Infectious complications in peritoneal dialysis

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Khabarovsk, October 2015

Overview

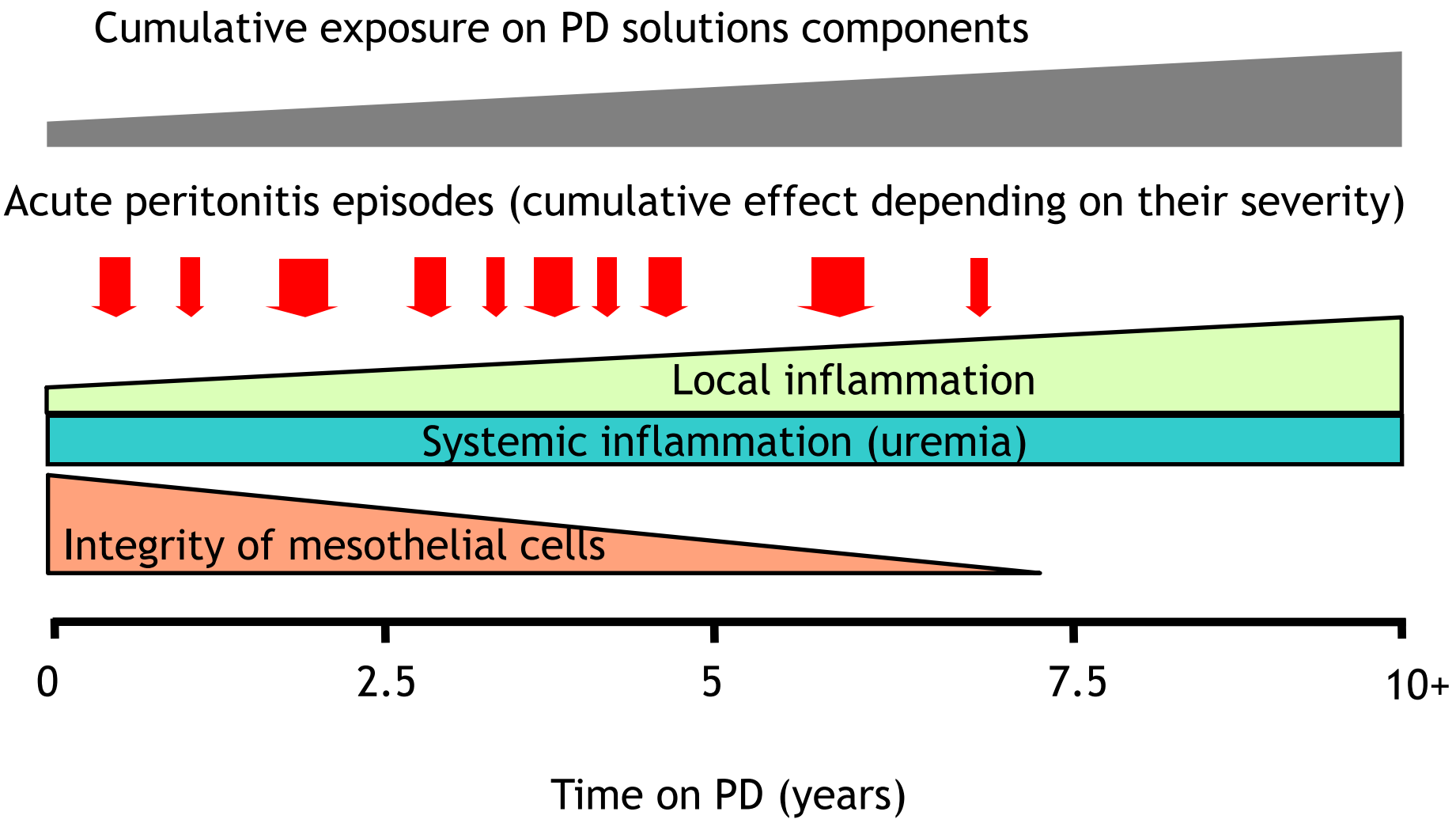
1. PD related infections – general overview

2. Infections in PD – treatment recommendations 2000
   a) Peritonitis
   b) Exit site infection
   c) Tunnel infection

3. Update 2005, 2010, 2012 (Pediatric)

4. Conclusions

Peritoneal membrane in PD



Infectious complications of PD

Peritonitis

1/24.0 pts/months US, Canada, Western Europe, Troidle, Semin in Dial 2003

1/21.9 pts/months Poland, Rutkowski et al. 2008

1/13.5 – 1/27.9 pts/months Scottish registry, Kavanagh, NDT 2004

1/12.0 – 1/85.7 pts/months London Thames group, Davenport, PDI 2009

1/20.0 – 1/171 pts/months Austrian Study Group, Kopriva-Altfahrt, PDI 2009

ESI (exit site infection) 1/85 pts/months - 1/111 pts/months

Rutkowski et al. „Report on RRT in Poland" 2002 vs. 2008

TI (tunnel infection) 1/325 pts/months - 1/830 pts/months

Rutkowski et al. „Report on RRT in Poland" 2002 vs. 2008

Infectious complications of PD

1. **Peritonitis**
2. ESI (exit site infection)
3. TI (tunnel infection)

Infectious complications of PD

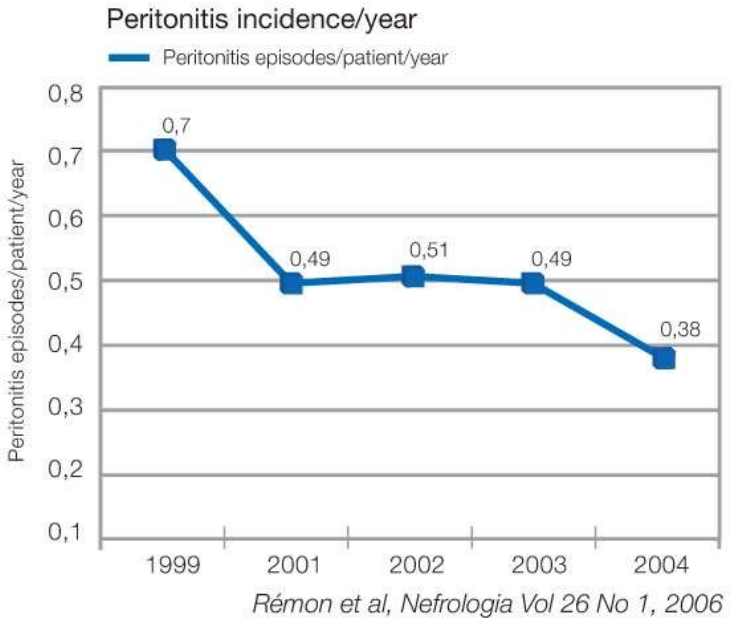
Peritoneal dialysis

Not necessarily

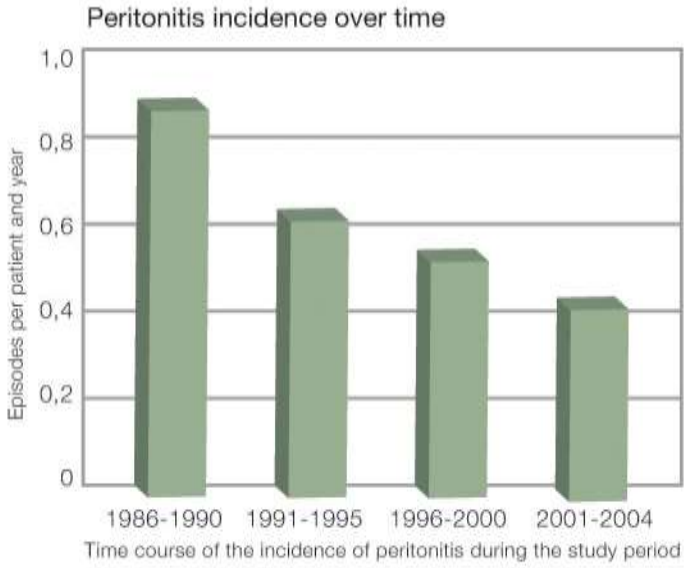
Peritonitis

Clinical issues in PD

Incidence of peritonitis related to PD decreased significantly during last decade.



Rémon et al, Nefrologia Vol 26 No 1, 2006

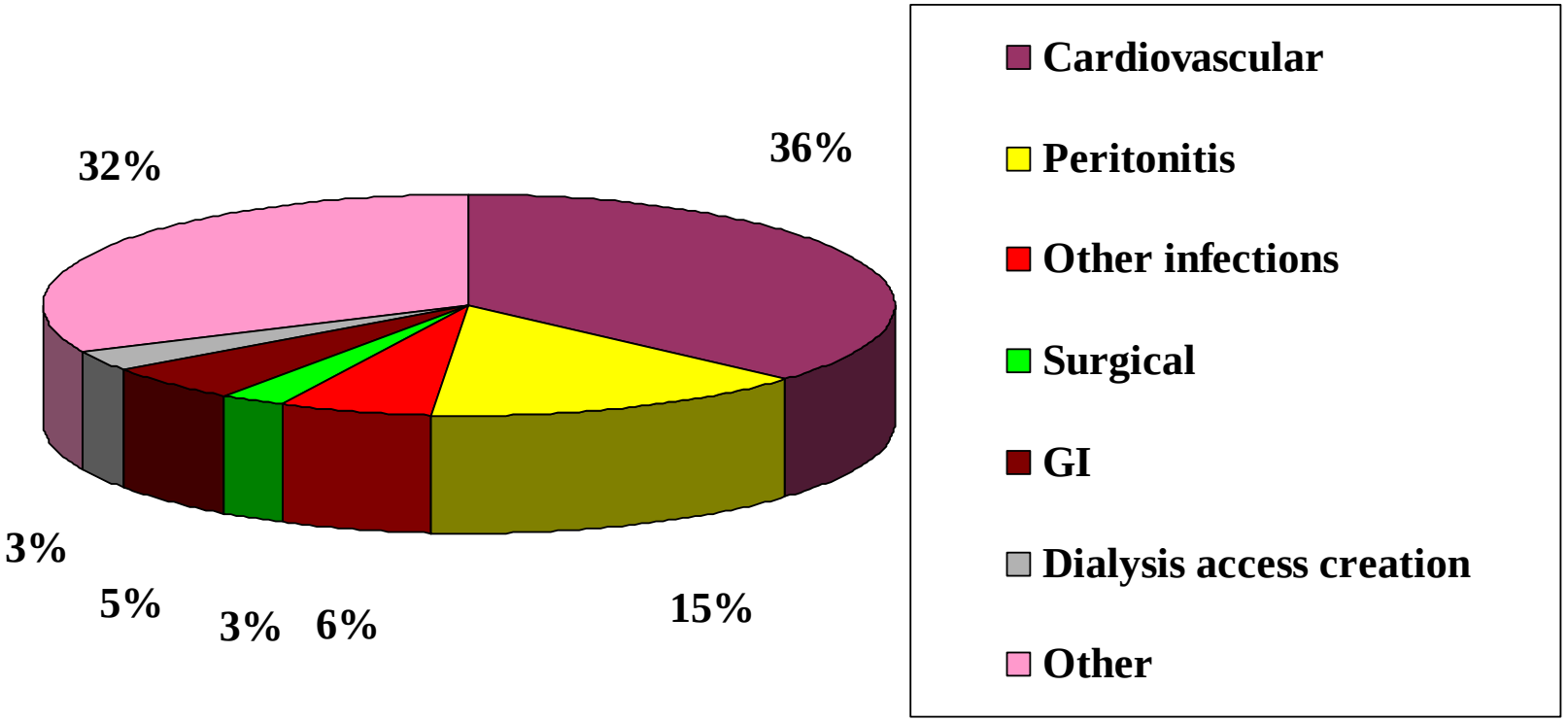


Perez-Fontan et al, PDI Vol 25, 2005

- Treatment period – 1999 – 2004
- 623 patients

- 693 peritonitis episodes in 565 patients
- Higher risk in: women 2.13, older 1.1/year, malnurished 2.51, high sCRP 4.04, low GFR 0.75/mL/min
- Other risk factors: comorbidities in general, depression, time on PD at onset of episode

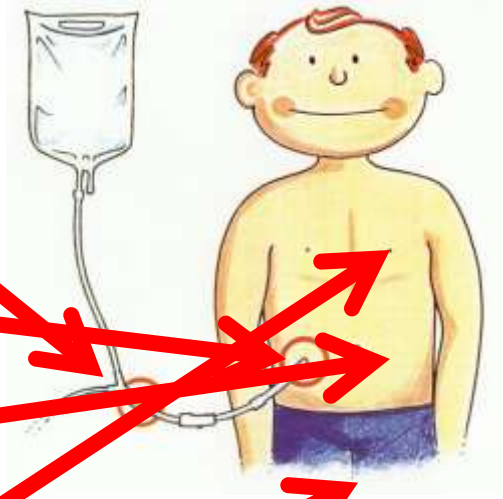
Reasons for hospitalisation in PD patients

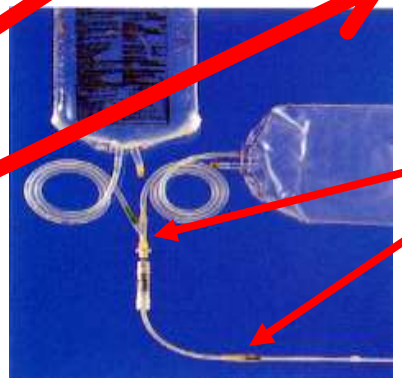


Murphy KI 2000; 57; 2357-2563

Contamination pathways

1. Intraluminal per catheter (damage of the connection, contamination of the connection, contamination of the PD solution)
2. Pericatheter (ESI, TI)
3. Intestinal (diverticulitis, bowel perforation)
4. Blood borne (systemic infections with bacteriemia, TBC)
5. Ascending (female genital)





PD related Peritonitis

Clinical symptoms:

1. Cloudy effluent and/or
2. Abdominal pain and/or
3. Fever and/or
4. Nausea, vomiting

Ultrafiltration failure

PD related Peritonitis

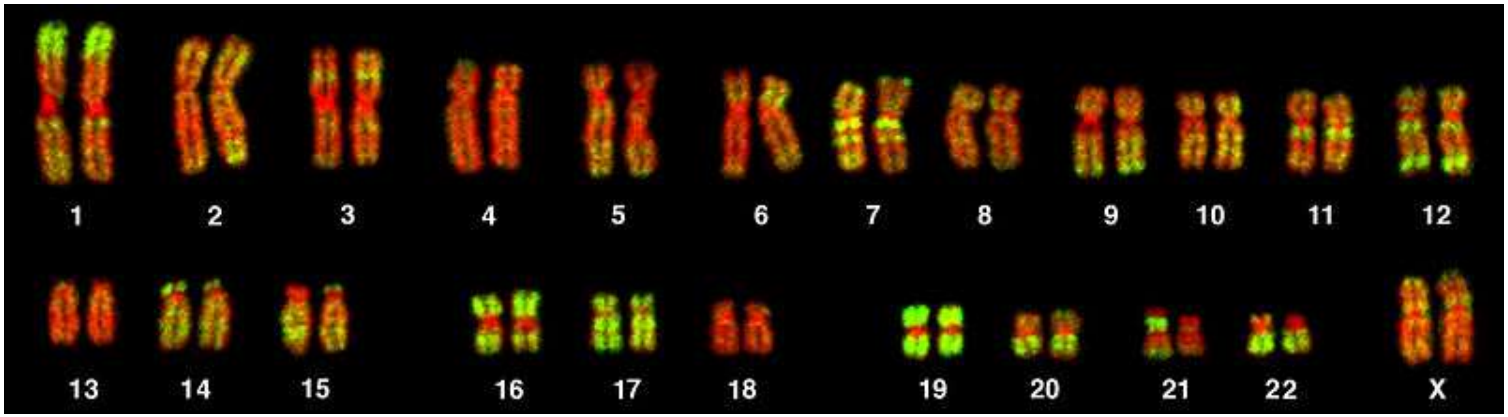
Lab tests:

1. PD effluent cell count
   - > 100 cells/mm^3
   - > 50% polynuclears
2. Peripheral leucocytosis
3. Positive culture
4. Gram assessment
5. Direct microscopy of PD effluent (fungal peritonitis suspected)
6. Serum amylase – to differentiate from pancreatitis

New diagnostic techniques complementary to culture

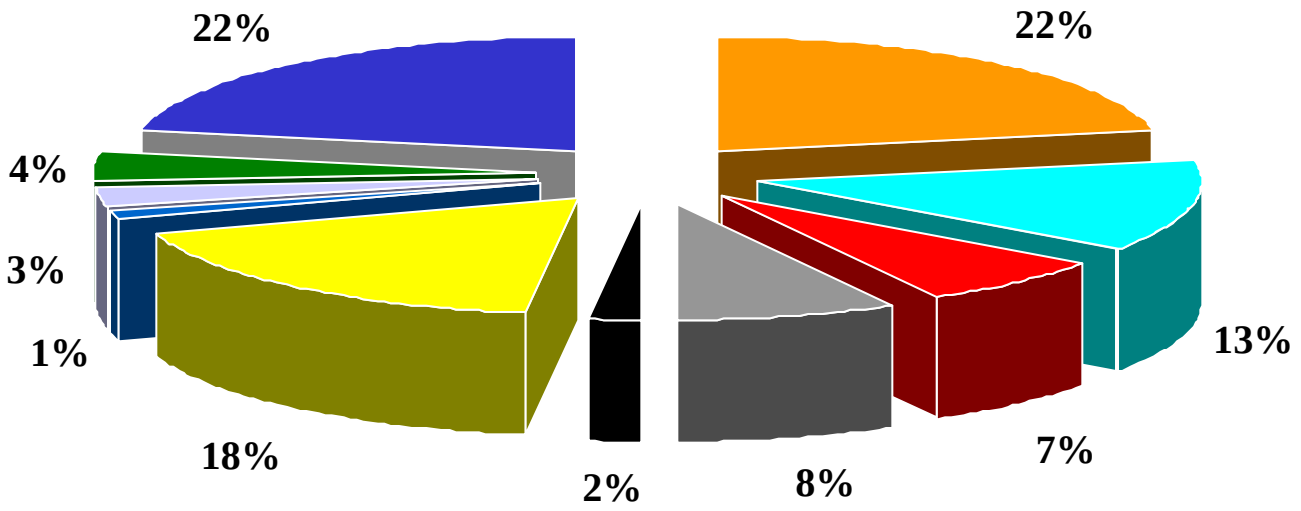
ISPD 2010

1. Strip test – leucocytes' esterase
2. Broad spectral PCR with sequentioning of RNA
3. Quantitative assessment of bacterial DNA in PCR
4. Test using metaloproteinase 9 for early diagnosis
5. Fluorescent *in situ* hybridisation (FISH)



PD related Peritonitis

Etiology



Harwell PDI 1997; 17 (6), 586-594

PD related Peritonitis

Etiology

- **Rare patogens**, recently registered as peritonitis pathogen:
  - *Haemofilus influenze*,
  - *Salmonella enteritidis*,
  - *Stenotrophomonas maltophilia*,
  - *Propionibacterium sp.* ,
  - *Corynebacterium diphtheriae*.

Azak et al. Am J Infect Control 2011 Sep;39(7):618.

- Responsible for the severe clinical course, **recurrency** and **resistancy**.

- Increased frequency of peritonitis caused by **vancomycin-resistant Enterococci** (VRE) and **vancomycin-resistant *Staphylococcus aureus*** (VRSA/VISA).

Chang CM, et al. Ren Fail. 2010;32(9):1121-2.

PD related Peritonitis

1. Initial – empirical (after the Gram test).

2. Modification – after the sensitivity test.

PD related Peritonitis

Treatment, further assessment

1. 1-3 quick exchanges with glucose 1,36% to diminish the pain.

2. IP heparin (500-1000 u/L).

3. Pain killers.

4. Assessment of exit site and tunnel
   - every control visit,
   - every peritonitis episode!

PD related Peritonitis

ISPD 2000

Empirical treatment:

	Diuresis < 100 mL/d	Diuresis > 100 mL/d
Cefazolin or Cefalotin	1 g / once daily i.p. or 15 mg/kg B.W./day	20 mg/kg B.W./day
Ceftazidime	1 g / once daily i.p.	20 mg/kg B.W./day once daily
Gentamicin Tobramicin Netilmicin	0,6 mg/kg B.W. / once daily i.p.	Not recommended

Keane, PDI 2000; 20: 396-411

PD related Peritonitis

Targeted treatment

ISPD 2000

1. Treat 14 days ip (preferable) or iv (po):
   a) most of G(+) germs;
   b) Single G(-) germs

2. 21 days
   a) Staph aur
   b) Stenotrophomonas, Pseudomonas
   c) Mixt G(-)

PD related Peritonitis

Fungal peritonitis

- 2,5% from 1375 peritonitis episodes
- Candida – 97% cases
- 70,6% patients received numerous antibiotics within last several months
- 94% patients needed catheter removal
- **Mortality – 26,5%**

Turp, PDI 2000; 20: 339-340

PD related fungal peritonitis

Flucytosine – loading dose 2 g p.o., maintenance1g p.o. AND

Fluconazole – 200 mg p.o. or i.p. /day

Resistance – consider itraconazole

If positive clinical response after 4 – 7 days: treat 4–6 weeks.	If no clinical response: 1. remove catheter, 2. treat i.v. 7 days after the catheter removal.

ISPD 2000

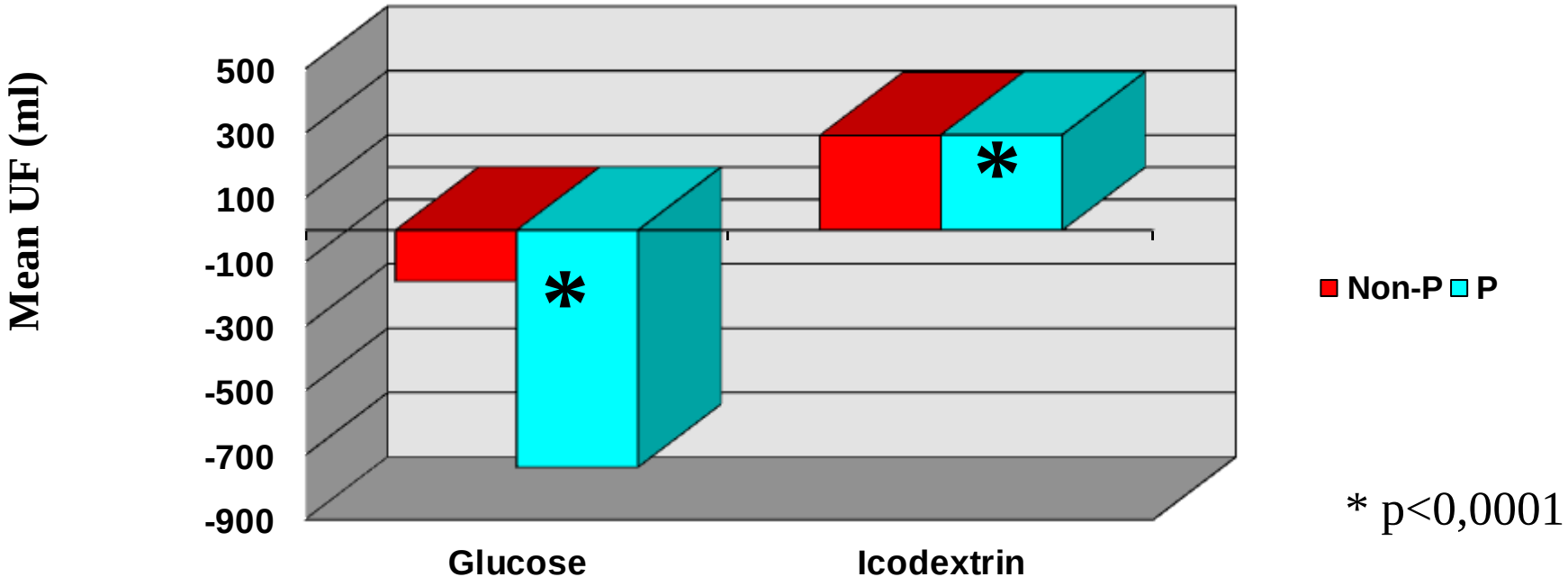
Voriconazole 200mg iv 2x day for 5 weeks

Caspofungin iv LD 70 mg, 50 mg every day ± amfotericin iv

ISPD 2010

Ultrafiltration

peritonitis (P) vs. without peritonitis (Non-P)
glucose based solution vs. icodextrin



* p<0,0001

Posthuma et al, EDTA Abstracts, 222, 1997.

PD related Peritonitis

Lactate solution (L) vs bicarbonate+lactate (B/L)

Solution	Peritonitis (P) incidence		Peritonitis treatment time		% of patients with P	
	Pts / Mths	Frequency	# Episodes	Average length	# Patients	% Patients
L (N=1519)*	2147	1 / 29	709	18,7 days	443	29%
B/L (N=553)*	5791	1 / 34	169	13,3 days	116	21%
	**p = 0.1093		p = 0.0002		** p = 0.0003	

***Adjustment for: differences between groups, age, gender and diabetes control*

*Group L – without B/L exchanges.
Group B/L - at least 1 B/L exchange / day.

Data from PDSR annual report 2002.

Infectious complications of PD

1. Peritonitis
2. **ESI (exit site infection)**
3. TI (tunnel infection)

Normal exit site

Exit site infection (acute)

Exit site infection (chronic)

ESI treatment

1. Dressing 1 – 2 times / day

2. Local antibiotics

   Gentamycin, Rifampin, Trim-Sulfa

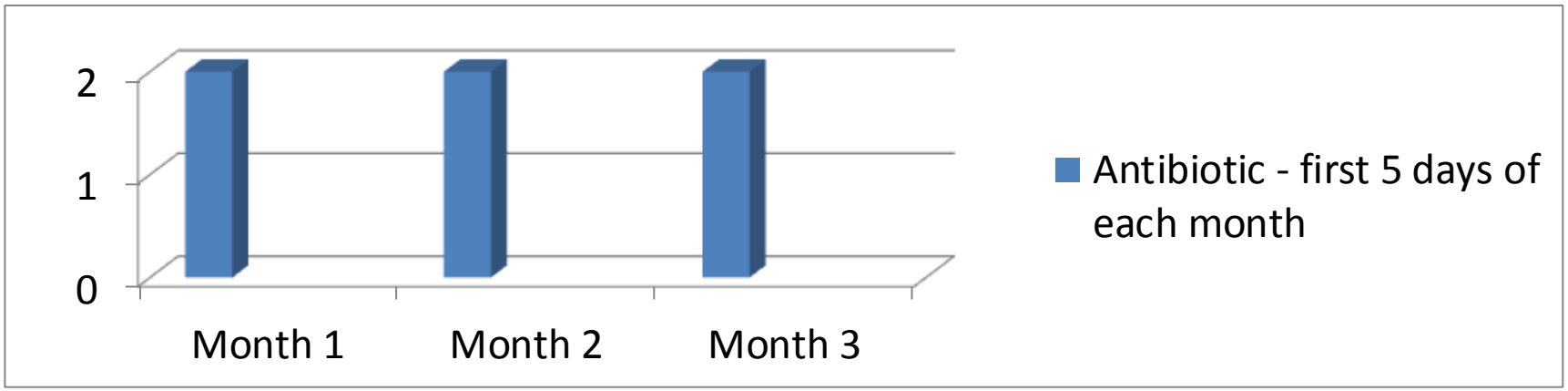
3. Antibiotics i.p.

4. Antibiotics generally (p.o., i.v.)

ESI prevention (2005)

Treatment of nasal Staph. aureus carriers:

- Mupirocin (Bactroban) – intranasally 2 times / day for first 5 days of each of 3 consecutive months



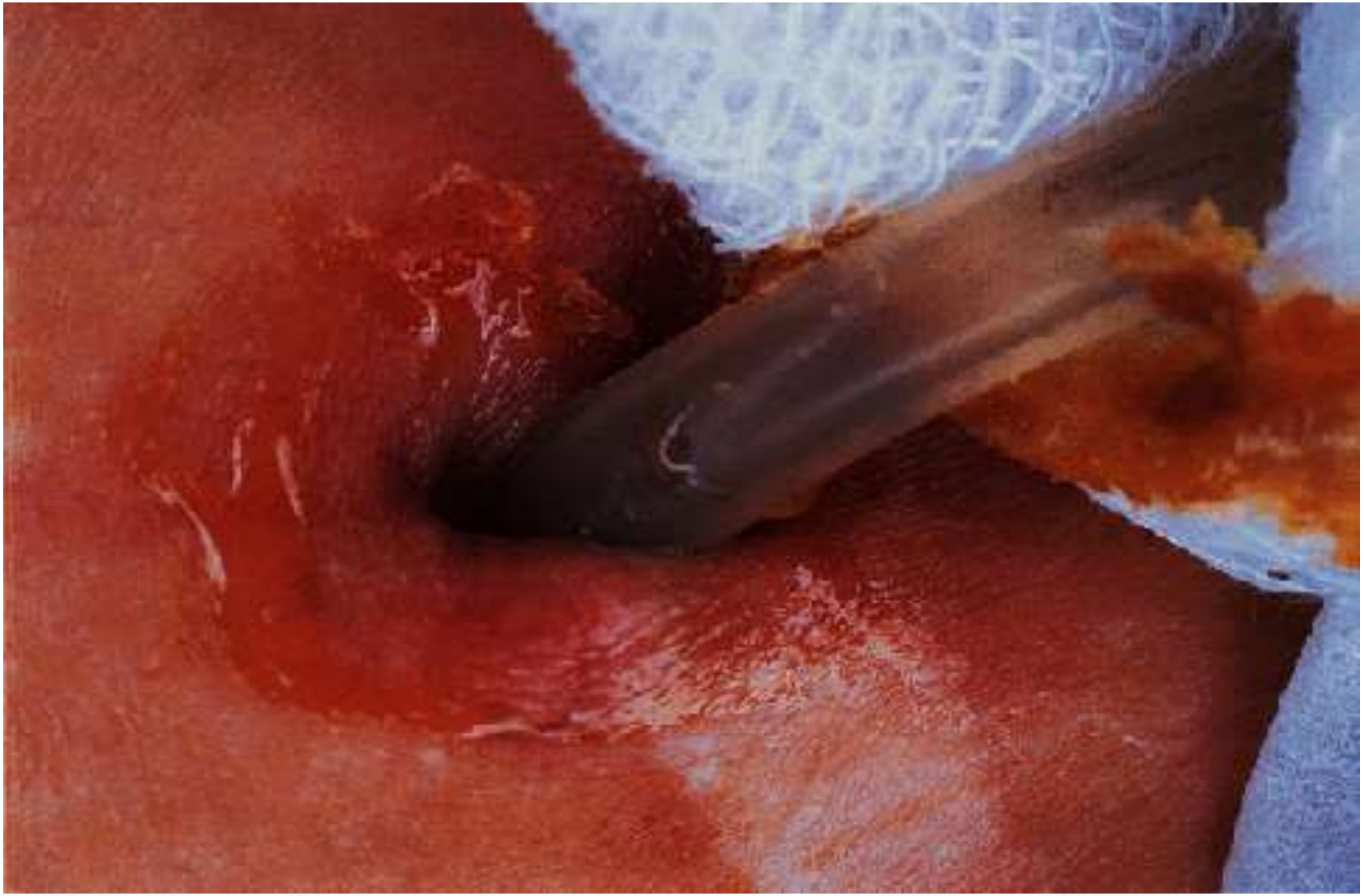
Infectious complications of PD

1. Peritonitis
2. ESI (exit site infection)
3. **TI (tunnel infection)**

Tunnel infection – symptoms

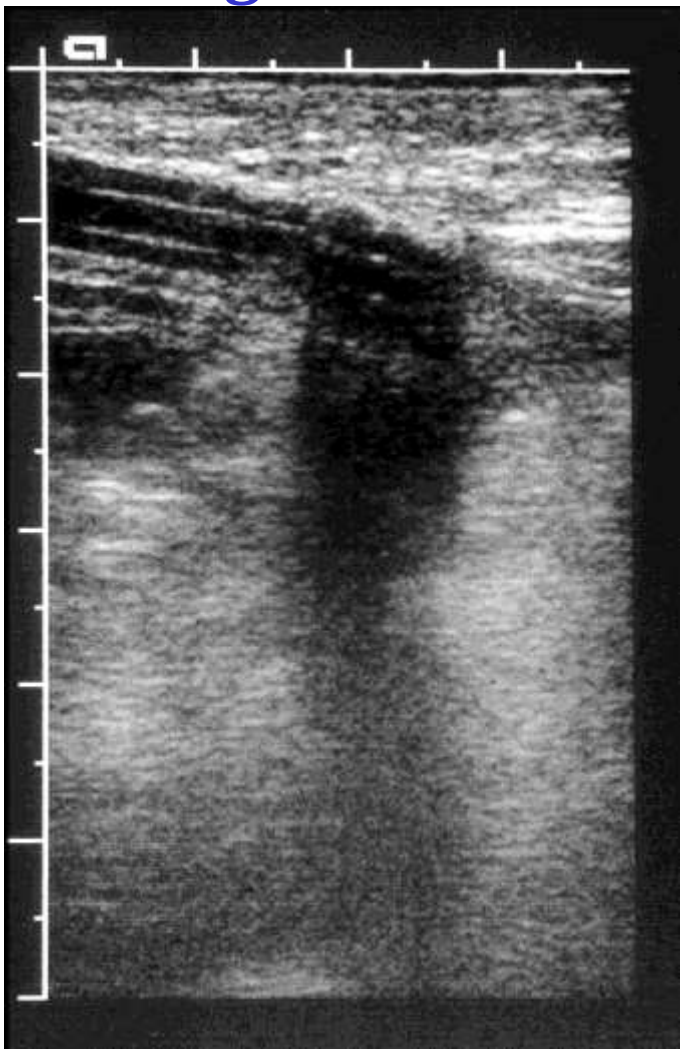
- Painfullness
- Redness
- Swelling
- Purulent leakage from the exit site

USG



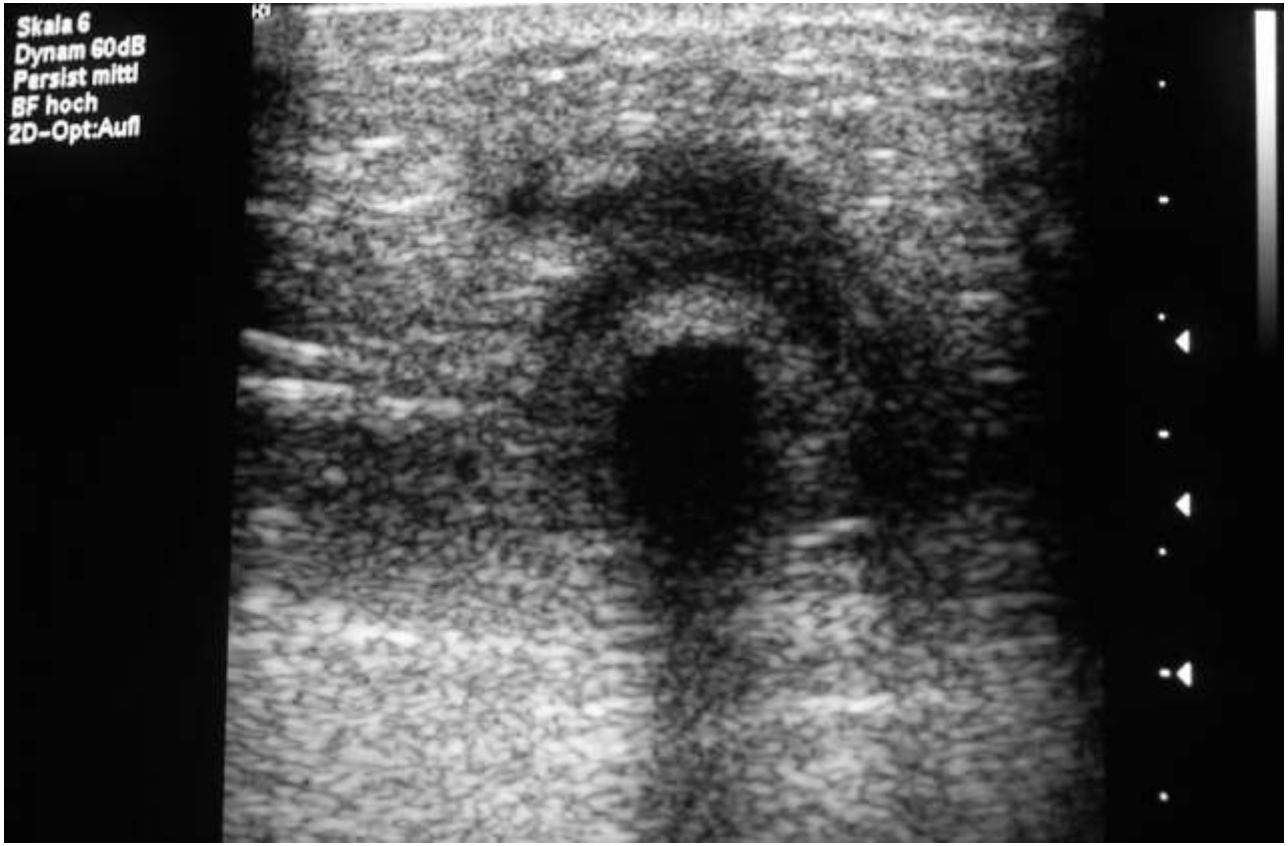
Ultrasonography of the tunnel – normal

Longitudinal view



Transverse view

Ultrasonography of the tunnel – infection
Collection of the purulent …



Tunnel infection – conservative treatment

1. Dressing with Gentamycin, Rifampin, Trim / Sulfa.

2. Flush of the tunnel with ↑ drugs – gentle injection to the tunnel.

3. Shaving of the external cuff if extruded.

What's new? (Annual Dialysis Conference, Tampa 2005)

Peritonitis treatment – ISPD 2005 guidelines

1. ESI and peritonitis **prevention**
   - **Antibiotic locally** (cream) – No direct indications which specific antibiotic, ALE ... Benefits of **gentamycin** over **mupirocin** – Pittsburgh centre experience

2. ESI / TI
   - **Agressive treatment**, min. 2 weeks
   - If **recurrent** ESI – **catheter** exchange

3. **Initial peritonitis treatment**
   - NO direct indications regarding antibiotics
   - Prefered IP way
   - Antibiotic to every exchange better than once daily – beside from vancomycyin
   - NO absolute need to change from APD to CAPD

Beth Piraino, Tampa 2005

When to remove the PD catheter?

ISPD 2005

1. Recurrent peritonitis – 2nd infection within 1 month with the same pathogen

2. Bad clinical results of the peritonitis treatment – cloudy effluent after 5 days

3. Fungal peritonitis

4. Peritonitis in cause of ESI / TI

Beth Piraino, Tampa 2005

ISPD 2010

Peritoneal Dialysis International, Vol. 30, pp. 393–423
doi:10.3747/pdi.2010.00049

0896-8608/10 $3.00 + .00

ISPD GUIDELINES/RECOMMENDATIONS

PERITONEAL DIALYSIS-RELATED INFECTIONS RECOMMENDATIONS: 2010 UPDATE

Philip Kam-Tao Li,[1] Cheuk Chun Szeto,[1] Beth Piraino,[2] Judith Bernardini,[2] Ana E. Figueiredo,[3] Amit Gupta,[4] David W. Johnson,[5] Ed J. Kuijper,[6] Wai-Choong Lye,[7] William Salzer,[8] Franz Schaefer,[9] and Dirk G. Struijk[10]

ISPD 2010

1. Methods of reporting PD-related infections.
2. ESI and TI management.
3. Peritonitis management
4. Patient education

TABLE 2
Oral Antibiotics Used in Exit-Site and Tunnel Infection

Amoxicillin	250–500 mg b.i.d.
Cephalexin	500 mg b.i.d. to t.i.d. (41)
Ciprofloxacin	250 mg b.i.d. (29)
Clarithromycin	500 mg loading dose, then 250 mg b.i.d. or q.d. (30)
Dicloxacillin	500 mg q.i.d.
Erythromycin	500 mg q.i.d.
Flucloxacillin (or cloxacillin)	500 mg q.i.d.
Fluconazole	200 mg q.d. for 2 days, then 100 mg q.d. (41)
Flucytosine	0.5–1 g/day titrated to response and serum trough levels (25–50 µg/mL) (41)
Isoniazid	200–300 mg q.d. (42)
Linezolid	400–600 mg b.i.d. (41)
Metronidazole	400 mg t.i.d.
Moxifloxacin	400 mg daily
Ofloxacin	400 mg first day, then 200 mg q.d.
Pyrazinamide	25–35 mg/kg 3 times per week (31)
Rifampicin	450 mg q.d. for <50 kg; 600 mg q.d. for >50 kg
Trimethoprim/sulfamethoxazole	80/400 mg q.d.

b.i.d. = 2 times per day; q.d. = every day; t.i.d. = 3 times per day; q.i.d. = 4 times daily.

ISPD 2010

Oral dosing of antibiotics.

ISPD 2010

TABLE 4
Intraperitoneal Antibiotic Dosing Recommendations for CAPD Patients[a]

	Intermittent (per exchange, once daily)	Continuous (mg/L; all exchanges)
Aminoglycosides		
Amikacin	2 mg/kg	LD 25, MD 12
Gentamicin, netilmicin, or tobramycin	0.6 mg/kg	LD 8, MD 4
Cephalosporins		
Cefazolin, cephalothin, or cephradine	15 mg/kg	LD 500, MD 125
Cefepime	1000 mg	LD 500, MD 125
Ceftazidime	1000–1500 mg	LD 500, MD 125
Ceftizoxime	1000 mg	LD 250, MD 125
Penicillins		
Amoxicillin	ND	LD 250–500, MD 50
Ampicillin, oxacillin, or nafcillin	ND	MD 125
Azlocillin	ND	LD 500, MD 250
Penicillin G	ND	LD 50 000 units, MD 25 000 units
Quinolones		
Ciprofloxacin	ND	LD 50, MD 25
Others		
Aztreonam	ND	LD 1000, MD 250
Daptomycin (115)	ND	LD 100, MD 20
Linezolid (41)	Oral 200–300 mg q.d.	
Teicoplanin	15 mg/kg	LD 400, MD 20
Vancomycin	15–30 mg/kg every 5–7 days	LD 1000, MD 25
Antifungals		
Amphotericin	NA	1.5
Fluconazole	200 mg IP every 24–48 hours	
Combinations		
Ampicillin/sulbactam	2 g every 12 hours	LD 1000, MD 100
Imipenem/cilastin	1 g b.i.d.	LD 250, MD 50
Quinupristin/dalfopristin	25 mg/L in alternate bags[b]	
Trimethoprim/sulfamethoxazole	Oral 960 mg b.i.d.	

ND = no data; q.d. = every day; NA = not applicable; IP = intraperitoneal; b.i.d. = 2 times per day; LD = loading dose in mg/L; MD = maintenance dose in mg/L.

[a] For dosing of drugs with renal clearance in patients with residual renal function (defined as >100 mL/day urine output), dose should be empirically increased by 25%.

[b] Given in conjunction with 500 mg intravenous twice daily.

IP dosing of antibiotics.

Dosing of antibiotics in APD

ISPD 2010

TABLE 5
Intermittent Dosing of Antibiotics in Automated Peritoneal Dialysis

Drug	IP dose
Cefazolin	20 mg/kg IP every day, in long day dwell (112)
Cefepime	1 g IP in 1 exchange per day
Fluconazole	200 mg IP in 1 exchange per day every 24–48 hours
Tobramycin	LD 1.5 mg/kg IP in long dwell, then 0.5 mg/kg IP each day in long dwell (112)
Vancomycin	LD 30 mg/kg IP in long dwell; repeat dosing 15 mg/kg IP in long dwell every 3–5 days (aim to keep serum trough levels above 15 µg/mL)

IP = intraperitoneal; LD = loading dose.

ISPD Pediatric guidelines on infectious complications 2012 (1)

ISPD 2012

- Guideline 1 – Training and periodic retraining
- Guideline 2 – Catheter type and placement – 2 cuff cath, antibiotic IV
- Guideline 3 – Early exit site care – 1/week dressing, cath immobilisation
- Guideline 4 – Chronic exit site care – antibiotic locally

ISPD Pediatric guidelines on infectious complications 2012 (2)

ISPD 2012

- Guideline 5 – Connectology – double bag, Y-set, spiking devices for APD

- Guideline 6 – Adjunctive antibiotic therapy – fungal antibiotics in risk patients, antibiotic prophylaxis in invasive therapy (dental, gastrointestinal, genitourinary)

- Guideline 7 – Ostomy patients – PD possible but some focus on safety needed, eg. Distance from the ostomy to the exit site.

- Guideline 8 – Diagnosis of PD-related peritonitis – considered only if cloudy effluent. Standard diagnostics.

ISPD Pediatric guidelines on infectious complications 2012 (3) ISPD 2012

- Guideline 9 – Administration of antibiotics – IP better than IV
- Guideline 10 – Empiric antibiotic therapy – center-specific. Cefepime monotherapy if available.
- Guideline 11 – Modification of therapy for Gram-positive peritonitis – List of antibiotics and treatment time – 2 or 3 weeks (MRSA, VRE).
- Guideline 12 – Modification of therapy for Gram-negative peritonitis - List of antibiotics and treatment time – 2 or 3 weeks (E.coli res to 3gC, Pseudomonas sp., Stenotrophomonas sp.).

ISPD Pediatric guidelines on infectious complications 2012 (4)

ISPD 2012

- Guideline 13 – Modification of therapy for culture-negative peritonitis – 2 weeks of cefepime or ceftazidme. AG for 72h.

- Guideline 14 – Modification of therapy for fungal peritonitis – antifungal therapy for 2 weeks after symptoms resolution. Catheter removal.

- Guideline 15 – Relapsing peritonitis – the same organism within 4 weeks

- Guideline 16 – Adjunctive therapy, eg. Heparin

- Guideline 17 – Catheter removal and replacement

ISPD 2012

ISPD Pediatric guidelines on infectious complications 2012

- Guideline 18 – Diagnosis of catheter-related infection
- Guideline 19 – Treatment of catheter-related infection
- Guideline 20 – Modification of APD
- Guideline 21 – Evaluation of primary response
- Guideline 22 – Failure to demonstrate improvement

Conclusions

1. The management of infectious complications is critical for the clinical outcome of PD patients in the **short** term as well as **long** term.

2. We **can** influence the infections' incidence.

3. We **can** manage infections.

4. HD patients **suffer** from infections too.

Спасибо Большое за внимание!