PERITONEAL DIALYSIS

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Contents

Summary

Chronic kidney disease has seen an alarming increase in its prevalence and the number of patients requiring renal replacement therapy (RRT) is growing every day. This rise is the result of an aging population associated with an increase in other chronic diseases such as diabetes and hypertension. The costs incurred are high and patient survival remains extremely unfavorable regardless of the chosen modality for RRT: hemodialysis (HD) or peritoneal dialysis (PD).

Peritoneal dialysis is an effective dialytic method that utilizes the peritoneal membrane for the removal of different uremic toxins. This method is equivalent to hemodialysis and presents similar clinical outcomes. When done properly, peritoneal dialysis keeps the patient with end-stage renal disease relatively stable and without symptoms until a kidney transplant is grafted or the technique itself fails, prompting a switch of modality.

This chapter aims to introduce to the reader a comprehensive overview of PD. Initially an introduction to the history of the therapy and its evolution over the past decades will be presented. We will then discuss PD in the worldwide setting, its physiology, the modalities of PD, the complications of PD and the morbidity/mortality associated with it. Lastly we will discuss quality of life issues and the choice of which modality to use.

1. A Brief History of Peritoneal Dialysis

The history of peritoneal dialysis begins in the nineteenth century when Wegener, in 1877, first performed experiments with the infusion of fluid into the peritoneal cavity. Fifty years passed before George Ganter published his first attempts to use PD in the treatment of uremic animals. In 1946 Frank, Seligman and Fine described the successful use of PD for acute kidney injury. However, difficulties in finding suitable materials for the realization of the method have held back its development (Wegner, 1877; Ganter, 1923, Frank et al 1946).

For several years the efforts have focused on developing strategies and technologies that could improve PD: from Arthur Grollman describing the first method for intermittent PD to Morton Maxwell simplifying the technique with the customization of a container, a plastic tube and a polyethylene catheter.

During the 1960s, home peritoneal dialysis, in the way we know it now, began to be shaped with the master's degree thesis of Fred Boen published in 1961. In about the 1950s, he described peritoneal dialysis as a simple and effective procedure that avoided abrupt changes in blood volume and allowed a better control on the balance of fluids

and electrolytes. Moreover, he claimed that PD could be carried out in the long term as a permanent method to replace the functions of the insufficient kidneys (Boen, 1961).

In 1968, Henry Tenckhoff, at the American Society of Artificial Internal Organs, presented a catheter modification to the Palmer and Quinton catheter from 1964 that had a wider opening at the tip and fenestrations along its side that significantly improve fluid escape and infection rates.

The beginning of continuous ambulatory peritoneal dialysis started with an engineer and a biomedical doctor in 1975, Jack Moncrief and Robert Popovich. Together they calculated and successfully performed a continuous dialysis consisting of five daily exchanges using 2 liters of dialysate. Later, they started to work together with Karl Nolph, Zylub Twardowsky and William Pyle. This technique had a major boost when Dimitri Oreopoulos replaced the glass jars, which were previously used, for plastic bags that, when empty, were kept attached to the patient's body until the next exchange. However, despite these innovations peritonitis rates remained extremely high until the early 1980s.

At that time, Karl Nolph and Umberto Buoncristiani produced a significant reduction in infection rates through their inventions. Karl Nolph invented the titanium connector place at the catheter tip and Umberto Buoncristiani introduced the stock twin system (Y) associated with the use of the "flush before fill" procedure. Thereafter, no new device showed such impact to decrease peritonitis rates. In contrast, there were important developments in the clinical management: the description of the peritoneum equilibration test by Twardowsky in 1987, the development of the cyclers and the more biocompatible solutions in early 1990s. A more detailed history is beyond the scope of this chapter but excellent references can be found for those who wish to undertake further reading (Gokal and Nolph,1994; Palmer, 1982).

2. Overview of PD in the World

Peritoneal dialysis was estimated to be the dialysis modality for almost 200,000 people in 2008. This number represents only 8 to 10% of the patients treated for end-stage renal disease (ESRD) worldwide. The reason for this low prevalence is not totally understood but includes medical factors, patient's educational level, psychological factors, local availability and reimbursement policies.

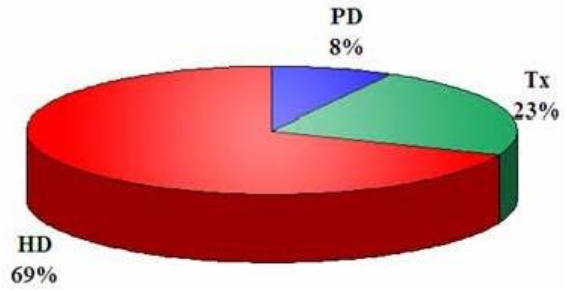

Figure 1. World estimated penetration of renal replacement therapies in the year of 2008.

In fact, economic issues are believed to be the most important factor. This matter can be best understood by looking at the considerable differences in the prevalence of this therapy worldwide and its corresponding health-economics reports (Jain et al, 2012).

Nowadays developing countries contribute to about 65% of all patients who receive PD. In contrast, over the past decade a reduction in the use of PD has been observed in developed countries. Paradoxically survival rates have been shown to be similar between therapies and a survey among nephrologists from developed countries reported that the ideal perceived prevalence of PD patients should be around 25-30% (Ledebo et al, 2000, 2001). The reasons to increase the penetrance of PD are to take advantage of the better survival of PD compared to HD during the first 2 years of treatment, the lower cost of therapy in general and all the conveniences of a home therapy.

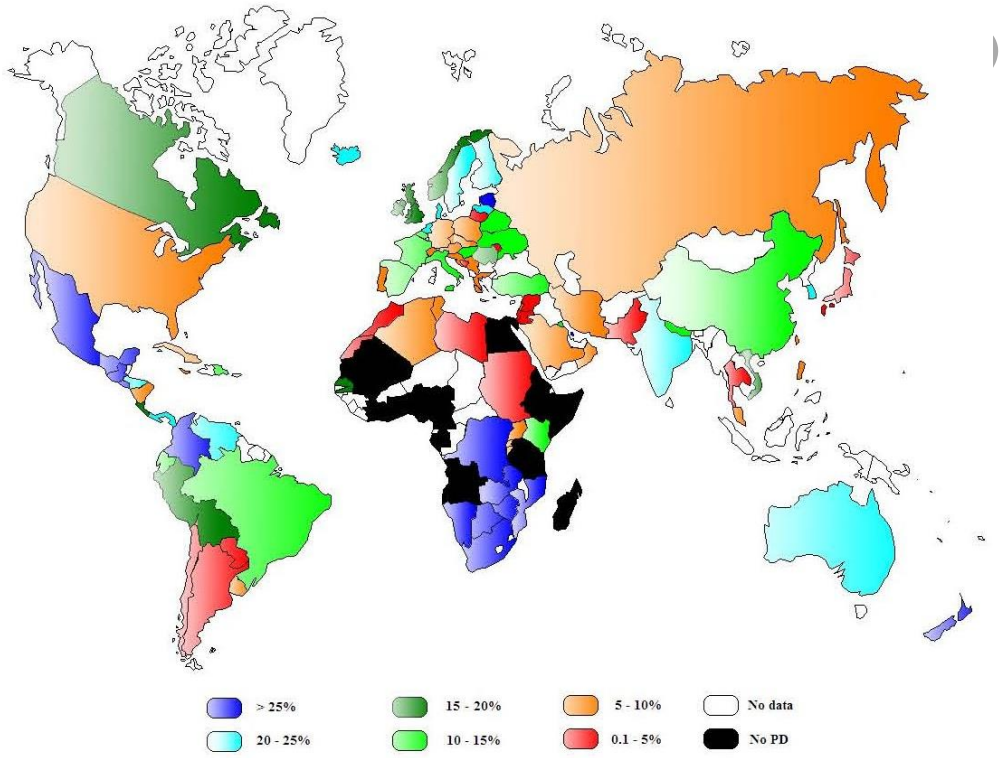

Figure 2. Percentage of peritoneal dialysis patients worldwide

Regarding PD modalities, the prevalence of automated peritoneal dialysis (APD) is growing fast. Its introduction provided a new modality with less disruption to the patient's lifestyle. The greater acceptance of this new modality was demonstrated by several reports such as the US Renal Data System publishing a 50% increase in the use of automated peritoneal dialysis (APD) from 1998 to 2005 (US Renal Data System: annual data report, 2008). More suitable reimbursement strategies, educational programs for patients and medical and non-medical healthcare teams carrying scientific support continue to be debated as potential policies to sustain the increased uptake of PD in the future.

3. Organization of a PD Program

The success of a PD program depends on numerous factors including the proper selection of patients, a committed multidisciplinary team, development of continuing education programs of both patients and the healthcare team and a minimum physical infrastructure. All PD programs should be integrated into a larger program of renal replacement therapies that involves all forms of dialysis and particularly renal transplantation. One should always remember that dialysis modalities should be seen as complementary to one another rather than competing. Last but not least, the implementation of clinical performance measurements can provide important information about the center, allowing the healthcare team to enhance the quality of care delivered. Below are discussed some important factors in the development of a good PD center.

3.1. Physical Space

The required physical space of a PD center should contain, whenever possible, a room for training on PD techniques; space to carry out procedures; a room for medical, nursing and multidisciplinary consultations; a waste room, a secretary and a waiting room.

- The training room: must be comfortable and quiet, with a door providing privacy when needed. It should be airy with good lighting with adequate work surfaces and have a sink for hand-washing. Above all, it must be clean and easily cleaned to provide a sterile environment in which to undertake PD. This area should contain all materials necessary to perform a manual exchange and/or cycler procedures and bandage materials. We suggest the minimum size of 15 to 20m² to this room.
- The office: The materials needed in an office for medical, nursing or multidisciplinary consults are very similar to a conventional office. These include a desk, chairs, a litterbin, light, telephone, some scales, apparatus for measuring blood pressure, paper or a computer to update patient records.
- The procedure room: similar to a small theatre (OR). It should facilitate dressing changes with aseptic technique following catheter insertion, tube changes and dialysis exchanges. For catheter insertion or removal a dedicated area should be used (in a clinic or at the hospital) with all the appropriate materials and patient monitoring equipment.

For a renal unit starting PD it is perfectly acceptable to adapt a smaller space for their work, especially when the number of patients is small. All PD centers must have a reference hospital to treat complications, whether they are or are not related to PD.

3.2. Human Resources

A good PD program should be composed of nephrologists, nurses, dieticians, social workers and, if possible, dentists, psychologists and podiatrists. Below is a small rationale for each member of the multidisciplinary team.

- Nursing: A well trained and motivated nurse is fundamental to any successful PD program. The nurse's most important function is to provide a good training on PD techniques for patients and/or caretakers. They must have good communication skills, be flexible and have the ability to work as a team member, firmly demonstrating the belief in patient self-care (Bernardini et al, 2006). We recommend a maximum of 1 nurse per 20 PD patients to avoid too large a workload.
- Dietitian: Malnutrition is extremely common in ESRD patients and its prevalence in PD is also very common. In addition, malnutrition is associated with greater morbidity and mortality (Chung et al, 2000) (Chung et al, 2000). Although believed to allow a more flexible diet due its continuous characteristic, PD has several clinical complications that may be attributed to dietary habits or the modality itself.
- Dentist: a large number of oral symptoms have been reported in dialysis patients, including periodontitis, dry mouth, mucosal lesions, halitosis, tooth mobility, malocclusion and dental erosion (Eltas et al, 2011). These symptoms will have a negative impact on nutrition and general health. Moreover, periodontitis was recently associated with increased risk of death (Chen et al, 2011).
- Psychologist: Depression appears to be more common in ESRD patients than in the general population. It is a modifiable risk factor that is associated with adverse outcomes including mortality and by itself justifies screening and treatment (Chilcot et al, 2008; Chilcot et al,2011).
- Podiatrist: An important but usually forgotten professional in dialysis clinics (Lavery et al 2010). This profession is of particular importance because up to 50% of dialysis patients have diabetes mellitus as their underlying renal disease and diabetic foot is a pathology highly associated with amputation and death. Additionally diabetic foot disease has a prevalence 250% higher in ESRD patients compared to patients without chronic kidney disease (CKD) (Ndip et al, 2010; Faglia et al, 2009).

4. Selection of Patients to PD

A proper patient selection is of extreme importance to optimize the treatment outcomes of ESRD patients. Several factors may affect outcomes. Center experience, age, diabetes, residual renal function, co-morbidity, obesity, socioeconomic status, social support are all aspects that should be taken into account when considering the initiation of PD. As a consequence, the choice regarding which patients should be offered PD should be carefully undertaken by nephrologists, nurses and patients. It is known that if sufficient and clear information is provided by the education programs, the percentage of patients choosing PD as their initial RRT raises (Li and Chow, 2009; Marron et al, 2005). However, there are several contraindications to PD. These can be divided into relative contraindications and absolute contraindications (Table 4.1).

Relative Contraindications
Abdominal wall hernias
Abdominal wall or skin infections
Advanced chronic pulmonary disease
Compliance adherence
Diverticulitis
Inflammatory or ischemic bowel disease

Morbid obesity
Ostomy
Peritoneal leaks
Severe gastroesophageal reflux
Severe malnutrition
Socioeconomic status
Social support
Absolute contraindications
Documented loss of peritoneal function
Extensive abdominal adhesions that limit dialysate flow
Physical or mental incapability in the absence of a caretaker
Third trimester pregnancy
Uncorrectable defects (irreparable hernia,omphalocele, bladder extrophy)

Table 1. Peritoneal Dialysis Contraindications

5. Peritoneal Access

High quality catheter placement and its timely availability are key to the success of PD initiation. Several factors, including mechanical and infectious complications, can interfere with catheter survival. For these reasons, catheter insertions should always be planned in advance of the need for dialysis. Care for the patient intending to undertake PD is divided into three distinct stages: pre-insertion care, catheter placement and post-implant care.

5.1 Pre-insertion Care

This stage begins, whenever possible, with a good pre dialysis care and the consequent early referral to a PD center. Ideally catheter insertion should be performed at least 2 weeks before starting PD. A prior visit to see the surgeon or interventional nephrologist to determine the ideal location for catheter placement is strongly recommended.

5.2 Catheter Placement

All PD programs should have protocols for catheter placement. This protocol should contain information that is summarized in the following bullet points:

- No particular catheter type has been proven to be superior to any other (Strippoli et al, 2004).
- Administration of prophylactic antibiotics at the time of insertion should be mandatory to decrease infection risk. Most centers prefer a first-generation cephalosporin, but recent data suggests that each program should analyze their local bacterial flora before determining which antibiotic to use. (Gadallah et al, 2000).
- Local expertise should drive implantation technique. Surgeons most often use open surgery while nephrologists tend to use percutaneous techniques. More recently, trocar insertions have been progressively substituted by Seldinger technique (Yip and Lo, 2010).

- Laparoscopic surgery with omentopexy appears to present better results but is expensive, particularly to developing countries where 65% of the world PD population is situated (Crabtree and Fishman, 2005).
- Although catheter insertion can be safely performed by nephrologists, the presence of a surgeon is important. In situations where multiple previous abdominal surgery has taken place or if a concomitant hernia correction is possible, a referral to the local surgeon is important. In dealing with complications such as visceral or vascular perforation, a surgeon is essential (Moraes et al, 2012).
- The most severe, but rare, complications are bowel perforation and severe hemorrhage. Lately we can see incisional hernias, dialysate leakage, infection, catheter dysfunction and cuff extrusion.

5.3 Post-Insertion Care

This stage starts once the catheter is placed and remains until the patient no-longer has a PD catheter *in situ*.

- Immobilization of the catheter in order to avoid trauma and hematoma.
- Cover the exit-site with a non-occlusive dressing to avoid infection.
- The dressing change should be done by a trained nurse employing an aseptic technique until healing is completed.
- Antibiotics for preventing exit-site infection are recommended. It can be done daily for all patients or only for *S.aureus* nasal carriage patients. Intermittent use has been more frequently associated with antibiotic resistance. Topical mupirocin or gentamycin are the most common antibiotics used.

Catheter insertion data should be included in the clinical performance measurement mentioned earlier and catheter-related function and complications should be audited every year. The following results should be the gold standard: a bowel perforation rate < 1%, an exit-site infection within 2 weeks of catheter placement < 5% and a mechanical problem such as catheter displacement requiring a new intervention < 20%.

6. Membrane Anatomy and Physiology

6.1 Anatomy

The peritoneum is a natural semipermeable membrane that lines the abdominal cavity. Its surface area is between 1 to 2m² in an adult and can be divided into parietal and visceral peritoneum. The former, attached to the abdominal wall, represents about 80% of the total peritoneal area and the latter, wrapped around the intestines and other internal organs, the remaining 20%.

The visceral peritoneum derives its blood supply from the superior mesenteric artery and the venous blood drains into the systemic circulation by the hepatic portal vein. In contrast, parietal peritoneum presents a much smaller surface area but with a greater contribution to PD. Its blood supply comes from the epigastric, lumbar and intercostal

arteries that drain to the inferior vena cava. Subdiaphragmatic lymphatics are responsible for up to 80% of the drainage from the peritoneal cavity.

The peritoneal membrane can also be divided histologically into six segments a stagnated liquid film coating, the capillary endothelium; the endothelium itself; the endothelial basement membrane; the interstitium; the mesothelium and another stagnated liquid film coating the mesothelium.

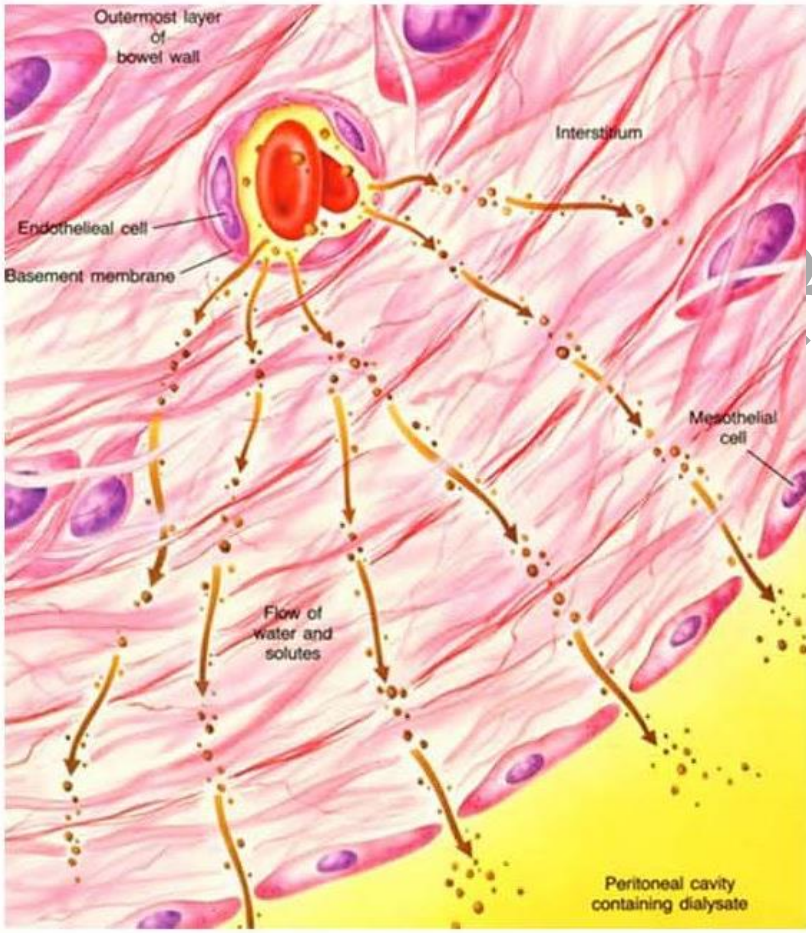

Figure 3. Peritoneal membrane

6.2 Physiology

Peritoneal dialysis begins with the infusion of a PD solution (from now on called dialysate) into the peritoneal cavity. Once the dialysate is in contact with the peritoneal membrane, the transport of solutes and water from the peritoneal capillaries, passing through the membrane, to the dialysate begins. This transport involves three concurrent processes: diffusion, ultrafiltration and liquid reabsorption.

Diffusion is the process whereby solutes on one side of a semipermeable membrane pass through it until the number of similar particles on either side of that membrane achieve the same concentration. For diffusion of the waste products produced by normal

metabolism, to pass through the peritoneal membrane into the dialysate, the particles encounter six cellular layers mentioned above.

The endothelium is considered the most important barrier as indicated by the three pore model, a widely accepted theory that describes the kinetics of peritoneal transport of solutes and fluids. Diffusion is also directly influenced by solute concentration gradient, molecular size, the membrane permeability and its surface area.

Ultrafiltration (UF) is the water transport induced by the presence of an osmotic agent in the dialysate. In addition, UF adds a convective component to solute transport (solvent drag). The following factors directly impact UF efficiency: overall osmotic gradient, reflection coefficient of the osmotic agent, peritoneal membrane hydraulic permeability and membrane surface area.

Liquid reabsorption is a relatively constant process that occurs primarily by lymphatic absorption, which in turn depends of the hydrostatic intraperitoneal pressure and the lymphatic effectiveness.

6.3 The Three Pore Model

First described more than 20 years ago, the three pore model affirms the solute transport through the capillary wall is consistent with a system of pores that differ in sizes (Figure 6.1)(Rippe et al, 2004; Rippe et al, 1991). These pores are size-selective and can be described as follows:

- Large pores – Comprise less than 0.1% of the total number of pores. Their average radius is greater than 150Å and they probably represent venular interendothelial gaps. These pores are involved in the transport of macromolecules contributing to part of the UF via convection of solutes from systemic circulation to peritoneal cavity.
- Small pores – These form the vast majority of the total pore surface. Responsible for the diffusion of small molecules, their average radius ranges from 40 to 50Å. They are likely to represent the gaps between endothelial cells.
- Aquaporins or ultra-small pores – These water specific channels located in the endothelial cells are of major importance to obtain a good daily UF. They are thought to mediate around 50% of the total UF acquired during a dwell with hypertonic glucose.

The distribution and number of these pores through the peritoneal membrane differs from patient to patient. Thus each patient has a different membrane profile with distinct characteristics of solute removal and ultrafiltration. In addition, the membrane profile is dynamic and prone to change during the therapy. Consequently PD prescriptions demand an individualized approach. A classification of peritoneal transport then becomes extremely helpful. The nature of peritoneal transport was characterized by Twardowski in 1987. This test, called Peritoneal Equilibration Test will be discussed below.

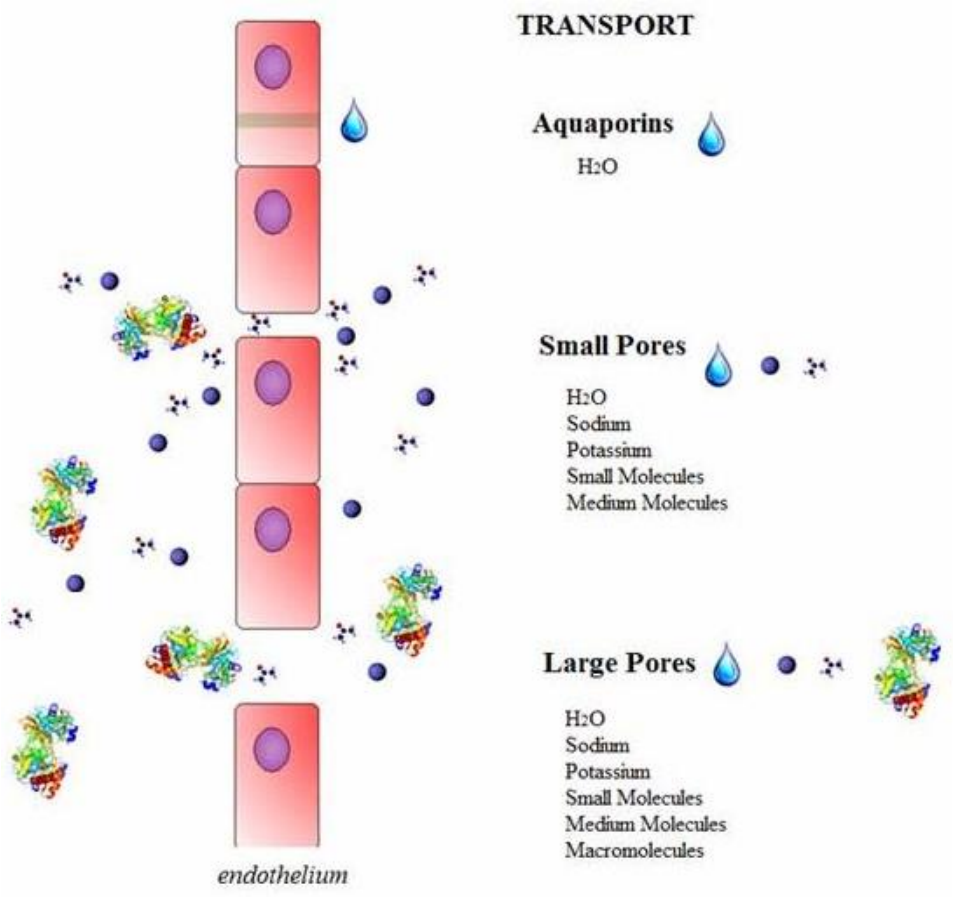

Figure 4. The three pore model

6.4 Peritoneal Equilibration Test

The PET is a semi quantitative assessment of peritoneal membrane transport characteristics that was first described in the 1980s. This test has several clinical applications (Table 2). Routinely the PET is performed approximately 4 weeks after the initiation of PD because significant changes occur in membrane characteristics within this period (Johnson et al, 2004).

Peritoneal Membrane Function Classification
Diagnosis of membrane injury
Diagnosis of causes of ultrafiltration failure
Diagnosis of causes of ineffective solute clearance
Long-term monitoring of membrane function
Selection of peritoneal dialysis modality
Analyze the impact of systemic diseases on peritoneal membrane function
Estimation of dialysis dose
Diagnosis of early ultrafiltration failure

Table 2. Peritoneal Equilibrations test applications

- Exchange preceding the test must dwell for 8 to 12 hours.
- The overnight exchange must be drained over 20 minutes.
- A sample of dialysis solution is obtained from the bag to be infused.
- The 2 liter of 2.5% glucose PD solution is infused in portions of 400ml every 2 minutes over a total of 10 minutes.
- Precisely 10 minutes after the start of infusion (dwell time zero), 200ml is drained, mixed and then 10ml is taken (the remaining 190ml is reinfused).
- During the four-hour dwell time, the patient can move about freely.
- A serum sample is obtained at 120 minutes.
- Samples of dialysate are taken at 60, 120 and 180 minutes.
- At four hours the dialysate is drained in the upright position (cannot exceed 20 min).
- The drain volume is measured and another dialysate sample is collected.
- Creatinine and glucose are measured in all collected samples.
- The serum and dialysate creatinine levels are corrected for the glucose level (Tam et al, 2009).
- The dialysate to plasma ratio for creatinine is calculated and the membrane transport rate is classified according to Figure 5.

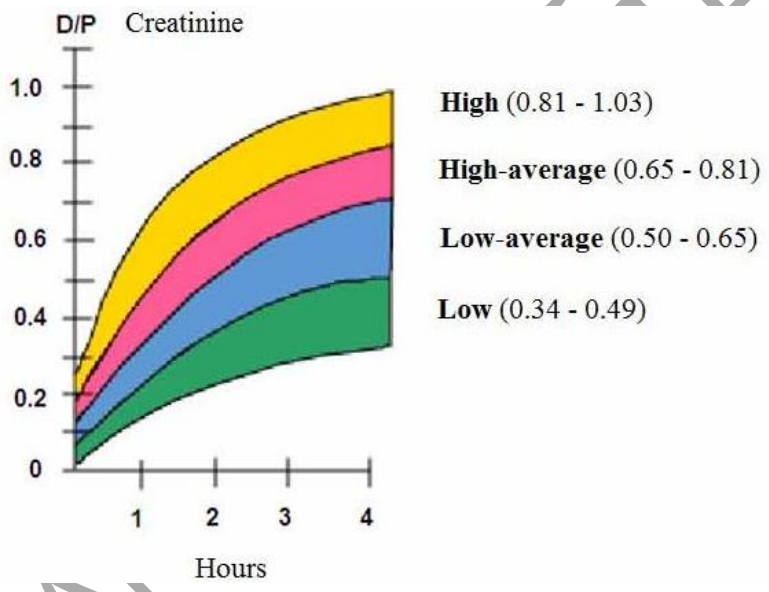

Figure 5. Transport classification according to the PET

The original PET, although very useful, is labor intensive, requires multiple blood and dialysate samples and is time consuming with 4 hours of nurse-patient interaction (Twardowski,1987). A simplified PET was developed three years later and its results were similar to the original PET (Twardowski, 1990). An alternative test called modified PET using a 4.25% glucose PD solution was described 10 years ago. This modified test presents some advantages compared with the traditional test with 2.5%. This test make possible to analyze UF failure concomitantly and without prejudice of transport characterization (Pride et al, 2002).

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Links

International Society for Peritoneal Dialysis: www.ispd.org

Peritoneal Dialysis International – Official Journal of the ISPD: www.pdiconnect.com

Advances in Peritoneal Dialysis: www.advancesinpd.com

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Biographical Sketches

Thyago Proença de Moraes, after graduating at Faculdade de Medicina de Marilia in 2001, he went to Evangelic University Hospital in Curitiba for his nephrology residency in 2005. In 2008 he became the coordinator of the pioneer peritoneal dialysis center in Brazil. In 2010 he was awarded with a motion of public recognition for services rendered on behalf of the population in the prevention and treatment of kidney disease by the Legislative Assembly of the State of Paraná. In 2011 appointed as Professor of

Medicine at Pontificia Universidade Católica do Paraná. In 2012 he assumed the position of project manager of the Brazilian Peritoneal Dialysis Study (BRAZPD), one of the largest PD database in the world containing data of more than 11.000 PD patients. Granted with a distinguished fellowship at Nottingham University under advisory of Christopher Macintyre in early 2012, nowadays he is a member of the International Society of Nephrology, American Society of Nephrology and the International Society for Peritoneal Dialysis in which he is a member of the education committee and member of the council representing Latin America. His main research activities are focused on peritoneal dialysis, particularly in carbohydrate and lipids disturbances, cardiovascular disease, inflammation and glucose-spared peritoneal dialysis solutions.