UWTASP
tele-antimicrobial stewardship program

April 16, 2024

Agenda

- Title: *Vancomycin – AUC monitoring*

Objectives

- Vancomycin trough/AUC refresher
- Cases
  - When would be most important to use AUC over trough-based monitoring
  - Threshold for dose adjustments
  - Utilizing transposition of vancomycin levels

Disclaimer

- Vancomycin dosing is subjective, recommendations may vary depending on pharmacist discretion.

Poll

How do you monitor vancomycin at your institution (not including SSTIs or UTIs)?

a. AUC for all patients on vancomycin
b. Vanco troughs 10-20 mcg/mL
c. Vanco troughs 15-20 mcg/mL
d. A mix of AUC and trough-based monitoring
e. Unsure/something else

Trough is used as a surrogate for AUC

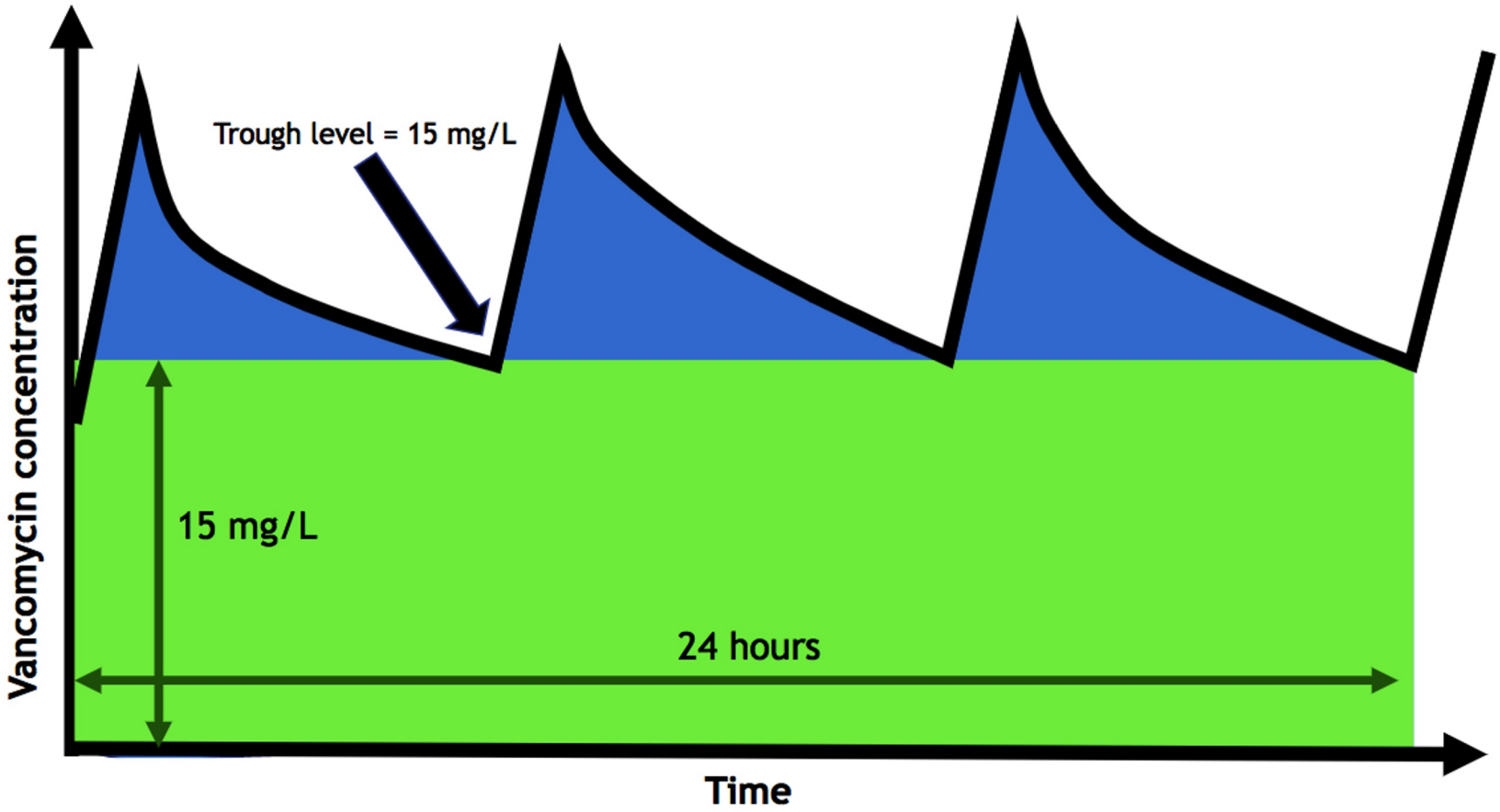

Photo credit: emcrit.org

A trough can be easily manipulated

Dose	Trough (mcg/mL)	Peak (mcg/mL)	24h AUC
750 mg IV Q6H	20	25	500
1000 mg IV Q8H	15	30	500
1500 mg IV Q12H	10	35	500
3000 mg IV Q24H	<0.5	40	500

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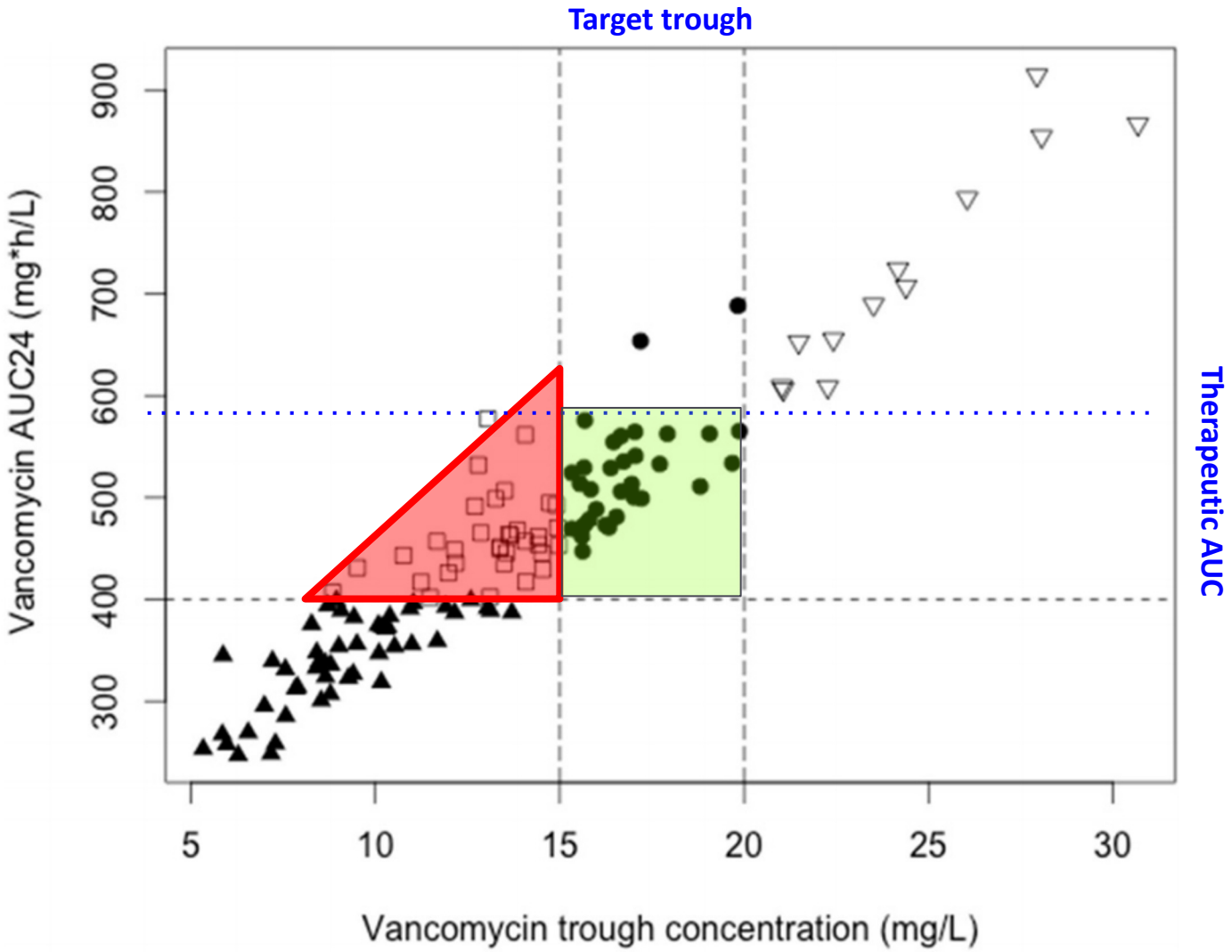
$$\text{AUC} = \frac{\text{Dose}}{\text{Ke x Vd}} \text{ x } \frac{24}{\text{T}} = \frac{\text{Total daily dose}}{\text{Clearance}}$$

Vanco trough>15 mcg/mL is a poor surrogate for AUC 400-600



Chavada R, Ghosh N, Sandaradura I, et al. Establishment of an AUC_{0-24} Threshold for Nephrotoxicity Is a Step towards Individualized Vancomycin Dosing for Methicillin-Resistant Staphylococcus aureus Bacteremia. Antimicrob Agents Chemother. 2017 Apr 24;61(5):e02535-16.

Clinical Infectious Diseases
MAJOR ARTICLE

The Emperor's New Clothes: PRospective Observational Evaluation of the Association Between Initial VancomycIn Exposure and Failure Rates Among ADult HospitalizEd Patients With Methicillin-resistant *Staphylococcus aureus* Bloodstream Infections (PROVIDE)

- Higher AUC was not correlated with lower treatment failure.
- Higher AUC was associated with increased nephrotoxicity.
- AUC monitoring was not correlated with improved clinical outcomes.

Bayesian approach

- Bayes' Theorem – Calculates the probability of an outcome occurring based on different patient conditions.
- Uses richly sampled PK data from studies to estimate an individual's pharmacokinetic parameters.

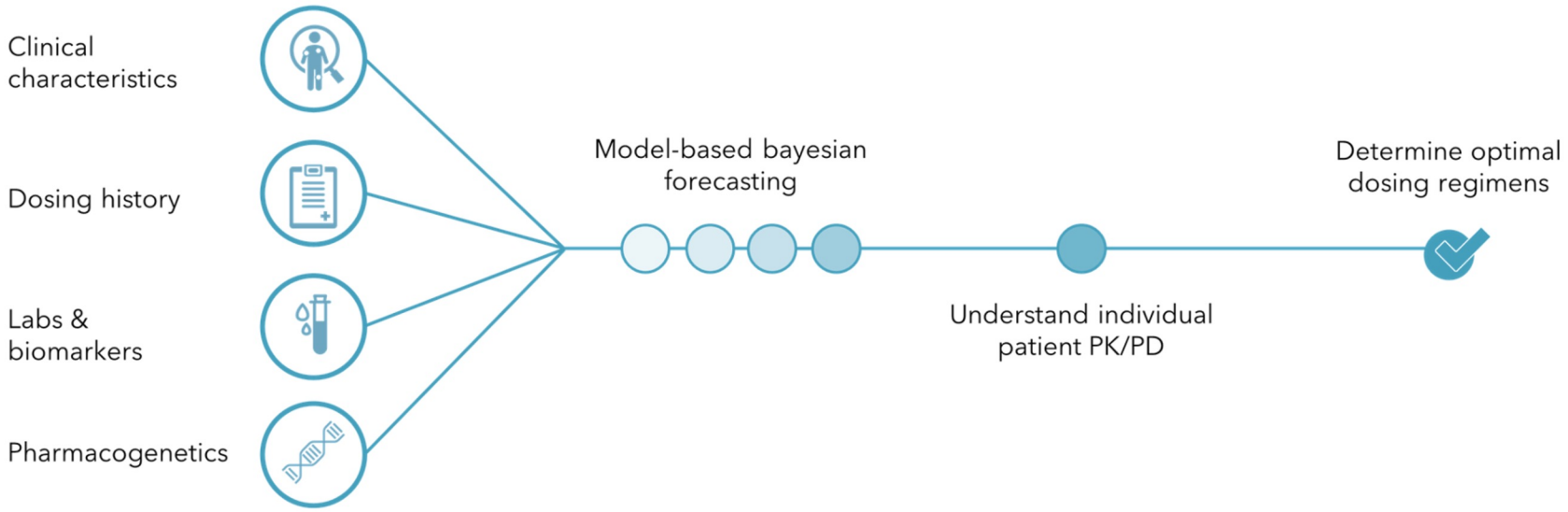
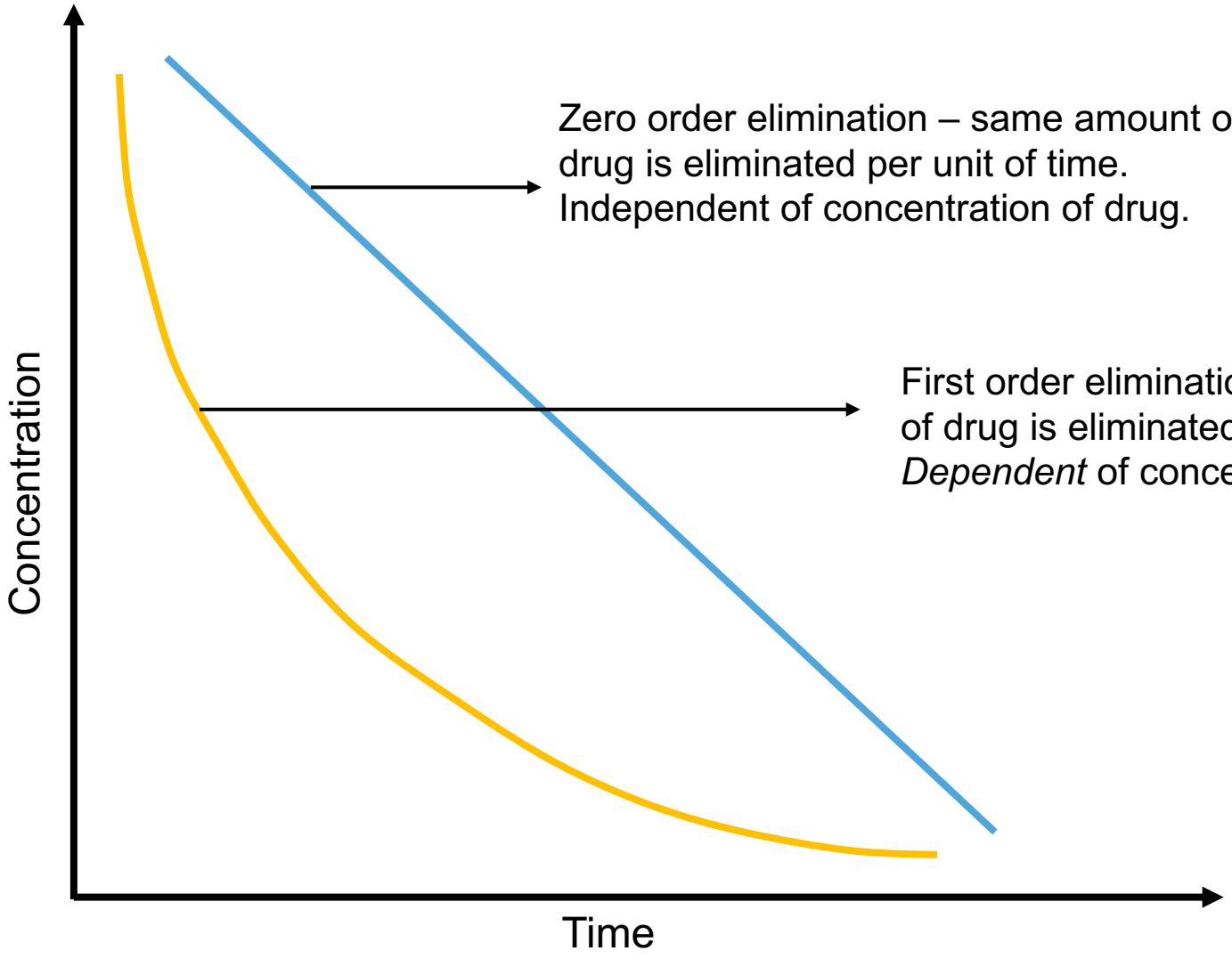


Photo credit: insightRx

Equation based approach

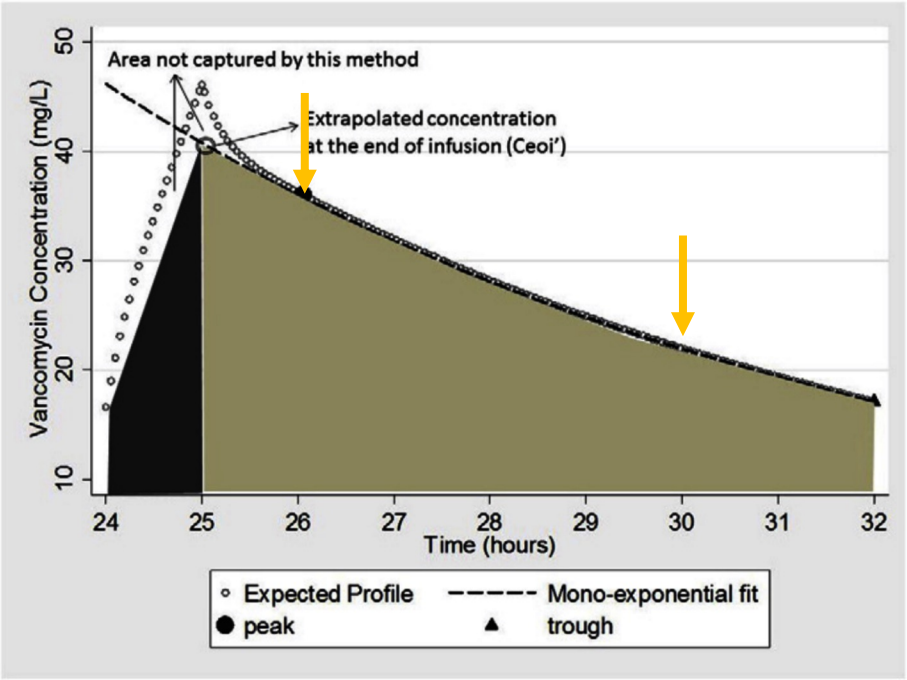


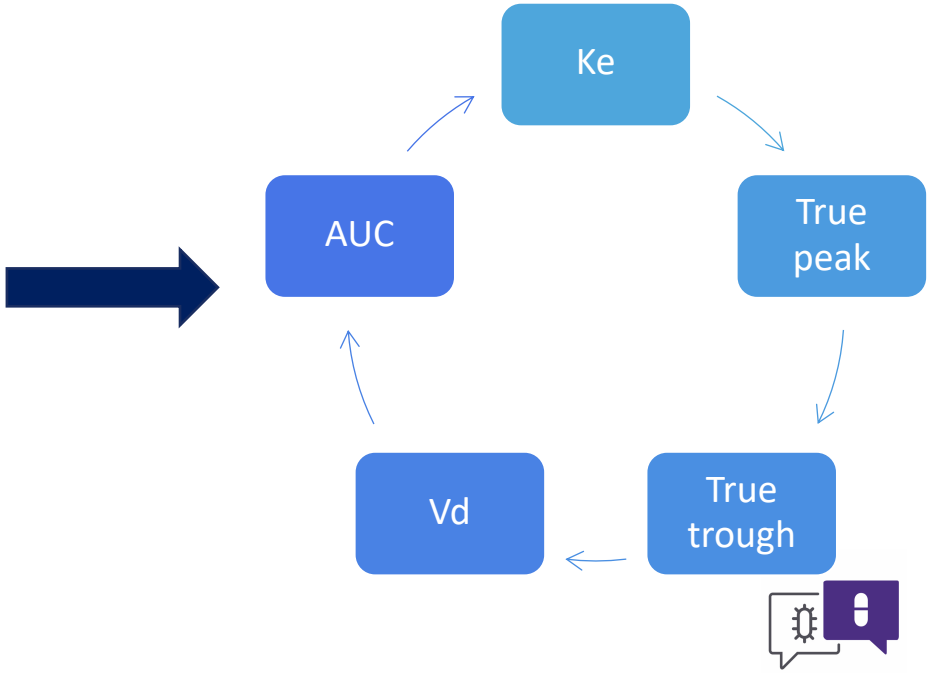
Zero order elimination – same amount of drug is eliminated per unit of time. Independent of concentration of drug.

First order elimination – same *proportion* of drug is eliminated per unit of time. *Dependent* of concentration of drug.

Equation based approach

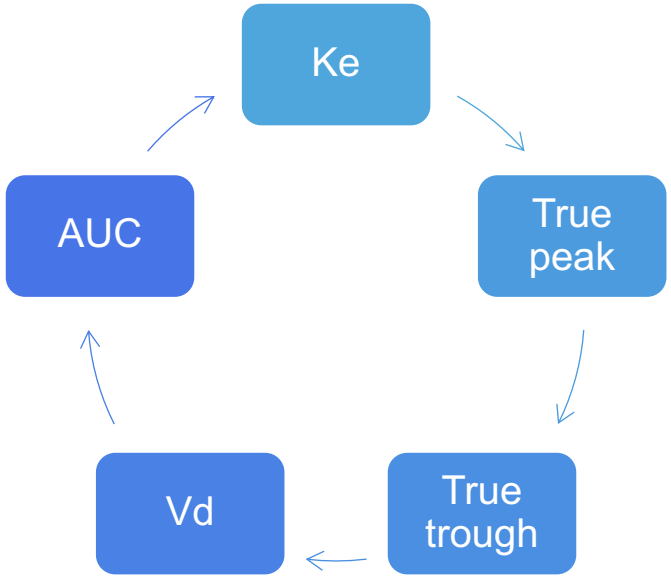
- Two level sampling: post-distributional peak and trough concentration.
- First-order kinetic formulas used to estimate exposure.





Equation based approach: Timing of levels matters

- First level drawn at least an hour after infusion.
- Levels should be drawn with ≥1 half-lives between each level (a minimum of 4 hours).
- If drawn too close together, likely downstream calculation errors due inaccurate Ke.



AUC calculators

- Homemade: excel
- Stanford Guide
- ClinCalc: https://clincalc.com/Vancomycin/

VANCOMYCIN AUC CALCULATOR	Input	Dosing parameter
Dose	1500	mg
Dosing interval	12	hours
Concentration$_1$ (Cmax)	40.0	mg/l
Concentration$_2$ (Cmin)	18.0	mg/l
Date/time of dose preceeding C1 and C2 (m/d/yyyy h:mm AM/PM)	12/22/2022 12:00 AM	Typing military time (hh:mm) will display correctly
Date/time Concentration 1	12/22/2022 3:00 AM	
Date/time Concentration 2	12/22/2022 11:00 AM	
Infusion time	1.5	hours
Calculated fields		
ke	0.10	hours^{-1}
Estimated half-life	6.94	hours
Cmax	46.46	mg/l
Cmin	16.29	mg/l
Vd	42.95	L
24-hour AUC	699	~~Goal 24h AUC = 400 [350 - 650] mg/l~~
If AUC within goal: Pt specific trough (lower limit)		mg/l
If AUC within goal: Pt specific trough (upper limit)		mg/l
Use this section to revise a regimen based on AUC above		
Suggested maintenance dose	1500	mg
Suggested dosing interval	24	hours
Dose change	1250	[new total daily dose = current total daily dose * (AUC desired/AUC calculated)] mg
Interval change	12	hours
New infusion time	1.5	hours
New Cmax	38.72	mg/l
New Cmin	13.58	mg/l
New AUC	582	
Pt specific trough (lower limit)	6	mg/l
Pt specific trough (upper limit)	9	mg/l

Fill in these areas, the rest with auto populate

24-hour AUC will turn red if supratherapeutic

Patient specific trough goal will be automatically calculated if 24-hour AUC is within goal. If dosing needs to be adjusted, refer to patient specific trough goal under revised regimen

Excellent review

Contents lists available at ScienceDirect

Advanced Drug Delivery Reviews

journal homepage: www.elsevier.com/locate/addr

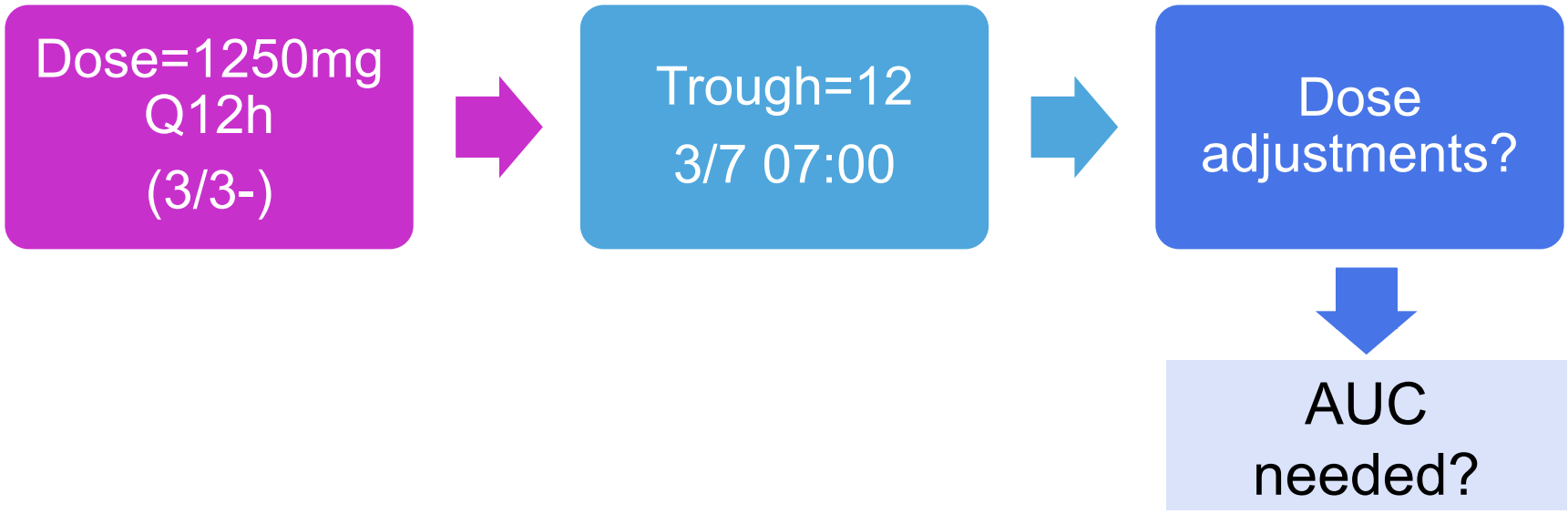
Innovative approaches to optimizing the delivery of vancomycin in individual patients ☆

Manjunath P. Pai [a], Michael Neely [b,c], Keith A. Rodvold [d], Thomas P. Lodise [a,*]

Pai MP, Neely M, Rodvold KA, et al. Innovative approaches to optimizing the delivery of vancomycin in individual patients. Adv Drug Deliv Rev. 2014 Nov 20;77:50-7.

Case 1: MRSA SSTI

58 yo M on vancomycin 1250mg Q12h for SSTI with abscesses s/p I&D growing MRSA. Clinically stable.



Poll

Dose adjustments and/or AUC needed?

a. Increase dose, no AUC
b. No change in dose, no AUC
c. No change in dose, obtain AUC
d. Unsure

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MRSA/Vancomycin guidelines: then and now

- 2011: “For most patients with SSTI who have normal renal function and are not obese, traditional doses of 1gm Q12h are adequate, and trough monitoring is not required (B-II)”.

- 2020: “In patients with suspected or definitive serious MRSA infections*, an individualized target of the AUC/MIC ratio of 400 to 600 should be advocated to achieve clinical efficacy while improving patient safety (A-II)”.

*Serious invasive MRSA infections exclude nonbacteremic SSTI and UTIs.

Liu C, Bayer A, Cosgrove SE, Daum RS, et al. Infectious Diseases Society of America. Clinical practice guidelines by the infectious diseases society of america for the treatment of methicillin-resistant Staphylococcus aureus infections in adults and children. Clin Infect Dis. 2011 Feb 1;52(3):e18-55.

Patient populations who may benefit from AUC

AUC

- Serious MRSA infections
- Prolonged courses of therapy
- Total daily needs >4gm/day

No AUC

- RRT (ex. HD, PD)
- Labile renal function
- Courses <7 days
- MRSA UTI/SSTI

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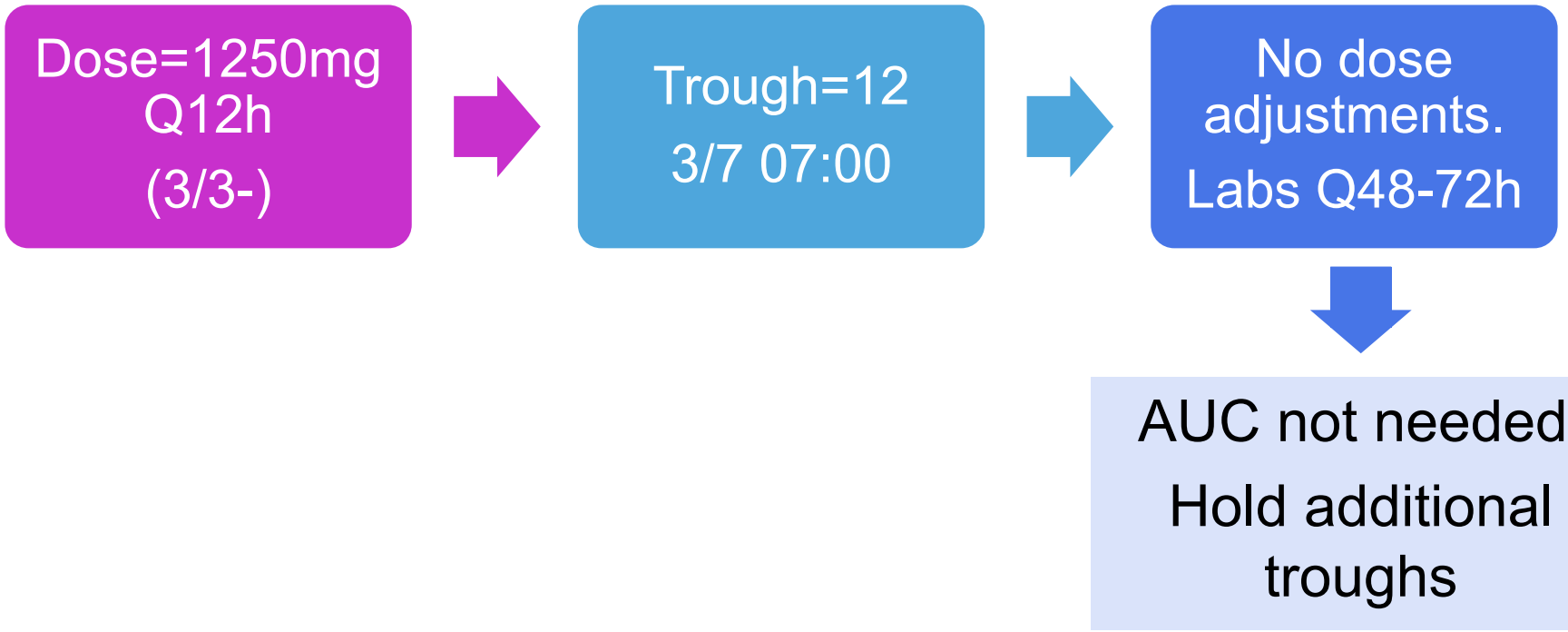
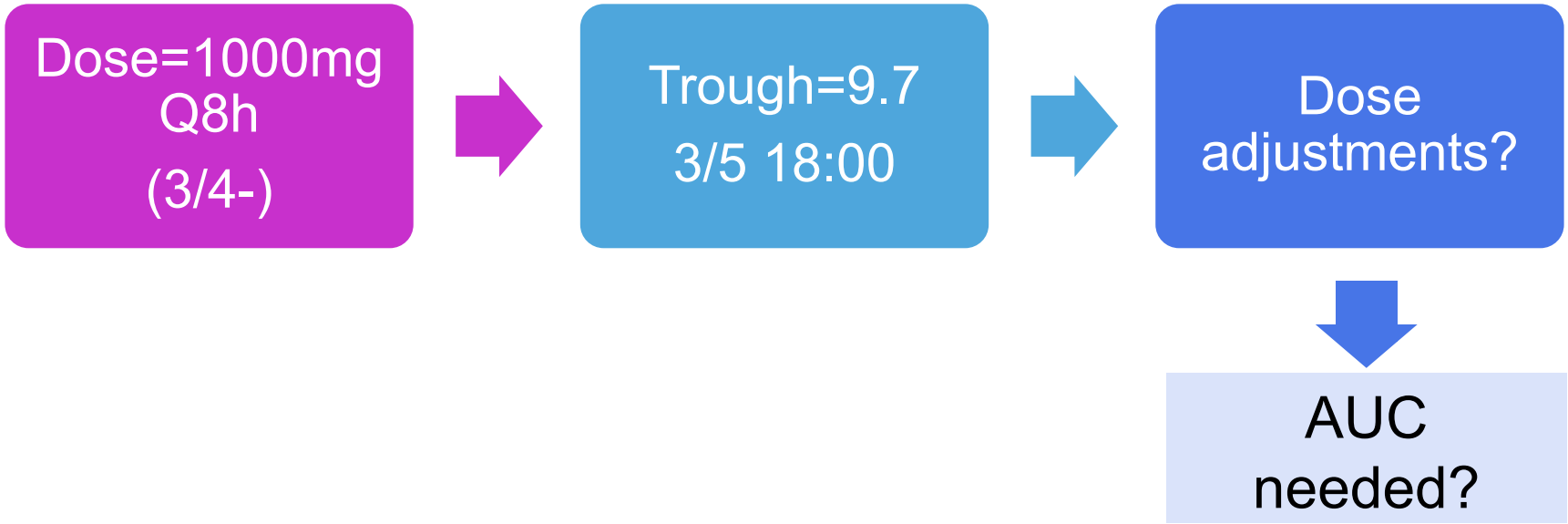


Takeaways

- For nonserious infections – no levels needed, but troughs of 10-15 may be aimed for safety.
- Trough goals of 15-20 are no longer commonly recommended.
- Reserve AUC for serious MRSA infections.
- Consider lab stewardship – vanc levels and lab frequency and timing.

Case 2: MRSA bacteremia

28 yo F on vancomycin 2gm x1, 1000mg Q8h for MRSA bacteremia. Repeat blood cultures clear. Clinically stable.



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Trough level adjustments

Trough Level :	<8	8 to 9.9	10 to 15	>15 to 20	>20
MRSA Infection	↑ consider AUC*	↔ consider AUC*	↔ consider AUC*	↔ consider AUC*	↓ consider AUC*
CoNS or Enterococcus	↑	↔	↔	↓	↓
CNS Infection	↑	Consider increase	Consider increase	↔	↓
SSTI, UTI, and Wound	↔	↔	↔	↓	↓
Empiric	↑	↔	↔	↓	↓
AUC Derived Trough Range Established	See patient specific trough range in previous EMR note				

Adapted from UW Medicine OCCAM Vancomycin Guidelines

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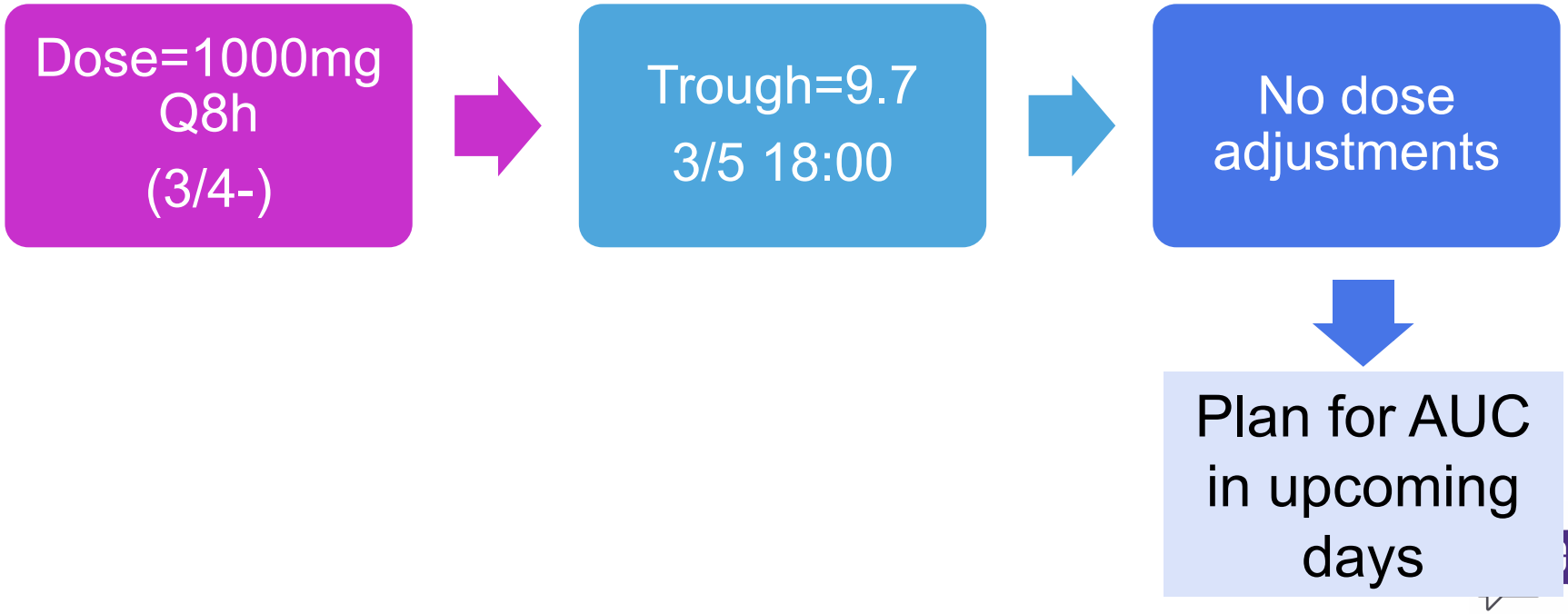

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Case 2: MRSA bacteremia

- AUC therapeutic but upper end of goal – decrease back down to 1000mg Q8h.
- If stable clearance, dose changes less than 25% typically do not need repeat AUC.
- Patient specific trough goal ~8-12.

Takeaways

- Trough/AUC levels can fluctuate.
- Do not chase trough values. Adjust if reasonably below trough goals.
- Patient-specific trough goals <10 with a therapeutic are ok to use.
- Narrow trough goal windows can be difficult to target, consider trough goals with a 5-point range.

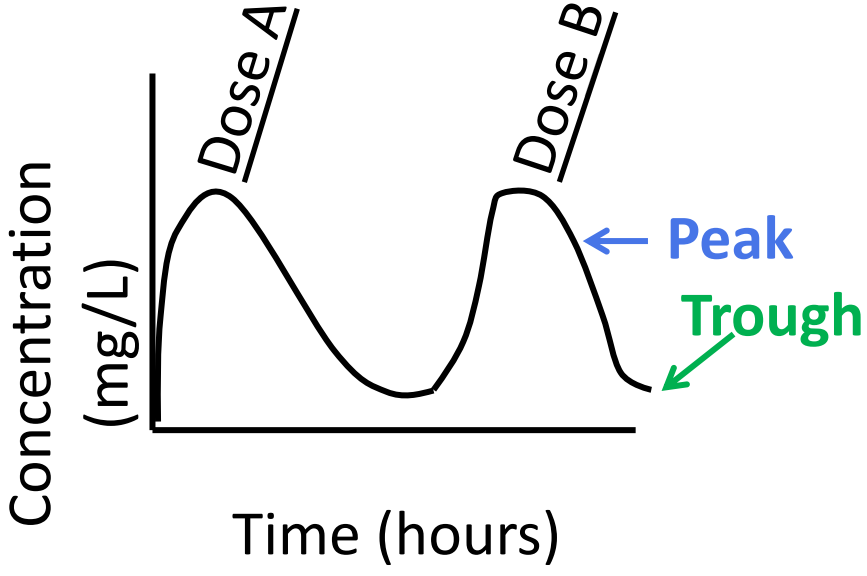
Case 3: MRSA bacteremia #3

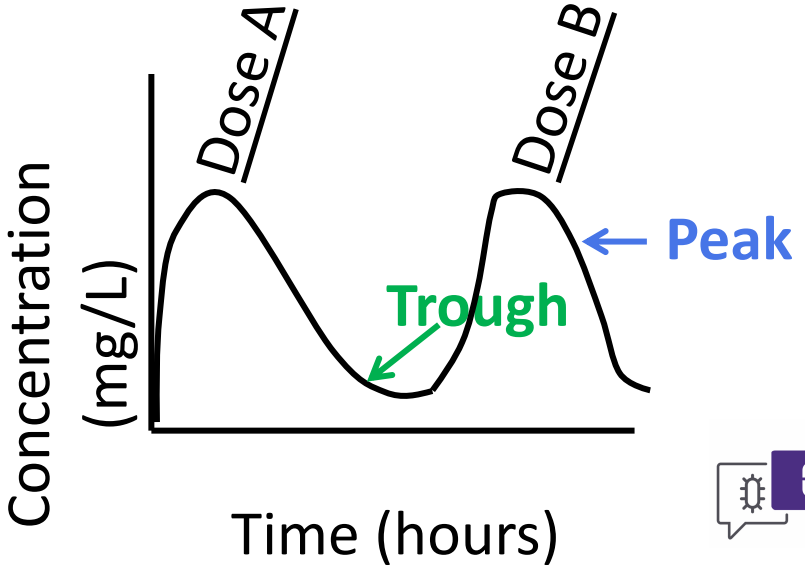
64 yo M on vancomycin 2gm x1, 1500mg Q12h for MRSA bacteremia. Clinically stable. Discharging soon.

- Has been monitored with troughs thus far, within goal (Troughs 10-20).
- Has not had AUC calculated.
- Planned 4 weeks of therapy.

Transposing levels

- Challenging lab draws/missed levels
- Cluster levels/labs that need to be drawn with prolonged dosing intervals (ie. Q12-24h)
- Facilitate discharge needs with AUC recommendations





Takeaways

- Consider transposing levels if time is a barrier.
- If no time, keep vanc trough goal 10-20. Safety is priority in clinically stable patients.

Summary

- Troughs 15-20 are now outdated for most vancomycin indications.
- Troughs and AUC monitoring is primarily for safety rather than efficacy.
- Monitoring clinical stability should be prioritize over correcting a subtherapeutic level.