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EDUCATIONAL REVIEW

Difficult peritonitis cases in children undergoing chronic peritoneal dialysis: relapsing, repeat, recurrent and zoonotic episodes

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Abstract Despite technological improvements in dialysis connectology and dialysis technique, peritonitis remains the most common and most significant complication of peritoneal dialysis (PD) in children. Most children undergoing chronic PD experience none or only one peritonitis episode, while others have multiple episodes or episodes secondary to unusual organisms. Knowledge of potential risk factors and likely patient outcome is imperative if treatment is to be optimized. In this review we will, in turn, describe episodes of peritonitis that are characterized as either relapsing, recurrent, repeat or zoonosis-related to highlight the clinical issues that are commonly encountered by clinicians treating these infections.

Keywords Peritonitis · Peritoneal dialysis · Relapsing peritonitis · Repeat peritonitis · Zoonotic peritonitis

Introduction

Peritoneal dialysis (PD) remains the preferred form of chronic dialytic therapy in children. Despite technological advances in PD connectology, the development of new PD solutions and the development of quality assurance performance improvement programs in many centers that are designed to improve PD outcomes, peritonitis remains the most common and most significant complication of PD [1–3]. The significance of peritonitis is derived not only from the resultant pain, hospitalization, loss of school (child) and work (parent) time, potential for removal of the PD catheter and the need for hemodialysis (HD) and cost, but it also may increase mortality in the pediatric patient population [2]. The 2011 annual report of the North American Pediatric Renal Trials and Collaborative Studies (NAPRTCS) showed that peritonitis and exit-site/tunnel infections accounted for 30 % of PD access revisions in children, although improvement in the annualized rate of peritonitis from 0.79 to 0.41 has occurred in recent years [4]. The registry also revealed that excessive infections accounted for more than 30 % of PD terminations (after exclusion for renal transplantation). Most importantly, the 2013 Annual Data Report from the United States Renal Data System (USRDS) has provided evidence that infection is the leading cause for hospitalization and the second-most common cause of death in children receiving PD [5].

Most recently, there has been hope that the use of newer, more "biocompatible" fluids might reduce the risk of peritonitis. However, available data are controversial. In the BALANZ trial, a multicenter, open-labeled, randomized clinical trial of PD patients in Australia and New Zealand, the use of biocompatible compared with conventional PD solutions was associated with a reduction of the overall peritonitis rate (0.30 vs. 0.49 episodes per patient-year) [6]. In contrast, a prospective longitudinal follow-up of almost 4,000 PD patients found no difference in peritonitis rate between newer, biocompatible PD solutions and conventional solutions [7]. In turn, the most recent Cochrane review concluded that there was no significant effect of biocompatible PD solutions on peritonitis rate [8].

Although many PD patients experience none or only one peritonitis episode over their "lifetime" of PD treatment, it is in those patients who have repeated episodes of peritonitis that additional morbidity is most likely to occur [1]. Repeated episodes may not only result in impaired function of the

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peritoneal membrane as a dialyzing membrane, but they can ultimately result in the serious complication of peritoneal sclerosis (see below), a disorder that not only precludes the use of PD, but one that can result in bowel obstruction, severe malnutrition and death in children and adults [9, 10]. Thus, a thorough understanding of factors associated with the risk of experiencing multiple episodes of peritonitis or episodes secondary to unusual organisms, along with an appreciation of the recommended approach to treatment of these infections, is desirable. In this review we will, in turn, describe several episodes of peritonitis that are characterized as either relapsing, recurrent or repeat, and highlight clinical issues that are commonly encountered by clinicians treating these infections. In the last part of this review, an interesting case of zoonotic peritonitis will be presented and discussed as a distinct entity.

Terminology

Two or more episodes of peritonitis can be characterized as either relapsing, recurrent or repeat [11, 12]. An episode that occurs within 4 weeks of completion of therapy of a prior episode with the same organism or one sterile episode is defined as relapsing peritonitis. An episode that occurs within 4 weeks of completion of therapy of a prior episode but with a different organism is defined as recurrent peritonitis. Finally, peritonitis that occurs more than 30 days after completion of therapy of a prior episode, but with the same organism that caused the prior episode, is defined as repeat peritonitis, whereas it is defined as a reinfection if the organism is different [13, 14] (Table 1).

The term "repeat infection" was first used by Piraino et al. in the Peritoneal Dialysis Related Infectious Recommendations—2005 update, published under the auspices of the International Society for Peritoneal Dialysis (ISPD) [13]. It has often been assumed that a repeat peritonitis episode is merely a delayed form of a relapsing episode. However, a recent study comparing the outcomes of 181 episodes of repeat peritonitis (observed from 1995 to 2009) with 91 episodes of relapsing peritonitis showed that the two groups of peritonitis episodes have different patterns of causative organisms and therapeutic response, which implies that they are indeed two distinct entities [15]. Although there was a debate and confusion regarding the terminology and a correction was proposed [14], the definitions of relapsing, recurrent and repeat peritonitis were not changed and were fully endorsed in the 2010 update of the adult guidelines [11] and the 2012 update of the pediatric peritonitis guidelines [12]. In these same guidelines, it has also been recommended that relapsing episodes of peritonitis should not be counted as an additional episode when calculating peritonitis rates, in contrast to recurrent and repeat episodes which should be counted.

Table 1 Terminology for peritonitis[a]

Time elapsed since completing antibiotics for prior peritonitis episode	Same organism	Different organism
≤4 weeks	Relapsing	Recurrent
>4 weeks	Repeat	Reinfection

[a] Adapted from Piraino et al. [13] and Bonadio et al. [14], with permission

Case 1: Replapsing peritonitis

An 11-year-old girl who had been undergoing chronic PD (CPD) for 17 months was admitted to the hospital with nausea, abdominal pain and cloudy dialysate effluent. Her renal failure was secondary to a complex anogenital malformation accompanied by a neurogenic bladder. She received nightly automated PD (APD) with a reduced fill volume (900 ml/m^2) and was prescribed six exchanges nightly with a dry abdomen during the day due to the presence of multiple incisional hernias secondary to repeated abdominal and pelvic surgeries. Five weeks earlier she had a prior peritonitis episode secondary to coagulase-negative *Staphylococcus* (CNS). That episode was treated with intermittent intraperitoneal (IP) cefazolin for 7 days, preceded by a 3-day course of empiric combination treatment with cefazolin and ceftazidime, with no associated change in her dialysis prescription. After a negative dialysate culture was obtained on the fifth day of treatment, along with clearing of the dialysate and resolution of her abdominal symptoms, the patient was discharged. Her mother continued IP antibiotic treatment at home over the subsequent 5 days.

On physical examination at the time of the most recent hospital admission, the patient had abdominal distension and diffuse abdominal tenderness. The catheter exit site was normal in appearance. Microscopic evaluation of the PD effluent showed 1,200 white blood cells/mm^3, with 85 % neutrophils. Blood, PD effluent and PD catheter exit-site cultures were obtained prior to initiating empiric antibiotic therapy with IP cefepime, in accordance with published treatment guidelines. The PD culture revealed CNS that was susceptible to cefepime, and cefepime was continued as monotherapy for 2 weeks. Since the causative agent was CNS, this was labeled as a relapsing peritonitis episode. The effluent gradually cleared over 5 days, and the patient experienced full functional recovery following 2 weeks of antibiotics.

Discussion

As noted previously, an episode of peritonitis that occurs within 4 weeks of completion of therapy for an earlier episode that is attributable to the same organism, or one sterile episode, is characterized as relapsing peritonitis [11, 12]. Relapsing

peritonitis follows approximately 5–20 % of primary peritonitis episodes in adult and pediatric series [16–19]. The Australian multicenter PD Registry recently analyzed the dialysis courses of 6,024 patients who received PD over a period of more than 4 years (1 October 2003 to 31 December 2007) and described 4,864 episodes of peritonitis in 2,542 (42 %) patients, with 669 episodes of relapsing peritonitis (14 % of all peritonitis episodes) occurring in 442 patients. Annualized rates for all and relapsing peritonitis were 0.52 and 0.05 episodes/patient-years of treatment, respectively [18].

In pediatric PD patients, the Australian and New Zealand Dialysis and Transplant (ANZDATA) registry reported a peritonitis relapse rate of only 5 %, in contrast to the Mid-European Pediatric Peritoneal Dialysis Study Group who reported a relapse rate of 20 % between 1993 and 1997 [16, 19]. By far the largest pediatric experience with relapsing peritonitis has come from the International Pediatric Peritonitis Registry (IPPR). IPPR data showed that out of 490 episodes of nonfungal peritonitis, 52 were followed by a relapse, for a relapse rate of 11 % [17, 20].

To date, there is no accurate laboratory test to help predict which patient is going to develop relapsing or recurrent peritonitis after completion of antibiotic treatment. A recent study designed to further evaluate this issue by measuring the level of bacteria-derived DNA fragments in the PD effluent found that bacterial DNA fragment levels in PD effluent were significantly higher, both 5 days before and on the date of completion of antibiotic therapy, among patients who subsequently developed relapsing or recurrent peritonitis episodes than among those without these infections [21]. Although this study deserves further attention, the results remain to be validated. It is also important to note that the presence of bacterial DNA fragments in PD effluent does not indicate the presence of living bacteria capable of causing an active infection.

In the IPPR experience, there was no significant difference in the distribution of causative organisms between cases of relapsing peritonitis and non-relapsing peritonitis. Of the episodes of relapsing peritonitis, 11 % were Gram-positive, 9.2 % were Gram-negative and 11.3 % were culture-negative. Overall, relapsing episodes consisted of 46 % Gram-positive organisms, 21 % Gram- negative organisms and 33 % culture-negative cases. *Staphylococcus aureus* and CNS was the causative organisms in 21 and 13 % of episodes of relapsing peritonitis, respectively [20]. CNS and *S. aureus* combined were more frequent causes of relapsing peritonitis episodes in the ANZDATA and Scottish Registries, accounting for 48 and 76 % of episodes, respectively [18, 22]. However, more recently and in contrast to this experience in the pediatric patient population, Szeto et al. described experience in the adult population in which the majority of organisms causing relapsing peritonitis were Gram-negative (62 %); *S. aureus* was isolated in only 5.5 % of relapsing peritonitis episodes [15]. The frequency of Gram-negative infections causing a relapsing infection in adult PD patients was also threefold higher than the frequency noted among pediatric PD patients [15].

Independent risk factors for relapsing peritonitis identified by the IPPR include young age, single-cuff catheter, downward-pointing exit site and chronic systemic antibiotic prophylaxis [20]. Adult data have also indicated that patients with repeated peritonitis had a higher risk of developing relapsing peritonitis than controls [15].

Treatment

Repeated episodes of peritonitis can lead to the loss of peritoneal membrane function resulting in reduced PD efficacy over time and eventual technique failure; consequently, prompt and efficacious treatment of relapsing peritonitis episodes is critical. Since, by definition, the bacterial etiology of relapsing peritonitis is the same as that of the preceding episode of peritonitis (except in the case of culture-negative peritonitis), it is prudent to empirically start the patient on an antibiotic that would treat the first organism identified based on the previously determined antibiotic susceptibilities whenever a new episode is diagnosed within 4 weeks of completion of therapy for a prior bout of peritonitis [12]. If the center-specific resistance rate of *S. aureus* isolates to methicillin or oxacillin exceeds 10 % or if the patient has a history of methicillin-resistant *S. aureus* (MRSA), IP administration of a glycopeptide combined with an antibiotic providing Gram-negative coverage should characterize the empiric treatment of any potential relapsing peritonitis episode, as is the case with an initial bout of peritonitis [12]. Treatment should be tailored once the new susceptibility pattern is identified.

In the IPPR data, neither the combination of ceftazidime with a first-generation cephalosporin or a glycopeptide (vancomycin or teicoplanin) as initial empiric therapy of sporadic peritonitis was associated with an increased incidence of relapse [12]. However, the subsequent prescription of monotherapy with a first-generation cephalosporin based on culture and susceptibility results was associated with higher relapse rate (23 %) than monotherapy with any other single antibiotic (0–9 %). As a result, it has been suggested that post-empiric antibiotic therapy of relapsing peritonitis be guided by in vitro susceptibility results, choosing an antibiotic other than cefazolin for monotherapy [12, 20]. However, whether or not monotherapy with a first-generation cephalosporin should ever be used for relapsing peritonitis management does require further study.

The results of a recent study in adults by Szeto et al. have suggested that the treatment of relapsing CNS peritonitis should be 3 weeks in duration [23]. In their retrospective evaluation of 232 peritonitis episodes, these authors found

that compared with the conventional 2-week treatment course, 3 weeks of antibiotic therapy was associated with a significantly higher complete cure rate [23]. The same recommendation is contained in the pediatric guidelines [12]. In relapsing peritonitis episodes secondary to *S. aureus* without a cuff or tunnel infection, at least a 3-week course of treatment also appears to be associated with the best outcome [12].

The cure rate of relapsing peritonitis following antibiotic therapy alone is similar in adult and pediatric relapsing peritonitis episodes (71 and 73 %, respectively) [15, 20]. However, in the IPPR, relapsing infections—in comparison to sporadic peritonitis episodes—were associated with a lower rate of full functional recovery (73 vs. 91 %), a higher rate of ultrafiltration (UF) problems (14 vs. 2 %) and a higher rate of permanent PD discontinuation (17 vs. 7 %) [20]. Finally, in the ANZDATA registry, relapsing peritonitis—relative to sporadic peritonitis—was associated with significantly higher rates of catheter removal (30 vs. 22 %) and permanent HD therapy transfer (25 vs. 20 %), but similar rates of hospitalization (70 vs. 73 %) and death (2.0 vs. 2.8 %) [18].

In view of the fact that the development of biofilms may complicate peritonitis and harbor causative organisms, intraluminal instillation of a fibrinolytic agent should be considered after the diagnosis of a first peritonitis relapse that is not explained by extraluminal pathology, such as a catheter tunnel infection or an intra-abdominal abscess [12]. Although intraluminal urokinase administration showed no effect on the clinical course and relapse risk when applied to adult patients with a first peritonitis episode in a placebo-controlled trial [24], studies using intraluminal fibrinolytic agents selectively in patients with resistant or relapsing peritonitis showed more promising results [25, 26]. For example, Klaus and colleagues [25] successfully used intraluminal high-dose urokinase (5,000 IU/mi) and antibiotic instillation in nine children with relapsing peritonitis. No second relapse occurred in the treated patients. In contrast, 75 % of patients from an untreated historical control group experienced a second relapse [25]. In a double-blind, placebo-controlled study of adult patients with resistant or relapsing peritonitis, Innes et al. found that resolution of peritonitis occurred within 4 days of intraluminal urokinase instillation (1,000 IU/ml) [26]. In addition, there was no recurrence with the same organism for 6 months in eight of 12 patients, an effect significantly better than that achieved with placebo [26]. Similarly, intraluminal administration of high-dose recombinant tissue plasminogen activator (1 mg/ml) has been found to be efficacious in anecdotal reports of patients with relapsing peritonitis [27, 28].

Catheter removal Catheter exchange is another treatment option and has been shown to be superior to urokinase in lowering treatment failure rates in relapsing or persistent peritonitis [29, 30]. Removal of the PD catheter is indicated as soon as peritonitis is controlled by antibiotic therapy in the setting of relapsing peritonitis associated with a persistent or recurrent tunnel infection, or when there is a second peritonitis relapse (Table 2) [12]. In most cases, simultaneous removal and replacement of the PD catheter is permissible and prevents the need for temporary HD [12, 30].

Case 2: repeat and recurrent peritonitis

A 17-year-old boy who had been receiving CPD for more than 10 years was admitted to the hospital with severe abdominal pain and abrupt UF failure.

His underlying kidney disorder leading to end-stage renal disease (ESRD) was CAKUT (congenital anomalies of the kidney and urinary tract). He also had severe cognitive delay secondary to perinatal asphyxia. His dialysis history included only a single peritonitis episode that occurred soon after the initiation of PD, with no additional episodes over the subsequent 9-year follow-up period. However, during the last year he had experienced four peritonitis episodes. The first of these four episodes was due to CNS that occurred as a result of touch contamination; this was followed by another episode with the same organism as a repeat infection after a 2-month interval. The initial infection was treated with cefazolin monotherapy and the repeat one with a 12-day course of cefepime, to which the organism was susceptible. Three weeks after completion of the IP cefepime therapy, another peritonitis episode was diagnosed—in this case due to *S. aureus* (recurrent peritonitis)—and an ultrasound examination of the PD catheter tunnel revealed a 2-mm fluid collection around the catheter. The patient's exit-site care did not include the use of an antibiotic ointment or cream. The exit site score was 3 based on predefined criteria [12]. Vancomycin was prescribed as treatment for peritonitis and provided by the IP route intermittently for 14 days. The results of a repeat catheter tunnel ultrasound after completion of the antibiotic therapy were normal, with no evidence of pericatheter fluid collection. However, 6 weeks later, the patient presented with another peritonitis episode, this time accompanied by purulent dialysate effluent; the exit site score was 5 with purulent secretion and tenderness across the tunnel tract. IP vancomycin and ceftazidime were prescribed, but persistence of effluent cloudiness prompted catheter removal due to the repeat and refractory peritonitis episode secondary to *S. aureus* and an accompanying tunnel infection. Intravenous teicoplanin treatment was continued during the course of HD. After a 4-week interval on HD during which time the peritonitis was treated and all associated symptoms resolved, the patient had a PD catheter reinserted and he returned to PD.

One month later, the patient began complaining about persistent abdominal pain. At the same time, his UF volumes decreased despite no change in his dialysis prescription, which

Table 2 Indications for catheter removal for peritoneal dialysis-associated infections[a]

Approach to catheter	Indication	Reinsertion
Definite removal	Refractory bacterial peritonitis	After 2–3 weeks
	Fungal peritonitis	After 2–3 weeks or more
	ESI/TI in conjunction with peritonitis with the same organism (mainly *Staphylococcus aureus* and *Pseudomonas aeruginosa*; except coagulase-negative staphylococci)	After 2–3 weeks
Simultaneous removal and replacement	Repeatedly relapsing or refractory ESI/TI (including *P. aeruginosa*); relapsing peritonitis	
Relative indication for removal	Repeat peritonitis	After 2–3 weeks
	Mycobacterial peritonitis	
	Peritonitis with multiple enteric organisms because of an intra-abdominal pathology or abscess; so-called surgical peritonitis	After 6 weeks
		Depends on the clinical course of the patient; after 2–3 weeks or more

ESI//TI, Exit-site infection/tunnel infection

[a] Adapted from Warady et al. [12], with permission

consisted of four exchanges/24 h with continuous ambulatory peritoneal dialysis (CAPD). Since there was no evidence of cloudy effluent, the child's mother tried several maneuvers at home for pain relief. In addition, unsuccessful prescribed efforts to increase UF included the use of a reduced fill volume, the use of PD solutions with a higher dextrose concentration, administration of enemas and, ultimately, a change of dialysis modality from CAPD to APD.

Subsequent clinical evidence compatible with a bowel obstruction prompted an abdominal ultrasound evaluation which revealed the trilaminar appearance of bowel wall thickening, small bowel dilatation and loculated ascites. An abdominal computed tomography scan confirmed the ultrasound findings and supported the diagnosis of encapsulated peritoneal sclerosis, leading to permanent transfer of the patient to HD and the initiation of parenteral nutritional support.

Discussion

As noted above, peritonitis episodes occurring more than 30 days after a prior episode are defined as repeat peritonitis, if the same organism is isolated from the peritoneal effluent [11]. In the Australian Registry (2004–2007), this represented 485 of 4,864 episodes (10 % of all peritonitis episodes) and in the Canadian multicenter Baxter POET (Peritonitis, Organism, Exit sites, Tunnel infections) registry (1996–2005), it accounted for 181 of 1,605 episodes (11 % of all peritonitis episodes) [31, 32]. The risk of having a repeat peritonitis episode appears to be much higher (25–30 %) in individuals with CNS and *S. aureus* peritonitis in series reported from China [23, 33] and Australia [34, 35]. A retrospective single-center observational cohort study of 181 consecutive cases of repeat peritonitis in 1995–2009 showed that Gram-positive organisms were responsible for more than half of the repeat peritonitis cases (56 %); 24 % of cases were caused by *S. aureus* and 18 % by CNS [15]. In the most recent Australian registry report, there was a similar frequency of *S. aureus* (24 %) infections, but CNS was isolated in a greater percentage of repeat peritonitis episodes (45 %) [31]. In the Canadian POET database, CNS was even more commonly isolated as a cause of repeat infections, accounting for 66 % of cases [32].

There may be several explanations for the high proportion of repeat peritonitis episodes with CNS relative to other organisms [32]. CNS is typically associated with the intraluminal introduction of organisms into the peritoneal cavity, and multiple CNS peritonitis episodes in a given patient might suggest a long-standing break in technique [32]. Another reason could be the shorter recommended duration of antibiotic therapy for CNS peritonitis in some centers (2 weeks for CNS vs. 3 weeks for other organisms) and the lower catheter removal rate for CNS infections compared to *S. aureus* peritonitis, both due to the lesser severity and more prompt response to therapy of the former infection [23, 34]. Additionally, CNS may have a propensity to colonize catheters with biofilms, with some limited data available to support the contention that CNS is different from other organisms in this regard [36]. Nodaira et al. investigated risk factors and causes of PD catheter removal in 63 patients receiving CAPD and showed that all catheters removed because of repeat peritonitis had an accompanying biofilm detected upon electron microscopic examination, whereas catheters removed for other reasons (e.g. gastrointestinal neoplasm or perforation) did not [37]. In another cohort of 198 patients with multiple peritonitis episodes [35], Finkelstein et al. also showed a significantly increased likelihood of Gram-positive organisms causing repeat peritonitis episodes and suggested that biofilm formation on PD catheters may be playing an important etiologic role [38].

As for the timing of the infection, an ANZDATA report revealed that after completion of therapy for a sporadic episode of peritonitis, the probability of a repeat peritonitis episode was highest in month 2 (41 %), then progressively decreased to a stable level of 14 % from 6 months onward [31]. The Canadian POET registry found that 15 % of repeat peritonitis episodes occurred within 3 months of the diagnosis of the prior episode and that an additional 33 % of cases occurred between 3 and 6 months [32].

A repeat peritonitis episode is generally believed not to be a delayed form of a relapsing episode [15]. As mentioned previously, Szeto et al. demonstrated that the two peritonitis groups, repeat and relapsing, had different patterns of causative organisms and therapeutic response, implying that they are two distinct entities and that the pathogenic mechanisms are probably different [15]. In that study, an exit-site infection with the same organism that caused the peritonitis episode was marginally more common in the repeat group than in the relapsing group (9.9 vs. 3.3 %). Similar to the finding in Szeto et al.'s study, repeat and non-repeated peritonitis episodes were compared in the ANZDATA registry; here also they were caused by a different spectrum of microorganisms and were associated with different outcomes [31].

Treatment of repeat peritonitis

The achievement of cure rates for repeat peritonitis comparable to what is experienced with relapsing peritonitis can be challenging. In their study of adult Chinese PD patients, Szeto et al. found that the repeat group had a lower complete-cure rate than the relapsing group (70.7 vs. 54.9 %), as well as a greater rate of further relapsing or repeat peritonitis episodes; however, the rates of primary response, catheter removal and mortality were similar [15]. Therefore, these authors concluded that in repeat peritonitis episodes, "aggressive" antibiotic treatment should be considered and that the presence of concomitant exit-site problems should be duly treated [15]. As in the case of relapsing peritonitis, these results suggest that treatment of repeat peritonitis secondary to CNS should be continued for 3 weeks to obtain the highest cure rate.

In addition, the data on these Chinese PD patients actually showed that those with repeat peritonitis episodes had a higher primary response rate and a lower rate of catheter removal than a control group of patients experiencing reinfection (infections preceded by another peritonitis episode secondary to a different organism 4 weeks to 24 months previously). On the other hand, among the patients with repeat peritonitis who had a primary favorable response, 46.6 % subsequently experienced a relapse, recurrent or repeat episode of peritonitis. Although Szeto et al. suggested a preference for the performance of catheter removal and replacement following the first repeat episode [15], this recommendation has not been endorsed by many and requires further study.

The ANZDATA registry shows that most patients with repeat peritonitis were treated first with either IP vancomycin or cefazolin combined with gentamicin. Compared with non-repeated peritonitis, repeat peritonitis episodes were more likely to be treated empirically with a vancomycin-based regimen instead of a cephalosporin-based regimen. Urokinase instillation in Tenckhoff catheters was also more common in repeat than in non-repeated peritonitis. Of interest, it has recently been suggested that the minimal biofilm eradication concentration, instead of the minimum inhibitory concentration, may be the preferred therapeutic target for determining antibiotic therapy for confirmed or suspected cases of biofilm-associated repeat infections [39]. On the other hand, it is generally not known whether repeat episodes are caused by the same strain of bacteria hidden in the biofilm—a determination which requires phage typing of the bacterial isolates for confirmation. Most importantly, on multivariate analysis, the ANZDATA results reveal that repeat peritonitis was independently associated with higher relapse rates, but not significantly associated with catheter removal, HD transfer or death [31].

Catheter removal It is well accepted that "saving the catheter" is not wise in many clinical settings (Table 2) [12]. As noted above, repeat peritonitis episodes, due to their high likelihood of subsequent relapsing, recurrent or repeat peritonitis [15], may be considered a relative indication for removal of the PD catheter. While delayed replacement of the catheter is usually recommended, simultaneous removal and replacement can be considered, provided that antibiotic therapy results in clearing of the dialysate effluent.

Recurrent peritonitis

Finally, and as previously defined, an episode that occurs within 4 weeks of completion of therapy of a prior episode but with a different organism is termed recurrent peritonitis, an example of which was the *S. aureus* infection described in our patient [11, 12]. Its prevalence is very low. The Australian multicenter PD Registry 4-year analysis of 6,024 PD patients showed that only 3 % of the patients had recurrent peritonitis episodes [18]. On the other hand, compared to uncomplicated and relapsing peritonitis episodes, recurrent peritonitis was much more frequently associated with fungal infections (13 %). CNS and *S. aureus* are rarely isolated in recurrent peritonitis [18].

Compared with uncomplicated peritonitis, recurrent peritonitis is associated with significantly higher rates of catheter removal (22 vs. 37 %) and permanent transfer to HD (20 vs.

32 %), but similar rates of hospitalization (73 vs. 70 %) and death (2.8 vs. 1.2 %) [18].

Case 3: zoonosis-related peritonitis

A 7-year-old girl with ESRD secondary to renal dysplasia presented to the Emergency Room with complaints of diffuse abdominal pain. The patient was treated with continuous cycling peritoneal dialysis (CCPD) and had a history of two prior episodes of peritonitis, both secondary to CNS. The pain was described as fairly severe in intensity and was accompanied by cloudy dialysis effluent upon initial drainage. The patient and parents did not admit to any break in technique with respect to the dialysis procedure. Upon further questioning, they did admit that they had several cats in the home but that the animals did not sleep with the patient; there was no evidence of dialysate leakage or of punctures of the dialysis tubing or bags.

Upon presentation, the patient's temperature was 37.5 °C and blood pressure was 110/60 mmHg. On physical examination, the abdomen was slightly distended and tender to palpation, with diffuse guarding present. There was no erythema or discharge at the PD catheter exit-site, and the tunnel was also without evidence of infection. Analysis of the dialysis effluent revealed a white blood cell count of 5.2×10^9/l with 95 % polymorphonuclear neutrophils. Gram stain was negative. A PD fluid culture was sent for laboratory analysis.

Initial therapy consisted of IP cefazolin and gentamicin. The patient's symptoms gradually resolved, but the culture remained negative at 48 h. The therapy was subsequently changed to IP ampicillin after the culture grew *Pasteurella multocida* at 72 h. The parents later admitted to not strictly adhering to hand hygiene recommendations and of frequently playing with their cats just prior to placing their daughter on dialysis.

Discussion

Peritonitis secondary to zoonotic microorganisms is uncommon, but must be considered in any patient on chronic PD because of the common presence of pets in the home [40]. Remarkably, there are more than 70 million pet cats and dogs in the USA and more than 40 million in Europe. Most importantly, pets are known to have a positive impact on the health of their owners as reflected by less response to mental stressors and less depression [41, 42].

At the same time, there have now been at least 125 cases of peritonitis caused by 12 different zoonotic agents; 31 of these infections have followed contact with an animal [40, 43]. Whereas a number of organisms can give rise to infections in humans as a result of the ingestion of contaminated food or water, organisms that have been associated with the development of peritonitis secondary to the direct transmission from dogs and cats to humans include *Pasteurella* spp., *Brucella* spp., *Capnocytophaga* spp., *Leptospira* spp., *Cryptosporidium* spp., *Septospira* spp., *Yersinia* spp., *Bordetella bronchiseptica*, *Listeria* spp. (dogs only) and *Bartonella henslae* (cats only).

Table 3 Recommendations to prevent pet-transmitted diseases and infections in patients on peritoneal dialysis[a]

Recommendations
Initial evaluation
• Inquire about exposure to pets through ownership or through exposure to pets from friends and neighbors at the start of PD training
• Ask about responsibilities for pet-care duties and how these duties are handled
• Question the patient's/parent's ability to contain the pet away from dialysis equipment and place where dialysis takes place
• Ask if pet containment will be problematic and examine possible solutions with patient and family
• Provide scenarios involving pet ownership in training so patients can learn to recognize potential harmful situations and become aware of symptoms to report
Ongoing patient/parent education
• Teach patients/parents that personal and procedural hygiene are extremely important in preventing zoonotic infections
• Stress the need for mandatory hand washing when in contact with a pet and performing connections and exchanges
• Consider mandatory exclusion of pets from room where dialysis takes place
• Inform patients that PD equipment, tubing, and bags can be an attraction for pets and the necessity of keeping pets away from areas where the equipment is stored and used
• Continue to inquire about pet containment strategies during clinic visits
• Teach patients to report scratches or bites
• Inquire about kennel placement of pets and remind patients that exposure to other animals in a community setting may increase the risk of a pet acquiring an infection
• Teach patients/parents to look for signs of illness in pets and the importance of prompt treatment
• Stress the importance of promptly reporting any animal bites or punctures to the PD equipment
Diagnosing peritonitis
• Consider a pet-acquired source of infection in differential diagnosis of peritonitis
• Be aware of the possibility of transmission of methicillin-resistant *Staphyloccus aureus* infection from pet to human
• Question patient and family members about recent exposure/contact with animals
• Inquire about the recent and past health of family pets
• Be aware that PD effluent culture results from zoonotic organisms can take 3–7 days
• Consider a zoonotic cause in culture-negative peritonitis

PD, Peritoneal dialysis

[a] Adapted from Schiller et al. [48], with permission

P. multocida is a small Gram-negative coccobacillus that is found in the nasal, gingival and tonsillar regions of cats and dogs [44]. It is a rare cause of peritonitis and in almost all cases, the patients have had close contact with domestic cats [45, 46]. The presumed mechanism of transmission is due to a cat bite or scratch of the peritoneal dialysis tubing or bags, although poor hand hygiene coupled with cats licking the hands of those performing dialysis has also been documented, as was the case in the patient described here [47]. This emphasizes the importance of addressing measures to be taken to help prevent pet-related infections as part of home PD training (Table 3) [48]. Interestingly, the majority (15/18) of reported cases of peritonitis secondary to animal bites or scratches when the dialysis modality is known are in patients receiving CCPD, with the long tubing apparently the "target" of the cats [49]. There are no characteristic findings on initial presentation with peritonitis, and culture positivity may require more than 48 h. Penicillin is the antibiotic of choice for the 2- to 3-week course of therapy, but the organism is also susceptible to aminoglycosides, fluoroquinolones and cephalosporins [40, 50]. Typically, patients are symptom free 48–96 h following the initiation of the appropriate antibiotic therapy.

Multiple choice questions (answers are given following the reference list)

1. Which of the following statements pertaining to relapsing peritonitis is true?

   a) An episode that occurs within 4 weeks of completion of therapy for an earlier episode attributable to the same organism, or one sterile episode is labeled as relapsing peritonitis.
   b) The majority of relapsing peritonitis episodes are caused by Gram-positive organisms in adults.
   c) Gram-negative organisms are most commonly identified in relapsing peritonitis episodes in children.
   d) Catheter removal and at least 3 weeks of antibiotic treatment are necessary before catheter reinsertion in relapsing peritonitis.

2. Which of the following statements about repeat peritonitis is true?

   a) A peritonitis episode occurring more than 30 days after a prior episode, if the different organism is isolated from the peritoneal effluent.
   b) Occurs following approximately 40 % of primary peritonitis episodes.
   c) Is not a delayed form of a relapsing episode.
   d) Has the same patterns of causative organisms and therapeutic response of relapsing peritonitis.

3. Which of the following statements pertaining to zoonotic peritonitis is correct?

   a) PD effluent culture results from zoonotic organisms can take 3–7 days until positive.
   b) Transmission of MRSA infection from pets to humans does not occur.
   c) Hand washing is unlikely to prevent peritonitis when regular contact with pets occurs in subjects performing PD.
   d) Exclusion of pets from the room where APD takes place is not recommended.

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Answers

1) a
2) c
3) a