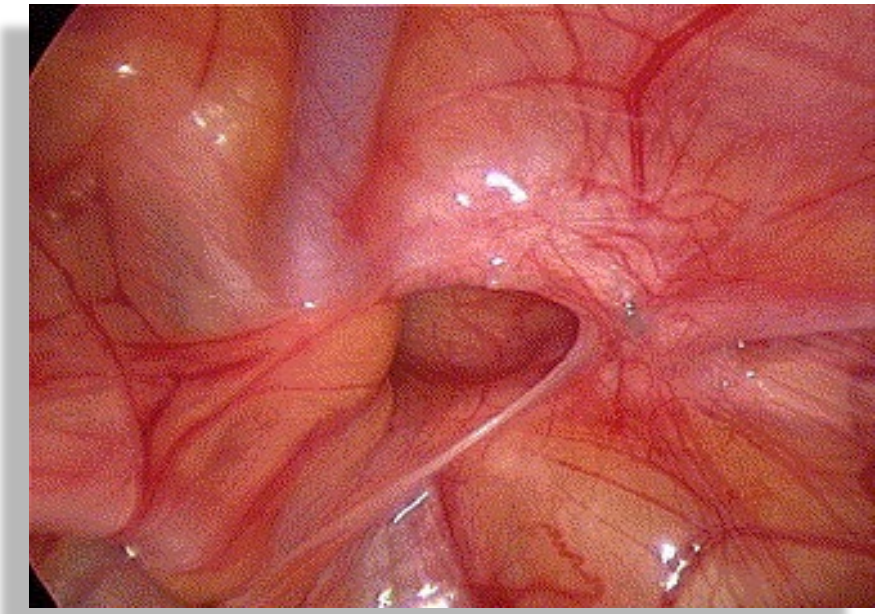
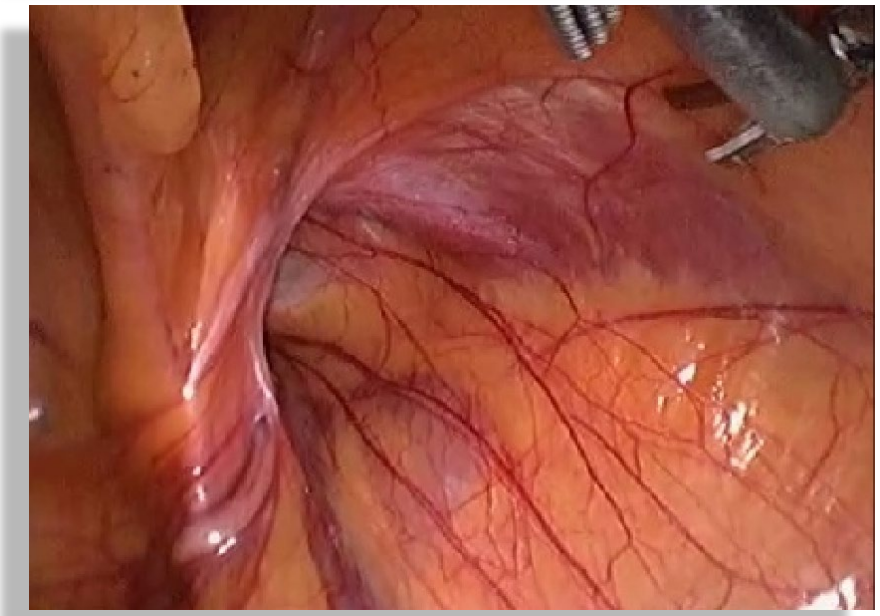
"Le peritoniti batteriche e le infezione dell'exite-site in dialisi peritoneale".

Valerio Vizzardi

ASST-Spedali Civili di Brescia

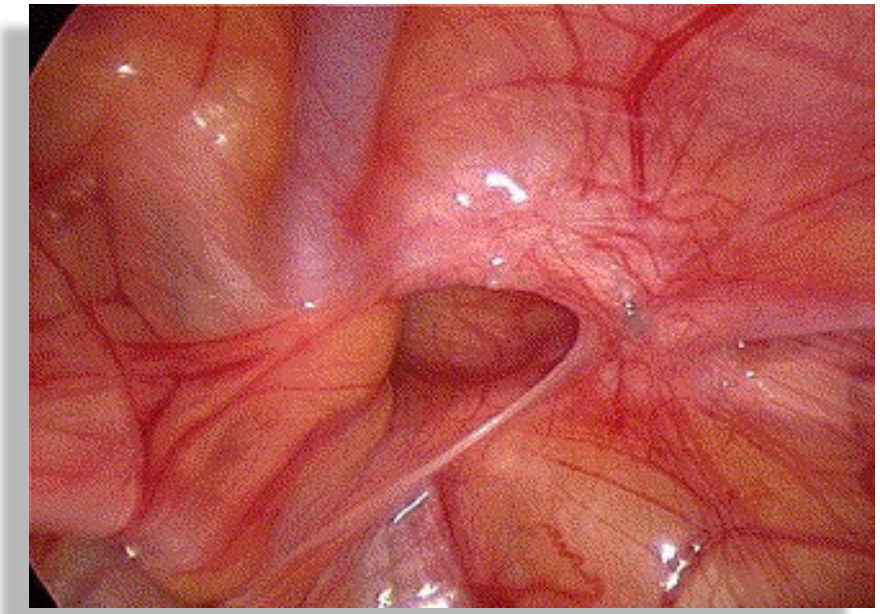


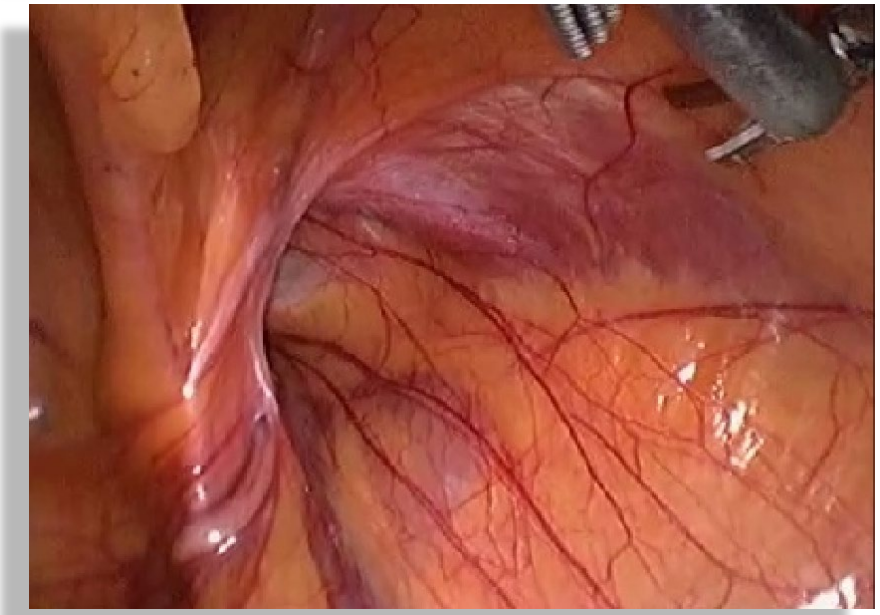


1730, James Douglas: "Il peritoneo si presenta liscio e piatto, lubrificato da un fluido allo scopo di preservarlo da quegli inconvenienti che altrimenti gli deriverebbero dal continuo attrito".

MEMBRANA BIOLOGICA:

- Membrana semipermeabile bidirezionale
- Superficie: 1.7-2 m^2 (circa la BSA)
- Drenaggio "linfatico": 1-2 ml/min
- Flusso ematico capillare: 50-100 ml/min
- Parietale (20%): spessore 0.1-0.2 mm
- Viscerale (80%): spessore 0.05 mm
- Caratteristiche di trasporto differenti da paziente a paziente
- Modificazioni "*acute*" (in corso di peritonite) e "*croniche*" delle caratteristiche cinetiche (tempo trascorso in DP)



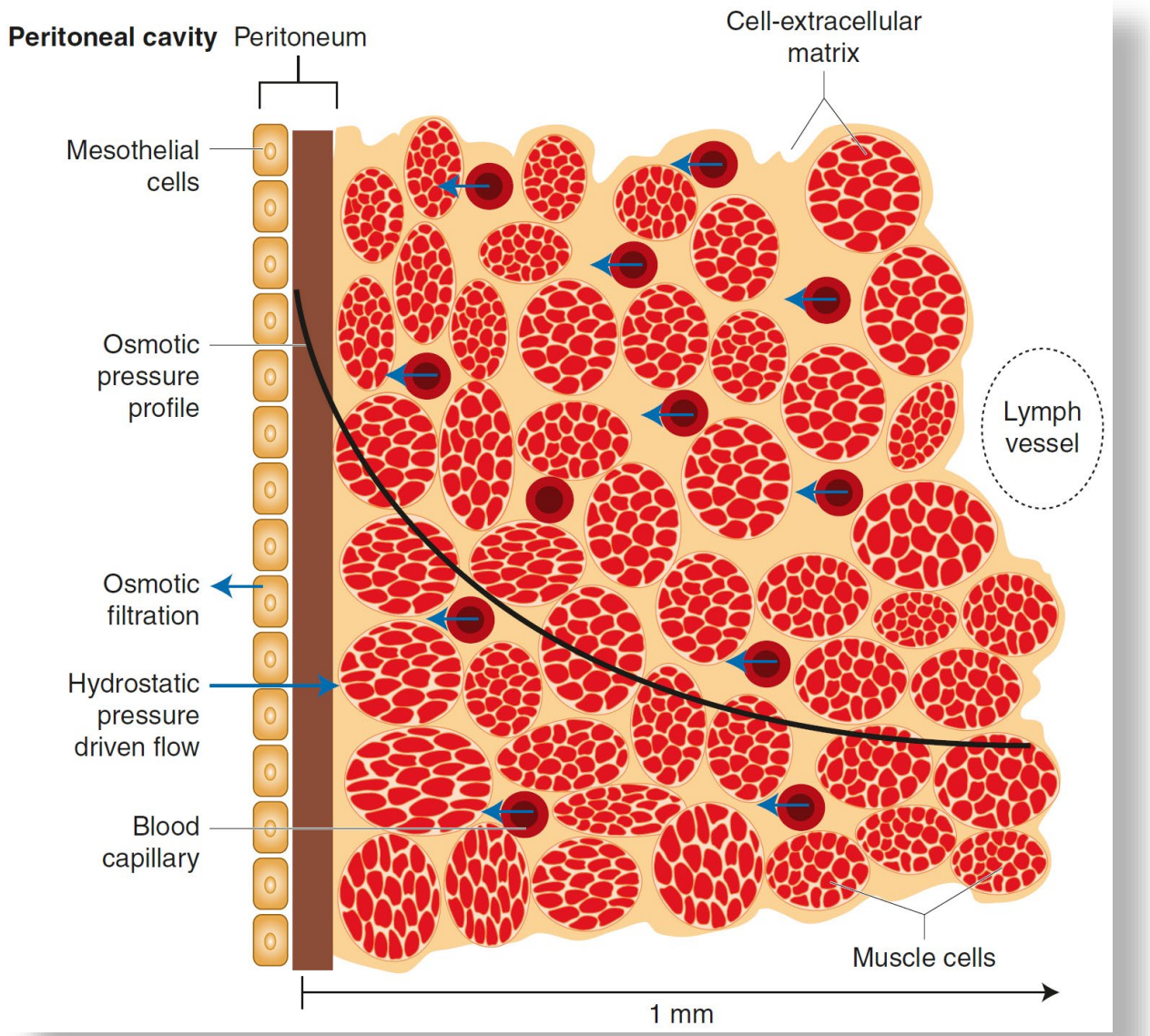


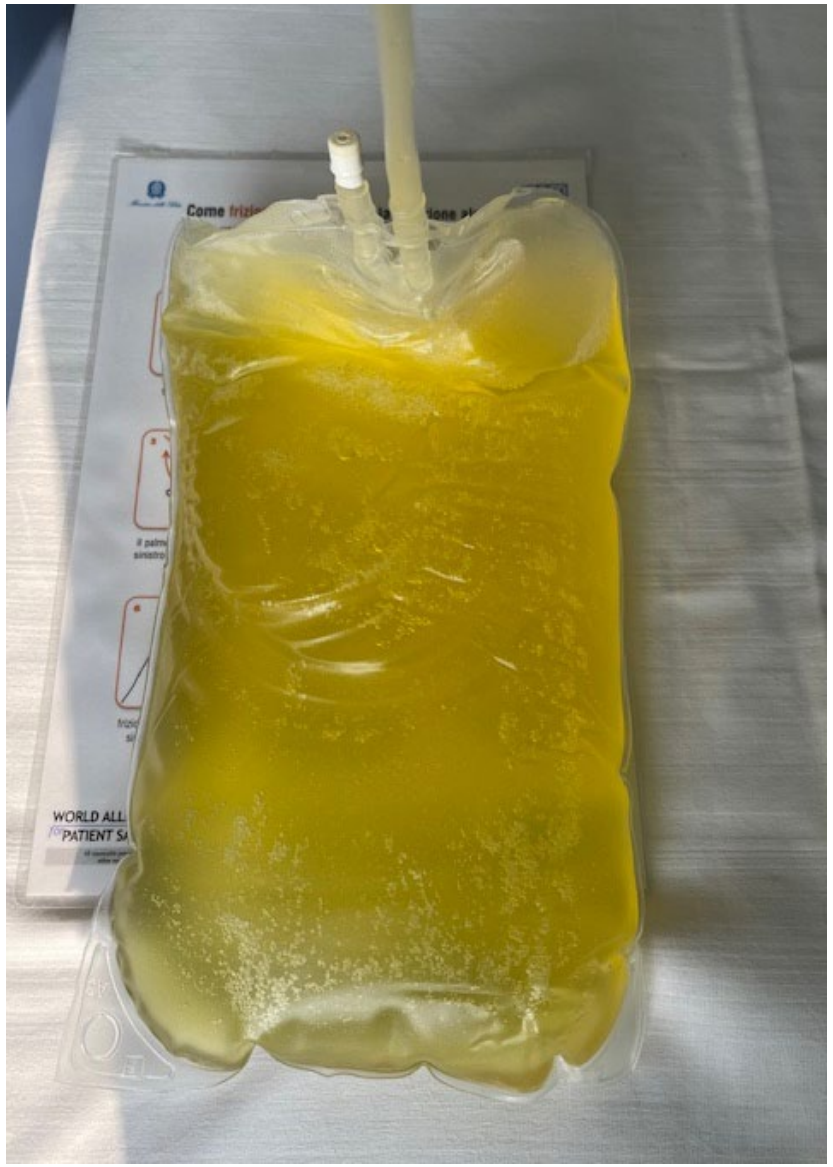
La peritonite è un'infiammazione della membrana sierosa che riveste i visceri e la cavità peritoneale dovuta, in genere, a contaminazione batterica. Si distingue in:

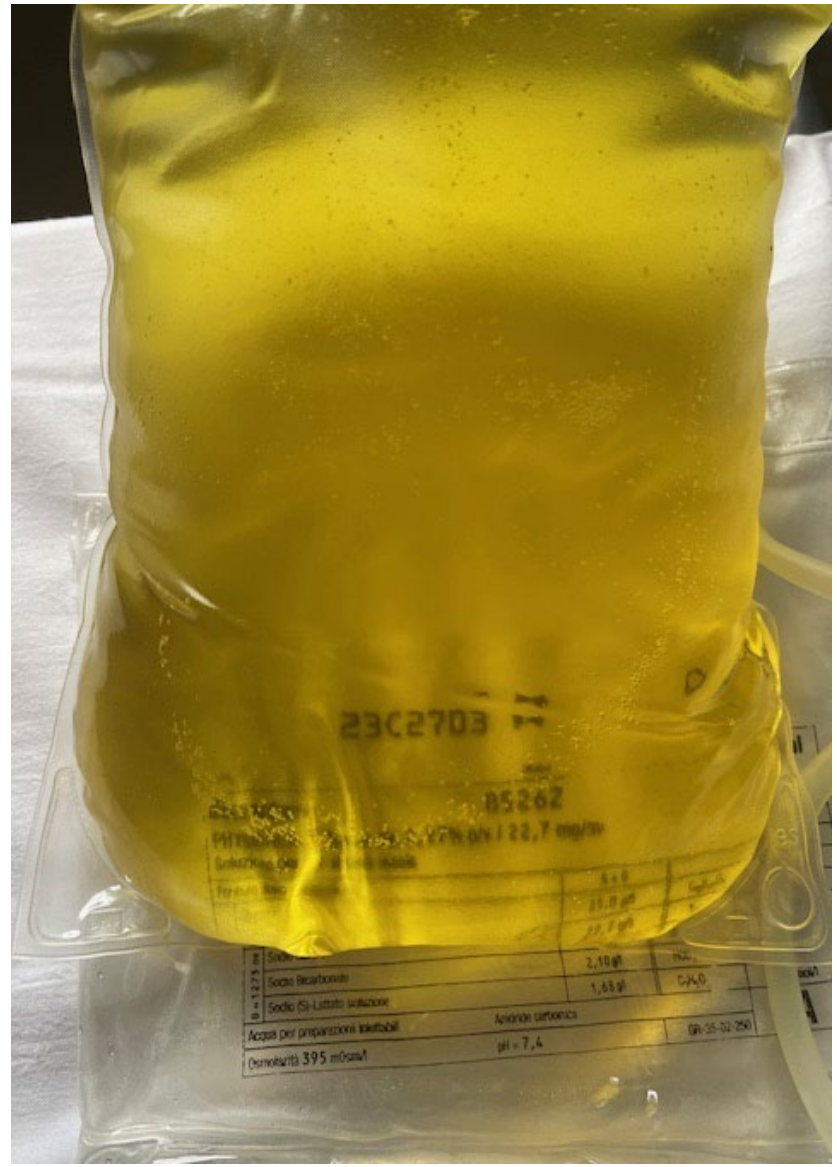
- *primitiva* (quando non c'è evidenza di un focolaio settico)
- *secondaria* (per invasione batterica o azione di agenti chimici a partenza da un focolaio tossi-infettivo del tubo digerente, del sistema epato-bilio-pancreatico, dell'apparato uro-genitale; per necrosi o perforazione di un viscere cavo o per deiscenza anastomotica; per un trauma chiuso o aperto)
- *terziaria* (per ricorrenza o persistenza di una peritonite secondaria o primaria in seguito a trattamento inefficace).

La peritonite può essere mortale se non curata immediatamente.

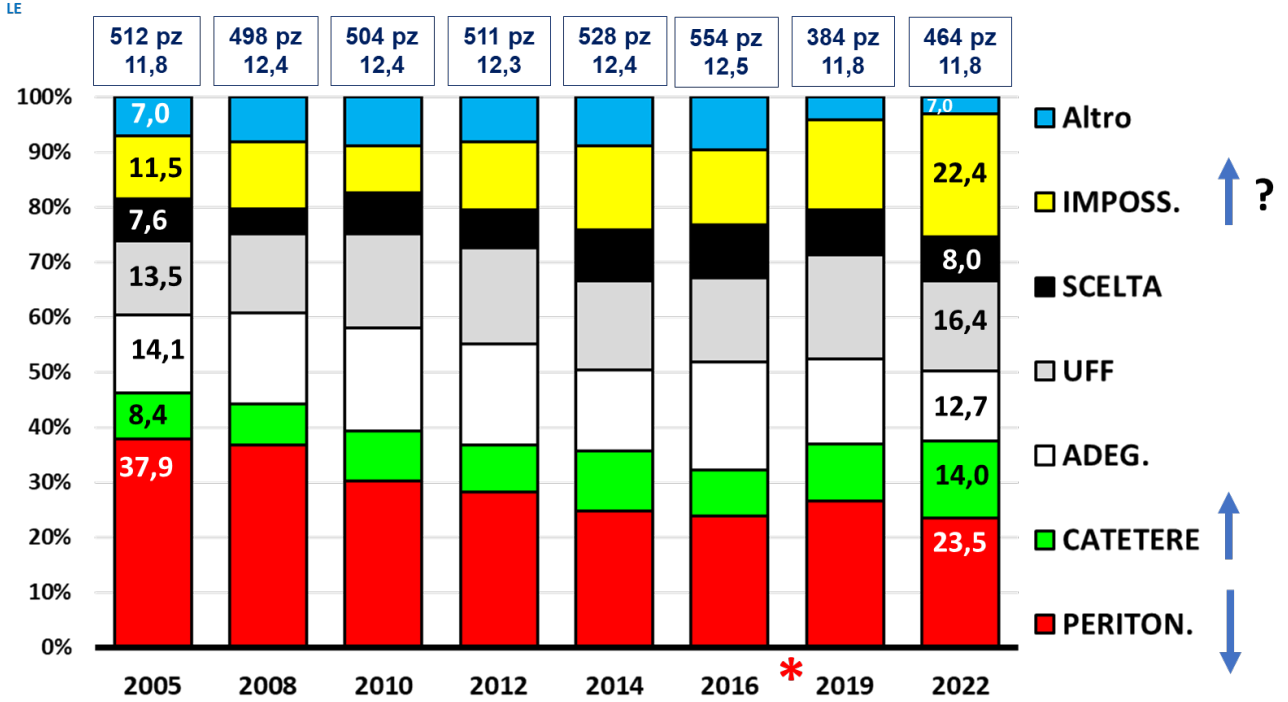
Acute peritonitis is associated with an increase in small-solute transport, as a result of inflammation-induced increases in peritoneal capillary surface area and vascular permeability.







The incidence of peritonitis has been decreasing over time in patients on chronic peritoneal dialysis, in part due to technological and procedural improvements in PD. Nevertheless, peritonitis remains the main infection seen in PD patients and is a major cause of PD catheter loss and transfer to HD. Furthermore, peritonitis can cause damage to the peritoneal membrane, sometimes irreversibly, and is a leading cause of hospitalization in PD patients.



Saxena AB. Applied Peritoneal Dialysis, 2021

Neri L. et al. Giorn Ital Nefrol, 2023

PERITONITIS DURING CAPD: A MIXED BAG

Perit Dial Int 1981

Stephen I. Vas

Our definition of peritonitis is based on the following criteria: (1) Abdominal pain, (2) cloudy drainage fluid (greater than 50 neutrophils/mm1, (3) demonstration of microorganisms from the drainage fluid. Combination of any two out of the three criteria above defines peritonitis.

"Nella pratica clinica corrente è la presenza dei primi due segni a far porre diagnosi di peritonite e a determinare l'inizio della terapia antibiotica empirica; questa verrà poi eventualmente modificata in base al risultato della colorazione di Gram e dell'antibiogramma".

La Milia V. et al. G Ital Nefrol, 2007

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

DOI: 10.1177/08968608221080586
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Philip Kam-Tao Li[1,2], Kai Ming Chow[1,2], Yeoungjee Cho[3,4], Stanley Fan[5], Ana E Figueiredo[6], Tess Harris[7], Talerngsak Kanjanabuch[8,9], Yong-Lim Kim[10], Magdalena Madero[11], Jolanta Malyszko[12], Rajnish Mehrotra[13], Ikechi G Okpechi[14], Jeff Perl[15], Beth Piraino[16], Naomi Runnegar[17], Isaac Teitelbaum[18], Jennifer Ka-Wah Wong[19], Xueqing Yu[20,21] and David W Johnson[3,4]

Initial presentation and management of peritonitis

- We recommend that peritonitis always be diagnosed when at least two of the following are present: (1) clinical features consistent with peritonitis, that is, abdominal pain and/or cloudy dialysis effluent; (2) dialysis effluent white cell count >100/μL or >0.1 × 10^9/L (after a dwell time of at least 2 h), with >50% PMN; and (3) positive dialysis effluent culture **(**1C**)**.
- We recommend that PD effluent be tested for cell count, differential, gram stain and culture whenever peritonitis is suspected **(**1B**)**.
- We recommend that PD patients presenting with cloudy effluent be presumed to have peritonitis and treated as such until the diagnosis can be confirmed or excluded **(**1C**).**

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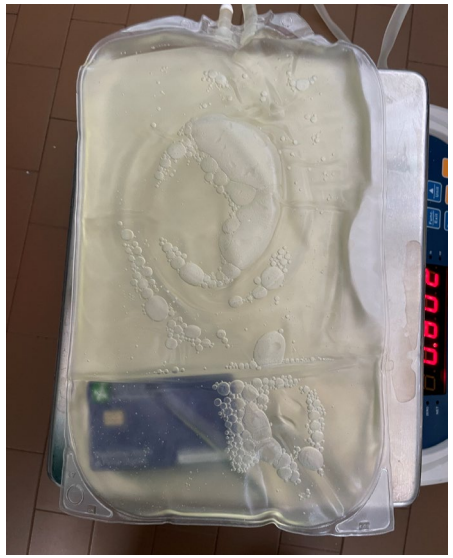
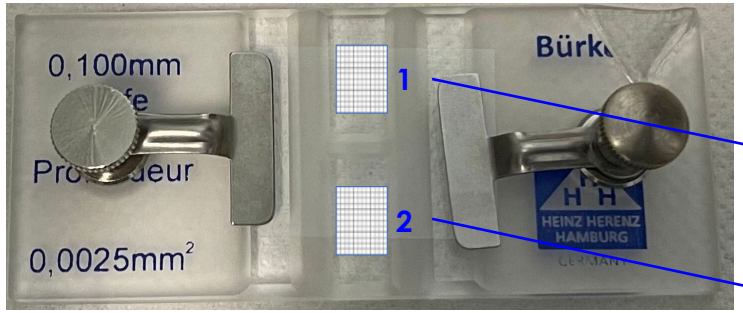


Il dubbio di peritonite in un paziente portatore di catetere peritoneale deve essere posto in presenza anche di ***una sola*** delle seguenti condizioni:

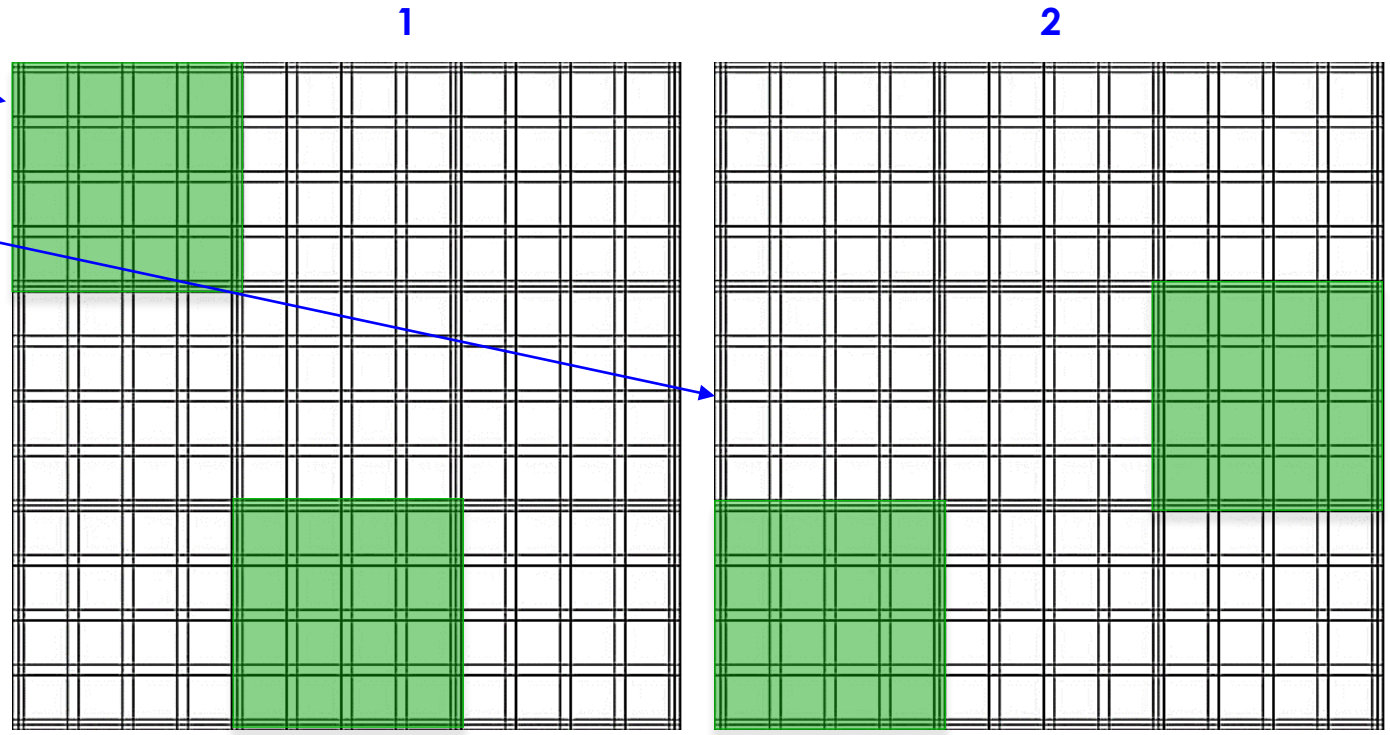
1. *Dolore addominale o altri segni/sintomi di flogosi peritoneale, anche se non associato a dialisato non limpido/torbido*
2. *Dialisato non limpido/torbido, anche senza segni/sintomi di flogosi peritoneale*

In presenza di una delle due condizioni è necessario provvedere ad una prima diagnostica, preferibilmente con la conta dei GB con camera di Bürker o, in alternativa, con Combur-test.

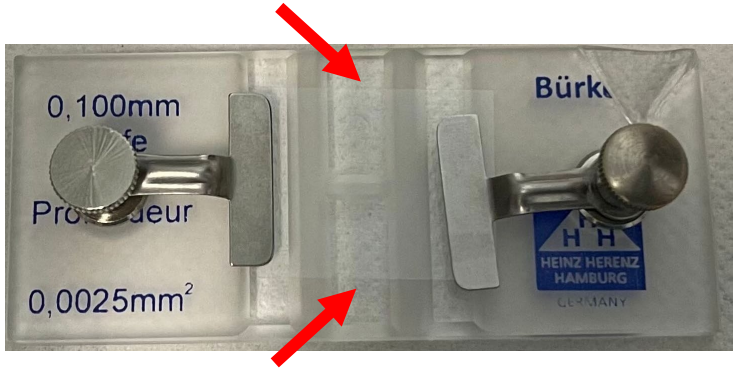
Camera di Bürcher



9 quadrati (1 mm) ciascuno formato da 4 quadrati (0.2 mm) + 4 spessori da 0.05 mm.

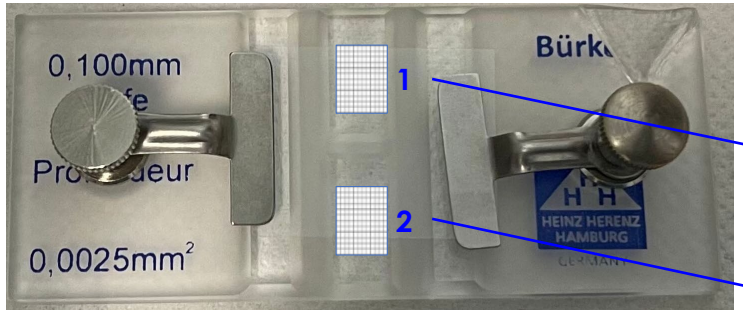


1. Si capovolge più volte la provetta con il liquido peritoneale
2. Si inserisce il vetrino nelle due mollette della CB
3. Con una pipetta si inseriscono alcune gocce di liquido per ciascun lato libero del vetrino in modo che si distribuisca uniformemente sotto di esso



Contare i GB presenti in almeno due quadrati grandi per ciascuno reticolo

Camera di Bürcher



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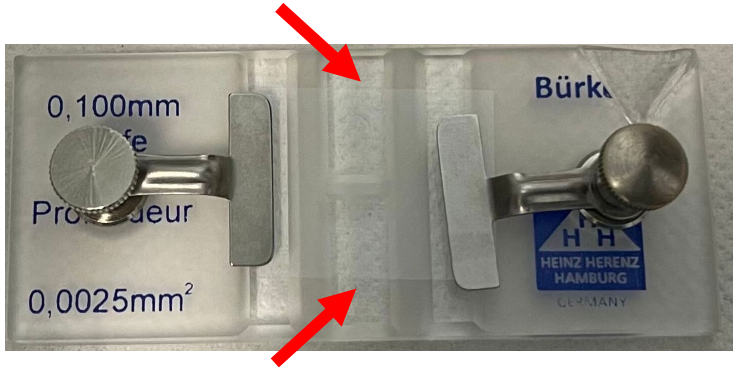

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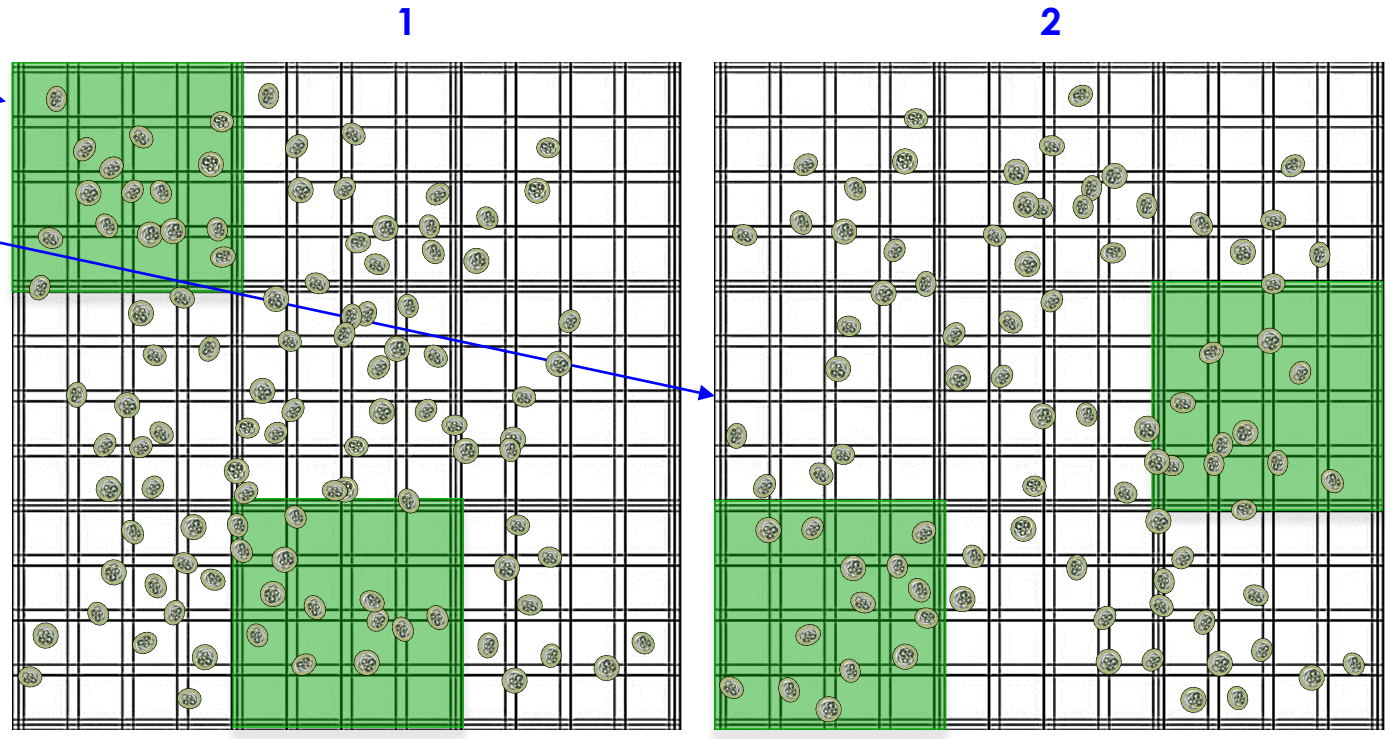
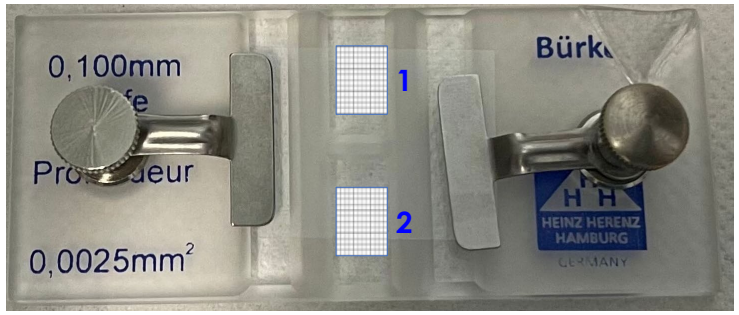
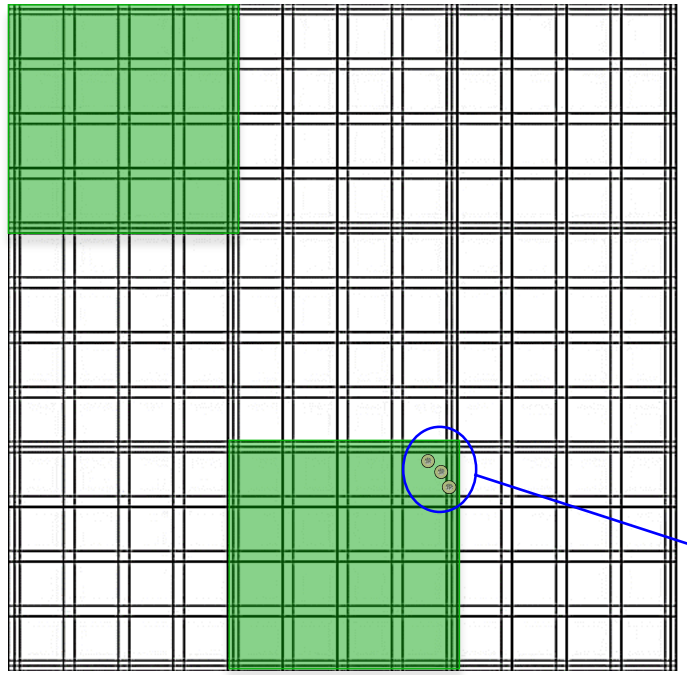


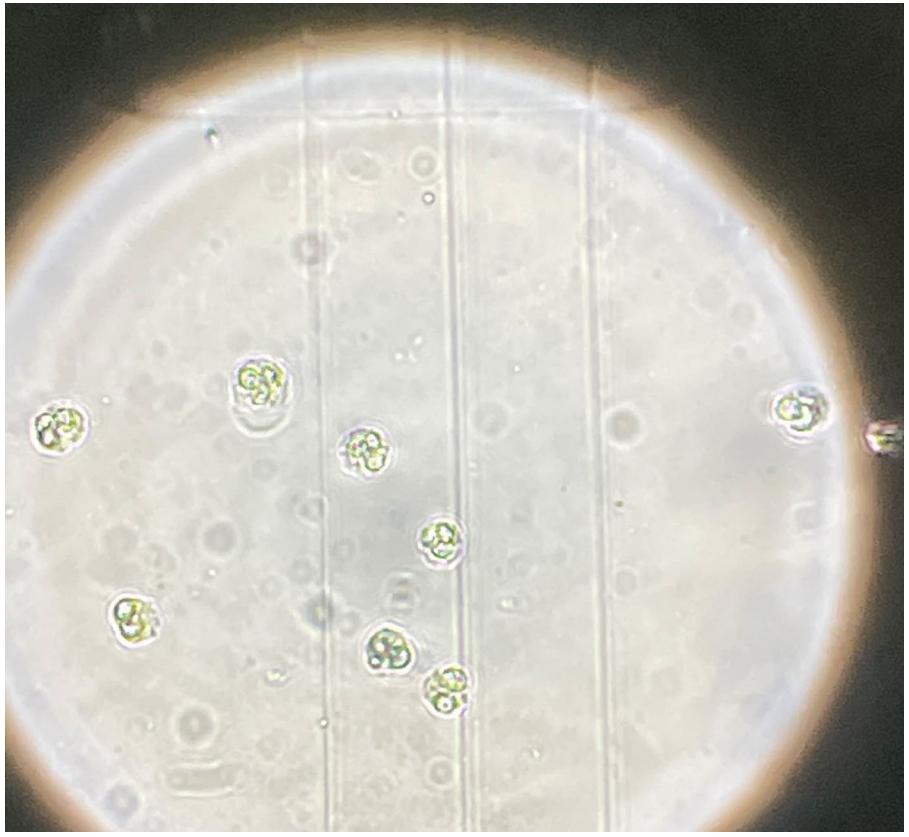
Contare i GB presenti in almeno due quadrati grandi per ciascuno reticolo

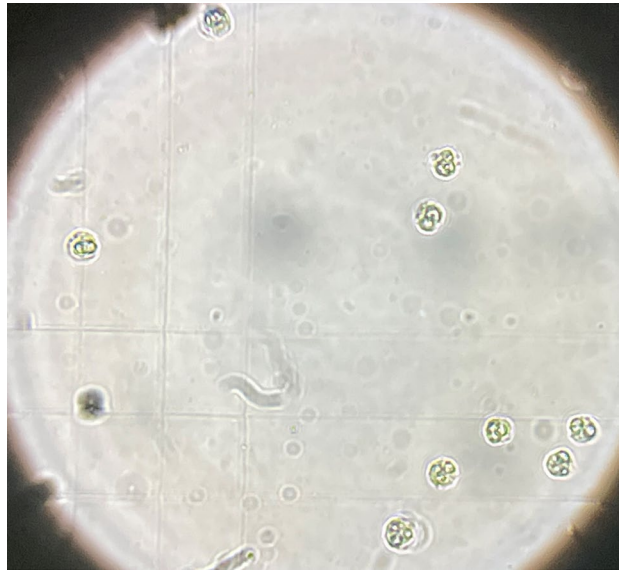
NB: se conti i GB presenti sulle righe di un lato del quadrato grande (tripla riga), non contare i GB presenti sulle righe del lato opposto

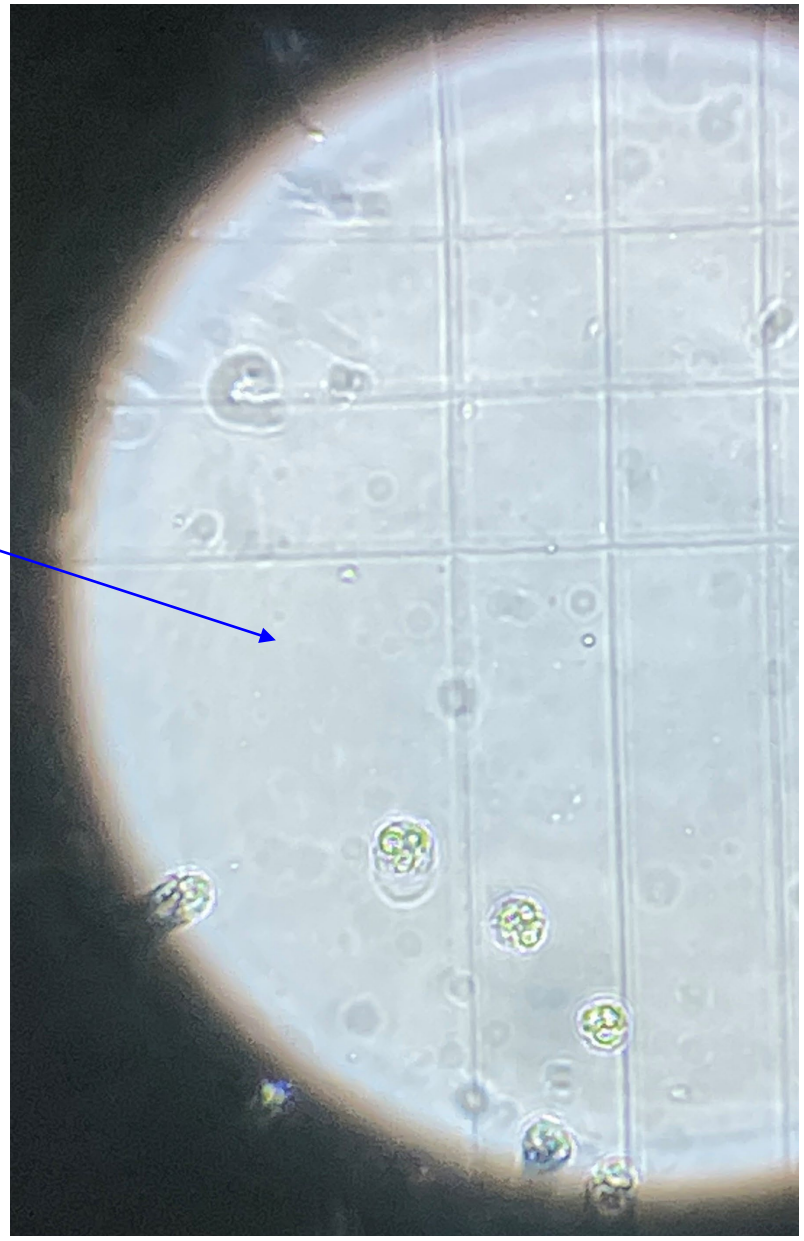
Camera di Bürcher

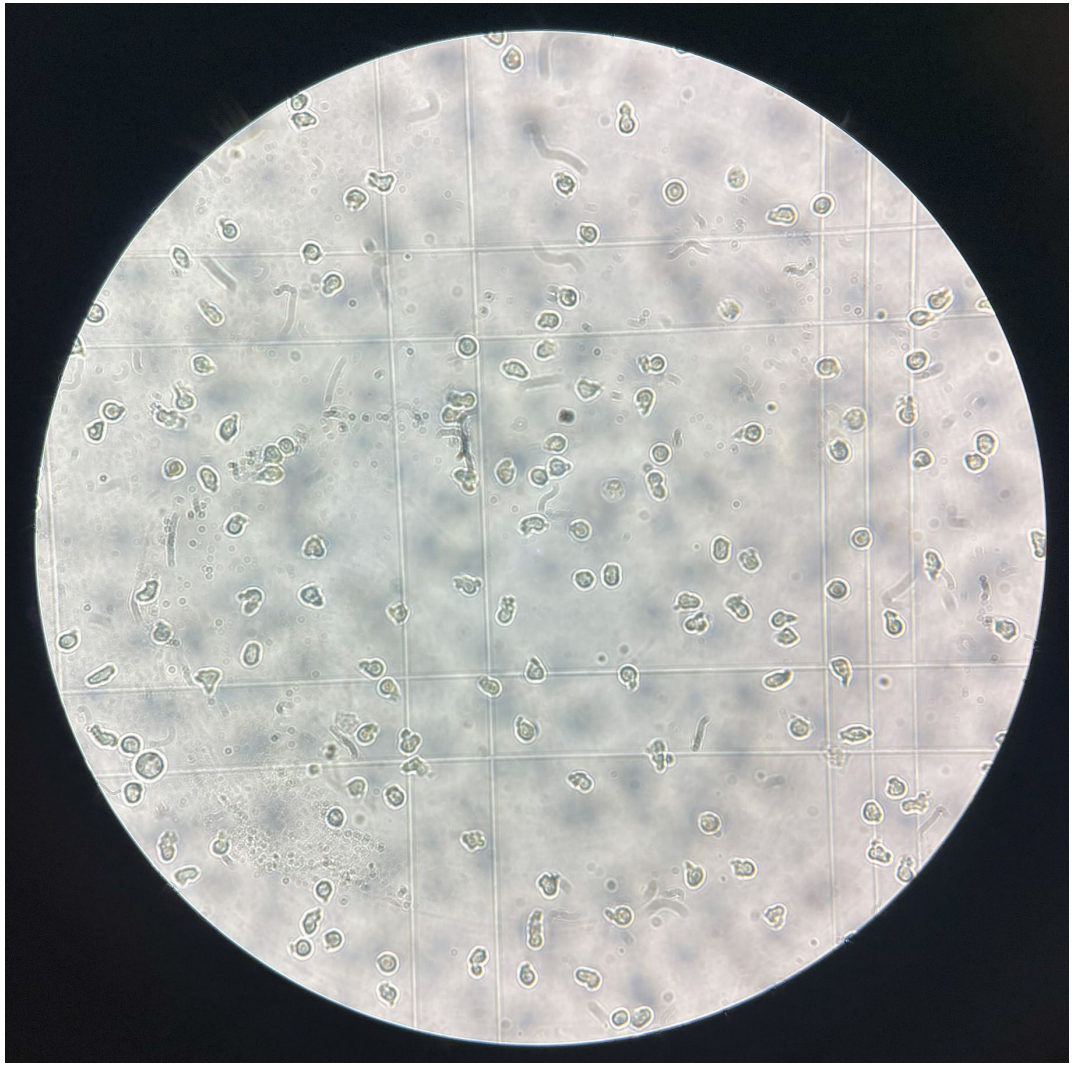


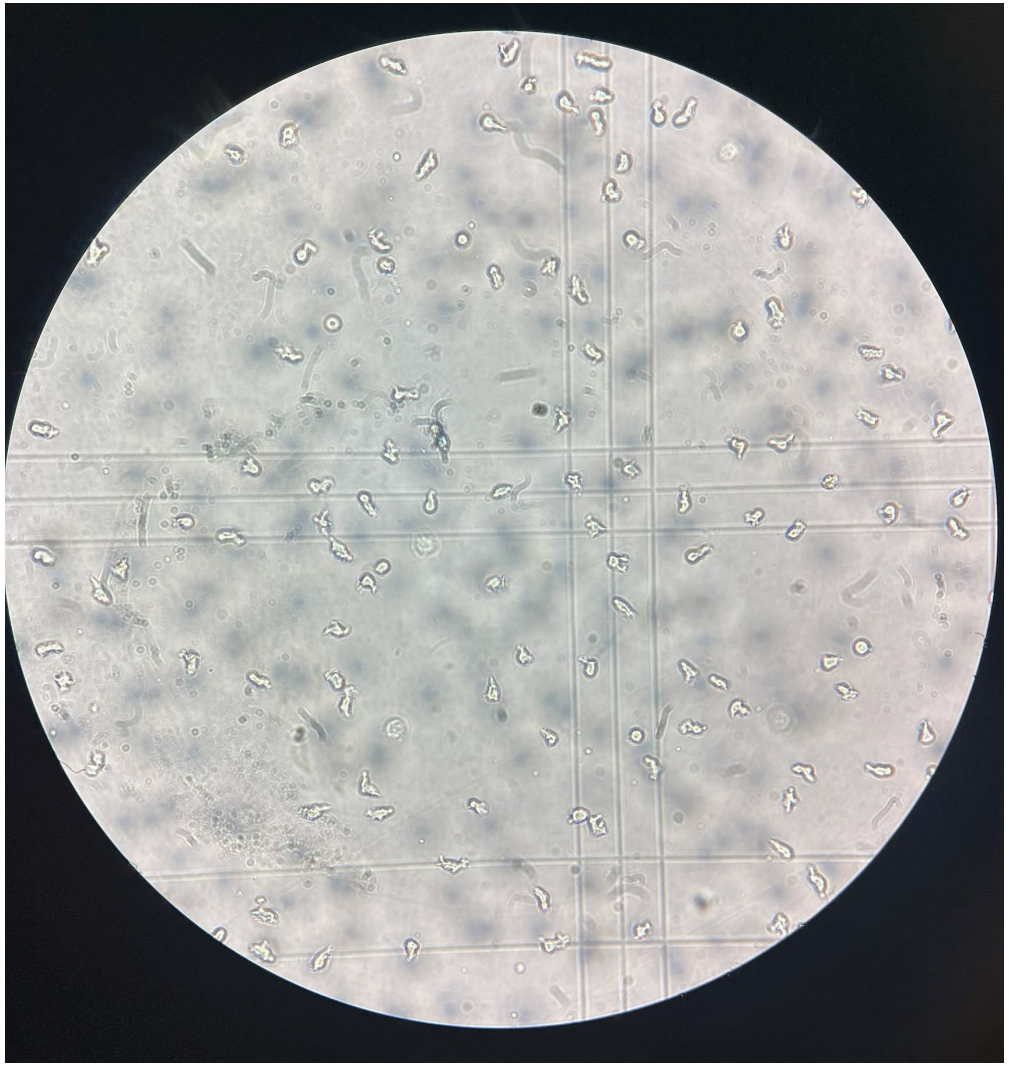


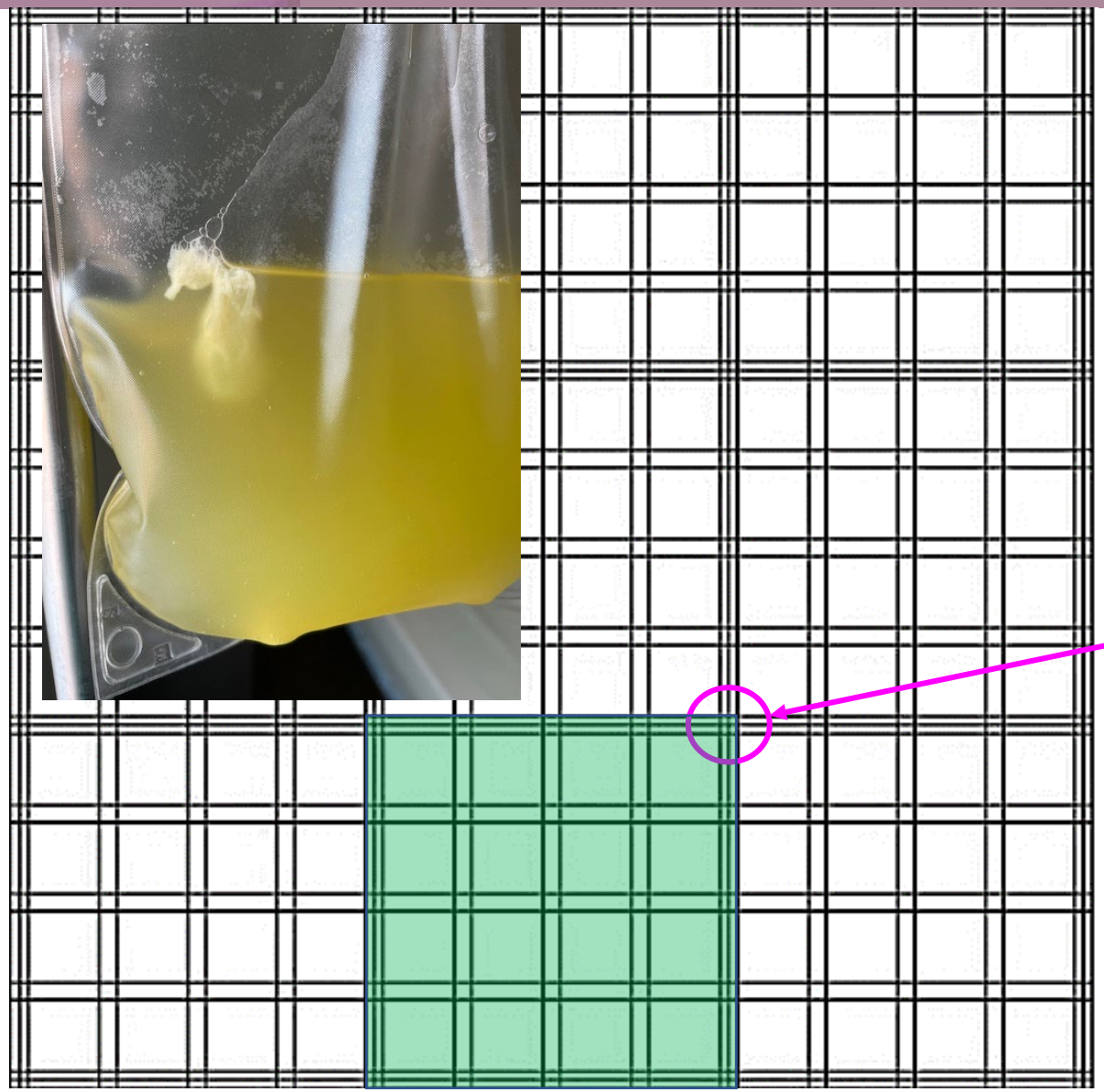


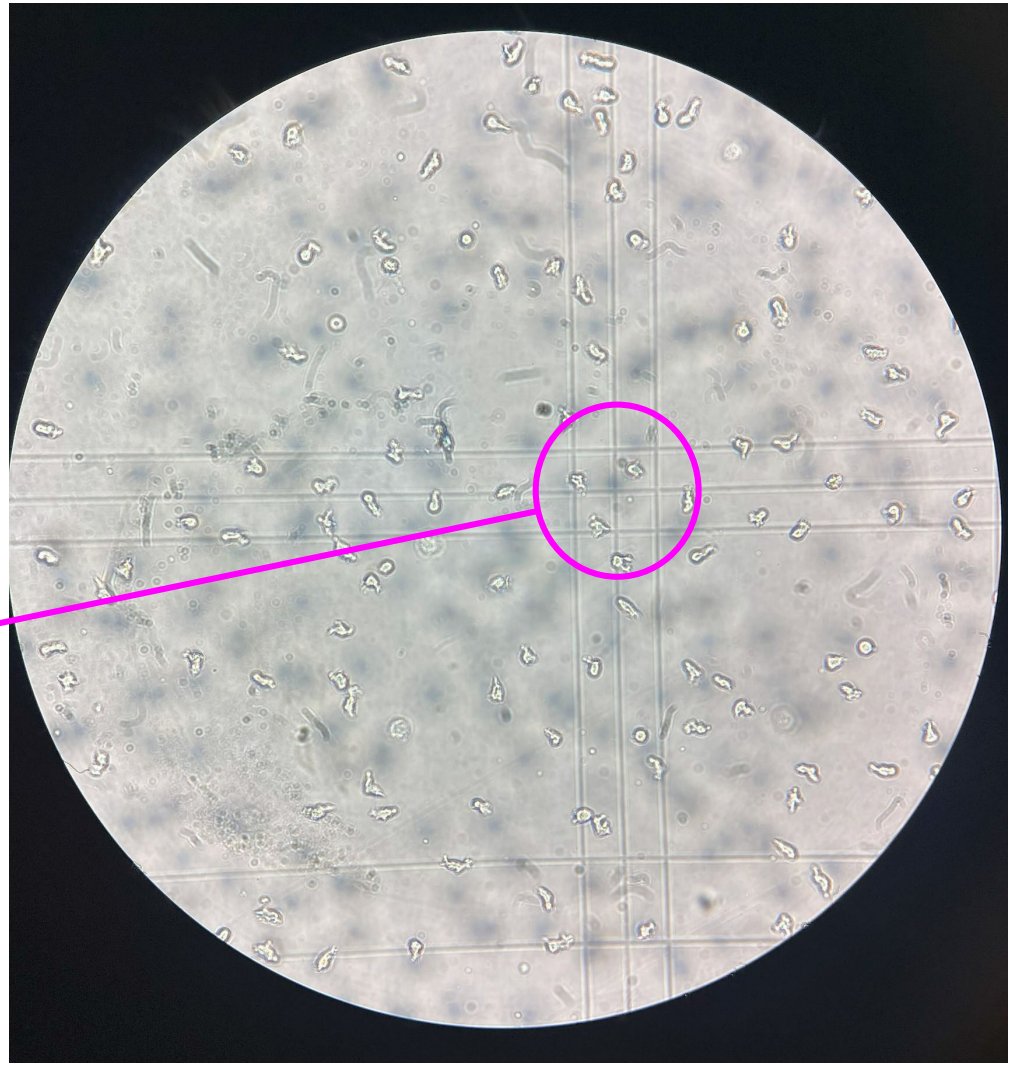












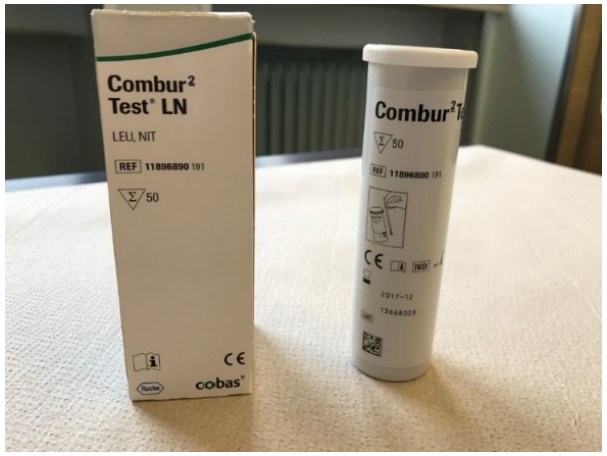
Standardizzare conta e colture

Criteri definiti per CAPD

- Positività: leucociti >100 /mm3 (dopo una stasi di 3-6 ore)
- Attenzione per stasi troppo brevi o troppo lunghe
- Attenzione a pazienti con periodi ad addome vuoto (es: DP incrementale)

Per pazienti in APD

- Attenzione per stasi troppo brevi o troppo lunghe
- Attenzione a pazienti con periodi ad addome vuoto
- Consigliato lavaggio seguito da stasi adeguata per esecuzione conta GB (NON MENO DI DUE ORE)
- Criterio aggiuntivo: polimorfonucleati >50% (indipendentemente dalla durata della stasi del dialisato raccolto)



1. Immergere la striscetta nel liquido peritoneale per 2-3 secondi
2. attendere 60-120''
3. Se il tampone si colora il test è positivo! Iniziare il protocollo per peritonite

NB: utile ripetere sempre il test

DOLORE ADDOMINALE E/O LIQUIDO ALTERATO

INFERMIERE: raccoglie informazioni avvisa il MDG

MDG: se dubbio di peritonite, invia il paziente in PS

INFERMIERE: se paz addome pieno, blocca il drenaggio

In PS con addome <u>PIENO</u> da >2 ore ma <6 ore:

▶ Drenaggio, colture, conta GB o Combur-test

Se addome <u>PIENO</u> da <2 ore o >6 ore:

1. Drenaggio, colture
2. **STASI** (un litro di 1.36% per minimo due ore)
3. Drenaggio, colture, conta GB o Combur-test

In PS con addome <u>VUOTO</u>:

1. Drenaggio, se presente fondo inviare colture
2. Lavaggio peritoneale (1.36% **<u>senza</u>** antibiotico)
3. **STASI** (un litro di 1.36% per minimo due ore)
4. Drenaggio, colture, conta GB o Combur-test

NEGATIVO

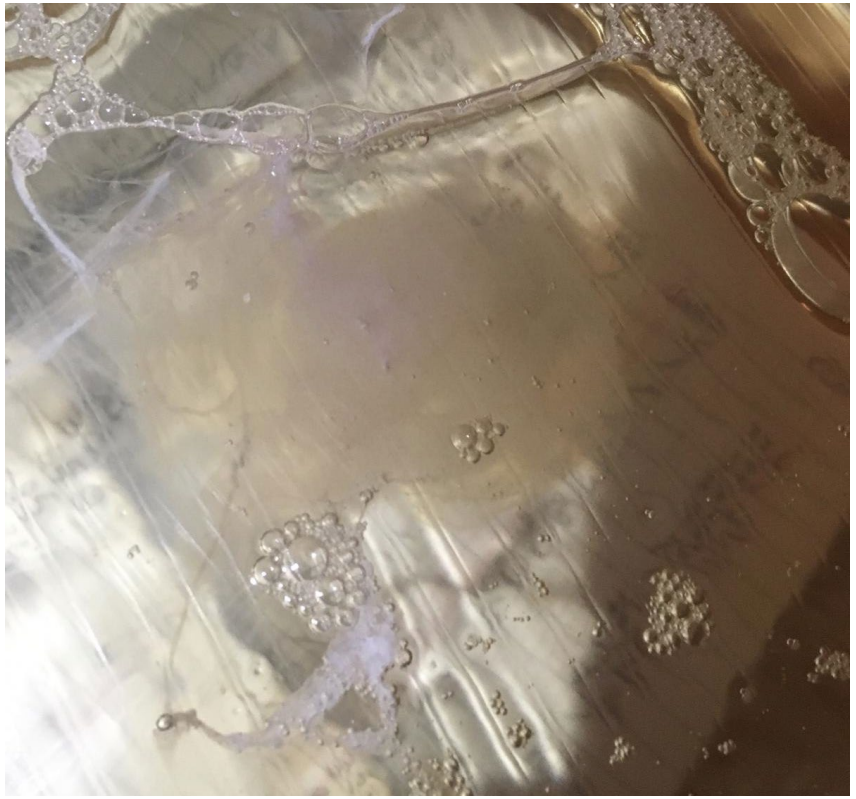
<u>DIMESSO</u> CONTROLLI IN REPARTO DP

POSITIVO

<u>RICOVERO</u> PROTOCOLLO PERITONITE

Table 4. Differential diagnosis of cloudy effluent.

Cellular causes
PMN leucocytes
Culture-positive infectious peritonitis
Infectious peritonitis with sterile cultures
Chemical peritonitis
Eosinophils
Dialysate eosinophilia
Chemical peritonitis
Monocyte/macrophages
Specimen taken from 'dry' abdomen (after prolonged peritoneal rest)
Red blood cells
Hemoperitoneum
Malignant cells
Lymphoma
Peritoneal metastasis
Non-cellular causes
Fibrin
Triglycerides (milky white appearance of effluent)
Calcium channel blockers
Lymphatic obstruction
Acute pancreatitis



CAUSES OF PERITONITIS

1. Contamination, most likely skin or environmental organisms
   - Contamination at the time of connection
   - Contamination from tubing
   - Hole in exchange tubing or catheter
   - Loss of cap on end of tubing or failure to close clamp with leaking
   - Product defects
2. Catheter related, most often staphylococcal species or *Pseudomonas aeruginosa*
   - Biofilm on internal portion of the catheter (relapsing, repeat peritonitis)
   - Exit-site and tunnel infection
3. Bowel-source enteric organisms including gram-negative rods, *Candida*, and anaerobes
   - Diverticulitis
   - Cholecystitis
   - Ischemic bowel
   - Colitis
   - Perforated stomach or intestine
   - Colonoscopy, especially with polypectomy
   - Constipation with transmural migration of organisms into peritoneum
4. Bacteremia, often *Streptococcus* or *Staphylococcus*
   - Transient from dental procedures
   - Infection of intravascular device
5. Gynecologic source, often *Streptococcus*, *Candida*, some gram-negative rods
   - Peritoneal vaginal leak
   - Vaginal delivery
   - Hysteroscopy

→ **INTRALUMINALE**: 30-40%
- ✓ Staphylococcus epidermidis
- ✓ Staphylococcus aureus
- ✓ Streptococcus viridans

→ **PERILUMINALE**: 20-30%
- ✓ Staphylococcus epidermidis
- ✓ Staphylococcus aureus
- ✓ Pseudomonas
- ✓ Miceti

→ **TRASMURALE**: 25-30%
- ✓ Colibacilli
- ✓ Anaerobi

→ **EMATOGENA**: 5-10%
- ✓ Streptococchi
- ✓ M. Tubercolosis

→ **ASCENDENTE**: 2-5%
- ✓ Lactobacilli
- ✓ Miceti

Piraino B. et al. Perit Dial Int 2011

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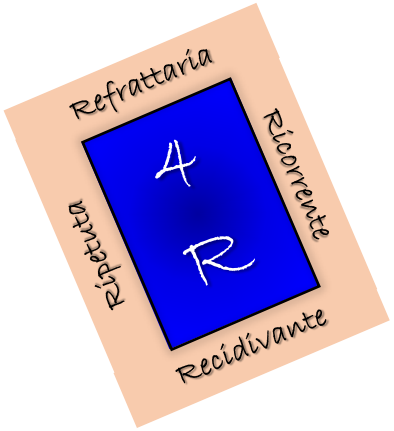
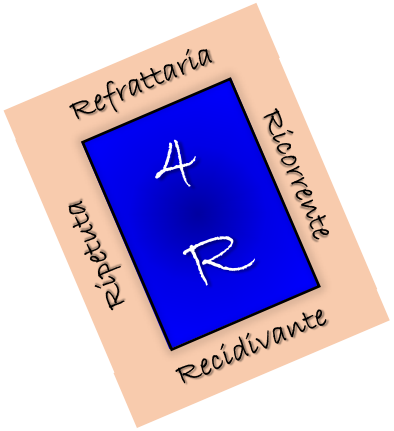


Table 1. Outcome specific definition following peritonitis.

Outcome	Definition
Medical cure	Complete resolution of peritonitis together with NONE of the following complications: relapse/ recurrent peritonitis, catheter removal, transfer to haemodialysis for ≥30 days or death
Refractory	Peritonitis episode with persistently cloudy bags or persistent dialysis effluent leukocyte count >100 × 10^9/L after 5 days of appropriate antibiotic therapy
Recurrent	Peritonitis episode that occurs within 4 weeks of completion of therapy of a prior episode but with a different organism
Relapsing	Peritonitis episode that occurs within 4 weeks of completion of therapy[a] of a prior episode with the same organism or one sterile (culture negative) episode (i.e. specific organism followed by the same organism, culture negative followed by a specific organism or specific organism followed by culture negative).
Repeat	Peritonitis episode that occurs more than 4 weeks after completion of therapy[a] of a prior episode with the same organism
Peritonitis-associated catheter removal	Removal of PD catheter as part of the treatment of an active peritonitis episode
Peritonitis-associated haemodialysis transfer	Transfer from PD to haemodialysis for any period of time as part of the treatment for a peritonitis episode
Peritonitis-associated death	Death occurring within 30 days of peritonitis onset or death during hospitalisation due to peritonitis
Peritonitis-associated hospitalisation	Hospitalisation precipitated by the occurrence of peritonitis for the purpose of peritonitis treatment delivery

PD: peritoneal dialysis.
[a]Completion of therapy is defined as the last day of antibiotic administration.

Tao Li PK, et al. Perit Dial Inter, 2022



Refractory peritonitis

- We recommend that PD catheter be removed in refractory peritonitis episodes, defined as failure of the PD effluent to clear after 5 days of appropriate antibiotics (1D).
- We suggest that observation for antibiotic effect longer than 5 days is appropriate if PD effluent white cell count is decreasing towards normal, instead of mandatory PD catheter removal if effluent does not clear up by day 5 (2C).

Relapsing, recurrent and repeat peritonitis

- We recommend timely PD catheter removal be considered for relapsing, recurrent or repeat peritonitis episodes (1C).
- We suggest that simultaneous PD catheter removal and reinsertion be considered after culture of the PD effluent has become negative and the PD effluent white cell count is below 100/μL, in the absence of concomitant exit site or tunnel infection (2C).

Tao Li PK, et al. Perit Dial Inter, 2022

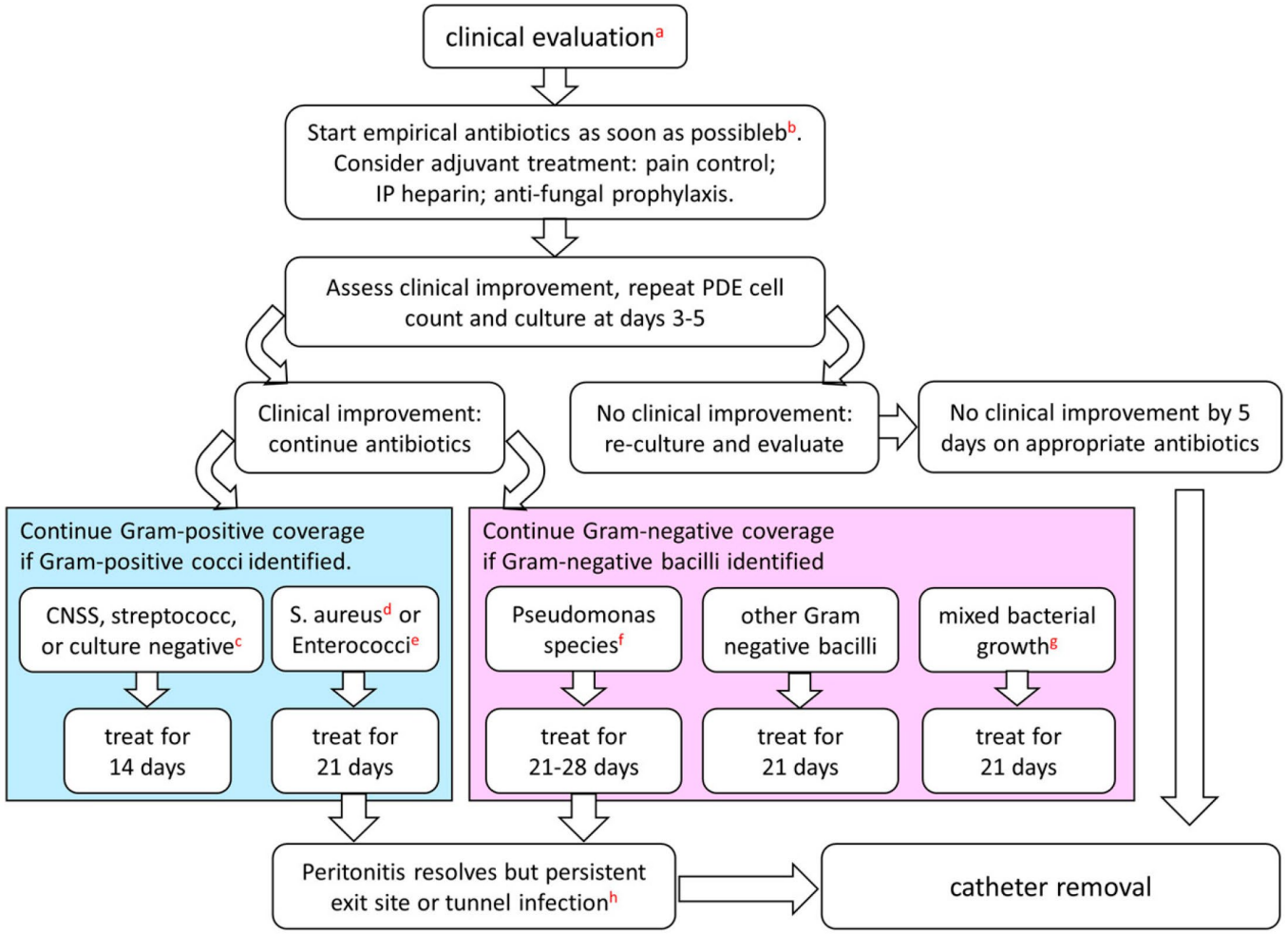
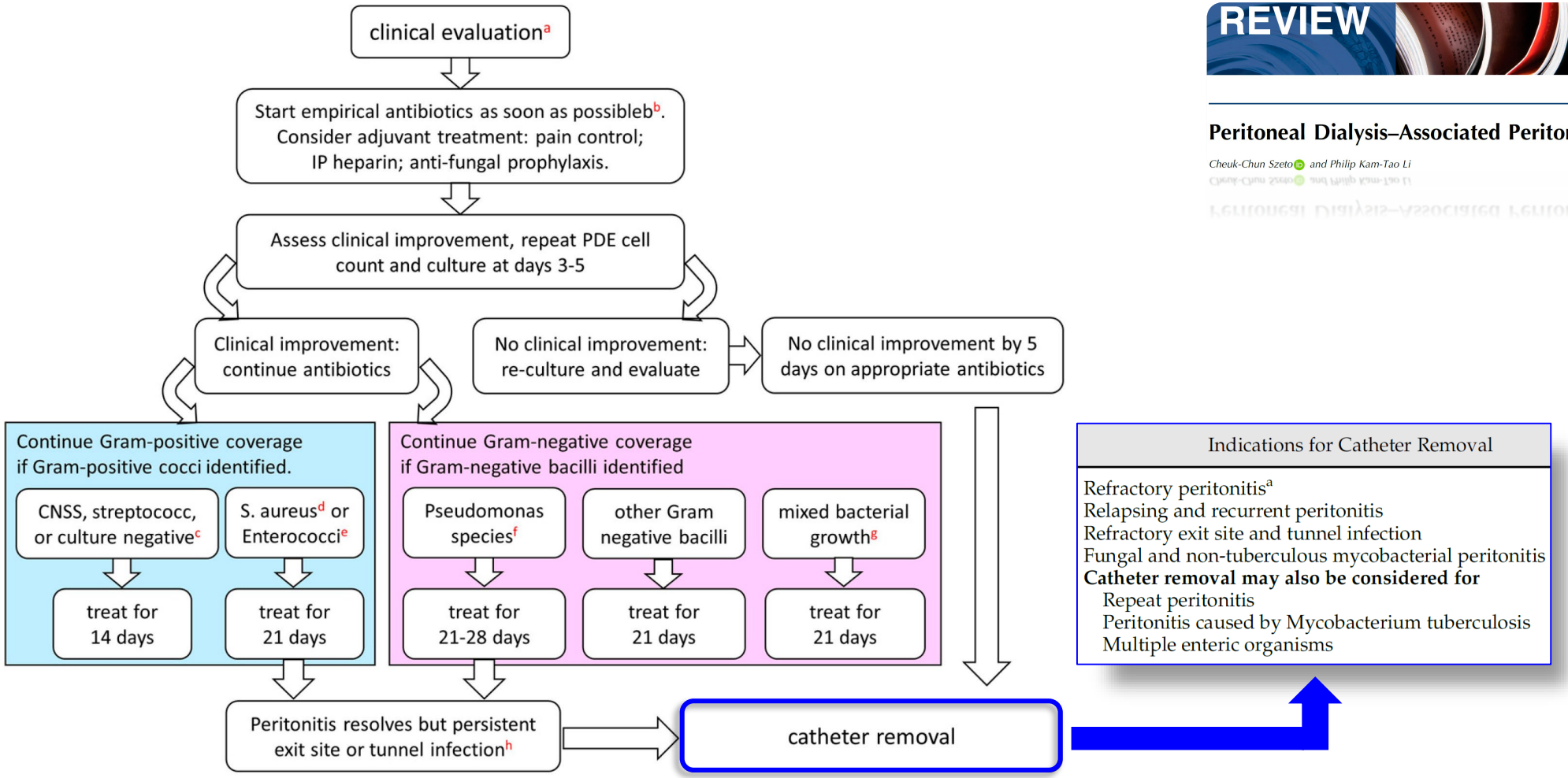


Figure 1. | Algorithm for the management of peritoneal dialysis-related peritonitis. **a** Clinical evaluation includes routine history, physical examination, examination of exit site and catheter tunnel, collection of PDE for cell count, differential count, Gram stain, and bacterial culture. **b** The choice of empirical antibiotics coverage should be on the basis of patient history and center sensitivity patterns. **c** In centers with a high prevalence of Gram-negative peritonitis, empirical Gram-negative coverage may be continued for culture negative peritonitis episodes. **d** Need to screen for S. aureus carrier. **e** Need to use vancomycin or other appropriate agents if enterococci identified. **f** Give two effective antibiotics according to sensitivity; also apply to Stenotrophomonas and other Pseudomonas-like species. **g** Consider surgical problem; in addition to Gram negative coverage, consider metronidazole and vancomycin. **h** Especially for peritonitis episodes caused by S. aureus or Pseudomonas species. CNSS, coagulase negative staphylococcal species; IP, intraperitoneal; PDE, peritoneal dialysis effluent.

Szeto CC, Li PK. Clin J Am Soc Nephrol, 2019



Peritoneal Dialysis–Associated Peritonitis

Cheuk-Chun Szeto and Philip Kam-Tao Li

Figure 1. | Algorithm for the management of peritoneal dialysis-related peritonitis. **a** Clinical evaluation includes routine history, physical examination, examination of exit site and catheter tunnel, collection of PDE for cell count, differential count, Gram stain, and bacterial culture. **b** The choice of empirical antibiotics coverage should be on the basis of patient history and center sensitivity patterns. **c** In centers with a high prevalence of Gram-negative peritonitis, empirical Gram-negative coverage may be continued for culture negative peritonitis episodes. **d** Need to screen for S. aureus carrier. **e** Need to use vancomycin or other appropriate agents if enterococci identified. **f** Give two effective antibiotics according to sensitivity; also apply to Stenotrophomonas and other Pseudomonas-like species. **g** Consider surgical problem; in addition to Gram negative coverage, consider metronidazole and vancomycin. **h** Especially for peritonitis episodes caused by S. aureus or Pseudomonas species. CNSS, coagulase negative staphylococcal species; IP, intraperitoneal; PDE, peritoneal dialysis effluent.

Szeto CC, Li PK. Clin J Am Soc Nephrol, 2019

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ISPD peritonitis guideline recommendations: 2022 update on prevention and treatment

Philip Kam-Tao Li[1,2], Kai Ming Chow[1,2], Yeoungjee Cho[3,4], Stanley Fan[5], Ana E Figueiredo[6], Tess Harris[7], Talerngsak Kanjanabuch[8,9], Yong-Lim Kim[10], Magdalena Madero[11], Jolanta Malyszko[12], Rajnish Mehrotra[13], Ikechi G Okpechi[14], Jeff Perl[15], Beth Piraino[16], Naomi Runnegar[17], Isaac Teitelbaum[18], Jennifer Ka-Wah Wong[19], Xueqing Yu[20,21] and David W Johnson[3,4]

..."The recommendations related to treatment are not intended to be implemented indiscriminately and may require adaptation according to local conditions, such as pattern of infection, causative organisms and microbial resistance".

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[d] [168]
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[210]	LD 400 mg/bag, MD 20 mg/L[211,140]
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]
Antifungal		
Fluconazole	IP 150–200 mg every 24 to 48 h[215,216] (oral route is preferred: see Table 6)	No data
Voriconazole	IP 2.5 mg/kg daily[217] (oral route is preferred: see Table 6)	No data

Tao Li PK, et al. Perit Dial Inter, 2022

No single antibiotic regimen has been proven to be superior to others, and the choice should be centre-specific. There should be adequate coverage for both gram-positive and gram negative organisms.

Tao Li PK, et al. Perit Dial Inter, 2022

Dosage of antibiotics

- We recommend that *IP antibiotics be the preferred route of administration* as long as the compatibility and stability of the IP antibiotics allow, unless the patient has features of systemic sepsis (1B).
- We suggest that IP aminoglycoside be administered as *daily intermittent dosing* (2B).
- We recommend that prolonged courses of IP aminoglycoside *be avoided* (1C).
- We suggest that adjunctive *oral N-acetylcysteine therapy* may help to prevent aminoglycoside ototoxicity (2B).
- There is *insufficient evidence* to make a recommendation as to whether patients on APD should be temporarily switched to CAPD during treatment of peritonitis (Not Graded).

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IP administration is preferred because nearly 90% is absorbed in the presence of peritonitis

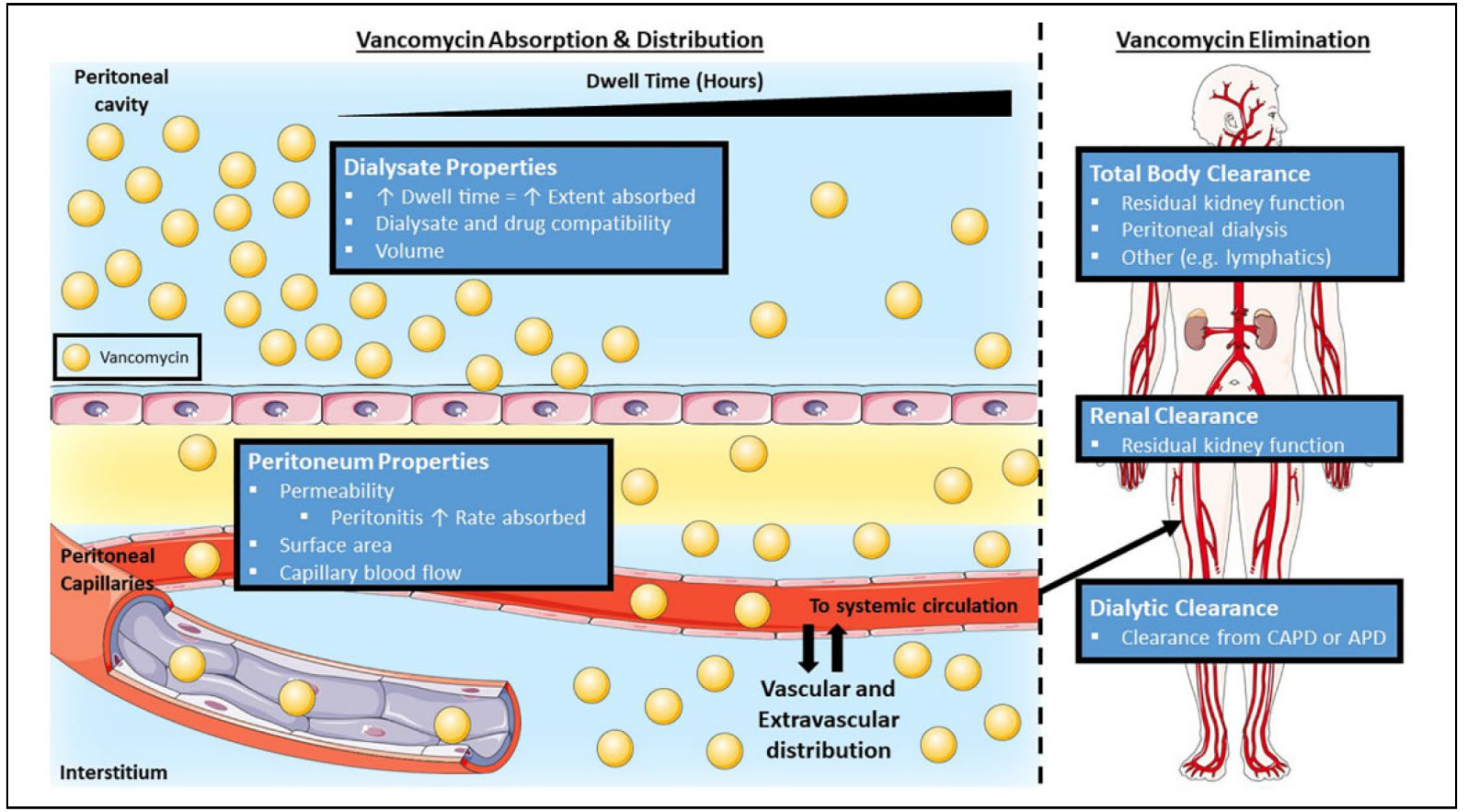

Figure 1. Illustration of vancomycin absorption, distribution, and elimination following an intraperitoneal dose.
Increasing the dwell time enhances vancomycin bioavailability. Peritoneum and dialysate properties should be considered as both these affect the rate and the extent of absorption following an intraperitoneal dose. Following dosing and an appreciable dwell time, vancomycin is eliminated by PD, renal, and nonrenal sources. These processes make up the total body clearance of vancomycin. This illustration is a derivative of "Simple squamous epithelium," "Arteries," "Arterial circulation," and "Bubble" by Servier Medical Art (https://smart.servier.com/) distributed under the Creative Commons License (CC BY 3.0). PD: peritoneal dialysis.

Lam E, et al. Pert Dial Int. 2020

Proprietà Farmacodinamiche

- *Antibiotici tempo-dipendenti* (beta-lattamine, cefalosporine, glicopeptidi, tetracocline, macrolidi, linezolid): l'efficacia dipende dalla durata in cui mantengono stabili nel tempo le loro concentrazioni plasmatiche sopra la MIC (minima concentrazione inibente). Quindi, per essere più efficaci è necessario frazionare il più possibile la posologia giornaliera fino all'infusione prolungata o a quella continua
- *Antibiotici concentrazione-dipendenti* (aminoglicosidi, fluorochinolonici, metronidazolo, daptomicina, tigecillina): garantiscono la loro maggiore efficacia, ma anche minore tossicità, se utilizzati in mono-somministrazione giornaliera.

Nella prima sacca (BOLO):

- CEFAZOLINA 500 mg/litro di soluzione dialitica (1 g/sacca 2 L)
- AMICACINA 25 mg/litro di soluzione dialitica (50 mg/sacca 2 L)

Mantenimento (somministrazione continua= nelle sacche diurne):

- CEFAZOLINA 125 mg/litro di soluzione dialitica (250 mg/sacca 2 L)

Mantenimento (somministrazione intermittente= solo nella sacca notturna):

- CEFAZOLINA 125 mg/litro di soluzione dialitica (250 mg/sacca 2 L)
- AMICACINA 2 mg/Kg peso corporeo/volume introdotto in addome

NB: EPARINA 1000 UI in ogni sacca (2 litri)

Proprietà Farmacodinamiche

- *Antibiotici tempo-dipendenti* (beta-lattamine, cefalosporine, glicopeptidi, tetracocline, macrolidi, linezolid): l'efficacia dipende dalla durata in cui mantengono stabili nel tempo le loro concentrazioni plasmatiche sopra la MIC (minima concentrazione inibente). Quindi, per essere più efficaci è necessario frazionare il più possibile la posologia giornaliera fino all'infusione prolungata o a quella continua
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Empiric antibiotic selection

- We recommend that empirical *antibiotic therapy be initiated as soon as possible*, using either IP or systemic route, after appropriate microbiological specimens have been obtained (1B).
- We recommend that empirical antibiotic regimens be centre-specific and *cover both gram-positive and gram-negative organisms* (1C).
- We recommend that gram-positive organisms be covered by a first-generation *cephalosporin or vancomycin* and gram-negative organisms by a *third-generation cephalosporin or an aminoglycoside* (1B).
- We suggest that cefepime monotherapy may be an acceptable alternative for empirical antibiotic regimens (2B).

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It is important to note that prompt administration of antibiotics has been consistently shown to be associated with better outcome of peritonitis treatment. In a prospective multicentre study of 159 peritonitis episodes in Western Australia, the contact-to-treatment time was independently associated with treatment failure, defined as either catheter removal or death at 30 days.

For each hour of delay in administering antibiotic therapy from the time of presentation to a hospital facility, the risk of PD failure or death was higher by 5.5%.

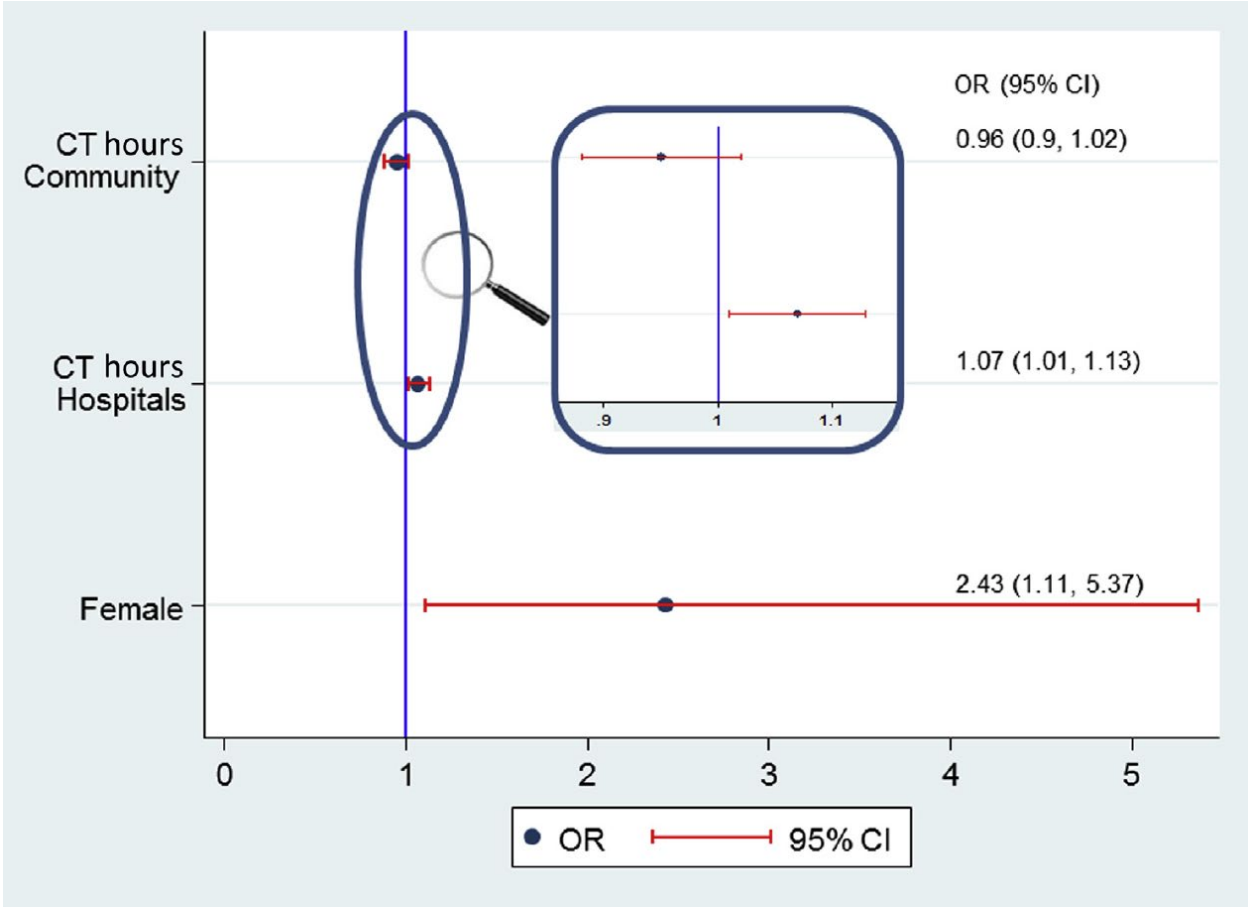

Figure 3. Multivariable model for predictors of the composite outcome PD-fail. CI, confidence interval; CT, contact-to treatment time; OR, odds ratio.

Muthucumarana K, et al. Kidney Int Rep. 2016

Coagulase-negative Staphylococcus

- We suggest that coagulase-negative staphylococci be treated with IP cephalosporin or vancomycin, according to susceptibility, for a period of *2 weeks (2C)*.
- We suggest that retraining be considered for patients with coagulase-negative staphylococcal peritonitis (Not Graded).

The leading cause of pathogenic coagulase-negative staphylococci peritonitis is Staphylococcus epidermidis, followed by Staphylococcus haemolyticus

Staphylococcus aureus

- We suggest that S. aureus peritonitis be treated with effective antibiotics for *3 weeks (2C)*.

Peritonitis episodes caused by S. aureus are often secondary to exit-site or tunnel infection, although touch contamination can be contributory.

Streptococcal peritonitis

- We suggest that streptococcal peritonitis be treated with appropriate antibiotics for *2 weeks (2C)*.

The reported cure rate of streptococcal peritonitis exceeds 85%, and most patients can continue PD.

Corynebacterium peritonitis

- We suggest that Corynebacterium peritonitis be treated with effective antibiotics for *2 weeks (2D)*.
- We suggest that peritonitis due to beta-lactam resistant trains, such as Corynebacterium jeikeium, should be treated with vancomycin (2C).

Tao Li PK, et al. Perit Dial Inter, 2022

Pseudomonas peritonitis

- We suggest that Pseudomonas peritonitis be treated with 2 antibiotics with different mechanisms of action and to which the organism is sensitive for 3 weeks (2C).
- We suggest that Pseudomonas peritonitis with concomitant exit-site and tunnel infection be treated with catheter removal (2D).
- If there is no clinical response after 5 days of effective antibiotic treatment, we suggest that Pseudomonas peritonitis be treated with early catheter removal instead of using three antibiotics as an attempt to salvage (2D).

Pseudomonas peritonitis is often severe and associated with less than 50% complete cure rate

Acinetobacter peritonitis

- We suggest that carbepenem-resistant Acinetobacter peritonitis be treated with aminoglycoside and a sulbactam-containing agent (2C).

Outcomes of Acinetobacter peritonitis are considered more favourable than those of Pseudomonas peritonitis. Empirical antibiotic therapy for Acinetobacter should be selected based on local susceptibility patterns and should consist of a broad spectrum cephalosporin, a combination beta-lactam/beta-lactamase inhibitor (combination including sulbactam) or a carbapenem (except ertapenem).

Stenotrophomonas maltophilia peritonitis

- We suggest that Stenotrophomonas maltophilia peritonitis be treated with trimethoprim–sulfamethoxazole (2D).
- *We suggest that S. maltophilia peritonitis be treated with two different classes of antibiotics for at least 3 weeks (2D).*

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Enteric gram-negative bacteria peritonitis

- We suggest that enteric gram-negative peritonitis be treated with effective antibiotics for at least 3 weeks (2C).

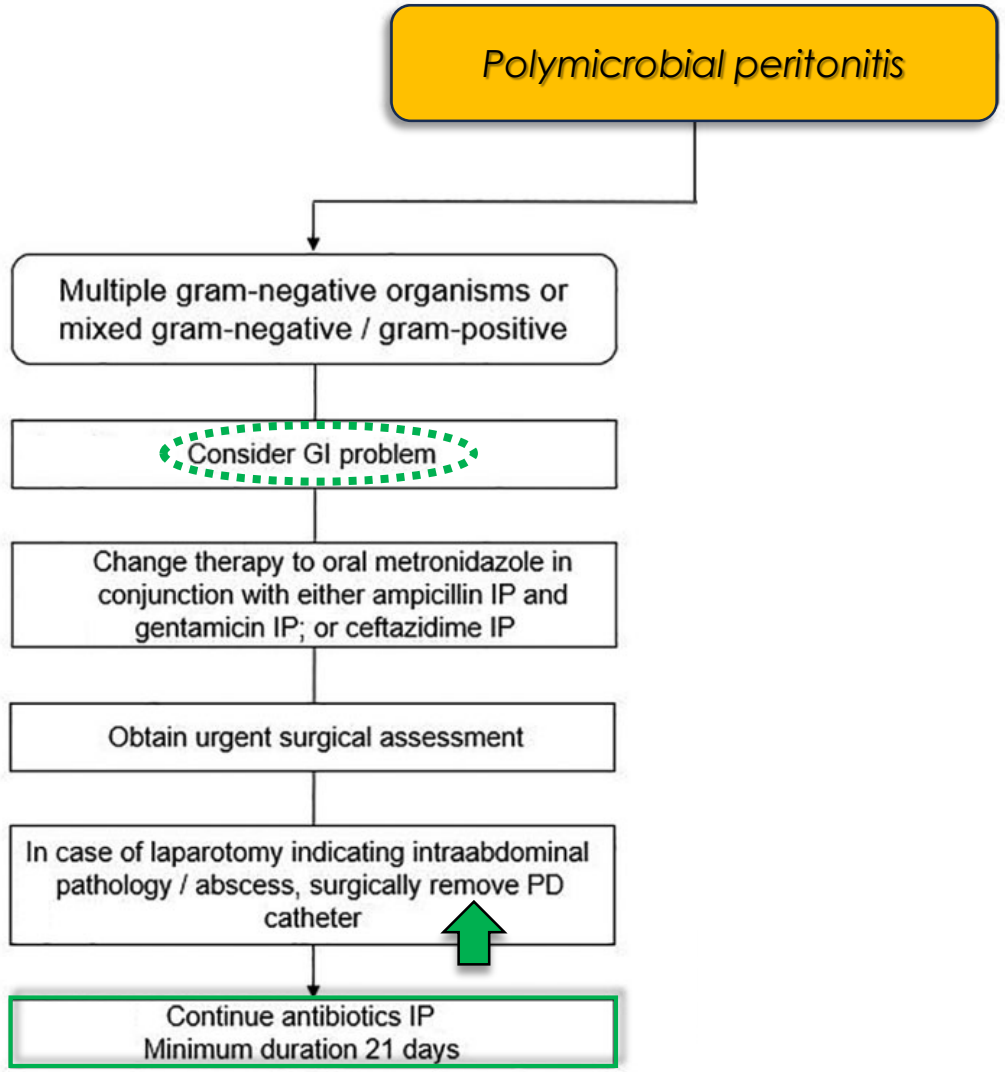
Besides non-fermenting gram-negative bacilli with high resistance to antibiotics, *several Enterobacterales species, such as E. coli, are reported to have increasing resistance and treatment failure rates.* The Enterobacterales order comprises several bacteria genera, including E. coli, Klebsiella and Enterobacter species. E. coli, the commonest member, accounts for one-third of single organism non-Pseudomonas gram-negative peritonitis in Australia. Treatment algorithms of enteric gram-negative peritonitis depend on the resistance pattern

Enterococcus peritonitis

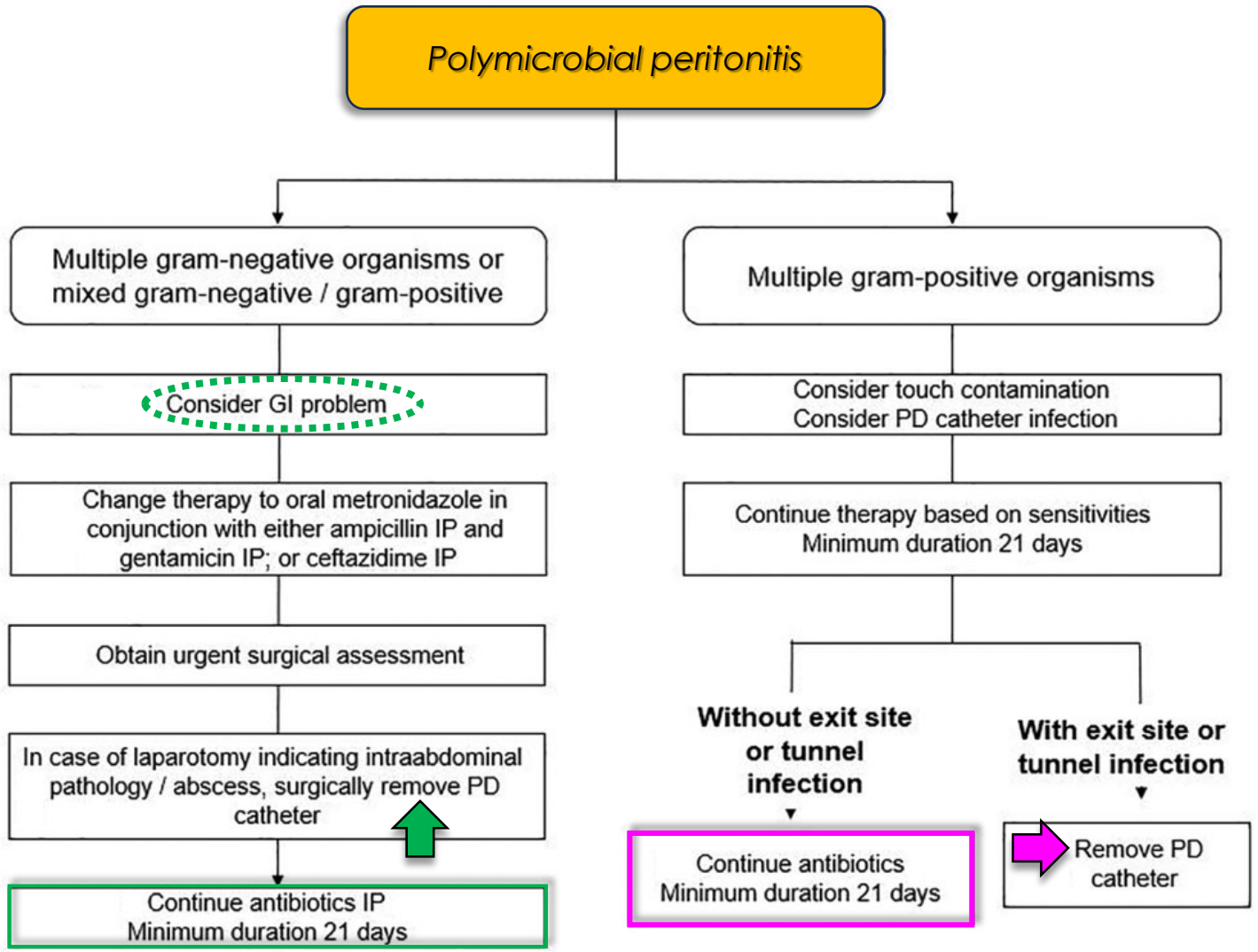
- We suggest that enterococcal peritonitis be treated for 3 weeks with oral amoxicillin (for ampicillinsusceptible enterococci) or IP vancomycin (2C).
- For peritonitis due to vancomycin-resistant Enterococcus (VRE) which are ampicillin-resistant, we suggest treatment with oral or intravenous linezolid or IP daptomycin, or teicoplanin if susceptibility is confirmed (2D).

Enterococci causing intra-abdominal infections are often enteric in origin, and sometimes enter the slime layer of intra-abdominal portion of PD catheter forming biofilm.

Tao Li PK, et al. Perit Dial Inter, 2022



Tao Li PK, et al. Perit Dial Inter, 2022



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Fungal peritonitis

- *We raccomend immediate catheter removal when fungi are identified in PD effluent (1C).*
- We suggest that treatment with an appropriate antifungal agent be continued for at least 2 weeks after catheter removal, and sometimes up to 4 weeks (2C).

  * Treatment failure and mortality rates of fungal peritonitis remain high, despite a slightly improved outcome with early catheter removal based on observational studies.

  * Irrespective of the treatment duration, catheter reinsertion and resumption of PD have been reported after a median period of 15 weeks in less than one-third of cases.

Culture-negative peritonitis

Reported risk factors for culture-negative peritonitis include *recent antibiotic usage and improper culture technique.* Data regarding the treatment outcomes of culture negative peritonitis based on large case series were in general favourable. Reported regimens for culture-negative peritonitis with suboptimal initial responses include a combination of ampicillin–sulbactam and amikacin, which demonstrated a response in 80% of 10 cases. PD catheter removal was required in around 10% of cases of culture-negative peritonitis

Tao Li PK, et al. Perit Dial Inter, 2022

Tuberculous peritonitis

- We suggest antituberculous therapy, instead of PD catheter removal, as the primary treatment of peritonitis caused by Mycobacterium tuberculosis (2C).

  The presenting symptoms of tuberculous peritonitis are abdominal pain in 89% and fever in 81% of PD patients. Many patients respond to anti-tuberculous therapy without catheter removal, although an attributable mortality of 15% has been reported. In a scoping review 216 cases of Mycobacterium tuberculosis peritonitis in patients on PD, catheter removal occurred in 52.4% of cases. Most of the cases requiring catheter removal were empirical, based on the rationale of failed treatment of 'bacterial' peritonitis before the diagnosis of tuberculous peritonitis was recognised. *PD catheter removal was not associated with an increased probability of survival.* Early diagnosis is essential in the management of tuberculous peritonitis complicating PD because treatment delay is the only significant factor predicting mortality.

Non-tuberculous mycobacterial peritonitis

- We suggest that Ziehl–Neelsen staining for acid-fast bacilli be requested when there is a clinical suggestion of non-tuberculous mycobacterial (NTM) peritonitis, including persistent culture-negative peritonitis (2D).
- *We suggest that NTM peritonitis be treated with both effective antibiotics and catheter removal (2D).*

  Mycobacterium fortuitum and chelonae account for the majority of NTM peritonitis episodes.

Tao Li PK, et al. Perit Dial Inter, 2022

PERITONITI-ESPOSIZIONE

	2022	Gennaio	Febbraio	Marzo	Aprile	Maggio	Giugno	Luglio	Agosto	Settembre	Ottobre	Novembre	Dicembre	TOT mesi trattamento 933,9	TOT n° peritoniti 12	Perit/mese-paz 77,8	Perit/anno-paz 0,16
APD																	
APD	n° Giorni DP										12	30	31	2,4	0		
APD	n° Peritoniti										0	0	0				
APD																	
APD	n° Giorni DP	31	20	0	0	0	0	0	0	0	0	0	0	1,7	1		
APD	n° Peritoniti	0	1	0	0	0	0	0	0	0	0	0	0				
APD																	
APD	n° Giorni DP	31	28	31	30	31	30	31	31	30	31	30	31	12,0	0		
APD	n° Peritoniti	0	0	0	0	0	0	0	0	0	0	0	0				
APD																	
APD	n° Giorni DP	31	28	31	30	31	30	31	31	30	31	30	31	12,0	0		
APD	n° Peritoniti	0	0	0	0	0	0	0	0	0	0	0	0				
APD																	
APD	n° Giorni DP	31	28	31	30	31	30	31	31	30	31	30	31	12,0	0		
APD	n° Peritoniti	0	0	0	0	0	0	0	0	0	0	0	0				
APD																	
APD	n° Giorni DP							15	25	0	0	0	0	1,3	0		
APD	n° Peritoniti							0	0	0	0	0	0				
APD																	
APD	n° Giorni DP				0	24	30	31	31	30	31	30	31	7,8	0		
APD	n° Peritoniti				0	0	0	0	0	0	0	0	0				
APD																	
APD	n° Giorni DP	31	28	31	30	31	30	31	31	30	31	30	31	12,0	0		
APD	n° Peritoniti	0	0	0	0	0	0	0	0	0	0	0	0				
APD																	
APD	n° Giorni DP	31	28	31	30	15	0	0	0	0	0	0	0	4,4	0		
APD	n° Peritoniti	0	0	0	0	0	0	0	0	0	0	0	0				
APD																	
APD	n° Giorni DP	31	28	31	30	31	30	31	31	30	31	30	31	12,0	0		
APD	n° Peritoniti	0	0	0	0	0	0	0	0	0	0	0	0				
APD																	

Table 2. Measurement and reporting of peritonitis.

	Unit of measure	**Minimum frequency**	**Target**
Peritonitis rates (overall and organism-specific)	Episodes per patient year	Yearly	<0.4 episodes per patient-year
Culture-negative peritonitis	% of all peritonitis episodes	Yearly	<15% of all peritonitis episodes
Time to first peritonitis episode	Mean unit time to first episode peritonitis	Quarterly (local report)	–
Proportion of patients free of peritonitis	% per unit time	Quarterly (local report)	>80% per year
Pre-PD peritonitis	% of all peritonitis episodes	Quarterly (local report)	–
PD catheter insertion-related peritonitis	% of all PD catheter insertions	Quarterly (local report)	<5%
Medical cure	% of all peritonitis episodes	Quarterly (local report)	–
Recurrent peritonitis	% of all peritonitis episodes	Quarterly (local report)	–
Relapsing peritonitis	% of all peritonitis episodes	Quarterly (local report)	–
Peritonitis-associated catheter removal	% of all peritonitis episodes	Quarterly (local report)	–
Peritonitis-associated haemodialysis transfer	% of all peritonitis episodes	Quarterly (local report)	–
Peritonitis-associated death	% of all peritonitis episodes	Quarterly (local report)	–

PD: peritoneal dialysis.

Tao Li PK, et al. Perit Dial Inter, 2022

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Pre-PD peritonitis	% of all peritonitis episodes	Quarterly (local report)	–
PD catheter insertion-related peritonitis	% of all PD catheter insertions	Quarterly (local report)	<5%
Medical cure	% of all peritonitis episodes	Quarterly (local report)	–
Recurrent peritonitis	% of all peritonitis episodes	Quarterly (local report)	–
Relapsing peritonitis	% of all peritonitis episodes	Quarterly (local report)	–
Peritonitis-associated catheter removal	% of all peritonitis episodes	Quarterly (local report)	–
Peritonitis-associated haemodialysis transfer	% of all peritonitis episodes	Quarterly (local report)	–
Peritonitis-associated death	% of all peritonitis episodes	Quarterly (local report)	–

PD: peritoneal dialysis.

Tao Li PK, et al. Perit Dial Inter, 2022

PREVENZIONE

Catheter placement

- *We recommend that systemic prophylactic antibiotics be administered immediately prior to catheter placement (1A).*

- Perioperative intravenous: Cefuroxime, Gentamicin, Vancomycin, Cefazolin.
- Although first-generation cephalosporin may be slightly less effective than vancomycin, the former is still commonly used because of the concern regarding vancomycin resistance.
- Each PD programme should determine its own choice of antibiotic for prophylaxis after considering the local spectrum of antibiotic resistance.
- No data exist on the effectiveness of routine screening and eradication of S. aureus nasal carriage before catheter insertion (such as intranasal mupirocin).

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PREVENZIONE

Exit-site care

- *Topical application of antibiotic cream or ointment to the PD catheter exit site is recommended* although such practice varied among centres internationally.
- Proper PD catheter immobilisation and avoidance of mechanical stress on the exit site may be useful to lower exit-site infection rate.
- Prompt treatment of exit-site or catheter tunnel infection is mandatory to reduce subsequent peritonitis risk.

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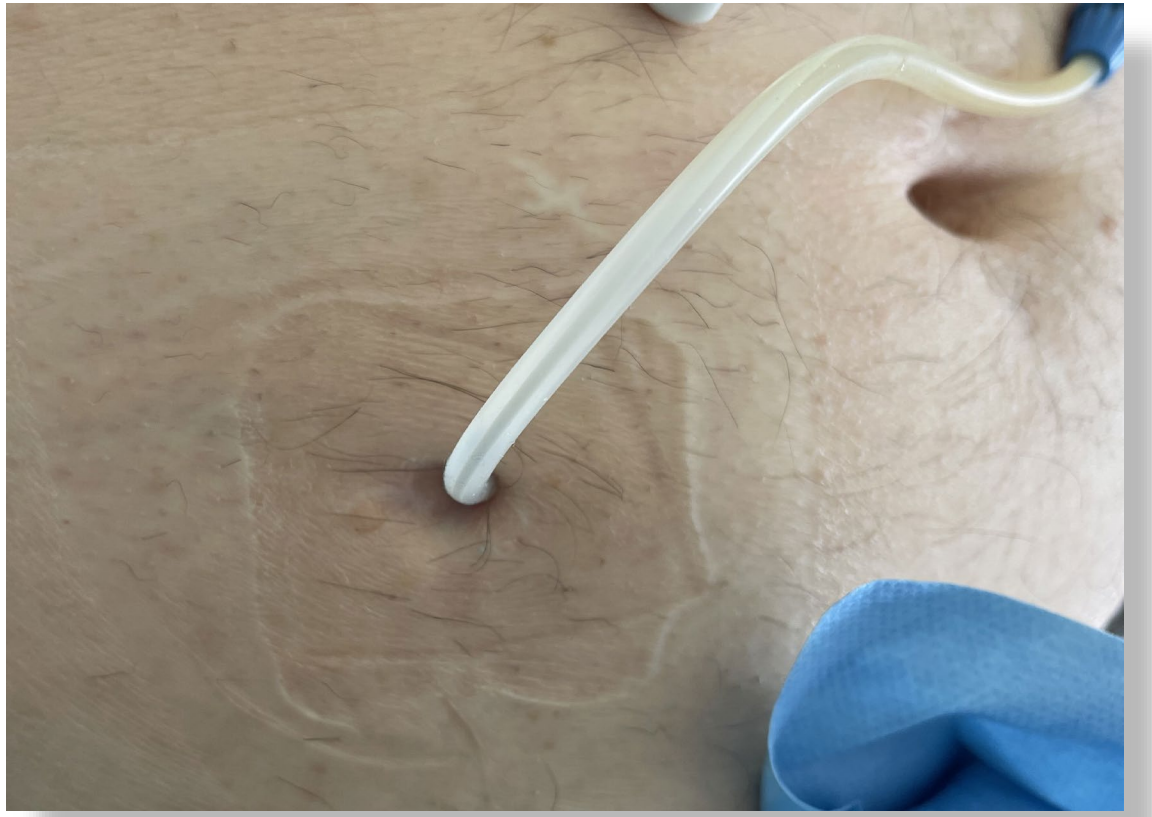
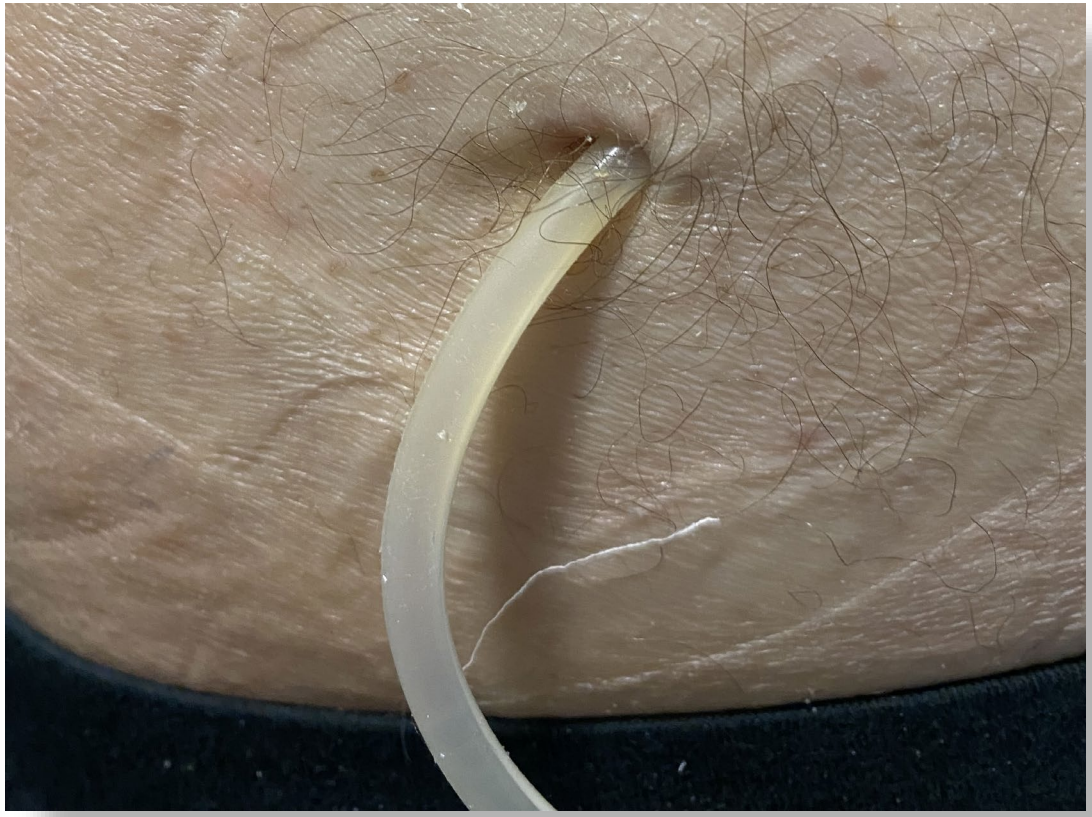
PREVENZIONE





PREVENZIONE

Contamination of PD system

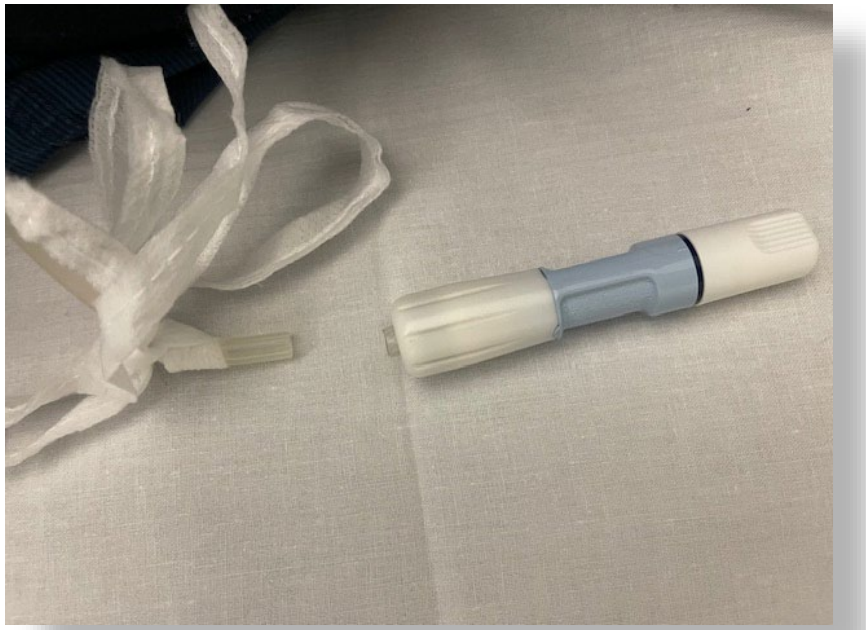
- We suggest advice be sought immediately from the treatment team if contamination during PD exchange is noted (Not Graded).
- We suggest prophylactic antibiotics *after wet contamination* of the PD system to prevent peritonitis (2D).

Wet contamination referring to contamination with an open system, when either dialysis fluid is infused after contamination or if the catheter administration set has been left open for an extended period). Examples of wet contamination include

a) leaks from dialysate bags
b) leaks or breaks in tubing proximal to the tubing clamp
c) breach of aseptic technique
d) touch contamination of the connection during a PD exchange.

Prophylactic antibiotics is only recommended after wet contamination.

Tao Li PK, et al. Perit Dial Inter, 2022



PREVENZIONE

Invasive gastrointestinal and gynaecological procedures

- We suggest antibiotic prophylaxis prior to colonoscopy (2C) and invasive gynaecological procedures (2D).
- We suggest drainage of PD fluid to keep the abdomen empty before endoscopic gastrointestinal and invasive or instrumental gynaecological procedures (2D).

Tao Li PK, et al. Perit Dial Inter, 2022

PREVENZIONE

The highest peritonitis complication rate after endoscopic or instrumental procedures in PD patients is reported after:

Colonoscopy without antibiotic prophylaxis, from 3.4% to 8.5%. More than half of reported peritonitis episodes occurring after colonoscopy are caused by ***E. coli*** The optimal antibiotic regimen for preventing peritonitis after colonoscopy has not been determined by clinical study: **IP** ceftazidime (1 g IP 1 h before the procedure). For **intravenous** antibiotic prophylaxis, potential choices include cephalosporins, amoxicillin–clavulanate, ampicillin–sulbactam, ampicillin plus aminoglycoside. **Oral** ampicillin 1000 mg, ciprofloxacin 500 mg and/or metronidazole 250 mg 1 to 2 h before colonoscopy.

Tao Li PK, et al. Perit Dial Inter, 2022

PREVENZIONE

The highest peritonitis complication rate after endoscopic or instrumental procedures in PD patients is reported after:

Gastroscopy, from 1.2% to 3.9%. The risk of PD patients developing peritonitis after gastroscopy is more uncertain. Commonly caused by organisms either enteric in origin or arising from the oral cavity, such as *Streptococcus.* Although there is insufficient evidence to recommend antibiotic prophylaxis prior to gastroscopy in PD patients, the study confirmed a lower odds of peritonitis after gastroscopy, after adjustment for confounding factors, *when antibiotics were used within 7 days of gastroscopy.*

Tao Li PK, et al. Perit Dial Inter, 2022

PREVENZIONE

The highest peritonitis complication rate after endoscopic or instrumental procedures in PD patients is reported after:

Invasive gynaecological procedures, from 26.9% to 38.5%. There is no standardised recommendation of antibiotic choice and administration route. However, reasonable regimens should cover gram-positive and gram-negative (aerobic and anaerobic) bacterial isolates from the upper tract of female reproductive tracts. Examples include intravenous cefazolin or ceftriaxone before the procedure or oral cefadroxil 500 mg once daily for 3 days.

Tao Li PK, et al. Perit Dial Inter, 2022

PREVENZIONE

PD effluent should be drained to keep patient's abdomen empty before colonoscopy (and gynaecological) procedure.

The argument for emptying the abdomen before colonoscopy is to enhance host defence, because the peritoneal macrophage phagocytic function and polymorphonuclear cell function are suppressed by the presence of dialysate. Furthermore, high fluid volumes can compromise efficiency of bacterial killing by disrupting the volume-to-surface-area ratio.

Tao Li PK, et al. Perit Dial Inter, 2022

PREVENZIONE

Domestic pet and zoonotic infection

- We recommend PD patients take extra precautions to prevent peritonitis if domestic pets are kept (1C).
- We suggest pets not be allowed in the room where PD exchange takes place, and where dialysis tubing, equipment and machine are stored (2A).

Secondary prevention

- *To prevent fungal peritonitis, we recommend that anti-fungal prophylaxis be co-prescribed whenever PD patients receive an antibiotic course, regardless of the indication for that antibiotic course (1B).*

The majority of fungal peritonitis episodes are preceded by courses of antibiotics. Two randomised control trials and a systematic review showed a significant benefit with oral nystatin (500,000 units qid) or fluconazole (200 mg every 48 h) as prophylaxis during antibiotic therapy.

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PREVENZIONE

Training programme

- We suggest that the characteristics of an optimal PD training programme (how, how long, where, when and by whom) remain uncertain (2C).
- *We recommend that PD exchange technique and knowledge be regularly reassessed and updated, with an emphasis on direct inspection of practice of PD technique (1C).*

Table 3. Indications for PD Retraining.

- Following prolonged hospitalisation
- Following peritonitis and/or catheter infection
- Following change in dexterity, vision or mental acuity
- Following change to another supplier or a different type of connection
- Following change in caregiver for PD exchange
- Following other interruption in PD (e.g. period of time on haemodialysis)

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Special Series/Guidelines

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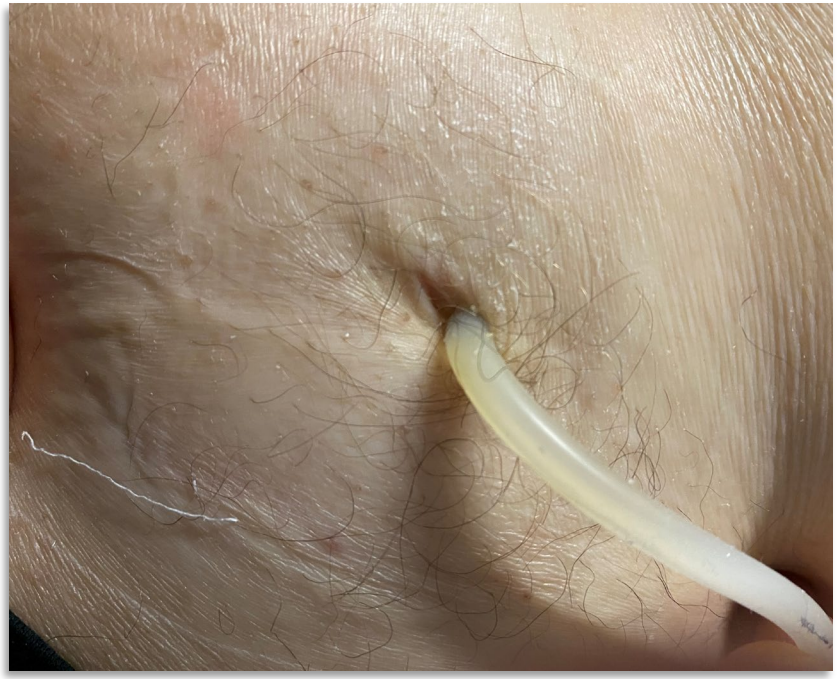
ISPD Catheter-related Infection Recommendations: 2023 Update

Kai Ming Chow[1,2], Philip Kam-Tao Li[1,2], Yeoungjee Cho[3,4], Ali Abu-Alfa[5,6], Sunita Bavanandan[7], Edwina A Brown[8], Brett Cullis[9], Dawn Edwards[10], Isabelle Ethier[11,12], Helen Hurst[13], Yasuhiko Ito[14], Thyago Proença de Moraes[15], Johann Morelle[16], Naomi Runnegar[17], Anjali Saxena[18,19], Simon Wai-Yin So[20], Na Tian[21] and David W Johnson[3,4]



Definitions

The definitions pertaining to catheter-related infections can be further classified according to type, cause, timing (in relation to catheter insertion and to previous episodes) and outcomes.

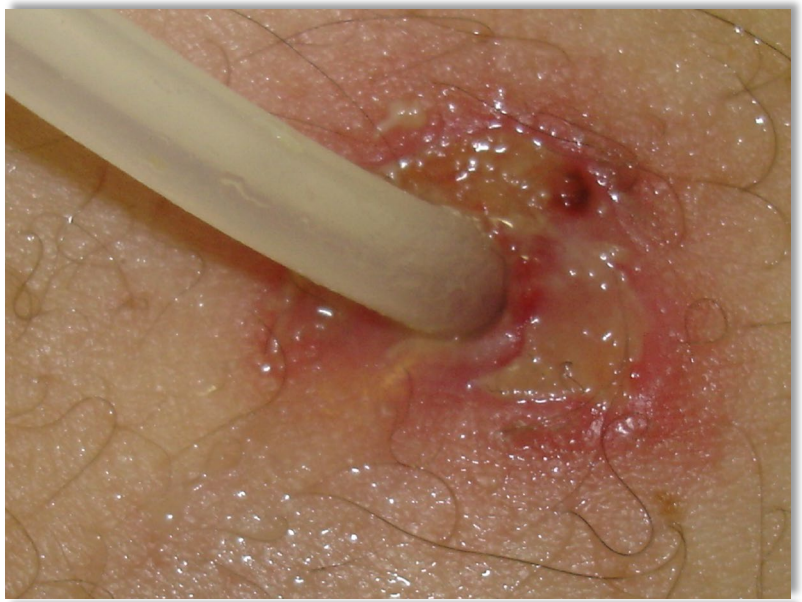
Types of catheter-related infection

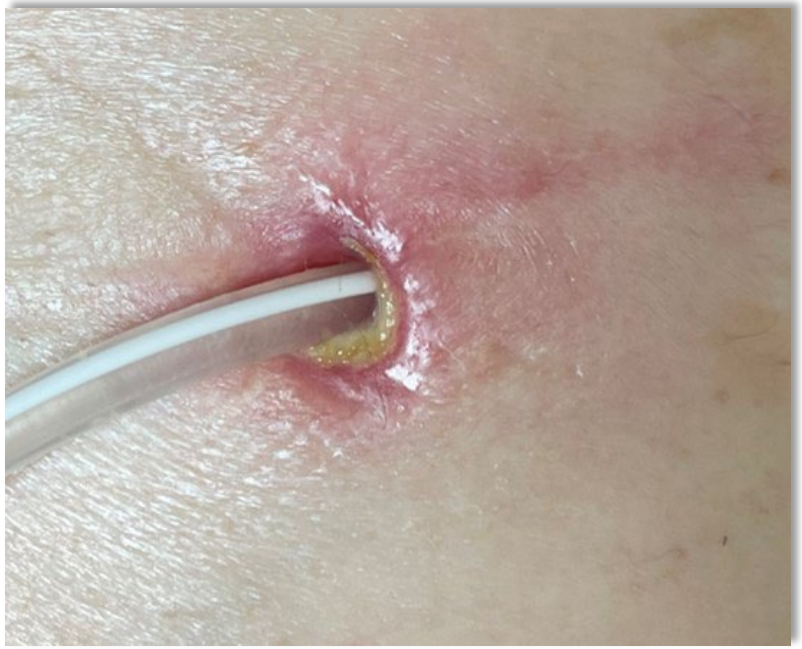
Exit site infection

- We suggest that definitive exit site infection is defined as the presence of purulent discharge, with or without erythema of the skin at the catheter-epidermal interface **(Not Graded)**.
- We suggest that, in the absence of purulent discharge, other signs of inflammation at the exit site (e.g. erythema, tenderness, swelling, granuloma or crust formation) are insufficient to definitively diagnose exit site infection **(Not Graded)**.

Tunnel infection

- We suggest that tunnel infection is defined as the presence of clinical inflammation (erythema, swelling, tenderness or induration) with or without ultrasonographic evidence of a fluid collection anywhere along the catheter tunnel **(Not Graded)**.

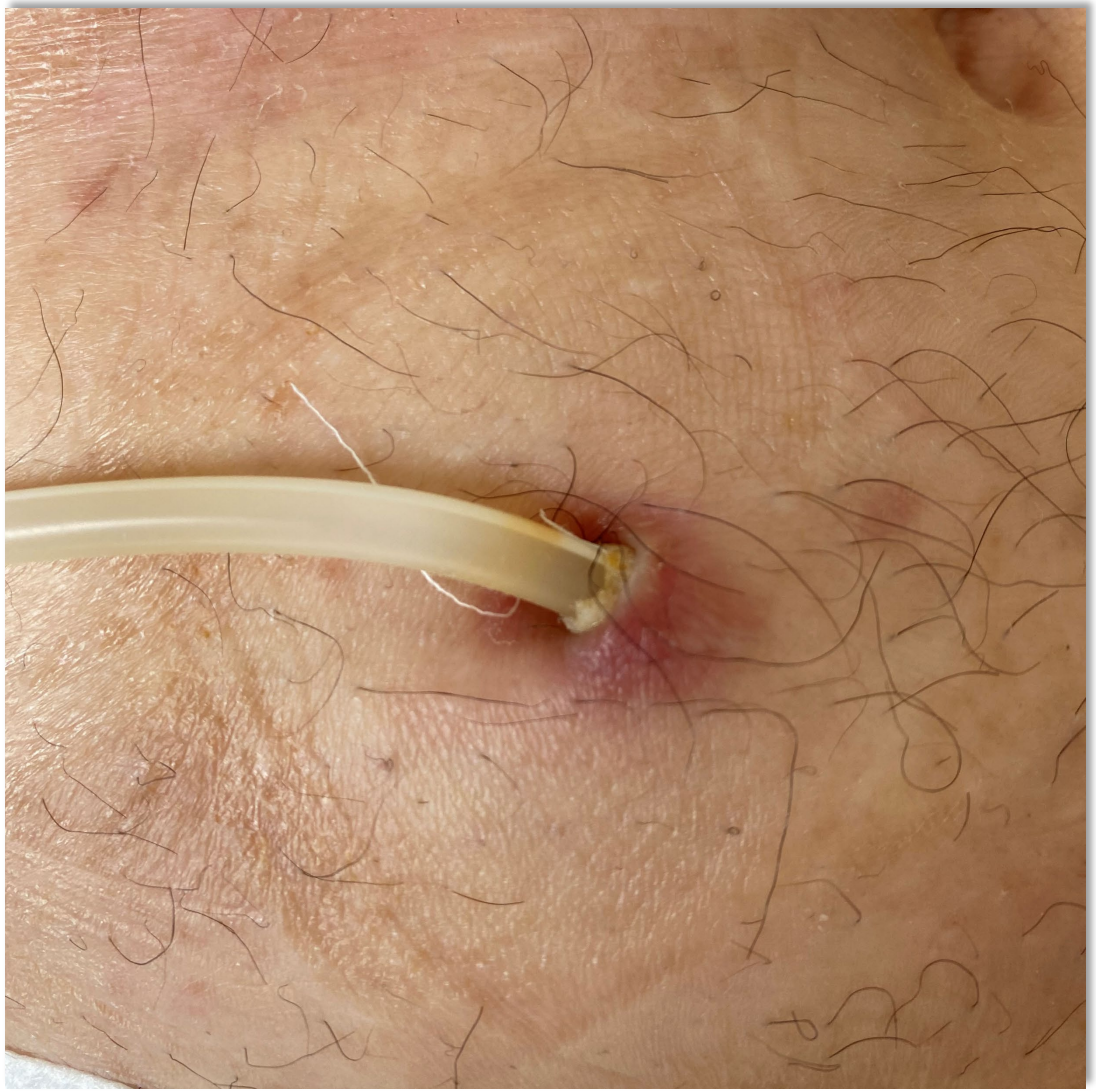


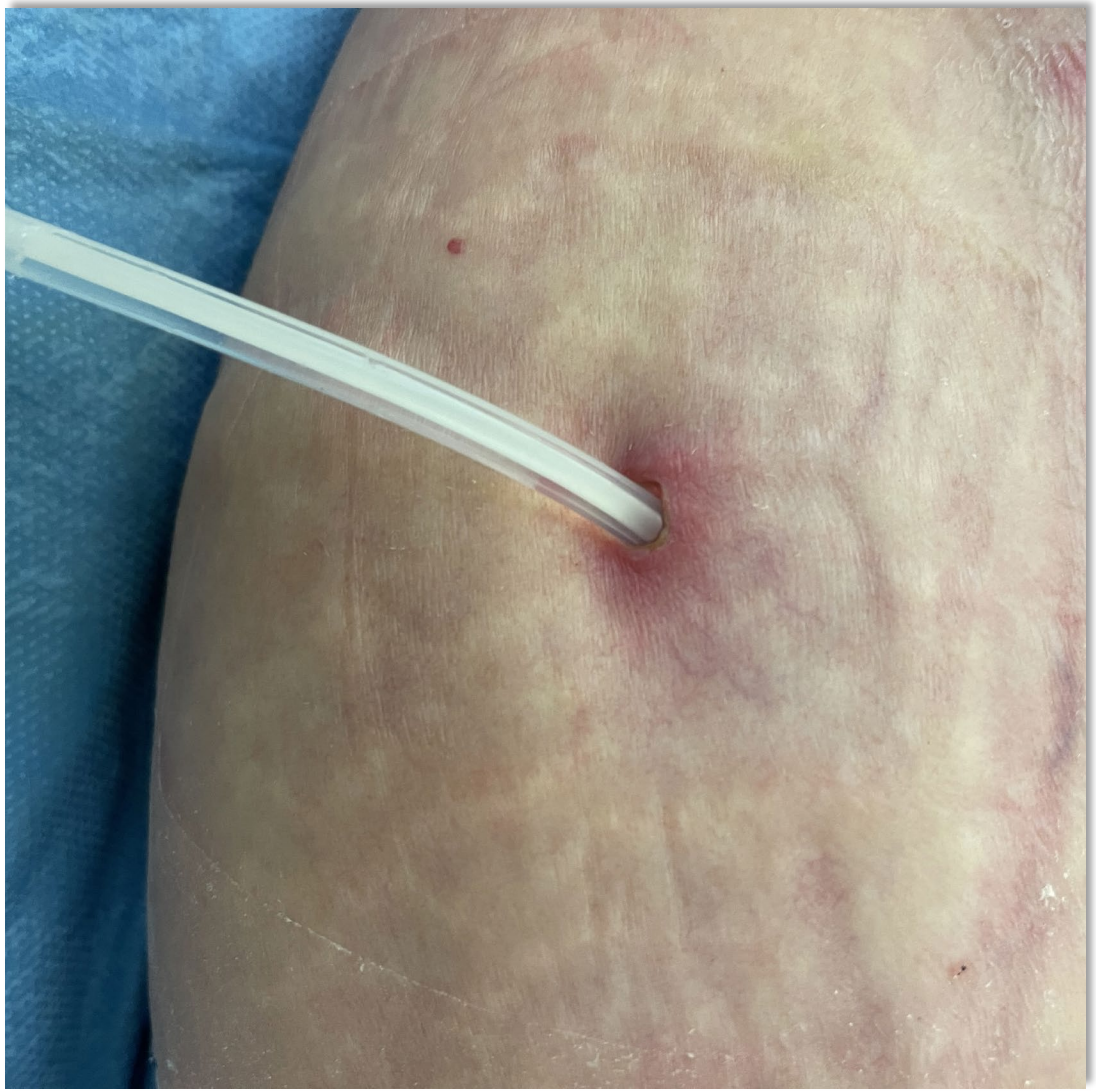


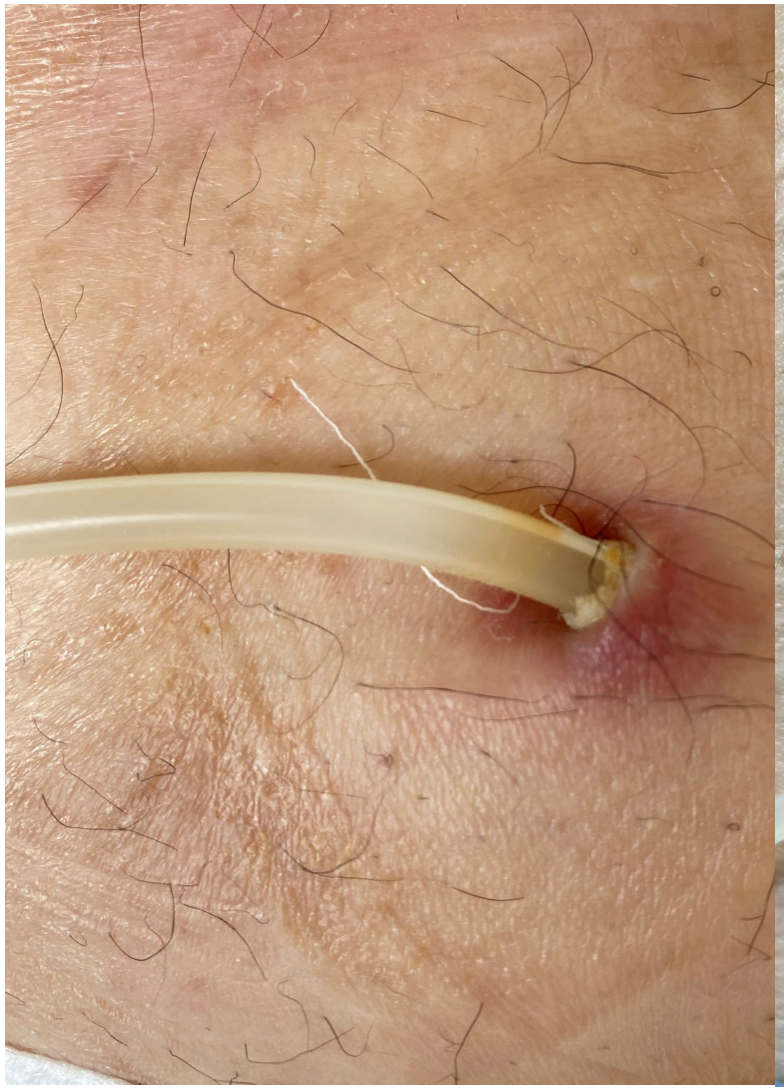
L'eritema pericatere senza secrezione purulenta può essere osservato a causa di

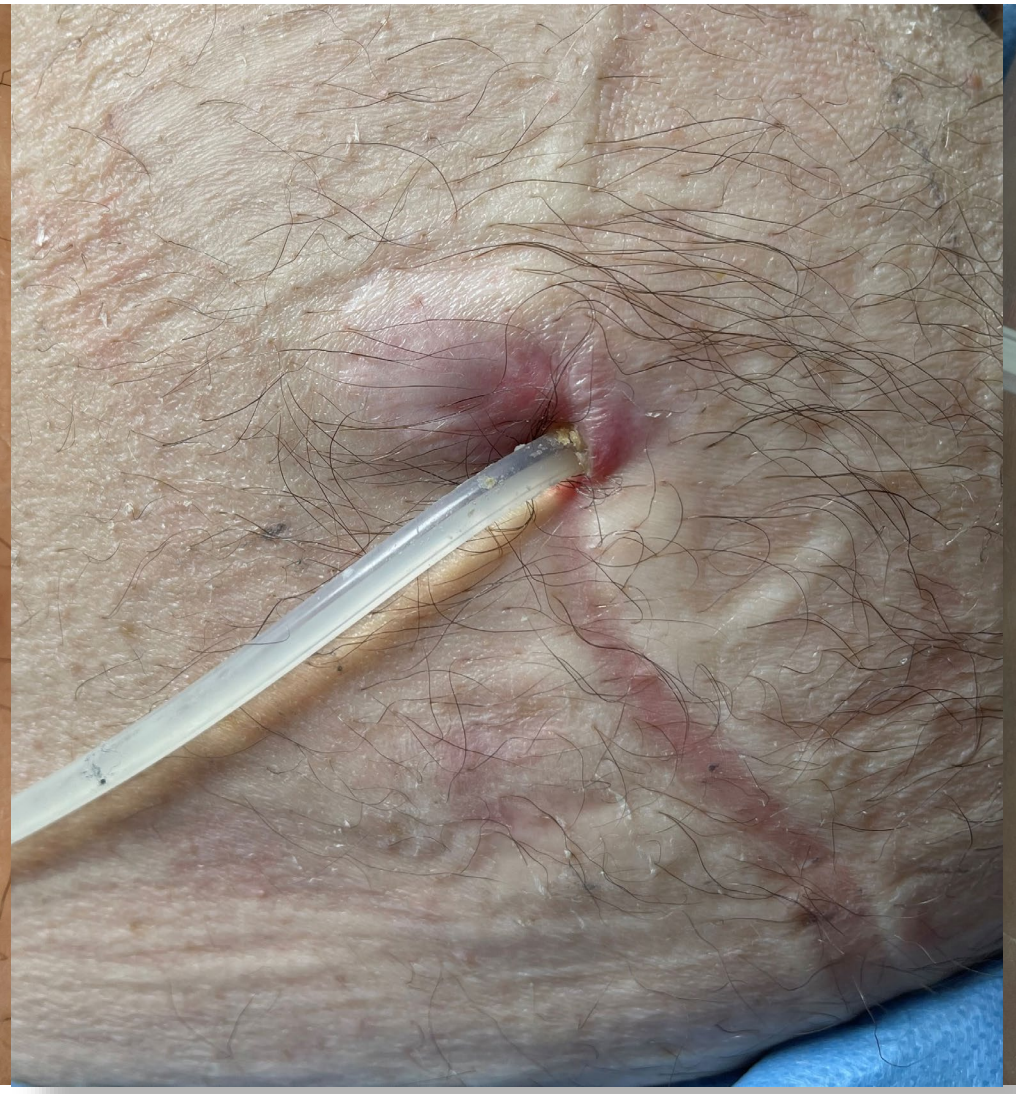
- una reazione allergica cutanea
- nel contesto di un catetere posizionato di recente
- in seguito a un trauma al catetere
- dopo un cambio della medicazione o dei materiali detergenti.
- A volte, l'eritema da solo può essere un'indicazione di un'infezione precoce che richiede un attento monitoraggio per l'eventuale sviluppo di secrezione purulenta e la necessità di un trattamento antimicrobico

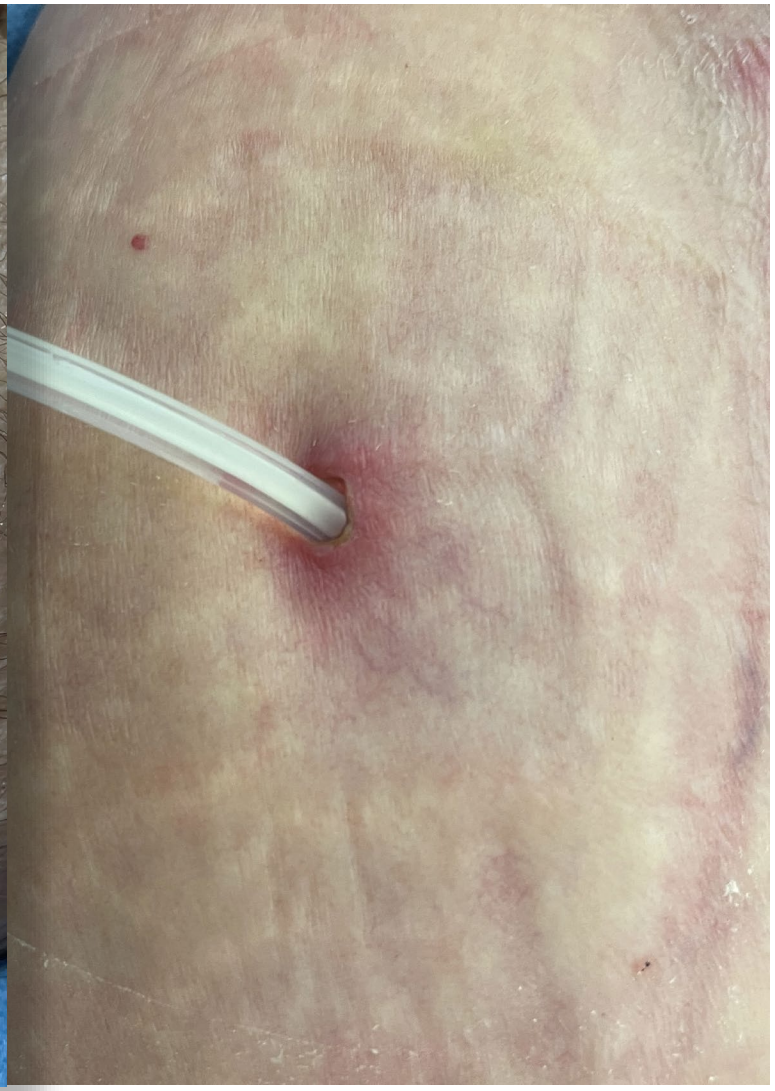
► *Una coltura positiva con un sito di uscita apparentemente normale (ad esempio senza secrezione purulenta) è indicativa di colonizzazione piuttosto che di vera infezione*

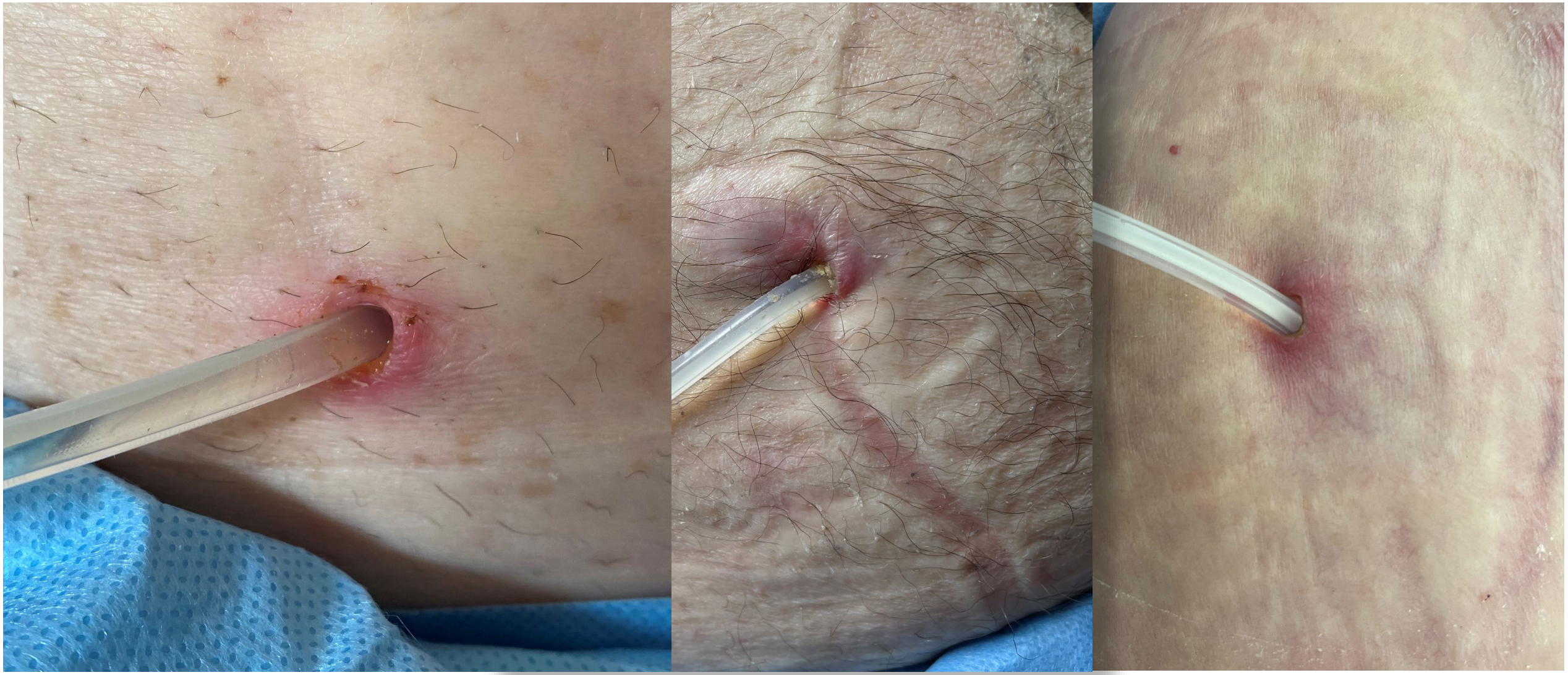


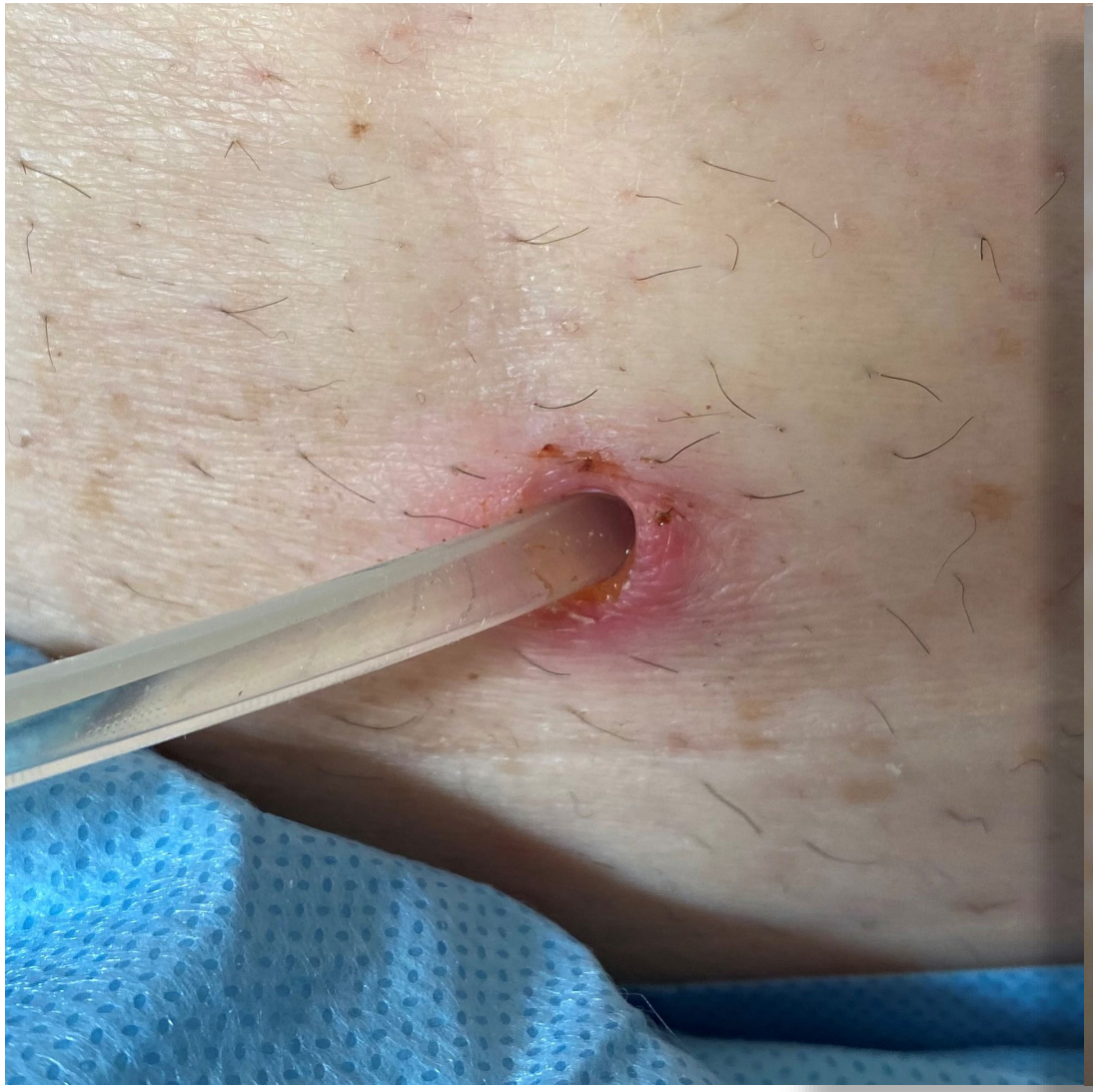


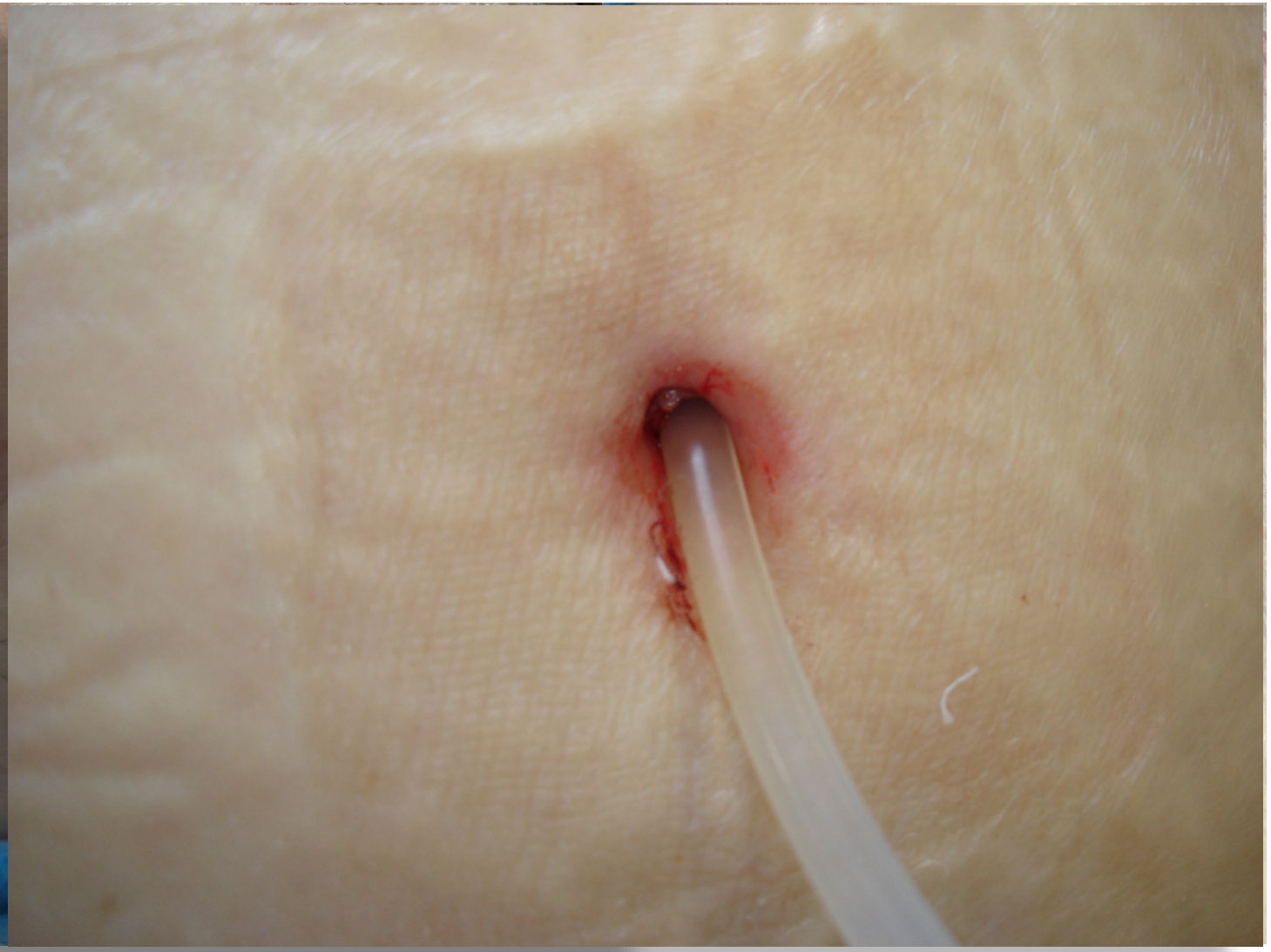


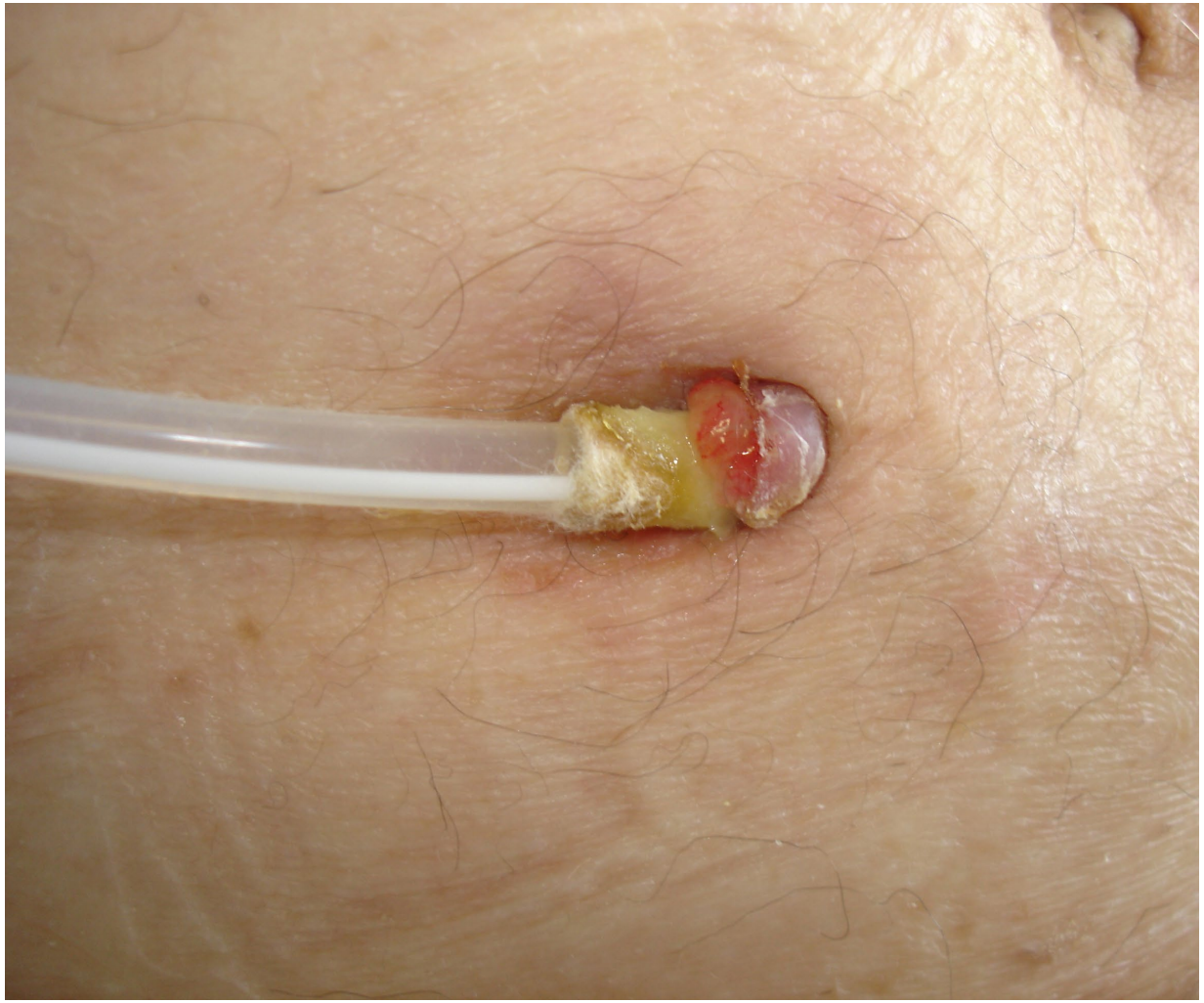


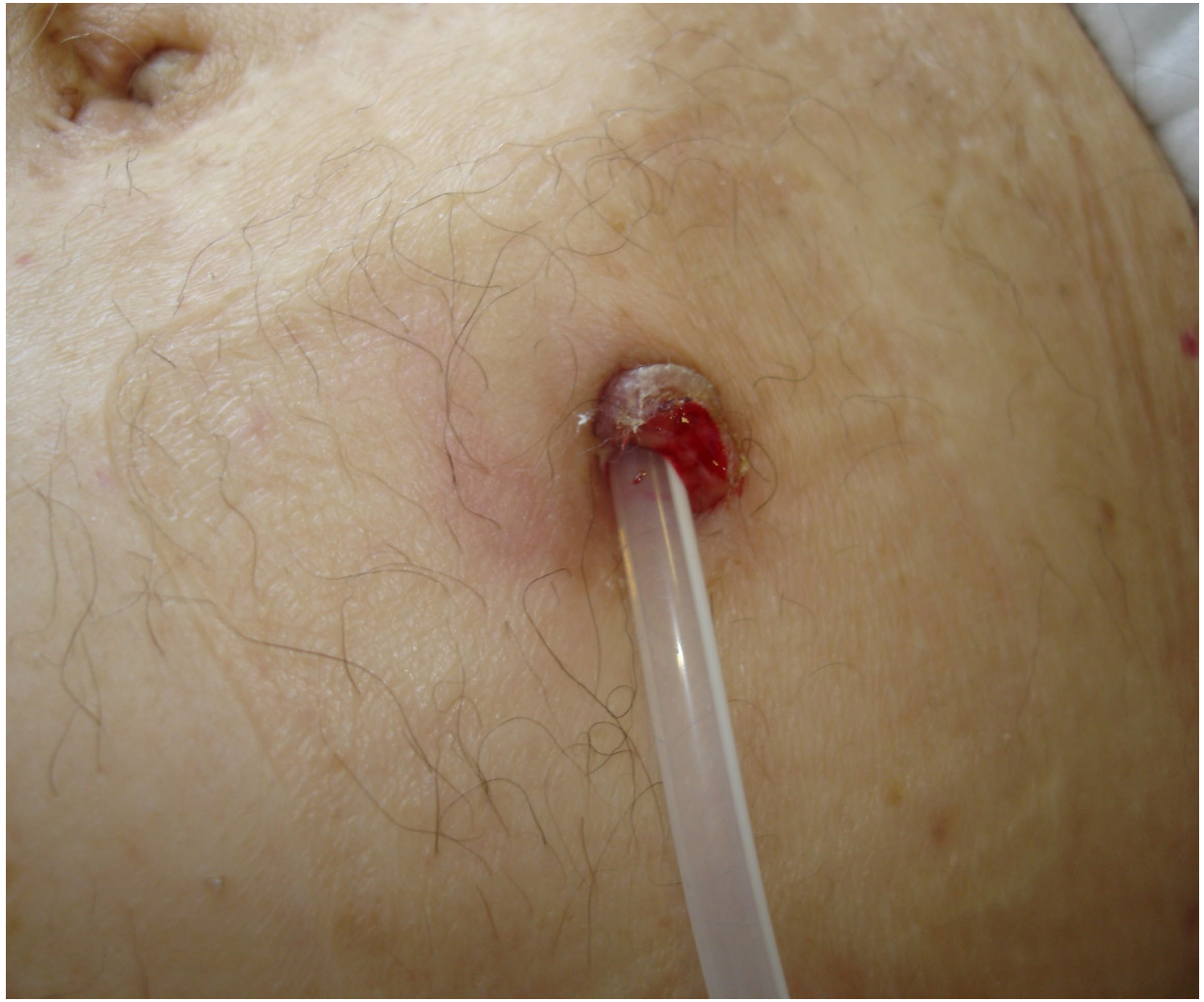












Exit-site care

★ We recommend daily topical application of antibiotic cream or ointment (mupirocin or gentamicin) to the catheter exit site to prevent catheter-related infection (1C).

★ We suggest that the comparative efficacies of topical mupirocin versus topical gentamicin or exit site versus nasal application of mupirocin for preventing catheter-related infection are uncertain (2C).

★ We suggest *that no cleansing agent has been shown to be superior* to any other with respect to preventing catheter-related infections (2B).

★ We recommend that *the exit site be cleansed* at least twice weekly and every time after a shower or vigorous exercise, including running, cycling, swimming and water sports (1C).

★ We recommend that *PD catheter exit site care be continued after interruption or discontinuation of PD* for as long as the catheter remains in place (Not Graded).

★ We suggest that a dressing cover over the exit site is not mandatory after exit site care and topical antibiotic application (2D).

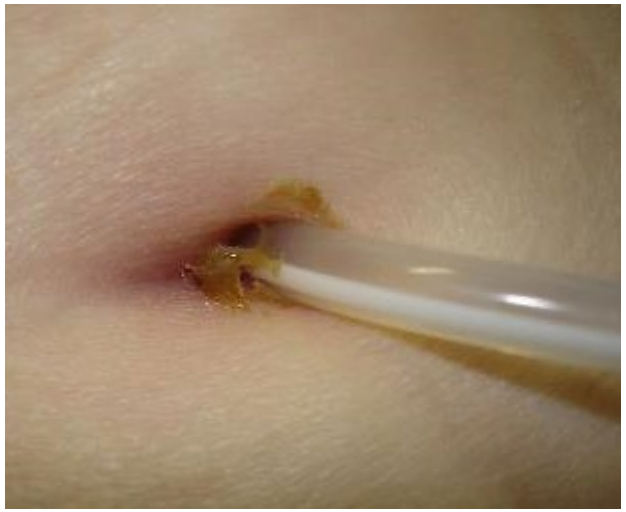
★ We recommend that the *PD catheter be immobilized* to avoid traction injury of the exit site (1C).

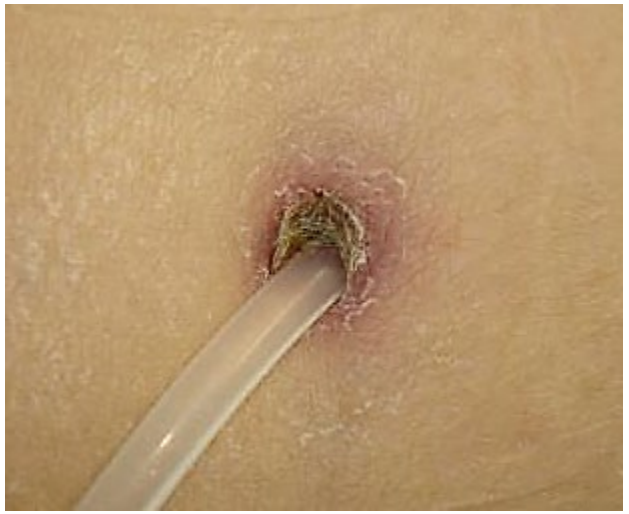
Chow KM, et al. Perit Dial Int, 2023

Exit-Site Scoring System[a]

	0 point	1 point	2 points
swelling	no	<0.5 cm	>0.5 cm[b]
crust	no	<0.5 cm	>0.5 cm
redness	no	<0.5 cm	>0.5 cm
pain	no	slight	severe
drainage	no	serous	purulent

[a] Modified from Schaefer F *et al.* (175).
[b] Or involve tunnel.





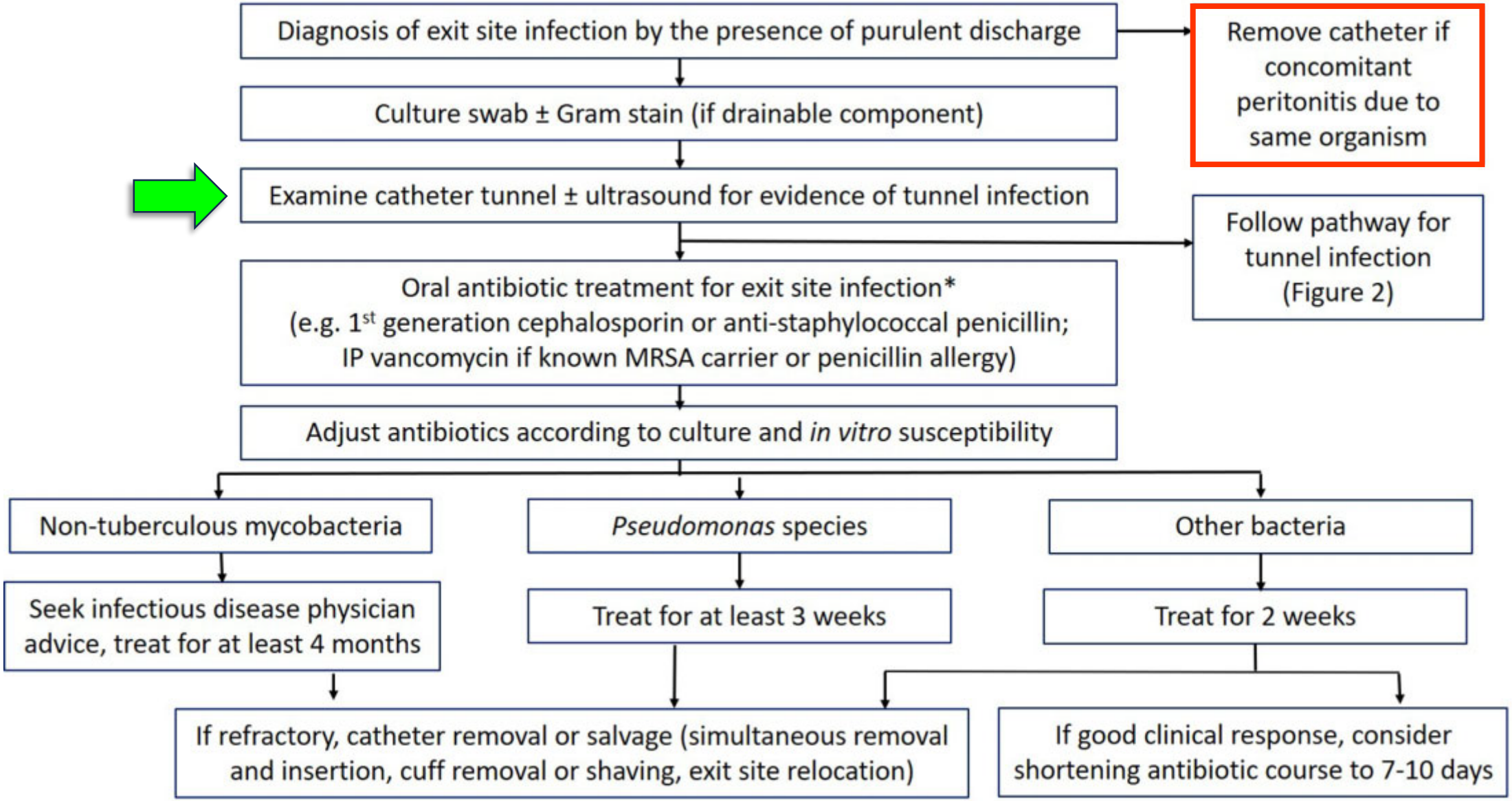
TOPICAL ANTIBACTERIAL AND ANTISEPTIC AGENTS

- We recommend daily topical application of antibiotic cream or ointment to the catheter exit site **(1A)**.
- We suggest that no cleansing agent has been shown to be superior with respect to preventing catheter-related infections **(2B)**.

Topical Antibacterials, Antiseptics, and Cleansing Agents for the Prevention of Catheter-Related Infections

- povidone-iodine (93–95)
- chlorhexidine solution (97,103)
- Amuchina solution/hypochlorite solution (98–102)
- mupirocin cream (25,56,106–113)
- gentamicin cream or ointment (107,108,123)
- ciprofloxacin otologic solution (121)
- antibacterial honey (128)
- polysporin triple ointment (129)
- polyhexanide (131)

Szeto CC, et al. Perit Dial Int, 2017



Szeto CC, et al. Perit Dial Int, 2017

EMPIRICAL ANTIBIOTIC TREATMENT

- We recommend empiric oral antibiotic treatment of exit-site infections with appropriate *S. aureus* cover such as a penicillinase-resistant penicillin (e.g. dicloxacillin or flucloxacillin) or first-generation cephalosporin, unless the patient has had a prior history of infection or colonization with methicillin-resistant *S. aureus* (MRSA) or *Pseudomonas* species (in these cases they should receive a glycopeptide or clindamycin, or appropriate anti-pseudomonal antibiotic, respectively) **(1C)**.

- *"Although anti-fungal prophylaxis (e.g. oral nystatin) is recommended for the prevention of secondary fungal peritonitis during antibiotic treatment of peritonitis, there is no study that directly supports the use of anti-fungal prophylaxis during treatment of catheter-related infections. However, a randomized controlled trial did report a lower risk of fungal peritonitis with nystatin prophylaxis whenever antibiotics were prescribed".*

Oral Antibiotics Used in Catheter-Related Infections

Amoxicillin	250–500 mg BD (182)
Amoxicillin/clavulanate	875 mg/125 mg BD (183)
Cephalexin	500 mg BD to TID (86)
Ciprofloxacin	250 mg BD (164) or 500 mg daily (184)
Clarithromycin	500 mg loading, then 250 mg BD (165)
Clindamycin	300–450 mg TID (185)
Cloxacillin/flucloxacillin	500 mg QID (186)
Erythromycin	250 mg QID (187)
Fluconazole	oral 200 mg loading, then 50–100 mg daily (188)
Levofloxacin	300 mg daily (189)
Linezolid	300–450 mg BD (190–192)
Metronidazole	400 mg TID (193)
Moxifloxacin	400 mg daily (194)
Rifampicin	450 mg daily for BW <50 kg; 600 mg daily for BW ≥50 kg (144,145)
Trimethoprim/ sulfamethoxazole	80 mg/400 mg daily (8) to 160 mg/800 mg BD (195)

BD = two times per day; TID = three times per day; QID = four times per day; BW = body weight.

Szeto CC, et al. Perit Dial Int, 2017

- We recommend that exit-site infection, *except episodes caused by Pseudomonas species*, be treated with at least 2 weeks of effective antibiotics **(1C)**.
- We recommend that exit-site infection caused by ***Pseudomonas*** species *and any tunnel infection* be treated with ***at least 3 weeks*** of effective antibiotics **(1C)**.
- If resolution of the ***infection is slow or if there is recurrent Pseudomonas ESI, a second anti-pseudomonal drug***, such as intraperitoneal (IP) aminoglycoside or ceftazidime, should be added. Generally speaking, tobramycin and amikacin are more active on Pseudomonas species than gentamicin.
- Oral fluoroquinolones are recommended as the first-line choice, but resistance may develop rapidly with fluoroquinolone monotherapy. If quinolones are given concomitantly with sevelamer, multivalent cations (e.g. calcium, iron, or zinc preparations), sucralfate, magnesium-aluminum antacids, or milk, chelation and reduced quinolone absorption may occur. Administration of the quinolone should therefore be separated from these drugs by at least 2 hours (with the quinolone administered first).
- For elderly and diabetic patients, **Achilles tendonitis** is an uncommon but well recognized complication of fluoroquinolone treatment.


Buon lavoro!