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# Chronic dialysis in the infant less than 1 year of age

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**Abstract.** Dialysis in the infant carries a mortality rate of 16%. Institution of dialysis may be the result of adequate nutritional intake, but avoidance of nutritional intake should never be seen as a way to prevent dialysis. Increased caloric intake, usually via enteral feeding tubes, is needed for optimal growth in the infant with end-stage renal disease (ESRD) in order to attain adequate nutrition with resulting good growth. "Renal" formulae may be constituted as dilute (as in the *polyuric* infant) or concentrated (as in the *anuric* infant) to fit the infants needs. Peritoneal dialysis (PD) is the usual mode of renal replacement therapy (97%), with access via a surgically placed cuffed catheter with attention to the placement of the exit site in order to avoid fecal or urinary contamination. PD volumes of 30–40 ml/kg per pass or 800–1,200 ml/m$^2$ per pass usually result in dialysis adequacy. Additional dietary sodium (3–5 mEq/kg per day) and protein (3–4 g/kg per day) are needed, due to sodium and protein losses in the dialysate. Protein losses are associated with significant infectious morbidity and nonresponsiveness to routine immunizations. Hemodialysis (HD) can be performed either as single- or dual-needle access that have minimal dead space (less then 2 ml) and recirculation rate (less then 5%). Attention to extracorporeal blood volume (< 10% of intravascular volume), blood flow rates (3–5 ml/kg per min), heparinization (activated clotting times), ultrafiltration (ultrafiltration monitor), and temperature control is imperative during each treatment. Because infants' nutrition is mostly fluid, HD may be needed 4–6 days/week (especially in the oligo-anuric infant) to avoid excessive volume overload between treatments. At the end of the treatment a slow blood return with minimal saline rinse is needed to avoid hemodynamic compromise. Infant dialysis, although technically challenging with a significant morbidity and mortality rate, can be safely carried out in the infant with ESRD but requires infant-specific equipment and trained personnel.

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## Introduction

End-stage renal disease (ESRD) requiring dialysis has an incidence rate of 6 per 1,000,000 in the pediatric age range from 0 to 4 years of age [1]. Although the incidence is quite low, the mortality rate in this population on dialysis approaches 16% per year or has an estimated mortality rate of 21% over a 2-year period. This is significantly greater then those children over 5 years, with a mortality rate of 3% per year. This high mortality rate makes both the care of the infant and the prevention of a complication an ongoing struggle effecting infant survival.

The etiologies of ESRD in the specific age group of 0–1 year are limited [2]. These include congenital anomalies that are associated with high-output renal failure, such as renal dysplasia or hypoplasia, infants with congenital nephrotic syndrome, as well as hemodynamic causes, including cortical necrosis, which may be associated with anuric renal failure. Understanding the etiology of ESRD will help in the management of the child. Dividing the infants into polyuric and anuric renal failure is helpful in differentiating the variations of either dialysis modality that may be necessary in the infant.

### *Polyuric renal failure*

Children with high-output renal failure are easier to manage either conservatively or on dialysis. These children typically have a urine output of 2 to 3 times normal, losing a significant amount of free water and sodium. Therefore, attention to water as well as sodium replacement in this population is important. Due to the fact that these children are usually struggling to maintain euvolemia (with the ongoing potential risk of hypovolemia), this group usually

requires dialysis primarily for urea, phosphorus, and potassium management, not ultrafiltration requirements. The down side of the urine output is that this group has a tendency to become rapidly dehydrated with an increased mortality rate secondary to dehydration.

This group may be managed "conservatively" without renal replacement therapy (RRT) if adequate nutrition and volume (including extra salt) are given to the infant. The use of enteral feeding tubes has become, in many centers, the "norm", making euvolemia maintenance easier to attain [3]. Because most infant "renal" formulae are low in sodium, the addition of sodium chloride and/or sodium bicarbonate of 2–4 mEq/100 ml of infant formula may be necessary to match the urinary sodium losses that occur in this population. Analysis of the urinary sodium at the time the infant is euvolemic may be helpful in determining the amount of sodium the polyuric infant requires.

*Anuric renal failure*

The infant with anuric ESRD is more difficult to care for because of the ongoing risk of volume overload. Due to the fact that more then 90% of the infant's nutrition is fluid based, frequent dialysis may be necessary, more for ultrafiltration than urea clearance. The use of concentrated formulae (see nutrition) may be needed in this population. These patients can not be managed for more then a few days without RRT. Nutrition should not be restricted in order to avoid dialysis, due to the ongoing catabolic needs of the growing infant.

## Dialysis techniques

*Peritoneal dialysis*

Peritoneal dialysis (PD) accounts for more than 95% of the mode of dialysis in infants [4]. Although there are no PD cyclers that are infant specific, most cyclers have the capability of delivering small volumes (50 ml) to the infant. Further, infants may be maintained on continuous ambulatory PD with the use of small dialysate bags and scales to weigh the amount of dialysate delivered and ultrafiltrated. Attention to the dead space of the dialysis tubing is important in order to avoid "recirculation" of the dialysate.

A typical infant requires somewhere between 800 and 1,200 ml/m$^2$ or 30–40 ml/kg of intraperitoneal volume per pass. This should result in adequate dialysis as well as ultrafiltration [5, 6]. A starting intraperitoneal volume of 10–12 ml/kg per pass and increasing to the previously mentioned volumes over a 3- to 4-week period can result in adequate dialysis. One of the difficulties with machines at this lower volume is that of low drain alarms on return. In the anuric infant, this is usually not an issue since the patient will usually return more than 100% of the infused volume because of the addition of the ultrafiltrate. In the polyuric infant it is common, due to these small volumes and because of absorption of dialysate, that the low-drain alarms are triggered causing additional anxiety to the infant and family. Most low-drain alarms are set to alarm if 85% of the dialysate is not returned within two-thirds of the allotted time. These can be adjusted on the machine. Care should be taken, however, to insure that the patient is not third spacing extraperitoneally, which may not be clinically apparent.

The standard sodium concentration of peritoneal dialysate is 132 mEq/l. This results in a net loss of sodium across the peritoneum in the majority of infants, usually requiring the addition of enteral or peritoneal sodium to mitigate this problem [7]. This negative sodium balance may be exacerbated in the infant with polyuric renal failure due to the ongoing urinary sodium loss. It is important in infants on PD with ESRD that sodium supplementation be given to maintain intravascular integrity. It may be necessary to supplement as much as 5–10 mEq/kg of additional sodium in these infants due to the combined losses of sodium in the urine and the dialysate.

The phosphorus and potassium clearance is less problematic in this population. Electrolyte normalization can be well obtained not only between phosphorus and potassium restrictive formulae, but also because most of these infants have adequate clearance due to increased (as opposed to older children) peritoneal membrane permeability. In the polyuric infant the absorbed dialysate will further increase urine output thereby increasing phosphorus and potassium clearance. Because of this phenomena, after some infants are started on PD, transition to a "normal" formula may be required for a period of time until further (and ongoing) deterioration of native kidney function occurs.

Ultrafiltration requirements in infants on PD will be dependent upon the degree of urine output and the amount of nutrition necessary for growth. In the polyuric infant, little need for ultrafiltration may exist. These infants can be well dialyzed on low-glucose-containing dialysate in order to avoid extra water losses through the peritoneal membrane. The ongoing polyuria that occurs in these infants places them at additional risk for dehydration if ultrafiltration does occur. It is not uncommon that infants with polyuria will absorb dialysate. In the face of lack of ultrafiltration, attention to the infant to ensure that third spacing of the dialysate is not occurring is important. In the anuric infant, ultrafiltration will be dependent upon formula intake. Therefore, a higher glucose content may be necessary in these infants in order to attain adequate ultrafiltration.

The infant on PD for 12–14 h a day, 7 days a week will easily attain adequate growth [8]. Remember that an infant may obtain 20–30 calories/kg per day of carbohydrate calories while on PD. Therefore, it is not surprising that many of these infants have weight growth out of proportion to height and head circumference growth.

*Hemodialysis*

Hemodialysis (HD) accounts for only 3% of ESRD therapies in infants in North America [4]. The obvious difficulties associated with HD is that of adequate access and

appropriate infant-specific HD machines [9, 10]. Recently an increased number of accesses have become available and many HD machines are adaptable for either infant-sized dual-needle or infant-specific single-needle HD [9, 11]. However despite these advances, HD continues to be less used for many reasons. The need for infant-specific trained nursing staff and pediatric nephologists to care for this high-risk population continues to be a major limitation.

Attention during a HD treatment is important to avoid excessive ultrafiltration [12]. Ultrafiltration monitors now exist in the majority of the newer HD machines in order to avoid excessive ultrafiltration. It should be noted that ultrafiltration monitors may have an error rate of ± of 50 ml/h, having as much as 150–200 ml error rate at the end of a 3-h treatment. This error rate can be minimized, in that once the variation is known the biomedical support system from the HD company can tighten the range of variation. Many centers utilize an infant scale during HD treatment. We have found at the University of Michigan that infant scales become more problematic. Strict attention to items placed and removed from these scales must be paid throughout the HD treatment in order to avoid a miscalculation of weight. We prefer to have a very strict and accurate ultrafiltration monitor for these infants.

Specific issues of access should include the understanding that they should be low resistance. Resistance of blood flow through the access is relative to the internal diameter as well as length of the catheter [13]. The best access is short and of wide diameter. The newer accesses that are specific for infants have become available and can be surgically placed in the superior vena cava right atrial junction for short-term "acute" or long-term "chronic" HD.

At the time of placing the HD lines on the machine, attention to the extracorporeal blood volume is important. The standard blood volume of the infant is 80 ml/kg. Thus, in a 5-kg infant the intravascular blood volume may only be 400 ml. As a rule, no more than 10% of the blood volume should be extracorporeal during the HD treatment, therefore maintaining a circuit of less than 40 ml is important. The smallest circuit currently available is 38 ml, which can be utilized in an infant as small as 4.5 kg without blood priming [9]. Circuits greater than 10% usually require blood priming. Blood priming is associated with an increased risk of antigen exposure, with negative impact upon transplantation. Increase in viscosity resistance is associated with high hematocrit blood bank blood, as well as a high potassium load in blood bank blood [9, 14]. If blood bank blood is utilized, diluting the blood with normal saline to a hematocrit of 30%–40% will be helpful in terms of the viscosity. This will have little to no benefit upon the potassium or the antigen expression. If blood bank blood is necessary then maneuvers such as using frozen deglycerolized cells or leukopore cells may be helpful in minimizing the white cell load and subsequent antigen exposure.

At the time that the blood lines are placed on the machine, attention that occlusion occurs at the site of blood pump compression upon the blood tubing is important. If the occlusion does not occur then reverse blood flow can result. This will result in recirculation and less-efficient treatments. If the occlusion is too tight then hemolysis may result. Most HD machines come equipped with an appropriate occluder device that measures the correct amount of gap at the size of occlusion.

Once HO commences, if one maintains less than 10% extracorporeal blood volume then either priming with saline or 5% albumin may be necessary at the beginning of the treatment. The standard blood flow rate for HD would be between 3 and 5 ml/kg per min with no more than 0.2 ml/kg per min of ultrafiltration to be carried out. Ultrafiltration above that will usually result in hemodynamic instability. Further, attention to appropriate-sized dialyzers is important. There are a number of newer hollow-fiber dialyzers that have small extracorporeal volume but have adequate surface area for adequate dialysis as ultrafiltration [9].

Many centers utilize "single-needle" access via a 2-mm or greater Hickman catheter [15]. This approach requires single-needle capability on the HD machine. Although potentially less efficient, attention to the arterial and venous times will help in maximizing both dialysis as well as ultrafiltration capability respectively. The use of "plate" dialyzers is necessary in order to have a compliant system necessary in single-needle HD.

Heparinization during the treatment can be easily maintained with a heparin load of 10–20 units/kg bolus then 10–20 kg/h. Many institutions utilize a bedside activated clotting time (ACT) in order to maintain a controlled heparinization [16]. An ACT between 150 and 200 s is adequate for a HD treatment. Centers using single-needle HD may need to utilize more heparin then stated above, due to the hemostasis in the dialyzer that occurs between arterial and venous components of single-needle HD.

Attention to the infant at the time of return of the extracorporeal blood volume is important. If one has 10% of the blood volume extracorporeal, then an infant could easily receive 5–8 ml/kg of blood transfusion rapidly. This is further exacerbated by the practice of rinsing the system once or twice with saline in order to give back all of the blood. This may result in replacement to the infant the total amount of ultrafiltration that was removed during the treatment. These maneuvers could result in hemodynamic instabilities as well as cardiac failure or malignant hypertension. Therefore, slow infusion of the extracorporeal blood volume is important. Many institutions utilize an "air return" to the patient. This would include a disconnection of the arterial port and turning down the blood pump rate when returning the blood. The arterial line is subsequently a system filled with air but the air leak detector is maintained in the *active* mode during this time in order to avoid the air emboli. This has the obvious risk of an air embolus to the patient. This has the benefit of avoiding excessive saline rinsing of the extracorporeal circuit and giving back excessive saline to the infant. Temperature control may be difficult in the infant due to a significant extracorporeal blood volume and relatively slow blood flow rates. Normothermia can be accomplished by increasing the dialysate bath temperature during each treatment.

In the volume-overloaded infant with pulmonary edema, attention to the oxygen requirements during the first 20–30 min of treatment is imperative. HD dialyzers may activate C5a during the initial part of the treatment, resulting in platelet and white cell aggregation within the

vasculature. In the face of an increased arterial-alveolar gradient from pulmonary edema, this may be exacerbated by the white blood cell and platelet layering along the vascular space. Therefore, FIO2 may need to be increased initially during the treatment [17].

Due to the fact that the majority of nutrition for infants is liquid based, as in PD, the number of dialysis treatments necessary per week may be partially based upon urine output. In the polyuric infant the indication for HD may be based more on the needs for dialysis as opposed to ultrafiltration. In the anuric infant more dialysis treatments per week may be necessary in order to maintain better volume control. Although not well studied, most centers will dialyze infants four to six times per week in order to maximize the attempt to maintain some degree of volume constance and in order to maximize "clearance" for improved growth. Because these children are dialyzed so frequently and due to the common use of infant "renal formulae," problems such as hyperphosphatemia are quite unusual.

## Infectious complications

Significant protein losses occur in the infant on PD [18]. Protein losses resulting in low plasma albumin as well as hypogammaglobulinemia may result in an increased risk of infection [19]. To date the dialysis database of the North American Pediatric Renal Transplant Cooperative Study has identified deaths in 15 infants while on dialysis; 14 of these deaths occurred on PD while 1 occurred on HD. Since at least 95% of infants undergoing RRT in North America are on PD, there is a roughly equal percentage of deaths in each modality group. Of the 14 deaths on PD, 5 were from infectious complications. Whether these patients were hypoalbuminemic or hypogammaglobulinemic is not specified in the database, yet one can speculate this may be an issue. Centers have shown that not only are these patients hypogammaglobulinemic but also have a poor responsiveness to normal infant immunizations [19–21]. Attention to these factors may improve the mortality rate in this population.

In HD protein losses are not similar to PD. It is believed that the protein losses and hypogammaglobulinemia that occur are directly related to the common protein losses of PD. No studies to date have adequately addressed whether or not hypogammaglobulinemia is a common finding in infants with chronic renal failure (CRF) or ESRD, irrespective of the mode of dialysis. A large number of infants with either CRF or ESRD should be investigated.

Exit site infections occur both in the PD and HD populations. Therefore, meticulous attention to side care is important to minimize this complication. In adults, HD access via a goretex shunt or fistula minimizes the risks of site infections when compared with an external access. Because infants do not have adequate-sized arteries or veins to support a subcutaneous shunt, the external access will continue to be associated with the risk of an "exit site infection."

## Growth

Fifty percent of the potential adult height is achieved in the first 18–24 months of life [22]. Attention to factors that impair growth in the infant with ESRD is important in order to minimize growth stunting. Studies to date have suggested that children on PD grow better than children on HD [23]. No studies to date have specifically addressed the issue of infants on PD versus HD. Factors that have been suggested to enhance growth in the child on PD have included: (1) increased dietary liberalness, (2) improved phosphorus control, and (3) most children on PD are dialyzed at home and are in a more comfortable environment.

## Nutrition

A number of formulae exist that are quite effective for the needs of the infant with ESRD. Ross (Columbus, Ohio, USA) makes PM 60/40 (0.67 calorie/ml), Suplena (2 calories/ml), and Nepro (2 calories/ml). These can be used either full strength as noted or diluted depending on the child's urine output. Suplena and Nepro may deliver too much magnesium to some infants, therefore monitoring of the magnesium may be necessary in some infants. Other formulae, such as S-29 (0.67 calories/ml, Wyeth, Philadelphia, Pa., USA) or Amin-Aid (2 calories/ml, American McGaw, Irvine, Calif., USA), can also be used for children with ESRD. S-29 requires replacement of electrolytes while Amin-Aid is depleted in trace elements and therefore both require additional additives.

The use of concentrated formulaes (with their high osmolality) in infants with high urine outputs must be avoided. This will result in an excessive osmolar load with the potential risk of dehydrating the infant who is already at risk for the same. Water-soluble vitamins are actively removed from the infant on dialysis; therefore, specific water-soluble vitamins should be replaced in this population. Avoidance of fat-soluble vitamins, including vitamin A, should be maintained. It is well documented that vitamin A can be retained in children with ESRD, resulting in secondary hypervitaminosis [24].

## Summary

In summary, infants can be supported on either PD or HD as treatment for ESRD. The infant with ESRD on dialysis has a significant mortality rate. Inadequate numbers on HD are available to address whether the mortality rate is higher on one modality than the other. Both modalities have their own unique associated risk. The important issue with either modality is that experienced nursing staff as well as a pediatric nephrologist be involved with the care of these patients because of their high mortality and risk of complications. Further, infant-specific equipment is important for use in this population in order to avoid equipment complications. The mortality rate of infants undergoing transplantation is less than in infants with ESRD on dialysis [1]. Therefore, because of the high mortality rate and the very high stress upon families as well as medical care givers,

dialysis in infants should only be seen as a bridge to transplantation.

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