

# THE THIRD NATIONAL KIDNEY FOUNDATION LECTURE CAPD — 1985

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Considering the fact that it is less than a decade since the concept of continuous ambulatory peritoneal dialysis (1) — now known as CAPD (2) — was described, it is truly remarkable that close to 20,000 patients with chronic renal failure are already being treated by this method world-wide (3, 4).

## INTRODUCTION

The modern era of peritoneal dialysis (PD) began when Boen published his results of treatment of a few patients in 1961 (5). Popularity was not widespread due to the need for repeated puncture of the peritoneal cavity and a staggering complication rate. Acceptance improved dramatically after 1968 when Tenckhoff described a chronic indwelling peritoneal catheter (6). Nevertheless, after ten years, only a few hundred patients were treated chronically by this method — very few by choice.

During this time, hemodialysis became feasible on a large scale due to tremendous technological advances. Smaller machines, disposable equipment, on-line water supply, improved biocompatibility of membranes and the economical benefits of mass production all contributed to the success of this form of treatment.

This was also the time when renal transplantation gradually became available to a larger population. Grafting was no longer restricted to identical twins, but large scale cadaveric transplantation was clearly spreading.

Intermittent peritoneal (IPD) dialysis was widely used in the treatment of acute renal failure in hospitalized patients, but very few people found it acceptable or attractive to dialyze 36 hours a week on IPD, even at home, when hemodialysis could be done in less than half the time in an outpatient center or at home.

Thus, in 1976, PD was barely used for chronic treatment except when transplantation and/or hemodialysis had failed. The WAK or wearable artificial kidney was thought of as a modified hemodialysis apparatus that the patient could carry as a back pack.

Things changed dramatically nine years ago, when Popovich and Moncrief described "The definition of a novel portable wearable equilibrium peritoneal dialysis technique" (1). Their concept of an intracorporeal form of treatment that could be applied chronically on an outpatient basis really stirred the imagination of clinicians. This is underscored by the subsequent explosive increase in research. Up until the mid 1970s, some 150 publications dealt with PD. Today more than one new publication is added to the PD literature every single day, most of them dealing with CAPD (7).

## CATHETERS

Access to the peritoneal cavity remains one of the cornerstones in the success or failure of any PD programme. Earlier, most catheters used in the U.S. were of the double cuff straight Tenckhoff type whereas single cuff catheters were used in many European centers. They were implanted often at the bedside, by nephrologists using local anesthetics only.

With CAPD, the demands for longevity have increased and the single cuff Tenckhoff, Toronto-Western, and Column disc catheters have gained in popularity.

Most catheters are now placed by surgeons. Whereas the bedside trocar technique was mainly applied to midline insertions below the umbilicus (8), it has been demonstrated that there are advantages to lateral placement through the bulk of the abdominal rectus muscle, such as better tissue ingrowth into cuffs and reduced leaks (9,10).

It is important to choose an exit site for the catheter before implanting it in order to avoid conflict with the patient's belt line and to make the subsequent dialysis as easy for the patient as possible. In this connection, it is important to realize that left-handed people may prefer a different exit from right-handed people.

The tunnel through which the catheter is placed serves three main purposes. First, it serves as an anchor around which the internal and external parts of the catheter are free to move. It is therefore essential that there is a tight fit between the soft tissues and the catheter. With the surgical technique, most people prefer to place a suture through the deep cuff and fascia covering the peritoneal cavity. Secondly, the tunnel must provide directional control for the intra-

peritoneal part of the catheters. Regardless of whether a straight or curved subcutaneous tunnel is preferred, the deep portion should always point straight towards the pelvis in order to avoid having the distal tip of the catheter float up towards the diaphragm, as this will impede drainage. Thirdly, the tunnel should serve to protect the peritoneum from intruding bacteria from the surface and prevent leakage of fluid in the opposite direction. This is only accomplished by soft-tissue ingrowth into the cuffs.

It is essential that the surgeon performing the catheter placement be very familiar with the objectives described. Meticulous attention must be paid to every detail of the insertion in order to obtain an access that will serve its purpose for years.

## THE PLASTIC BAG

It was definitely the advent of the plastic bag containing mass produced dialysis solution that made PD ambulatory (11). Today, several companies are offering a full line of dialysis solutions in plastic bags in sizes and content to meet almost any need from the smallest pediatric patient to the largest adult.

The dialysis solution itself has undergone very little change over the past 20 years. The basic principle is still a sodium chloride solution with glucose added to obtain the desired osmolarity, lactate added as a buffer, plus calcium and magnesium to prevent depletion of these substances. The solution is still autoclaved to insure sterility.

The great advantage of the plastic bag is its flexibility. After instilling the dialysis solution into the peritoneal cavity, the bag can be folded without opening the system, and can then be carried on the body without taking up more space than a small billfold, until it is time to drain.

## SELF CARE

Following the placement of the permanent indwelling catheter, most patients go through the so-called break-in period designed to maintain the patency of the catheter, facilitate the healing of the tissues, prevent leaks of dialysate around the newly implanted catheter and provide dialysis for control of uremia (12). If dialysis is necessary, the patient is kept in a supine position to minimize intraabdominal pressure. IPD is carried out starting no earlier than 24 hours post-surgery if at all possible using 500-1000ml volumes only. As the healing progresses, the volume of the dialysis fluid is gradually increased. Regular CAPD is generally not attempted until 10-14 days after catheter implantation.

The patient is trained on an outpatient basis immediately following the break-in period. Training usually lasts from 7 to 14 days. The patient learns to connect and disconnect bags to and from the tubing attached to the catheter using anti-septic technique which is essential to prevent the introduction of microorganisms into the system. The patient also learns to cope with problems that might arise from accidental disconnections or breakdown in the materials used.

Filling of the peritoneal cavity is accomplished by hooking up a fresh bag to the catheter and letting it flow in by gravity. When inflow is complete, the bag is rolled or folded as the individual patient prefers. The dwell time, which is the time the dialysate remains inside the peritoneal cavity, is usually decided by the number of daily exchanges, the time of day, and the specific individual needs of the patient. Outflow is;

accomplished by placing the unfolded bag in a position lower than the abdomen. A new cycle is then begun by disconnecting the old bag and immediately repeating the cycle with a fresh solution.

CCPD (Continuous Cycling Peritoneal Dialysis) which is a hybrid between CAPD and IPD uses only 1 bag hook-up every morning (13). The dialysis solution is then left in the abdomen all day and is only drained at night when the patient connects to a machine that automatically will do 4-6 short dwell cycles during the night.

The patient may also learn how to add medications or other sterile solutions to the bags through a separate port provided on every bag. Again, anti-septic technique is of utmost importance. Prime examples of substances added to the bag are insulin to control blood sugar in diabetics and antibiotics to treat peritonitis.

### DIETARY CONSIDERATIONS

The special considerations necessary in the dietary management of patients on CAPD all come from factors that are inherent to the technique (14). Protein loss averages 1 gram per liter of dialysate in steady state. With episodes of peritonitis losses increase substantially. Most of the protein lost is albumin, but even large molecular weight substances such as the immunoglobulins are lost during long dwell times. It is generally agreed that a positive nitrogen balance can be maintained with an average protein intake of 1.2 grams per kg body weight per day. Supplementation is needed as losses increase.

Water soluble vitamins are lost in the dialysate and must be replaced (15). This can conveniently be accomplished with folate containing multi-vitamin tablets.

Since glucose, which is used, as an osmotic agent in the dialysis solution is readily absorbed from the peritoneal cavity, less carbohydrate will be needed orally. Total recommended carbohydrate intake is usually one-third of the total calories. Adequate calorie intake is around 2,500 kcal per day for a 70 kilogram person.

For diabetics, intraperitoneal administration of insulin along with the glucose load offers a more physiological control of blood sugar. Tight blood glucose control without a high rate of hypoglycemic episodes is greatly facilitated by this approach.

Children treated with CAPD generally need much higher calorie and protein intake than do adults. As is the case with children in general, the requirement correlates inversely with age. The ultimate measurement of success with the dietary management of children on dialysis is normal growth including catch-up growth.

### COMPLICATIONS

Traditionally, the complications of CAPD have been divided into infectious complications which will be dealt with below and those that are not associated with infection (16).

Non-infectious complications can be divided in many ways. Drainage problems are associated with catheter migration.

Problems with dehydration or volume overload are not nearly as frequent as was seen with IPD. This is largely due to the continuous nature of the therapy and the option that the patient has of choosing a more or a less hypertonic solution for the next exchange according to the current fluid status.

Whereas, an entity like the dysequilibrium syndrome is unknown by virtue of the continuous treatment, other problems have surfaced. High levels of triglyceride has been seen in many patients probably as a result of the high glucose load. It has not been determined, however, what impact this and other metabolic abnormalities may have on morbidity and mortality, largely because of an insufficient number of patients and time of follow up. No treatment is presently advocated.

### PERITONITIS

Infectious complications remain a major cause of morbidity and treatment failure in CAPD (17). It is therefore of utmost importance that the diagnosis be established as soon as possible so that treatment can be initiated without delay. According to the USA National CAPD registry, more than 60% of patients started on CAPD will have had peritonitis by 12 month of therapy and more than 80% by 2 years (3). The diagnosis of peritonitis remains controversial but most centers subscribe to the definition outlined below. This has the distinct advantage of allowing early treatment, and thereby minimizing the need for hospitalization and limiting the number and severity of systemic complications. It is realized that a few patients will be treated without ever having had peritonitis. The cost and morbidity of treatment, however, is so low that it is negligible compared to the risk of letting just one episode go untreated for a few days.

As a matter of definition, at least two of the following three groups of criteria must be present in any combination to establish the diagnosis of peritonitis. Signs and symptoms not included in these three groupings are thought to be of no consequence in the diagnosis because they occur with low incidence and very little consistency. The criteria are 1) cloudy drainage and/or more than 100 white blood cells per cubic mm effluent, 2) abdominal tenderness and/or abdominal pain, and 3) positive culture and/or organism seen on fresh gram stain. It is noteworthy that symptoms such as fever, nausea, vomiting, diarrhoea, and constipation all occur so infrequently that they are of no use in establishing the diagnosis, although they may indicate a more severe course of infection. Once the diagnosis has been established, treatment is indicated (again as a matter of definition).

Greater than 90% of peritonitis episodes are usually bacterial, less than 5% are fungal, and, in experienced laboratories, usually less than 5% are culture negative (for instance, the so-called eosinophilic peritonitis). Roughly two-thirds of all infections are caused by gram positive organisms, while gram negative bacteria cause one fourth. *Staphylococcus epidermidis* remains the single most frequent causative organism.

Whereas the indication for treatment is automatically established by the diagnostic criteria, it remains a matter of debate as to the best treatment. Often initial treatment will be empiric as it may take up to 48 hours to get the offending organism identified and its sensitivity to antibiotics established. Treatment should be directed against the suspected agent either based on the individual centers experience with the most frequently occurring organisms or based on the type of organism seen in fresh gram stain (if any). The standard treatment for suspected bacterial peritonitis consists of the following: 1. Dialysate is immediately drained from the abdomen. Specimens are taken for gram stain, cell count and differential. Specimens are prepared for culture and sensitivity in the manner appropriate for the particular laboratory.

2. Three rapid in and out exchanges are carried out to rinse out debris from the peritoneal cavity. 3. Heparin is added in a concentration of 500 to 1,000 international units per liter to every bag used until the effluent is clear. 4. Antibiotics are added to solutions according to the type of organism encountered, or if unknown, initial therapy is governed by the particular center's standard protocol. In our center, we use a loading dose of 250 mg of cefazolin per liter combined with a loading dose of 1.7 mg per kg body weight of tobramycin. Maintenance doses in subsequent bags are kept at 125 mg of cefazolin and 8 mg of tobramycin per liter of dialysis fluid. Treatment is continued for a total of 10 days. 5. Treatment is adjusted according to the result of culture and sensitivity.

Bacterial peritonitis usually responds very rapidly and very well to the treatment outlined above. Hospitalization is not routine and the whole procedure of diagnosing and treating peritonitis is part of the patient's basic training. However, if there are exceptions to this course, patients should be promptly admitted for further evaluation. If a tuberculous or fungal peritonitis is diagnosed, the treatment of choice is removal of the catheter and discontinuance of the standard antibiotic therapy. Patients will have to be switched to another mode of treatment at least until the infections are eradicated. If more than one organism is encountered, one should suspect intestinal perforation. This is mainly seen with diverticular disease of the large bowel, and one should be aware that continued peritoneal dialysis with antibiotics may mask the extent of the problem, and that early surgical evaluation is indicated. It should be remembered that bonafide surgical conditions like perforated gastric ulcer, cholecystitis, pancreatitis, or appendicitis may all present as CAPD peritonitis. Simple constipation may also give rise to similar symptoms. Meticulous attention to any deviation from the usual pattern should facilitate early diagnosis and correct treatment in these cases.

Local infection around the site where the catheter exits the skin is a frequent occurrence in CAPD patients and is known as exit site infection. It is often diagnosed on routine check-up. It usually presents with redness and variable tenderness around the catheter and pus can usually be seen around the catheter. It is essential to keep the area well drained, and to obtain a culture of the material without contaminating the specimen with patient's normal skin flora. Treatment consists of appropriate exit site care with drainage and antibiotics as necessary. Topical antibiotics are not recommended.

If the infection is extending deeper than the outer cuff or deeper than 1-2 cm with only a single internal cuff, the diagnosis of a tunnel infection can be made. Treatment problems with tunnel infection are related to the poor tissue penetration of the antibiotics used in treating peritonitis and the presence of a foreign body in a confined area. If intensive treatment with appropriate agents fails to resolve the infection, catheter removal may become necessary. Usually the patient will then have to be maintained on a different kind of therapy for a couple of weeks until a new catheter can be placed electively.

Although mortality from peritonitis and associated infectious complications is very low, it is a very frequent cause of treatment failure. There is evidence to suggest that the rate of infectious complications decreases with the experience of a particular center (3). Meticulous attention to detail and accurate execution of the procedures are key elements in avoiding

infections. No effective prophylaxis is known, and routine use of antibiotics is not recommended.

Prevention is as always a key to success.

## RECENT DEVELOPMENTS

In the last few years there has been growing concern in Europe over loss of ultrafiltration in an increasing number of patients (18-20). An International Ultrafiltration Survey has been initiated (21) and preliminary results indicate a higher rate of glucose absorption as well as lower ultrafiltration in patients dialysed with acetate as a buffer as compared to patients using lactate. With rapid glucose absorption the osmotic gradient across the peritoneal membrane dissipates quickly and the patient can no longer sustain adequate ultrafiltration using four to eight hour dwell times. This has made change of therapy necessary in some cases.

Encapsulating peritoneal sclerosis (most commonly known as sclerosing peritonitis, even though the role of infectious peritonitis has not been established) has likewise been reported from a number of European centers (22). This serious condition associated with loss of ultrafiltration, is characterized by solid fibrous encasement of the bowel and gross thickening of the peritoneal membrane leads to mandatory termination of peritoneal dialysis. It carries a high morbidity from the intestinal complications and has been seen almost exclusively in patients dialysed with European made dialysate, mainly the variety containing acetate as a buffer. Despite longer experience with more patients, no North American center has reported any significant incidence of these problems.

Whether acetate itself can be implicated as the offending agent remains doubtful. Our own animal studies were able to reproduce the clinical findings, but not with every acetate-containing solution (23). Contaminants, plasticizers and infections may also play important roles. With more information, a multifactorial origin seems more likely.

Early detection of peritonitis remains a clinical enigma. It is generally accepted that 12-48 hours elapse from onset of infection to the first clinical symptoms. To minimize not only the systemic effects and complications but also the damage to the peritoneal membrane, rapid detection and treatment is a *sine qua non*. Most methods try to identify an increased number of white blood cells or bacterial by-products in the dialysate (24, 25). However, so far no test has proven sensitive, specific and inexpensive enough, to enable or justify routine testing of every single bag of dialysate as it is drained. Such immediate testing would be needed to achieve the goal of early diagnosis and treatment in order to reduce membrane injury. It should be stressed however, that it is unknown whether even multiple uncomplicated infections cause any clinically important permanent damage to the peritoneum (26).

Glucose as an osmotic agent has certain drawbacks. The extra calories lead to weight gain, sometimes even frank adiposity. Triglyceride blood levels are commonly elevated (27) and a few patients have very high levels. Even though accelerated arteriosclerosis and increased cardiovascular morbidity have not yet been proven (28, 36) there is reason to be concerned. Because of this alternate substances have been looked for.

The ideal osmotic agent should be non-absorbable, non-metabolizable, atoxic, sterile and inexpensive. It should also be able to generate sufficient ultrafiltra-

tion over the dwell times utilized in CAPD and CCPD i.e. 3-12 hours.

So far no such agent has been identified, but promising results have been achieved in preliminary animal studies (29, 30). There is little doubt, that alternatives to the classical PD solutions will be available for clinical use within a few years.

### CHOOSING A THERAPY

When ESRD ensues, there are now three different approaches to treatment.

Transplantation was thought to be the ultimate therapy, and living related donor transplantation indeed has a very high rate of success. However, the increasing number of diabetics and the increasing age of the ESRD population raises very real problems. Even with cyclosporin A, there is significant morbidity and mortality with cadaveric transplantation.

Hemodialysis and all its variants is still the most common mode of therapy. It offers well proven results, and great flexibility. People capable of self care can perform treatment in their home, and with sorbent cartridges travel is feasible. Limited care centers offer assistance when the patient is in need of a helping hand. Hospital or center dialysis is widely available for those who need the most care. The problems with vascular access, heparinization, metabolic and volume instability, osteodystrophy and aluminum toxicity just to mention a few, are well-known to us all.

CAPD is by definition a home care — usually self care therapy. Next to a functioning kidney it offers the greatest versatility and flexibility known. Because of its continuous nature, the patient is not subjected to intermittent fluctuations in volume or azotemia. Because of the membrane, CAPD is six times better at removing middle molecules than is hemodialysis.

CAPD is well suited to sparsely populated areas, because only a few visits to the outpatient clinic (center) will be needed in a year.

Blind people have been trained successfully to self care with CAPD, and with the availability of simple assist devices, people with other physical handicaps need not be excluded from this therapy. Blood sugar control seems superior in diabetics (31, 32) on CAPD, and preservation of vision is at least as good as with other modes of dialysis.

CAPD is rapidly becoming the preferred mode of dialysis for children and infants with ESRD (33). The need for vascular access, repeated needlesticks and use of machines is obviated, and a much more appropriate diet can be employed (36), in an attempt to normalize development. Treatment can be managed by the parents at home in their usual environment.

These three modes of ESRD treatment are by no means mutually exclusive but rather they compliment each other nicely. It gives the patient — and the physician — a choice. The preference may change with time, and transfer from one therapy to another may be the answer, if a patient does not do well on the current treatment.

How the different forms of treatment compare over long periods of time is not yet known. Short term survival compares very favorably for CAPD, even in some high risk categories. Sources of this kind of information will be for instance the U.S. National CAPD Registry (3) and the European Dialysis and Transplant Association (EDTA) (4). With the establishment of the International Society for Peritoneal Dialysis in 1984 (35), world wide data could soon become available for comparison.

Quality of life remains the ultimate measure of success. What is right for one may not be right for all, and what is right may change with time. We believe that CAPD has increased the possibility substantially for a good quality of life for some of the ESRD population.

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