

Bradley A. Warady
Franz Schaefer
Steven R. Alexander
Editors

Pediatric Dialysis

Second Edition

 Springer

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*We thank our families for the support they provide us.
We thank our colleagues for the insight they share with us.
We thank our patients for the trust they have in us.*

The editors

Preface

The provision of optimal dialysis therapy to children requires a thorough understanding of the multidisciplinary manner in which the pediatric patient is affected by renal insufficiency. It was based on this philosophy that the inaugural edition of *Pediatric Dialysis* was published in 2004. Since that time, advances have taken place in dialysis-related care with the creation of a wealth of new knowledge, outpacing much of the content that occupied a prominent place in the original text. In response, we believe that even in this age of the electronic transmission of information, the availability of a contemporary, comprehensive, and authoritative source of information such as *Pediatric Dialysis* cannot only help facilitate the provision of superb patient care by seasoned clinicians, but it also can help meet the demand of our young trainees for the information that they require as a foundation for the future advances that they will surely initiate.

We are, in turn, fortunate to have been able to enlist the collaboration of over 70 colleagues from North America, Europe, and Asia to thoroughly update this text, which remains the most comprehensive source of state-of-the-art information on the dialysis of infants, children, and adolescents currently available. To them, we are eternally grateful for their commitment to this project. The inclusion of a host of new authors from “both sides of the pond” with their unique and fresh perspectives, combined with many authors from the first edition and all with recognized expertise on the topic chosen for their review, has resulted in a text that is clinically relevant and that will someday hopefully duplicate the appearance of one of the initial editions, owned by a dialysis nurse and characterized as being “full of worn pages as a result of almost daily use.” The addition of several new chapters, including *Conservation of Residual Renal Function in Children Reaching End-Stage Renal Disease*, *Intensified Hemodialysis in Children*, and *Transitioning the Adolescent Dialysis Patient to Adult Care*, should contribute to that end.

As clinicians ourselves who have spent many hours over the past three decades on hospital wards, in the intensive care unit, and in the dialysis unit applying what we have learned from the documented experience of others, we know that this text is undoubtedly the product of the hard work and ingenuity exhibited by the global pediatric nephrology community and, as such,

cannot help but to serve as a valuable tool with a singular emphasis on successfully caring for our challenging patient population. If that goal can be achieved through the publication of the second edition of *Pediatric Dialysis* and even one child benefits from our combined efforts, it will all have been worthwhile.

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Part I

Essential Primers

Notes on the History of Dialysis Therapy in Children

1

Steven R. Alexander and Pierre Cochat

Key Words

Dialysis therapy • Children • History

Introduction

In his authoritative and entertaining monograph on the history of dialysis, Stewart Cameron calls attention to the important role played by the development of dialysis technology in the founding of nephrology as a medical specialty [1]. Prior to the 1950s and 1960s, the study and management of disorders of the kidney was the province of general physicians. Along with the introduction of the renal biopsy and its interpretation [2], the introduction of dialysis was "...an important motor which accelerated the emergence of nephrology as a specialty. Suddenly there was a need for specialist knowledge to apply the complex data from the increasing number of critically ill patients who survived their primary disease only to go into acute

renal failure..." [1]. When long-term dialysis became possible in the 1960s, hundreds of units sprang up in North America and Europe spawning a new breed of physicians who "...trained frantically to run them..." These physicians adopted a culture that was more "active" than the traditional contemplative approach of medicine specialties, and by the 1970s, nephrology had become "...an autonomous specialty with an uneasy relationship to general internal medicine. There is no doubt that those physicians who chose to make dialysis their principal interest were to some extent a breed apart, with whom physicians in general found it difficult to relate..." [1].

In contrast, the discipline of pediatric nephrology emerged in response to different drivers. Based on the classic work of pediatric physiologists on fluid and electrolyte metabolism, regulation of intracellular and extracellular fluid, acid-base homeostasis, and parenteral fluid therapy, the first generation of pediatric nephrologists who arose in the 1950s and 1960s were rarely exposed to the care of children with acute or chronic renal failure [3, 4]. It is emblematic that the early starting point of pediatric nephrology as a specialty is traced by some to the organization of the International Study of Kidney Disease in Children (ISKDC) in the 1960s, which was a study of childhood nephrotic syndrome [1]. Early pediatric nephrologists rarely

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cared for children suffering what is now called acute kidney injury (AKI), a role more often played by pediatric surgeons. Those who cared for children with what is now known as chronic kidney disease (CKD) focused on dietary restrictions and diuretic, antibiotic, and electrolyte therapies, attempting to ease the progression to end-stage renal disease (ESRD). When ESRD was reached, older children and adolescents often had to look to adult ESRD programs for access to chronic dialysis and transplantation; infants and younger children were frequently offered only palliative care [5].

During the past five decades, the landscape has changed dramatically. Acute and chronic dialysis is now routinely available for children throughout the world, and the study of dialysis therapy and the disordered physiology of the pediatric patient with AKI or ESRD has come to occupy a prominent if not dominant place in pediatric nephrology research [4]. Pediatric nephrology training programs worldwide are expected to teach trainees how to dialyze children of all ages, and modern pediatric nephrology training program graduates come equipped with technical skills unimagined by the founders of the specialty. With increasing acceptance of universal access to dialysis therapy for children has come a concomitant growth in the demand for pediatric nephrologists, leading to a steady increase in the size of pediatric nephrology programs. Unlike adult dialysis programs, many of which long ago separated from their academic roots, pediatric dialysis programs remain firmly grounded in university medical centers and medical school-affiliated children's hospitals, a fortunate association that has promoted, sustained, and demanded a culture of scientific inquiry in what easily could have become a purely technical and derivative discipline.

In this chapter, we have attempted to briefly review selected high points in the development of dialysis therapy for children. We have left to the chapters that follow a detailed description of these innovations. Our goal is to place them in historical context, acknowledging the debt owed to those pioneering pediatric nephrologists, nurses, engineers, dieticians, and social workers and their young patients whose efforts have helped make a complex and life-sustaining therapy a part of routine medical management for children throughout the world.

Dialysis: The Founding Fathers

The term *dialysis* has both Latin and Greek roots and refers to a separation or dissolution: (from *dialyein* – to separate; *dia* – apart; *lyein* – to loose) [6]. The modern understanding of the term is the result of the work of a Scottish physical chemist, Thomas Graham (1805–1869) who redefined *dialysis* to reflect his newfound understanding of the ability of a semipermeable membrane (Graham's own concept) to separate solutions containing a crystalloid from a colloid [7]. Using sheets of vegetable parchment impregnated with starch as the membrane, Graham observed that some substances (e.g., sugars) crossed the membrane and would crystallize on drying, while larger molecules like gum arabic would remain in the original solution. Based on his own discovery of the laws governing diffusion of gasses, Graham realized that the crystalloid molecules moved by the force of diffusion across the membrane which prevented the movement of larger molecules. For this work, Graham is known as the “father of modern dialysis” [8].

Earlier work by a Frenchman, Rene' Dutochet (1776–1847) introduced the term *osmosis* to describe the movement of water down concentration gradients of salts across membranes that retard the movement of solutes. Dutochet's *osmotic pressure* forms the basis of osmotic-induced ultrafiltration and has earned him the sobriquet, “grandfather of dialysis” [9].

Application of these principles led scientists in the late nineteenth century to explore the use of semipermeable membranes in the laboratory to investigate the properties of many substances. Animal membranes were popular, including the peritoneal membrane (of calves), but the concept was limited to separation and purification of substances. Beginning with the animal experiments of John Jacob Abel (1857–1938) and his team in Baltimore, the early twentieth century saw much progress in the ability to perform dialysis in living animals. In 1913, Abel's team built an apparatus using hollow collodion tubes encased in a glass cylinder that foretold the design of modern hollow fiber dialyzers. They called the process

“vividiffusion” and were the first to conceive of dialysis as a means of removing “...substances from the blood whose accumulation is detrimental to life...” [10]. However, clinical application of these techniques would be delayed until mid-century when both hemodialysis (HD) and peritoneal dialysis gained traction as treatments for renal failure in humans.

Peritoneal Dialysis

The roots of the use of peritoneal dialysis (PD) in children can be traced to the use of the peritoneal cavity to treat dehydration in infants. In 1918, two Johns Hopkins pediatricians, Kenneth Blackfan and Kenneth Maxcy, first described the successful fluid resuscitation of dehydrated infants using intraperitoneal injections of saline solution [11]. At that time, dehydrated infants too small or dehydrated to permit intravenous access, were treated by injecting fluids into the subcutaneous tissues (“clysis”), a method Blackfan and Maxcy noted was often “disappointing,” because “...absorption from the subcutaneous tissues is often very slow and after repeated injections is almost nil...” Injection of physiologic sodium chloride solution directly into the peritoneal cavity was “...simple...practicable and accompanied by a minimum of risk to the patient...” [11]. These same characteristic features, simplicity, practicality, and safety, have made peritoneal dialysis particularly well suited for use in children for the past 60 years.

The first reports of the use of the peritoneum to treat children with renal failure appeared in 1948 [12] and 1949 [13] at a time when worldwide reported clinical experience with PD totaled only 100 patients [14]. These first pediatric acute PD reports are of interest in part because they describe in arresting detail many of the problems that have continued to complicate the use of PD in children.

Writing in the premier issue of the journal *Pediatrics*, a pediatrician, Allan Bloxsum, and his urologist colleague at Houston’s St. Joseph’s Hospital, Norborne Powell, described the treatment of an oliguric 10-year-old boy who suffered

acute glomerulonephritis complicating scarlet fever. Severely hypertensive, fluid overloaded, and becoming increasingly cyanotic, “...it appeared that the boy was going to die...” [12]. Modeling their technique on methods first described in adults in 1946 [15], Bloxsum and Powell had #30 Fr. mushroom catheters surgically placed into the right and left lower quadrants to serve as irrigating tubes. The irrigating solution was mammalian Tyrode’s solution, then in common use as a surgical irrigant. It contained sodium, potassium, chloride, magnesium, phosphate, bicarbonate, and dextrose in near-physiologic concentrations, along with penicillin (only 5,000 units/L), sulfadiazine, and heparin. Fluid from 1-L autoclaved flasks was dripped continuously at 10 mL/min into one catheter while being drained by gravity from the other. Peritoneal lavage was continued for 4 days, during which the patient’s azotemia worsened, but enough ultrafiltration occurred to improve blood pressure from 186/130 to 148/105. Fortunately, a spontaneous diuresis began almost immediately, and by the third day of treatment, the boy had begun to recover. During lavage, the drainage catheter often became obstructed requiring reversal of flow through the two catheters and eventual application of suction to the drainage line. By the fourth day, the system would no longer drain at all, with fluid leaking freely around both catheters. Peritoneal fluid cultures were positive for three organisms, which may have been contaminants, as the boy did not display signs of clinical peritonitis. Although Bloxsum and Powell entitled their paper: “The treatment of acute temporary dysfunction of the kidneys by peritoneal irrigation: Successful treatment of a 10-year old male child,” the contribution of peritoneal irrigation to the child’s successful recovery is questionable.

The 1949 experience of Henry Swan and Harry H. Gordon was more promising [13]. These pioneering Denver pediatric surgeons employed continuous peritoneal lavage to treat three acutely anuric children, 9 months, 3 years, and 8 years of age. Rigid surgical suction tips covered by metal sheaths with multiple perforations were implanted into the upper abdomen and pelvis allowing large volumes (~33 L/day) of sterile, physiologic

Tyrod's solution to flow by gravity from 20-L carboys continuously into and out of the abdomen. Ultrafiltration was controlled by adjusting the dextrose concentration between 2% and 4%, while dialysate temperature was regulated by changing the number of illuminated incandescent 60-W lightbulbs in a box placed over the inflow tubing. The two older children regained normal renal function and survived after 9 and 12 days of peritoneal lavage; the infant was sustained for 28 days, but did not regain renal function and succumbed to obscure complications. Peritonitis occurred only once and responded to intraperitoneal antibiotics. Removal of urea and maintenance of fluid balance were successful in all three children, although obviously herculean efforts were required to deliver this therapy [13]. Although impractical and technically difficult to deliver, the continuous peritoneal lavage of Swan and Gordon should be credited as the first conclusive demonstration of the lifesaving potential of PD when used to treat acute renal failure in children.

It was more than a decade before the use of PD in children was again reported. During the 1950s and early 1960s, the development of disposable nylon catheters [16] and commercially prepared dialysis solutions led to the replacement of continuous peritoneal lavage techniques with intermittent forms of PD, allowing the routine use of peritoneal dialysis as a treatment for AKI and some intoxications in adults [17]. These methods were adapted for use in children in the early 1960s by teams in Indianapolis and Memphis [18, 19] who also showed how PD could be effective in the treatment of the boric acid and salicylate intoxications commonly seen in small children at that time [20, 21]. Subsequent reports established PD as the most frequently employed renal replacement therapy (RRT) for AKI in pediatric patients [22–28]. Compared to hemodialysis (HD), PD appeared ideally suited for use in children. It was intrinsically simple, practical, safe, and easily adapted for use in patients of all ages and sizes, from premature newborn infants to fully grown adolescents. In contrast, HD at this early stage of development required large extracorporeal blood circuits and vascular access that was difficult to achieve and maintain in pediatric patients (see later in this chapter).

Although successful as a treatment for AKI, early PD techniques were poorly suited for the child with end-stage renal disease (ESRD). The need to reinsert the dialysis catheter for each treatment made prolonged use of PD in young patients problematic. In the largest published pediatric series from the disposable catheter period, Feldman, Baliah, and Drummond maintained seven children, ages 6–14 years on intermittent peritoneal dialysis (IPD) for 3.5–8 months while awaiting transplantation. Treatments were infrequent, ranging from every 7–12 days to every 4–12 weeks. Although complications were few, at the time of the report, two children had died, two had been transferred to hemodialysis, and three remained on IPD; no child had been successfully transplanted [29].

More than any other advance, it was the development of a permanent peritoneal catheter that made long-term PD an acceptable form of treatment for pediatric patients. First proposed by Palmer, Quinton, and Gray in 1964 [30] and later refined by Tenckhoff and Schechter in 1968 [31], the permanent PD catheter revolutionized chronic PD for adults and children in the same way the Scribner shunt transformed chronic hemodialysis, making long-term renal replacement therapy possible. In Seattle, the new permanent peritoneal catheters were combined with an existing automated dialysate delivery system that had been designed by Boen, Mion, Curtis, and Shilipetar for use in the home [32, 33]. In the early 1970s, this work culminated in Seattle in the establishment of the first pediatric chronic home PD program [34]. The success of the Seattle program throughout the 1970s showed that chronic IPD could be a practical option for some children with ESRD [35].

Additional limited experience with chronic IPD was reported from several other pediatric centers [36–39], but enthusiasm for the technique was limited. Chronic IPD seemed to involve many of the least desirable features of chronic HD, including substantial fluid and dietary restrictions, immobility during treatments that lasted many hours, and the need for complex machinery requiring parental or nursing supervision, without providing the one great advantage of HD: efficiency. Moreover, it became clear from efforts

to maintain adult ESRD patients on chronic IPD that long-term technique survival was not often achieved [40]. Inadequate dialysis and frequent peritonitis were cited as the most common causes of IPD failure in the 1970s, leading to widespread reliance on HD among adult dialysis programs and limited access to chronic RRT for children, especially infants. In fact, pediatric dialysis and transplant programs at the time routinely excluded infants and small children, reasoning with Hurley that "...although it is technically possible to perform hemodialysis and transplantation in these children, the myriad of well-known problems... should contraindicate such therapy ..." [41], and with Reinhart: "...we may find the price the child pays for life too great..." [42]. During a period in which advances in ESRD therapy pushed the upper age limits for successful therapy well into the seventh and eighth decades, the youngest ESRD patients remained therapeutic orphans, considered by many to have severely limited chances for survival [43, 44].

The description of what became known as continuous ambulatory peritoneal dialysis (CAPD) by Robert Popovich and Jack Moncrief and associates in 1976 heralded a new era in the treatment of ESRD in children [44]. As originally described, 2 L of dialysate were infused into an adult and retained for 4–5 h, then drained and repeated a total of five times per day while the patient went about regular daily activities [45]. As early experience with CAPD in adults was analyzed by pediatric nephrologists it became clear that this new modality offered theoretical advantages to children when compared to HD and IPD that included near steady-state biochemical control, no disequilibrium syndrome, greatly reduced fluid and dietary restrictions, and freedom from repeated dialysis needle punctures. CAPD allowed children of all ages to receive dialysis at home, which offered a more normal childhood. And for the first time, CAPD made it possible to routinely provide chronic dialysis for infants and small children, which meant that this population could now be safely maintained on CAPD until they reached transplantable age and size.

The first child to receive CAPD was a 3-year-old girl in Toronto in 1978 [46, 47]. Although a number of pediatric dialysis programs in North

America [48–51] and Europe [52, 53] quickly followed suit, enthusiasm in many areas was tempered by the availability of dialysis fluid only in 2,000-mL containers. In Canada, small-volume plastic dialysis fluid containers were provided by Baxter, Inc. soon after the first pediatric CAPD patients were trained there in 1978, but it would be another 2 years before small-volume containers became available in the United States and much of the rest of the world [54].

During the 1980s, the popularity of CAPD for children spread worldwide [55]. In Japan, where transplantation was less common due to religious prohibitions on organ donation, Masataka Honda and other pioneers established large CAPD programs that demonstrated the long-term capabilities of the modality in children [56]. Pediatric nephrologists in developing countries soon realized that CAPD was relatively affordable, which meant that ESRD was no longer an inexorably lethal condition for children from families with limited resources [57–59]. And throughout the world, the survival of so many more children with ESRD increased the demand for the multidisciplinary pediatric specialists required to care for them.

The next big step in the evolution of PD for children was the resurgence of automated cycling machinery. As we have seen, during the 1960s and 1970s, automated PD machinery was used to deliver chronic IPD, but treatments were infrequent, with patients often receiving three PD treatments per week, usually for 12 h overnight. Following the success of CAPD, in the early 1980s quality of life issues made a revival of interest in automated PD inevitable in those countries that could afford it. The CAPD technique required interruption of daily activities several times each day for dialysis exchanges; how much easier and less intrusive it would be to relegate dialysis to nightly exchanges performed by automated cyclers while the patient and family slept.

The first reports of an automated dialysis fluid cycling device adapted to provide "continuous" cycler PD (CCPD) were published in 1981 by groups in Charlotte, North Carolina and Houston, Texas [60, 61]. The technique maintained the principle of continuous PD by cycling dialysate exchanges through the night and leaving an exchange in place during the day. CCPD was first

shown to work in a pediatric patient by the Houston group in 1981 [61]. Soon CCPD became extremely popular among pediatric dialysis programs in developed countries worldwide [62–66].

During the late 1980s improvements in renal transplantation increased renal allograft and patient survival rates so dramatically in children that all forms of dialysis were viewed even more as a bridge to get children safely to or between kidney transplants [62]. The ready availability of potent vitamin D analogues, ESRD-friendly phosphate binders and nutritional supplements and formulas, controlled enteral nutrition via gastrostomy or nasogastric tubes, recombinant human erythropoietin, and recombinant human growth hormone (see Chaps. 22, 23, 25, and 27) gave pediatric nephrologists a powerful armamentarium with which to bring the child on chronic dialysis safely to transplantation in optimal condition – well nourished, normally grown, with minimal renal anemia and bone disease. Attention could then be turned to quality of life issues, scholastic and emotional development, and child and family psychosocial adjustment to the rigors of ESRD and chronic dialysis (see Chaps. 29, 30, and 33).

Before 1982, fewer than 100 pediatric patients had been treated with CAPD worldwide, and CCPD for children was virtually unknown. During the ensuing three decades, continuous forms of PD became available in pediatric dialysis centers throughout the world. Regional, national, and international multicenter study groups and registries developed during this period have since added much to our knowledge of peritoneal dialysis in children [63–67]. These efforts have spawned an extensive series of clinical guidelines and treatment options that will be discussed in many of the chapters that follow.

Hemodialysis

The clinical use of an “artificial kidney” was pioneered in 1944 in adult patients suffering from acute renal failure by Willem J (“Pim”) Kolff [68], a Dutch physician in Nazi-occupied Holland during the Second World War. Kolff’s interest in dialysis grew from his experiences caring for

young patients with renal failure for whom treatment options were essentially nonexistent at that time [69]. Prior to Kolff’s remarkable invention, the stage had been set for the introduction of an extracorporeal dialysis device by the availability of two key elements: heparin and cellophane.

Heparin was first purified from an extract of liver tissue in 1916 by a second year medical student at Johns Hopkins, Jay MacLean, working in the laboratory of a prominent hematologist, William H. Howell [70]. Heparin rapidly replaced hirudin, a naturally occurring, but often toxic anticoagulant extracted from the heads and gullets of leeches.

The basis for cellophane is cellulose, a substance first purified from wood in 1885. Cellophane had been available since 1910 as sheets of cellulose acetate used in the packing industry, but it had the necessary qualities of a good dialysis membrane: It could be easily sterilized without injury to the material and had a long shelf life. When cellophane tubes became widely available as sausage casings in the 1920s, studies in animals showed the casings also made excellent diffusion membranes [71]. Clinical application of cellophane and heparin in the construction of a dialysis device awaited Kolff’s invention of the rotating drum kidney in 1944.

Pediatric application of the Kolff artificial kidney was first reported in 1950 by John Merrill and his colleagues in Boston who included a 3½-year-old boy with nephrotic syndrome in their initial series of 42 adult patients dialyzed using a rotating drum machine essentially the same as Kolff’s original design [72]. As described by Merrill:

Blood is led from the radial artery by means of an inlying glass cannula through a rotating coupling to the surface of a revolving metal drum. Here it passes through a length of cellophane tubing (~20 meters) wound spirally around the drum, and is carried by the motion of the drum to the distal end. During its course, the blood-filled tubing is passed through a rinsing fluid maintained at a constant temperature of 101 degrees F in a 100 liter container. Into this medium, diffusion from the blood takes place through the cellophane membrane. Distally, the blood is passed through a second rotating coupling, and pumped to inflow flasks, whence it is fed by gravity to a vein in the forearm through another inlying cannula. [72]

Merrill's pediatric patient received a single 4-h dialysis treatment and was said to have had "...modest improvement, but of short duration..." [72].

In 1955, FM Mateer, L. Greenman, and T.S. Danowski described their experience at the Children's Hospital of Pittsburgh with eight hemodialysis treatments in five severely uremic children, 7–15 years of age, all of whom were "...either stuporous or confused... overbreathing present in three of the five... (one child) had developed pulmonary edema, and convulsions had appeared in (two children)..." [73]. Their equipment was built by the Westinghouse Company based on an Alwall coil kidney design [74]. Alwall's coil kidney in effect turned Kolff's rotating drum on its end submerging the coils of cellophane tubing completely in the dialysate bath. Mateer's version of the coil kidney was more compact than the Kolff machine, consisting of ~15 m of $1\frac{1}{8}$ in. cellophane tubing wound on stainless steel screens submerged in a warmed 32 L bath of dialysate. An in-line roller pump propelled heparinized blood through the tubing from radial artery through the cellophane coils to return via the saphenous vein. Dialysate consisted of Pittsburgh tap water to which were added sodium, calcium, chloride, bicarbonate, glucose, and variable amounts of potassium; a fresh batch was mixed every 200 min, and with every bath change an antibiotic (usually oxytetracycline) was injected into the tubing leading to the artificial kidney [73].

For these severely uremic children, dialysis was clearly a heroic treatment that was surprisingly effective, if only temporarily. After treatments lasting 2–13 h, all patients became more alert, pulmonary edema and overbreathing improved, phosphorus levels fell, and blood nonprotein nitrogen levels decreased from an average of 231 to 113 mg/dL. Two of the five children survived, one recovering normal renal function after an episode of what may have been hemolytic uremic syndrome ("...previously well...bloody diarrhea...oliguria, albuminuria, profound anemia..."). Mateer concluded that,

while dialysis had been successful in supporting this child's reversible ATN, "...in view of the difficulty in assessing elements of reversibility of renal failure in chronic states, more frequent use of dialysis is indicated in these situations..." [73].

In 1957, Frank H Carter and a team at the Cleveland Clinic that included Willem Kolff, who had emigrated to the United States in 1950, next described eight hemodialysis treatments in five children (2–14 years of age) using an improved disposable Alwall twin coil kidney that could be modified for children <20 kg by using only one of the two coils, thereby reducing priming volume from 750 to 400 mL [75]. The coils sat in the warmed rinsing bath with rinsing fluid circulating over the blood-filled cellophane tubing. Vascular access was via a large-bore polyvinyl catheter inserted into the inferior vena cava via a saphenous vein cutdown with return of dialyzed blood to a large vein in the arm. Roller pump speed was 200–400 mL/min. Catheters remained in place until the child died or recovered sufficient renal function to no longer need dialysis [75].

Four of the five children survived, including a 2-year-old boy with probable acute glomerulonephritis who presented anuric with a blood urea nitrogen (BUN) of 322 mg/dL. Carter noted that "...in the hands of a well-trained team, hemodialysis is not only helpful in producing a smoother course in these children, but it may also be life-saving..." [75].

Unlike the concise and constricted prose demanded by modern journal editors, the papers by Mateer and Carter published 50 years ago are wonderfully detailed, conveying the intensity and drama that must have attended these early hemodialysis sessions. While some laboratory testing was available, management decisions relied primarily on clinical judgment. Presaging modern use of aggressive RRT in critically ill children, Mateer concluded that:

...the relative safety of the procedure (hemodialysis) warrants an increased use in uremic patients whose prognosis has been considered hopeless, with the goal that time will thereby be provided for recovery for those who have reversible lesions... [73]

Intoxications with salicylates or barbiturates represented another potential use for hemodialysis in children [76], but while potentially lifesaving in cases of reversible AKI or intoxications, the role of periodic hemodialysis in the management of irreversible renal failure in children faced daunting technical challenges, the first of which was the absence of a reusable vascular access. This problem was first solved in 1960 by Belding Scribner and the team in Seattle with the development of a Teflon(R)-silastic shunt that still bears his name [77]. The Scribner shunt consisted of silastic-teflon cannulas inserted in the radial artery and a nearby forearm vein that were connected to each other between dialysis treatments and could be separated and connected to the arterial and venous tubing of a dialysis apparatus. Smaller versions of the Scribner shunt were soon adapted for use in children [78], and by the mid-1960s the availability of repeated vascular access via these shunts made chronic hemodialysis in children a reality.

Using a pumpless system developed for pediatric patients by Robert Hickman and Belding Scribner in Seattle in the early 1960s [79], the first large pediatric chronic hemodialysis programs were established in Seattle [80], San Francisco [81], Los Angeles [82], Minneapolis [83], London [84], and Paris [85].

The San Francisco experience is illustrative of the problems encountered and overcome by these pioneering pediatric centers during this early period so critical to the successful adaptation of chronic hemodialysis for children. In a report summarizing their initial experience from 1966 to 1969, Donald Potter and his associates at San Francisco General Hospital described the chronic hemodialysis of 14 children 2–16 years of age weighing 10–52 kg [81]. Time on dialysis ranged from 1 to 27 months, with five children receiving dialysis at home. For the first 3 years of the pediatric dialysis program, children were selected for dialysis in competition with adult patients by a committee, a stark reminder of the earliest days of chronic hemodialysis when the scarcity of this resource forced painful decisions into the hands of so-called “Life and Death Committees” [86]. By 1969, a separate pediatric unit had been created in San Francisco, and children were accepted “...

on a first-come, first served basis if they were medically stable...” [81].

Using the Seattle pumpless method [79], Potter’s patients were dialyzed thrice weekly primarily using the recently introduced flat plate dialyzers and an automated dialysate delivery system. The basic flat plate device, known as a Kiil kidney [87], consisted of two grooved polypropylene plates separated by a sheet of cellophane clamped tightly together. Blood flowed through the enclosed dialyzer down the grooves on one side of the cellophane membrane across from dialysate flowing in the grooves of the plate on the other side of the membrane in a counter current direction. One or more of these membrane “sandwiches” could be clamped together to construct the dialyzer. The parents of the children treated at home in the early days of the program were required to construct a Kiil dialyzer for every treatment (Donald Potter, MD, personal communication, 2011).

Vascular access was via arteriovenous shunts originating in the radial, brachial, posterior tibial, or femoral artery. Extracorporeal volume during treatment averaged 14% of estimated blood volume, and blood loss with each treatment was 20–40 mL. Transfusions were given when the hematocrit fell to 15%, leading to a mean transfusion requirement of 0.5 unit of packed red blood cells per month. The highest dialyzer clearance available was 128 mL/min, and because of this low clearance, five of the children were dialyzed 18–27 h/week. Dialysis prescriptions were adjusted according to pre-dialysis BUN, which averaged 70–86 mg/dL [81].

There were many complications, including hemodynamic decompensation due to the a-v shunt, shunt clotting and infection, anemia, hypertension, renal bone disease, congestive heart failure, uremic pericarditis, and growth delay. Despite these difficulties, there was only one death, and at the time of the 1970 report, seven children had received successful kidney transplants [81]. Looking back on his early experience, Potter recently recalled that although hemodialysis in 1970 appeared to be a potentially successful therapy for uremic children, there were many who doubted its technical problems