



Fluids, Membranes, and Magic

The Fundamentals of Peritoneal Dialysis

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April 9th, 2026

Disclosures

The planner(s) and speaker(s) have indicated that there are no relevant financial relationships with any ineligible companies to disclose.

Learning Objectives

At the end of this session, learners should be able to:

- Recognize the physiologic mechanism of peritoneal dialysis, including solute clearance and ultrafiltration.
- Name the two common modalities of peritoneal dialysis and their place in therapy.
- Recall the benefits, limitations, and common complications associated with peritoneal dialysis.
- Identify the clinical resources available to guide management of antimicrobials for peritoneal dialysis-related peritonitis.

Outline

1. An Overview of Peritoneal Dialysis

- Understanding Peritoneal Dialysis
- Peritoneal Dialysis Modalities
- Peritoneal Dialysis versus Hemodialysis
- Peritoneal Dialysis in the Hospital

2. Peritonitis

- Peritoneal Dialysis-Associated Peritonitis
- Exit-Site Care
- Empiric Treatment
- Culture-Specific Peritonitis Treatment
- Secondary Prophylaxis: Antifungals
- Subsequent Management of Peritonitis

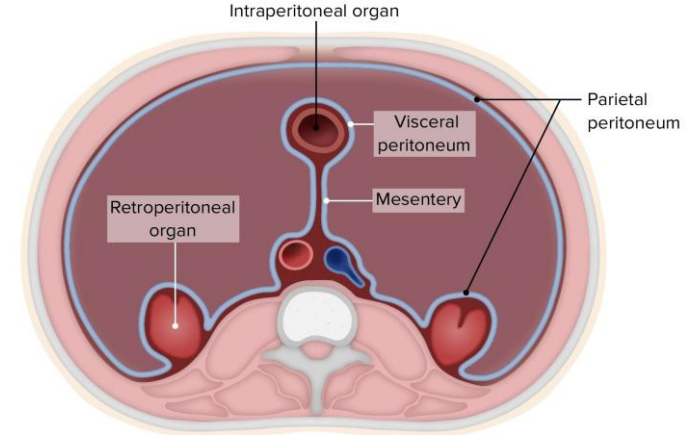
Abbreviation Key

- APD: Automated Peritoneal Dialysis
- CAPD: Continuous Ambulatory Peritoneal Dialysis
- CI: Confidence Interval
- GI: Gastrointestinal
- HD: Hemodialysis
- IP: Intraperitoneal
- ISPD: International Society for Peritoneal Dialysis
- LD: Loading dose
- MD: Maintenance dose
- MRSA: Methicillin resistant *Staphylococcus aureus*
- PD: Peritoneal Dialysis
- SBP: Spontaneous Bacterial Peritonitis

Understanding Peritoneal Dialysis (PD)

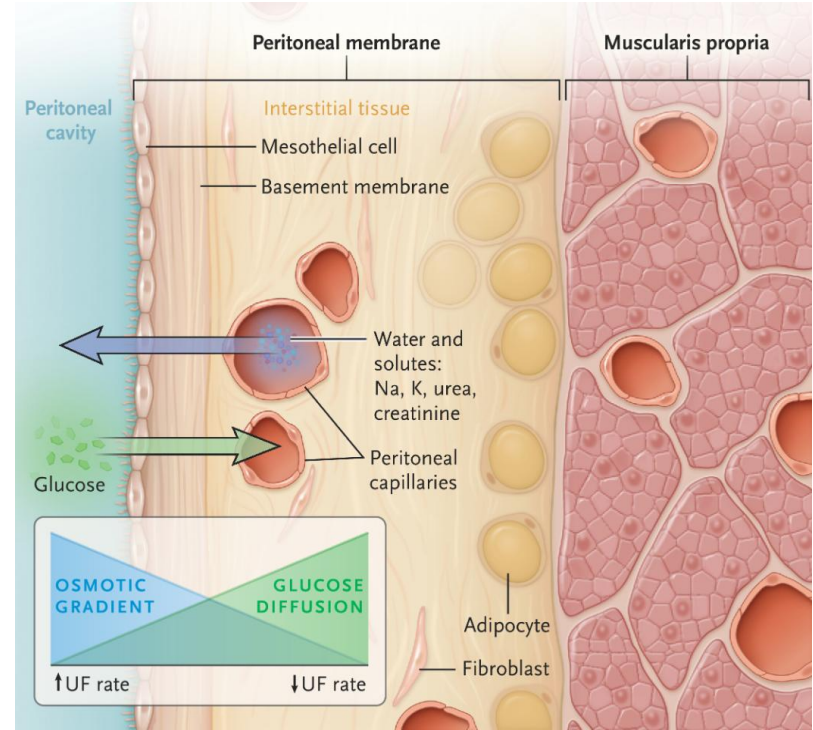
The Peritoneal Membrane

- A two-part membrane that encloses the abdominal cavity
 - Visceral peritoneum – covers the abdominal organs
 - Parietal Peritoneum – lines the abdominal wall and underside of diaphragm
- A single layer of mesothelial cells sits atop vascular interstitial tissue

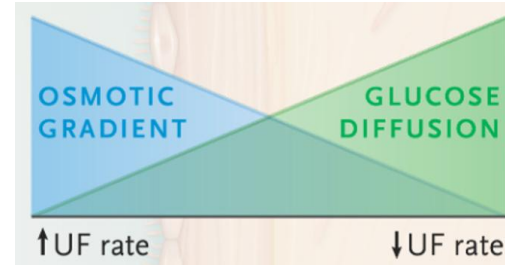


The Concept of PD

- Solutes diffuse across the thin layer of mesothelial cells and into or out of the peritoneal capillaries
- Water transport is dependent on the pressure gradient created by the dialysate

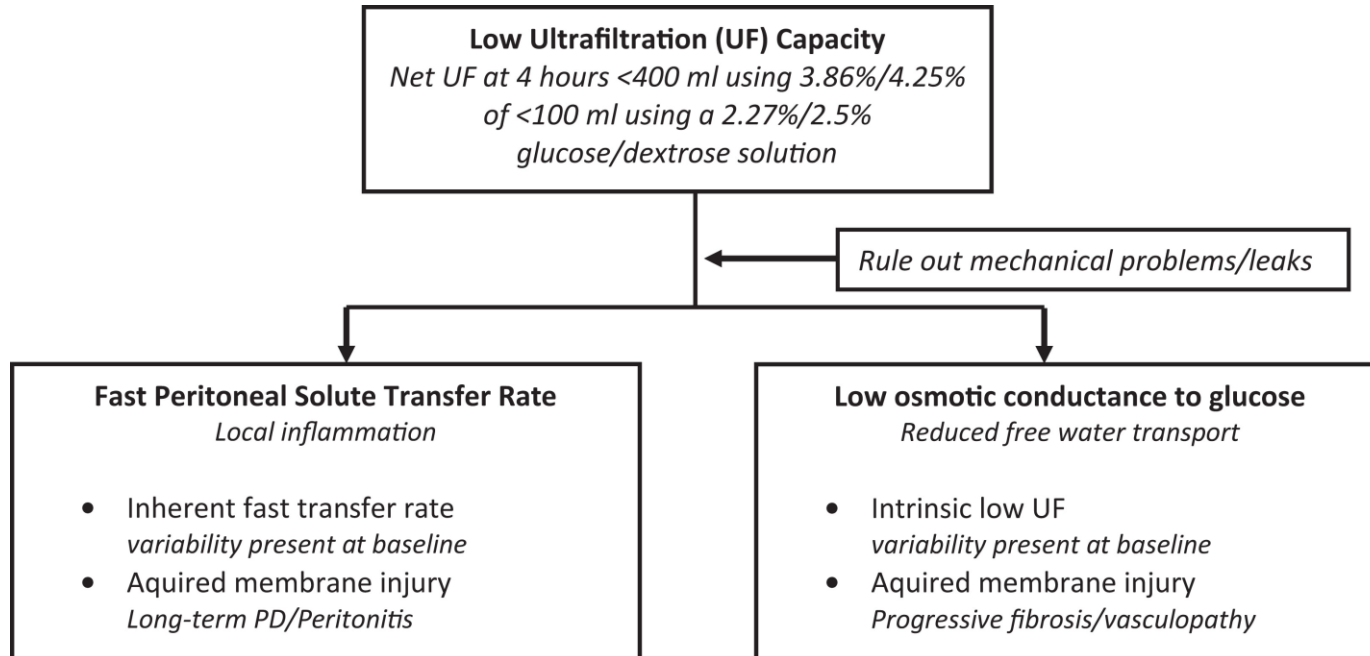


Ultrafiltration



- PD fluid is a hypertonic solution
- Different concentrations of glucose drive different rates of fluid removal, or ultrafiltration
- As fluid moves to the dialysate and glucose moves into the blood, the osmotic gradient is depleted and ultrafiltration slows
 - Patients with more peritoneal vascularity have less successful ultrafiltration during long dwells
 - Icodextrin may improve ultrafiltration in these patients

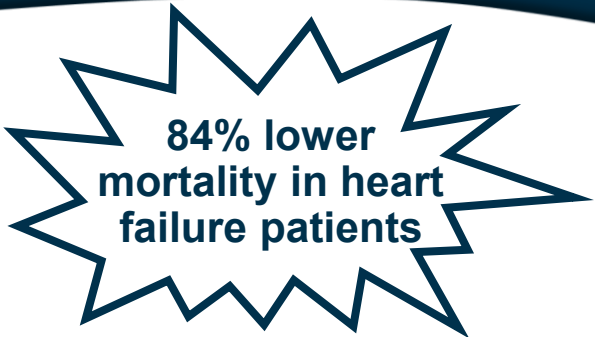
Monitoring Efficacy



Peritoneal Dialysate Contents

- Osmotic agent
 - Dextrose 1.5%, 2.5%, and 4.25%
 - Icodextrin 7.5%
- Electrolytes
 - Sodium, magnesium, chloride
 - Calcium – standard and low concentrations
- Buffer
 - Lactate

Icodextrin

A starburst graphic with a dark blue outline and a white fill, containing text.

84% lower
mortality in heart
failure patients

- A large polymer, icodextrin maintains an osmotic gradient better than glucose
- Use of icodextrin during one long-dwell each day improves long term survival and decreases uncontrolled fluid overload
- Patients who use icodextrin absorb 40g less glucose per dwell
 - This has not been reflected in fasting glucose levels and A1c
- Expensive – maximize glucose-containing fluids first

Pharmacokinetic Impact

- PD is not an effective means of systemic drug elimination
- Effective drug removal requires a low volume of distribution, a small molecular size, and low protein binding
 - Aminoglycosides and some cephalosporins
- Patients often do not require supplemental doses after PD is completed
- Vancomycin
 - ~25%-40% of total drug is removed during an HD session
 - PD patients may be able to go as long as 7 days between doses

Assessment Question #1

AK is not achieving adequate ultrafiltration during her overnight dwell, and often ends the night with minimal fluid removal. She is utilizing Dianeal PD-2/2.5% Dextrose dialysate fluid. Which of the following would be a potential solution to this problem?

- A. Decrease the dextrose concentration
- B. Switch to an icodextrin-based dialysate
- C. Decrease the dwell volume
- D. Increase the dwell time

Peritoneal Dialysis Modalities

CAPD versus APD

Continuous Ambulatory Peritoneal Dialysis (CAPD)

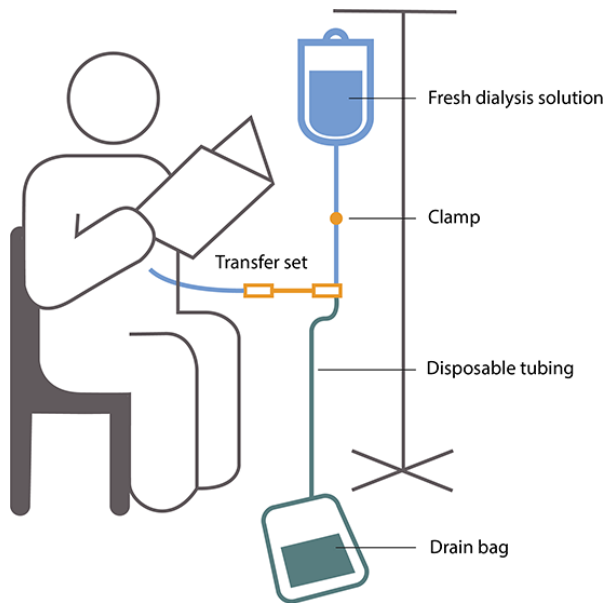
- Typically 3-6 gravity exchanges per day
- 4-6 hours per dwell
- Does not require electricity
- Each exchange takes about 40 minutes

Automated Peritoneal Dialysis (APD)

- A cycler machine automatically exchanges PD fluid multiple times over several hours
- Usually done overnight, but a dwell can be added during the day as renal function declines

CAPD versus APD

CAPD



APD



CAPD versus APD

- There is no solid evidence supporting a mortality difference between modalities
- APD has been shown to have lower risk of peritonitis
- APD may accelerate loss of residual kidney function, but data is conflicting
- APD may be better for highly vascular patients due to shorter dwell times

Teitelbaum I. *NEJM*. 2021;385(19):1786-1795.

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Peritoneal Dialysis vs Hemodialysis

Hemodialysis

- Blood is removed from the body and flows through a dialyzer
- A concentration gradient between blood and dialysate drives solute diffusion
- Fluid removal can be performed by increasing hydrostatic pressure within the dialyzer
- Usually done for 4 hours, 3 times a week, most often in a clinic setting
- Studies have shown no clear survival or quality of life difference

Complications

Hemodialysis (HD)

- Catheter-related bloodstream infections (54%)
- Hemodynamic instability
- Heart failure exacerbations
- Fatigue
- Arrhythmias

Peritoneal Dialysis (PD)

- Peritonitis (28%)
- Hyperglycemia
- Peritoneal sclerosis
- Abdominal/back pain
- Catheter leak

Lifestyle Impact

HD

- Usually requires clinic visits
- Requires less patient/caregiver knowledge
- 4 dialysis-free days a week
- Easy for trained personnel to control dialysis parameters

PD

- Done at home
- The patient and/or caregiver must be able to manage the exchanges independently
- A daily commitment
- Parameters such as ultrafiltration rates are more difficult to acutely adjust

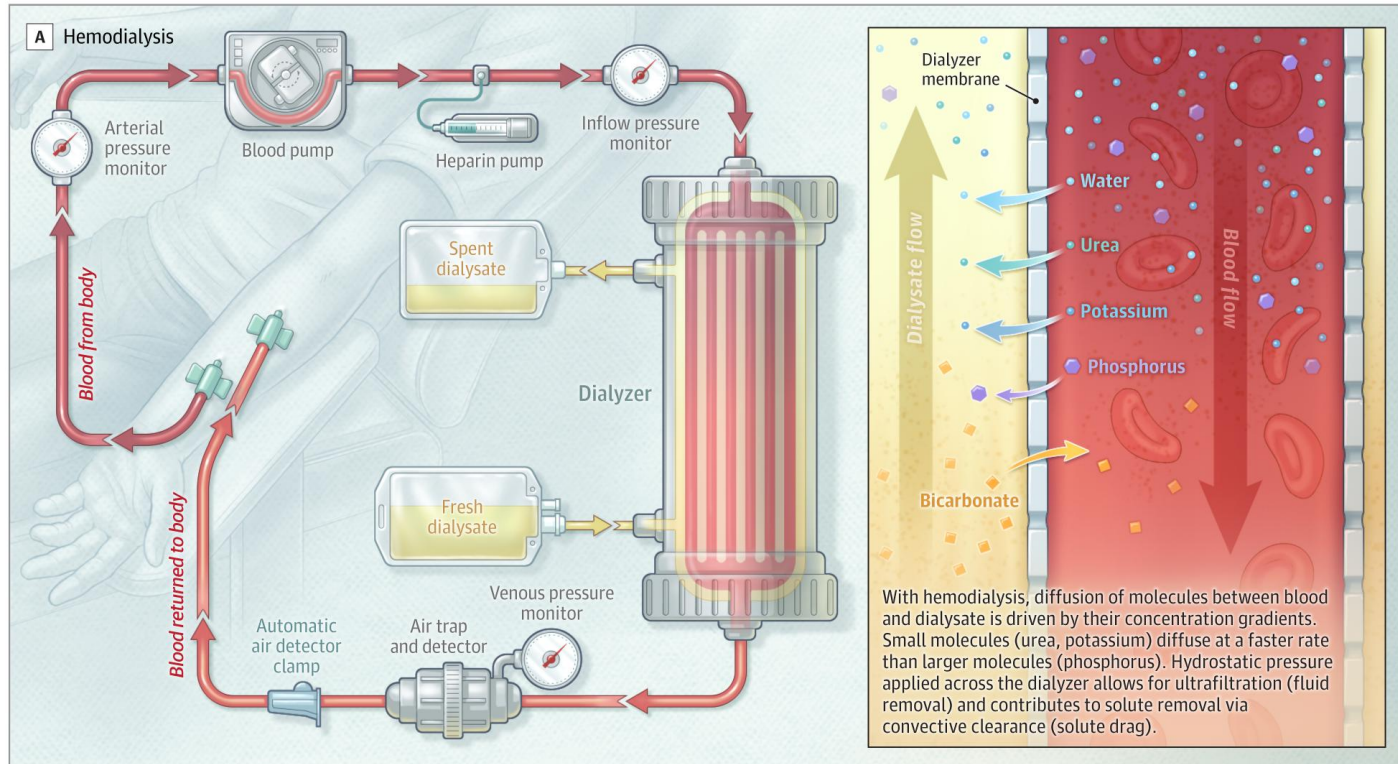
PD Contraindications

- An unclean home environment to perform exchanges
- Patient and/or caregiver unable to effectively manage PD at home
- A peritoneum that is severely scarred or has many adhesions
- Other issues may be perceived as barriers but have available solutions

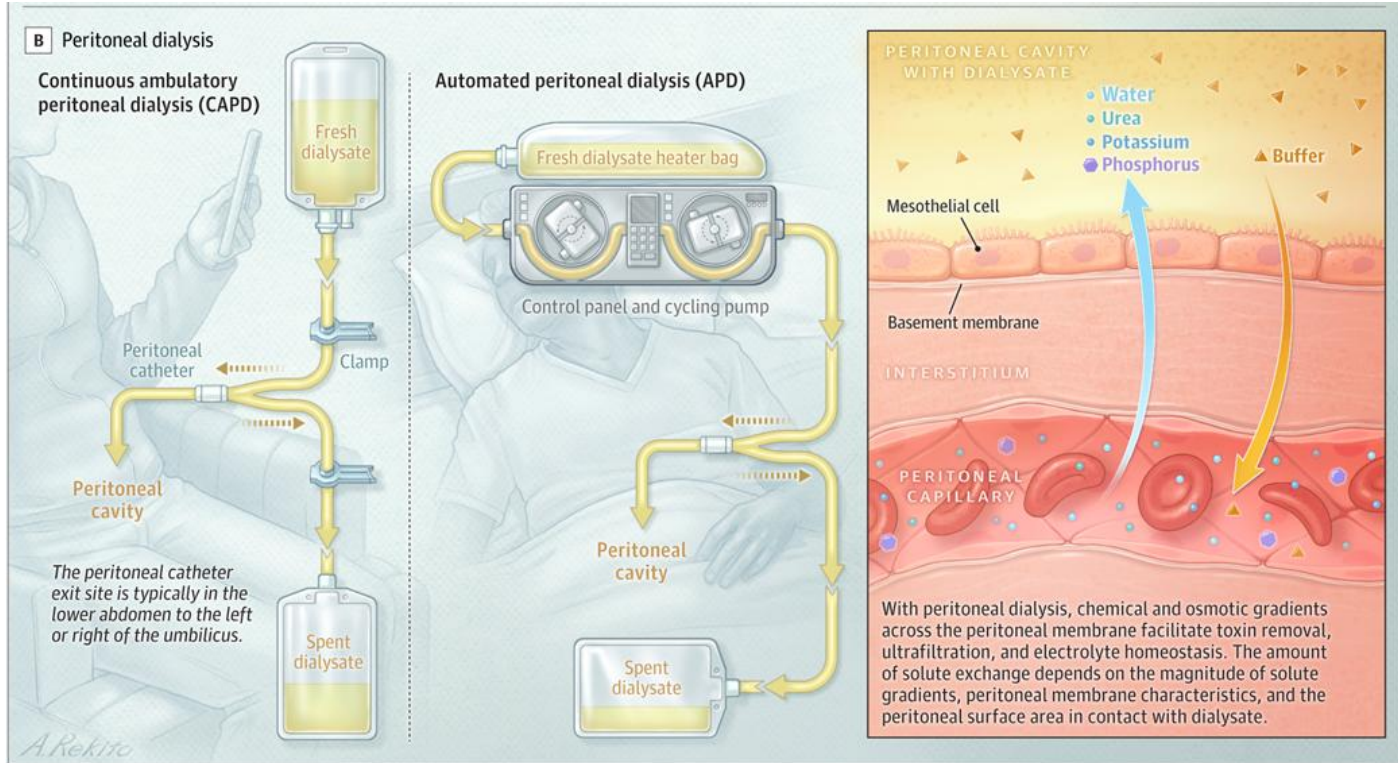
PD Barriers

Barrier	Solution
Morbid Obesity	A presternal catheter that exits through the chest bypasses the abdominal wall.
Polycystic Kidney Disease	Frequent low-volume exchanges minimize pressure in the abdominal cavity.
Ostomy	Presternal catheters maximize distance between the ostomy and exit site, decreasing contamination.
Severe Cognitive/Physical Impairment	Management of PD by a caregiver allows these patients greater freedom.

Hemodialysis Mechanism

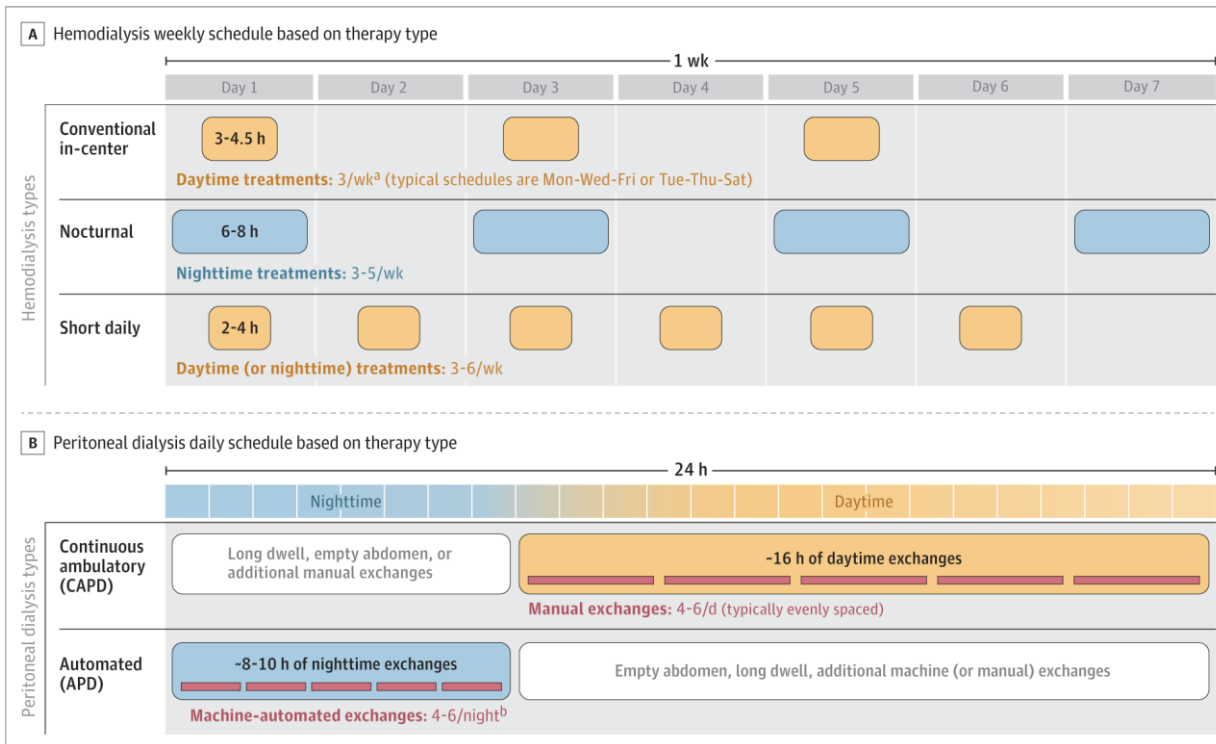


Peritoneal Dialysis Mechanism



Patient Schedule

HD



PD

Pharmacist Considerations During Hospitalization

Medication Considerations

- Remember: PD is not an effective means of drug removal
- Drug dosing is dependent upon residual kidney function
- Medications that are administered intraperitoneally achieve rapid systemic circulation
 - Always consider drug stability and compatibility within the dialysate
- Protect residual kidney function by screening for nephrotoxins
 - Avoid NSAIDs and iodinated contrast media when possible

Metabolic Disturbances

- Up to 55% of PD patients develop a metabolic derangement
- PD fluids usually contain glucose, which is absorbed into the blood
- Hyperglycemia is common
 - Monitor glucose levels and insulin needs
 - PD glucose concentrations may change due to ultrafiltration requirements
- Supplement potassium for hypokalemia

PD in Epic

- There is a NEPH IP Peritoneal Dialysis order set in Epic
- Ordering provider selects the PD modality and selects an appropriate dialysate solution
 - Multiple solutions can be selected (i.e. if the patient uses Dianeal PD-2/1.5% Dextrose during the day and Icodextrin 7.5% at night)
- Additives include heparin, lidocaine, insulin, antibiotics, and electrolytes
- Specify exchange volume, cycles per day, and dwell times

Pharmacist Tips

- If multiple dialysate fluids are used, the order of use should be in the administration instructions
- Manual PD exchanges are able to use partial bags by using a hanging scale to track instillation volume
- Ensure compatibility of additives
 - Cross check when multiple additives are ordered
- If modifications are made during verification, every other dialysate bag order must be modified at the same time

Assessment Question #2

HA is an at-home PD patient. She is experiencing a lithium overdose, and the medical team wants to enhance drug clearance with dialysis. Which dialysis modality would be the best option for drug clearance?

- A. Continue her PTA CAPD as prescribed
- B. Continue her PTA CAPD but increase the exchanges
- C. Switch to APD
- D. Switch to HD

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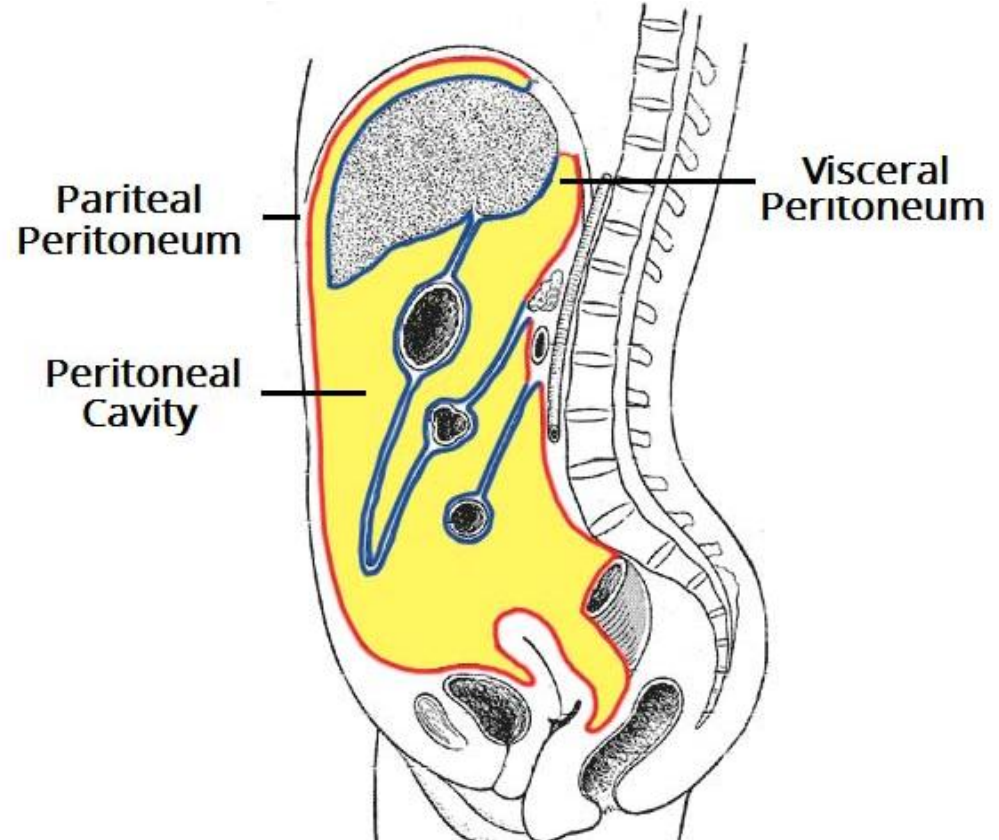
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Peritonitis

Peritonitis

- Inflammation of the peritoneum



Categories of Infective Peritonitis

- Primary
 - Infection not directly related to intra-abdominal abnormalities
 - Spontaneous bacterial peritonitis (SBP)
- Secondary
 - Infections that can result from a variety of intra-abdominal events
- Tertiary
 - Peritonitis and sign of sepsis are present after treatment
- PD-associated

Peritoneal Dialysis-Associated Peritonitis

PD Peritonitis Guidelines

Special Series/Guidelines

PERITONEAL
DIALYSIS
INTERNATIONAL



ISPD peritonitis guideline recommendations: 2022 update on prevention and treatment

Peritoneal Dialysis International
2022, Vol. 42(2) 110–153

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DOI: 10.1177/08968608221080586

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Goals of Treatment

Medical Cure

Prevent Complications

Salvage Catheter (if able)

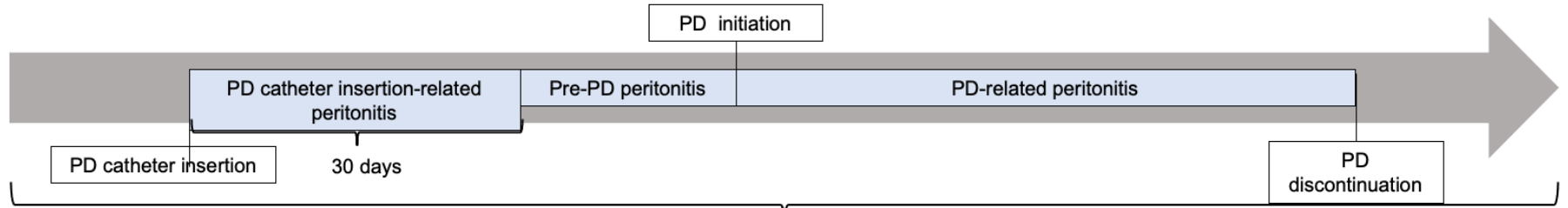
Diagnosis

- When two of the following are present:
 1. Clinical features consistent with peritonitis (i.e. abdominal pain and/or cloudy dialysis effluent)
 2. Dialysis effluent white cell count $> 100/\mu\text{L}$ or $> 0.1 \times 10^9/\text{L}$ (after dwell time of at least 2 hours) with $> 50\%$ polymorphonuclear leukocytes
 3. Positive dialysis effluent culture

Cause-specific Peritonitis

- Culture-negative peritonitis: no organism on culture
- Catheter-related peritonitis: within 3 months of a catheter infection with the same organism
- Enteric peritonitis: occurring from an intestinal source

Time-specific Peritonitis



Risk Factors

- Hypokalemia
- GI problems such as constipation, enteritis, GI bleed
- Histamine-2 receptor antagonists use
- Endoscopic gastrointestinal and invasive or instrumental gynecological procedures
- Improper PD technique/training
- Domestic pets

Exit-Site Care

Catheter-related Infections

PERITONEAL
DIALYSIS
INTERNATIONAL



Special Series/Guidelines

ISPD Catheter-related Infection Recommendations: 2023 Update

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Peritoneal Dialysis International

1–19

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DOI: 10.1177/08968608231172740

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Exit-Site Care

- Daily topical antibiotic cream or ointment to catheter exit site is recommended (1C)
- Mupirocin vs gentamicin
 - Exit-site vs nasal mupirocin

Exit-Site Antibiotic Prophylaxis

Study	Design	Intervention	Results
Tacconelli et al., 2003 USA and Israel n = 2445	Meta-analysis 10 studies	Mupirocin vs placebo/no intervention	<i>S. aureus</i> infections (peritonitis and exit site) risk reduced by 63% (P < 0.001) <i>S. aureus</i> peritonitis risk reduced by 66% (P < 0.001)
Xu et al., 2010 China n = 2450	Meta-analysis 14 studies	Mupirocin vs placebo/no intervention	Peritonitis due to <i>S. aureus</i> risk reduced by 70% (P < 0.00001) Peritonitis due to all organisms risk reduced by 41% (P < 0.0001)
Obata et al., 2020 Japan n = 657	Systemic review and Meta-analysis of Randomized Control Trials 6 studies	Mupirocin vs no antibiotic ointment and mupirocin vs gentamicin	Uncertain the effect of mupirocin in prevention of peritonitis (95% CI: 0.05-1.21) No difference in mupirocin vs gentamicin (95% CI: 0.32-2.26)

Bernardini et al., 2005
USA
n = 133

Randomized, double-blind trial

Mupirocin vs gentamicin

Gentamicin was as effective as mupirocin in preventing *S. aureus* infections (P = 0.44)

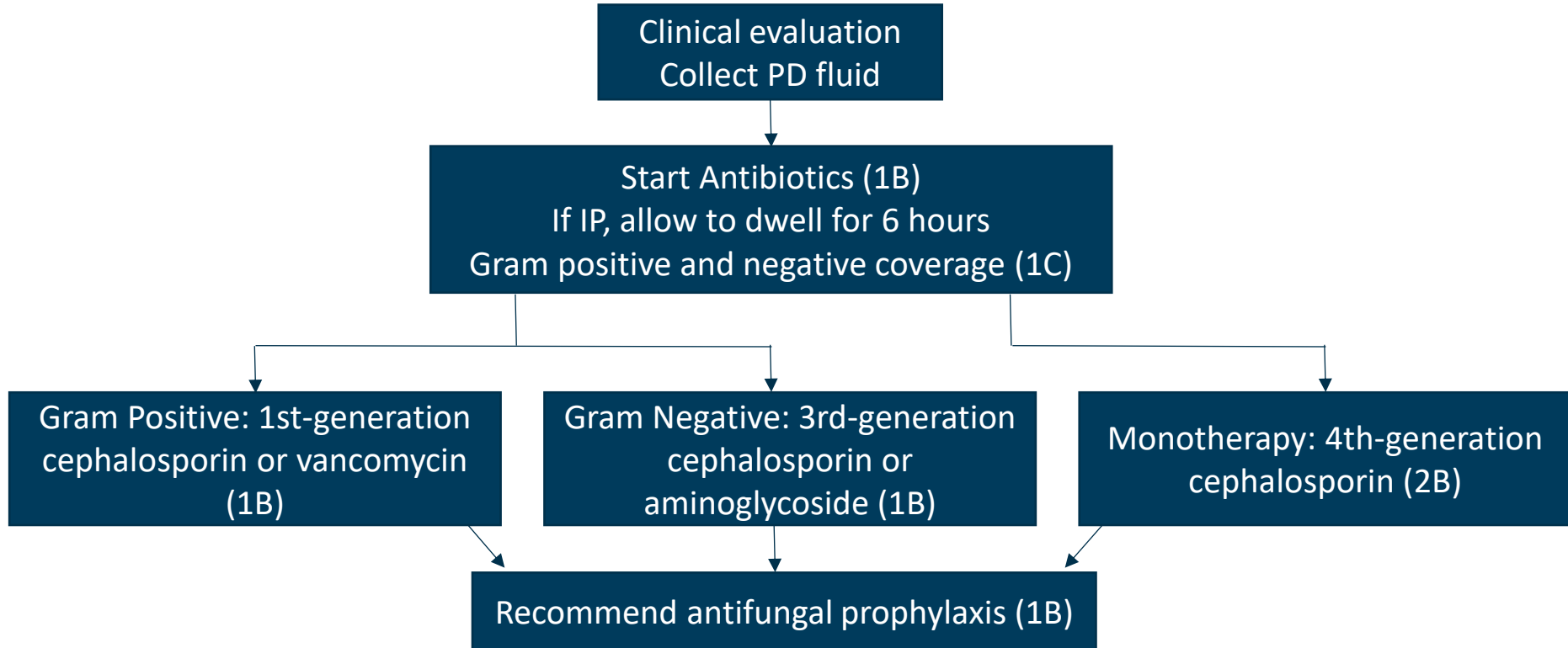
Catheter infection rates: 0.23/year with gentamicin vs 0.54/year with mupirocin (P=0.005)

COSMO-PD Trial

- Multi-center, double blind randomized controlled trial in Thailand
- Local application of chlorhexidine gluconate, mupirocin ointment and normal saline for PD-related infection prevention
- Currently in progress

Empiric Treatment

Empiric Treatment



IP Antibiotic Dosing

Antibiotic	Intermittent (Usually Once Daily)	Continuous (every PD bag)
Amikacin	2 mg/kg daily	Not advised
Gentamicin	0.6 mg/kg daily	Not advised
Tobramycin	0.6 mg/kg daily	Not advised
Cefazolin	15 mg/kg daily (for long dwell) 20 mg/kg daily (for short dwell)	LD: 500 mg/L MD: 125 mg/L
Cefepime	1000 mg daily	LD: 500 mg/L MD: 125 mg/L
Cefotaxime	500–1000 mg daily	No data
Ceftazidime	1000–1500 mg daily (for long dwell) 20 mg/kg daily (for short dwell)	LD: 500 mg/L MD: 125 mg/L
Ceftriaxone	1000 mg daily	No data
Vancomycin	CAPD: 15–30 mg/kg every 5–7 days APD: 15 mg/kg every 4 days	LD: 20–25 mg/kg MD: 25 mg/L

IP Antibiotic Stability

Antibiotic	Dextrose based PD-solution	Icodextrin based PD-solution	Stability	Room Temperature	Refrigerated
Gentamicin	X		14 days	X	X
		X	14 days	X	X
Cefazolin	X		8 days	X	
	X		14 days		X
		X	7 days	X	
		X	14 days		X
Ceftazidime	X		4 days	X	
	X		7 days		X
		X	2 days	X	
		X	14 days		X
Cefepime	X		14 days		X
Vancomycin	X		28 days	X	
		X	14 days	X	X

Culture Specific Peritonitis Treatment

Coagulase-Negative *Staphylococcus*

Coagulase-Negative *Staphylococcus* on culture

De-escalate/optimize antibiotics

Repeat cell count and culture at day 3

Clinical improvement: continue IP antibiotics for 14 days (2C)

No clinical improvement by 5 days: surgically remove PD catheter (1D) then continue treatment for 14 days

Staphylococcus aureus

Staphylococcus aureus on culture

De-escalate/optimize antibiotics

Repeat cell count and culture at day 3

Clinical improvement: continue IP antibiotics
for 21 days (2C)

No clinical improvement by 5 days: surgically
remove PD catheter (1D) then continue
treatment for 14 days

Streptococci

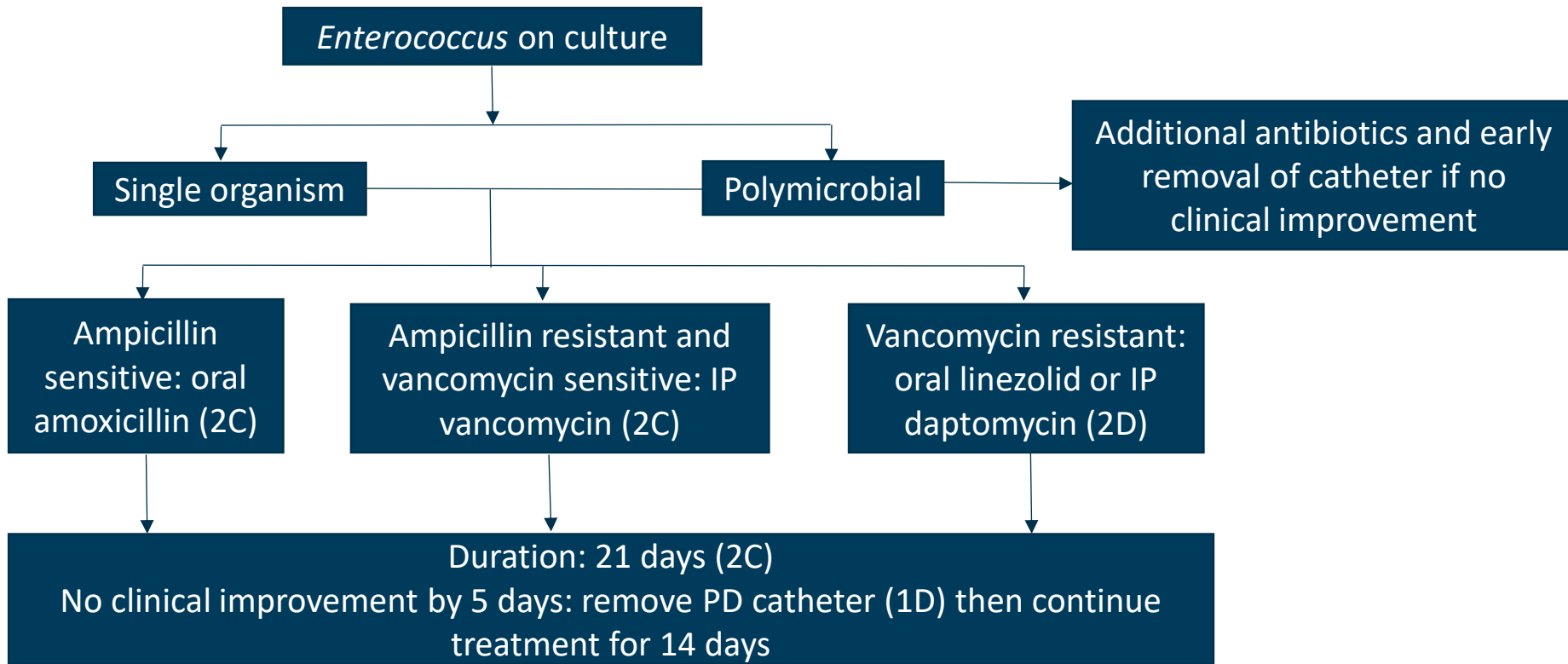
Streptococcus on culture

De-escalate/optimize antibiotics

Clinical improvement: continue IP antibiotics
for 14 days (2C)

No clinical improvement by 5 days: surgically
remove PD catheter (1D) then continue
treatment for 14 days

Enterococcus



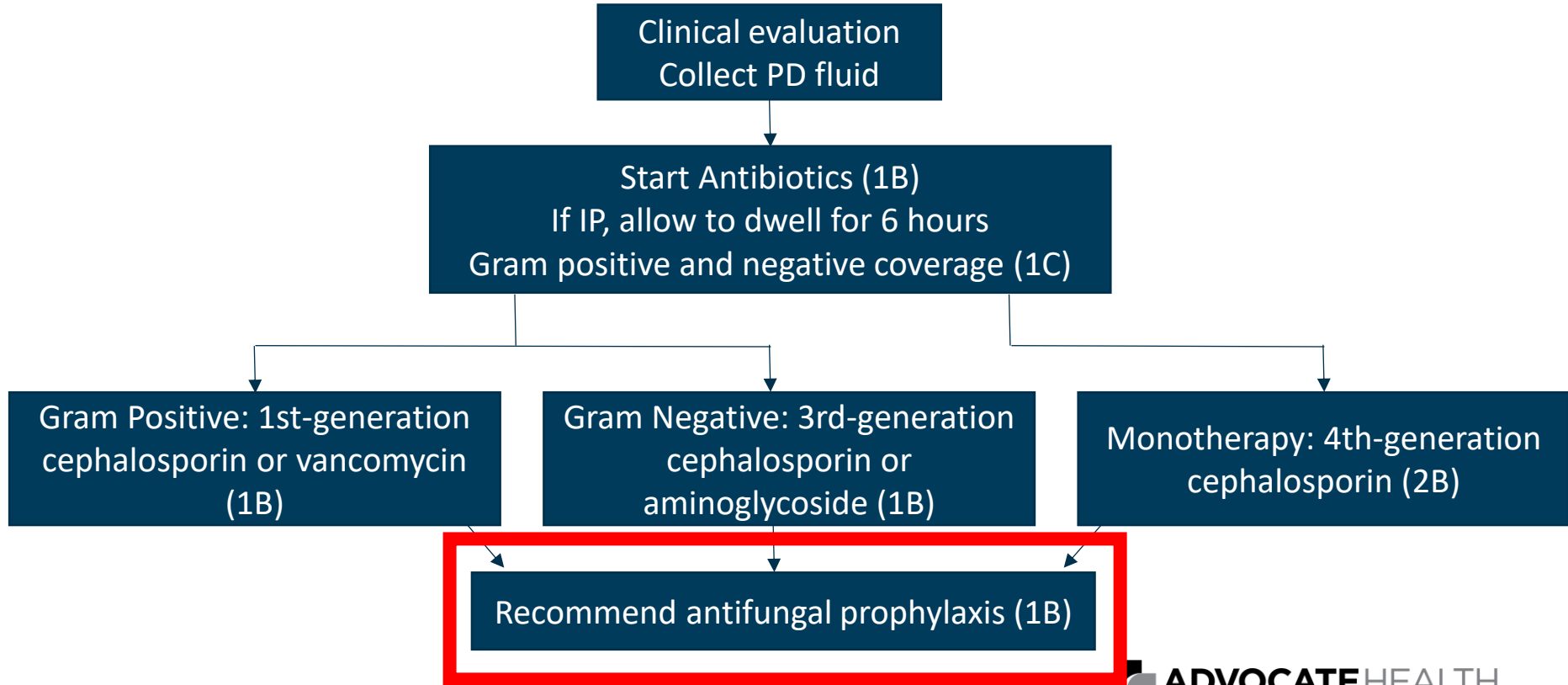
Assessment Question #3

GB, a patient on PD, presents to the ED with abdominal pain and cloudy dialysis effluent. The fluid is sent and cultures are obtained. The culture results positive for MRSA within two days. Vancomycin is started. After two days, GB begins clinically improving. Which of the following is the recommended antibiotic duration?

- A. 14 days
- B. 7 days
- C. 21 days
- D. 5 days

Secondary Prophylaxis: Antifungal

Empiric Treatment



Antifungal Prophylaxis

Study	Design	Intervention	Results
Lo et al., 1996 Hong Kong n = 397	Randomized Control Trial	Nystatin 500,000 units 4 times daily (group 1) vs no antifungal (group 2)	4 episodes of fungal peritonitis in group 1 vs 12 episodes in group 2 Probability of candida peritonitis free survival at 2 years was higher in group 1 (P < 0.05)
Restrepo et al., 2010 Colombia n = 434	Randomized Control Trial	Fluconazole 200 mg every 48 hours vs no antifungal	0.92% of fluconazole patients had fungal peritonitis vs 6.46% in the no antifungal group (P = 0.0051)
Kumar et al., 2014 India n = 142	Observational cohort comparing 2 time periods	No prophylactic antifungal (period I) vs fluconazole (period II)	Period I: 18 of 102 episodes were fungal peritonitis (17.6%) Period II: 2 of 40 episodes were fungal peritonitis (5%) P = 0.04

Antifungal Dosing

Antifungal	Oral
Fluconazole	LD: 200 mg MD: 100 mg daily
Nystatin	500,000 units 3 or 4 times daily

Same duration as the antibiotic course
(May extend by 3 days after last aminoglycoside dose or 7
days after last vancomycin dose)

Assessment Question #4

A patient presents with PD-associated peritonitis prior to culture results. Which resource is most appropriate to guide empiric antibiotic recommendations?

- A. Hospital antibiogram
- B. IDSA guidelines for Skin and Soft tissue Infections
- C. International Society for Peritoneal Dialysis Peritonitis Guidelines
- D. The Sanford Guide to Antimicrobial Therapy

Summary/Conclusion

- Peritoneal dialysis is an effective but infrequently utilized means of renal replacement therapy
- CAPD and APD offer distinct benefits and drawbacks that should be considered when selecting a modality
- PD introduces unique challenges for pharmacists
- Infective peritonitis treatment should be adjusted based on culture growth and sensitivities
- Antifungal prophylaxis should be given whenever PD patients receive an antibiotic course

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Questions?

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