Pediatric Dialysis

Bradley A. Warady
Steven R. Alexander
Franz Schaefer
Editors

Third Edition

Springer

Editors
Bradley A. Warady
Department of Pediatrics
University of Missouri-Kansas City
School of Medicine, Division of
Pediatric Nephrology, Children's
Mercy Kansas City
Kansas City, MO
USA

Franz Schaefer
Division of Pediatric Nephrology
Center for Pediatrics and Adolescent
Medicine, University of Heidelberg
Heidelberg, Germany

Steven R. Alexander
Stanford University School of Medicine
Division of Pediatric Nephrology
Department of Pediatrics
Palo Alto, CA
USA

ISBN 978-3-030-66860-0 ISBN 978-3-030-66861-7 (eBook)
https://doi.org/10.1007/978-3-030-66861-7

© Springer Nature Switzerland AG 2021
This work is subject to copyright. All rights are reserved by the Publisher, whether the whole or part of the material is concerned, specifically the rights of translation, reprinting, reuse of illustrations, recitation, broadcasting, reproduction on microfilms or in any other physical way, and transmission or information storage and retrieval, electronic adaptation, computer software, or by similar or dissimilar methodology now known or hereafter developed.
The use of general descriptive names, registered names, trademarks, service marks, etc. in this publication does not imply, even in the absence of a specific statement, that such names are exempt from the relevant protective laws and regulations and therefore free for general use.
The publisher, the authors, and the editors are safe to assume that the advice and information in this book are believed to be true and accurate at the date of publication. Neither the publisher nor the authors or the editors give a warranty, expressed or implied, with respect to the material contained herein or for any errors or omissions that may have been made. The publisher remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

This Springer imprint is published by the registered company Springer Nature Switzerland AG
The registered company address is: Gewerbestrasse 11, 6330 Cham, Switzerland

11 **Preservation of Residual Renal Function in Children Reaching End-Stage Renal Disease** 157
Il-Soo Ha and Franz Schaefer

Part III Peritoneal Dialysis

12 **Peritoneal Access in Children Receiving Dialysis** 175
Bradley A. Warady and Walter S. Andrews

13 **Technical Aspects and Prescription of Peritoneal Dialysis in Children** 193
Enrico Eugenio Verrina and Lyndsay A. Harshman

14 **Peritoneal Dialysis Solutions** 229
Elizabeth Harvey

15 **Peritoneal Dialysis During Infancy** 249
Enrico Vidal and Joshua Zaritsky

16 **Infectious Complications of Peritoneal Dialysis in Children** 265
Alicia M. Neu, Bradley A. Warady, and Franz Schaefer

17 **Noninfectious Complications of Peritoneal Dialysis in Children** 291
Sevcan A. Bakkaloğlu and Christine B. Sethna

18 **Remote Patient Monitoring in Peritoneal Dialysis** 315
Claus Peter Schmitt and Daljit K. Hothi

Part IV Hemodialysis

19 **Hemodialysis Vascular Access in Children** 325
Michael Boehm, Deepa H. Chand, and Mary L. Brandt

20 **Technical Aspects of Hemodialysis in Children** 341
Franz Schaefer and Jordan M. Symons

21 **Haemodiafiltration: Principles, Technique, and Advantages over Conventional Haemodialysis** 359
Rukshana Shroff, Evgenia Preka, and Bruno Ranchin

22 **Maintenance Hemodialysis During Infancy** 379
Sarah J. Swartz and Fabio Paglialonga

23 **Home Haemodialysis in Children** 389
Daljit K. Hothi and Claus Peter Schmitt

24 **Infectious Complications of Hemodialysis in Children** 401
Ali Mirza Onder and Michael J. G. Somers

25 **Non-infectious Complications of Hemodialysis in Children** 437
Dagmara Borzych-Dużałka and Elizabeth Harvey

Noninfectious Complications of Peritoneal Dialysis in Children

17

Sevcan A. Bakkaloğlu and Christine B. Sethna

Noninfectious (NI) complications, mainly related to the dialysis catheter, are the major causes of peritoneal dialysis (PD) technique failure and patient morbidity. These complications can be categorized into mechanical (catheter-related and related to intra-abdominal pressure) and technique-related (ultrafiltration problems and metabolic effects of the absorption of glucose and its degradation products) (Table 17.1) [1–4]. Membrane failure, characterized by ultrafiltration failure and inadequate solute removal, was responsible for 8–27% of cases of chronic PD (CPD) termination in pediatric series [5–7]. Additionally, adverse metabolic effects of PD may further exacerbate the increased cardiovascular risk in end-stage kidney disease (ESKD).

Mechanical Complications of PD

Long-term catheter survival rates seem to be improved over time [8–10]; however, in reality it is highly variable in different registries; at 4 years, it was reported to be 73% in a recent report of the International Pediatric Peritoneal Dialysis Network (IPPN; based on the date from 2007 to 2014) [9] and 75% in an earlier Turkish registry (1989–2002) [11], but 35% in a national registry from Italy [8]. In line with this, while two large retrospective studies from Germany [12] and from the USA [13] showed catheter exchange rates of 34%, other studies and registry reports revealed lower catheter replacement rates (7–17%), due to noninfectious complications [7–9, 14].

Data from 2453 patients enrolled in the IPPN between 2007 and 2015 showed that mechanical catheter-related problems (malfunction and leakage) doubled the risk of technique failure compared with infectious causes (peritonitis and exit-site infection – 28%) [9].

The most common mechanical complications associated with PD catheters in children are inflow/outflow problems, catheter malposition, pericatheter leak, and hernia. Children under 2 years of age or weighing less than 10 kg are at a higher risk of these complications [12–16].

Pain is another important complication of PD for children. It may occur during infusion – possibly related to the jet of fluid – or at the end of draining [3]. This discomfort is frequently transient, resolving shortly after PD is initiated. Coiled catheter design [17], usage of warm, biocompatible fluids, slowing the rate of infusion, and tidal dialysis may minimize infusion and pressure pain.

S. A. Bakkaloğlu (✉)
Department of Pediatric Nephrology, Gazi University School of Medicine, Ankara, Turkey
e-mail: sevcan@gazi.edu.tr

C. B. Sethna
Pediatric Nephrology, Cohen Children's Medical Center of New York, Zucker School of Medicine at Hofstra/Northwell, Feinstein for Medical Research, New Hyde Park, NY, USA
e-mail: csethna@northwell.edu

© Springer Nature Switzerland AG 2021

B. A. Warady et al. (eds.), *Pediatric Dialysis*, https://doi.org/10.1007/978-3-030-66861-7_17

Table 17.1 Noninfectious complications of peritoneal dialysis [1–4]

Mechanical complications
Catheter-related
Perioperative (perforation of viscus or hemorrhage)
Obstruction to flow
Inflow problems
Catheter kinking
Outflow failure
Constipation
Catheter malposition, kinking
Catheter occlusion (internal by fibrin or external by omentum)
Leakage (exit-site or concealed)
Pain (on infusion or drainage)
Catheter cuff extrusion, tunnel erosion
Related to increased intra-abdominal pressure
Hernia
Pleural leak (hydrothorax)
Back pain
Gastroesophageal reflux and delayed gastric emptying
Technique-related complications
Adequacy and ultrafiltration problems
Inadequate solute clearance
Poor compliance
Decreased peritoneal permeability
Inadequate ultrafiltration
Fast transport status
Encapsulated peritoneal sclerosis
Metabolic complications
Hyperglycemia
Hyperinsulinemia
Hypertriglyceridemia
Hypokalemia
Magnesium alterations
Other complications
Hemoperitoneum
Pneumoperitoneum
Pancreatitis
Ischemic colitis and necrotizing enterocolitis
Subcapsular steatosis

Obstruction of PD Fluid Flow

Inflow obstruction suggests intraluminal blockage with fibrin or blood and may be due to kinking of the catheter (Fig. 17.1a). It usually becomes obvious soon after catheter placement. Outflow failure, which is defined as incomplete drain of instilled dialysate, most commonly occurs because of constipation, catheter malposition, intraluminal catheter occlusion (often by thrombus and fibrin), extraluminal catheter occlusion (by omentum, adhesions, epiploid fat appendices, fallopian tubes), and catheter kinking [1, 2].

Migration of the catheter out of the pelvic cavity (Fig. 17.1b) usually causes poor drainage and sometimes poor inflow of the dialysate, which is usually evident within days of placement. Omental occlusion is commonly observed within several weeks of catheter implantation and may also cause migration. Large side holes on the intraperitoneal portion of PD catheter may cause omental entrapment [15]. Large pediatric series showed the rate of malfunction/obstruction between 5% and 36% (Table 17.1) [7–10, 12–16, 18–20]. Age less than 1–2 years is a significant risk factor for dislocation [13] and malfunction [16]. A recent retrospective report analyzing infants only (n = 25, median: 18 months) demonstrated that malfunction and malposition of the catheters were seen in 44% of the cases [18].

Prevention Strategies

A simple strategy against malfunctioning migrated catheters is avoiding constipation. In addition to spontaneous repositioning, saline flushing into the peritoneal cavity, enema administration, and modification of the patient's position are conservative methods used by clinicians to reposition a migrated catheter. Liberal use of laxatives or enemas is an underappreciated strategy to promote good catheter function via inducing bowel peristalsis, since fecal impaction can cause catheter migration and external compression of the lumen by the bowel [1].

Other strategies to prevent early catheter malfunction include appropriate catheter selection, optimal surgical technique by center's best experience, good postimplantation care, and education of patients and caregivers. Insertion of catheters by experienced and dedicated physicians is advised [1, 15]. A number of modifications of PD catheter design have been proposed; however, overall, the intraperitoneal configuration, straight vs coiled, or tunnel configuration,

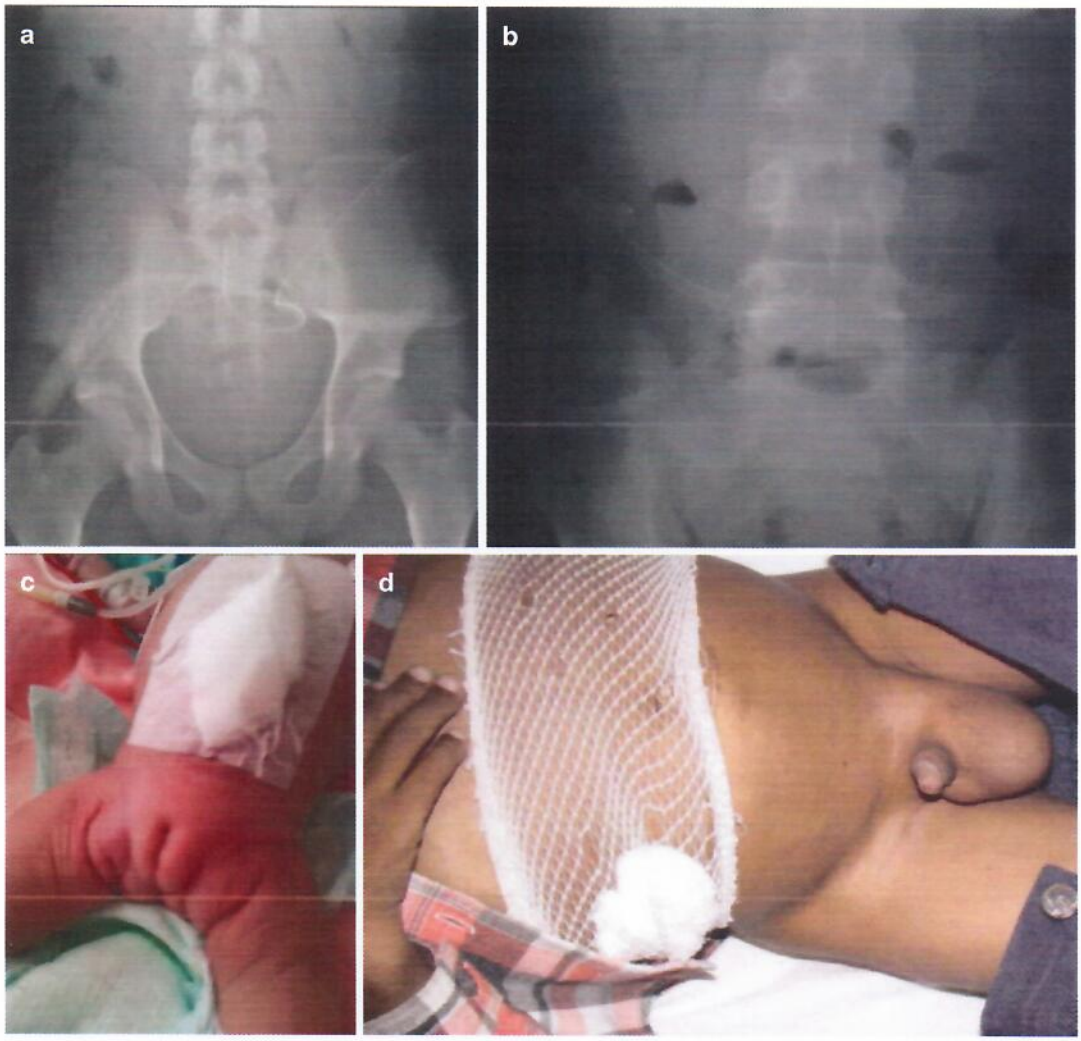


Fig. 17.1 (**a**) Catheter kinking, (**b**) catheter migration out of the pelvic cavity, (**c**) genital swelling due to leakage in an infant on chronic peritoneal dialysis, (**d**) inguinal hernia in a child on nightly intermittent peritoneal dialysis. (With permission of Sevcan A. Bakkaloglu, MD)

swan-neck vs straight, does not seem to modify this risk [1, 2, 9, 14, 17]. In the experience of the International Pediatric Peritonitis Registry (IPPR), the use of Tenckhoff catheters with a straight ending was associated with an increased rate of post-peritonitis technique failure [8]; however, in the IPPN registry, swan-neck tunnel with a curled intraperitoneal portion had a significantly higher percentage of catheter revisions secondary to mechanical dysfunction and peritonitis compared with other catheter types [9]. On the other hand, a recent cohort from the USA reported that lateral exit-site was associated with catheter migration in small infants with single-cuff catheters [14]. A single cuff may act as a fulcrum about which the catheter may rotate and cause malfunction. Tunneling these catheters straight superiorly is suggested [14]. In line with this, a recent RCT demonstrated that a new open surgical technique, involving catheter fixation to the lower abdominal wall combined with a straight upward tunnel configuration and low implant position (i.e., a shorter intra-abdominal catheter section), was successful in reducing

catheter malfunction, due to migration and omental entrapment [21]. Straight upward tunnel configuration for preventing catheter malfunction should be evaluated in pediatric RCTs.

There is a controversial data about the effect of omentectomy on catheter patency [13–16, 19]. Some studies showed 2–3 times reduced catheter replacement rate in patients undergoing an omentectomy (7–15% vs 23–27%) [14, 16, 19]. On the other hand, recent retrospective studies suggested that omentectomy did not change early or late mechanical complications and the reoperation rate [13, 15]. Therefore, omentectomy is left to physician's discretion in the current practice.

The catheter tip should sit deep in the pelvis. Selection of a catheter that is too short will result in poor drainage because the catheter will sit higher in the abdomen, where it is vulnerable to interference with omentum. Compared with other methods of PD catheter placement, positioning of the catheter can be done more accurately with laparoscopy [22]. However, studies and meta-analyses have yielded conflicting results; some are in favor of laparoscopic placement [13, 23] in terms of long-term catheter complications, while others are not [24–26]. Advanced laparoscopic techniques might further improve clinical outcome. Crabtree et al. have described advanced laparoscopic management with rectus sheath tunneling, prophylactic adhesiolysis, and prophylactic omentopexy (fixing the redundant omentum to the upper abdomen by means of a suture) and reported a reduction in the rate of catheter flow complications to <1% compared with 12% with standard laparoscopic technique [27]. In adults, nephroscope-assisted laparoscopic technique may also provide additional advantages over standard laparoscopy, including a single port entry and less leakage, less surgical time, and lower cost [28]. Particularly for patients at higher risk for catheter malfunction as a result of previous complicated abdominal surgery, advanced laparoscopic techniques provide good results in experienced hands. In children, the reported frequencies of flow problems are similar with both implantation techniques, varying between 5% and 36% [8, 10, 19, 22, 29–31]. Furthermore, recent studies in infants/neonates who had their catheters implanted mainly laparoscopically observed 2–3 times more noninfectious complications compared to those implanted open surgically in different centers [7, 18]. While awaiting convincing data from pediatric RCTs, it should be realized that the frequency of complications decreases as the experience gained by the operator increases [15], regardless of the surgical technique.

Treatment Options

Guidewire manipulation should be considered when poor drainage persists, despite an adequate trial of conservative methods. This treatment is usually reserved for catheters with radiographic evidence of migration to the hypochondriac region, although malfunctioning catheters that are properly positioned in the true pelvis may be entrapped in an adhesion and benefit from guidewire manipulation. Using a stiff rod and a stiff wire under fluoroscopy guidance, catheters can be drawn back into the rectovesical pouch with a promising long-term patency [32]. In an analysis of CPD outcomes in infants reported to the Italian registry, a successful catheter reposition rate of 25% was noted [7]. If fluoroscopically guided manipulations fail, open or laparoscopic surgery is necessary to reposition the catheter. In omental trapping, laparoscopic mobilization of the catheter can also be possible [33].

Intraluminal instillation of thrombolytics is helpful if intraluminal obstruction persists after vigorous flushing and results in a high rate of restoration of flow. Administration of tissue plasminogen activator (tPA, 8 mg in 10 mL of sterile water injected into the catheter and allowed to dwell for 1 h) in 29 cases of catheter obstruction resulted in restored patency in 24 instances with no adverse effects [34]. In children, empirically and partly based on patient and catheter size, 2.5–5 mg of tPA (1 mg/mL) in 10–20 mL saline may be used [35]. Pure tPA at a volume of 4 mL (4 mg) was shown to be effective in a newborn [36]. The reusability of tPA due to its nonallergenic properties makes it an attractive option, preventing unnecessary replacement of PD catheters.

Outcome

Although catheter patency can be sustained by conservative or interventional manipulations, obstruction to flow is still an important cause of catheter removal up to the rate of 22% in different single-center retrospective series (Table 17.2). There were no significant differences between early and delayed catheter use groups in terms of mechanical catheter problems [9, 10, 20]. However, newborns and small infants should be accepted as exception. In a study from the USA, usage of catheter within 3 days postimplantation resulted in catheter removal in 72% of these babies (median age 18 days, 60% neonates), and obstruction was the second most common cause following leakage [18].

Dialysate Leakage

An exit-site leak refers to the appearance of any moisture around the PD catheter identified as dialysate; however, the spectrum of dialysate leaks also includes any dialysate loss from the peritoneal cavity other than via the lumen of the catheter. Early leaks occur within 30 days of PD catheter insertion, and late leaks occur after this period. Early leakage most often manifests as a pericatheter leak and most commonly in newborns and infants [12, 14–16, 18]. Abdominal weakness appears to predispose mostly to late leaks, which may present more subtly with subcutaneous swelling and edema, weight gain, peripheral or genital edema, and apparent ultrafiltration failure. This reduced dialysate drainage may easily be mistaken for ultrafiltration failure at the peritoneal membrane level. Additionally, it is important to be aware that mechanical damage to the catheter will produce identical symptoms. A catheter puncture during suturing will be followed by leakage of dialysis fluid at the exit-site [33].

Risk Factors and Prevention

Leakage of dialysate at the pericatheter site tends to occur early after catheter placement, in association with high dialysate volumes, and in those with a weak abdominal wall (such as those with a history of multiple surgeries or newborns/small infants) or loose purse-string suture on the peritoneum and improperly sutured fascia [14, 33]. Intra-abdominal pressure increases linearly with the volume of dialysate infused and exponentially when abdominal compliance is exhausted. So, initiating PD with low dialysate volume (300 mL/m^2 body surface area) has been recommended as a good practice measure [37]. In addition, leaks frequently occur only after a patient becomes physically active and are less common in those who undergo dialysate exchanges when supine. Adult reports indicate that the incidence of dialysate leakage is seen in slightly more than 5% of CAPD patients [37]. The reported incidence of pericatheter leak is widely variable (3–41.5%) in different pediatric series [8, 10, 12–16, 18–20, 22, 29–31, 38] (Table 17.2). Infants with a body weight of <10 kg have 3–5 times higher risk of leakage compared to the older children [14, 15, 18]. Frequency of leakage can be as high as 71% in newborns [18]. So, the increased likelihood of leakage may be explained by patient size and delayed healing due to decreased subcutaneous tissue [18]. Although higher incidence of leakage may in part be attributed to surgical catheter placement in adult studies, the implantation method, either open surgical or percutaneous or laparoscopic, did not appear to make significant difference in pediatric series [8, 10, 18, 22].

Other factors suggested as potentially related to dialysate leak include the immediate initiation of PD [18] and median PD catheter insertion [37]. In a retrospective pediatric study, the delayed use of peritoneal catheter after its implantation (>14 days) was associated with a lower incidence of dialysate leak [29]. In line with this, the use of PD catheters within 3 days of placement was associated with catheter failure in newborns and infants [18]. Recent, large retrospective studies confirmed the impact of small age on leakage [12, 13, 15, 18]. On the other hand, the incidence of dialysate leakage in the IPPN cohort including 2453 patients with a median age of 10.5 (IQR, 3.4–14.2) years was similar for early (<7 days) and late (>7 days) PD start [9].

Table 17.2 Noninfectious complications of peritoneal dialysis: summary of pediatric studies from different countries

	Rinaldi [8]	Rahim [29]	Donmez [30]	Macchini [31]	Aksu [10]	Stringel [22]	Hooman [38]	Ladd [19]	Vidal [7]	Phan [16]
Publication year	2004, Italy	2004, USA	2005, Turkey	2006, Italy	2007, Turkey	2008, USA	2009, Iran	2011, USA	2012, Italy	2013, USA
Study period	1986–2000	1990–2000	1997–2004	1986–2002	1995–2005	–	1993–2006	1986–2008 Retrospective, single center	1995–2007 Registry data	1994–2009 Retrospective, single center
Number of patients	363 (503 catheters)	90 (127 catheters)	53 (72 catheters)	78 (89 catheters)	93 (108 catheters)	21	122	163	84	207
Age	<15 years	0–21 years	3 days–19 years		3 months–16 years	3 months–16 years	<14 years	Mean: 6.25 ± 5.58 years	All are infants started dx <1 years	Median: 12 (range: 0–21) years
Insertion technique	Surgical, omentectomy in 82.4%		Percutaneous Surgical laparoscopic	Open surgical + omentectomy in 70%	Percutaneous	Laparoscopic + omentectomy	Surgical	All open but 1% laparoscopic, 53% partial omentectomy	Open surgical + omentectomy (97%)	Mainly open, (laparoscopic in 9%) + partial or total omentectomy in 75%
PD modality		CCPD	CAPD	CAPD/CCPD	CAPD/CCPD	–	CAPD	CPD and acute (15% idiopathic acute renal failure)	CPD (70% APD 30% CAPD then APD)	CPD
Catheter type	Mainly double-cuff straight		Mainly double-cuff swan-neck curled and straight	Mainly double-cuff straight	Double-cuff swan-neck curled	Single-cuff curled, downward or lateral exit-site	Double-cuff straight or swan-neck curled	Curl or straight Quinton catheters	Mainly double cuffed, curled, downward-pointing exit-site	Mostly curled
Timing of catheter use		Early vs late	Early vs late		Early vs late	After 1 week	Early vs late	–		
Hernia			15.1%	1.5%	No		20%			33% for patients <1 year vs 10% for those >1 year

Leak	5.8%	14.2%	41.5%	2.5%	No	Several minor leaks	15%	13%	3	18% for patients <1 year vs 3% for those >1 year
Kink					7%					
Dislocation	5.8%			3.5%	12%			11%	6	
Malfunction (obstruction, drainage problems)	5.3%	21.3%	20.8%	5%	7%	7 catheters		36%	9	
Cuff extrusion	4.8%		5.7%						3	
Catheter exchange	7.6% (38 catheters (17 obstruction, 14 dislocation, 4 cuff extrusion, 3 leakage))	Catheter malfunction in 11.8% of the patients, leak with infection in 1.6%	39.6% (21 catheters from 20 patients, malfunction in 11 patients and leak in 9 patients)	7.9% (7 catheters (6 dislocation, 1 obstruction))	12% (13 catheters from 11 patients (malfunction in 6, dislocation in 3, omental capture in 2, kink in 2))	7 interventions in 5 patients (24%) due to adhesions	Catheter obstruction in 8.7% of the patients	63 (39%) underwent catheter revision (obstruction in 23, leak in 8, malposition in 7)	Catheter replacement in 15% of cases, all mechanical complications. 21 catheters were repositioned, due to NI complication	46 (22%) catheters were removed for malfunction 34% adhesions, 24% leak, 17% fibrin plugs, 17% migration, and 8% other reasons

(continued)

Table 17.2 (continued)

	Kim[a] [3]	Carpenter [13]	Radtke [12]	Borzych-Duzalka [9]	LaPlant [14]	Radtke [15]	Imani [18]	Nikibakhsh [20]
Publication year	2015, Korea	2016; USA	2016, Germany	2017, international	2018, USA	2018, Germany	2018, USA	2018, Iran
Study period	1986–2012 Retrospective, single center	2002–2014 Retrospective, single center	2009–2014 Retrospective, single center	2007–2015 Registry data International	2005–2017 Retrospective Two centers	2009–2015 Retrospective Two centers	Retrospective, single center, 2002–2015	2005–2011 Retrospective, single center
Number of patients	60 patients (70 catheters)	116 patients, 173 catheters	60 (71 catheters)	2453 (824 incident, 1629 prevalent)	130 patients, 157 catheters	122 patients, 154 catheters	25 catheters, only <2 years	56
Age at dialysis initiation	9.9 ± 5.5 (at dx initiation)	9.7 ± 6.3 years (2 days to 22 years)	Median: 3.3 (0.01–15.5) years	Median 10.5 (IQR: 3.4–14.2) years	4 ± 5.3 years (1 day to 23 years) – 46% infants	Median: 3.0 (0.01–17.1) years	Median: 18 (7–121) days, 60% neonate	Median: 6.5 y (1 month – 14 years)
Insertion technique	–	Open (122) and laparoscopic (51) ± partial omentectomy (34%)	Open surgical	All	Mainly open and laparoscopic (n = 20, 13%) + omentectomy	Open ± partial omentectomy	Laparoscopic (84%) ± omentectomy (40%)	Open surgical ± omentectomy
PD modality	CAPD	All CPD	33 CPD, 37 acute	Chronic PD	Acute and CPD	89 catheters for CPD, remaining for acute use	CPD	Acute (21) and CPD (35) (>3 weeks on PD)
Catheter type	Two-cuffed straight Tenckhoff, downward-pointing ES	Double cuffed catheters	One cuffed	All types	Argyle curl catheters (no straight tunnel) upward-pointing ES	One-/double-cuffed curled and straight catheters in small children (n = 19), downward ES	One/double (29%)-cuffed curled (48%) and straight catheters	Swan-neck coil two cuff
Timing of catheter use				Immediately, <7 day, ≥7 day	Same day and later on – 22% delayed use		Use within 3 days (48%)	Immediate use
Hernia	Hernia (8.6%)				10% 15% in infants, and 5% in older children		20% hernia at catheter insertion (60% of newborns)	

Leak	Leakage (10.0%)		7.1% (only in <10 kg)	29 (%1)	14% 21% leakage for infants vs 8% for others	18 (11.7% of catheters) (25.5% for pts. < 10 kg vs 5.6% for pts. > 10 kg)	32% (71% of newborns)	5.35%
Dislocation	Catheter tip migration (2.9%)	7% (15% for pts. < 2 years vs 5% for those >2 years)	10%		6%	16 (10.4% of the catheters)	18%	
Malfunction (obstruction, drainage problems)	Outflow failure (14.3%)	24% (including leak and kink)	12.9%	270 (%11)	6% – adhesion	31 (20.1% of catheters) (15 – omental trapping)	26%	21.4%
Catheter exchange	Catheter malfunction, injury, and oozing resulted in catheter removal in 7 (11.6%) patients – catheter exchange rate is 7.1% (n = 5)	34% of the patients had their catheter exchanged due to NI causes (dysfunction more in children <2 years)	17 out of 70 catheters (24.3%) needed a surgical revision within 6 months after implantation	Catheter malfunction and leakage resulted in catheter exchange in 7.8% of the pts. (n = 192)[b]	17% of the patients had their catheter exchanged (8 for leakage, 3 migration, 1 adhesion, 1 hernia)	53 (34.4%) catheters underwent revision	18 new catheters (72%) were inserted within 12-month follow-up	8.3% of CPD patients transferred to HD NI complications are same with immediate use.

CPD chronic peritoneal dialysis, *ES* exit-site, *IQR* interquartile range, *NI* non-infectious, *y* years, *d* days, *pts.* patients

[a]Other noninfectious complications: peritoneal bleeding (7.1%), inflow or outflow pain (4.3%), catheter injury by patient or caregiver (2.9%), and abdominal distension (1.4%); metabolic complications: 5% of the patients

[b]Access revision: 13% of all patients and 23% of incident patients required one or more access revisions

A decreasing overall incidence of leakage was reported by the Italian registry, possibly related to improved surgical experience [8]. In a prospective, open-label randomized study performed in a single pediatric center, the application of fibrin glue to the peritoneal cuff suture prevented early dialysate leakage [39]. Overall, the surgical approach, the number of cuffs, and the primary renal diagnosis were not predictors of initial catheter complications [18]; however, omentectomy may be a risk factor for leakage by recognizing the rate of leakage as 25% vs 5% in patients with or without omentectomy [19].

Diagnosis

The presence of fluid around a peritoneal catheter may be due to leakage of dialysate or to serosanguineous fluid extruding from the subcutaneous tissue. If the etiology of the fluid is unclear, a dialysate leak can be confirmed by checking the glucose concentration of the leaking fluid.

Fluid infiltration of the abdominal wall is easily overlooked, particularly in obese patients. Reduced drain volumes may occur because a substantial portion of the dialysate leaks into the abdominal wall and once a steady state is achieved is absorbed at a rate equal to the leakage rate. Normal solute equilibration in the PET, with apparently lacking ultrafiltration, suggests the diagnosis of "internal" leakage. The most widely used approach to confirm the diagnosis and to determine the exact site of fluid leaking into the abdominal subcutaneous tissue and/or intermuscular layers is T2-weighted MRI with an empty and filled abdominal cavity or CT with contrast agent-added PD fluid [33, 37].

Groin or genital swelling caused by leaks (Fig. 17.1c) is usually related to underlying hernias (which are often palpable), with a patent processus vaginalis, or a peritoneal membrane defect along the catheter tract. Scrotal swelling is much more common than labial swelling; it is generally bilateral. Leakage into the pleural space will be discussed separately below.

Management

Successful management of pericatheter leaks can usually be accomplished by decreasing the dialysate volume. Occasionally, converting the patient to continuous peritoneal modalities in which exchanges occur when supine or application of temporary hemodialysis may resolve dialysate leakage. Leaks that do not respond to conservative management may require minor surgical repair of the deep cuff or rarely catheter replacement. Surgical repair has been strongly suggested for leakage causing genital swelling [33, 37].

Hernia

Hernia is a common complication in children on PD, with a reported incidence up to 30% across pediatric series (Table 17.2). Several different types of hernias have been described in PD patients. The sites of anatomic weakness that predispose to hernia formation include the inguinal canals with or without patent processus vaginalis, the umbilicus, the linea alba, the exit site, and any sites of prior surgical incision (Fig. 17.1d).

Risk Factors

The risk of PD-associated hernia in children is affected by the intraperitoneal pressure (IPP), the patient age [14, 16, 18, 40–42], and the presence of anatomically weak sites in the abdominal wall [40]. Infants compared to older children had a three times higher risk of hernia development (15% vs 5% and 33% vs 11%, in different series) [14, 16]. In a study from the USA, 20% of 25 infants starting CPD during the first 2 years of life had hernia at catheter insertion; 60% of those cases were newborns, and presence of a hernia was one of the main predictors of initial PD catheter failure in small infants [18]. Therefore, the risk of hernia seems to be confined to neonates and infants [14, 16, 18], due to their high incidence of patent

processus vaginalis and, possibly, higher intra-abdominal pressure. These findings support the concept of prophylactic closure of the processus vaginalis at the time of catheter insertion in neonates and young infants. Recently in adults, combined hernia repair and PD catheter placement has been shown as a safe procedure [43]. However, the presence of a hernia at PD catheter placement with or without repair was associated with dialysate leak in neonates and infants [18].

Abdominal wall hernias are not uncommon in patients on CAPD, and some risk factors have been identified in adult patients. These include female gender, increasing age, longer time on peritoneal dialysis, increasing number of laparotomies, and multiparity [44]. However, there is no clear data in children.

Clinical Features

The most common presentation of the hernia is a painless swelling. Other symptoms associated with abdominal hernia in PD patients include discomfort or disfigurement and problems related to a complication from the hernia. Complicated hernias present as a tender lump, recurrent gram-negative peritonitis, bowel obstruction, and perforation, if there is strangulation or incarceration of the bowel. An umbilical hernia has a special predilection for strangulation. Catheter and other incisional site hernias and least commonly inguinal hernias may lead to incarceration and strangulation of the bowel. These complications are also more likely when the hernia is small, preventing the free movement of bowel into and out of the hernia sac. The presence of genital swelling may suggest occult indirect inguinal hernias [2]. Additionally, hernias may be associated with poor PD outcomes because of ineffective dialysis from increases in hernia size with increasing dwell volumes.

Diagnosis

Patients can easily be diagnosed clinically. MRI or CT peritoneography is a useful confirmatory diagnostic procedure. Peritoneal scintigraphy is usually used in patients who are allergic to contrast dye and in centers where MR peritoneography is not available [2].

Prevention

There are several implantation best practice recommendations for preventing leakage and hernias. Two-cuff designs and placement of the deep cuff at an intramuscular location are preferred. Intramuscular cuff placement results in fewer pericatheter leaks and hernias. In infants and children, a paramedian fascial incision is usually preferred in order to avoid herniation or dialysate leakage [8]. However, surprisingly, the number of catheter cuffs was not significantly associated with catheter outcomes in a recent cohort of infant PD [18]. Laparoscopic catheter placement is an attractive alternative to open surgical insertion, since it allows complete visualization of the peritoneal cavity, including inspection of the inner inguinal ring and prophylactic closure of patent processus vaginalis in infants [22]. A recent paper from the USA reported that three umbilical hernias, three bilateral inguinal hernias, and two ventral hernias were successfully repaired in 8 of 21 pediatric patients during laparoscopic PD catheter placement [22].

Intraperitoneal pressure (IPP) can be easily measured using a central venous pressure scale attached to the PD tubing system as the mean of inspiratory and expiratory pressure in the midaxillary line in the supine position. IPP in the empty abdominal cavity is 0.5–2.2 cmH_2O, increasing with rising amounts of fluid volume and change in posture. The supine position generates the lowest IPP for a given volume of IP fluid [2]. Biocompatible PD solutions reduce IPP by 15–20%. On the other hand, IPP increases with obesity and organomegaly, for example, autosomal recessive polycystic kidney disease. Likewise, abdominal pain and constipation increase IPP [45]. IPP monitoring may be used as an objective measure to guide fill volume prescription by determining how much intraperitoneal volume is tolerated and potentially lower the risk of mechanical complications such as hernia and leakage [40, 41, 45], although the concept has not been verified in RCTs. In children, IPP is usually acceptable up to 13–14 cmH_2O, which corresponds to a mean fill volume of 1400 mL/m^2. Abdominal pain is not reported below 12 cmH_2O. Below 2 years of age, IPP should not be above 8–10 cmH_2O, that is,

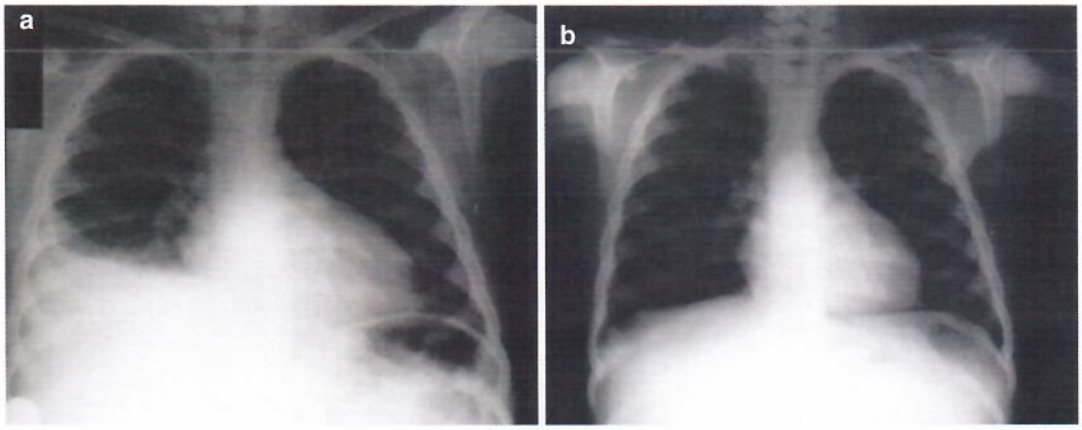


Fig. 17.2 (**a**) Right-sided massive pleural effusion. (**b**) Complete resolution of pleural effusion after pleurodesis with tetracycline. (With permission of Sevcan A. Bakkaloglu, MD)

in most cases fill volume not above 800 mL/m^2. Otherwise, the risk of hernia and leakage increases considerably in infants [45].

Treatment

Most hernias need surgical repair [33]. Repair of preexisting hernias and delaying PD catheter use to allow for a longer period of healing reduces the risk of complications and improves the overall catheter survival [18]. If immediate use of PD catheter is necessary, patients should be maintained on low-volume nocturnal cyclic PD, with an empty or small-volume dwell during daytime.

Hydrothorax

Hydrothorax is an uncommon but well-recognized complication of peritoneal dialysis. The reported incidence of hydrothorax varies from 1.6% to 10%. It can present as an asymptomatic effusion found on a chest radiograph ([46], Fig. 17.2a), or it can be massive, causing major respiratory symptoms. Hydrothorax can follow the first few dialysate exchanges or occur after years of uneventful PD [37]. Increased intra-abdominal pressure after instillation of fluid into the peritoneal cavity can result in leakage of the PD solution from the peritoneal cavity into the pleural space across the diaphragm. The pleural to peritoneal connection is almost always on the right side. The presence of the heart and pericardium may prevent the leak of fluid across the left hemidiaphragm. The condition should be differentiated from other causes of transudative pleural effusion, such as congestive cardiac failure, hypoalbuminemia, or fluid overload for any reason [2, 37]. Spontaneous leakage of dialysate fluid from the peritoneal cavity into the pericardium via a pericardioperitoneal fistula, "hydropericardium," is an extremely rare, potentially life-threatening complication of PD [47].

Pathogenesis

The physiopathology of hydrothorax is not entirely clear. It is most commonly secondary to a pleuroperitoneal communication. Possible mechanisms include a disorder of lymphatic drainage, pleuroperitoneal pressure gradient, and congenital diaphragmatic defects. A disorder of lymphatic drainage was suggested by the finding of diaphragmatic lymphatic swelling after peritoneal fluid instillation during surgical exploration. In autopsy studies, discontinuities in the tendinous portions of the hemidiaphragms have been

observed, thereby supporting the presence of diaphragmatic defects. In addition, the negative intrathoracic pressure combined with an increased intra-abdominal pressure caused by dialysate instillation may open small defects in the diaphragm and promote the flow of dialysate into the pleural space [2, 37].

Clinical Features

The most common clinical symptom is shortness of breath, which can be mistaken for congestive heart failure. Patients may use more hypertonic dialysis solution to increase ultrafiltration; however, that will lead to a further increase in the intra-abdominal pressure and subsequently worsening of symptoms. Physical examination will reveal decreased or absent breath sounds and stony dullness on percussion.

Diagnosis

Chest X-ray may show right-sided pleural effusion (Fig. 17.2a). The presence of left-sided pleural effusion should prompt the clinician to evaluate for other secondary causes of hydrothorax. Thoracocentesis with biochemical analysis of pleural fluid is the first-line investigation. A transudative effusion with high glucose content (>300–400 mg/dL or pleural fluid to serum glucose concentration gradient >50 mg/dL) proves the peritoneal origin of the pleural fluid. In patients with icodextrin solution, iodine mixed with the effluent results in a bluish-black discoloration, which is diagnostic for PD-induced hydrothorax [48]. In uncertain cases, or when there is a clinical need to demonstrate the anatomy of the communication, an imaging approach such as MRI or CT peritoneography can also be used [2, 49].

Treatment

Once hydrothorax secondary to pleuroperitoneal communication is confirmed, temporary cessation of PD remains the first-line treatment. Frequent small-volume exchanges can be a feasible alternative in children. In case of acute shortness of breath, discontinuation of PD and immediate thoracocentesis are indicated. PD can often be resumed after temporary cessation, presumably because of spontaneous resolution of the leakage.

Current evidence in adults shows that video-assisted thoracoscopic pleurodesis or diaphragmatic repair should be the treatment of choice in patients who failed conservative management [49]. Chemical pleurodesis has been performed with talc, autologous blood, and tetracycline ([46], Fig. 17.2b), with uneventful recovery both in children and adults [2, 46, 49]. There is no evidence to suggest that one agent is superior to another. The main side effect of these sclerosing agents is pain. Open surgical treatment is the last option for recurrent hydrothorax [2, 49].

Technique-Related Complications

Peritoneal Membrane Failure

Peritoneal membrane failure is an important complication of PD characterized by ultrafiltration failure (UFF) and/or inadequate solute removal. It ensues due mainly to structural and functional changes in the peritoneal membrane attributable to severe, persistent, and/or relapsing intraperitoneal infection and the use of conventional bio-incompatible PD solutions, which are hyperosmolar, acidic, has lactate buffer and contains high concentrations of glucose and glucose degradation products (GDPs) (see Chap. 12).

Pathogenesis

Continuous exposure to bio-incompatible PD solutions and bacterial infection triggers inflammation of the peritoneal membrane, which leads to the release of endogenous cellular compo-

nents and matrix degradation products that cause progressive fibrosis, neoangiogenesis, vasculopathy, epithelial-to-mesenchymal transition (EMT) of mesothelial cells, collagen deposition in the sub-mesothelial compact zone and, ultimately, UFF. A peritoneal biopsy study clearly showed that PD treatment per se had a strong impact on peritoneal fibrosis and vasculopathy. The thickness of the sub-mesothelial zone and the extent of vasculopathy were positively correlated with the duration of PD, and inversely with UF capacity [50].

There is emerging evidence that toll-like receptor (TLR) activation of peritoneal mesothelial cells is linked to fibrosis of the membrane; thus, TLRs may be a potential therapeutic target for preventing fibrosis and membrane failure [51]. EMT of peritoneal mesothelial cells is also an important mechanism involved in the process of peritoneal membrane failure. EMT is induced by multiple stimuli, which include GDPs and advanced glycation end products and inflammatory cytokines, such as TGF-beta. Mesothelial cells that undergo EMT promote neoangiogenesis through VEGF expression. Dysfunctional aquaporin 1 (AQP1) in peritoneal endothelial cells is another putative mechanism of UFF. Peritoneal neoangiogenesis is probably the main effector of increased solute transport and UFF in long-term PD. In addition, mast cells and various genetic factors controlling angiogenesis and fibrosis and effects of medications may modulate the rate at which UFF develops. However, the relative roles of fluid components, bacterial inflammation, genetic disposition, drugs and other factors, and the precise sequence of the pathophysiologic events, initiating and propagating peritoneal fibrosis and angiogenesis, remain elusive [50].

Differential Diagnosis

The ability to evaluate for UFF is of major clinical importance. In the case of low drain volumes, a distinction must be made between catheter dysfunction, leakage of fluid either externally through the catheter tunnel or internally from the peritoneal cavity to the pleural space, and impairment of the peritoneal membrane. In fact, multiple membrane-related causes should be considered, which include the following:

1. Large functional peritoneal surface area relative to the size of the fill volume, the result of either too low a prescribed fill volume or too large a vascular surface area secondary to hyperperfusion (e.g., GDP-induced neoangiogenesis)
2. Impaired free-water transport as a result of aquaporin dysfunction
3. High lymphatic absorption associated with a marked elevation of IPP
4. Limited peritoneal surface area available for exchange, as might occur with postinfectious or postsurgical adhesions, peritoneal fibrosis, or peritoneal sclerosis [41]

The causes of membrane failure can be distinguished in part by the peritoneal equilibration test (PET, see Chap. 11). The peritoneal membranes can be classified according to PET results into high, high-average, low-average, and low transporter categories. The high transporter status is associated with a poor technique and even patient survival in adults, probably due to increased glucose resorption, leading to UFF, fluid overload, hypertension and left ventricular hypertrophy, increased atherogenesis, and malnutrition related to increased peritoneal protein losses [52, 53]. Children with high transporter status are at risk for poor longitudinal growth [54].

Management

The traditional method to treat membrane failure is to use short exchanges with hypertonic dialysate. However, exposure to the high glucose concentration in hypertonic dialysate can accelerate the process of peritoneal inflammation and neoangiogenesis, thereby further aggravating UFF. Therefore, the protection of the peritoneal membrane from the long-term toxic and metabolic effects of conventional high GDP-containing, glucose-based solutions would be ideal [53, 55]. More biocompatible PD solutions may preserve peritoneal membrane function and

promote ultrafiltration (see Chap. 12 for details). In children with established UFF, PD fluids containing icodextrin as osmotic agent may be of some value, both by their greater efficacy in inducing ultrafiltration [55, 56] and by minimizing peritoneal glucose exposure (see Chap. 12 for details). However, the level of evidence to support the use of biocompatible fluid to prevent or treat peritoneal membrane failure is not adequate. In a recent Cochrane review of 42 studies including adults and children, due to the inconsistency of reporting and low methodologic quality of studies, the impact of biocompatible solutions on long-term peritoneal membrane function was determined to be uncertain [57].

Prognosis

Membrane failure is responsible for up to 27% of CPD termination in different pediatric series [5, 6, 58]. Altered peritoneal membrane function over time has a significant impact on both technique and patient survival. As the prevalence of UF failure increases, it becomes the predominant reason for dropout in long-term PD, particularly in anephric and oliguric patients. According to the Japanese long-term experience, the frequency of PD termination due to UFF steadily increases with time on PD, from 14% in the first 5 years of treatment to 33% thereafter [58]. In contrast, insufficient solute removal was a constant cause of technique failure in 13% of cases before and after 5 years on PD.

The prognosis of membrane failure is not unvariably poor and likely depends on the underlying mechanism of the high transporter phenotype. Recent classification attempts to differentiate the various types: "type 1," an early inherent type of membrane failure associated with increased mortality related to marked underlying comorbidity and inflammation; "type 2," an early inherent type with a large peritoneal surface area; and "type 3," a late-acquired type with peritoneal membrane changes which develop with time on PD. The latter two types have a good prognosis provided that fluid balance is controlled using APD and icodextrin-based PD solution [52].

Ultrafiltration failure due to an elevated peritoneal solute transport may be transient or sustained. Transient increases are seen during episodes of peritonitis. In some cases, repeated episodes of peritonitis lead to a sustained increase in solute transport and a persistent loss of ultrafiltration. Other factors like prolonged PD vintage, dialysate buffer, glucose and buffer byproducts used in the dialysate, and the use of beta-blockers may contribute to impaired ultrafiltration [53].

Encapsulating Peritoneal Sclerosis

Encapsulating peritoneal sclerosis (EPS) is a rare, but serious, complication of long-term PD, characterized by encasement of the bowel loops accompanied by extensive sclerotic thickening of the peritoneal membrane. Clinical features of EPS result from underlying pathogenic processes, particularly ileus, inflammation, and/or peritoneal adhesions. Signs and symptoms frequently include abdominal pain, nausea, vomiting, fatigue, loss of appetite, constipation, diarrhea, abdominal mass, ascites, weight loss, low-grade fever, and hemorrhagic effluent [59]. It is also typically associated with a progressive loss of ultrafiltration, resulting in fluid retention and edema. Unlike other causes associated with these clinical findings, EPS is an insidious, gradual, non-acute clinical syndrome [58]. It is important to recognize that EPS may also present long after the cessation of PD [60].

Pediatric registries from Japan, Italy, and the European Pediatric Dialysis Working Group (EPDWG) report an incidence of 1.5–2% for EPS in children on PD [61–63]. In the Japanese registry, all patients who developed EPS had received PD for longer than 5 years, with a mean PD duration of 10.3 years. The incidence of EPS was 6.6% among all patients on PD for longer than 5 years and 22% among those who had received PD for longer than 10 years [62]. Similar results were found in the Italian and EPDWG registries [61–63].

Pathogenesis

The etiology of EPS is believed to be multifactorial. Potential risk factors for the development of EPS include extended duration of PD; previous frequent severe peritonitis episodes; a reaction to other foreign agents, such as plasticizers from catheters; exit-site cleansing agents, such as povidone-iodine or chlorhexidine; and extended exposure to bio-incompatible dialysis solutions [58]. Of note, there was no difference reported in the incidence of EPS between biocompatible and standard PD solutions in the Italian and EPDWG registries [61–63].

Diagnosis

The diagnosis of EPS is suspected in the patient with a long history of PD, signs and symptoms consistent with SEP, and/or progression to a high peritoneal permeability state and is confirmed with radiographic or histological findings of bowel encapsulation. Imaging with computed tomographic (CT) scanning is recommended to evaluate for characteristic signs, such as peritoneal calcification, bowel thickening, bowel tethering, bowel dilatation, and localized ascites. (Fig. 17.3) [64, 65]. Peritoneal membrane thickening is common among long-term PD patients and without symptoms is not, in and of itself, diagnostic of EPS.

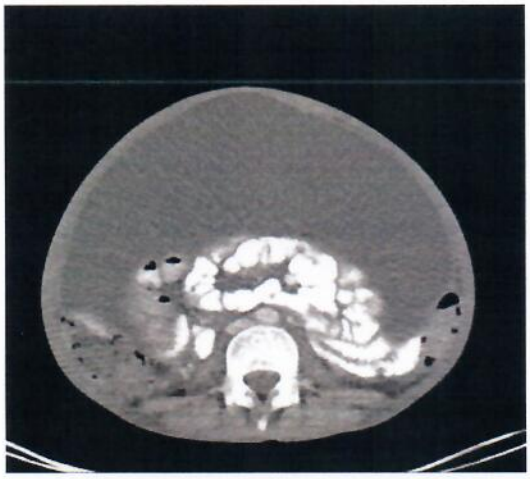


Fig. 17.3 Massive ascites secondary to EPS pushing stomach and intestinal loops posteriorly. (With permission of Sevcan A. Bakkaloglu, MD)

Treatment

Although frequently unsuccessful, the treatment of sclerosing peritonitis most commonly entails cessation of PD with transfer to hemodialysis and bowel rest with total parenteral nutrition (TPN). In addition, drug therapy with corticosteroids, tamoxifen (a selective estrogen receptor modulator that inhibits the production of TGF-β by fibroblasts), and other immunosuppressive agents including, azathioprine, sirolimus, and mycophenolate mofetil have been tried with variable results [58, 65]. There are no consensus guidelines for the use of drug therapy in EPS [61–63]. Surgery is indicated for bowel obstruction, bowel perforation, hemoperitoneum, or lack of improvement with drug therapy.

Prognosis

EPS is the most serious complication of long-term PD with a mortality ranging from 14% to 38% [61–63]. The major causes of death are almost invariably related to problems concerning bowel obstruction or complications of surgery, such as malnutrition or septicemia. Therefore, a high index of suspicion and elective discontinuation of PD in high-risk patients is of particular importance for the early diagnosis and prevention of potentially fatal outcome. The development of UFF, a high dialysate/plasma creatinine ratio, peritoneal calcification, a persistently elevated C-reactive protein level, and severe peritonitis in patients on PD for longer than 5 years are signals that should prompt the clinician to consider terminating PD as a possible means of preventing the development of EPS [58]. However, there is no evidence to support the benefit of routine transitioning to hemodialysis for all long-term PD patients as EPS is very rare.

Metabolic Complications

Dyslipidemia and Insulin Resistance

Disturbances of lipid and glucose metabolism are the common complications of chronic renal failure and persist or deteriorate during renal replacement therapy. The few reports available in

pediatric PD patients are consistent with findings of adult studies, indicating insulin resistance, hyperleptinemia, dyslipidemia, and an atherogenic lipid profile [4, 66–69]. The pathophysiology of these metabolic complications in PD patients is multifactorial, including the continuous administration of glucose in the dialysate, albumin and HDL losses into the peritoneal cavity, and reduced lipolytic enzyme activity.

Serum total cholesterol, triglyceride, low-density lipoprotein cholesterol, apolipoprotein A, and lipoprotein (a) levels are elevated, and HDL lipoprotein levels are decreased in children on PD. The prevalence of dyslipidemia differs by dialysis modality, with PD conferring an increased risk for dyslipidemia compared to hemodialysis. Dyslipidemia was reported in 85.1% of PD patients and 76.1% of hemodialysis patients in the European ESPN/ERA-EDTA registry of 976 children with ESRD. Interestingly, younger age on PD was associated with a more adverse lipid profile. Monitoring for dyslipidemia with annual fasting lipid level measurements is recommended in children on chronic PD [70]. Therapeutic lifestyle modifications including moderate-to-vigorous exercise and reduction in sedentary activities and dietary fat are vital for primary prevention of dyslipidemia. There is currently a lack of evidence regarding the efficacy of pharmacological treatment of dyslipidemia in children, although statin therapy can be considered for children ≥10 years old that fail non-pharmacologic treatment [71]. The direct benefit of statin therapy in reducing the mortality from cardiovascular disease in children on dialysis is not yet proven.

As has been shown in adults, glucose intolerance and insulin resistance are of concern because they may be risk factors for cardiovascular disease in children on PD. In a study that included 31 pediatric PD patients, 54.8% demonstrated glucose intolerance, 25.8% had impaired fasting glucose, 22.6% had impaired glucose tolerance, 6.5% were diagnosed with diabetes mellitus, and 9.7% had insulin resistance. There were no differences in these parameters when compared to hemodialysis patients [69]. There are currently no pediatric specific guidelines for the monitoring of glucose metabolism. Minimization of glucose in the PD prescription and the use of icodextrin for the long-dwell dialysis solution are strategies that can be implemented in children with glucose abnormalities.

Hypokalemia

As compared with pediatric patients on hemodialysis, patients on PD are at increased risk of hypokalemia because of the greater cumulative clearance of potassium by PD [72]. Also, enhanced cellular uptake of potassium, prompted by the intraperitoneal glucose load with subsequent insulin release, and bowel losses may also play a role in the hypokalemia observed in PD patients. Furthermore, cultural dietary preferences are likely to affect the disposition to hypokalemia on PD. Kt/V urea, the etiology of renal failure, age, the peritoneal membrane transport type, and oral protein and caloric intake appear not to be related to hypokalemia [73].

Hypokalemic patients complain of weakness more often than those with normal potassium levels. For stable chronic outpatients, liberalization of dietary potassium restriction and, when needed, oral potassium replacement (based upon individual patient serum potassium determinations) are usually successful treatments for hypokalemia.

Hypermagnesemia

Hypermagnesemia, a common finding in PD patients, is due to positive magnesium balance, resulting from renal failure and the relatively high dialysate magnesium concentration. The typical serum magnesium level in patients with ESKD is 2.4–3.6 mg/dL (1.0–1.5 mmol/L), a value usually not associated with clinical symptoms. Serum magnesium levels are usually elevated in those dialyzed against solutions containing magnesium concentrations of 0.75 mmol/L (1.8 mg/dL) [74]. Since there is an inverse relationship between concentrations of magnesium and intact parathyroid hormone

(PTH), raising the possibility that hypermagnesemia may contribute to adynamic bone disease [75], the 0.50 mmol/L (1.2 mg/dL) concentration dialysate may generally be preferable. Hypomagnesemia may develop in patients utilizing 0.25 mmol/L (0.6 mg/dL) magnesium concentration [74].

Other Complications

Hemoperitoneum

The presence of blood in PD effluent is called hemoperitoneum. This is a benign complication of chronic PD. Only a very small amount of bleeding is required to make dialysate appear bloody. As little as 1 mL of whole blood injected into 2 L of an effluent bag can make the fluid readily blood tinged, and injection of 7 mL of blood can make the entire volume as red as fruit juice.

Pathogenesis

Hemoperitoneum has a wide differential diagnosis. Blood tinging of dialysate is commonly seen after PD catheter placement, as a result of direct vascular and visceral damage. It rapidly clears with a few in-and-out exchanges. The most common and benign cause of hemoperitoneum in adolescent girls is menstruation. Two theories are proposed to explain its mechanism. First, endometrial tissue, if present in the peritoneum, will shed simultaneously with uterine endometrium. Secondly, shed endometrial tissue and blood moves out of the cervix through the fallopian tubes in a retrograde fashion. Peritoneal bleeding starts a few days before vaginal menstrual flow. Other causes of hemoperitoneum in adolescent girls are ovulation (with a typical mid-cycle timing of occurrence) and ruptured ovarian cysts.

Trauma (including strenuous exercising), procedures to the abdominal area, bleeding disorders, or anticoagulation therapy can also predispose to hemoperitoneum. Bleeding into a hepatic or renal cyst with rupture into the peritoneal cavity, acute and chronic pancreatitis, sclerosing peritonitis, and peritoneal calcification in patients with severe CKD-associated mineral-bone disorder are further, less frequent causes of hemoperitoneum [2].

Diagnosis

The extent of bleeding and associated symptoms are of primary importance in determining further evaluation. If bleeding is very mild, self-limited, and not associated with other symptoms, the patient may not require further evaluation. This is especially likely if the patient is menstruating. If the bleeding is severe, recurrent, and/or associated with pain and fever, urgent evaluation is required to exclude underlying intra-abdominal pathology, such as cyst rupture or a vascular catastrophe. Findings on physical examination such as a rebound or guarding do not occur with benign intraperitoneal bleeding and should be treated as a surgical emergency. In this setting, peritoneal fluid cell count, culture and sensitivity, and peritoneal amylase level (>50 μU/L suggests an intra-abdominal process) should be obtained. Peritoneal dialysate hematocrit >2% suggests an intraperitoneal pathology. All of the possible disorders in this setting are cause for great concern, and merit surgical consultation and consideration of early laparoscopy or laparotomy [2].

Abdominal imaging by CT, ultrasound, or MRI may also be indicated. A CT scan of the abdomen and pelvis should be performed if ultrasound is negative or inconclusive. In patients with persistent bleeding, isotope-labeled RBC scan can be done to localize the site of bleeding, which can then be selectively embolized. Contrast agents should be avoided in patients with preserved residual function. Angiography is the last option that may be required for more definitive diagnosis [2].

Management

Treatment of the underlying cause is essential, and curative management may require emergent evaluation and care. Menstruating adolescent girls should be reassured that asymptomatic hemoperitoneum is benign and that it will likely resolve spontaneously. Rapid flushes and instillation of heparin in the dialysate to prevent catheter clotting are usually done. Infusing cool dialysate

(i.e., room temperature) may also be helpful. Most commonly, the hemoperitoneum will clear after one to three rapid flushes. In severe conditions, extensive diagnostic studies and required surgical interventions should be done as indicated [2, 76].

Acute Pancreatitis

Acute pancreatitis (AP) is characterized by inflammation of the pancreas, which presents with acute onset of epigastric abdominal pain accompanied by epigastric tenderness on physical exam. The incidence rate of AP in children on PD was reported to be 6.2 per 1000 person-years in the Italian Registry of Pediatric Chronic Dialysis [77]. The risk of AP is higher in hemodialysis patients compared to PD, and patients on dialysis appear to be at a higher risk for AP than the general population.

Pathogenesis

Patients with ESKD may be at increased risk for AP due to the decreased catabolism of gastric hormones that may lead to hypersecretion of the pancreatic enzyme trypsin. Trypsin hypersecretion is thought to induce morphologic changes in the pancreas that could make the pancreas more susceptible to inflammation. In addition, it has been hypothesized – but not proven – that PD may directly contribute to the risk for AP. Dialysate fluid containing glucose and calcium may theoretically irritate the pancreas. Hyperglycemia, hypercalcemia, as well as hypertriglyceridemia are known causes of AP in the general population. Furthermore, it has been suggested that repeated episodes of peritonitis may release enzymes that irritate and cause inflammation of the pancreas.

Diagnosis

The diagnosis of AP may be difficult to distinguish from peritonitis in children on PD. Patients with AP present with an acute onset of severe epigastric abdominal pain. Pain will often radiate to the back, which may be relieved by sitting forward. AP is usually accompanied by nausea and vomiting. On physical examination, there is tenderness to palpation in the epigastric region or there may be diffuse abdominal tenderness. Abdominal distension and hypoactive bowel signs may be present due to underlying ileus. Patients with severe AP often present with fever, dyspnea, tachypnea, and hypotension.

Diagnostic criteria for AP include two of the following: (1) characteristic epigastric pain or pain radiating to the back, (2) elevated serum lipase or amylase to three times the upper limit of normal, or (3) radiographic evidence of AP by CT, MRI, or ultrasound. Reliance on serum pancreatic marker criteria may not be possible in children on PD, since amylase and lipase are often elevated above three times the upper limit in asymptomatic patients. The elevation in pancreatic enzymes is due to decreased urinary excretion and the minimal clearance of the enzymes by PD [78]. In children treated with icodextrin, amylase may be reduced due to the competitive inhibition by icodextrin on the amylase assay [79]. Therefore, radiologic studies may be required to aid in the diagnosis of AP. Focal or diffuse enlargement of the pancreas is suggestive of AP. Imaging may also be required later in the clinical course to evaluate for necrotizing pancreatitis and other complications.

Management

Treatment of AP is mainly supportive with recommendations for bowel rest, intravenous fluids or parenteral nutrition, and pain control. Prophylactic antibiotics can be considered for prevention/treatment of necrotizing pancreatitis. Continuation of PD during AP is often possible. Surgical treatment may be necessary in cases of necrotizing pancreatitis or pseudocyst.

Prognosis

Most episodes of AP are mild and most patients recover without complications or recurrence; however, AP can be severe with complications. Complications include pancreatic pseudocyst, necrosis, systemic inflammatory response syndrome, and organ failure. Mortality reported among adult dialysis patients varies from 8% to 58%. A culmination of 32 children on dialysis

from pediatric series reported in the literature demonstrated the prevalence of mortality to be 22% [77].

References

1. McCormick BB, Bargman JM. Noninfectious complications of peritoneal dialysis: implications for patient and technique survival. J Am Soc Nephrol. 2007;18:3023–5.
2. Saha TC, Singh H. Noninfectious complications of peritoneal dialysis. South Med J. 2007;100:54–8.
3. Kim JE, Park SJ, Oh JY, Kim JH, Lee JS, Kim PK, Shin JI. Noninfectious complications of peritoneal dialysis in Korean children: a 26-year single-center study. Yonsei Med J. 2015;56:1359–64.
4. Bakkaloglu SA, Ekim M, Tumer N, Soylu K. The effect of CAPD on the lipid profile of pediatric patients. Perit Dial Int. 2000;20:568–71.
5. Verrina E, Edefonti A, Gianoglio B, Rinaldi S, Sorino P, Zacchello G, Lavoratti G, Maringhini S, Pecoraro C, Calevo MG, Turrini Dertenois L, Perfumo F. A multicenter experience on patient and technique survival in children on chronic dialysis. Pediatr Nephrol. 2004;19:82–90.
6. Honda M. The 1997 report of the Japanese National Registry data on pediatric peritoneal dialysis patients. Perit Dial Int. 1999;19(Suppl 2):S473–8.
7. Vidal E, Edefonti A, Murer L, Gianoglio B, Maringhini S, Pecoraro C, Sorino P, Leozappa G, Lavoratti G, Ratsch IM, Chimenz R, Verrina E, Italian Registry of Paediatric Chronic Dialysis. Peritoneal dialysis in infants: the experience of the Italian Registry of Paediatric Chronic Dialysis. Nephrol Dial Transplant. 2012;27:388–95.
8. Rinaldi S, Sera F, Verrina E, Edefonti A, Gianoglio B, Perfumo F, Sorino P, Zacchello G, Cutaia I, Lavoratti G, Leozappa G, Pecoraro C, Rizzoni G, Italian Registry of Pediatric Chronic Peritoneal Dialysis. Chronic peritoneal dialysis catheters in children: a fifteen-year experience of the Italian Registry of Pediatric Chronic Peritoneal Dialysis. Perit Dial Int. 2004;24:481–6.
9. Borzych-Duzalka D, Aki TF, Azocar M, White C, Harvey E, Mir S, Adragna M, Serdaroglu E, Sinha R, Samaille C, Vanegas JJ, Kari J, Barbosa L, Bagga A, Galanti M, Yavascan O, Leozappa G, Szczepanska M, Vondrak K, Tse KC, Schaefer F, Warady BA, International Pediatric Peritoneal Dialysis Network Registry. Peritoneal dialysis access revision in children: causes, interventions, and outcomes. Clin J Am Soc Nephrol. 2017;12:105–12.
10. Aksu N, Yavascan O, Anil M, Kara OD, Erdogan H, Bal A. A ten-year single-centre experience in children on chronic peritoneal dialysis – significance of percutaneous placement of peritoneal dialysis catheters. Nephrol Dial Transplant. 2007;22:2045–51.
11. Bakkaloglu SA, Ekim M, Sever L, Noyan A, Aksu N, Akman S, Elhan AH, Yalcinkaya F, Oner A, Kara OD, Caliskan S, Anarat A, Dusunsel R, Donmez O, Guven AG, Bakkaloglu A, Denizmen Y, Soylemezoglu O, Ozcelik G. Chronic peritoneal dialysis in Turkish children: a multicenter study. Pediatr Nephrol. 2005;20:644–51.
12. Radtke J, Lemke A, Kemper MJ, Nashan B, Koch M. Surgical complications after peritoneal dialysis catheter implantation depend on children's weight. J Pediatr Surg. 2016;51:1317–20.
13. Carpenter JL, Fallon SC, Swartz SJ, Minifee PK, Cass DL, Nuchtern JG, Pimpalwar AP, Brandt ML. Outcomes after peritoneal dialysis catheter placement. J Pediatr Surg. 2016;51:730–3.
14. LaPlant MB, Saltzman DA, Segura BJ, Acton RD, Feltis BA, Hess DJ. Peritoneal dialysis catheter placement, outcomes and complications. Pediatr Surg Int. 2018;34:1239–44.
15. Radtke J, Schild R, Reismann M, Ridwelski RR, Kempf C, Nashan B, Rothe K, Koch M. Obstruction of peritoneal dialysis catheter is associated with catheter type and independent of omentectomy: a comparative data analysis from a transplant surgical and a pediatric surgical department. J Pediatr Surg. 2018;53:640–3.
16. Phan J, Stanford S, Zaritsky JJ, DeUgarte DA. Risk factors for morbidity and mortality in pediatric patients with peritoneal dialysis catheters. J Pediatr Surg. 2013;48:197–202.
17. Hagen SM, Lafranca JA, IJzermans JN, Dor FJ. A systematic review and meta-analysis of the influence of peritoneal dialysis catheter type on complication rate and catheter survival. Kidney Int. 2014;85:920–32.
18. Imani PD, Carpenter JL, Bell CS, Brandt ML, Braun MC, Swartz SJ. Peritoneal dialysis catheter outcomes in infants initiating peritoneal dialysis for end-stage renal disease. BMC Nephrol. 2018;19:231.
19. Ladd AP, Breckler FD, Novotny NM. Impact of primary omentectomy on longevity of peritoneal dialysis catheters in children. Am J Surg. 2011;201:401–4; discussion 404–405.
20. Nikibakhsh AA, Mahmoodzadeh H, Vali M, Enashaei A, Asem A, Yekta Z. Outcome of immediate use of the permanent peritoneal dialysis catheter in children with acute and chronic renal failure. Iran J Pediatr. 2013;23:171–6.
21. Zhang Q, Jiang C, Zhu W, Sun C, Xia Y, Tang T, Wan C, Shao Q, Liu J, Jin B, Zhang M. Peritoneal catheter fixation combined with straight upward tunnel and low implant position to prevent catheter malfunction. Nephrology (Carlton). 2018;23:247–52.
22. Stringel G, McBride W, Weiss R. Laparoscopic placement of peritoneal dialysis catheters in children. J Pediatr Surg. 2008;43:857–60.
23. Chen Y, Shao Y, Xu J. The survival and complication rates of laparoscopic versus open catheter placement in peritoneal dialysis patients: a meta-analysis. Surg Laparosc Endosc Percutan Tech. 2015;25:440–3.

24. Xie H, Zhang W, Cheng J, He Q. Laparoscopic versus open catheter placement in peritoneal dialysis patients: a systematic review and meta-analysis. BMC Nephrol. 2012;13:69.
25. Strippoli GF, Tong A, Johnson D, Schena FP, Craig JC. Catheter type, placement and insertion techniques for preventing peritonitis in peritoneal dialysis patients. Cochrane Database Syst Rev. 2004;(4):CD004680.
26. van Laanen JHH, Cornelis T, Mees BM, Litjens EJ, van Loon MM, Tordoir JHM, Peppelenbosch AG. Randomized controlled trial comparing open versus laparoscopic placement of a peritoneal dialysis catheter and outcomes: the CAPD I trial. Perit Dial Int. 2018;38:104–12.
27. Crabtree JH, Fishman A. A laparoscopic method for optimal peritoneal dialysis access. Am Surg. 2005;71:135–43.
28. Hu JC, Chiu KY, Wang SS, Chen CS, Ho HC, Yang CK, Chen CC, Wang SC, Lin CY, Hung SC, Cheng CL, Li JR. A modified application of peritoneal dialysis catheter implantation: a revolution from the laparoscope- to the nephroscope-assisted surgery. J Endourol. 2018;32:502–8.
29. Rahim KA, Seidel K, McDonald RA. Risk factors for catheter-related complications in pediatric peritoneal dialysis. Pediatr Nephrol. 2004;19:1021–8.
30. Donmez O, Durmaz O, Ediz B, Cigerdelen N, Kocak S. Catheter-related complications in children on chronic peritoneal dialysis. Adv Perit Dial. 2005;21:200–3.
31. Macchini F, Valade A, Ardissino G, Testa S, Edefonti A, Torricelli M, Luzzani S. Chronic peritoneal dialysis in children: catheter related complications. A single centre experience. Pediatr Surg Int. 2006;22:524–8.
32. Ozyer U, Harman A, Aytekin C, Boyvat F, Ozdemir N. Correction of displaced peritoneal dialysis catheters with an angular stiff rod. Acta Radiol. 2009;50:139–43.
33. Ratajczak A, Lange-Ratajczak M, Bobkiewicz A, Studniarek A. Surgical management of complications with peritoneal dialysis. Semin Dial. 2017;30:63–8.
34. Zorzanello MM, Fleming WJ, Prowant BE. Use of tissue plasminogen activator in peritoneal dialysis catheters: a literature review and one center's experience. Nephrol Nurs J. 2004;31:534–7.
35. Krishnan RG, Moghal NE. Tissue plasminogen activator for blocked peritoneal dialysis catheters. Pediatr Nephrol. 2006;21:300.
36. Sakarcan A, Stallworth JR. Tissue plasminogen activator for occluded peritoneal dialysis catheter. Pediatr Nephrol. 2002;17:155–6.
37. Leblanc M, Ouimet D, Pichette V. Dialysate leaks in peritoneal dialysis. Semin Dial. 2001;14:50–4.
38. Hooman N, Esfahani ST, Mohkam M, Derakhshan A, Gheissari A, Vazirian S, Mortazavi F, Ghane-Sherbaff F, Falak-Aflaki B, Otoukesh H, Madani A, Sharifian-Dorcheh M, Mahdavi A, Esmaeile M, Naseri M, Azhir A, Merikhi A, Mohseni P, Ataei N, Fallahzadeh MH, Basiratnia M, Hosseini-Al-Hashemi G. The outcome of Iranian children on continuous ambulatory peritoneal dialysis: the first report of Iranian National Registry. Arch Iran Med. 2009;12:24–8.
39. Sojo ET, Grosman MD, Monteverde ML, Bailez MM, Delgado N. Fibrin glue is useful in preventing early dialysate leakage in children on chronic peritoneal dialysis. Perit Dial Int. 2004;24:186–90.
40. Aranda RA, Romao Junior JE, Kakehashi E, Domingos W, Sabbaga E, Marcondes M, Abensur H. Intraperitoneal pressure and hernias in children on peritoneal dialysis. Pediatr Nephrol. 2000;14:22–4.
41. Fischbach M, Warady BA. Peritoneal dialysis prescription in children: bedside principles for optimal practice. Pediatr Nephrol. 2009;24:1633–42; quiz 1640, 1642.
42. Jander A, Nowicki M, Tkaczyk M, Makulska I, Zwolinska D, Latoszynska J, Boguszewska-Baczkowska A, Grenda R, Balasz-Chmielewska I, Zagozdzon I, Zaluska-Lesniewska I, Zurowska A, Stefaniak E, Zachwieja J, Leszczynska B, Roszkowska-Blaim M, Zachwieja K, Pietrzyk JA, Wiercinski R, Zoch-Zwierz W, Stankiewicz R. Chronic peritoneal dialysis in infants – preliminary results of the multicenter survey. Przegl Lek. 2006;63(Suppl 3):72–4.
43. Tom CM, Dubina ED, Simms ER, de Virgilio C, Moazzez A. Outcomes of combined hernia repair and peritoneal dialysis catheter placement: a NSQIP analysis. Am Surg. 2018;84:1604–7.
44. Bargman JM. Complications of peritoneal dialysis related to increased intraabdominal pressure. Kidney Int Suppl. 1993;40:S75–80.
45. Schmitt CP, Zaloszyc A, Schaefer B, Fischbach M. Peritoneal dialysis tailored to pediatric needs. Int J Nephrol. 2011;2011:940267.
46. Bakkaloglu SA, Ekim M, Tumer N, Gungor A, Yilmaz S. Pleurodesis treatment with tetracycline in peritoneal dialysis-complicated hydrothorax. Pediatr Nephrol. 1999;13:637–8.
47. Borzych D, Ley S, Schaefer F, Billing H, Ley-Zaporozhan J, Schenk J, Schmitt CP. Dialysate leakage into pericardium in an infant on long-term peritoneal dialysis. Pediatr Nephrol. 2008;23:335–8.
48. Camilleri B, Glancey G, Pledger D, Williams P. The icodextrin black line sign to confirm a pleural leak in a patient on peritoneal dialysis. Perit Dial Int. 2004;24:197.
49. Szeto CC, Chow KM. Pathogenesis and management of hydrothorax complicating peritoneal dialysis. Curr Opin Pulm Med. 2004;10:315–9.
50. Kim YL. Update on mechanisms of ultrafiltration failure. Perit Dial Int. 2009;29(Suppl 2):S123–7.
51. Raby AC, Gonzalez-Mateo GT, Williams A, Topley N, Fraser D, Lopez-Cabrera M, Labeta MO. Targeting Toll-like receptors with soluble Toll-like receptor 2 prevents peritoneal dialysis solution-induced fibrosis. Kidney Int. 2018;94:346–62.
52. Chung SH, Heimburger O, Lindholm B. Poor outcomes for fast transporters on PD: the rise and fall of a clinical concern. Semin Dial. 2008;21:7–10.

53. Saxena R. Pathogenesis and treatment of peritoneal membrane failure. Pediatr Nephrol. 2008;23:695–703.
54. Schaefer F, Klaus G, Mehls O. Peritoneal transport properties and dialysis dose affect growth and nutritional status in children on chronic peritoneal dialysis. Mid-European Pediatric Peritoneal Dialysis Study Group. J Am Soc Nephrol. 1999;10:1786–92.
55. Canepa A, Verrina E, Perfumo F. Use of new peritoneal dialysis solutions in children. Kidney Int Suppl. 2008;(108):S137–44.
56. Michallat AC, Dheu C, Loichot C, Danner S, Fischbach M. Long daytime exchange in children on continuous cycling peritoneal dialysis: preservation of drained volume because of icodextrin use. Adv Perit Dial. 2005;21:195–9.
57. Htay H, Johnson DW, Wiggins KJ, Badve SV, Craig JC, Strippoli GF, Cho Y. Biocompatible dialysis fluids for peritoneal dialysis. Cochrane Database Syst Rev. 2018;10:CD007554.
58. Honda M, Warady BA. Long-term peritoneal dialysis and encapsulating peritoneal sclerosis in children. Pediatr Nephrol. 2010;25:75–81.
59. Stefanidis CJ, Shroff R. Encapsulating peritoneal sclerosis in children. Pediatr Nephrol. 2014;29:2093–103.
60. Brown EA, Bargman J, van Biesen W, Chang MY, Finkelstein FO, Hurst H, Johnson DW, Kawanishi H, Lambie M, de Moraes TP, Morelle J, Woodrow G. Length of time on peritoneal dialysis and encapsulating peritoneal sclerosis – position paper for ISPD: 2017 update. Perit Dial Int. 2017;37:362–74.
61. Vidal E, Edefonti A, Puteo F, Chimenz R, Gianoglio B, Lavoratti G, Leozappa G, Maringhini S, Mencarelli F, Pecoraro C, Ratsch IM, Cannavo R, De Palo T, Testa S, Murer L, Verrina E, Italian Registry of Pediatric Chronic Dialysis. Encapsulating peritoneal sclerosis in paediatric peritoneal dialysis patients: the experience of the Italian Registry of Pediatric Chronic Dialysis. Nephrol Dial Transplant. 2013;28:1603–9.
62. Hoshii S, Honda M. High incidence of encapsulating peritoneal sclerosis in pediatric patients on peritoneal dialysis longer than 10 years. Perit Dial Int. 2002;22:730–1.
63. Shroff R, Stefanidis CJ, Askiti V, Edefonti A, Testa S, Ekim M, Kavaz A, Ariceta G, Bakkaloglu S, Fischbach M, Klaus G, Zurowska A, Holtta T, Jankauskiene A, Vondrak K, Vande Walle J, Schmitt CP, Watson AR, European Paediatric Dialysis Working Group. Encapsulating peritoneal sclerosis in children on chronic PD: a survey from the European Paediatric Dialysis Working Group. Nephrol Dial Transplant. 2013;28:1908–14.
64. Ekim M, Fitoz S, Yagmurlu A, Ensari A, Yuksel S, Acar B, Ozcakar ZB, Kendirli T, Bingoler B, Yalcinkaya F. Encapsulating peritoneal sclerosis in paediatric peritoneal dialysis patients. Nephrology (Carlton). 2005;10:341–3.
65. Kawaguchi Y, Saito A, Kawanishi H, Nakayama M, Miyazaki M, Nakamoto H, Tranaeus A. Recommendations on the management of encapsulating peritoneal sclerosis in Japan, 2005: diagnosis, predictive markers, treatment, and preventive measures. Perit Dial Int. 2005;25(Suppl 4):S83–95.
66. Bakkaloglu SA, Saygili A, Sever L, Noyan A, Akman S, Ekim M, Aksu N, Doganay B, Yildiz N, Duzova A, Soylu A, Alpay H, Sonmez F, Civilibal M, Erdem S, Kardelen F. Assessment of cardiovascular risk in paediatric peritoneal dialysis patients: a Turkish Pediatric Peritoneal Dialysis Study Group (TUPEPD) report. Nephrol Dial Transplant. 2009;24:3525–32.
67. Bonthuis M, van Stralen KJ, Jager KJ, Baiko S, Jahnukainen T, Laube GF, Podracka L, Seeman T, Tyerman K, Ulinski T, Groothoff JW, Schaefer F, Verrina E. Dyslipidaemia in children on renal replacement therapy. Nephrol Dial Transplant. 2014;29:594–603.
68. Buyan N, Bideci A, Ozkaya O, Ortac E, Bakkaloglu S, Gonen S, Peru H, Soylemezoglu O, Cinaz P. Leptin and resistin levels and their relationships with glucose metabolism in children with chronic renal insufficiency and undergoing dialysis. Nephrology (Carlton). 2006;11:192–6.
69. Canpolat N, Caliskan S, Sever L, Guzeltas A, Kantarci F, Candan C, Civilibal M, Kasapcopur O, Arisoy N. Glucose intolerance: is it a risk factor for cardiovascular disease in children with chronic kidney disease? Pediatr Nephrol. 2012;27:627–35.
70. KDIGO. KDIGO clinical practice guideline for lipid management in chronic kidney disease. Kidney Int Suppl. 2013;3(3):259.
71. Kavey RE, Allada V, Daniels SR, Hayman LL, McCrindle BW, Newburger JW, Parekh RS, Steinberger J, American Heart Association Expert Panel on Population and Prevention Science; the Councils on Cardiovascular Disease in the Young, Epidemiology and Prevention, Nutrition, Physical Activity and Metabolism, High Blood Pressure Research, Cardiovascular Nursing, and the Kidney in Heart Disease; and the Interdisciplinary Working Group on Quality of Care and Outcomes Research. Cardiovascular risk reduction in high-risk pediatric patients: a scientific statement from the American Heart Association Expert Panel on Population and Prevention Science; the Councils on Cardiovascular Disease in the Young, Epidemiology and Prevention, Nutrition, Physical Activity and Metabolism, High Blood Pressure Research, Cardiovascular Nursing, and the Kidney in Heart Disease; and the Interdisciplinary Working Group on Quality of Care and Outcomes Research. J Cardiovasc Nurs. 2007;22:218–53.
72. Factor KF. Potassium management in pediatric peritoneal dialysis patients: can a diet with increased potassium maintain a normal serum potassium without a potassium supplement? Adv Perit Dial. 2007;23:167–9.
73. Khan AN, Bernardini J, Johnston JR, Piraino B. Hypokalemia in peritoneal dialysis patients. Perit Dial Int. 1996;16:652.
74. Hutchinson AJ. Serum magnesium and end-stage renal disease. Perit Dial Int. 1997;17:327–9.

75. Wei M, Esbaei K, Bargman JM, Oreopoulos DG. Inverse correlation between serum magnesium and parathyroid hormone in peritoneal dialysis patients: a contributing factor to adynamic bone disease? Int Urol Nephrol. 2006;38:317–22.
76. Greenberg A, Bernardini J, Piraino BM, Johnston JR, Perlmutter JA. Hemoperitoneum complicating chronic peritoneal dialysis: single-center experience and literature review. Am J Kidney Dis. 1992;19:252–6.
77. Vidal E, Alberici I, Verrina E, Italian Registry of Pediatric Chronic Dialysis. Acute pancreatitis in children on chronic maintenance dialysis. Pediatr Nephrol. 2019;34(9):1501–12.
78. Bastani B, Mifflin TE, Lovell MA, Westervelt FB, Bruns DE. Serum amylases in chronic and end-stage renal failure: effects of mode of therapy, race, diabetes and peritonitis. Am J Nephrol. 1987;7:292–9.
79. Wang R, Leesch V, Turner P, Moberly JB, Martis L. Kinetic analysis of icodextrin interference with serum amylase assays. Adv Perit Dial. 2002;18:96–9.