Complications of Peritoneal Dialysis and How to Avoid Them

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Outcomes are at least equal, if not better, for patients on peritoneal compared with haemodialysis [1] – however, most of the data is from registries, with only one randomised controlled trial comparing the modalities which was underpowered [2]. A whole range of factors influence the comparison including comorbidity, age, residual renal function, late presentation and the access used for HD. Commonly undue emphasis is placed on the risk that patients on peritoneal dialysis face, without due recognition of the potential complications associated with HD, infection presenting as much a risk for patients on PD as on patients on HD. Although peritonitis is a concern for patients on PD, bacteraemia is rare and hospitalisation for infection is similar between the modalities [3]. When it comes to access, a very important issue, there is an appreciation of the difficulties that can occur when PD catheters do not work properly, but the burden to the average patient is no greater than that experienced by HD patients requiring revision of their vascular access. The spectre that is commonly raised is that of encapsulating peritoneal sclerosis – clearly a dreaded potential complication of PD and deservedly the focus of considerable research attention. However, this is exceptionally rare in the early years of PD and is not as significant a risk factor as the major causes of adverse outcome that affect our patients.

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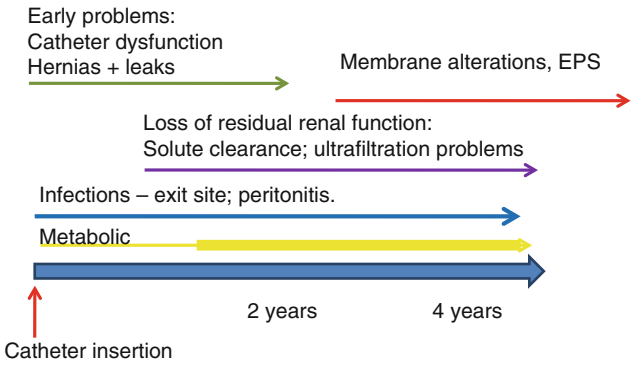


Fig. 64.1 A graphic demonstration of the timeline of PD-related complications

In general, effective management of PD requires careful practice patterns underpinned by regular audit, and in this area there is much work to do. Low infection rates are possible through a careful multidisciplinary team-based approach, which for optimal care should be combined with regular review of patient progress, prescription management and planned transfer to HD if this becomes necessary. For many patients PD is an excellent therapy in which they can be the master of their own care and remain independent from hospital. The likelihood of a particular peritoneal dialysis-related complication is influenced to some extent by the time that the patient has been on PD, and a schema is presented in Fig. 64.1. Patients discontinue peritoneal dialysis for a range of reasons including infection, social reasons and problems with ultrafiltration and clearance [4] (Fig. 64.2).

Peritoneal Dialysis-Associated Infection

Prevention of PD-Associated Infection

In the early days of peritoneal dialysis, infection was a common and difficult problem with peritonitis occurring every few months. Considerable attention has been given to this

complication with the result being a marked improvement. Over the last three decades, technical developments have included the change from glass bottles to plastic bags, improved systems (with the disconnect system and flush before fill) and more recently the use of prophylactic antibacterial creams at the exit site. Emphasis has been placed on the importance of training for staff, patients and carers and the role of audit to understand infection rates and causative organisms (Fig. 64.3). There is evidence that the degree of nursing experience and patient training methods influence

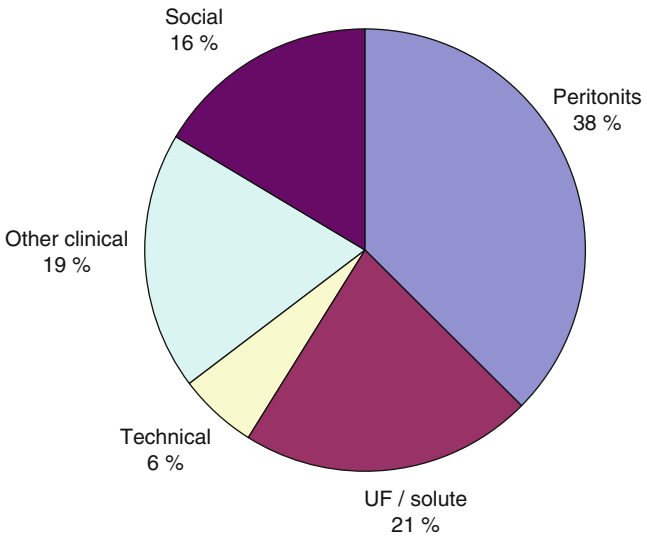
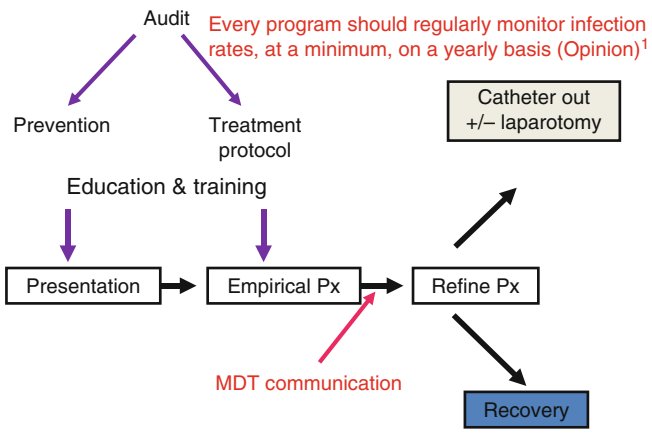


Fig. 64.2 Causes of discontinuation of peritoneal dialysis (Created using data obtained from Verger et al. [4])



[1] ISPD 2010 peritoneal related infection guidelines doc

Fig. 64.3 A schema describing optimal prevention and management of PD peritonitis

Table 64.1 Methods for reducing the risk of PD peritonitis

Catheter-related interventions
Double-cuffed catheter
Careful catheter insertion protocols as outlined in the ISPD guidance [7]
Systems
Flush-before-fill technology
Avoiding spike systems
Antibiotic prophylaxis
Before catheter insertion
As part of exit site care
Before interventional procedures – e.g. colonoscopy
Training
Careful training and directed retraining for patients and staff
Clear points of contact for patients, carers and staff
Clear protocols for the management of PD-related infection and contamination events that are accessible and easily understood
Review
Regular audit or continuous quality improvement (at least annually) to be presented at unit meetings
Regular multidisciplinary team meetings to review patient care, developing problems and practice development requirements
Regular update of unit protocols in the light of new developments or data presented from the audit meetings

the risk of PD infections which should be based on the principles of adult education. Refresher courses are recommended 3 months after initial training and routinely thereafter at a minimum of once a year as well as following hospitalisation, episodes of peritonitis and catheter infection or if there is a change in dexterity, vision or mental acuity. Examples of training programmes are available at www.ispd.org.

Table 64.1 summarises the multidisciplinary team-based initiatives that have an impact on preventing peritoneal dialysis-associated infection. The best centres have peritonitis rates that are less than 1 per 36 patient month on treatment, and, for example, data from the French registry showed that half of the patients did not experience this complication in 31 months [5]. There are many publications on PD-associated infection, but few randomised controlled trials. The best resources are the guidelines from the International Society of Peritoneal Dialysis [6] which are free to download from www.ispd.org.

An important part of infection prevention relates to the procedures for catheter placement and techniques focussed on the prevention of exit site infection. Catheter placement should be governed by clear protocols [7] with the exit site being located preoperatively and placed in a suitable position. Recommendations regarding post-operative management of

Table 64.2 Strategies to prevent exit site infection (ISPD guideline)

Dressings should be done by a trained dialysis nurse using sterile technique until the exit site is healed
If possible do not remove dressing for 5 days post-insertion
The exit site should be kept dry until well healed – thus avoid baths and showers for this period
Once the exit site is well healed, the patient should be taught how to perform exit site care – antibacterial soap and water or an antiseptic wash are acceptable; scabs should not be picked off!
The catheter should be kept immobile to avoid to prevent pulling and trauma to the exit site
If possible avoid using the catheter until healed

Table 64.3 Causes of culture negative peritonitis

In appropriate sampling or culture technique
Presence of antibiotics – e.g. treatment for an exit site infection
Presence of fastidious organisms, e.g. fungi or mycobacterium tuberculosis
Chemical or allergic peritonitis, e.g. due to antibiotic allergy
Intra-abdominal disease – e.g. carcinoma or lymphoma

the PD catheter in order to minimise the risk of exist site infection are summarised in Table 64.2. There is good evidence for the value of the preventative use of antibiotic creams at the exit site with meta-analysis showing benefit for mupirocin use on both exit site infection and peritonitis rates [8].

PD Peritonitis

PD peritonitis is the leading cause of technique failure, confers an increased mortality risk and if severe and prolonged can be associated with peritoneal membrane damage. It is diagnosed by the presence of abdominal pain and cloudy dialysate effluent that has a leucocyte count of greater than 100/mm^3. In APD the larger drain bag may result in a lower cell count – therefore a differential count of >50 % neutrophils is considered diagnostic. It is possible to overlook the diagnosis of peritonitis in APD patients if the effluent line runs straight to a drain without collecting in a bag, and leucocyte esterase sticks are sometimes used by patients to test the effluent dialysate. Patients presenting with peritonitis range from the mildly unwell, who can be managed easily as an outpatient, to those with marked features of systemic sepsis requiring admission to hospital. The principal sources of contamination include a break in the sterile technique and infection at the exit site – others are organisms within the catheter biofilm, transmural migration of organisms across the bowel wall and rarely haematogenous spread or vaginal leak.

Root cause analysis should be performed after every episode of peritonitis to understand modifiable risk factors as much as possible and plan an intervention strategy. There are a number of potentially modifiable risk factors associated with PD peritonitis including depression, hypoalbuminaemia, hypokalemia, constipation, exit site colonisation, infection, connection methodology, technique errors, prolonged antibiotics and medical procedures.

It is important that peritonitis is diagnosed promptly so that appropriate treatment can be started immediately, and therefore the patient and their carers require clear contact details of the unit. The health-care team should be experienced in the diagnosis and management of peritonitis, supported by evidence-based protocols. Presentation to the incorrect hospital department can potentially lead to misdiagnosis and inappropriate management. A suitable technique for dialysate sampling is required in order to maximise the opportunity for identifying the causative organism. The recommended approach to dialysate sampling is either the inoculation of blood culture bottles or centrifugation of 50 mL of peritoneal effluent at 3,000 g for 15 min, followed by resuspension of the sediment in 3–5 mL of sterile saline and inoculation of this material both on solid culture media and into a standard blood culture medium. With this method, less than 5 % will be culture negative [6].

The differential diagnosis of cloudy dialysate fluid includes noninfectious causes such as chemical and allergic peritonitis, haemoperitoneum, malignancy and chylous effluent. A dialysate sample should ideally be taken after a 2-h dwell, and samples taken from a "dry" abdomen can give a spuriously elevated WCC.

Inability to identify the causative organism has implications for primary cure rates with most studies showing poorer outcomes where the organism has not been identified. Causes of sterile peritonitis include poor dialysate sampling and culture techniques, as well as recent courses of antibiotics – for example, for the treatment of an exit site infection (Table 64.3). It is important to have a low threshold for the possibility of surgical peritonitis in a PD patient which can pose diagnostic and therapeutic challenges and may occur in 10 % of cases, resulting from inflammation, perforation or ischaemia of intra-abdominal organs. There are several possible pitfalls in the diagnosis of surgical peritonitis including the innocent finding of air under the diaphragm patients on PD, the possibility that serum amylase may be spuriously low in patients on icodextrin and poor diagnostic sensitivity

of CT scanning. Delays in institution of appropriate treatment, particularly surgical intervention, leads to increased morbidity and mortality [9].

The nature of organisms causing PD peritonitis has changed over the last three decades. Whereas gram-positive organisms were the commonest, their relative frequency has been reduced by improvements in technology and technique as demonstrated by a 25-year single-centre experience from Brazil [10]. As a result, patients presenting with PD peritonitis are more likely than previously to have gram-negative infections, which needs to be considered when designing treatment protocols. It is important that individual centres examine their own patterns of infection, causative organisms and sensitivities and adapt protocols as necessary for local conditions.

Treatment of PD Peritonitis

The ideal antibiotic should give broad coverage of organisms, avoid disturbing normal bacterial flora, have a low side effect profile, not provoke the emergence of resistant organisms and be convenient to administer and cheap. This will be influenced by the pharmacokinetic and pharmacodynamic profile as well as the potential side effects of particular antibiotics [11]. A number of factors have influenced this choice, including the emergence of vancomycin-resistant enterococci, reports of vancomycin intermediately sensitive *S. aureus*, the emergence of methicillin resistance and extended spectrum beta-lactamase-producing enterobacteriaceae (ESBLs) as well as the concern regarding the impact of aminoglycosides on residual renal function.

Initial empirical treatment for PD peritonitis should cover both gram-positive and gram-negative organisms and be governed by an understanding of local organisms and their sensitivities. The International Society of Peritoneal Dialysis (ISPD) infection guidelines recommend possible antibiotic schedules including either the combination of a third-generation cephalosporin (ceftazidime) or an aminoglycoside for gram-negative cover with a first-generation cephalosporin (cephazolin) or vancomycin for gram-positive cover. A systematic review did not identify superior antibiotic regimens [12]. There are potential hazards with all antibiotics, and it is important to liaise with the local microbiological team regarding the most appropriate protocol. Treatment should be adjusted once the organism has been identified, and for detailed discussion the reader should access the ISPD infection guidelines at www.ispd.org. Emphasis should be on preservation of the peritoneal membrane and the patient rather than persisting with PD when the infection is not responding to treatment. Guidelines recommend catheter removal if the patient does not respond with 5 days of treatment (Table 64.4); however, there should be a low threshold to remove the catheter earlier than this if the patient is significantly unwell. Vancomycin and aminoglycoside doses require adjustment based on antibiotic levels due to complex pharmacodynamics which are influenced by a range of factors including patient size, dialysate flow rates, peritoneal membrane characteristics, the molecular weight of the antibiotic, degree of residual renal function, whether the patient is on CAPD or APD and whether it is administered continuously or intermittently [13].

Table 64.4 Indications for PD catheter removal for peritoneal dialysis-associated infections

Refractory peritonitis (persisting for more than 5 days despite appropriate therapy)
Peritonitis associated with tunnel infections
Some cases of chronic exit site or tunnel infection
Certain organisms – fungal infections or the combination of an exit site infection with peritonitis due to *Staphylococcus aureus* or *Pseudomonas aeruginosa*
Polymicrobial peritonitis or other significant intra-abdominal pathology
Continually relapsing peritonitis with no obvious cause

Adapted from Ref. [6]

Exit Site Infection (ESI)

The importance of ESI is that it is a risk factor for PD peritonitis. If the exit site becomes infected, eradication may be difficult and require prolonged courses of antibiotics, therefore strategies to reduce the risk of this complication are essential. These start before the catheter is placed with a careful discussion with the patient regarding the location of the exit site, catheter placement protocols to minimise the risk of infection, and a rigorous approach to post-operative exit site care. In recent years exit site prophylaxis with antibacterial creams has been demonstrated to have an impact on both exit site and peritonitis rates, in particular with gram-positive organisms [8]. A positive nose swab for *Staphylococcus aureus* is associated with an increased likelihood of developing exit site infection.

Although purulent drainage from the exit site indicates the presence of infection, erythema is not specific. The identification of an organism in the absence of inflammation indicates colonisation and does not require treatment. An exit site scoring system recommended by the ISPD is based on the presence of swelling, redness, pain and discharge [14] (Fig. 64.4).

Treatment of an infected exit site requires appropriate antibiotics based on swab results, and a prolonged course of antibiotics may be necessary. Infecting organisms are most commonly *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Pseudomonas aeruginosa* and *Escherichia coli*. For chronic exit site infections, a combination of synergistic antibiotics is preferred to avoid the development of resistance. Response may be slow, appearances may change only gradually and de-roofing of the tunnel with exteriorisation or shaving of the cuff may be required. A variety of topical agents have been recommended for exit site care; however,

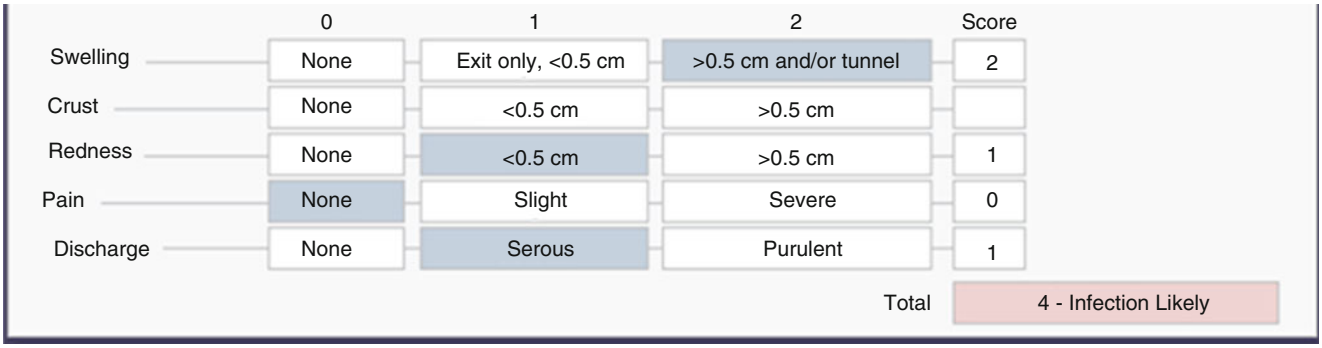


Fig. 64.4 Exit site scoring using the ISPD recommended system [14]

care should be taken not to use agents that are potentially damaging to the skin. A tunnel infection may present as exit site discharge, erythema, oedema or tenderness over the subcutaneous pathway but is often clinically occult. *Staphylococcus aureus* and *Pseudomonas aeruginosa* exit site infections are very often associated with concomitant tunnel infections and are the organisms that most often result in catheter infection-related peritonitis; aggressive management is always indicated for these organisms. Ultrasound examination of the tunnel can assist diagnosis. Catheter removal is required in non-responding tunnel infections.

Audit Standards for PD-Related Infection

These are summarised in UK Renal Association standards document (www.renal.org) which details annual audits of infection and prevention strategies. The key points are peritonitis rates of less than 1 episode per 18 months in adults and 12 months in children, a primary cure rate of ≥80 % and a culture negative rate of <20 %.

Peritoneal Access-Related Problems

An adequately functioning peritoneal dialysis catheter is essential for successful PD, and when the catheter does not work adequately, this can lead to considerable heartache for patients and staff as well as increased costs to the health-care system. Although it might appear that PD catheters are frequently causing problems and requiring replacement or repositioning, it is relevant to note that vascular access causes at least as much of a problem for patients on HD [15]. Regular audit of primary catheter function and the main complications is essential to ensure that high standards are maintained. There are many papers describing single-centre experiences of catheter placement techniques; however, many of these are confounded by patient selection and publication bias. The publications of John Crabtree give a rigorous discussion of the topic and conclude that the laparoscopic approach in the best hands probably has the best success rate [16]. However, this is by no means essential and each approach has its protagonist. The medical Seldinger technique performed under local anaesthetic has the advantage of being mastered by nephrologist or specialist nurse, giving the control of catheter placement to the medical team. On the other hand, for services that have a team of renal transplant surgeons, the open surgical approach is favoured for logistical reasons. It is important that there is a team-based approach, that the service is responsive and it is essential that there is good access to surgical support when required.

Common Catheter-Related Complications

The main complication of PD catheters is dysfunction. Since a PD catheter requires a flow of up to 150 mL/min, it is necessary that the side holes are not obstructed and that the tip is well placed in the sump of the pelvis where the residual dialysate will be retained. If the tip is not appropriately placed, this will result in a large residual volume resulting in reduced clearance, reduced ultrafiltration, increased intra-abdominal pressure and associated complications. It is important to remember that APD is more demanding on catheter function than CAPD with poor flows resulting in drainage alarms on the machine. This can be managed to some extent by the use of a tidal prescription (where a small amount of fluid is left in the peritoneal cavity at the end of a dwell); however, if it results in problems with clearance or ultrafiltration, the catheter may need to be repositioned or replaced. Good early catheter function is essential if PD is to be used as treatment for late-presenting patients.

Catheter dysfunction has several common causes including catheter migration which can be diagnosed by a plain abdominal film (Fig. 64.5). Faecal loading is commonly cited as a cause and often treated with beneficial results. Interestingly HD patients may have slower bowel transit times than PD patients; however, bowel function is given priority in PD patients since faecal loading can have an impact on catheter function. Adequate bowel preparation is an essential part of the catheter insertion protocol. An uncommon cause of catheter dysfunction is the omental wrap which

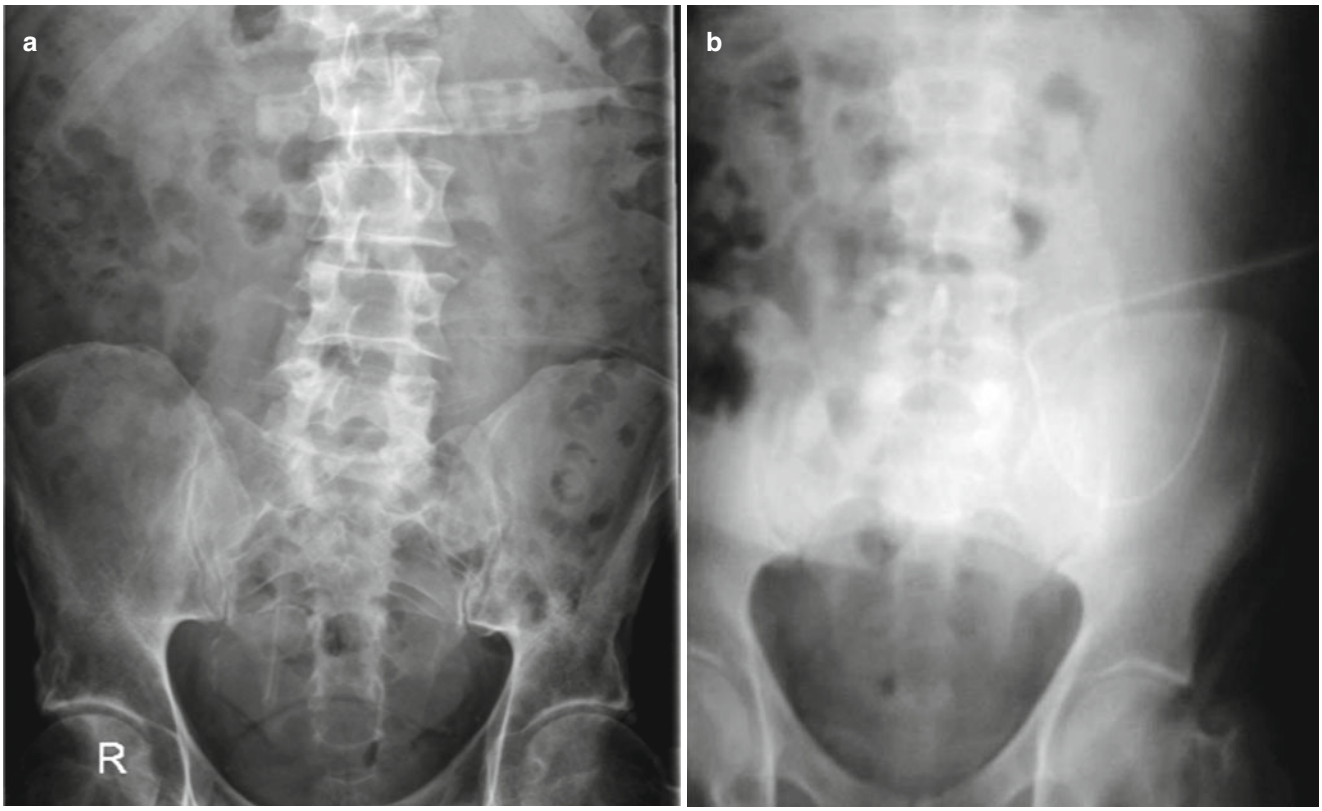


Fig. 64.5 Plain abdominal X-rays demonstrating the PD catheter located in the pelvis (**a**) demonstrating a PD catheter where the tip has migrated out of the pelvis (**b**)

can be diagnosed and treated by laparoscopy. Catheter obstruction may result from fibrin or blood clots which can be resolved by the use of a urokinase lock into the catheter. Of course, catheter dysfunction is not easy to define, being described in practice more by the impact on the patient or nursing staff rather than objective measurements of flow. The most objective measure of the success of catheter placement is whether the patient is using it for their treatment at 1-year post-insertion censored for death, transplantation and other causes of elective transfer from PD.

Patients may complain of pain on inflow or drainage of PD fluid. This may be due to the irritant effect of acidic dialysate, a consequence of negative pressure (suction) particularly in APD or a mechanical consequence of tube position. Techniques available to manage these issues include the use of tidal PD, and it is possible to use the machine software to identify dialysate flow profiles and optimise the tidal prescription. The use of more biocompatible neutral pH dialysates may ameliorate inflow pain possibly due to less chemical irritation of the membrane resulting in reduced stimulation of nociceptors. The position of the tube in the pelvis can lead to mechanical irritation which may be resolved by tube repositioning. If such problems are not resolved promptly, some patients may be discouraged from persisting with PD.

Audit Standards for Catheter Placement

The minimisation of catheter-related complications requires care and attention from the operator in the context of a consistent team-based approach supported by clear guidelines and protocols [7]. These describe the conditions necessary for optimal catheter function with minimisation of complications. The only registry that reports primary catheter function is the French-speaking registry, and this gives really excellent catheter function data [5]. However, in reality, many centres describe results that are considerably lower. The ISPD audit standards for catheter placement include a 1-year catheter survival of at least 80 % and peritonitis within 2 weeks of catheter insertion of less than 5 % [7].

Surgical Complications of PD

The surgical complications related to the insertion of the PD catheter can lead to morbidity, which can seriously compromise outcomes and result in loss of confidence for patients. Early complications include haemorrhage, perforated viscus, wound infection, catheter obstruction and displacement and dialysate leak. Later complications

include external cuff extrusion, dialysate leaks, hernias, erosion of abdominal organs, haemoperitoneum and chylous effluent. Independent of the insertion technique, the operator must be able to recognise and manage of complications promptly and effectively. Preoperative evaluation and identification of potential risk factors are essential to prevent them [17].

Haemorrhage

Intraperitoneal haemorrhage may arise from trauma to the omental or mesenteric vessels, particularly during closed or blind insertion. This usually presents with blood staining of the effluent, which may be heavy. Slight bleeding may be treated expectantly; however, heavy bleeding, particularly in association with hypotension, will require return to theatre for localisation of the source of the bleeding and haemostasis. Extraperitoneal bleeding may be obvious from the wound edge (main wound or exit site) or an enlarging wound haematoma. Skin edge bleeding can be dealt with using either additional sutures or local injection with a local anaesthetic solution containing adrenaline. Failure to evacuate a haematoma predisposes to delayed wound healing, dehiscence and infection with potential risk of tunnel infection and peritonitis.

Haemoperitoneum

Haemoperitoneum can give a dramatic appearance, but generally settles spontaneously without the patient suffering harm. Many causes exist and have been summarised in an excellent review article [18]. There are rare occasions when it can signify a significant intraperitoneal haemorrhage – for example, following the rupture of a splenic artery aneurysm, although most commonly the cause is a bleed from a peritoneal capillary or due to either ovulation or retroperitoneal menstruation in women. In one series, the incidence of haemoperitoneum was 6 % of all patients on PD. Seventy percent of these did not require any active intervention apart from addition of heparin to the dialysate, with 20 % requiring active intervention for significant haemorrhage and the remaining 10 % having significant intra-abdominal pathology but minor haemoperitoneum [19]. Blood transfusion may be required in severe bleeding due to follicular or ovarian cyst rupture or coagulopathies.

Perforation or Laceration

Perforation of bowel and urinary bladder is a well-recognised complication of closed PD catheter insertion, which rarely occurs with open insertion. Injuries to liver, a polycystic kidney, aorta, mesenteric artery and hernial sac have been reported. Predisposing factors include abdominal adhesions and distensions due to paralytic ileus or bowel obstruction and unconscious, cachectic or heavily sedated patients. The bladder is at risk of injury if it is of high volume, for example, in patients with chronic bladder outflow obstruction, which can be avoided by preoperative voiding or urethral catheterisation if urinary retention is demonstrated on a post-voiding bladder ultrasound scan. Evidence of peritonitis associated with contaminated effluent is an indication for laparotomy and repair of the perforation. Delayed perforation of intestine, bladder and vagina caused by pressure necrosis and erosion from an unused catheter has been described.

Wound Infection

Although rare, this is a serious complication, which may lead to catheter loss. Usual organisms are *Staphylococcus aureus* and *Pseudomonas species*. Contamination of the wound should be prevented by strict adherence to aseptic technique, prophylactic antibiotics and meticulous haemostasis. Treatment of established infection requires antibiotics, surgical drainage and possibly catheter removal for intractable infection involving the catheter. ESI or peritonitis directly as a consequence of catheter placement should be a rare event.

Hernias

It is estimated that between 10 and 20 % of the CAPD population develop hernias due to raised intra-abdominal pressure associated with PD, which can be inguinal, para-umbilical and peri-catheter in location. Part of the preoperative assessment of the prospective PD patient is to assess for the presence of hernias since these can be repaired at the time of catheter placement. However, often these are not present at the time of catheter insertion and develop later, more commonly in patients who use larger intraperitoneal volumes and in patients with adult polycystic kidney disease.

Elective hernia repair should be undertaken if possible and if the peritoneum remains intact and the hernia repair is not extensive, disruption of PD is not required. A small volume and short cycle dwell regimen can be continued postoperatively. However, where the peritoneum is breeched during hernia repair, change to haemodialysis for at least 3 weeks to allow healing of the peritoneum should be considered since leakage of dialysis fluid through the hernia wound encourages infection of mesh used to reinforce the repair. Peri-catheter hernias, which usually occur in the midline, are difficult to manage without removing the catheter. Any

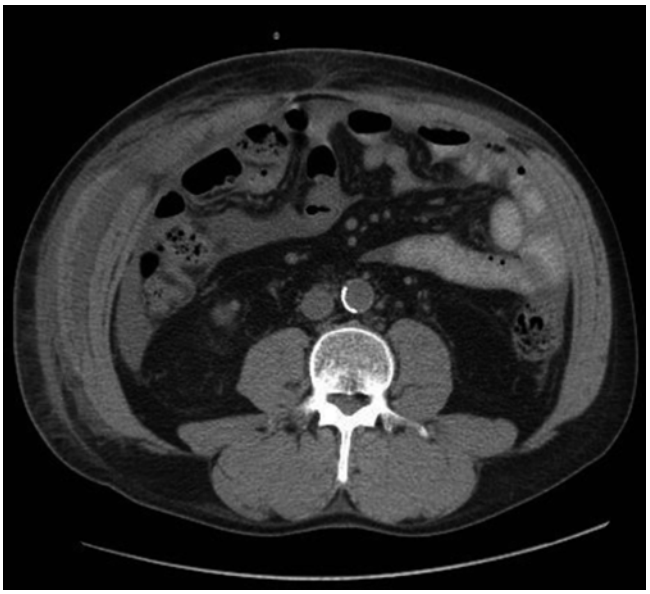


Fig. 64.6 An abdominal wall peritoneal leak at this site of a previous transplant scar demonstrated on CT scan in a patient on peritoneal dialysis following a failed renal transplant

attempt to repair a peri-catheter hernia leaving the catheter intact will either compromise the hernia repair or the catheter function. Meticulous attention to the technique in placement of the catheter will usually prevent such hernias from developing.

Leaks

A dialysate leak can occur months or even years after starting PD in up to 25 % of catheters placed through the midline, but is less common with a paramedian incision and has been reported in 7.4 % of cases following a laparoscopic PD catheter insertion [20]. Clinically, leakage presents as a clear dialysis fluid around the catheter at its exit site or as a localised swelling and oedema of the abdominal wall, due to infiltration with fluid (peau d'orange). The passage of dialysis fluid through a patent processus vaginalis may lead to gross scrotal and penile oedema in the male and labial oedema in the female. Occasionally, the oedema may be so marked that it is not possible to decide the side of origin of the leak. Hydrothorax, in a patient on PD, can result from leak of fluid through a congenital pleura-peritoneal communication or an acquired diaphragmatic hernia, which presents with chest pain and dyspnoea. The presence of leak can be suggested by the presence of a relatively high glucose (between dialysate and serum), low protein or LDH concentration in the pleural fluid and confirmed by an ultrasound, CT (Fig. 64.6) or an MR scan. An isotope scan (peritoneo-scrotogram or pleural scintigraphy) will delineate the side of the leak (Fig. 64.7a, b), and a negative scintigraphy allows the therapy to be continued while other causes are pursued.

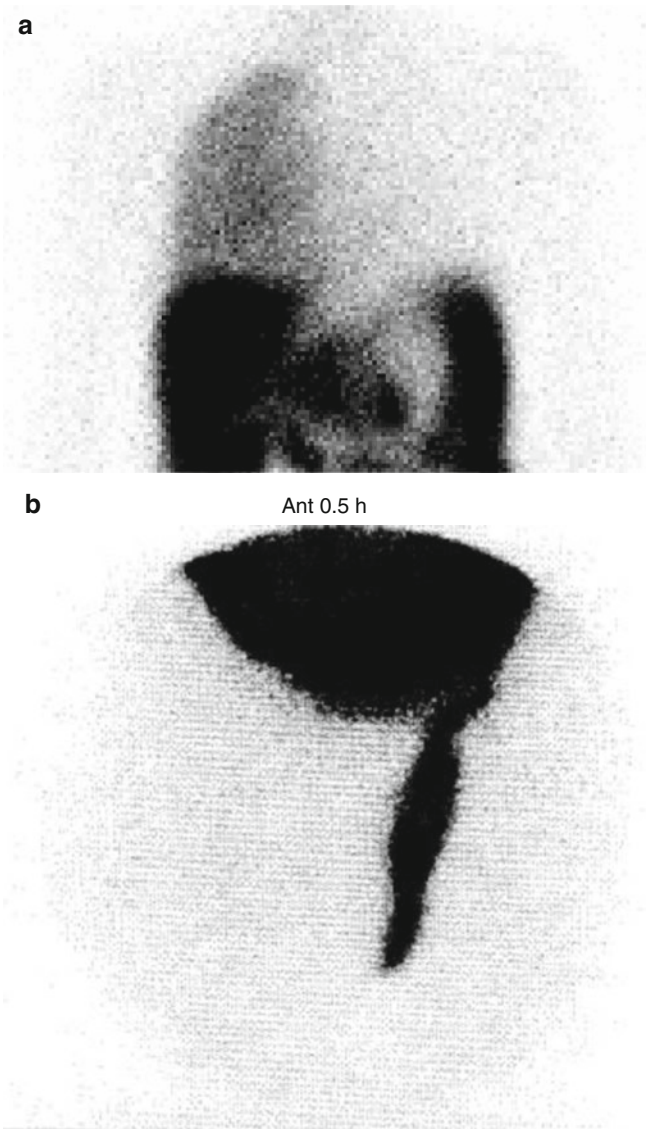


Fig. 64.7 (**a**) Scintigraphy – a positive study from a peritoneal dialysis patient with a pleural effusion. (**b**) Scintigraphy demonstrating peritoneal fluid leaking into the scrotum

Securing the PD catheter tightly at the deep cuff level reduces the risk of early leak and is recommended if there are plans to use the catheter early [21]. Early leaks can be managed by temporary discontinuation of PD; however, catheter replacement may be required. In a leak through patent processus vaginalis, PD should be discontinued until the oedema has subsided, and then repair should be undertaken as for an inguinal hernia. If possible the patient should be temporarily converted to haemodialysis for about 2 weeks following repair.

External Cuff Extrusion

Location of the subcutaneous cuff close to the exit site may lead to its protrusion, which either can result if the catheter

becomes inadvertently pulled or may occur spontaneously due the shape memory resulting in straightening of the catheter. This complication can be avoided by placing the external cuff approximately 2–3 cm from the exit site. If the subcutaneous cuff of the catheter begins to extrude, it may result in a persistent exit site infection. In the absence of signs of tunnel or deep cuff infection, removal of the subcutaneous cuff (shaving) allows the exit site infection to resolve in 50 % of cases unresponsive to antibiotic treatment. Failure of the infection to resolve mandates removal of the catheter.

Chylous Effluent

Chylous ascites, as defined by the presence of chylomicrons causing cloudiness of the effluent, is a rare entity which can occur with either no identifiable cause or in association with intra-abdominal malignancies (lymphoma and ovarian carcinoma), cirrhosis of liver, chronic pancreatitis, amyloidosis, cardiac failure and patients on calcium channel blockers. In cases with no obvious cause, microtrauma to the peritoneal lymphatics is presumed to be the aetiology, where improvement has been reported with cessation of PD, administration of medium-chain triglycerides and octreotide. Continued loss of lymph (lymphocytes and fat) leads to malnutrition and immunosuppression, which may necessitate discontinuation of PD.

Indications for Catheter Removal

Catheter removal may be required for malfunction which can result from intraluminal obstruction with blood or fibrin clots, omental tissue incarceration, catheter tip migration out of the pelvis with poor drainage, a catheter kink, catheter tip caught in an adhesion following severe peritonitis or an accidental break. Indications for removal of a functioning catheter include severe, unresponsive or recurrent peritonitis, peritonitis due to exit site and/or tunnel infection, persistent exit site infection, tunnel infection with abscess, late recurrent dialysate leak, atypical peritonitis, bowel perforation, severe abdominal pain due to the catheter impinging on internal organs, and catheter cuff extrusion with infection.

Metabolic Complications of Peritoneal Dialysis

PD has been used in general clinical practice for over 40 years, but it is only in recent years that metabolic consequences associated with its use have begun to be clarified. The majority of peritoneal dialysis exchanges rely on hypertonic glucose solutions to provide osmotic clearance of water in combination with a buffer for acid base correction. Perhaps unsurprisingly this process can lead to metabolic complications that may be either systemic or local effects on the peritoneal membrane. Components of peritoneal dialysis fluid other than glucose can also have metabolic consequences, and these will be considered. The potential for PD to cause adverse effects resulting in morbidity and mortality underlines the need to prescribe and manage PD responsibly. Research is a priority to identify mechanisms to ameliorate these complications.

Systemic Metabolic Complications of Peritoneal Dialysis

The use of glucose as the osmotic agent in PD leads to the absorption of approximately 800 g of glucose per week. In healthy people an excess of glucose will be utilised and stored as glycogen or later as lipids. It is therefore reasonable to propose that PD patients may manage excess glucose in this manner resulting in an increase in fat mass or body weight. However, the relationship between glucose exposure, fat mass and body weight is not consistent, suggesting that many factors influence metabolism in this group of patients.

Dialysis has the potential to impact on appetite in several ways. Leptin, the product of the Ob gene, is secreted by fat cells and regulates food intake and energy expenditure in animal models. Whether the hyperleptinaemia observed in uraemic patients is involved in the anorexia often identified in this group is unclear. Studies have observed that in PD patients, particularly those with diabetes, leptin levels and body fat content increase. In those that lost lean body mass, higher leptin and initial CRP levels were recorded [22]. It is of interest that insulin has been identified as a regulator of leptin gene expression. With chronic hyperinsulinaemia leptin levels can increase significantly.

The impact of glucose-based PD on the glucose-insulin system has been investigated [23]. Galach et al. studied 3.86 % glucose dwells lasting 6 h in 13 nondiabetic patients who were clinically stable and fasting. Significant increases in plasma glucose and insulin were identified. Insulin resistance was noted in the majority of patients although they were, in general, able to control the glucose peaks related to PD. Disruption of the glucose-insulin axis is one factor defining the metabolic syndrome. Other elements include hypertension, raised BMI, depressed high-density lipoprotein levels and raised triglycerides. Metabolic syndrome had been identified in approximately 50 % of PD patients and is recognised as a risk factor for cardiovascular death [24]. The management of the metabolic syndrome in PD patients is challenging as it can at least in part be attributed to the effects of exposure to hypertonic glucose dialysis solutions. Advice includes increased exercise to limit the effect of absorbed glucose and consequent fat deposition, often difficult to follow for patients with comorbid conditions.

Pharmaceutical management of dyslipidaemia is advisable as is BP control through appropriate salt water balance and use of hypotensive agents. Techniques to limit glucose exposure in peritoneal dialysis include the appropriate scheduling of exchanges, the use of non-glucose-based fluids and optimisation of residual renal function. A recently reported randomised controlled trial demonstrated the effect of a glucose sparing dialysate regimen to improve blood sugar control in diabetic patients [25].

Long-Term Changes to the Peritoneal Membrane: Impact on Ultrafiltration Capacity and Patient Outcome

The Cardiff peritoneal biopsy registry explored the relationship between peritoneal structural changes and membrane function in patients on PD [26]. Most prominently was the development of submesothelial fibrosis which increased significantly with the duration of PD, for example, 180 μm (microm) in those 0–24 months up to 700 μm (microm) in those on PD for 97 months. Vascular abnormalities were also a prominent finding with degrees of vessel wall thickening and capillary dilation which was graded from 1 to 4 according to the degree of subendothelial hyaline material, luminal distortion or obliteration. The findings suggested a causal relationship between the vasculopathy and the membrane thickening suggesting that vasculopathy may result in relative ischaemia exacerbating the fibrosis.

From the clinical perspective, long-term changes to the peritoneal membrane are demonstrated by a time-dependent increase in solute transfer associated with a decline in ultrafiltration capacity (the amount of water moving across the membrane in response to a particular glucose concentration over a defined time) occurring after about 4 years of treatment. In a study of 210 consecutive patients commencing PD, peritoneal kinetics stabilised in the first 6 months of treatment, but thereafter there was a time-dependent increase in solute transport which became significant at 42 months. In that study high solute transport (measured using the peritoneal equilibration test[1]) and earlier loss of residual renal function were associated poor outcome in patients on CAPD [27]. The patients with increasing solute transport had earlier loss in residual renal function and had been exposed to significantly more hypertonic glucose during the first 2 years of treatment that preceded the increase in solute transport. This was associated with greater achieved UF compensating for reduced residual renal function. This finding was confirmed in a 2003 report in which early and higher dialysate glucose exposure, which was in the context of higher comorbidity and lower residual renal function, was associated with a more rapid deterioration in membrane function [28]. Thus the changes in the structural-functional relationship of the membrane could be predicted to some extent by clinical factors present within the first year. Patients with PD technique survival beyond 5 years were more likely to have preserved residual renal function, maintained nutrition and medium-small solute transport characteristics [4]. The coupling between the increase in D/P creatinine and the reduction in UF is due to the earlier loss of the osmotic gradient leading to reduced aquaporin-mediated water transport and increased water reabsorption. Importantly a group of patients develop a disproportionate fall in UF with time on PD due to a marked loss of UF capacity which may be an important marker of significant membrane damage. Icodextrin and automated peritoneal dialysis can be used to improve volume status in patients with higher transport status who have insufficient urine volume, and there is evidence from various reports of benefits of this approach and in particular a meta-analysis suggesting that the adverse effect of the high transport status on outcome has been mitigated in recent years [29].

With time on PD, patients are often prescribed increasing glucose loads. The chicken and egg question has been whether increased glucose load results in changes to the membrane leading to impaired ultrafiltration or whether impaired ultrafiltration related to membrane changes comes first causing physicians to increase the glucose concentrations in the patients' prescription. A retrospective analysis of prospectively gathered data from PD patients by Davies et al. [30] provided supporting evidence that the primary event is the exposure of the peritoneal membrane to hypertonic glucose which in turn contributes to changes in membrane function. A cohort of patients who had performed continuous PD for 5 years were identified and divided into those who had stable membrane function and those with increasing membrane transport characteristics. When these 2 groups were compared, the patients with increasing membrane transport were noted to have experienced earlier loss of residual renal function and were exposed to higher glucose loads to compensate for this in advance of the recorded changes in membrane characteristics.

Potentially cytotoxic components with the dialysis fluid may be partly responsible for peritoneal membrane changes. Using in vitro techniques including cell growth inhibition and assessment of advanced glycosylation end products (AGEs) formation, Wieslander and colleagues demonstrated that the low pH of glucose dialysates causes significant cytotoxicity with glucose degradation products (GDP) and to a lesser extent osmolality and presence of lactate also causing damage [31]. GDP are formed by the exposure of the dialysate glucose to heat during sterilisation. The condensation of a carbonyl group on these sugars with a reactive amino group

[1]The peritoneal equilibration test measures the dialysate to plasma ratio of creatinine (D/P creatinine) at the end of a 4-h dwell using a dialysate with a 2.27 % glucose concentration.

of a protein produces AGEs. In vivo studies have confirmed that the interaction of the AGE with their receptor (RAGE) leads to damage of the peritoneum in humans. Peritoneal membrane in uraemic patients not on dialysis already shows changes of fibrosis, angiogenesis and RAGE activation. Those patients exposed to peritoneal dialysis with glucose-based fluids demonstrated further increase in these parameters. The AGE molecules have a physical effect on structure causing disruption to the matrix of the membrane as well as a functional effect. The AGE/RAGE interaction triggers cellular signal pathways involved in inflammation and fibrosis.

The observed long-term changes in the integrity of the peritoneal membrane have lead to the development of dialysis solutions that are intended to be more "biocompatible" utilising a neutral pH and lower concentrations of glucose degradation products and in some cases bicarbonate as a buffer. This development requires more complex (and consequently expensive) technology, including the use of twin chamber bags to separate the buffer from the electrolyte components until mixing just prior to use and to allow the glucose to be heat sterilised at a lower pH than conventionally which reduces the formation of GDPs. Several studies have tested these more biocompatible solutions examining their impact on biomarkers of peritoneal membrane integrity or inflammation and clinical aspects including UF, residual renal function and solute transport [32]. The recently published BalANZ study is the largest randomised controlled trial of biocompatible peritoneal dialysate vs standard dialysate to date [33] recruiting 185 incident peritoneal dialysis patients to this 2-year study. Patients were randomised 1:1 to receive either a neutral pH, lactate-buffered, low GDP Balance solution (Fresenius Medical Care, Bad Homburg, Germany) or a conventional, standard, lactate-buffered PD solution. The primary outcome measure was the difference in the slope of the decline in residual renal function, and this was not met. However, there was a significant difference between the groups in both time to anuria ($p=0.009$) and time to first peritonitis episode ($p=0.01$) in favour of the more biocompatible solution. Indeed the peritonitis rate in the biocompatible group was 0.30 vs 0.49 ($p=0.01$) episodes per year. In addition there was a significant reduction in over all infection in the biocompatible group (4 non-PD infections out of 91 patients vs 20 out of 91 in the control group). Thus the biocompatible group demonstrated meaningful benefits in terms of infection and time to anuria compared with the control solution.

Encapsulating Peritoneal Sclerosis

Encapsulating peritoneal sclerosis (EPS) is a rare but potentially devastating complication of peritoneal dialysis (PD). Diagnostic criteria have been published by the International Society of Peritoneal Dialysis and are based on a combination of clinical features (such as the presence of inflammation, disturbance of gastrointestinal function) supported by confirmation with imaging (Fig. 64.8) or by laparotomy [34]. Onset is often insidious, presenting with non-specific features of inflammation, weight loss and abdominal discomfort. In full-blown form it causes failure of the gastrointestinal tract and death. Its sporadic nature, the difficulty in early diagnosis as well as the lack of suitable animal models means that at present the understanding of risk factors is incomplete and evidence-based therapies are lacking. In some patients EPS seems to be a self-limiting condition that can be managed with appropriate nutritional support, whereas in others, the progression is rapid with the development of obstructive features, and in these cases there is growing evidence that timely surgical intervention can be successful.

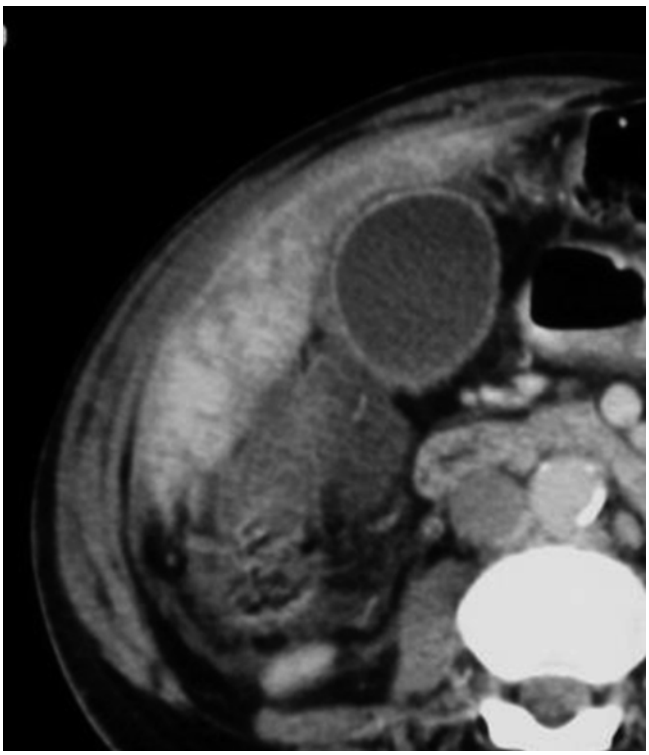


Fig. 64.8 CT scan from a patient with encapsulating peritoneal sclerosis demonstrating peritoneal thickening and cocoon formation

The Scottish Renal Registry reviewed all cases of encapsulating peritoneal sclerosis (EPS) [35] identified in Scotland from 1 January 2000 until 31 December 2007 and found an overall rate of 1.5 %; however, the incidence increased with time on PD, reaching 8.1 % (95 % confidence interval 3.6–17.6 %) for those with 4–5 years exposure to the therapy. The Scottish data gave a similar prevalence of EPS to other key papers published since the millennium of approximately 2–3 % [36–38], generally higher than that reported in earlier papers.

In the Scottish study, at diagnosis 26 % were on PD, whereas 63 % were diagnosed within 1 year and 72 % within 2 years of stopping PD; in 50 % cases patients had received a renal transplant before the diagnosis of EPS. Patients were likely to have discontinued PD because of ultrafiltration failure or inadequate dialysis, and 65 % of the cohort had used high-strength dextrose (3.86 %), and 98 % had used icodextrin, whereas no patients had used "biocompatible" dialysis fluids exclusively. The cumulative risk is modest at 2.6 % by 5 years, reflecting the reality that few patients continue PD beyond 4 years, and thus in a sense EPS is a condition of survivors damaging the otherwise good prognosis in this younger group of patients. The mortality rate was 42 % within 1 year of diagnosis, with the median survival from diagnosis being 180 days (range 1–1,075).

There have been several more recent cohort studies [39–42] each of which seems to suggest either an increased disease frequency or at least an improved rate of diagnosis of PD-associated EPS in recent years. Associated factors include PD exposure (time on PD), dialysate glucose concentrations and the possibility that icodextrin has a role. There is also an association with discontinuing PD and possibly renal transplantation. The epidemiology of EPS is complex, and given its rarity, the difficulties with delayed diagnosis, associations with reduced residual renal function and ultrafiltration failure, it is difficult to disentangle the true risk factors. Good quality information on treatment for EPS is lacking and is based on case series reports, including nutritional optimisation, the use of immunosuppressant agents and tamoxifen and specialist surgery if clinical features fail to resolve with focused nutritional and medical treatment. The surgical method combines enterolysis with excision of the diseased peritoneum and cocooning membrane and should be performed at dedicated national centres [43]. Major outstanding questions remain around risk factors, diagnosis and treatment, and large prospective studies are required.

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