Treatment of Peritonitis: CAPD vs APD Patients

Peritonitis Management: Case-based Presentations
Monday, March 6, 2023

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Disclosures

- None

Case 1

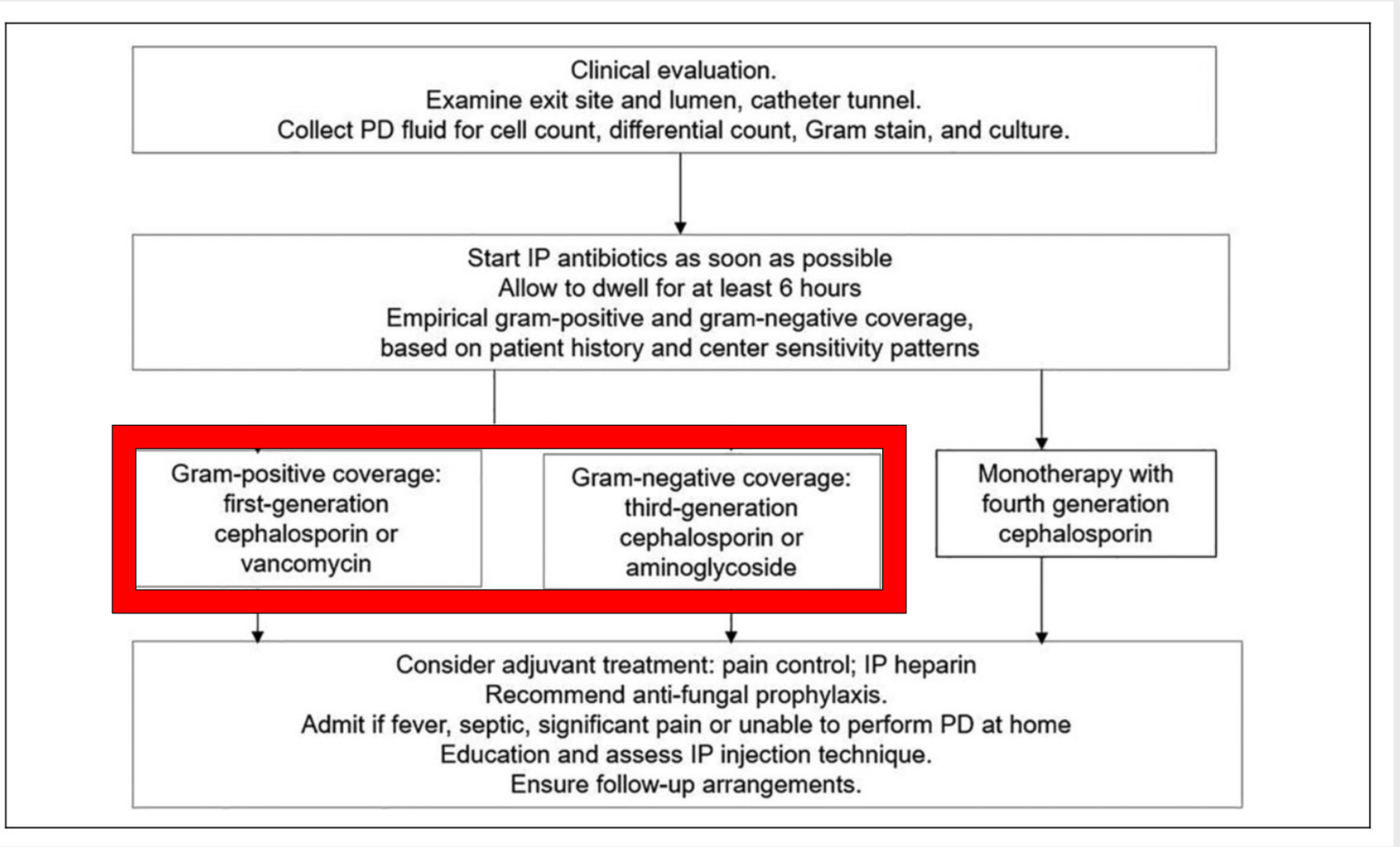
- 60 year old woman, 70kg
- ESRD secondary to IgA Nephropathy on PD for about 2 years.
- Presenting with cloudy fluid and abdominal pain
  - Current prescription CAPD
  - 2000cc Exchanges, 4x/day
  - No Residual Renal Function

Case 1 Treatment

- Empiric treatment: Intermittent dosing regimen
  - 1g Ceftazidime IP daily
  - 2g Vancomycin IP every 5 days
    - following levels of vancomycin to maintain a level > 15 mg/L

- Await culture/cell count data to determine final antibiotics choice and course duration

ISPD Guideline Based Treatment



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Principles of Effective Treatment

- Adequate Coverage
  - Empiric Gram Positive and Gram Negative Coverage
- Adequate Dose
  - Adjust for residual renal function and dialysis clearance of medication
  - Intermittent vs Continuous dosing
- Adequate Delivery
  - Correct Administration
- Adequate Duration
  - Based on culture/sensitivities

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Empiric Gram Positive Coverage

- First generation Cephalosporin or Vancomycin
- Most popular 1st gen cephalosporin would be cefazolin

Table 5. IP antibiotic dosing recommendations for treatment of peritonitis.

Antibiotic	Intermittent (1 exchange daily for at least 6 h)	Continuous (all exchanges)
Aminoglycosides		
Amikacin	2 mg/kg daily[173]	Not advised
Gentamicin	0.6 mg/kg daily[174,175]	Not advised
Netilmicin	0.6 mg/kg daily[165]	Not advised
Tobramycin	0.6 mg/kg daily	Not advised
Cephalosporins		
Cefazolin	15 mg/kg daily (for long dwell)[176,177] 20 mg/kg daily (for short dwell)[178,176]	LD 500 mg/L, MD 125 mg/L[d] [168,179]
Cefepime	1000 mg daily	LD 500 mg/L, MD 125 mg/L
Cefoperazone	No data	LD 500 mg/L, MD 62.5–125 mg/L[180]
Cefotaxime	500–1000 mg daily[181]	no data
Ceftazidime	1000–1500 mg daily (for long dwell) 20 mg/kg daily (for short dwell)[178]	LD 500 mg/L, MD 125 mg/L[d] [168,182]
Ceftriaxone	1000 mg daily[183]	No data
Penicillins		
Penicillin G	No data	LD 50,000 unit/L, MD 25,000 unit/L[13]
Amoxicillin	No data	MD 150 mg/L[184]
Ampicillin[a]	4 gm daily[185]	MD 125 mg/L[186]
Ampicillin/sulbactam		LD 1000 mg/500 mg, MD 133.3 mg/66.7 mg[187,188]
Piperacillin/tazobactam	No data	LD 4 gm/0.5 gm, MD 1 gm/0.125 gm[189]
Ticarcillin/clavulanic acid	No data	LD 3 gm/0.2 gm, MD 300 mg/20 mg/L[190]
Others		
Aztreonam	2 gm daily[191]	LD 500 mg/L[192], MD 250 mg/L[192,193]
Ciprofloxacin	No data	MD 50 mg/L[194]
Clindamycin	No data	MD 600 mg/bag[195]
Daptomycin	300 mg daily[196]	LD 100 mg/L[197,198,199], MD 20 mg/L[197,200]
Fosfomycin	4 g daily[201,202]	No data
Imipenem/cilastatin	500 mg in alternate exchange[203]	LD 250 mg/L, MD 50 mg/L[182]
Ofloxacin	No data	LD 200 mg, MD 25 mg/L[204]
Polymyxin B	No data	MD 300,000 unit (30 mg)/bag[188]
Quinupristin/dalfopristin	25 mg/L in alternate exchanges[b205]	No data
Meropenem	500 mg daily (for long dwell in APD)[207] 1000 mg daily (for short dwell in CAPD)[208,209]	MD 125 mg/L[206]
Teicoplanin	15 mg/kg every 5 days	LD 400 mg/bag, MD 20 mg/L
Vancomycin	15–30 mg/kg every 5–7 days[c141,212] for CAPD 15 mg/kg every 4 days[213] for APD	LD 20–25 mg/kg, MD 25 mg/L[214]

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Empiric Gram Negative Coverage

- Third generation Cephalosporin or Aminoglycoside
- Most popular choices Ceftazidime and Gentamicin
- ISPD Guidelines recommend intermittent dosing of gentamicin only

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Netilmicin	0.6 mg/kg daily[165]	Not advised
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Cephalosporins		
Cefazolin	15 mg/kg daily (for long dwell)[176,177] 20 mg/kg daily (for short dwell)[178,176]	LD 500 mg/L, MD 125 mg/L[d 168,179]
Cefepime	1000 mg daily	LD 500 mg/L, MD 125 mg/L[d 168]
Cefoperazone	No data	LD 500 mg/L, MD 62.5–125 mg/L[180]
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Intermittent vs Continuous Dosing

- Intermittent Dosing
  - Antibiotics in 1 exchange each day
- Continuous Dosing
  - Antibiotics in all exchanges each day

ISPD guidelines allow the use of either dosing strategy

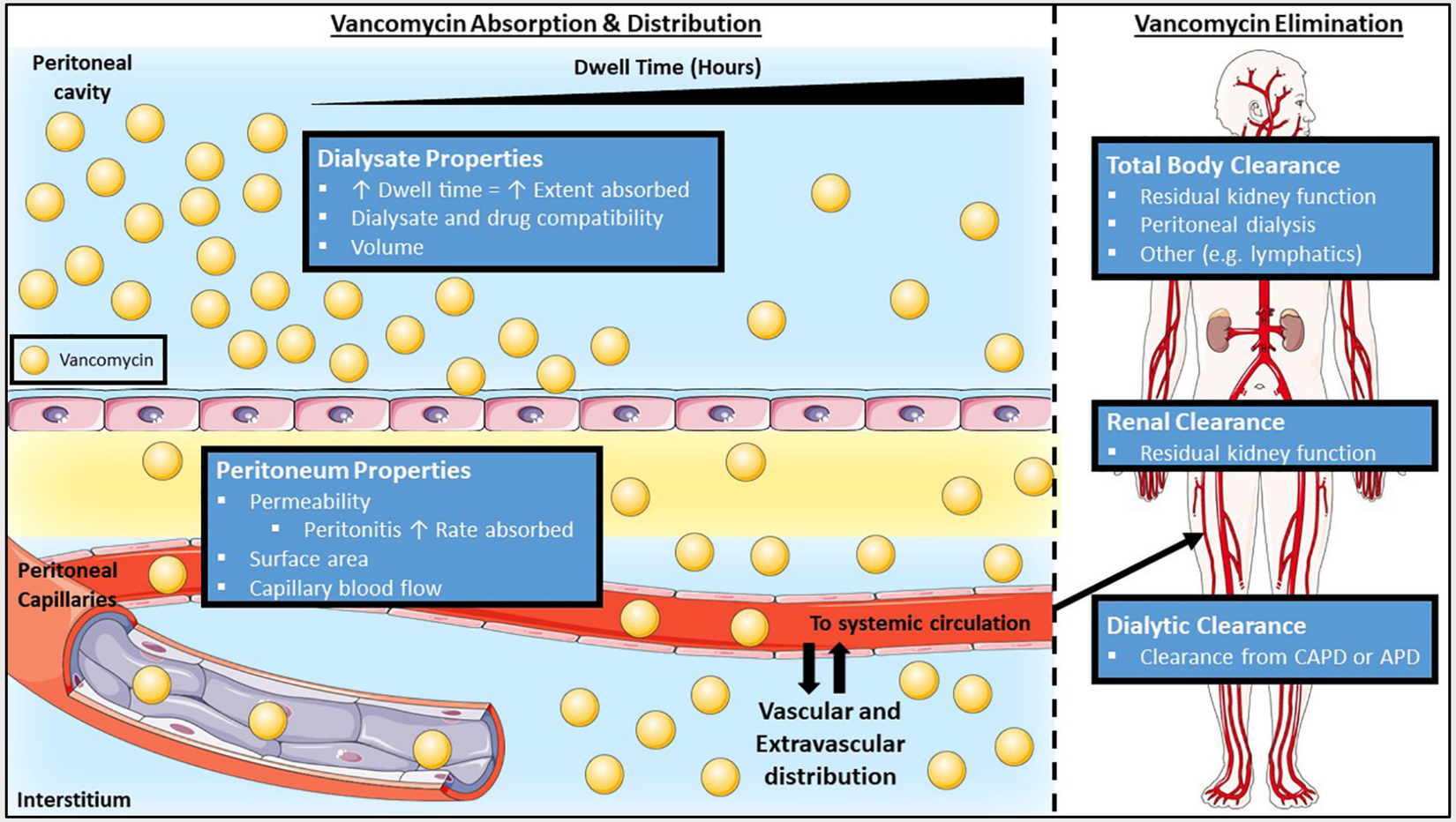
Therapeutic Principle

Ensure adequate local concentration of antibiotic in the peritoneal cavity to eliminate infection

- Intermittent Dosing
  - High concentration in 1 exchange each day
  - The body acts as a drug reservoir to deliver an adequate amount to the site of infection throughout the period between intermittent doses.
- Continuous Dosing
  - High concentration in all exchanges each day
  - Ensure that every PD bag is getting the correct amount of antibiotic

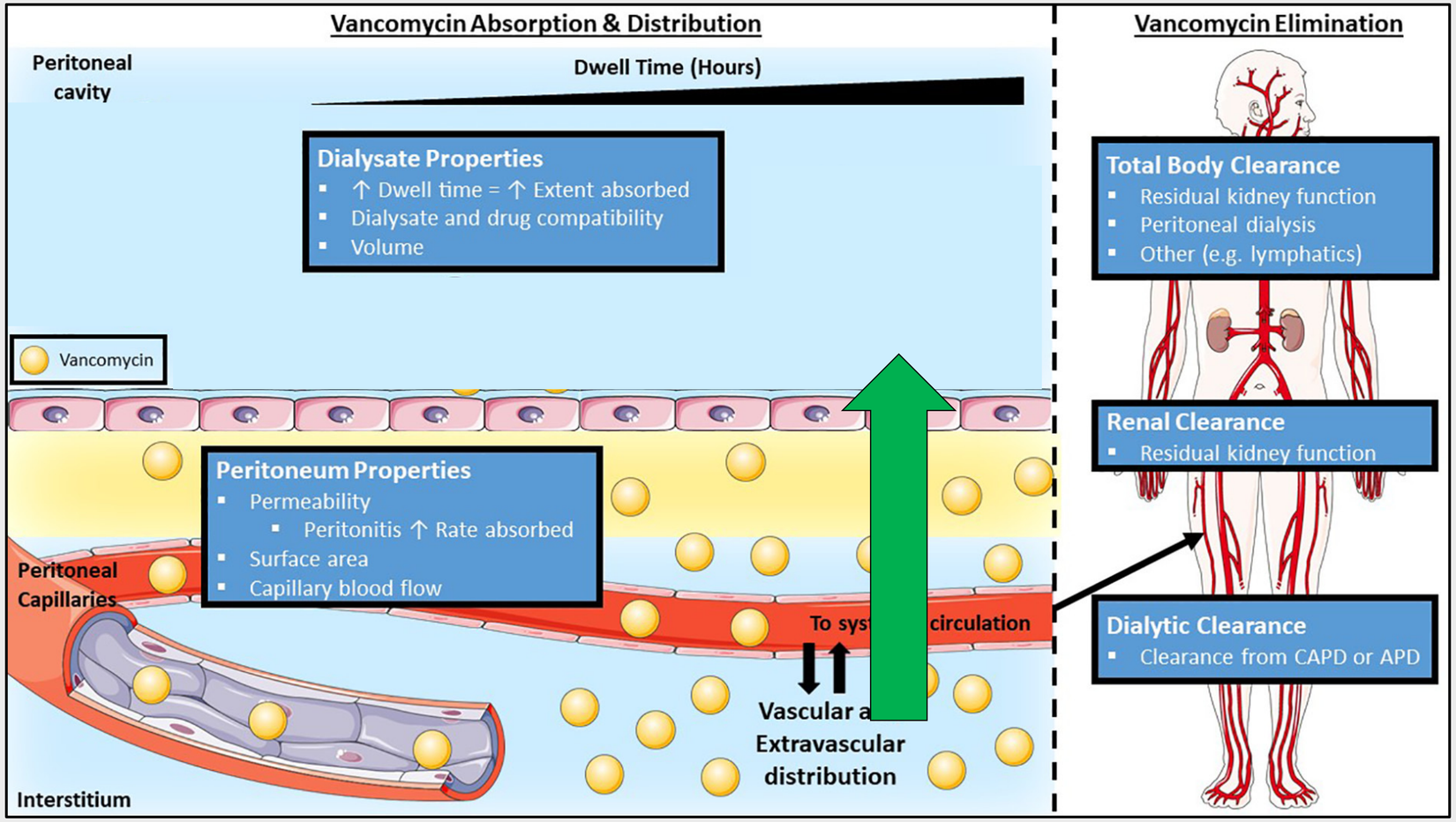
Golper T. Intermittent versus continuous antibiotics for PD-related peritonitis. Perit Dial Int. 1997 Jan-Feb;17(1):11-2. PMID: 9068015.

Pharmacology of Vancomycin in PD



Lam E, Lien YT (Kayla), Kraft WK, et al. Vancomycin in peritoneal dialysis: Clinical pharmacology considerations in therapy. Peritoneal Dialysis International. 2020;40(4):384-393. doi:10.1177/0896860819889774

Vancomycin must diffuse back into Peritoneal space during an exchange with no antibiotic



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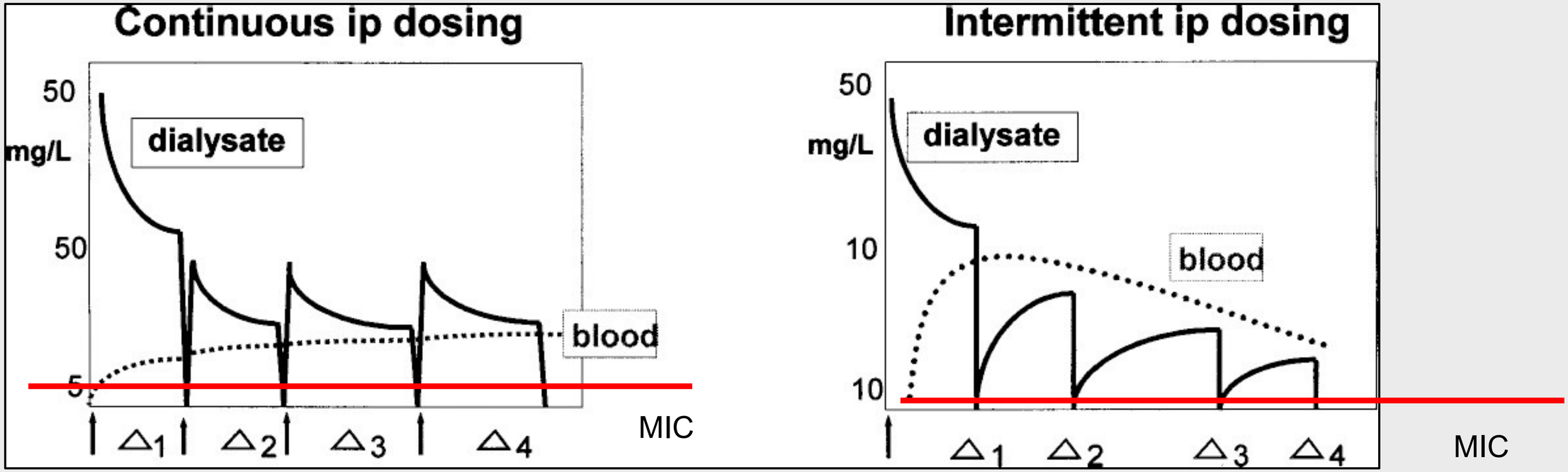
Modelled Drug Concentration in Intermittent vs Continuous Dosing



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Case 1 Treatment

- Empiric treatment:
- Continuous dosing regimen
  - 1g Ceftazidime IP in first exchange 500mg in each exchange thereafter
  - 2g Vancomycin IP in first exchange 50mg in each exchange thereafter
    - Following levels of vancomycin to maintain a level > 15 mg/L

- Await culture/cell count data to determine final antibiotics choice and course duration

Case 2

- 38 year old man, 70kg
- ESRD secondary to GPA on PD for about 6 months.
- Avid soccer player, sweats all the time, doesn’t clean the exit site well
- Presenting with cloudy fluid and abdominal pain
  - Current prescription CAPD is incremental
  - 2000cc Exchanges, 2-3x/day
  - Significant Residual Renal Function
  - Sleeps empty, or has other long periods of dry abdomen (playing soccer).
  - Even worse he does not dwell the full 2L volume each exchange

Case 2 Treatment

- Empiric treatment:
  - –1g Ceftazidime IP daily
  - –2g Vancomycin IP every other day to start
    - Following levels of vancomycin to maintain a level >15 mg/L
  - –Day 3 culture Methicillin resistant Staph Epi (MRSE)
    - He needed 2g Vanco daily to maintain level >15 mg/L
      - –Almost certainly was not dwelling 2L each exchange
      - –Cleared after 2 weeks of treatment

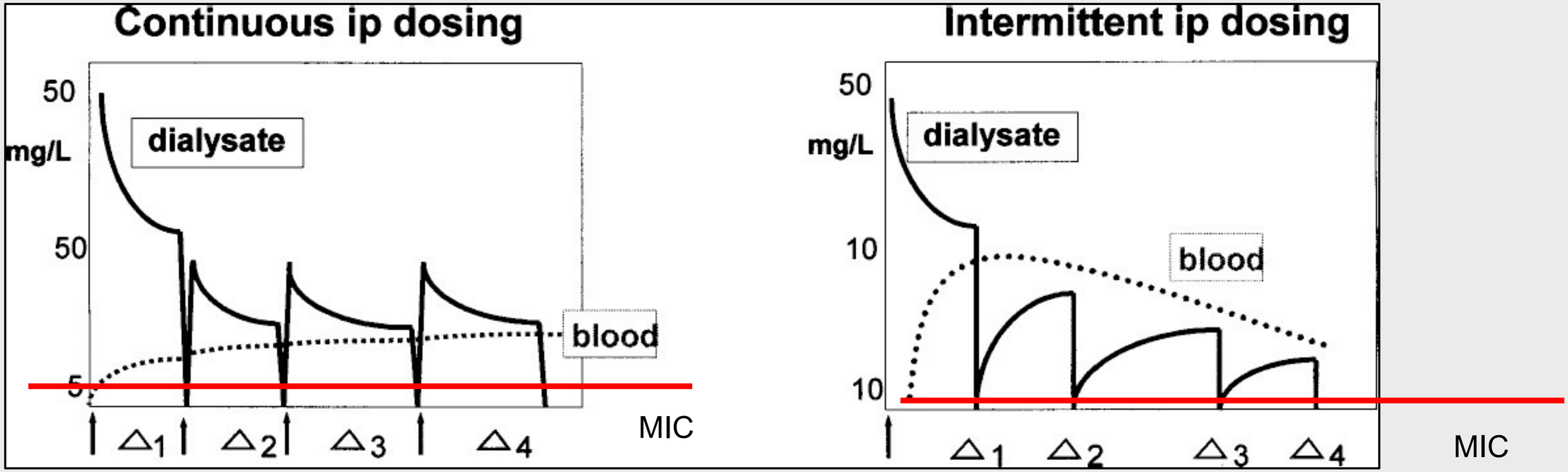
Case 3

- 78 year old man, 70kg
- ESRD secondary to Diabetic Nephropathy on PD for about 1.5 years.
- Presenting with cloudy fluid and abdominal pain
  - Current prescription APD
  - 2000cc x4 cycles at night
  - 2000cc last fill
  - Some Residual Renal Function

Case 3 Treatment Considerations

- Empiric Gram Positive and Gram Negative Coverage
- Switch to CAPD?
  - Some patients would switch to CAPD and can use the previously mentioned empiric intermittent or continuous regimens
  - Generally, most patients will want to stay on APD

Modelled Drug Concentration in Intermittent vs Continuous Dosing



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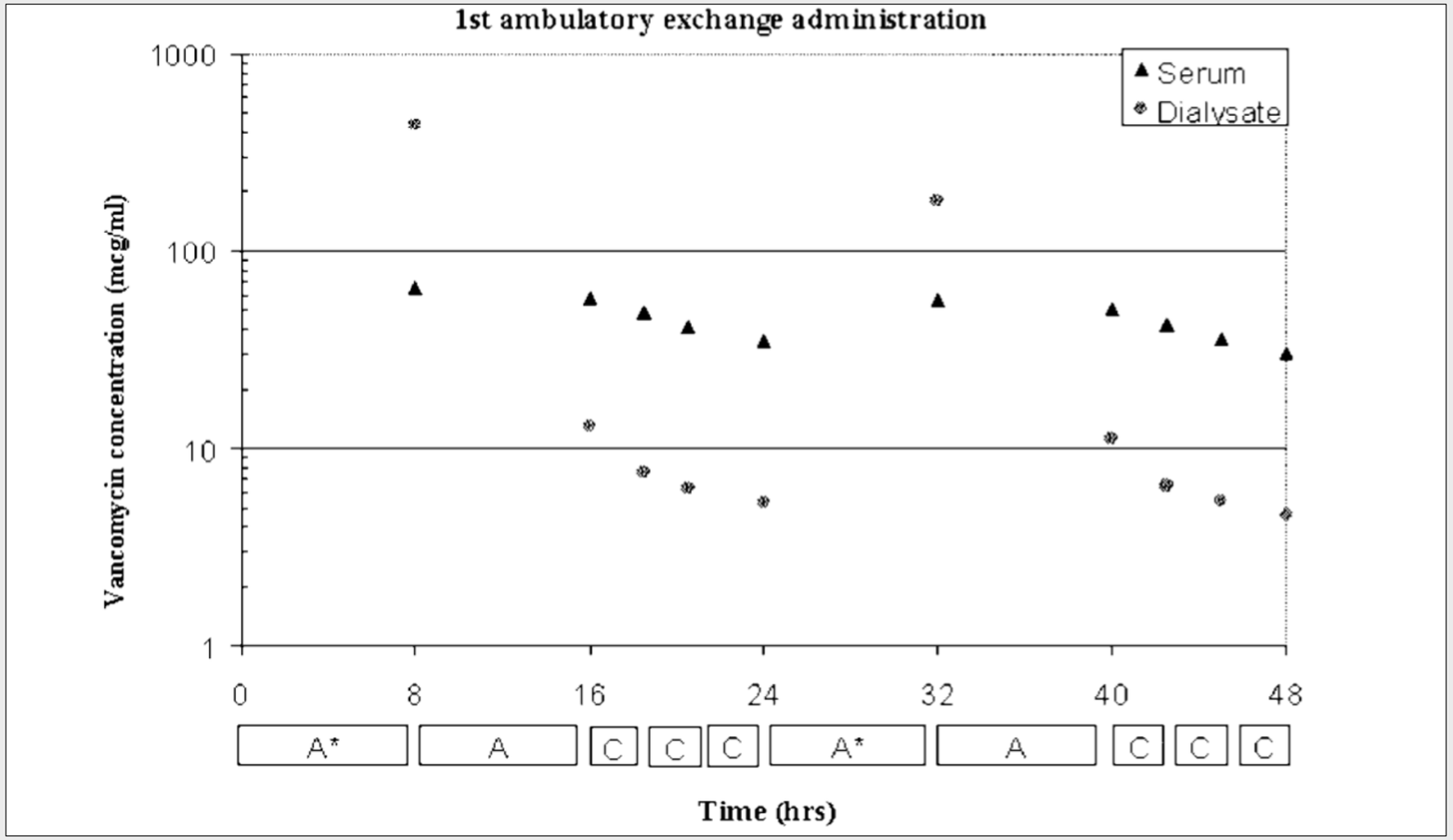
Pharmacologic Considerations in APD for Intermittent dosing of vancomycin



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Vancomycin dosing in APD

- Not clear what serum vancomycin trough level is necessary for peritonitis resolution.
- Dialysate levels of vancomycin are lower than serum levels.

TABLE 2
Vancomycin

Author/year	Type of study	Number of patients and peritonitis yes/no	Pharmacokinetic data	Outcomes
Manley 2001 (25)	Prospective observational Vancomycin 15 mg/kg given IV	10 APD no peritonitis	Yes	– Serum vancomycin and dialysate vancomycin levels above MIC only during 1st & 2nd dwell. – In APD vancomycin clearance is significant & daily IP dosing needed to provide adequate dialysate concentrations.
Fish 2012 (26)	Prospective observational Vancomycin 30 mg/kg IP Day 5 checked serum & dialysate vancomycin levels after a 4-h dwell	19 APD with peritonitis	Yes	– Serum vancomycin >12 mg/L 98% pts – Dialysate vancomycin <4 mg/L 23% pts – Conclude serum levels alone are not to be used to predict dialysate level due to low correlation coefficient – Suggest smaller more frequent dosing may be preferable
Mulhern 1995 (27)	Retrospective review Vancomycin 15 mg/kg IV Q week × 4	10 APD 21 CAPD All with peritonitis	Yes	– 9 episodes relapsed – Cumulative trough of <12 mg/L or initial day 7 trough <9 mg/L were predictive of relapse
Stevenson 2015 (28)	Retrospective cohort	3 APD 27 CAPD All with peritonitis	Yes	– Vancomycin levels were similar in patients achieving cure vs no cure – Conclude outcomes not associated with serum levels
Blunden 2010 (29)	Retrospective observational Vancomycin 25 mg/kg for anuric (increased by 25% for non-anuric	120 APD 267 CAPD All with peritonitis	Yes	– Vancomycin level did not predict cure or relapse of gram-positive or culture-negative peritonitis
Schaefer 1999 (30)	Prospective observational Vancomycin 30 mg/L continuous dosing vs initial loading dose 15 mg/kg followed by 2nd dose of 30 mg/kg after 7 days	152 pediatric pts with 166 episodes of bacterial peritonitis Both APD and CAPD utilized (no breakdown given on number of APD vs CAPD)	No	– No breakdown between outcomes of CAPD and APD pts Overall: – No difference in relapse rate continuous vs intermittent vancomycin – Eradication of causative organism more frequent in continuous vs intermittent at both 60 hours (p<0.001) and 7 days (p=0.004)

APD = automated peritoneal dialysis; IV = intravenous; MIC = minimum inhibitory concentration; IP = intraperitoneal; pts = patients; CAPD = continuous ambulatory peritoneal dialysis; pts = patients; Q week = weekly.

Mancini A, Piraino B. Review of Antibiotic Dosing with Peritonitis in APD. Peritoneal Dialysis International. 2019;39(4):299-305. doi:10.3747/pdi.2018.00209

Vancomycin dosing in APD

- Patients who relapsed had lower serum vancomycin levels (7.8 ± 0.6 mg/L during relapse vs 13.7 ± 0.9mg/L during relapse-free episodes p = 0.0004)
- No episodes of relapsing peritonitis were found in patients with a mean serum vancomycin trough of > 16 mg/L. This is higher than the 15 mg/L recommended by ISPD.

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Ceftazidime in APD

- ISPD guidelines recommend an intermittent once-daily dose
- Studied in CAPD but is widely extrapolated to APD.

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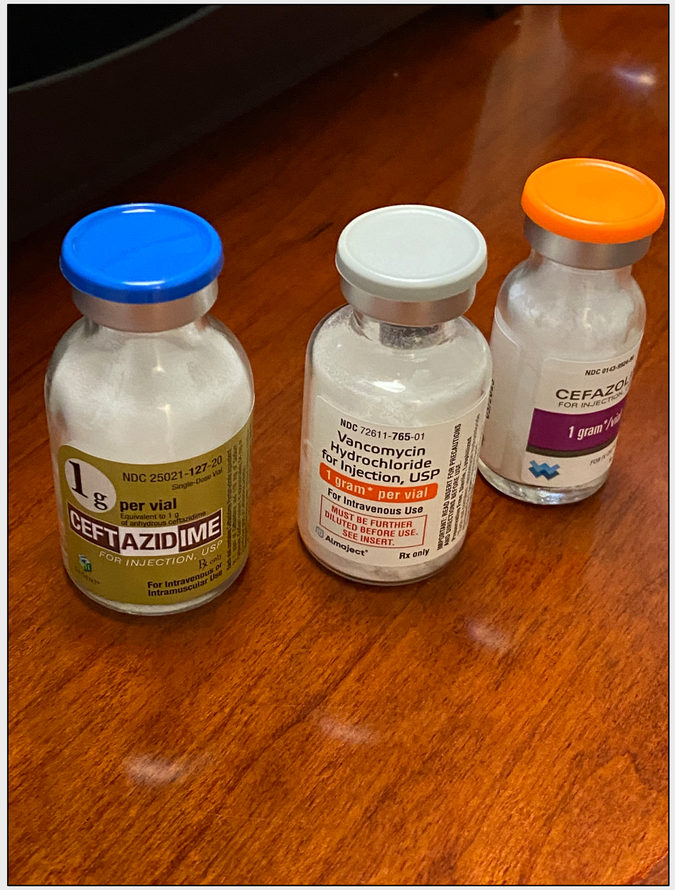
Case 3 Treatment

- Empiric Regimen:
  - 1g Ceftazidime daily in the long day dwell
  - 2g vancomycin every 3 days in the long day dwell
    - Following levels of vancomycin to maintain a level >15 mg/L

Considerations for the patient

- Ceftazidime/Cefazolin ISPD recommended continuous dosing
  - LD 500 mg/L, MD 125 mg/L



Conclusions

- Empiric antibiotics for PD peritonitis should focus on ensuring adequate coverage, dosing, delivery, and duration of medication
- CAPD patients are the reference case, intermittent vs continuous dosing can be used and advantages and disadvantages understood.
- Increased clearance with APD patients must be accounted for in terms of antibiotic dosing.

Questions?

- Questions?