INTRODUCTION

In the inpatient setting, a high proportion of nephrology consultations are requested for patients in the intensive care unit (ICU). These patients may have acute kidney injury (AKI) or may be critically ill and have end-stage renal disease (ESRD). Thus, nephrologists need to understand recent evidence-based advances in the field of critical care, as well as areas of ongoing controversy and investigation. In this article, we summarize the diagnosis and management of shock, as well as the management of sepsis, acute lung injury/acute respiratory distress syndrome (ALI/ARDS), and fulminant hepatic failure, all of which are associated with high mortality in the critical care setting. We discuss infectious complications of critical care, including ventilator-associated pneumonia and catheter-related infections. Supportive care, including nutrition, insulin therapy, and anemia management, are reviewed. Dialysis considerations in critically ill patients are discussed. Last, we review the management of several life-threatening intoxications, many of which require early recognition and consideration of dialysis.

SHOCK

Definition: absolute hypotension (eg, systolic blood pressure < 90 mm Hg or mean arterial pressure [MAP] < 60 mm Hg) or relative hypotension (eg, decrease in systolic blood pressure > 40 mm Hg) resulting in inadequate end-organ perfusion.1,2

Causes

I. Hypovolemic: hemorrhage, volume depletion due to decreased fluid intake or excessive fluid losses
II. Distributive: low systemic vascular resistance
   A. Sepsis
   B. Anaphylaxis
   C. Endocrine: adrenal insufficiency
   D. Neurogenic: spinal shock
III. Cardiogenic: acute myocardial infarction, heart failure, valvular heart disease, arrhythmias
IV. Obstructive: extracardiac disease resulting in poor cardiac function: decreased cardiac filling (eg, tamponade, mechanical ventilation with high positive end-expiratory pressure resulting in decreased venous return) or increased cardiac afterload (massive pulmonary embolism)

Diagnosis3

I. Echocardiography: transthoracic or transesophageal
II. Invasive hemodynamic monitoring
   A. Central venous catheter
      1. Central venous pressure (CVP) may be artificially high in patients on mechanical ventilation and high levels of positive end-expiratory pressure (increases intrathoracic pressure)
      2. Superior vena cava oxygen saturation (ScVO₂) as a correlate of mixed venous oxygen saturation (which can be measured only with a pulmonary artery catheter)
         a. Correlation with mixed venous oxygen saturation somewhat controversial4
   B. Pulmonary artery catheter
      1. Pulmonary artery occlusion pressure/pulmonary capillary wedge pressure reflects left atrial pressure in the absence of significant valvular heart disease
2. Cardiac output monitoring: Fick or thermodilution
   a. Thermodilution cardiac output monitoring unreliable with tricuspid valve disease
   b. Fick cardiac output monitoring uses mixed venous oxygen saturation (obtained from the pulmonary artery) to calculate cardiac output; assumes normal oxygen consumption
C. Cardiac output, systemic vascular resistance, and CVP can be used to distinguish between the different types of shock (Table 1)
D. Pulmonary artery catheterization has not been shown to be of benefit in critically ill or surgical populations. In general, CVP monitoring is sufficient. Pulmonary artery catheters may be associated with complications, including infection, arrhythmias, and pulmonary artery rupture. However, in cases of mixed shock (eg, septic and cardiogenic), invasive cardiac output monitoring may be useful to tailor vasoressor therapy. Echocardiography also may be useful in the management of complex (eg, mixed cause) shock or shock in a patient with known heart failure
III. Other methods to monitor cardiac output (partial carbon dioxide rebreathing, pulse contour analysis) are less well validated
   A. Arterial catheter
      1. Allows for beat-to-beat blood pressure monitoring
      2. Radial, femoral, or dorsalis pedis sites preferred
      3. Perform Allen test before radial arterial catheter placement to confirm adequate collateral circulation
   B. Serum tryptase levels can be useful in anaphylaxis
   C. Commonly used medications include:
      1. Phenylephrine (neosynephrine): pure α agonist
      2. Dopamine: dopamine receptor, β and α agonist (dose dependent)
      3. Dobutamine: β1 and β2 agonist, use can be associated with hypotension; often used to increase cardiac output in patients with cardiogenic shock caused by congestive heart failure
      4. Epinephrine: β1 greater than α1, β2 receptor agonist
      5. Norepinephrine (Levophed): α1 and β1 agonist, associated with less tachycardia than epinephrine
      6. Vasopressin: has been used as a second-line pressor for refractory septic shock; use can be associated with significant mesenteric ischemia
      7. Milrinone/amrinone: phosphodiesterase inhibitors with inotropic and vasodilatory effects; used along with dobutamine for the treatment of patients with cardiogenic shock in the setting of congestive heart failure
IV. Early goal-directed therapy for sepsis (see Sepsis IV)
V. Corticosteroids for adrenal insufficiency (see Sepsis VI)
VI. Anaphylaxis: epinephrine, H1 and H2 blockers, steroids
VII. Supportive care: intubation and mechanical ventilation if needed

SEPSIS

Diagnosis

I. Systemic inflammatory response syndrome (SIRS): characterized by the presence of: (1) temperature greater than 38°C or less than 36°C, (2) heart rate greater than 90 beats/min, (3) respiratory rate greater than 20 breaths/min or need for support with mechanical ventilation, and (4) white blood cell count greater than 12,000 cells/µL or less than 4,000 cells/µL
II. Sepsis: suspected or documented infection in association with 2 or more SIRS criteria
III. Severe sepsis: sepsis with acute organ dysfunction
IV. Septic shock: severe sepsis with hypotension despite adequate fluid resuscitation

Prognosis

I. Approximately 750,000 cases/y in the United States, resulting in approximately 200,000 deaths
II. Mortality rate approximately 30% to 40%, but greater in sicker populations
III. Major risk factor for AKI

Treatment

I. Appropriate broad-spectrum antibiotics and control of source of infection (eg, debridement, removal of infected catheter)
II. Volume resuscitation
III. Vasopressors as needed
   A. Data supporting choice of first vasopressor limited
   B. Norepinephrine/Levophed may be reasonable because it will increase systemic vascular resistance and increase cardiac output
   C. A recent clinical trial does not support the use of vasopressin as a first-line agent in combination with norepinephrine (Vasopressin and Septic Shock Trial [VAST])
IV. Early goal-directed therapy: refers to the combination of volume resuscitation/vasopressors and inotropes/transfusion guided by CVP (target CVP, 8 to 12 mm Hg), arterial blood pressure (MAP > 65 mm Hg), ScVO₂ (ScVO₂ > 70%), and evidence of end-organ perfusion (urine output > 0.5 mL/kg/h)
   A. A single-center randomized clinical trial showed mortality benefit with early institution of these interventions (within 6 hours of diagnosis)

Table 2. Summary of Vasopressor and Inotropic Agents

<table>
<thead>
<tr>
<th>Vasopressors</th>
<th>Comments</th>
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<tbody>
<tr>
<td>α Agonists</td>
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<tr>
<td>Phenylephrine (neosynephrine)</td>
<td>High doses can be associated with reflex bradycardia</td>
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<tr>
<td>Mixed α/β agonists</td>
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<tr>
<td>Norepinephrine (Levophed)</td>
<td>Causes less tachycardia than epinephrine</td>
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<td>Epinephrine</td>
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<tr>
<td>Dopamine agonists</td>
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<tr>
<td>Dopamine</td>
<td>Like epinephrine, associated with significant tachycardia</td>
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<tr>
<td>Other</td>
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<tr>
<td>Vasopressin</td>
<td>Increases vascular smooth muscle receptor tone via V1 receptor</td>
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<td>Inotropes</td>
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<tr>
<td>β Agonists</td>
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<tr>
<td>Dobutamine</td>
<td>Use can be associated with hypotension</td>
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<tr>
<td>Phosphodiesterase inhibitors</td>
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<td>Milrinone</td>
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<td>Amrinone</td>
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Shock [PROCESS]) is ongoing to confirm results of the initial study and try to better correlate these interventions with benefit

V. Activated protein C was shown to have mortality benefit for patients with severe sepsis with Acute Physiology and Chronic Health Evaluation (APACHE) II score of 25 or higher in a large randomized multicenter clinical trial16
   A. Activated protein C has not been shown to be of benefit in children or less critically ill adults17,18
   B. A clinical trial of critically ill adults with refractory shock (PROWESS-SHOCK) is ongoing19

VI. Role of steroids for relative adrenal insufficiency is controversial20
   A. Diagnosis of relative adrenal insufficiency should be considered with refractory shock after volume resuscitation
   B. Both basal cortisol level and response to high-dose corticotropin (ACTH) stimulation test have been used to define adrenal insufficiency in the critically ill,21 although criteria for adrenal insufficiency are controversial
   C. Annane et al22 showed a mortality benefit with hydrocortisone/fludrocortisone treatment for 7 days in patients with relative adrenal insufficiency and early septic shock in a multicenter placebo-controlled randomized clinical trial
   D. However, in a subsequent multicenter placebo-controlled randomized clinical trial, low-dose hydrocortisone therapy did not improve survival in patients with septic shock23
      1. Treatment with hydrocortisone was associated with a shorter time on vasoressor therapy, but also with an increase in new sepsis and new septic shock
      2. Differing results may be attributable to differences in duration of septic shock, severity of illness, steroid administration (patients in study by Annane et al22 randomly assigned earlier, had higher severity of illness scores, and received fludrocortisone and hydrocortisone)
   E. In both studies, patients were randomly assigned after the ACTH stimulation test, but before results were available; thus, patients should be treated empirically with steroids if there is a concern for relative adrenal insufficiency, rather than waiting for results of the stimulation test

VII. Other supportive care as warranted by the clinical condition: intubation and mechanical ventilation, nutrition, glycemic control

VIII. Data for some of the Surviving Sepsis guidelines are limited

ALI/ADULT RDS

Diagnosis24
Acute onset (<7 days) of:
   I. Hypoxemia: PaO2/fraction of inspired oxygen (FIO2) less than 300 for ALI, less than 200 for ARDS
   II. Bilateral infiltrates on chest radiograph
   III. No clinical evidence of left atrial hypertension

Risk Factors25
   I. Infection: pneumonia, sepsis
   II. Aspiration
   III. Trauma
   IV. Transfusion

Prognosis26
   I. Mortality rate 25% to 40% in most recent studies

Treatment
   I. Lung protection with a low tidal volume ventilation strategy has mortality benefit for patients with ALI/ARDS27
      A. Tidal volume, 6 mL/kg ideal body weight (versus 12 mL/kg ideal body weight)
      B. Ideal body weight: 50 + 2.3 × (height in inches – 60) for men, 45.5 + 2.3 × (height in inches – 60) for women
      C. Plateau pressure less than 30 mm H2O
      D. Goal PaO2, 55 to 80 mm Hg
      E. Target pH, 7.30 to 7.45
1. For moderate acidosis (pH, 7.15 to 7.30), can increase respiratory rate (not to exceed 35) until pH 7.35 or PaCO₂ less than 25 mm Hg
2. For severe acidosis (pH < 7.15), can increase respiratory rate (not to exceed 35), increase tidal volume, or administer intravenous bicarbonate

F. Permissive hypercapnia/respiratory acidosis may be problematic in patients with concomitant AKI or chronic kidney disease who may have concurrent metabolic acidosis.²⁸

II. A fluid conservative management strategy increases ventilator-free days in patients with ALI/ARDS²⁹

A. Patients with ESRD or AKI requiring dialysis at the time of study enrollment were excluded from the fluid management study
B. The fluid conservative management strategy was not associated with an increased requirement for dialysis
C. Patients in the fluid-conservative group received diuretics to achieve a target CVP of 4 to 8 mm Hg or pulmonary artery occlusion pressure of 8 to 12 mm Hg provided they: (1) were out of shock for 12 hours, (2) had effective circulation based on cardiac index or physical examination, and (3) were not oliguric, defined as urine output less than 0.5 mL/kg/h

III. Higher levels of positive end-expiratory pressure do not appear to have mortality benefit for patients with ALI³⁰-³²

IV. Rescue therapies include:
   A. Extracorporeal membrane oxygenation (ECMO)
   B. High-frequency ventilation
   C. Partial liquid ventilation with a perfluorocarbon
   D. Inhaled nitric oxide
   E. Prostacyclin

V. Animal studies suggest that injurious mechanical ventilation (eg, high tidal volume) and lung injury can lead to AKI,³³-³⁵ although the molecular mechanisms have not been fully elucidated. Similarly, AKI may lead to or exacerbate existing lung injury in animal models

VENTILATOR-ASSOCIATED PNEUMONIA³⁶

I. Clinical suspicion of infection: new fevers, leukocytosis or purulent respiratory secretions, worsening respiratory failure/increased ventilator support
II. Culture: gold-standard methods are unclear
   A. Many ways to obtain culture specimens, including such quantitative methods as bronchoalveolar lavage and protected specimen brush, as well as nonquantitative cultures and endotracheal aspirates
   B. Although bronchoalveolar lavage and protected brush specimens with quantitative cultures may allow for more rapid antibiotic deescalation, superiority to nonquantitative methods is not clear³⁷-³⁹

III. Appropriate empiric initial antibiotic therapy is key: antibiotics should be tailored to known local antimicrobial resistance patterns

IV. Patients with ventilator-associated pneumonia are at high risk of sepsis and associated AKI

CATHETER-RELATED INFECTIONS

Definitions³⁰

I. Catheter colonization: presence of bacteria or fungi in a quantitative or semiquantitative culture of catheter material, but without signs of local or systemic infection. Microorganisms grow in a biofilm that coats the surface of the catheter
II. Exit-site/insertion-site infection: erythema, tenderness, induration, or purulence at the site the catheter exits the skin
III. Tunnel infection: erythema, tenderness, induration, or purulence in the tract where a venous catheter is tunneled under the skin
IV. Catheter-related bloodstream infection: bacteremia in the presence of positive cultures from the catheter itself (see Diagnosis section)

Incidence

I. Catheter-related bloodstream infections are more common with nontunneled than tunneled central catheters
II. Major risk factors for infection include duration of catheter use, number of catheter
lumens (multilumen catheters carry greater risk of infection), poor technique at the time of catheter insertion, use of total parenteral nutrition (TPN)41

III. Although subclavian catheters generally are associated with lower risk of infections compared with internal jugular and femoral catheters, these should be avoided in patients with AKI or ESRD because of the risk of subclavian stenosis

IV. Although the internal jugular site generally is believed to be associated with less risk of infection than the femoral site, a recent randomized clinical trial suggests that the risk of infection is similar with nontunnelled femoral and internal jugular dialysis catheters in critically ill immobilized patients.42 However, in patients in the highest tertile of body mass index (≥28.4 kg/m²), femoral catheters were associated with increased risk of infection compared with internal jugular catheters. Furthermore, these results cannot be generalized to mobile non–critically ill individuals

Diagnosis43

I. Differential time to positivity: if a blood sample drawn from the catheter is positive more than 2 hours before the peripheral-blood culture, this is highly suggestive of catheter-related bloodstream infection

II. Quantitative blood cultures: if a blood sample drawn through the catheter has a greater concentration (≥5:1 ratio) of microorganisms than the peripheral-blood culture, this is highly suggestive of catheter-related bloodstream infection

III. Quantitative culture of catheter segment or catheter tip: requires removal of central venous catheter

Treatment44

I. Empirc broad-spectrum antibiotics; staphylococci are common pathogens

II. Removal of central venous catheter; however, this decision will depend on: (1) ongoing need for central venous access, (2) ability to replace the catheter at another site, (3) clinical status of the patient, and (4) type of infection/pathogen

III. Indications for catheter removal include: septic shock, presence of a tunnel infection, polymicrobial bacteremia, gram-negative rod bacteremia, fungemia, evidence of distant infection (abscesses, endocarditis), and failure to respond to antibiotic therapy

NUTRITION/TPN

I. Patients who are critically ill frequently are hypermetabolic/hypercatabolic and therefore at increased risk of nutritional complications45

II. Calorie requirements can be estimated by using predictive equations (Harris-Benedict or Mifflin-St Jeor for obesity) or measured by using indirect calorimetry (in which oxygen consumption and carbon dioxide generation are measured in expired gas and used to calculate resting energy expenditure and the respiratory quotient [RQ])

A. Indirect calorimetry is less accurate as oxygen requirements increase and generally is not useful when the patient requires an Fio₂ greater than 0.60

B. Indirect calorimetry also allows for calculation of the RQ; a high RQ (≥1.0) suggests overfeeding (of either total calories or carbohydrates) or a hypermetabolic state

III. Nitrogen balance can be used to determine whether provision of nutrition therapy (particularly protein) is adequate

A. Protein requirements of patients with AKI vary based on the underlying cause of AKI and type of renal support provided (both intermittent hemodialysis and continuous renal replacement therapy [CRRT] associated with ongoing protein losses)46

B. Patients on CRRT likely will require at least 1.6 to 1.8 g/kg/d of amino acids and, in some studies, have received up to 2.5 g/kg/d without complications

IV. Serum markers for nutritional adequacy in the critically ill are controversial45

A. Although serum albumin level is a valuable prognostic indicator of morbidity and mortality, serum albumin levels decrease with metabolic stress and with specific disease states that are common in the ICU, such as liver failure
B. Transferrin, prealbumin, and retinol-binding protein levels may be superior markers of nutritional status; however, in patients with critical illness, synthesis of these proteins may decrease because of preferential production of acute-phase reactants (ie, C-reactive protein).

C. Prealbumin level may be falsely increased in patients with kidney failure because of reduced clearance and in patients on high-dose steroid therapy.

D. Trends of prealbumin and C-reactive protein levels may be more useful than absolute values to follow up response to nutrition therapy.

V. In an observational cohort study, critically ill patients with AKI did not have significantly more major gastrointestinal complications (vomiting, diarrhea, abdominal distention) or more infectious complications (aspiration pneumonia) 47

VI. TPN is associated with increased risk of infection and should be used only if efforts to provide enteral nutrition have failed or the patient has a strict contraindication to enteral feeding.

INTENSIVE INSULIN THERAPY

I. A large randomized clinical trial of surgical patients showed mortality benefit and decreased length of ICU stay in patients who received intensive insulin therapy (target blood glucose, 80 to 110 mg/dL [4.4 to 6.1 mmol/L]) 48

II. A subsequent randomized clinical trial of medical patients did not show the same mortality benefit 49

A. However, patients who had longer ICU stays (defined as ≥3 days) had decreased in-hospital and ICU mortality with intensive insulin therapy.

III. Intensive insulin therapy is associated with an increased incidence of severe hypoglycemia 50

IV. It is unclear whether the benefit is from glycemic control or a direct effect of the insulin itself.

V. A pooled analysis of the large medical and surgical clinical trials suggest that patients with better glycemic control had lower mortality rates; however, it is unclear whether this was a result of the improved glycemic control or differences in severity of illness 51

VI. Similarly, a pooled analysis of the 2 large clinical trials and a meta-analysis suggest that intensive insulin therapy has a renoprotective effect 52,53

VII. However, a recent meta-analysis of 29 clinical trials (8,432 patients) did not show a difference in mortality or need for dialysis therapy between patients randomly assigned to tight versus usual glucose control. 54 There was a decreased incidence of bacteremia and marked increase in the incidence of hypoglycemia (glucose < 40 mg/dL [<2.2 mmol/L]) in the tight-control group. Of note, target glucose level in the tight-control group varied across these studies from less than 100 to less than 144 mg/dL (<5.6 to <8.0 mmol/L).

VIII. Thus, the optimum target glucose level in critically ill patients is unclear at present.

ANEMIA MANAGEMENT

Target Hemoglobin in Critically Ill Patients

I. A large randomized clinical trial suggested that a restrictive transfusion strategy (transfusions only for hemoglobin < 7 g/dL) was safe and associated with a trend toward improved clinical outcomes compared with a liberal transfusion strategy (transfusions for hemoglobin < 10 g/dL) 55

II. Of note, patients with chronic anemia (hemoglobin < 9 g/dL) and those with active bleeding were excluded. In addition, the investigators noted that results may be less applicable to patients with active myocardial ischemia because a greater proportion of these patients were not enrolled in the trial because of refusal on the part of the treating physician to allow study participation.

Role of Erythropoietin Therapy in Critically Ill Patients

I. In a recent placebo-controlled randomized clinical trial, recombinant erythropoietin did not decrease the number of transfusions needed or the proportion of patients who received transfusions 56
II. Erythropoietin therapy was associated with an increased number of thrombotic events.

III. Given recent findings of significant complications associated with erythropoiesis-stimulating agents in clinical trials of patients with chronic kidney disease and oncology patients, routine use in the critical care setting cannot be recommended at this time in the absence of kidney disease.

DIALYSIS CONSIDERATIONS

Modality

I. Intermittent dialysis and CRRT can be considered equivalent modalities for the treatment of patients with AKI.

II. There may be a subset of patients who are critically ill with refractory hypotension or increased intracranial pressure (eg, patients with fulminant hepatic failure) in whom CRRT is preferable.

A. CRRT: continuous fluid/volume management and slow clearance
   1. Arteriovenous (AV) and venovenous (VV) modalities, now primarily VV modalities
   2. Continuous VV hemofiltration (CVVH): convective clearance
   3. Continuous VV hemodialysis (CVVHD): diffusive clearance
   4. Continuous VV hemodiafiltration (CVVHDF): convective and diffusive clearance

B. CRRT may necessitate anticoagulation to prolong the half-life of the filter

C. Anticoagulation typically administered prefilter to minimize systemic anticoagulation
   1. Heparin and citrate are most common types of therapy
   2. Citrate chelates calcium, a necessary cofactor in the coagulation cascade
      a. Major risk of citrate anticoagulation is hypocalcemia
      b. Can also be associated with metabolic alkalosis (1 molecule of citrate is converted to 3 molecules of bicarbonate)

D. Drug dosing: in general, medications should be dosed for a creatinine clearance of 10 to 50 mL/min; if possible, follow up drug levels to optimize dosing

III. Slow low-efficiency dialysis (SLED): 8 to 12 h/treatment, 6 treatments/wk; hybrid technique with improved hemodynamic tolerance.

Access

I. For critically ill patients with ESRD, CRRT modalities require placement of a temporary or tunneled catheter.

Membrane

I. Biocompatible membranes are in more common use and may be associated with improved survival and shorter time to renal recovery.

II. Cuprophane membranes can lead to complement activation and infiltration of the kidneys by inflammatory cells, including neutrophils, which may increase renal injury and thereby delay renal recovery.

Dose

I. A recent large multicenter randomized clinical trial (Acute Renal Failure Trial Network [ATN] study) suggested there was no benefit with more intensive dialysis (CVVHDF with effluent flow rate of 35 mL/kg/h or intermittent hemodialysis 6 times/wk with Kt/V of 1.2/session) compared with less intensive dialysis (CVVHDF with effluent flow rate of 20 mL/kg/h or 3 times/wk intermittent hemodialysis).

A. Patients with chronic kidney disease (defined as creatinine > 2.0 mg/dL [>177 μmol/L] in men and 1.5 mg/dL [133 μmol/L] in women) were excluded.

II. These results are supported by a large single-center study comparing 2 doses of CRRT; a multicenter study of 2 doses of CVVHDF is ongoing.

III. Conversely, single-center clinical trials suggested mortality benefit with greater doses of CVVH and intermittent dialysis.

A. For the CRRT study, there may have been differences in the characteristics of patients treated and treatment characteristics (including a greater proportion of surgical patients, fewer patients with sepsis, and inclusion of patients with chronic kidney disease, as well as use of lactate-based replacement fluid and postfilter replacement fluid administration).
B. For the intermittent hemodialysis (IHD) study, doses of dialysis provided per treatment were lower than in the ATN study.

**Timing**

I. Optimum timing of the initiation of dialysis therapy for patients with AKI is unclear, although observational studies have suggested potential benefit to earlier initiation of dialysis therapy.

II. A number of the critical care practices described in this article may impact on the metabolic parameters that trigger the decision to initiate dialysis therapy. Specifically, low tidal volume ventilation and permissive hypercapnia may exacerbate acidemia in a patient with AKI and associated metabolic acidosis. Early goal-directed therapy may ultimately result in volume overload, and, depending on the fluid selected for resuscitation, hyperchloremic metabolic acidosis. Steroid administration for relative adrenal insufficiency may exacerbate azotemia and volume retention. Thus, these changes in critical care practice may necessitate earlier initiation of dialysis therapy in selected patients.

**FULMINANT HEPATIC FAILURE**


II. Orthotopic liver transplantation is definitive therapy.

III. Mortality high with supportive care alone.

IV. Common complications include:

A. Hepatic encephalopathy

B. Cerebral edema: can lead to increased intracranial pressure and brain stem herniation
   1. Major cause of mortality in this population
   2. Patients with compromised kidney function may require CRRT to avoid fluctuations in intracranial pressure and tight volume control (especially in setting of transfusions of large volumes of blood products)

C. AKI: altered hemodynamics, direct toxicity
   1. Because of large volume of blood products and cerebral edema, may require support with CRRT before conventional “indications” are met.

D. Coagulopathy

E. Hypoglycemia

F. Infection/sepsis

**INTOXICATIONS**

I. Acetaminophen
   A. *N*-Acetylcysteine

   B. Supportive care for fulminant hepatic failure, including metabolic acidosis (hepatocyte necrosis and inability to metabolize lactate can result in severe lactic acidosis)

   C. AKI, may be direct effect of acetaminophen leading to acute tubular necrosis or hepatorenal syndrome; usually recovers spontaneously, but may require dialytic support

   D. 5-Oxoprolinuria and associated metabolic acidosis may occur in susceptible individuals, even when only recommended doses of acetaminophen are administered.
      1. Consider in a patient with recent acetaminophen use, unexplained metabolic acidosis, altered mental status
      2. *N*-Acetylcysteine may increase glutathione levels and be of benefit

II. Salicylates
   A. Classically presents with respiratory alkalosis and anion gap metabolic acidosis

   B. Symptoms include tinnitus, altered mental status, nausea/vomiting

   C. Activated charcoal for gut decontamination

   D. Glucose should be administered if the patient has altered mental status because aspirin can cause central nervous system (CNS) hypoglycemia, even with normal serum glucose concentrations
E. Sodium bicarbonate to promote mobilization of salicylates from tissue stores to plasma and urinary excretion
F. Hemodialysis: altered mental status, volume overload, plasma salicylate concentration greater than 100 mg/dL

III. Methanol/ethylene glycol\textsuperscript{72,73}
A. Present with anion gap acidosis and osmolar gap
B. Early recognition is critical
C. Visual changes, including blurry vision, central scotomata, blindness, retinal edema, and hyperemia of the optic disk, are characteristic of methanol poisoning
D. Oliguria and calcium oxalate crystals in urine are characteristic of ethylene glycol toxicity; can use UV light (Woods lamp) to look for fluorescence in urine (fluorescein added to most antifreeze)
E. Fomepizole/ethanol competitively inhibit alcohol dehydrogenase and prevents the formation of toxic metabolites (methanol is converted to formate, ethylene glycol is converted to glycolate/glyoxylate/oxalate)
F. Dialysis will remove both the alcohols and toxic metabolites
   1. Should not wait for confirmatory testing result to initiate treatment
   2. Consider empiric therapy in a patient with unexplained anion gap acidosis, osmolar gap, and suspected ingestion/evidence of end-organ dysfunction
G. Additional supportive care, including folic acid/thiamine

IV. Lithium\textsuperscript{74}
A. Presents with altered mental status, neuromuscular excitability, tremors, nausea, vomiting, seizures
B. Consider dialysis based on absolute level and symptoms
C. Slow equilibration between intracellular and extracellular lithium may lead to plasma rebound and necessitate extended dialysis sessions (8 to 12 hours)

V. Metformin\textsuperscript{75}
A. Can be associated with life-threatening lactic acidosis, in particular, when used in patients with reduced kidney function or hepatic dysfunction, heart failure, history of lactic acidosis, or ongoing hypoperfusion or hemodynamic instability
B. Metformin should be held if a patient requires parenteral contrast for a computed tomographic scan for at least 48 hours poststudy to ensure normal kidney function
C. In patients with life-threatening acidosis, dialysis will remove metformin and allow for the provision of bicarbonate to treat the acidosis

VI. Other toxicities to consider for treatment with hemodialysis: paraquat, isopropanol, theophylline (cleared by means of dialysis, but more efficiently cleared by using charcoal hemoperfusion)

**SPECIAL ACID-BASE AND ELECTROLYTE ABNORMALITIES**

I. Propofol can be associated with life-threatening metabolic acidosis, especially in children\textsuperscript{76}
II. Lorazepam (Ativan) infusions contain polyethylene glycol as a carrier agent and can be associated with anion gap acidosis\textsuperscript{76}
III. Cerebral salt wasting with CNS disease (subarachnoid hemorrhage, postneurosurgery) can lead to profound hyponatremia\textsuperscript{77}
   A. Can be differentiated from CNS-associated syndrome of inappropriate antidiuretic hormone (SIADH) by volume status: cerebral salt wasting leads to hypovolemia, patients with SIADH are euvolemic

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