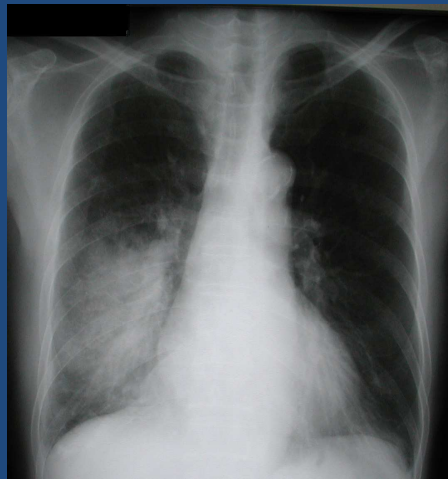


# Vancomycin-Associated Nephrotoxicity

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## CASE STUDY



## Patient Case

60 yo AAM c/o increasing shortness of breath over several weeks

PMH: DM, HTN

- Recent hospitalization
- WBC 17, SCr 0.7
- HAP suspected
- Empiric IV antibiotics initiated

## Intravenous Vancomycin

- Glycopeptide antibiotic
- MOA
  - Inhibits bacterial cell wall synthesis
- DOC: Methicillin-resistant staphylococcus aureus (MRSA)
- Widely distributes into body tissues/fluids
- Renally eliminated
- Adverse Effects

## History of Vancomycin

- 1950s: “Mississippi Mud”
  - 1958: FDA approved
- 1980s: 0 % to 5 % nephrotoxicity
- Currently: > 90 % purity
- Current rate of nephrotoxicity

## Dosing

- Loading Dose
  - Critically ill
  - Complicated infections
- Maintenance Dose
  - Standard dose
  - Population kinetics
  - Patient-specific kinetics
- Patient weight

## Patient Case

- Vancomycin, pharmacy consult
  - Ht: 74"    Wt: 83 kg
  - Baseline SCr 0.7 – 1.0
  
  - Loading Dose
  - Maintenance Dose
  - Goal trough level

## Monitoring

- Therapeutic Drug Monitoring (TDM)
  - Peak vs trough
  - AUC/MIC
- Renal function
- Accumulation
- Adjust maintenance dose

## Elevated Target Troughs

- 2009 ASHP/IDSA recommendation
  - Minimum of 10 mg/L
    - Prevent resistance, treatment failure
  - 15-20 mg/L

## Patient Case

Day	Vancomycin Dosage	SCr	Vancomycin Level
1	1500 mg x 1	--	
2	1 g Q8 x 3	0.63	
3	1 g Q8 x 2 1.5 g Q8 x 1	0.64	11.6
4	1.5 g Q8 x 3	0.66	
5	1.5 g Q8 x 1 1.75 g Q8 x 2	0.61, 0.52	13.8
6	1.75 g Q8 x 1 1.5 g Q8 x 1	0.69	
7	1.5 g Q8 x 1	<b>3.10, 4.03</b>	<b>75.2</b>

## Mechanism of Toxicity

- Definition (ASHP/IDSA 2009)
  - SCr increase by  $\geq 0.5$  from baseline on at least two consecutive readings
  - OR SCr increase by  $\geq 50\%$  from baseline on at least two consecutive readings
    - VS CLcr increase by  $\geq 50\%$  from baseline on two consecutive readings
- Proximal renal tubular toxicity
  - Oxidative stressor
- Reversible

## Vancomycin Causes Toxicity?

- Elevated baseline risk of nephrotoxicity
  - Critically ill/ICU residence
  - Renal dysfunction
- $\geq 4$  grams vancomycin daily (Lodise et al. 2008)
- Elevated trough concentrations
  - $\geq 15$  mg/L (van Hal, et al. 2012)
  - Initial trough (Lodise et al. 2009)

## Patient Case

Days Post-Vancomycin	SCr	Vancomycin Level
1	5.24, 5.76	
2	<b>7.03, 7.34</b>	HEMODIALYSIS INITIATED
<b>3</b>	6.28, 6.51	<b>58.8</b>
4	5.42	
<b>6</b>	<b>7.82</b>	<b>31.5</b>
7	5.78	
8	6.42	
9	4.62	
12	2.83	
13	2.63	
14	2.07	

## Vancomycin Causes Toxicity?

- Prolonged course of therapy
  - $\geq 7$  days
- Direct glomerular toxicity
- Consistent, prospective study data lacking
  - One meta-analysis
  - Few prospective studies
  - Multiple retrospective studies

## Prevention of Toxicity

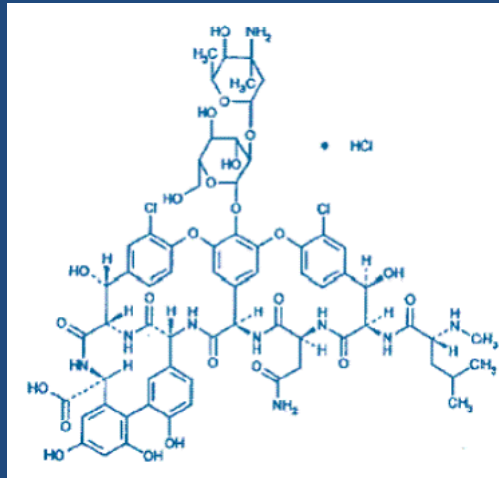
- Trough monitoring
  - Lower trough target range?
- Renal function monitoring
  - Alternative method for identifying toxicity
- Awareness of concurrent nephrotoxic agents
  - Ex: ACE-I, contrast dye
- Alternative anti-MRSA antibiotics

## Conclusions

- Vancomycin nephrotoxicity exists
  - Induced/related/associated
- Published data inconsistent
- Awareness of unstable renal function required
  - Optimal clinical outcomes
  - Patient safety
- Caution
  - Prolonged courses of therapy
  - Avoid  $\geq 4$  grams per day



## Questions?



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