Preventing Peritonitis:

Why do some do it better? Reducing Risks in PD

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Peritonitis Rates Around the World

Piraino et al, ISPD Position Statement on the role of reducing the risks of peritoneal dialysis-related infections. PDI 31(6) 2011

country	reference	year	# centers or #pts	episodes /yr
Taiwan	Tzen-Wen	2008	100 adults	0.06
Japan	Hoshii	2006	130 children	0.17
China	Fang	2008	496 adults	0.20
Japan	Nakamoto	2006	139 adults	0.22
US	Qamar	2009	137 adults*	0.24
Austria	Kipriva-Altfart	2009	332 adults	0.24
Qatar	Shigidi	2010	241 adults	0.24
Canada	Fang	2008	312 adults	0.33
Canada	Nessim	2009	4247 adults*	0.36
France	Castrale	2010	1631 elderly	0.36
US	Mujais	2006	35 centers*	0.37
Spain	Perez Fontan	2009	641 adults	0.38
Portugal	Rodrigues	2006	312 adults	0.39
Canada	Mujais	2006	26 centers	0.43
Australia	Jarvis	2010	4675 adults*	0.60
Netherlands	Ruger	2009	205 adults*	0.60
Scotland	Kavanaugh	2004	1205 adults*	0.62
Aus/NZ	Fahim	2010	4675 adults*	0.62
Brazil	Mores	2009	680 adults*	0.74
Turkey	Akman	2009	132 children	0.77
UK	Davenport	2009	1904 pt yrs*	0.82 CAPD, 0.66 APD
Israel	Cleper	2010	29 children	1.66

* Registry data

The differences…

- An individual patient, on average, may expect to have peritonitis as rarely as
  - once every 17 years in one center,
  - or as frequently as once every 7 months in another.
- Even at centers within a single country, there is often a marked variation in the peritonitis rate.
  - Scottish registry has centers with rates that range from 0.43 episodes (28mo) to 0.89 episodes per year (13mo)
  - London Thames centers vary from 0.14 episodes (>7yrs) to 1.0 episodes per year (12 mo)
  - Austrian Study Group centers range from 0.07 episodes (>14yrs) to 0.60 episodes per year (20mo)

Technique survival

- highly affected by infection rates
  - Infection is leading cause of transfer off PD

Possible reasons for differences in infection rates…

- differences in patient training
- differences in infection-prevention protocols
- variations in the accuracy with which peritonitis data is collected and reported

GOOD OUTCOMES

- Achieved when a dedicated group of professionals continuously work to improve the care for PD patients.

Key Issue:

Goal: *to reduce the risk* of poor outcomes for PD patients.

What outcomes do you want to improve?

Remember…

If you cannot measure it,
you cannot manage it or improve it.

Reducing Risk of Infections

Prevention of infectious complications in peritoneal dialysis: best demonstrated practices. Bender F, Bernardini J, Piraino B. KI suppl, 2006;103:S44-54.
ISPD Position Paper: Prevention of Peritonitis and Exit Site Infection. Piraino et al,. PDI 31(6): 614-630.

- Proper catheter insertion and post-op care
- Chronic exit site care
- S.aureus prophylaxis
- Hand washing per CDC / WHO protocols
- Careful training/retraining of the patient
- Contamination protocols
- Reducing the risk of peritonitis relapse
- Fungal and procedure-related prophylaxis
- Assessment of patient in their home
- Continuous Quality Improvement

Prevention Begins with Catheter Insertion

Figueiredo A, Goh BL, Jenkins S, Johnson DW, Mactier R, Ramalakshmi S, Shrestha B, Struijk, Wilkie M. Clinical Practice Guidelines for Peritoneal Access. Perit Dial Int. 2010;30:424-429.

- Access team
  - Coordinate exit site location and timing of referral for surgery
  - Includes availability of catheter manipulation and urgent removal
  - Bowel prep pre-op, flushing post insertion
- Local expertise guide insertion techniques
  - No catheter shown to be superior
- Antibiotics pre-op : single dose peri-operatively
  - Gadallah MF, Ramdeen G, Mignone J, Patel D, Mitchell L, Tatro S. Role of preoperative antibiotic prophylaxis in preventing postoperative peritonitis in newly placed peritoneal dialysis catheters. Am J Kidney Dis 2000; 36(5): 1014–19.
- Sterile post op care
- Immobilize catheter to promote healing and reduce trauma
- Annual audit of catheter insertions
  - >80% functioning at 1 year
  - Bowel perforation <1%, significant hemorrhage <1%,
  - ESI or peritonitis within 2 weeks <5%.

Goals of Post-op care:

- Prevent colonization during healing
- Reduce trauma at exit and cuff(s)
  - restrict dressing changes to PD staff
    - *aseptic technique*
  - cleanse with non-irritating agent
  - non-occlusive dressing
  - immobilize catheter

Chronic Exit Site Care

Prevention of infectious complications in peritoneal dialysis: best demonstrated practices. Bender F, Bernardini J, Piraino B. KI suppl, 2006;103:S44-54

- Begins after complete healing
  - immobilize catheter
  - hand washing prior to exit site care
  - daily exit site care
    - liquid antibacterial soap or disinfectant
    - examine visually, then cleanse gently
    - dry thoroughly
    - *S.aureus* prophylaxis

Well Healed Exit Sites

Choices for cleansing exit site:

	Cytotoxic ?
Povidone-iodine	yes (if >0.001% conc)
Hydrogen peroxide	yes (if >0.003% conc)
Sodium hypochlorite	yes (if >0.24% conc)
Chlorhexidine	yes (if >0.005% conc)
Acetic acid	yes (if >0.24% conc)
Alcohol	yes (to open wound)
Non-ionic surfactant	(not antiseptic)
○ Pure soap	
○ Antibacterial soap	

- Lineaweaver et al, Topical antimicrobial toxicity. Arch Gen Surgery 120(3), 1985
- Heling et al, Bactericidal and cytotoxic effects of sodium hypochlorite and sodium dichlorosiocyanurate solutions in vitro. J Endodontics 27(4), 2001
- Lineaweaver et al. Cellular and bacterial toxicities of topical antimicrobials. Plast Reconstr Surg 75(3), 1985
- Doughty D. A rational approach to the use of topical antiseptics. J Wound Ost Cont Nurs 21(6), 1994
- Tatnall et al, Comparative study of antiseptic toxicity on basal keratinocytes, transformed human keratinocytes and fibroblasts. Skin Pharm 3(3), 1990
- Tatnall et al, Assay of antiseptic agents in cell culture: conditions affecting cytotoxicity. J Hosp Inf 17(4), 1991
- Harsbargen et al. Exit-site care;is it time for a change? Perit Dial Int, 13 (suppl 2), 1993

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S.Aureus prophlyaxis: ISPD Recommendations 2010

Piraino B, Bernardini, J, Price V, Szeto CC, Li PK et al. ISPD position statement on reducing the risks of peritoneal dialysis-related infections. Perit Dial Int 2011.

Choose one:

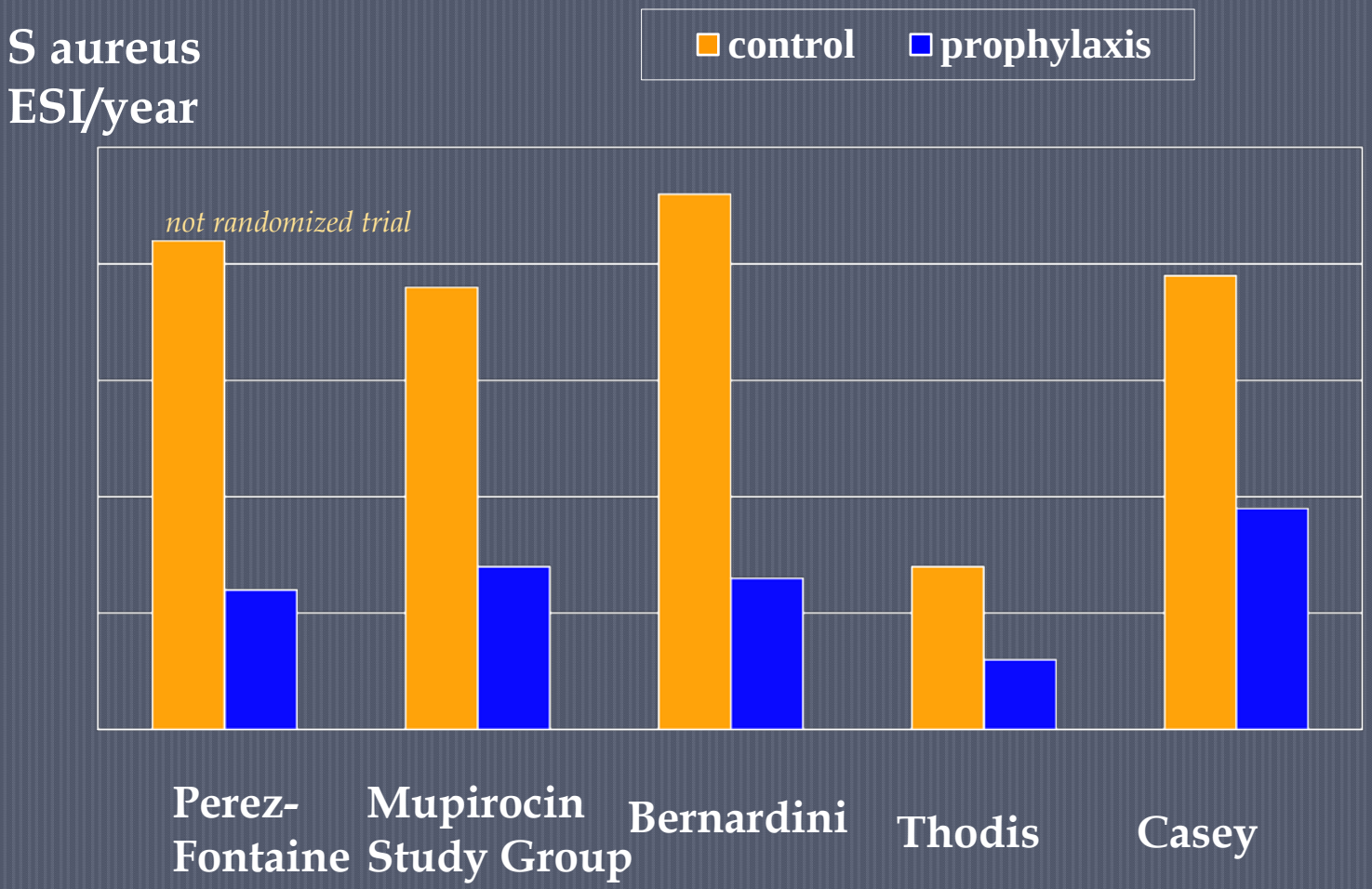
- *Exit site mupirocin or gentamicin*
  - daily after cleansing
  - in all patients
- *Intranasal mupirocin*
  - Monthly, BID x 5 days
  - *Reduces SA exit site infections, not SA peritonitis*

Target rates of infection:

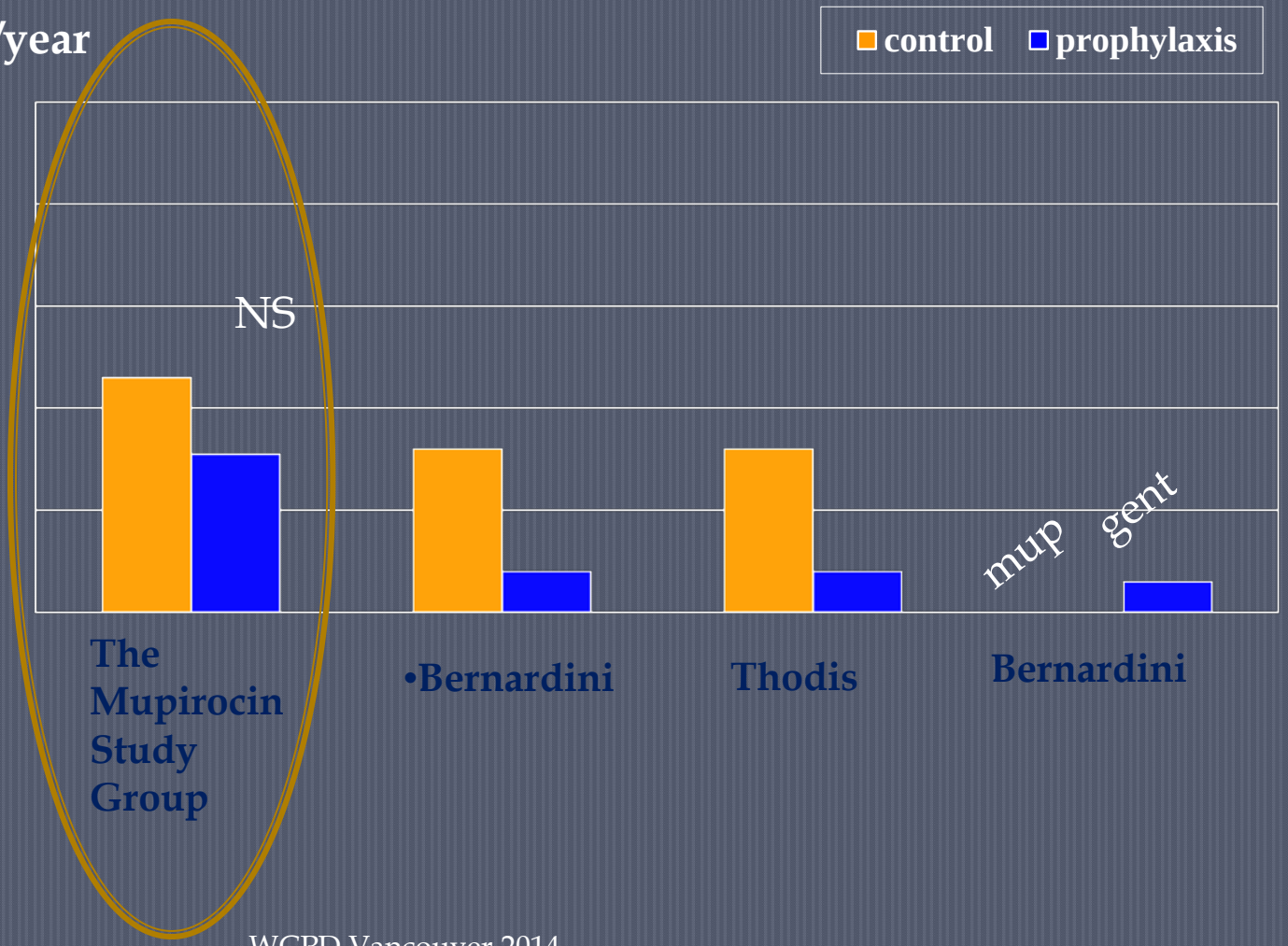
S.Aureus catheter infections <0.05/year
1 episode every 240 months or 20 years

S. Aureus peritonitis <0.06/year
1 episode every 200 months or 16.7 years

S aureus ESI are reduced with mupirocin prophylaxis



Effect of *S aureus* prophylaxis on prevention of *S. aureus* peritonitis



Meta-Analysis of Mupirocin Prophylaxis to prevent S.aureus infections in PD patients

- 10 studies (3 RCT's and 7 historical cohort studies)
  - 63% reduction in all S. aureus infection risk with the prophylaxis
    - 66% reduction in S. aureus peritonitis
    - 62% reduction in S.aureus exit site infection
  - Tacconelli E, Carmeli Y, Aizer A, Ferreira G, Foreman MG, D'Agata EM. Mupirocin prophylaxis to prevent Staphylococcus aureus infection in patients undergoing dialysis: a meta-analysis. Clin Infect Dis 2003; 37(12):1629–38.

- 2009 meta –analysis and RCT's
  - 72% reduction in S.aureus exit site infections by
  - 40% reduction in S.aureus peritonitis
    - Xu G, Tu W, Xu C. Mupirocin for preventing exit-site infection and peritonitis in patients undergoing peritoneal dialysis. Nephrol Dial Transplant. 2009

Exit site mupirocin has been found to be more effective than intranasal mupirocin in reducing S.aureus peritonitis

Mupirocin versus Gentamicin at the Exit Site

- prospective, double-blind, multi-centered, randomized trial:

Bernardini J, Bender F, Florio T, Sloand J, PalmMontalbano L, Fried L, Piraino B. Randomized Double Blinded Trial of exit site Cream for Prevention of Exit Site Infection in Peritoneal Dialysis Patients. J Am Soc of Nephrology. 16:539-545:2005

	mup	gent	p
Catheter infections	0.54	0.23	<0.003
S. aureus	0.06	0.08	0.44
Pseudomonas	0.11	0	<0.003
Peritonitis	0.52	0.34	0.03
S. aureus	0	0.03	0.14
Pseudomonas	0.04	0	0.14

Replication studies: mupirocin vs gentamicin at exit site

Chu KH et al. Perit Dial Int:28(5);505-8, 2008.

- Prospective trial, assigned 1:1 to either daily exit site gentamicin or daily exit site mupirocin
- 81 patients at single center followed for 1 year; not controlled for *S.aureus* nasal carriage; no power calculations.
- Mupirocin group significantly older with more comorbidities

Chu KH et al. Perit Dial Int:28(5);505-8, 2008.

	gentamicin	mupirocin	p
ESI/yr	**0.38**	**0.20**	ns
S.Aureus	0.13	0	
meth sens	0.05	--	
MRSA	0.08	--	
P.Aeruginosa	*0.18*	*0.13*	
Peritonitis/yr	***0.33***	***0.27***	*ns*
S. aureus	*0.03*	*0.02*	
P.Aeruginosa	*0.05*	*0.02*	
total Gm neg	*0.20*	*0.20*	

Conclusion: *gentamicin equivalent to mupirocin applied daily to exit site but underpowered with short follow-up*

Mahaldar et al. Comparison of gentamicin and mupirocin in the prevention of exit site infection and peritonitis in peritoneal dialysis. Adv Perit Dial 2009:25;56-59.

- Retrospective review 2003-2007; no method for assignment to mup or gent
- 100 patients on either mup or gent at least 6 months; follow-up about 1 yr
- Excluded infections 1st 3 months after PD catheter inserted

	gent	mup		p
Patients, n	50	50		
Catheter inf	0.03	0.08	(episodes/year)	ns
S.aureus	0.03	0		
g neg	0	0.01		
pseudo	0	0.04		
Peritonitis	0.61	0.32		0.07
S.aureus	0.10	0.06		
G neg	0.10	0.10		
pseudo	0	0		
CNS	0.20	0.10		
strept	0.10	0		

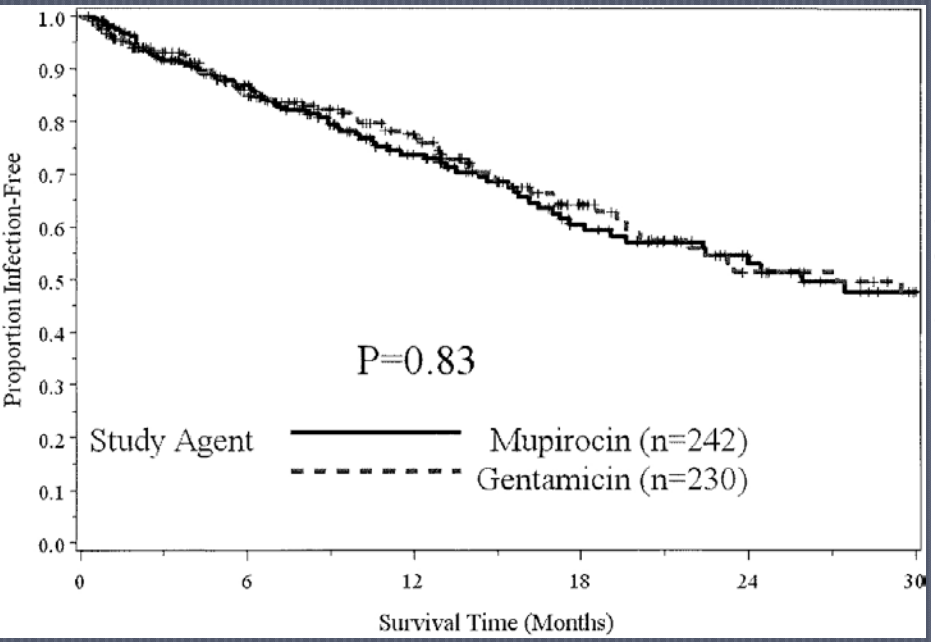
Study concluded gentamicin not superior to mupirocin at exit site.

The Effect on Pathogens for Changing Antibiotic Prophylaxis

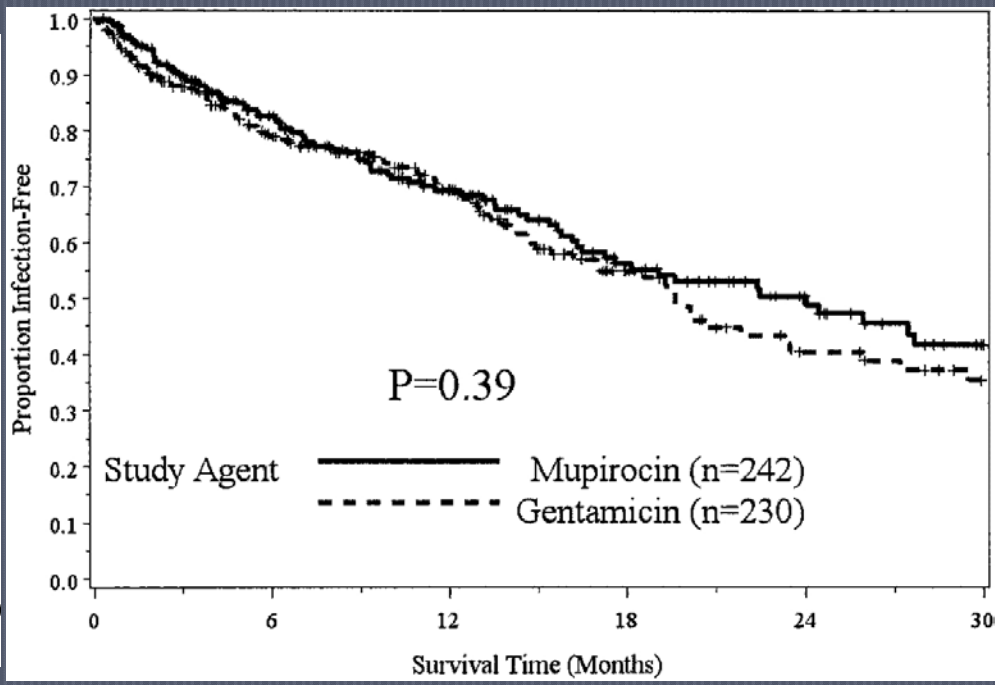
Pierce DA et al. PDI 32(5):525-530: 2012

Retrospective observational study of two periods of prophylaxis
Decreased susceptibility Enterobacter and Pseudomonas with gent
Limitation: high rate no growth cultures both groups (30% & 19%)

Peritonitis rates



Overall Infections rates



The Honeypot Study

Johnson DW et al Antibacterial honey for the prevention of PD related infections: a randomized trial. Lancet Inf Dis October 2013

- Randomized study of 370 patients
- Comparing S.aureus prophylaxis
  - intranasal mupirocin 1 / month
  - Medihoney antibacterial gel at exit site daily

Results:

rates of exit site infection and peritonitis not different.

But… Medihoney group had increased risk of infection for peritonitis in patients with DM.

Also… Medihoney group had high dropout rate due to skin irritation.

Effectiveness of different types of care of the peritoneal dialysis catheter: a systematic review.

Ques Aam et al. JB Database Systemic Review and Implementation Reprots. 11(9), 133-179, 2013

- reviewed all randomized studies 1996-2009
  - 9 randomized trials
- conclusions:
  - gentamicin cream at exit site better than mupirocin to decrease ESI and peritonitis
  - chlorhexidine better than povidone iodine to decrease ESI and P at 5-6 months
  - strict sterile technique imperative post op

Exit Site Infection of peritoneal catheter is reduced by the use of polyhexidine.

PDI in Press: doi:10.3747.

- Prospective randomized trial of daily exit site care for 12 months, single center
- S.aureus carriers Rx with intranasal mup BID x 7d

	NS+Povidone	NS+polyhexidine	
n	30	30	
ESI/yr	0.33	0.12 *	p<0.04
SA	0.11	0	
Pseudo	0.04	0.12	
P/yr	0.51	0.37	p<0.04

* all 3 ESI Pseudomonas aeruginosa

Reducing Risk by Preventing Infections

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HANDWASHING

Indications for Hand Hygiene

- When hands are visibly dirty, contaminated, or soiled, wash with non-antimicrobial or antimicrobial soap and water.

- If hands are not visibly soiled, use an alcohol-based handrub for routinely decontaminating hands.

Guideline for Hand Hygiene in Health-care Settings.
MMWR 2002; vol. 51, no. RR-16.
WHO 2009

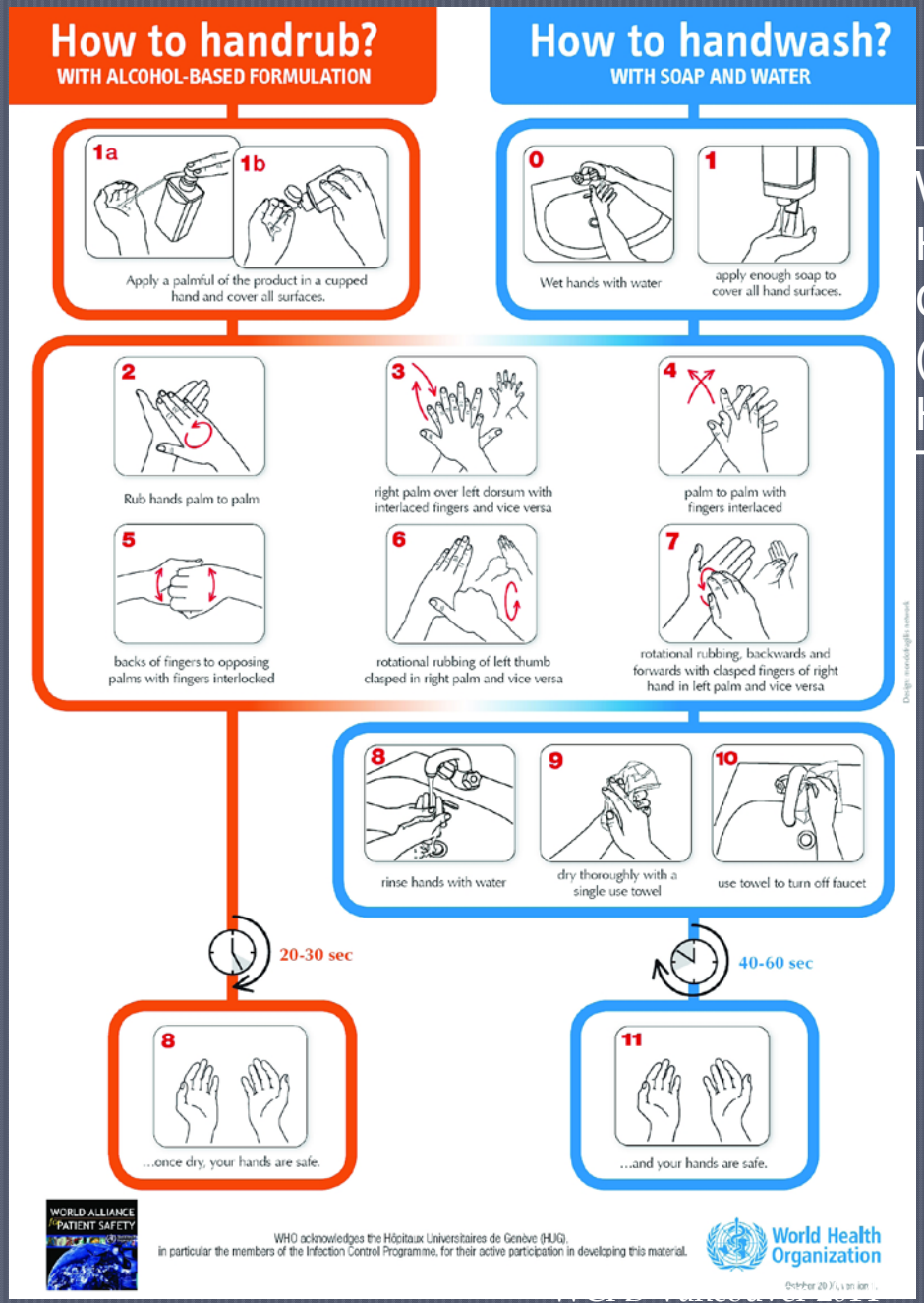
Recommended Hand Hygiene

www.CDC.gov/Handhygiene whqlibdoc.who.int/publications

- Handrubs
  - Apply 3mL of 60-80% alcohol gel to palm of one hand, rub hands together covering all surfaces until dry
  - Volume: should take 20-30 seconds to dry

- Handwashing
  - Wet hands with warm water (not hot), apply 3mL soap, rub hands together for at least 20 seconds
  - Rinse and dry with disposable towel
  - Use towel to turn off faucet
  - Entire procedure takes 40-60 seconds
  - If use bar soap, must use rack to drain and dry between uses

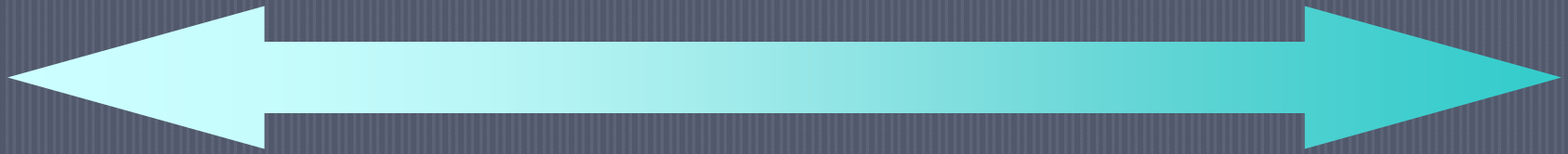
CDC.Gov and WHO 2009



World Health Organization Guidelines on Hand Hygiene in Health Care (2009) and Center for Disease Control and Prevention (CDC) Guideline for Hand Hygiene in Health-Care Settings (2002)

PD Patients must be taught aseptic technique, with emphasis on proper hand washing techniques.

Efficacy of Hand Hygiene Preparations in Killing Bacteria



Plain Soap

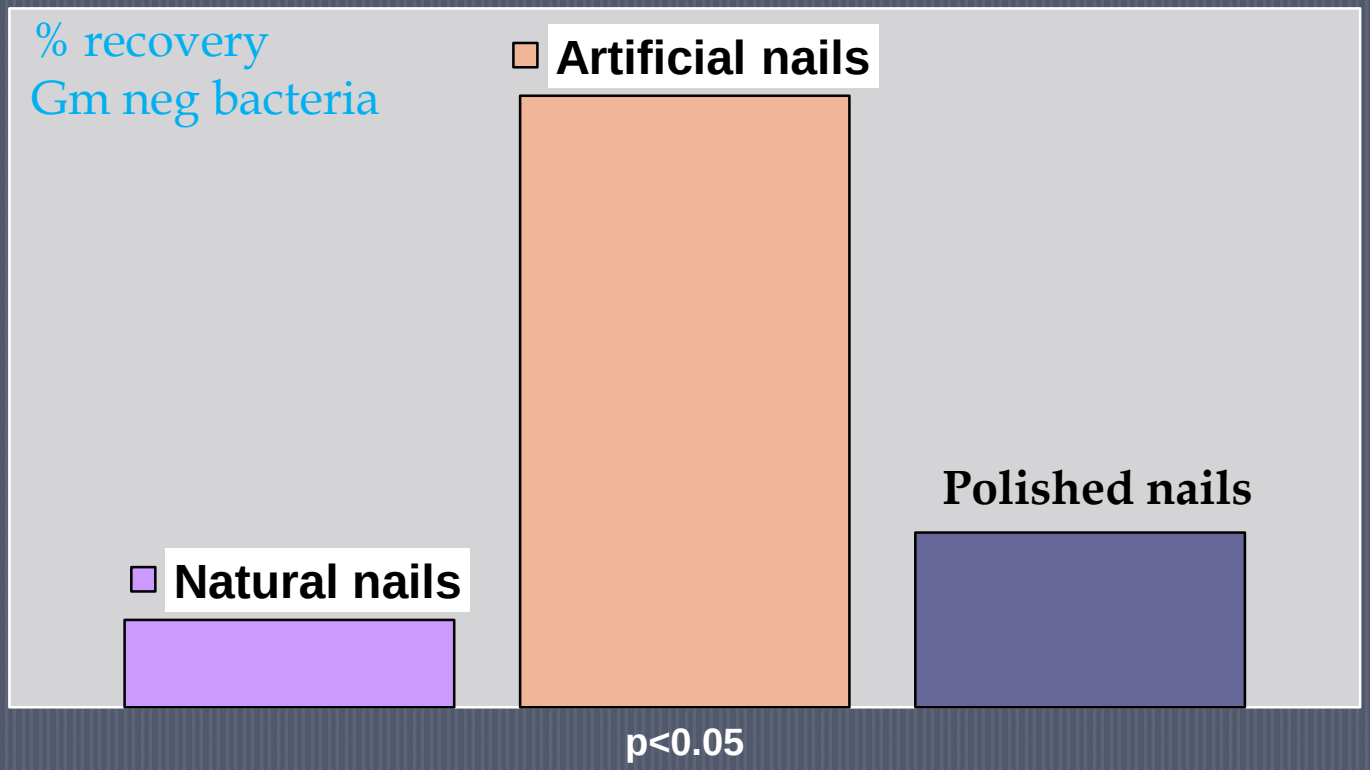
Antimicrobial soap

Alcohol-based handrub*

** C. Difficile is NOT killed by alcohol---soap required*

www.CDC.gov/Handhygiene

Can a Fashion Statement Harm the Patient?



% Recovery of gram negative bacteria

Avoid wearing artificial nails,

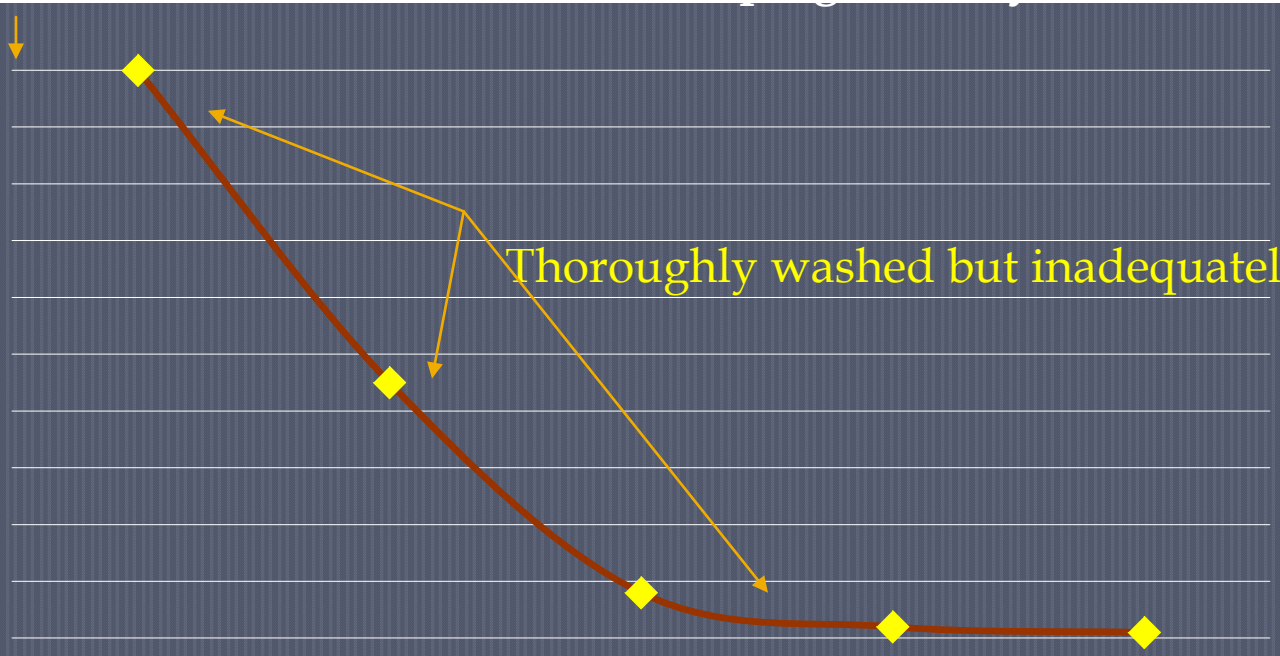
keep natural nails <1/4 inch if caring for high risk patients (ICU, OR)

Edel et. al, *Nursing Research* 1998:47;54-59
WHO 2009

Relationship of hand dampness after hand washing to bacterial translocation following touch contamination

From Miller TE, Findon G. Perit Dial Int.17;1997:560-567

% decrease in bacterial numbers with wet and progressively drier hands



Time air drier used on hands, in seconds

Hand hygiene in peritoneal dialysis patients: a comparison of two techniques.

Figueiredo A et al. Perit Dial Int.33;655-61, 3013.

- Simple soap and water + alcohol gel versus alcohol gel alone.
- 22 PD patients
  - Cultured prior to hand hygiene procedure and after
  - Colony forming units significantly lower after use of alcohol alone
  - Concluded that 70% alcohol gel alone is more effective in cleaning hands

Reducing Risk by Preventing Infections

Bender, Bernardini, Piraino. KI suppl, 2006;S44-54

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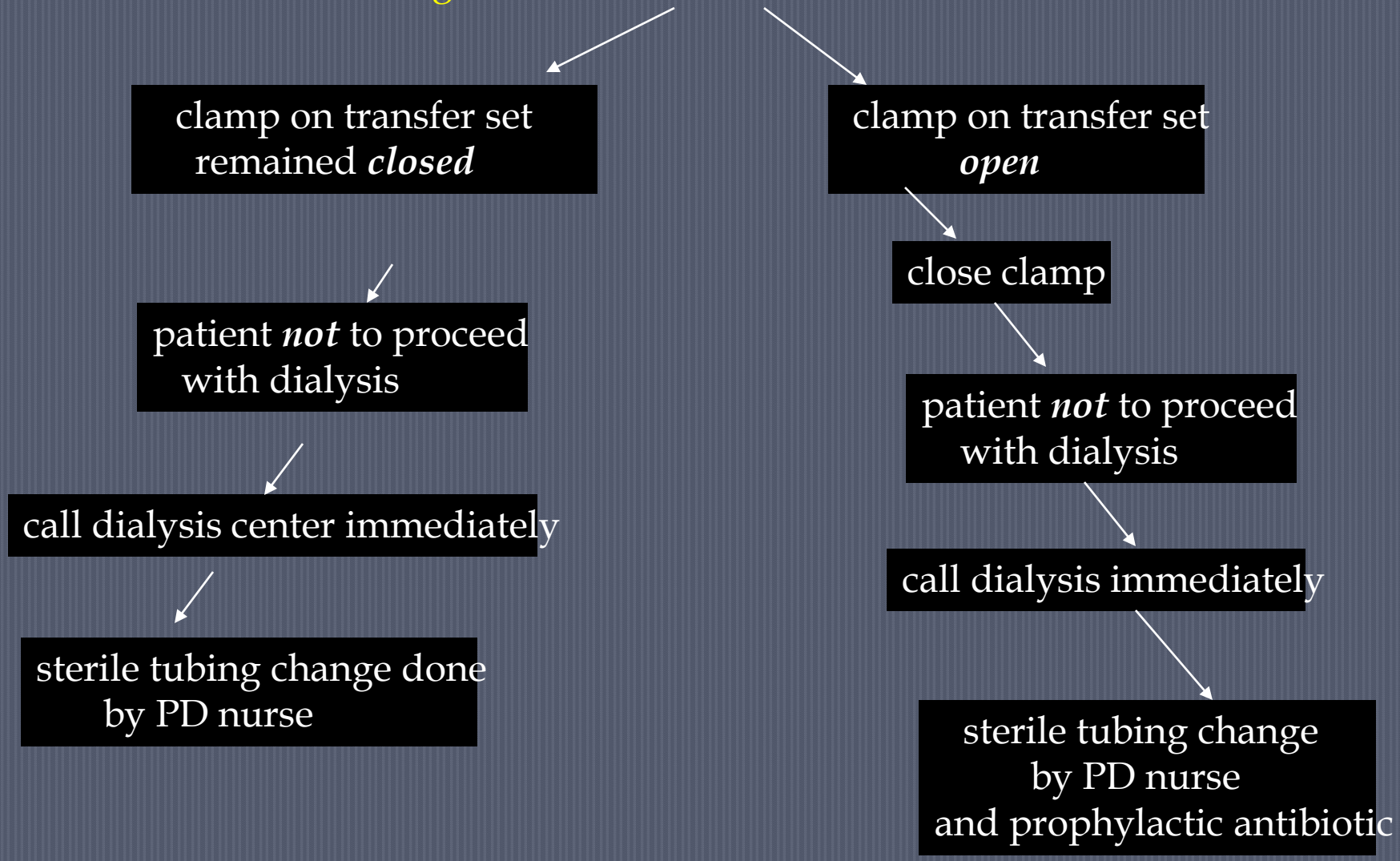
Contamination Protocols

- If unclear whether clamp open or closed, assume it was open.
- Culture effluent post-contamination
  - If positive (even if effluent clear), full course of antibiotic Rx
    - Goal is to prevent inflammatory response of peritoneum to contaminant
  - Apply new sterile transfer set to re-establish sterile pathway
    - No alternative appropriate post contamination
- Pets in room of exchange may also cause contamination—especially with cycler
- Accidental disconnections and hole in systems will also cause contamination

Algorithm for PD Contamination



Additional predictors of increased peritonitis risk:

Malnutrition

- Initial albumin <2.9 g/dL predicts >2 times higher rate of peritonitis
  - Wang Q. Bernardini J. Piraino B. Fried L. Albumin at the start of peritoneal dialysis predicts the development of peritonitis. AmJ of Kidney Dis. 2003:41(3):664-9.

Hypokalemia

- Transmural migration of enterobacter
  - Chuang YW, Shu KH, Yu TM, Cheng CH. Hypokalaemia: an independent risk factor of Enterobacteriaceae peritonitis in CAPD patients.NDT 2009; 24(5):1603-8.
  - Szeto CC, Chow KM, Kwan BC, Leung CB, Chung KY, Law MC, Li PK. Hypokalemia in Chinese peritoneal dialysis patients: prevalence and prognostic implication.. Am J Kidney Dis 2005; 46(1):128-35.
  - Shu KH. Chang CS. Chuang YW. Chen CH. Cheng CH. Wu MJ. Yu TM. Intestinal bacterial overgrowth in CAPD patients with hypokalaemia. Nephrol Dialy Transplant 2009; 24(4):1289-92.

- Depression
  - Troidle L. et al Depression and its association with peritonitis in long term peritoneal dialysis patients. AJKD 2003;42(2):350.

- Vitamin D
  - Rudnicki M. et al. Risk factors for peritoneal dialysis associated peritonitis: the role or oral active vitamin D. Perit Dial Int. 2010;30:541.

Reducing Risks by Preventing Infections

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Reduce risk of peritonitis due to relapse

- Defined as 2nd episode with same organism within 2-4 weeks of stopping antibiotics
- May be due to occult catheter infection
- Catheter replacement prevents further episodes

Reducing risks by Preventing Infections

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Nystatin Prophylaxis to prevent Candida Peritonitis

- 10 year study (non-randomized) using historical controls
- Nystatin 500,000 u QID while on antibiotics

	Nystatin 1995-1999	Control 1999-2005	
Patients, n	320	481	
Overall peritonitis	0.56/yr	0.44/yr	
Candidia peritonitis	14	13	ns
	0.019/yr	0.011/yr	ns
Antibiotic-related Candidia peritonitis	10/14	4/13	<0.05
	0.014/yr	0.003/yr	<0.05

Wong PN, Lo KY, Tong GM, Chan SF, Lo MW, Mak SK, Wong AK. Prevention of fungal peritonitis with nystatin prophylaxis in patients receiving CAPD. Perit Dial Int. 2007 Sep-Oct;27(5):531-6.

Peritonitis due to procedures

ISPD 2010 Guidelines

- Transplant
  - empty abdomen of fluid
  - antibiotic prophylaxis pre
- Colonoscopy with polypectomy
  - single IV dose ampicillin 2 gm + single dose aminoglycoside with or without metronidazole just prior to procedure
  - empty abdomen of fluid
- Dental procedures
  - single oral dose amoxicillin 2 gm two hours pre
- Uterine biopsy
  - empty abdomen of fluid
  - prophylaxis with antibiotic

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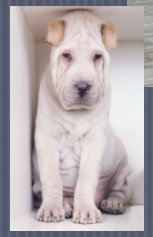
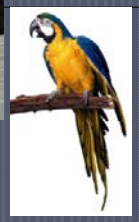
Home Visits

Remember– sometimes we do not see the problem until we see them at home!

Accidental Delivery

- No pets in the room





- No connections in front of vents or fans

- Well water---use bottled water to clean exit site

- Periodically re-evaluate patient
  - home situation
  - ability to perform connections safely
  - appropriateness of equipment & technology

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Dialysate cultures

- Important to identify the organism
  - for appropriate antibiotic treatment
  - for identification of resistant organisms
  - to establish probable cause of infection
  - Ideally <10% culture negative (but always<20%)
    - Li PK, Szeto CC, Piraino B, Bernardini J, Figueiredo AE, Gupta A, Johnson DW, Kuijper EJ, Wai -Choong L, Salzer W, Schaefer F, Struijk DG. ISPD Guidelines;recommendations. Peritoneal Dialysis-related infections. Recommendations: 2010 update. 2010;30:393-423.
- Blood culture bottles are best
  - 10 ml injected into aerobic and anaerobic bottles (ISPD)
    - Prep injection site for effluent sample with betadine drop for 5 minutes
    - Innoculated bottles incubated at 37◦C
  - 50mL centrifuged has lowest culture-negative rate
    - Chow KM, Chow VC, Szeto CC, Law MC, Leung CB, Li PK. Continuous ambulatory peritoneal dialysis peritonitis: broth inoculation culture versus water lysis method. Nephron Cliin Pract 2007;105:c121-5.
    - <5% culture negative
    - …but not always practical

Summary of Prevention Tactics

- Reduce risks for developing catheter infection and peritonitis.
  - Reduce risks associated with PD catheter
  - Attention to handwashing
  - Careful training and retraining of patients
  - S.aureus prophylaxis
  - Fungal prophylaxis and procedure prophylaxis
  - Contamination protocols
  - Reduce risk of peritonitis relapse
  - Continuous Quality Improvement
    - Determine root cause of each peritonitis
  - Re-evaluate patient at home

Thank you.