The New Vancomycin Guideline: Insights On Key Elements From An Experienced Antimicrobial Stewardship Pharmacist

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In this article a leading antimicrobial stewardship pharmacist with decades of experience shares insights on the new vancomycin guideline.

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Vancomycin is a glycopeptide antibiotic with activity versus clinically important Gram positive bacteria including methicillin-resistant *Staphylococcus aureus* (MRSA). It was first used in the 1950s and is presently the workhorse for anti-MRSA antibiotic therapy in hospitalized patients.

When vancomycin is given intravenously it is common for clinicians to do therapeutic drug monitoring (TDM), collecting blood samples from patients to determine how much vancomycin is in the body. TDM is used to adjust doses of vancomycin and many times institutions have pharmacy-to-dose vancomycin protocols, which allow pharmacists to order labs and change vancomycin orders to optimize care. In hospitals, vancomycin dosing and monitoring is kind of a big deal. It involves prescribers, pharmacists, nurses, lab, and others.

Prior to the vancomycin guideline just published in 2020, the previous vancomycin guideline was from 2009. Now over 10 years later, this latest iteration of the vancomycin guideline is recommending some pretty substantial practice changes.

In this article, a leader in the field of antimicrobial stewardship is interviewed. The purpose of this interview is to provide insights on the new vancomycin guideline and help people understand the context surrounding this highly anticipated publication.

1. Do you recall how you were first introduced to vancomycin? In what capacity have you worked with it during your career?

I was first introduced to vancomycin over 20 years ago, when I was a pharmacy student working at a large, academic medical center. This institution had a well-established, pharmacist-led, pharmacokinetics dosing program that has been in place for decades. As a student intern, we assisted with monitoring levels and making trough-based dosing recommendations (under the supervision of the floor pharmacists).

As is typical, I continued to dose vancomycin when I entered my career as hospital-based clinical pharmacist. As I moved into roles that allowed me to work with large groups of hospitals, my experience with vancomycin transitioned more into monitoring antibiotic utilization at a national level, developing formulary management guidelines (especially for when to move to non-vancomycin based therapies), and creating vancomycin dosing and monitoring protocols for adaptation by acute care hospitals. I have also developed several vancomycin pharmacokinetic training programs for acute care pharmacists over the years.

Now my focus on vancomycin has shifted to the application of Bayesian dosing principles through clinical decision support in order to calculate key pharmacokinetic parameters including AUC.

2. There has been a lot of buzz surrounding the new vancomycin guidelines. Which part(s) of the guidelines are you most excited about?

Finally moving to AUC based dosing! It is something that we have been talking about for a long time, but we can now move forward with putting it into practice. I am excited to be in a position that allows me to follow the transitions that emerge in clinical practice moving from pre- to post-guideline implementation.

I also am happy to see a whole section that addresses how to calculate AUC, including through the use of Bayesian-derived AUC monitoring. In the 2009 guidelines, the word "Bayesian" is mentioned only one time and now there is an entire section dedicated to it in the new guidelines.

Other points of excitement around new guidelines include the expanded discussion about the nuances associated with MIC testing and how the method of testing can impact the AUC:MIC ratio. Also, having clearer guidance on special populations is very helpful. When there is a lack of evidence, safety can be compromised, so the expanded discussions on dosing vancomycin in dialysis, pediatrics, and neonates will also be beneficial.

3. The new vancomycin guideline recommends AUC-based monitoring for patients with MRSA infections. Many patients that receive vancomycin ultimately are not found to have an MRSA infection. What advice do you have for institutions looking to do AUC-based monitoring for select patients only?

Creating a reference table or guide for pharmacists that lists the indications for when AUC monitoring is needed is a great place to start. Also, evaluating vancomycin utilization patterns and creating exception lists for when monitoring is not necessary in the first place is also helpful.

Resources of this nature would not only be good to communicate to pharmacists, but also to prescribers so that they are aware that not every patient who receives vancomycin will require AUC dosing (or in some cases therapeutic monitoring at all).

4. The new vancomycin guideline recommends continuous vancomycin infusion to achieve a steady-state concentration between 20 – 25 mg/L. Can you discuss some of the challenges and provide practical advice for institutions seeking to implement this dosing option?

I think we can take what we have learned from years of implementing continuous and extended infusion programs for beta-lactams and use this as a guide for the best way to approach how to implement continuous infusion (CI) vancomycin.

The first phase involves taking the standard approach of creating criteria for patient types that would benefit from vancomycin continuous infusion (*e.g.,* critically ill patients), developing prescriber and pharmacist educational materials, updating vancomycin dosing protocols, and developing order entry options in the Electronic Health Record (EHR). Not only should these resources address the therapeutics of CI, but also common logistical challenges like IV compatibility, when to obtain levels, and how to transition a patient from intermittent to CI and vice versa. However, one key group to engage early in the conversation is nursing. Start by working with a small group of trusted nurses from the units where CI is most likely to be administered who can help you address the operational issues that are involved with implementing a CI protocol. This pilot group can provide feedback on the process, recommend nursing specific information that should be included in any support materials and can help to troubleshoot any issues early. It is always easier to make changes in the program when you are dealing with a small group vs trying to course correct with the entire nursing staff. These nurses can also serve as a resource for other nurses who are unfamiliar with administering vancomycin CI.

Finally, similar resources should be developed that provide guidance for how to discharge a patient on CI vancomycin as well as outpatient parenteral antibiotic therapy (OPAT) guidelines, if applicable.

6. For decades pharmacists have debated vancomycin dosing strategies in dialysis patients. In your role, working with hospitals across the US and even internationally, what have you observed as it relates to the practice of dosing vancomycin in dialysis patients?

The diversity of dosing protocols in dialysis is astounding. This is one of the most challenging areas for vancomycin dosing for several reasons. Vancomycin dosing can often be very individualized from institution to institution due to prescriber or outside dialysis provider preference and can be impacted by filter permeability, flow rates, and time of administration during the session. Even more variability is introduced when you move into the topic of dosing patients on continuous renal replacement therapy (CRRT).

Although this iteration of the guidelines provides helpful guidance and a place to start, we need to identify better ways to dose vancomycin to achieve therapeutic targets. In addition, it would be helpful if more granular information about dialysis practices could be included in the manuscripts for pharmacokinetic studies, such as filter types used, flow rates, and dialysis frequency. This information is often generalized in studies.

7. All guideline content considered, in which patient population do you feel vancomycin dosing is the most challenging and why?

Aside from dialysis (as mentioned previously), dosing in obesity is by far the biggest challenge. As we know, the average weight of patients has steadily increased and we are seeing higher rates of morbid obesity in our patient population [1]. Although the guidelines provide recommendations for dosing in this category of patients, the dose cap makes it difficult to reach the recommended mg/kg doses, especially when we are dosing based on actual body weight.

Of interest, when I looked at the distribution of adult vancomycin doses given across the US in 2019 (based on our DoseMeRx data), only a small percentage of individual doses given were more than 2 grams. This is not surprising since many institutions still have dosing policies which prohibit administration of a single dose above 2 grams, even if the calculated dose is higher. The guidelines highlight the controversy regarding the optimal body size metric to use for this population. This is an area of research for us since we have a large amount of AUC and dosing data in Class I, II, and III obese patients that will be useful to inform the development of innovative dosing models in this population [2].

In regards to vancomycin dosing in pediatrics and neonates, I am pleased to see such a comprehensive pediatrics section. I think that this will help address some of the challenges that we have encountered in this population in the past and improve the safety of the use of vancomycin in this population.

8. Is there anything you feel was missed in this vancomycin guideline that you hope to see addressed in a future iteration?

I would like to see a “Future state” section that provides a summary of clinical situations or disease states where more research is needed.

A couple of example topics that might be included in this section are vancomycin dosing for patients receiving extracorporeal membrane oxygenation (ECMO) or how to incorporate new biomarkers (*e.g.*, cystatin C) into our dosing decisions. It would be great to have a list of these under-researched areas in the guidelines, even in the absence of any formal recommendations. This would be a great resource for researchers and clinicians looking for new research ideas for an already extensively studied drug.

Closing Comments

Vancomycin has stood the test of time. It is amazing how a drug, discovered over 60 years ago, continues to be one of the most commonly used IV medications in healthcare. The new vancomycin guidelines are an excellent resource for any pharmacist or prescriber, and not only provide specific recommendations for dosing, but serve as a great literature review.

Although moving to AUC dosing will be a big paradigm shift, there are great tools and resources out there to help guide pharmacists. It will also be exciting to see how pharmacist adapt to using of Bayesian science to dose medications. This has such wide applicability, not only across other antibiotic classes but also outside of ID. This will become important as we move into the modern era of precision medication dosing.

For a complete literature review on vancomycin AUC dosing, readers may find this helpful:

REFERENCES

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Disclosures KK is an employee of and TG has served as a consultant for DoseMe/ Tabula Rasa HealthCare. The views expressed in this interview represent that of the individuals and do not necessarily reflect the position or policy of their previous, current, or potential future employers or other organizations in which they serve.

ABOUT THE INTERVIEWEE

Dr. Kristi Kuper is Director of Clinical Pharmacy for DoseMe, a Tabula Rasa Healthcare Company. Kristi has spent the majority of her 20-year career in pharmacy focusing on antibiotic stewardship and clinical pharmacy. In more recent years, Kristi has developed a passion for harnessing technology to improve medication use through precision medication dosing in the acute care setting. Through her current and previous roles in healthcare, she has worked in various capacities with over 500 hospitals both nationally and internationally, ranging in size from 10 to 1200 beds.

She has served on a number of committees related to antibiotic stewardship, including past CDC, SHEA, and Pew Trust workgroups on antibiotic stewardship, the IHI Antimicrobial Stewardship Driver Diagram development committee, the National Quality Forum's Antibiotic Stewardship Acute Care "Playbook" and was an invited attendee at the White House Forum on Antibiotic Stewardship. She currently serves as a technical advisor for the AHRQ Safety Program for Improving Antibiotic Use, is recent past Chair of the SIDP Policy and Government Affairs Committee and is a tenured member of the City of Houston Antibiotic Stewardship Executive Committee.

She received her Doctor of Pharmacy degree from the University of Nebraska Medical Center and completed a post graduate pharmacy practice residency at the James A. Haley Veterans Hospital in Tampa, Florida. She is currently pursuing a Graduate Certificate in Biomedical Informatics through the University of Texas Health Science Center.

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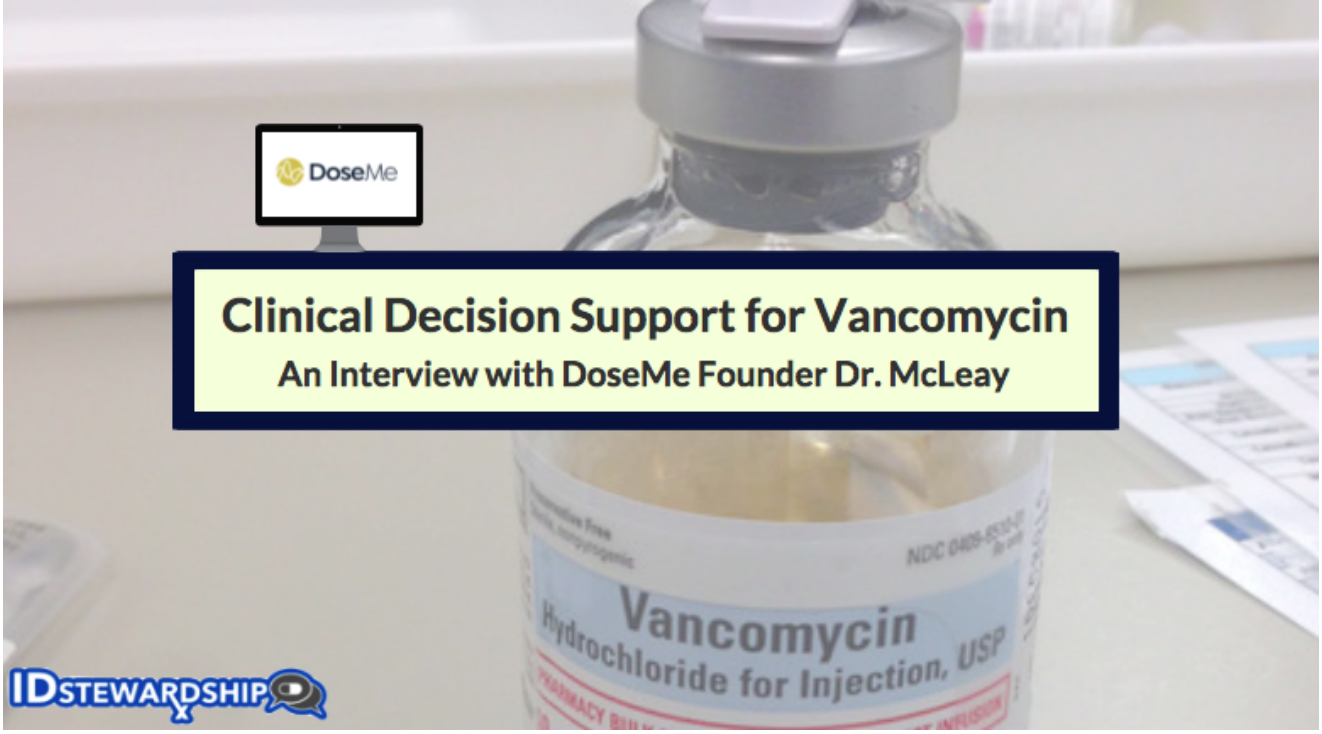
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