Notes on the History of Dialysis Therapy in Children

1

Steven R. Alexander and Pierre Cochat

Introduction

Prior to the 1950s and 1960s, the study and management of disorders of the kidney was the province of general physicians. As described by Stuart Cameron, along with the introduction of the renal biopsy and its interpretation, 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, 2]. When long-term dialysis became possible in the 1960s, hundreds of adult dialysis units sprang up in North America and Europe, 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…" [1].

In contrast, the discipline of pediatric nephrology emerged in response to different drivers. Based in 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 many 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 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 therapy, attempting to ease the progression to end-stage kidney disease (ESKD). When ESKD was reached, older children and adolescents often had to look to adult ESKD programs for access to chronic dialysis and transplantation; infants and younger children were frequently offered only palliative care [5].

During the past six 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 ESKD has come to occupy a prominent if not dominant place in pediatric

S. R. Alexander (✉)
Department of Pediatrics, Lucile Packard Children's Hospital at Stanford, Stanford, CA, USA
e-mail: sralex@stanford.edu

P. Cochat
Service de néphrologie rhumatologie dermatologie pédiatriques, Centre de référence des maladies rénales rares, Hospices Civils de Lyon & Université Claude-Bernard Lyon 1, Lyon, France

B. A. Warady et al. (eds.), *Pediatric Dialysis*, https://doi.org/10.1007/978-3-030-66861-7_1

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 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, focusing on the ingenuity and resourcefulness of some of these early pioneers. It is an exciting story. We have left a detailed description of these innovations to the chapters that follow. Our goal is to place these advances in historical context, acknowledging the debt owed those pioneering pediatric nephrologists, nurses, engineers, dieticians, and social workers and their young patients and their families. All have helped make a complex and life-sustaining therapy a part of routine medical management for children throughout the world.

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 [6]. At that time, dehydrated infants too small or dehydrated to permit intravenous access were treated by "clysis," injecting fluids into the subcutaneous tissues. Blackfan and Maxcy noted that clysis 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…" [6]. These same characteristic features, simplicity, practicality, and safety, have made peritoneal dialysis particularly well suited for use in children for the past 100 years.

The 1949 experience of Henry Swan and Harry H. Gordon should be credited as the first conclusive demonstration of the lifesaving potential of PD when used to treat acute renal failure in children [7]. 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 liters/day) of sterile, physiologic Tyrode's solution to flow by gravity from 20-liter 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 light bulbs 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 [7]. 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 kidney injury (AKI) 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 [8–11]. These methods were adapted for use in children in the early 1960s by teams in Indianapolis and Memphis [12, 13] 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 [14, 15]. Subsequent reports established PD as the most frequently employed renal replacement therapy (RRT) for AKI in pediatric patients [16–22]. 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 ESKD. The need to re-insert the dialysis catheter for each treatment made prolonged use of PD in small 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 [23]. 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 HD, and three remained on PD; no child had been successfully transplanted [23].

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 [24] and later refined by Tenckhoff and Schechter in 1968 [25], the permanent PD catheter revolutionized chronic PD for adults and children in the same way the Scribner shunt transformed chronic HD, both making long-term renal support 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 [26, 27]. In the early 1970s, this work culminated in the establishment in Seattle of the first pediatric chronic home PD program [28]. The success of the Seattle program throughout the 1970s showed that chronic IPD could be a practical option for some children with ESKD [29].

Additional limited experience with chronic IPD was reported from several other pediatric centers [30–33], 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 efficiency of HD. Moreover, it became clear from efforts to maintain adult ESKD patients on chronic IPD that long-term technique survival was not often achieved [34]. Inadequate dialysis resulting in severe undernutrition 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 dialysis for children, especially infants. 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…" [35], and with Reinhart, "…we may find the price the child pays for life too great…" [36]. During a period in which advances in ESKD therapy pushed the upper age limits for successful therapy well into the seventh and eighth decades, the youngest ESKD patients remained therapeutic orphans, considered by many to have severely limited chances for survival [36, 37].

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 ESKD in children [38]. As originally described, 2 liters of dialysate were infused into an adult's peritoneal cavity and retained for 4–5 hours, then drained, and repeated a total of five times per day while the patient went about regular daily activities [39]. 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 a transplantable age and size.

The first child to receive CAPD was a 3-year-old girl in Toronto in 1978 [40, 41]. Although a number of pediatric dialysis programs in North America [42–45] and Europe [46, 47] quickly followed suit, enthusiasm in many areas was tempered by the availability of dialysis fluid only in 2000-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 the rest of the world [48].

During the 1980s, the popularity of CAPD for children spread worldwide [49]. 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 [50]. Pediatric nephrologists in developing countries soon realized that CAPD was relatively affordable, which meant that ESKD was no longer an inexorably lethal condition for children from families with limited resources [51–53], and throughout the world, the survival of so many more children with ESKD increased 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 hours 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 where it could be afforded. 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 [54, 55]. 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 [55]. Soon, CCPD became extremely popular among pediatric dialysis programs in developed countries worldwide [56–61].

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 [56]. The ready availability of potent vitamin D analogues, ESKD-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. 26, 27, 28, 29, 30, 31, and 32) gave pediatric nephrologists a power-

ful armamentarium with which to bring the child on chronic dialysis safely to transplantation in relatively good condition. Attention could then be turned to quality of life issues, scholastic and emotional development, and child and family psychosocial adjustment to the rigors of ESKD and chronic dialysis (see Chaps. 34 and 35).

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 [57–62]. 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 [63], 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 [64]. 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 [65]. 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; in addition, 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 [66]. 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 3 1/2-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 [67].

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…." [67]

Merrill's pediatric patient received a single 4-hour dialysis treatment and was said to have had "…modest improvement, but of short duration…" [67].

In 1955, FM Mateer, L Greenman, and TS 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)…" [68]. Their equipment was built by the Westinghouse Company based on an Alwall coil kidney design [69]. 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 meters of 1 1/8-inch cellophane tubing wound on stainless steel screens submerged in a warmed 32-liter bath of dialysate. An in-line roller pump propelled heparinized blood through the tubing from the radial artery through the cellophane coils to return via the saphenous vein. Dialysate consisted of Pittsburgh tap water to which was added sodium, calcium, chloride, bicarbonate, glucose, and variable amounts of potassium; a fresh batch was mixed every 200 minutes, and with every bath change, an antibiotic (usually oxytetracycline) was injected into the tubing leading to the artificial kidney [68].

For these severely uremic children, hemodialysis was clearly a heroic treatment that was surprisingly effective, if only temporarily. After treatments lasting 2–13 hours, 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..." [68].

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 HD treatments in five children (2–14 years of age) using an improved and disposable Alwall twin coil kidney that could be modified for children <20 kg by using only one of the two coils, thereby reducing the priming volume from 750 ml to 400 ml [70]. 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 [70].

Four of the five children survived, including a 2-year-old boy with probable acute post-infectious 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 lifesaving..." [70].

Unlike the concise and constricted prose demanded by modern journal editors, the papers by Mateer and Carter published more than 60 years ago are wonderfully detailed, conveying the intensity and drama that must have attended these early pediatric HD 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...." [68]

Intoxications with salicylates or barbiturates represented another potential use for HD in children [71]. However, while potentially lifesaving in cases of reversible AKI or intoxications, the role of periodic HD 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 [72]. The Scribner shunt consisted of Silastic-Teflon^{R} 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 [73], and by the mid-1960s, the availability of repeated vascular access via these shunts made chronic HD in children a reality.

Using a pumpless system developed for pediatric patients by Robert Hickman and Belding Scribner in Seattle in the early 1960s [74], the first large pediatric chronic HD programs were established in Seattle [75], San Francisco [76], Los Angeles [77], Minneapolis [78], London [79], and Paris [80].

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 HD 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 HD provided to 14 children 2–16 years of age weighing 10–52 kg [76]. 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 HD when the scarcity of this resource forced painful decisions into the hands of so-called Life and Death Committees [81]. 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..." [76].

Using the Seattle pumpless method, 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 [82], consisted of two grooved polypropylene plates clamped tightly together and separated by a sheet of cellophane. 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 an arteriovenous shunt originating in either 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/minute, and because of this low clearance, five of the children were dialyzed 18–27 hours per week. Dialysis prescriptions were adjusted according to the pre-dialysis BUN, which averaged 70–86 mg/dL [76].

There were many complications, including hemodynamic decompensation, 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 a successful kidney transplant. Looking back on his early experience, Potter recalled that although HD in 1970 appeared to be a potentially successful therapy for some uremic children, there were many who doubted its technical problems could be overcome sufficiently to allow its routine use in children. According to Potter, three major subsequent advances turned the tide: (1) improved vascular access with the introduction of arteriovenous fistulas and permanent double-lumen catheters; (2) the introduction of smaller more efficient dialyzers and lower-volume dialysis circuits; and (3) the development of dialysis equipment with more precise ultrafiltration monitoring and control capability (Donald Potter, personal communication, 2011).

The critical problem of ultrafiltration monitoring in infants, most critical due to their small body size and narrow blood volume safety limits, was solved ingeniously by another pioneering pediatric HD program in Minneapolis led by Michael Mauer and Carl Kjellstrand who developed electronic weighing equipment on which the dialyzing infant lay throughout the procedure. The equipment required meticulous calibration but was able to very accurately measure weight changes to within 3 g [83]. In a review published in 1976, Mauer and R.E. Lynch addressed these issues and others in an engaging description of the state of the art of pediatric HD in North America in the early 1970s [84].

Developments in Europe paralleled those in North America. In 1975, the second edition of the famous French textbook of pediatric nephrology was co-edited by Pierre Royer, Renée Habib, Michel Broyer, and Chantal Loirat. There were six pages about HD, stating as follows: "…The management of end-stage renal disease in children is a recent experience, and pediatric maintenance hemodialysis had really begun in 1969-70 in Europe…" [85]. According to these authors, there were three major contraindications to chronic dialysis in children: (i) systemic disease such as lupus, (ii) mental retardation, and (iii) young age, i.e., below 18 months. Vascular accesses included only radial or femoral arteriovenous shunt or fistula, so that such a procedure was limited to children older than 2–3 years. There was no specific device for pediatric dialysis, and children suffered from many uncomfortable/unacceptable side effects (seizures, severe hypotension) during HD sessions. Morbidity primarily consisted of arterial hypertension, renal osteodystrophy, anemia, undernutrition, and poor growth velocity. However, actuarial patient survival was reported to be 90% after 3 years on chronic HD [85].

By the late 1980s, chronic HD for children had become widely available throughout Europe and North America. While the goal was always preparation for a successful kidney transplant, further technical improvements in the delivery of dialysis therapy allowed the focus to shift from simply prolonging life to rehabilitation and the achievement of more normal physical, intellectual, and social development [86].

Among the most recent advances, some have brought significant improvement in HD for children:

- Daily on-line hemodiafiltration allows better nutrition, reduces blood pressure, improves left ventricular size and function, improves calcium × phosphate control, better controls chronic microinflammation, and promotes catch-up growth in children [87].
- The lowest age limit for starting HD in children has dropped to include neonates thanks to specific devices and improvement in general care of such patients [88].
- There is better worldwide knowledge and investigation of cardiovascular risk factors leading to better long-term control and prevention of cardiovascular disease (see Chap. 30).
- The use of on-line monitoring equipment for chemical/physical signals during HD and biofeedback is growing, such as continuous noninvasive monitoring of relative blood volume changes during HD, patient-dialysate sodium gradient assessment, ionic dialysance and plasma conductivity (calculated from on-line inlet and outlet dialysate conductivity measurements), estimation of sodium concentration derived from conductivity, intra-HD urea kinetics and delivered dialysis dose from on-line urea monitors, and dialysate temperature modulation according to blood temperature monitoring [89].

Patient Registries and Multicenter Studies

By the early 1970s, it became clear among pediatric nephrologists in North America and Europe that the care of children with ESKD required separate facilities from those in which adult patients were dialyzed. The concept of specialized pediatric dialysis centers was pioneered in Europe by Michel Broyer, Karl Scharer, Cyril Chantler, RA Donckerwolke, Gianfranco

Rizzoni, and many others who stressed the importance of concentrating pediatric ESKD patients in multidisciplinary pediatric centers specially equipped for children and with the experience and expertise to care for children on dialysis and their families [86]. These units were usually attached to university departments of pediatrics, as was the case in similar units established in North America. However, no single pediatric center in Europe or North America could hope to treat enough patients to properly develop the therapy. As a result, the concept of large national and international patient databases or registries of children receiving dialysis was born.

The first of these was the work of the European Dialysis and Transplant Association (EDTA), which in 1971 published the first report devoted entirely to the care of pediatric dialysis patients [90]. The 1971 report presented data on 296 patients less than 15 years of age at the start of RRT who were receiving treatment at 122 centers, only 5 of which had treated 3 or more pediatric patients, reflecting the practice in Europe at that time of managing children on dialysis in adult units. In 1976, the components of a pediatric dialysis center were rigorously defined by the EDTA to include pediatricians, pediatric nurses, dieticians, social workers, child psychologists, and school facilities, along with a separate children's ward in which therapy was provided away from adult patients [91]. Close association with a transplant program was also prescribed, reflecting early recognition of the critical importance of transplantation as the therapy of choice for children with ESKD. By 1989, nearly 80% of all children receiving dialysis in the countries of the EDTA were cared for in specialized pediatric centers [92].

Pediatric dialysis in Europe was summarized in 2010 with a report on 483 incident and 2512 prevalent pediatric dialysis patients (age <15 years) from 28 countries [93]. In comparison to a previous demographic report of the former EDTA registry 14 years earlier, the authors found a nearly threefold higher incidence and prevalence of RRT among children aged younger than 15 years. They speculated that the difference was likely to be due to underreporting to the previous EDTA registry, the recent achievement of RRT programs for all children in many countries and an increasing acceptance and survival of infants and children with multiple comorbidities in pediatric RRT programs in Europe, resulting in a truly increased incidence and prevalence of RRT [93].

In North America, the success of the EDTA pediatric registry prompted over 60 pediatric ESKD programs to band together in 1987 under the leadership of Amir Tejani, Richard Fine, Steven Alexander, William Harmon and others to form what is now called the North American Pediatric Renal Trials and Collaborative Studies (NAPRTCS) [94]. The NAPRTCS is a voluntary registry restricted to pediatric centers in Canada, the United States, Mexico, and Costa Rica that initially focused on transplant patients. In 1992, the NAPRTCS expanded to include dialysis patients and in 1994 expanded again to include children with chronic kidney disease (CKD). As of July 2019, data have been recorded on 21,316 children entered into the NAPRTCS registry. This includes 10,874 courses of dialysis among 8507 children and 13,611 kidney transplants performed in 12,525 children and young adults. A complete listing of the more than 150 publications based on NAPRTCS data that have appeared since 1990 is available on the NAPRTCS website, as are all of its most recent Annual Data Reports (http://web.emmes.com/study/peds).

The most recent addition to the international pediatric patient registries is the International Pediatric Dialysis Network (IPDN). The IPDN is a global consortium of pediatric nephrology centers dedicated to the care of children on chronic dialysis. Currently, 245 institutions participate in the network from Europe; Scandinavia; North, Central, and South America; and Oceania. The IPDN is composed of the IPPN registry for children on chronic peritoneal dialysis and the IPHN registry for children on hemodialysis. To date 3773 patients have been enrolled in the IPPN registry at 128 contributing centers in 43 countries, and 1005 patients have been enrolled in the IPHN at 85 contributing centers in 36 countries (http://pedpd.org).

Conclusion

The EDTA, NAPRTCS, and the IPDN registries have catalogued and promoted the steady growth and development of RRT for children that has occurred since the 1970s and 1980s. During the last four decades, HD and PD in children have dramatically improved, with the near disappearance of many of the complications that once plagued pediatric hemodialysis; advances in peritoneal dialysis have occurred in parallel with those in hemodialysis for children, although not always at the same pace.

The history of maintenance HD and PD in children has been characterized by a series of major developments, nearly all of which are discussed in the ensuing chapters [95–100]:

- Introduction of more efficient and biocompatible synthetic membranes and peritoneal dialysis solutions (Chaps. 13 and 20)
- Erythropoietin treatment (Chap. 32)
- Growth hormone therapy (Chap. 28)
- The development of new therapeutic approaches to bone disease and calcium-phosphate disorders (Chap. 29)
- Advances in vascular accesses (microsurgery for arteriovenous fistulae, new materials for cuffed tunnelled venous catheters) (Chap. 19)
- Introduction of pediatric data for dialysis adequacy measurement (Kt/V, urea reduction ratio) (Chaps. 13 and 20)
- Novel dialysis strategies (e.g., high-flux dialysis, hemodiafiltration) (Chap. 21)
- Optimizing the use of anticoagulation (low molecular weight heparins, regional trisodium citrate) (Chap. 20)
- Improving dialysis water quality and bacterial safety (ultrapure dialysate)
- Non-invasive investigation of vascular access blood flow
- Using urokinase or tPA for the management of the thrombosed hemodialysis catheter (Chap. 25)
- Improving nutritional assessment and support (Chap. 27)
- Using new machines with precise control of ultrafiltration by volumetric assessment and continuous blood volume monitoring during dialysis sessions
- The availability of specific small-size dialyzers and tubing for infants (Chap. 22)
- The use of sodium modelling

In the meantime, HD and PD practice has benefited from specific medical and staff training, including educational courses, fellowship programs, and congresses. Specific regulations have also been established for HD and PD practice in children. During this period, patient morbidity and mortality have significantly decreased. Worldwide clinical experience has resulted in general practical guidelines for pediatric HD and PD, many of which will be discussed in the chapters that follow.

All these improvements have led to better quality of life, better nutritional status, better neurological development, better psychosocial outcome, and better patient survival for those children who receive chronic dialysis. All have their origins in the work of pioneering medical teams, patients, and families beginning almost a century ago. It has been a truly exciting story that continues to this day. The chapters that follow in this text will address these and other recent advances in dialysis therapy for children.

References

1. Cameron JS. A history of the treatment of renal failure by dialysis. New York: Oxford University Press Inc; 2002. p. 179–85.
2. Cameron JS, Hicks J. The introduction of renal biopsy into nephrology from 1901 to 1961: a paradigm of the forming of nephrology by technology. Am J Nephrol. 1997;17:347–58.
3. Barnett HL, Edelmann CM Jr. Development of pediatric nephrology. Am J Kidney Dis. 1990;16:557–62.
4. Chesney RW. The development of pediatric nephrology. Pediatr Res. 2002;52:770–8.
5. Scharer K, Fine RN. The history of dialysis therapy in children. In: Warady BA, Schaefer FS, Fine RN, Alexander SR, editors. Pediatric dialysis. Dordrecht: Kluwer Academic Publishers Inc; 2004. p. 1–11.

6. Blackfan KD, Maxcy KF. The intraperitoneal injection of saline solution. Am J Dis Child. 1918;15:19–28.
7. Swan H, Gordon HH. Peritoneal lavage in the treatment of anuria in children. Pediatrics. 1949;4:586–95.
8. Odel HM, Ferris DO, Power MH. Peritoneal lavage as an effective means of extra-renal excretion. Am J Med. 1950;9:63–77.
9. Fine J, Frank HA, Seligman AM. The treatment of acute renal failure by peritoneal irrigation. Ann Surg. 1946;124:857–75.
10. Weston RE, Roberts M. Clinical use of a stylet catheter for peritoneal dialysis. Arch Intern Med. 1965;15:659–62.
11. Maxwell MH, Rockney RB, Kleeman CR, Twiss MR. Peritoneal dialysis: technique and applications. JAMA. 1959;170:917–24.
12. Segar WE, Gibson RK, Rhamy R. Peritoneal dialysis in infants and small children. Pediatrics. 1961;27:603–13.
13. Etteldorf JN, Dobbins WT, Sweeney MJ, Smith JD, Whittington GL, Sheffield JA, Meadows RW. Intermittent peritoneal dialysis in the management of acute renal failure in children. J Pediatr. 1962;60:327–39.
14. Segar WE. Peritoneal dialysis in treatment of boric acid poisoning. N Engl J Med. 1960;262:708–800.
15. Ettledorf JN, Dobbins WT, Summitt RL, Rainwater WT, Fischer RL. Intermittent peritoneal dialysis using 5 per cent albumin in the treatment of salicylate intoxication in children. J Pediatr. 1961;58:226–36.
16. Lloyd-Still JD, Atwell JD. Renal failure in infancy, with special reference to the use of peritoneal dialysis. J Pediatr Surg. 1966;1:466–75.
17. Manley GL, Collipp PJ. Renal failure in the newborn: treatment with peritoneal dialysis. Am J Dis Child. 1968;115:107–10.
18. Lugo G, Ceballos R, Brown W, Polhill R, Cassady G. Acute renal failure in the neonate managed by peritoneal dialysis: preliminary report of two cases. Am J Dis Child. 1969;118:655–9.
19. Giantantonio CA, Vitacco M, Mendilaharzu J, Mendilaharzu F, Rutty A. Acute renal failure in infancy and childhood: clinical course and treatment of 41 patients. J Pediatr. 1962;61:660–78.
20. Wiggelinkhuizen J. Peritoneal dialysis in children. S Afr Med J. 1971;45:1047–54.
21. Day RE, White RHR. Peritoneal dialysis in children: review of 8 years' experience. Arch Dis Child. 1977;52:56–61.
22. Chan JCM. Peritoneal dialysis for renal failure in childhood. Clin Pediatr. 1978;17:349–54.
23. Feldman W, Baliah T, Drummond KN. Intermittent peritoneal dialysis in the management of chronic renal failure in children. Am J Dis Child. 1968;116:30–6.
24. Palmer RA, Quinton WE, Gray J-F. Prolonged peritoneal dialysis for chronic renal failure. Lancet. 1964;1:700–2.
25. Tenckhoff H, Schechter H. A bacteriologically safe peritoneal access device. Trans Am Soc Artif Intern Organs. 1968;14:181–7.
26. Boen ST, Mion CM, Curtis FK, Shilitar G. Periodic peritoneal dialysis using the repeated puncture technique and an automatic cycling machine. Trans Am Soc Artif Intern Organs. 1964;10:409–14.
27. Tenckhoff H, Meston B, Shilipetar G. A simplified automatic peritoneal dialysis system. Trans Am Soc Artif Intern Organs. 1972;18:436–40.
28. Counts S, Hickman R, Garbaccio A, Tenckhoff H. Chronic home peritoneal dialysis in children. Trans Am Soc Artif Intern Organs. 1973;19:157–67.
29. Hickman RO. Nine years' experience with chronic peritoneal dialysis in childhood. Dial Transplant. 1978;7:803.
30. Brouhard BH, Berger M, Cunningham RJ, Petrusik T, Allen W, Lynch RE, Travis LB. Trans Am Soc Artif Intern Organs. 1979;25:90–4.
31. Baluarte HJ, Grossman MB, Polinsky MS, Elzouki AY, Prebis JW, Gruskin AB. Experience with intermittent home peritoneal dialysis (IHPD) in children. (Abstract). Pediatr Res. 1980;14:994.
32. Lorentz WB, Hamilton RW, Disher B. Home peritoneal dialysis during infancy. Clin Nephrol. 1981;15:194–7.
33. Potter DE, McDaid TK, Ramirez JA. Peritoneal dialysis in children. In: Atkins RC, Thomson NM, Farrell PC, editors. Peritoneal dialysis. New York: Churchill Livingstone; 1981. p. 356–61.
34. Ahmad S, Gallagher N, Shen S. Intermittent peritoneal dialysis: status re-assessed. Trans Am Soc Artif Intern Organs. 1979;25:86–8.
35. Hurley JK. Kidney transplantation in infants. (Letter). J Pediatr. 1978;93:538.
36. Reinhart JB. The doctor's dilemma: whether or not to recommend continuous renal dialysis or renal homotransplantations for the child with end-stage renal disease. J Pediatr. 1970;77:505.
37. Oreopoulos DG, Katirtzoglou A, Arbus G, Cordy P. Dialysis and transplantation in young children. (Editorial). Br Med J. 1979;2:1033.
38. Popovich RP, Moncrief JW, Dechard JF. The definition of a novel portable/wearable equilibrium dialysis technique (Abstract). Trans Am Soc Artif Intern Organs. 1976;5:64.
39. Moncrief JW, Popovich RP, Nolph KD. The history and current status of continuous ambulatory peritoneal dialysis. Am J Kidney Dis. 1990;16:579–84.
40. Oreopoulos DG, Katirtzoglou A, Arbus G, Cordy P. Dialysis and transplantation in young children (Letter). Br Med J. 1979;1:1628–9.
41. Balfe JW, Irwin MA. Continuous ambulatory peritoneal dialysis in pediatrics. In: Legain M, edi-

tor. Continuous ambulatory peritoneal dialysis. Amsterdam: Excerpta Medica; 1980. p. 131–6.
42. Alexander SR, Tseng CH, Maksym KA, Talwalker YA. Clinical parameters in continuous ambulatory peritoneal dialysis for infants and young children. In: Moncrief JW, Popovich RP, editors. CAPD update. New York: Masson Publ; 1981. p. 195–209.
43. Kohaut EC. Continuous ambulatory peritoneal dialysis: a preliminary pediatric experience. Am J Dis Child. 1981;135:270–1.
44. Potter DE, McDaid TK, McHenry K, Mar H. Continuous ambulatory peritoneal dialysis (CAPD) in children. Trans Am Soc Artif Intern Organs. 1981;27:64–7.
45. Salusky IB, Lucullo L, Nelson P, Fine RN. Continuous ambulatory peritoneal dialysis in children. Pediatr Clin N Am. 1982;29:1005–12.
46. Guillot M, Clermont M-J, Gagnadoux M-F, Broyer M. Nineteen months' experience with continuous ambulatory peritoneal dialysis in children: main clinical and biological results. In: Gahl GM, Kessel M, Nolph KD, editors. Advances in peritoneal dialysis. Amsterdam: Excerpta Medica; 1981. p. 203–7.
47. Eastham EJ, Kirplani H, Francis D, Gokal R, Jackson RH. Pediatric continuous ambulatory peritoneal dialysis. Arch Dis Child. 1982;57:677–80.
48. Alexander SR. Pediatric CAPD update-1983. Perit Dial Bull (Suppl). 1983;3:S15–22.
49. Alexander SR, Honda M. Continuous ambulatory peritoneal dialysis for children: a decade of worldwide growth and development. Kidney Int. 1993;43(Suppl):S65–74.
50. Honda M, Itaka K, Kawaguchi H, et al. The Japanese data on CAPD: a ten year experience. A report of the Study Group of the Pediatric PD Conference. Perit Dial Int. 1996;16:269–75.
51. Munoz AR, Salazar GML, Gordillo PG. Adequacy of chronic peritoneal dialysis in low socioeconomic class uremic children. Int J Pediatr Nephrol. 1986;7:81–4.
52. Bakkaloglu SA, Ekim M, Sever L, et al. Chronic peritoneal dialysis in Turkish children: a multicenter study. Pediatr Nephrol. 2005;20:644–51.
53. Grunberg J, Verocay MC, Rebori A, et al. Twenty years' pediatric chronic peritoneal dialysis in Uruguay: patient and technique survival. Pediatr Nephrol. 2005;20:1315–9.
54. Diaz-Buxo JA, Farmer CD, Walker PJ, Chandler JT, Holt KL. Continuous cyclic peritoneal dialysis: a preliminary report. Artif Organs. 1981;5:157–61.
55. Price CG, Suki WN. Newer modifications of peritoneal dialysis: options in treatment of patients with renal failure. Am J Nephrol. 1981;1:97.
56. Seikaly M, Ho PL, Emmett L, Tejani A. The 12th annual report of the North American Pediatric Renal Transplant Cooperative Study: renal transplantation from 1987 to 1998. Pediatr Transplant. 2001;5:215–31.
57. Warady BA, Sullivan EK, Alexander SR. Lessons from the peritoneal dialysis patient database: a report of the North American Pediatric Renal Transplant Cooperative Study. Kidney Int. 1996;49(Suppl):S68–71.
58. Edefonti A, Verrina E, Schaefer F, Fischbach M, Watson A. The European experience with CAPD/CCPD in children. In: Fine RN, Alexander SR, Warady B, editors. CAPD/CCPD in children. Boston: Kluwer Academic Publ; 1998. p. 17–34.
59. Fine RN, Ho M. The role of APD in the management of pediatric patients: a report of the North American Pediatric Renal Transplant Cooperative Study. Semin Dial. 2002;15:427–9.
60. Neu AM, Sander A, Borzych-Dazualka D, Watson AR, Valles PG, Ha IS, Patel H, Azkenazi D, Balasz-Chmielewska I, Lauronen J, Groothoff JW, Feber J, Schaefer F, Warady BA, IPPN investigators. Comorbidities in chronic pediatric peritoneal dialysis patients: a report of the International Pediatric Peritoneal Dialysis Network. Perit Dial Int. 2012;32:410–8.
61. Van der Heijden BJ, van Dijk PC, Vernier-Jones K, Jager KJ, Briggs JD. Renal replacement therapy in children: data from 12 registries in Europe. Pediatr Nephrol. 2004;19:213–21.
62. Verrina E, Edefonti A, Gianglio B, et al. A multicenter experience on patient and technique survival in children on chronic dialysis. Pedatr Nephrol. 2004;19:82–90.
63. Kolff WJ, Berk HTH, Ter Welle M, van der Leg JW, van Dijk EC, van Noordwijk J. The artificial kidney: a dialyser with great area. Acta Medica Scand. 1944;117:121–34.
64. Kolff WJ. First clinical experience with the artificial kidney. Ann Intern Med. 1965;62:608–19.
65. MacLean J. The thromboplastic action of cephalin. Am J Phys. 1916;41:250–7.
66. Andrus FC. Use of Visking sausage casing for ultrafiltration. Proc Soc Exp Biol Med. 1919;27:127–8.
67. Merrill JP, Smith S III, Callahan EJ III, Thorn GW. The use of an artificial kidney. II Clinical experience. J Clin Invest. 1950;29:425–38.
68. Mateer FM, Greenman L, Danowski TS. Hemodialysis of the uremic child. Am J Dis Child. 1955;89:645–55.
69. Alwall N. Apparatus for dialysis of the blood in vivo. Acta Med Scand. 1947;128:317–35.
70. Carter FH, Aoyama S, Mercer RD, Kolff WJ. Hemodialysis in children: report of five cases. J Pediatr. 1957;51:125–36.
71. Kallen RJ, Zaltzman S, Coe FL, Metcoff J. Hemodialysis in children: technique, kinetic aspects related to varying body size, and application to salicylate intoxication, acute renal failure and some other disorders. Medicine. 1966;45:1–50.
72. Quinton W, Dillard D, Scribner B. Cannulation of blood vessels for prolonged hemodialysis. Trans ASAIO. 1960;6:104.
73. Morse TS. Synthetic arteriovenous shunts for hemodialysis in children. J Ped Surg. 1970;5:23–31.

74. Hickman RO, Scribner BH. Application of the pumpless hemodialysis system to infants and children. Trans Am Soc Artif Intern Organs. 1962;8:309–14.
75. Hutchings RH, Hickman R, Scribner BH. Chronic hemodialysis in a pre-adolescent. Pediatrics. 1966;37:68–73.
76. Potter D, Larsen D, Leumann E, Perin D, Simmons J, Piel CF, Holliday MA. Treatment of chronic uremia in childhood. II Hemodialysis. Pediatrics. 1970;46:678–89.
77. Fine RN, DePalma JR, Lieberman E, Donnell GN, Gordon A, Maxwell MH. Extended hemodialysis in children with chronic renal failure. J Pediatr. 1968;73:706–13.
78. Mauer SM, Shideman JR, Buselmeier TJ, Kjellstrand CM. Long-term hemodialysis in the neonatal period. Am J Dis Child. 1973;125:269–72.
79. Boulton-Jones JM, Cameron JS, Bewick M, Ogg CS, Meadow SR, Ellis FG. Treatment of terminal renal failure in children by home dialysis and transplantation. Arch Dis Child. 1971;46:457–64.
80. Broyer M, Loirat C, Kleinknecht C. Technical aspects and results of regular hemodialysis in children. Acta Paediat Scand. 1972;61:677–84.
81. Lenzer J. Obituary: Belding Scribner: inventor of shunt dialysis. BMJ. 2003;327(7407):167.
82. Cole JJ, Pollard TL, Murray JS. Studies on the modified polypropylene Kiil dialyser. Trans Am Soc Artif Intern Organs. 1963;9:67–72.
83. Kjellstrand CM, Mauer SM, Shideman JR, Buselmeier TJ. Accurate weight monitoring during pediatric hemodialysis. Nephrom. 1973;10:302–5.
84. Mauer SM, Lynch RE. Hemodialysis techniques for infants and children. Ped Clin N America. 1976;23:843–56.
85. Broyer M. Dialyse et transplantation rénale. In: Royer P, Habib R, Broyer M, Loirat C, editors. Néphrologie Pédiatrique. Paris: Flammarion Médecin-Sciences; 1975. p. 302–13.
86. Broyer M, Chantler C, Donckerwolke R, Rizzoni G. Renal replacement therapy in children. In: Mahaer JF, editor. Replacement of renal function by dialysis. 3rd ed. Boston: Kluwer Academic Publisher; 1989. p. 720–49.
87. Fischbach M, Terzic J, Menouer S, Dheu C, Seuge L, Zalosczic A. Daily online haemodiafiltration promotes catch-up growth in children on chronic dialysis. Nephrol Dial Transplant. 2010;25:867–73.
88. Shroff R, Wright E, Ledermann S, Hutchinson C, Rees L. Chronic hemodialysis in infants and children under 2 years of age. Pediatr Nephrol. 2003;18:378–83.
89. Locatelli F, Buoncristiani U, Canaud B, Köhler H, Petitclerc T, Zucchelli P. Haemodialysis with on-line monitoring equipments: tools or toys? Nephrol Dial Transplant. 2005;20:22–3.
90. Scharer K, Brunner FP, Gurland HJ, Harlen H, Parsons FM. Combined report on regular dialysis and renal transplantation of children in Europe, 1971. Proc Eur Dial Transplant Assoc. 1972;9:191–200.
91. Chantler C, Donckerwolke RA, Brunner FP, Gurland H, Hathway RA, Jacobs C, Selwood NH, Wing AJ. Combined report on regular dialysis and renal transplantation of children in Europe, 1976. Proc Eur Dial Transplant Assoc. 1977;14:70–112.
92. Ehrich JHH, Rizzoni G, Brunner FP, Brynger H, Gerlings W, Fasbinder W, Raine AEG, Selwood NH, Tufveson G. Combined report on regular dialysis and transplantation of children in Europe, 1989. Nephrol Dial Transplant. 1991;6(Suppl 1):37–47.
93. Van Stralen KJ, Tizard EJ, Verrina E, Schaefer F, Jager KJ, on behalf of the European Society for Paediatric Nephrology/European Renal Association-European Dialysis and Transplant Association (ESRN/ERA-EDTA). Demographics of paediatric renal replacement therapy in Europe: 2007 annual report of the ESPN/ERA-EDTA registry. Pediatr Nephrol. 2010;25:1379–82.
94. Alexander SR, Sullivan EK, Harmon WE, Stablein DM, Tejani A. Maintenance dialysis in North American children: a preliminary report of the NAPRTCS. Kidney Int Suppl. 1993;43:S104–9.
95. Shroff R, Ledermann S. Long-term outcome of chronic dialysis in children. Pediatr Nephrol. 2009;24:463–74.
96. Goldstein SL, Allsteadt A. Ultrasound dilution evaluation of pediatric hemodialysis vascular access. Kidney Int. 2001;59:2357–60.
97. Sheth RD, Brandt ML, Brewer ED, Nuchtern JG, Kale AS, Goldstein SL. Permanent hemodialysis vascular access survival in children and adolescents with end-stage renal disease. Kidney Int. 2002;62:1864–9.
98. Bourquelot P, Raynaud F, Pirozzi N. Microsurgery in children for creation of arteriovenous fistula for renal and non-renal diseases. Ther Apher Dial. 2003;7:498–503.
99. Krause I, Birk E, Davidovits M, Cleper R, Blieden L, Pinhas L, Gamzo Z, Eisentsein B. Inferior vena cava diameter: a useful method for estimation of fluid status in children on haemodialysis. Nephrol Dial Transplant. 2001;16:1203–6.
100. Fischbach M, Edefonti A, Schröder C, Watson A, the European Pediatric Dialysis Working Group. Hemodialysis in children: general practical guidelines. Pediatr Nephrol. 2005;20:1054–66.