeting AUC

• Calculate dose to target $AUC_{24}$ between 400 to 600 with maintaining a trough of 10 to 20 mcg/ml

• Estimate vancomycin clearance

\[
Cl_{van} = Ke \times Vd
\]

• Estimate total daily dose required (in mg) and determine appropriate maintenance dose (round to nearest 250 mg)

\[
TDD = Cl_{van} \times \text{Desired } AUC_{24} \\
MD = \frac{TDD}{(24/\tau U)}
\]
Patient Case

- Vd = 39.2 L
- CrCl: 77.4 mL/min
- ke = 0.069 hr⁻¹
- T₁/₂ = 10 hours
- Dosing interval = 12 hours

Calculate the patient’s vancomycin clearance, total daily dose, and maintenance dose

Vancomycin clearance = 0.69 hr⁻¹ x 39.2 L = 2.7 L/hr
Total Daily Dose = 2.7 L/hr x 500 = 1352.4 mg
Maintenance Dose = 1352.4 mg/(24/12) = 676.2 mg → round to 750 mg
Maintenance Dose Equations – when targeting AUC

- Predict steady state $C_{\text{max}}$ and $C_{\text{min}}$

\[
\text{Peak} = \frac{\left(\frac{MD}{t}\right)}{k_e \times V_D} \times \left(\frac{1 - e^{-kt}}{1 - e^{-kT}}\right)
\]

\[
\text{Trough} = \text{Peak} \times e^{-k(T-t)}
\]
Patient Case

- $V_d = 39.2 \text{ L}$
- $\text{CrCl}: 77.4 \text{ mL/min}$
- $k_e = 0.069 \text{ hr}^{-1}$
- $T_{1/2} = 10 \text{ hours}$
- Dosing interval = 12 hours
- Dose = 750 mg

Calculate the patient’s estimated peak/trough with this dose

Estimated peak/trough with a regimen of 750 mg IV q12h = 32.8 mcg/mL and 15.4 mcg/mL
Calculate predicted steady-state AUC$^{24}_{24}$
Patient Case

- \( V_d = 39.2 \) L
- \( \text{CrCl: 77.4 mL/min} \)
- \( k_e = 0.069 \) hr\(^{-1} \)
- \( T_{1/2} = 10 \) hours
- Dosing interval = 12 hours
- Dose – 750 mg q12h
- Predicted C\(_{\text{max}}\) and C\(_{\text{min}}\) 32.8 and 15.4 respectively

Calculate the patient’s predicted AUC

\[
\begin{align*}
\text{AUC}_{\text{inf}} &= 24.1 \\
\text{AUC}_{\text{elim}} &= 252.2 \\
\text{AUC}_{24} &= 552.6 \\
\text{AUC:MIC ratio using actual MIC if culture data available, or institutional average for empiric calculations (usually 1)}
\end{align*}
\]
Dosing in Patients with Renal Dysfunction

• Chronic Kidney Disease (CKD)
  – Approach just described can be used for patients with CKD if their SCr is near baseline

• Acute Kidney Injury (AKI)
  – Vancomycin clearance is unpredictable in patients with AKI
  – PK equations can be used initially but will not accurately predict $k_e$ as renal function not at steady state
Monitoring

• Checking levels after first dose
  – Patients at high risk for nephrotoxicity and/or when $K_e$ cannot be accurately predicted (i.e. morbidly obese, AKI)
  – Meningitis/CNS infections
  – Nephrotoxins include, but are not limited to: IV aminoglycosides, IV colistin/polymyxin, amphotericin, IV contrast within last 72 hours (e.g. that used for CT, cardiac catheterization, vascular imaging)

• Checking levels at steady state
  – Not clear whether vancomycin will be continued following an initial dose
  – If 2 levels have not been checked after the initial dose

• Repeat trough levels
  – At least weekly for hemodynamically stable patients with stable renal function
  – More frequent or daily monitoring in the hemodynamically unstable, have fluctuating renal function, or are at high risk for nephrotoxicity
Monitoring in Renal Dysfunction

- **CKD**
  - Levels can be checked after first dose, or at a minimum once concentrations are near steady state or within 72 hours, whichever is sooner.

- **AKI**
  - Checking 2 levels has minimal value in unstable patients with AKI, single serum levels should be checked early and frequently.
Timing of Levels

• Both levels should be drawn following the same dose
• Level 1 – Approximately 2 hours after the completion of the infusion
• Level 2 – at least 1 half-life after the first level
# Adjusting Based on Two Serum Levels

<table>
<thead>
<tr>
<th>Calculation</th>
<th>Formula</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calculate patient’s true $k_e$ from two measured concentrations.</td>
<td>$k_e = \frac{\ln \left( \frac{C_1}{C_2} \right)}{t_2 - t_1}$</td>
</tr>
<tr>
<td>Calculate patient’s true $t_{1/2}$.</td>
<td>$t_{1/2} = \frac{0.693}{k_e}$</td>
</tr>
<tr>
<td>Calculate patient’s true $C_{\text{max}}$.</td>
<td>$C_{\text{max}} = \frac{C_1}{1 - \left( e^{-k_e \Delta T} \right)}$</td>
</tr>
<tr>
<td>Calculate patient’s true $C_{\text{min}}$. Skip step if only 1 dose received.</td>
<td>$C_{\text{min}} = C_{\text{max}} \times \left( e^{-k_e \left( T_{\text{au}} - t \right)} \right)$</td>
</tr>
<tr>
<td>Calculate patient’s $V_d$.</td>
<td>$V_d = \frac{Dose}{t} \times \frac{1 - e^{-kt}}{k_e \times C_{\text{max}}}$</td>
</tr>
<tr>
<td>- If patient has received only 1 dose:</td>
<td>$V_d = \frac{Dose}{t} \times \frac{1 - e^{-kt}}{k_e \times \left( C_{\text{max}} - C_{\text{min}} \times e^{-kt} \right)}$</td>
</tr>
<tr>
<td>- Steady-state condition:</td>
<td></td>
</tr>
</tbody>
</table>
Adjusting based on Two Serum Levels
Cont’d

<table>
<thead>
<tr>
<th>Calculation</th>
<th>Equation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calculate actual vancomycin clearance ($Cl_{van}$).</td>
<td>$Cl_{van} = Vd \times k_e$</td>
</tr>
<tr>
<td>If $C_{min}$ concentration obtained is high, calculate time needed to reach desired range.</td>
<td>$T = \frac{\ln\left(\frac{C_{min}}{C_{des}}\right)}{k_e}$</td>
</tr>
<tr>
<td>Calculate the new Tau.</td>
<td>$\frac{\ln\left(\frac{C_{max,des}}{C_{min,des}}\right)}{k_e} + t$</td>
</tr>
<tr>
<td>Estimate total daily dose (TDD) needed to achieve target $AUC_{0-24}$.</td>
<td>$TDD (mg) = Cl_{van} \times Desired\ AUC_{0-24}$</td>
</tr>
<tr>
<td>Calculate new maintenance dose (MD).</td>
<td>$MD = \frac{TDD}{\left(\frac{24}{\tau}\right)}$</td>
</tr>
<tr>
<td>Calculate predicted steady-state $C_{max}$ for new dosing regimen.</td>
<td>$C_{max} = \frac{\left(\frac{Dose}{Vd}\right)}{(1 - e^{-k\cdot\tau})}$</td>
</tr>
<tr>
<td>Calculate predicted steady-state $C_{min}$ for new dosing regimen.</td>
<td>$C_{min} = C_{max} \cdot (e^{-k\cdot(\tau-t)})$</td>
</tr>
</tbody>
</table>
### Adjusting Based on Two Serum Levels Cont’d

<table>
<thead>
<tr>
<th>Calculate predicted steady-state $AUC_{24}$ based on new dosing regimen. (see figure below)</th>
</tr>
</thead>
</table>
| a. Use linear trapezoidal rule to calculate $AUC$ during infusion.  
$AUC_{inf} = \frac{(C_{max} + C_{min})}{2} \times t$ |
| b. Use logarithmic trapezoidal rule to calculate $AUC$ during elimination.  
$AUC_{elim} = \frac{(C_{max} - C_{min})}{k_e}$ |
| c. Sum areas from above and multiply by # doses / 24 hours.  
$AUC_{0-24} = (AUC_{inf} + AUC_{elim}) \times \left(\frac{24}{\text{Tau}}\right)$ |
What MIC?

- Remember the goal parameter is AUC: $\text{MIC} \geq 400$
- Always use patient, culture-specific data if available
- For empiric dosing or culture negative situations, use local/institutional average (typically 1) – ask your lab!
• Always want to maintain a trough of at least 10 to prevent the development of resistance
• An AUC range of 400-600 is ideal, risk of AKI significantly increased with AUC > 1300
• When the MIC is 2 or greater, an AUC:MIC ratio of ≥ 400 may not be possible without compromising toxicity and alternative agents should be considered
Benefits of an AUC Based Dosing Strategy

- Analysis carried out by Cox-regression showed AUC-target dosing as protective against nephrotoxicity.
- Bayesian exposure profiles of 160 patients with bacteremia showed a significant decrease in vancomycin exposure for AUC-targeted dosing patients.

Practical Implementation

- **Dosing calculators**
  - Excel based/homegrown
  - Commercial products

<table>
<thead>
<tr>
<th></th>
<th>BestDose</th>
<th>ID-ODS</th>
<th>First-Dose</th>
<th>ClinCalc</th>
</tr>
</thead>
<tbody>
<tr>
<td>Method of PK assessment</td>
<td>Bayesian non-parametric approach</td>
<td>Bayesian parametric approach</td>
<td>Population parametric approach</td>
<td>Population parametric approach</td>
</tr>
<tr>
<td>Cost</td>
<td>Current version is free</td>
<td>Trial period free</td>
<td>Free</td>
<td>Free (web), small fee (app)</td>
</tr>
<tr>
<td>Smart phone app</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>

Challenges to Implementation

• Culture change!
  – Panic over ‘high’ peak levels
  – Adjustment to 2 levels versus single trough

• Training required
  – Physicians/prescribers
  – Pharmacists
  – Nursing
Conclusions

- Trough based vancomycin dosing strategies are sub-optimal and may lead to unnecessarily high doses for many patients.
- AUC:MIC ratio is the best PK/PD parameter to describe vancomycin efficacy.
- AUC-based dosing strategies may offer a better way to dose vancomycin.
I don't get it. Not a single person has joined since we opened.