Therapeutics Bulletin

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PAEDIATRIC VANCOMYCIN DOSING

KEY POINTS TO REMEMBER:

- All patients should receive loading doses.
- Trough concentrations should be done prior to the 2nd maintenance dose.
- All patients should have a baseline creatinine, or a creatinine taken with the trough concentration prior to the 2nd maintenance dose.
- Do not dose-adjust vancomycin according to trough concentrations.
- Clinical Pharmacology should be contacted when vancomycin is commenced for assistance with AUC calculations.

Paediatric vancomycin dosing

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Vancomycin, a glycopeptide antimicrobial, inhibits cell wall synthesis by binding to cell wall precursors and inhibiting glycopeptide polymerization.[1] Vancomycin is effective against gram-positive bacteria, including methicillin-resistant *Staphylococcus aureus*, penicillin-resistant streptococci and ampicillin-resistant enterococci.[1]

What are the indications and antibiotic policy for prescribing vancomycin?

Vancomycin should be used for suspected or confirmed methicillin-resistant *Staphylococcus aureus*. It is important to remember that vancomycin is less effective than beta-lactams against *Staphylococcus aureus* that is susceptible to cloxacillin/methicillin. All vancomycin prescriptions should be discussed with, and authorized (written signature or telephonic with pharmacy) by the managing consultant. In addition, they should be discussed on weekly stewardship rounds.

Table 1: Vancomycin intermitted dosing in the paediatric population[2–5]

Patient groups	**Neonates#**		**Children 1 month to < 18 years (unless admitted to neonatal ward)**
Loading dose (mg/kg)	25		25
Maintenance dose (mg/kg)	15*		20* (Maximum daily empirical dose is 3600mg)
Corrected gestational age (weeks)	< 35	> 35	
Dosing interval (hours)	12	8	8

#All infants < 28 days and any baby admitted to the neonatal wards
*Dose adjustment is required in children with renal dysfunction
In selected patients a continuous infusion may be the preferred dosing strategy.
This can be discussed with Infectious Diseases and Clinical Pharmacology

FIGURE 1:

Process to follow when prescribing and monitoring vancomycin

- ¥ Special populations include patients with renal impairment, obese or critically ill patients.
- # A trough concentration is taken within 30 minutes before the next dose.
- + Creatinine concentration to be done if the patient does not have a baseline creatinine prior to vancomycin commencement or if the patient has renal impairment.
- * The Clinical Pharmacology Laboratory is situated on the 7th floor of the Clinical Building, Tygerberg Campus. Contact no.: 021 938 6168



Patient with indication for vancomycin:

Obtain authorisation for vancomycin use from managing consultant or microbiology



Administer loading dose followed by maintence dose as per *Table 1*.

For dosing in special populations¥ consult *Clinical Pharmacologist on call*



Take a trough concentration# and creatinine+ before the 2nd maintenance dose and send to the Clinical Pharmacology Therapeutic Drug Monitoring Laboratory*



Contact the *Clinical Pharmacologist* on *call* to evaluate AUC/MIC ratio and for dose optimization, as needed

How should vancomycin be dosed?

The pharmacokinetic/pharmacodynamic (PK/PD) parameter of efficacy for vancomycin is the area under the concentration-time curve over the minimum inhibitory concentration (AUC/MIC). A loading dose is recommended to achieve optimal AUC/MIC early in the treatment course. This is particularly important for patients who may have a significantly increased volume of distribution and in the setting of severe sepsis and septic shock.

How should vancomycin be administered?

Vancomycin should be diluted to 500 mg/100 mL and given intravenously as a slow infusion over 60 minutes. The infusion should not run at a rate of more than 500 mg per 30 minutes.

How should vancomycin be monitored?

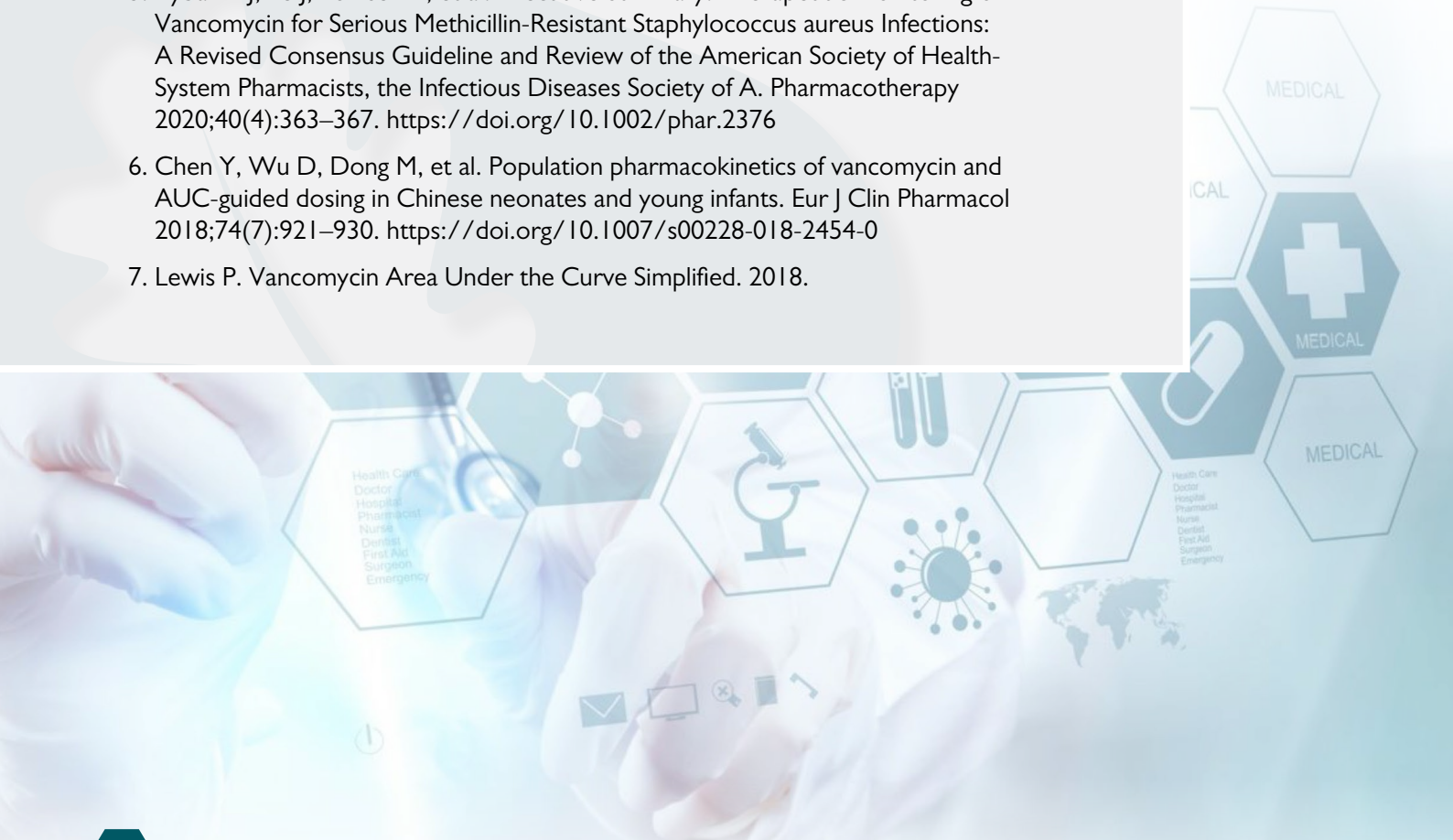
Vancomycin has a narrow therapeutic index. Adequate concentrations are essential for effective clinical response and reduced toxicity. Inappropriate dosing is associated with treatment failure, resistance and toxicity. Traditionally, trough concentrations were used to monitor vancomycin because it is convenient and pragmatic.[5] A trough concentration is the lowest concentration in the dosing interval. However, this is not the best measure to assess exposures of vancomycin.[6,7] An AUC of 400-600 is associated with better outcomes provided that the MIC of the suspected organism is 1 mg/L.[5] This is also a safer way to monitor the exposure and prevent complications.

An AUC can be calculated and used to individualize the vancomycin dose using software that utilizes Bayesian analysis. The Division of Clinical Pharmacology has a license to access this software and can use the trough concentrations to assess the appropriateness of the dose and to predict dosing for individual patients. Trough concentrations should be performed just prior to the 3rd dose and weekly for children in longer term therapy with stable renal function. Vancomycin is eliminated almost exclusively via the kidneys,[1] and therefore a change in renal function could affect vancomycin exposures. Conversely, toxic vancomycin concentrations can cause renal dysfunction and care should be taken when vancomycin is administered with other nephrotoxic drugs.

The *Clinical Pharmacologist* on call must be consulted when administering vancomycin in a patient with impaired renal function for renally adjusted doses, for AUC/MIC ratio calculations, or for any other vancomycin related queries.

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