Determinants of Survival in Pediatric Continuous Hemofiltration

William E. Smoyer, Cathy McAdams, Bernard S. Kaplan, and Joseph R. Sherbotie

ABSTRACT
Continuous hemofiltration (CH) is being used in increasing numbers of pediatric intensive care unit patients. Experience with 114 CH treatments in 98 critically ill children from March 1988 to March 1993 is presented in this study. Ages ranged from 1 day to 23 yr (mean ± SE = 7.1 ± 0.7 yr), and 54% of patients were male. Seventeen percent of all treatments were performed in neonates under 1 month of age. The most common primary diagnoses were sepsis and adult respiratory distress syndrome (11 patients each), liver transplantation and hypoplastic left heart syndrome (10 patients each), and hemolytic uremic syndrome (9 patients). The most frequent indications for CH were fluid overload and acute renal failure (42% each). Choices for CH included: continuous arteriovenous hemofiltration (CAVH, 50%), continuous arteriovenous hemodiafiltration (CAVH-D, 23%), continuous venovenous hemofiltration (CVVH, 18%), and continuous venovenous hemodiafiltration (CVVH-D, 9%). Choices for anticoagulation included: none (47%), regional (49%), and systemic (4%). Treatment duration ranged from 1 to 25 days (mean = 5.3 ± 0.4 days). Mean filter life span for 363 filters was 0.94 ± 0.1 filters/patient per day. Despite an overall survival rate of 43%, survival to discharge varied greatly (0 to 100%) among the 24 diagnostic groups: tumor lysis syndrome and systemic lupus erythematosus (3/3 patients each, 100%), hemolytic uremic syndrome (8/9 patients, 89%). This compares with: bone marrow transplantation (0/6 patients, 0%), hypoplastic left heart syndrome (2/10 patients, 20%), and leukemia (1/4 patients, 25%). Survival to hospital discharge was better in patients who did not receive pressors (P < 0.005) and in patients treated with combined ultrafiltration and dialysis (CAVH-D, CVVH-D) compared with ultrafiltration alone (CAVH, CVVH) (P < 0.005), but was not notably affected by patient age, sex, use of anticoagulation, filter life span, blood pump-assisted versus spontaneous CH, or duration of therapy. Filter life span was not affected by use of anticoagulation, but was remarkably longer in patients with arteriovenous versus venovenous CH (P < 0.004). It was concluded that: (1) empirical anticoagulation of patients treated with CH is not necessary; (2) children with a minority of underlying diseases and those requiring pressor support at initiation of CH appear to have relatively poor survival rates despite the technically effective use of CH; and (3) the addition of countercurrent dialysis to routine CH may enhance patient survival to hospital discharge.

Key Words: Dialysis, ultrafiltration, anticoagulation, filter life span
METHODS

Patients

This study was a retrospective review of the charts of all patients who received CH at The Children’s Hospital of Philadelphia between March 1988 and March 1993. A total of 114 treatments were performed on 98 critically ill patients (12 patients received two separate treatments and 3 patients received three separate treatments). A separate treatment was defined as treatment of: (1) different patients; (2) the same patient on different occasions, or (3) the same patient, requiring a change in the type of hemofiltration. All treatments were carried out in the intensive care unit. For the purposes of this study, all survival data represent patient survival to discharge from the hospital.

Equipment

The equipment used for CH varied, and was based on patient size, blood pressure, and type of CH. Vascular catheters used included Vygon (8F; Ecouen, France), Medcomp (16g, 5F; Harleysville, PA), Mudge (14-21 g; Cooke Critical Care, Bloomington, IN), and Jenkins (Cooke Critical Care, Bloomington, IN) catheters. The majority of catheters for arteriovenous therapy were placed in femoral arteries and veins, although subclavian veins were occasionally used for venous return. More than 95% of the hemofilters used were hollow fiber (D-20 and D-10; Amicon, Danvers, MA, and HF-250; Renal Systems, Minneapolis, MN), although a few parallel plate filters (Hospal, Meyzieu, France) were also used. Ultrafiltration rate was controlled by modified intravenous pumps (IVION, Boulder, CO) connected directly to the ultrafiltrate line (20).

When blood pump-assisted CH (CVVH, CVVH-D) was performed, a calibrated blood pump (Renal Systems, Minneapolis, MN) was used, with blood flows ranging from 25 to 200 mL/min. Target blood flows ranged from 2 to 10 mL/kg per min. A venous side air detector and a venous pressure monitor (Renal Systems, Minneapolis, MN) were added to the circuit to protect the patient in case an air embolism developed. Hemodialysis tubing with volumes of 45 to 75 mL was used (Medisystems, San Francisco, CA). Whole blood was used to prime the extracorporeal circuit when the total circuit volume exceeded 7 to 10% of the patient’s estimated blood volume. Vascular access was accomplished with the use of separate catheters as described above for arteriovenous therapies, or by using double lumen hemodialysis catheters (6.5F to 12F, Medcomp, Harleysville, PA, and Vascath, Ontario, Canada) placed into femoral or subclavian veins.

Fluids

Replacement fluid (used for CAVH, CVVH-D) consisted of either lactated Ringer’s solution with additional sodium chloride added to a final sodium concentration of 140 to 145 mEq/L, or bicarbonate-based replacement fluid, which was prepared in the hospital pharmacy. Standard bicarbonate-based replacement fluid consisted of sterile water with the following additives: NaCl 100 mEq/L, NaHCO₃ 40 mEq/L, KCl 2 mEq/L, K₂PO₄ 2 mEq/L, glucose 150 mg/dL, and MgSO₄ 1.5 mEq/L. When indicated, bicarbonate concentrations were varied from 25 to 60 mEq/L and potassium from 0 to 4 mEq/L. Replacement fluid was routinely infused pre-filter, into the “arterial” limb of the hemofilter circuit. Replacement fluid flow rates were relatively low compared with blood flow, so a "predilution" effect to minimize filter clotting and to enhance urea clearance was unlikely. Ultrafiltrate and dialysate flow rates were varied between 0 and 2000 mL/hr and were adjusted according to the patient’s clinical status. Target combined ultrafiltration and dialysate flow rates in most patients ranged from 10 to 20 mL/min per M², but rates of 50 to 65 mL/min per M² were used in neonates treated for hyperammonemia. Urea clearance was not routinely measured. When measured, urea clearance ranged from 8 to 18 mL/min per M² with the ultrafiltration and dialysate flows as described.

Dialysate (used for CAVH-D, CVVH-D) consisted of standard sterile peritoneal dialysis solution (Inpersol; Abbott, North Chicago, IL) with 1.5% dextrose (and sodium chloride, potassium chloride, and potassium phosphate adjusted to physiologic concentrations), or bicarbonate-based dialysate (prepared in the hospital pharmacy, as described above for replacement fluid). Dextrose concentrations, except when standard peritoneal dialysate fluid was being used, were adjusted to 100 to 200 mg/dL (0.1 to 0.2% dextrose). Dialysate was infused into the hemofilter casing countercurrent to blood flow.

Bicarbonate-based replacement fluid and dialysate were used in the majority of patients, although the composition of the fluid was chosen by the attending pediatric nephrologist. When bicarbonate-based dialysate or replacement fluid was used, a separate infusion of 10% calcium gluconate was added to replace filtration and dialysate losses and to correct deficits. This infusion was begun at 0.5 mL/h per 100 mL ultrafiltrate or dialysate and adjusted to maintain normal serum calcium levels. Calcium was infused post-hemofilter, separate from the replacement fluid or dialysate, to prevent precipitation in solutions containing bicarbonate and phosphorus. Conductivity measurements of all hospital-made replacement and dialysis solutions were used to assure proper electrolyte concentrations. Attempts were made to convert all fluids, including hyperalimentation, to physiologic concentrations of electrolytes (particularly sodium) while the patients were on CH.

Anticoagulation

Decisions regarding the use of heparin were made on the basis of platelet counts, prothrombin time and partial thromboplastin time values, and evidence of bleeding. Heparin was not used when there was bleeding, when a risk of bleeding was present, when prothrombin time or partial thromboplastin time was greater than 130% of normal for age, or when the platelet count was less than 70,000/µL. When used, anticoagulation was initiated with a slow continuous infusion of heparin (without an initial bolus) into an arterial (pre-filter) port of the CH circuit to maintain the activated clotting time (ACT; Hemochron Whole Blood Coagulation System; International Technidyne Corporation, Edison, NJ) on the venous (post-filter) side of the CH circuit at 130 to 150% of normal. No attempt was made to systemically anticoagulate the patients. Protamine was used in only a few patients to reverse anticoagulation.

Statistics

Statistical analyses were performed using a chi-squared test or t test, as indicated. Results are expressed as mean ± SEM. Differences between groups were considered statistically significant if P < 0.05.
RESULTS

Age and Sex Distribution

The age distribution of patients treated with CH ranged from 1 day to almost 23 yr (Figure 1). Fifty-four percent of patients were male and 46% were female.

Primary Diagnoses

The total number of patients in each of 24 primary diagnostic categories is shown in Figure 2. Although many of these patients also had several secondary diagnoses, the classification of patients was based on the primary diagnosis for that particular hospital admission. Five primary diagnoses were included in the category labeled "Other" in Figure 2: (1) inflammatory bowel disease; (2) abdominal gunshot wound; (3) Rh incompatibility; (4) rhabdomyolysis; and (5) thalassemia.

Indications for CH

The indications for initiating CH are displayed in Figure 3. There were a total of 179 indications, because several patients had more than one indication for CH at the time of initiation of therapy. Indications were classified according to the underlying or major reason(s) for initiating CH. The "Metabolic Abnormalities" category consisted of inborn errors of metabolism (urea cycle defects associated with hyperammonemia, maple syrup urine disease, and primary lactic acidosis), idiopathic hyperammonemia, and hyperammonemia associated with liver failure. The "Other" category consisted of a single patient with early adult respiratory distress syndrome (ARDS) who was entered in a prospective study, but had no other indication for beginning CH.

Type of CH

Figure 4 shows the distribution of the types of CH used for our patients. The type of CH used was chosen by the attending pediatric nephrologist. Although slow continuous ultrafiltration is frequently used in the treatment of neonates during Extra-Corporeal Membrane Oxygenation (ECMO) at our hospital, its use is considered routine and these patients are not included in our analysis.

Anticoagulation

Almost half (47%) of all CH treatments were performed without the use of any anticoagulation. Forty-nine percent were performed using "regional" anticoagulation (described in "Methods") and 4% with systemic anticoagulation. An initial bolus of heparin was rarely used. There was no notable difference in the frequency of heparin use in arteriovenous CH compared with venovenous CH ($P = \text{not significant, by chi-squared test}$).

Figure 1. Age distribution in 98 children treated with CH; median 4.5 years, range 1.0 day to 22.8 yr; percentage of total patients is shown above the bars.
Duration of CH

A total of 607 patient days of CH treatment were evaluated. The duration of individual therapy with CH ranged from less than one day to 25 days. The median treatment time was 4 days, and the mean duration was 5.3 ± 0.4 days. The majority of treatments lasted only a few days, but several patients were treated for longer than 2 wk.

Filter Life Span

We were able to document filter usage in 96 of the 114 treatments (84%). This produced data on the use of 363 filters. In the majority of treatments, filters were replaced only if they were clotted. In a few treatments, filters were replaced after 24 h of use. The mean filter life span was 0.94 ± 0.1 filters/patient per day, with a range from 0.20 to 3.0 filters/patient per day. Mean filter life span was not affected by the use of anticoagulation (1.00 versus 0.89 filters/patient per day, anticoagulation versus none; P = not significant, by unpaired t test), but was remarkably longer in arteriovenous compared with venovenous CH (AV -0.81 filters/patient per day versus VV -1.26 filters/patient per day; P < 0.004 by unpaired t test) with the same frequency of heparin use.

Complications

Sixteen percent of all treatments (18/114) had complications associated with the use of hemofiltration (0.03 events/patient treatment day; Table 1). Most complications had no significant clinical consequences or were easily remedied (e.g., transient hypotension with excessive fluid removal). Several complications deserve special consideration. The requirement for close monitoring of patients on CH is exemplified by one patient who removed his femoral venous access and subsequently required transfusion. Hyperkalemia occurred in another patient after use of a replacement fluid that inadvertently contained an excessive concentration of potassium. Electrolyte imbalances associated with additives to the replacement or dialysate solutions occurred in <3% (3/114) of treatments. It is unclear if the two treatments complicated by seizures and line sepsis were actually related to the CH treatments. Two treatments were unsuccessful because of inadequate vascular access, both for arteriovenous and venovenous CH.

Patient Survival

The percent survival for the 13 primary diagnostic groups containing three or more patients is shown in Figure 5. Although the overall survival rate was 43%, there were striking differences among diagnostic groups. Among the diagnostic groups containing three or more children, patient survival ranged from 0 to 100%. The single patient with hemolytic uremic syndrome who died had an atypical recurrent form and survived initial CH treatment. Two of the three patients diagnosed with "acute renal failure" subsequently developed multiple organ failure during their hospitalization. The patient who did not develop multiple organ failure survived to discharge.

An evaluation of the correlation between several patient- and CH-related factors and patient survival is displayed in Table 2. The overall survival rate of 35% for all neonates (<1 month of age) was not signifi-
Figure 3. Indications for beginning CH in 98 children, 114 treatments; $N = 179$ indications, as several patients had multiple indications; percentage of total indications is shown to the right of the bars.

Figure 4. Modality of CH used to treat 98 children; $N = 114$ treatments. "CHD with ECMO" refers to CH with the filter connected in parallel with an ECMO circuit (1 patient); percentage of total treatments is shown above the bars.

Significantly different from the survival rate for patients older than 1 month, and compared favorably with the study population as a whole (43%). Analysis of available data revealed that survival was also not significantly affected by patient sex, use of anticoagulation, pump-assisted (CVVH, CVVH-D) versus spontaneous (CAVH, CAVH-D) hemofiltration, filter life span, or duration of therapy (all analyzed by chi-squared test). Survival to discharge was significantly better in patients who did not receive vasopressor support ($P < 0.005$ by chi-squared test, Table 2). Although 15 patients were treated with more than one type of CH, analysis of the remaining 83 patients suggested improved survival in patients treated with combined ultrafiltration and dialysis (CAVH-D, CVVH-D) compared with ultrafiltration alone (CAVH, CVVH) ($P < 0.005$ by chi-squared test).
0.005 by chi-squared test). There were no significant differences between these two groups (CAVH, CVVH versus CAVH-D, CVVH-D) in the use of vasopressors or in filter lifespan.

**DISCUSSION**

This study contains the most extensive experience compiled to date regarding CH in infants and children. Our results demonstrate that patient outcome after CH in these critically ill children (43% overall patient survival to hospital discharge) compares very favorably with that observed in adults, in which survival rates range from 23 to 45% (21-25). In addition, we have shown that CH can be as effective in neonates as in older children.

The indications for treatment with CH in our patients were similar to those reported in other studies (15-19,21,26). Peritoneal dialysis and hemodialysis are routinely used in our institution for the treatment of uncomplicated acute renal failure. Nearly all of our patients had or developed multiple organ involvement before or during CH treatment, and 70% required pressor support. Liberal administration of parenteral nutrition, and blood products when necessary, was routine. Electrolyte imbalances (particularly hypokalemia) resulting from the removal of large volumes of plasma water and small dissolved solutes were minimized by converting all intravenous fluids to physiologic concentrations of electrolytes during CH, and by increasing the sodium concentration of commercially available peritoneal dialysate to a physiologic level when used in CAVH-D or CVVH-D. As reported by others, supplementation with phosphorus and potassium was necessary when serum levels normalized during CH (22).

Our study suggests that CH may also represent a novel and effective approach to the treatment of a number of clinical states other than acute renal failure and its consequences, including ARDS and several metabolic disorders. Our experience in a small group of children with ARDS demonstrated significant improvement in pulmonary gas exchange after 48 hours of CAVH-D (27). Other reports have suggested that CAVH and CVVH are effective in the treatment of neonates with urea cycle enzymopathy-associated hyperammonemia, maple syrup urine disease, and several other metabolic disorders (28-30). Our experience confirms that aggressive CAVH-D or CVVH-D may result in even more effective ammonium and amino acid clearance in newborns with these disorders (Sherbotie JR, manuscript in preparation).

Previous studies have documented improved solute clearances by using the diffusive component provided by countercurrent dialysate flow during CH (CAVH-D, CVVH-D) (3,4,31). Despite this, we found that neither hemodialysis nor the addition of countercurrent dialysate to CH were required for control of azotemia or the metabolic derangements associated with acute renal failure in two-thirds (68%) of the treatments.

Other studies have suggested that blood pump-assisted venovenous CH is at least equally efficacious and is safer than arteriovenous CH because the need for a large arterial vascular access is eliminated (23,32,33). One study has also reported improved survival in adults treated with blood pump-assisted CH (CVVH) compared to spontaneous CH (CAVH) (24). These authors suggested that the improved survival may have been due to the higher daily ultrafiltration volumes achieved with pump-assisted CH. The relative ultrafiltration volumes achieved with CAVH in this study were less than the target volumes in our patients. In sharp contrast to this, a recent pediatric study reported a significantly worse survival rate for children treated with CVVH compared to CAVH (17). No data were presented, however, comparing daily ultrafiltrate volumes between modalities. Our results suggest that the use of pump-assisted CH (CVVH) does not have a notable effect on patient survival at comparable dialysate plus ultrafiltrate flow rates.

The study presented here further demonstrates that arteriovenous CH can be performed with minimal problems in children. Access was consistently achieved without complications. Arteriovenous CH offers several advantages over venovenous therapies: (1) there is no need for a blood pump; (2) the extracorporeal circuit volume is generally smaller; and (3) the potential problems associated with negative pressure generated by a blood pump at the "arterial" access of the venovenous circuit are eliminated. In addition, our results show that mean filter life span was longer in patients treated with arteriovenous compared with venovenous CH. Several patients could not be effectively treated with arteriovenous CH because of poor blood flow (e.g., congenital heart disease with low mean arterial pressures and elevated central venous pressures), and venovenous CH was required. Anticoagulation of critically ill patients treated with CH is not without risk. Bleeding and hematoma formation are among the most frequent complications.

**TABLE 1. Complications associated with CH in 98 children**

<table>
<thead>
<tr>
<th>Complications</th>
<th>Number of Treatments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bleeding around access</td>
<td>2</td>
</tr>
<tr>
<td>Patient removed access</td>
<td>1</td>
</tr>
<tr>
<td>Hypotension</td>
<td>4</td>
</tr>
<tr>
<td>Hypokalemia</td>
<td>1</td>
</tr>
<tr>
<td>Hemofilter membrane rupture</td>
<td>2</td>
</tr>
<tr>
<td>Hyperkalemia</td>
<td>2</td>
</tr>
<tr>
<td>Seizures</td>
<td>1</td>
</tr>
<tr>
<td>Inadequate vascular access</td>
<td>2</td>
</tr>
<tr>
<td>Hemolysis</td>
<td>1</td>
</tr>
<tr>
<td>Line sepsis</td>
<td>1</td>
</tr>
</tbody>
</table>

* N = 18/114 treatments. Percentage of treatments with complication(s): 16% (0.03 events/patient treatment day).
Figure 5. Diagnosis-related patient survival for the 13 primary diagnostic groups containing three or more patients; (shaded bars) number of patients surviving to hospital discharge; (open bars) number of patients treated in each group; percent survival for each category is shown to the right of the bars; N = 98 patients.

The incidence of reported complications related to CH ranges from 5 to 31% (13, 21, 32–34). Although 16% of CH treatments in this study were associated with complications, far fewer resulted in any clinically significant sequelae. The most potentially serious complications included electrolyte imbalances related to incorrect additives in hospital-made replacement or dialysis fluids, and problems associated with maintaining large arterial or venous access in uncooperative patients.

Our analysis of several patient- and CH-related factors identified only two poor prognostic factors during CH. First, patients who required vasopressor support while on CH had a notably worse survival rate than those not needing vasopressors. Clearly the decision regarding the use of pressors was based on clinical factors, and the worse survival rates for those patients requiring pressors may simply reflect treatment of a more critically ill group of patients. The need for vasopressors has also been shown in adult studies to be one of the most important predictors of a poor outcome (19). Second, patients with a few specific primary diagnoses had particularly poor outcomes. These included patients who had undergone bone marrow transplantation (0% survival), patients who had undergone corrective or partially corrective surgery for hypoplastic left heart syndrome (20% survival), and patients with leukemia (25% survival). The reasons for the high mortality rate in these small groups of patients could not be determined from this study. While it is possible that these patients were also simply more ill than those in other diagnostic groups when CH was begun, stratification of patients according to the severity of illness was not performed in this retrospective review. Furthermore, the rela-
TABLE 2. Effects of several patient- and CH-related factors on patient survival to hospital dischargea

<table>
<thead>
<tr>
<th>Factor</th>
<th>% Survival (N)</th>
<th>P Value</th>
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<tbody>
<tr>
<td>Age</td>
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<td></td>
</tr>
<tr>
<td>&lt; 1 month</td>
<td>35 (6/17)</td>
<td>NS</td>
</tr>
<tr>
<td>&gt; 1 month</td>
<td>44 (36/81)</td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>46 (25/54)</td>
<td>NS</td>
</tr>
<tr>
<td>Female</td>
<td>39 (17/44)</td>
<td></td>
</tr>
<tr>
<td>Pressorsc</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>31 (18/59)</td>
<td>&lt; 0.005</td>
</tr>
<tr>
<td>No</td>
<td>68 (17/25)</td>
<td></td>
</tr>
<tr>
<td>Anticoagulation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heparin</td>
<td>53 (28/53)</td>
<td>NS</td>
</tr>
<tr>
<td>None</td>
<td>31 (14/45)</td>
<td></td>
</tr>
<tr>
<td>Blood Flow</td>
<td></td>
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</tr>
<tr>
<td>Arteriovenous</td>
<td>40 (25/62)</td>
<td>NS</td>
</tr>
<tr>
<td>Venovenous</td>
<td>47 (17/36)</td>
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<tr>
<td>Filter Life Spand</td>
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<tr>
<td>≤ 1 Filter/patient per day</td>
<td>45 (29/64)</td>
<td>NS</td>
</tr>
<tr>
<td>&gt; 1 Filter/patient per day</td>
<td>33 (6/18)</td>
<td></td>
</tr>
<tr>
<td>Duration of Therapy</td>
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<td></td>
</tr>
<tr>
<td>≤ 5 days</td>
<td>44 (27/62)</td>
<td>NS</td>
</tr>
<tr>
<td>&gt; 5 days</td>
<td>42 (15/36)</td>
<td></td>
</tr>
<tr>
<td>Type of CH*</td>
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<td></td>
</tr>
<tr>
<td>UF alone</td>
<td>29 (17/58)</td>
<td>&lt; 0.005</td>
</tr>
<tr>
<td>UF + Dialysis</td>
<td>68 (17/25)</td>
<td></td>
</tr>
</tbody>
</table>

a Numbers in parentheses represent the number of patients for whom data was available regarding each factor analyzed. All analyses were performed using chi-squared test.

b NS, not significant.
c Pressor data available for 86% of patients.
d Filter life span data available for 84% of patients.

e Type of CH data available for 85% of patients.

were similar to target ultrafiltration flow rates during CAVH and CVVH, although actual volumes were not retrieved. This suggests the possibility that the addition of dialysis to the CH treatment may have an independent therapeutic effect, regardless of patient diagnosis or severity of illness. The addition of dialysis to ultrafiltration may improve small solute removal. To date, however, there have been no reports of a beneficial effect on survival by the addition of dialysis to ultrafiltration. Confirmation of such an effect would require a prospective, controlled study carefully assessing the relative contribution of diffusion and convection to solute clearance and to overall patient outcome.

In summary, this study of a large group of children treated with CH has resulted in a number of observations of interest to clinicians involved either in the use of CH or the management of critically ill infants and children: (1) empirical anticoagulation of patients treated with CH is not necessary; (2) children with a minority of underlying diseases and those requiring pressor support at initiation of CH appear to have relatively poor survival rates despite the technically effective use of CH; and (3) the addition of countercurrent dialysis to routine CH may enhance patient survival to hospital discharge, but the mechanism(s) remain speculative.

REFERENCES

12. Zobel G, Ringer E, Muller W: Continuous arteriovenous
24. Storck M, Hartl WH, Zimmerer E, Inthorn D: Comparison of pump-driven and spontaneous continuous hae-