UNDERSTANDING PERITONEAL DIALYSIS

THE INVENTION AND DEVELOPMENT OF PERITONEAL DIALYSIS

FRESENIUS MEDICAL CARE

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PERITONEAL DIALYSIS – FROM THE BEGINNING TO THE PRESENT

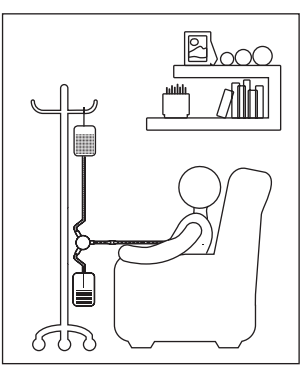
When symptoms of uremia first appear in the body, it is a sign that the kidneys are not functioning properly or have stopped filtering toxins from the blood. The Greek origin of the word shows that awareness of the disease goes back much further than our ability to effectively treat people with this life-threatening illness.

Only within the last 100 years has medical research been able to lay the foundation for replacing the kidneys' functions through dialysis.

Essentially, there are two types of dialysis. Hemodialysis is an extracorporeal procedure, or procedure outside the body, for filtering uremic substances from the blood of patients. This is the preferred treatment for almost 90% of all dialysis patients. The alternative is peritoneal dialysis, which most patients carry out themselves – either at home or at work. This type of treatment uses the peritoneum as a dialysis membrane.

The first significant progress with peritoneal dialysis was made during the 1920s, but it would take a number of subsequent discoveries in the following decades to make it accessible for a larger number of patients with chronic kidney disease.

The following pages provide an insight into the fascinating history of peritoneal dialysis.



PERITONEAL DIALYSIS ENABLES DIALYSIS PATIENTS TO CARRY ON WITH THEIR LIVES AS NORMAL DESPITE CHRONIC KIDNEY FAILURE.

PERITONEAL DIALYSIS

The **peritoneum** is the lining of the abdomen. With a surface area of as much as two square meters, this thin, shiny membrane covers the abdominal cavity and its internal organs. The peritoneum's very good blood circulation makes it an excellent natural filter membrane. In addition, it has similar attributes to the artificial filter used in hemodialysis – its pores allow the passage of certain substances while retaining others. Peritoneal dialysis (PD) exploits these unique traits.

PERITONEUM
the lining of the abdomen – it is used as a natural filter in peritoneal dialysis.

A sterile **dialysis solution** is introduced at regular intervals into the abdominal cavity through a permanent catheter. It initially remains here to absorb waste products such as urea or creatinine from the blood. Excess water is also removed from the body. After a time, this fluid is drained into a bag and replaced by fresh solution.

Peritoneal dialysis is the preferred treatment for over

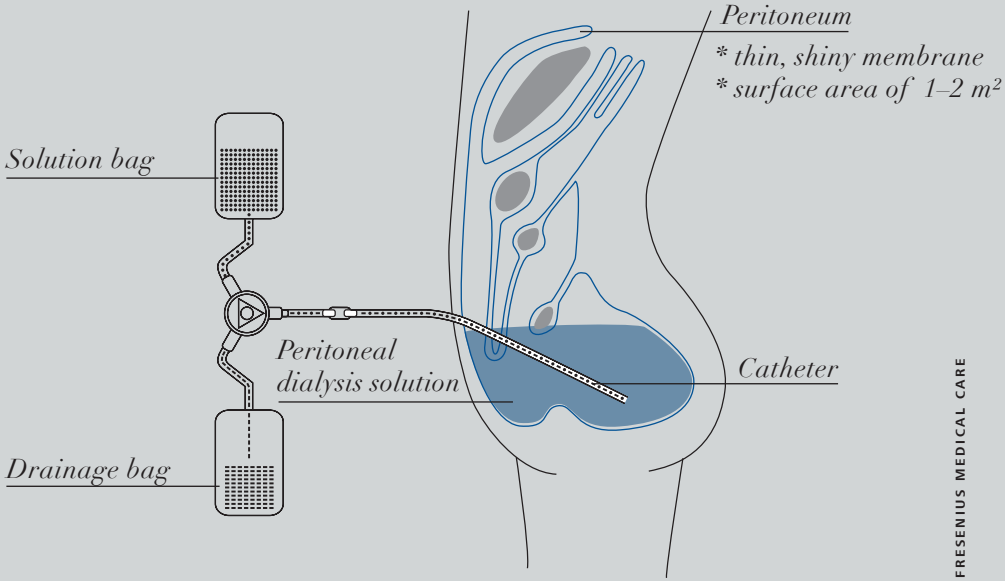
10%

of all dialysis patients.

There are various types of peritoneal dialysis. With **continuous ambulant peritoneal dialysis (CAPD),** patients change the dialysis solution themselves four to five times a day. No machine is needed to change the bag.

Automated peritoneal dialysis (APD) uses a programmable machine, or cycler, that controls the volume, filling, dwell time and drainage of the solution. Thanks to automated dialysis, patients can now be dialyzed while asleep at home.

PERITONEAL DIALYSIS



THE FIRST STEPS TOWARD PERITONEAL DIALYSIS

Removing water from the abdomen in the 17th century

The term "peritoneum" comes from the Greek word "peritonaion" and means "to stretch". The famous Greek physician Galen and other medical scholars of ancient Greece were the first to study the abdominal cavity. Early anatomists and surgeons described the size and features of the peritoneal membrane but failed to discover its detailed structure or function.

1744, physiologist and physicist Stephen Hales joined forces with surgeon and fellow Englishman Christopher Warrick to lay the foundation for peritoneal dialysis in humans. They attempted to treat a 50-year-old patient with ascites by first removing the excess abdominal fluid from the woman before using a leather tube to introduce a solution consisting of 50% water and 50% wine into her abdomen.

Stephen Hales

In **1862,** Friedrich Daniel von Recklinghausen gave the first scientific description of the peritoneum's cellular composition.

In **1877,** the German Georg Wegner performed the first animal experiments to observe the metabolic transport processes occurring through the peritoneum. In doing so, he discovered that a concentrated sugar solution would lead to an increased amount of fluid in the abdominal cavity – the basis for using the peritoneum for fluid removal, or peritoneal ultrafiltration.

In **1894,** two Englishmen – Ernest Henry Starling and Alfred Herbert Tubby – discovered that fluid removal through the peritoneum was effected by its blood vessels.

FIRST TREATMENTS OF HUMAN BEINGS

It took until **1923** for Georg Ganter at the University of Würzburg to perform the first peritoneal dialysis for patients with chronic kidney disease. He introduced 1.5 liters of a physiological saline solution – one with the same salt concentration as the human blood – into the abdomen of a woman who was suffering from a blocked ureter. Although the treatment alleviated the symptoms temporarily, the patient died a short time later.

Between **1924** and **1938,** a number of medical teams in the U.S. and Germany performed the first regularly repeated – or intermittent – peritoneal dialysis treatments, thereby proving that this form of treatment can be a short-term replacement for the kidneys' natural function.

In the **following years,** the careful selection of materials that were easy to sterilize – such as porcelain, metal, latex and glass – for the first time made it possible to ensure reasonably hygienic conditions during peritoneal dialysis. The main reason why this did not result in more widespread use of the procedure was the lack of a safe method of accessing the patient's abdomen.

PERITONEAL DIALYSIS CATHETER

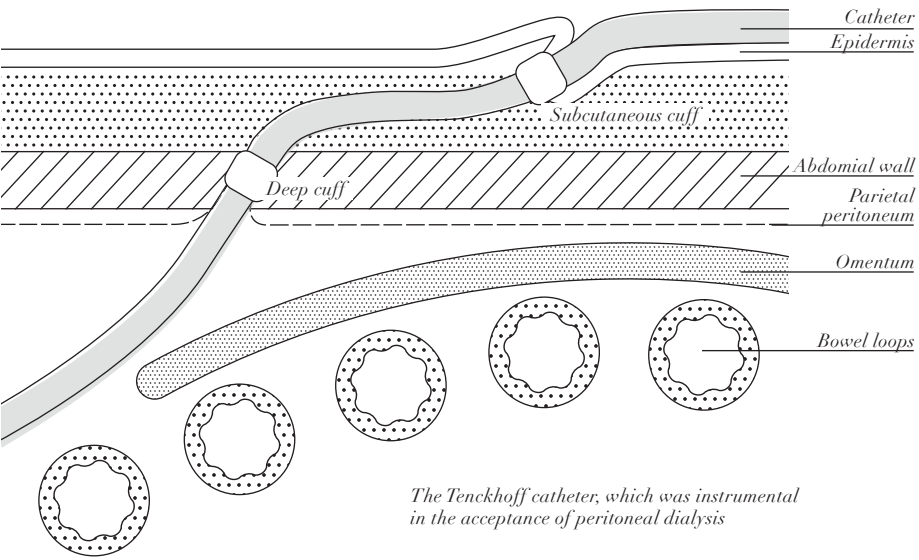
Safe access to the abdomen for peritoneal dialysis is provided by a catheter. Metal cannulae were originally used to gain access to the abdominal cavity, but these were replaced by stomach and oxygen tubes later on.

In **1952,** Arthur Grollman from Southwestern Medical School in Dallas developed a catheter that would make peritoneal dialysis treatments accessible for patients with chronic kidney failure. Grollman used a one-liter container with a cap to which a plastic tube was attached. This tube was in turn connected to a polyethylene catheter. His revolutionary idea was to use a flexible catheter rather than a stiff tube, as had been the case in the past. In addition, the tip of the catheter remaining in the abdominal cavity had several small holes to allow an optimal inflow and outflow of dialysis solution.

In **1959,** the American Paul Doolan designed a catheter for long-term use that could remain in the patient's abdominal cavity. Richard Ruben, another American, used this Doolan catheter to perform the first peritoneal dialysis over a period of seven months.

In **1968,** the American Henry Tenckhoff developed the catheter named after him. Up until then, the widely used stylet catheter had already made it possible to treat patients with chronic kidney failure using peritoneal dialysis. However, this meant placing a new catheter in the abdominal cavity for each treatment – a time-consuming process for patient and medical staff alike. The permanent catheter developed by Tenckhoff, which proved instrumental in the wide acceptance of peritoneal dialysis, is still in use today. Made from silicone, it has one or two cuffs, which help the catheter to grow into the peritoneum as well as into deeper layers of connective tissue.

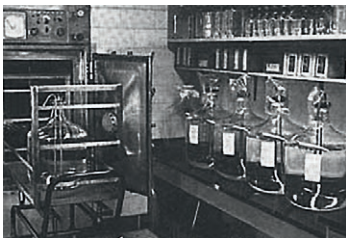
TENCKHOFF CATHETER



The Tenckhoff catheter, which was instrumental in the acceptance of peritoneal dialysis

BAGS AND TUBES

In addition to improvement of the catheters, the development of bags and tubes also played a decisive role in the long-term success of peritoneal dialysis. As the most common complication, peritonitis prevented peritoneal dialysis from becoming more widely used.



Sterilization of peritoneal dialysis solutions in large glass containers

Until the fall of **1978,** peritoneal dialysis solution (PD solution) was only available in glass containers connected to the permanent catheter with plastic tubes. Patients had to attach the tubes to the catheter every time they added or removed solution. Because of the repeated connections and disconnections, the risk of infection – and thus the peritonitis rate – was extremely high.

Dimitrios Oreopoulos from Toronto finally made peritoneal dialysis practical by introducing disposable plastic bags. The new technique significantly lowered the **peritonitis** rate while also giving patients far greater freedom of movement. Once the dialysis solution had been introduced into the abdominal cavity, the bag could simply be rolled up and remained connected to the patient's body. To remove the solution, the patient unrolled the bag and allowed the used solution to drain into it. The bag was then disconnected from the catheter and replaced by a new one.

PERITONITIS
inflammation of the abdominal lining

Several Italian research teams also made a valuable contribution to the prevention of peritonitis – most notably Umberto Buoncristiani, who invented the Y-System. This system consists of an initially empty drainage bag, a Y-shaped tube system and a bag filled with dialysis solution. The used solution initially runs into the drainage bag, also removing any bacteria from the catheter connector. The fresh dialysis solution is then flushed through the tube system into the almost completely filled

drainage bag for about three seconds in order to remove air from the feed tube. The connection to the abdominal cavity remains closed during this procedure. Only after this flushing is fresh dialysis solution introduced (flush-before-fill principle). Depending on the system, the direction of flow is controlled with clamps or a disc. Another advantage of this technology is that patients do not have to carry a bag attached to their bodies.

The double-bag system is an improvement of the Y-system. This innovation not only provides an empty bag already attached to the Y-shaped tube system but also a bag with fresh dialysis solution. This eliminates yet another connection and further decreases the risk of infection.

REPLACEMENT FLUID:
** approx. 1,500 to 2,500 ml depending on body volume*

Double chamber bag

Standard single bag solution

Drainage set

THE AGE OF CONTINUOUS AMBULANT PERITONEAL DIALYSIS (CAPD)

Robert Popovich and Jack Moncrief were the first to describe CAPD (1976).

CAPD originated in Austin, Texas, in **1975,** when Robert Popovich and Jack Moncrief discussed ways of dialyzing a patient who was unable to undergo hemodialysis. Comprehensive calculations were used to determine the amount of dialysis solution and the dwell time required for effective removal of uremic toxins. This led to the conclusion that a two-liter bag should be changed up to five times a day and a PD solution should constantly remain in the patient's body. Initial reports detailing the practical findings with this method were not taken seriously to start with and it took until **1978** for the researchers to win over the medical community with their clinical successes. The method they developed made it possible to remove fluids and filter the blood more steadily and continuously than with intermittent procedures

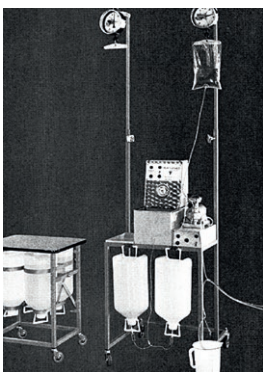
The new generation of cyclers developed by Fresenius Medical Care

AUTOMATED PERITONEAL DIALYSIS (APD)

In addition to constantly lowering the rate of infection, costs for medical staff and materials also had to be cut. Machines for automated peritoneal dialysis (APD) were developed for this purpose.

Automated peritoneal dialysis was introduced in **1962** by Fred Boen from Washington University. The machine he developed required a 40-liter container of PD solution. The invention significantly cut the amount of time needed to open and close the tubing system and connect or disconnect bags, as required up to that point. Full containers were delivered to the patients' homes and retrieved when empty. This form of peritoneal dialysis was performed once a week.

It was again Tenckhoff who further simplified automated peritoneal dialysis. To eliminate the difficult task of maneuvering the 40-liter containers, he suggested installing water preparation equipment that could provide sterile water at the patients' homes. A concentrate was added to the sterile water to produce dialysis solution.



Precursors of the current peritoneal dialysis machine, developed by Henry Tenckhoff and Norman Lasker

In **1970,** the first patients received home dialysis with a cycler. The American Norman Lasker combined the developments of Boen, Tenckhoff and Russel Palmer in this cycler technology.

In **1981,** José Diaz-Buxo proposed the continuous cyclic peritoneal dialysis (CCPD) that is now the most commonly used APD method. Here, excess water and toxins are removed from patients overnight using ten to 15 liters of dialysis solution. During the day, 1.5 to two liters of dialysis solution remain in the abdominal cavity.

NEW, BIOCOMPATIBLE PERITONEAL DIALYSIS SOLUTIONS

Dialysis solutions play an increasingly important role in peritoneal dialysis research and development.

In the **1920s,** Ganter used a physiological saline solution, to which glucose was later added.

In **1938,** Jonathan Rhoads began adding lactate to the solution to correct metabolic acidosis. This occurs if the kidneys are no longer able to eliminate acidic metabolic products. Lactate is still used to this day, but there are also PD solutions containing either pure bicarbonate or a mixture of the two substances – bicarbonate and lactate – to balance the acid-base status. As a substitute for glucose, dialysis solutions can also contain amino acids or glucose polymers.

In the early **1980s,** Axel Duwe for the first time discussed the effects of individual components of the PD solution on peritoneal efficiency in preventing infections. A few years later, the term "bio(in)compatibility" was coined to indicate the body's (in)tolerance of dialysis solutions. Studies showed that conventional PD solutions could inhibit the activities of key cells in the peritoneum and cause long-term damage to the membrane. This could lead to a gradual weakening of the peritoneal membrane and make it unsuitable for further use as a dialyzer.

More than
300,000
peritoneal dialysis patients worldwide

Conventional dialysis solutions have a low pH and a high concentration of glucose degradation products, both of which contribute to the bioincompatibility of solutions. The new generation of PD solutions, however, has a neutral to physiological pH and a significantly lower amount of glucose degradation products. This was made technically possible by developing the double chamber bag.

The solution in the first chamber contains electrolytes and glucose, while the second chamber holds a buffer solution. Filling, sterilizing and keeping the two solutions in two separate chambers prevents excessive formation of undesirable glucose degradation products.

The fascinating interaction between the ideas and determination of a great many pioneers and dedicated scientists is reflected in modern-day peritoneal dialysis. It is the leading form of home dialysis and gives patients the flexibility to integrate the treatment into their everyday life.

New, biocompatible peritoneal dialysis solution in a double bag

Fresenius Medical Care is the world's leading provider of products and services for patients with kidney disease, millions of whom are undergoing dialysis treatment. We look after hundreds of thousands of dialysis patients in our global network of dialysis centers. Fresenius Medical Care is also the leading provider of dialysis products such as dialysis equipment and dialysis filters. Additionally, in the field of Care Coordination, the company is expanding its portfolio of supplementary medical services related to dialysis.

Further information about our company and the history of dialysis can be found online at:

www.freseniusmedicalcare.com

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