American College of Surgeons Critical Care Review Course
Renal, Fluids and Electrolytes

Lewis J. Kaplan, MD, FACS, FCCM, FCCP
Associate Professor of Surgery
Yale University School of Medicine
Department of Surgery
Section of Trauma, Surgical Critical Care and Surgical Emergencies
330 Cedar Street, BB-310
New Haven, CT 06520-8062
Tel (203) 785-2572; FAX (203) 785-3950
Lewis.Kaplan@yale.edu

Director of Tactical Medicine
North Haven Police Department
Tactical Police Surgeon
North Haven/North Branford, CT SWAT Team
LMAKKCCP@gmail.com

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Dear Dr. Frankel,

Below please find my detailed outline for the inaugural American College of Surgeon's Critical Care Review course. It should serve as an adequate study guide for those preparing for their Board examination, and is drawn from published data rather than local practice. Areas of controversy are identified, as are standards of care.

The outline is accompanied by 5 Board style review questions with one correct answer and three incorrect distractors. The correct answer is in a light blue colored font. I hope that my outline and questions are appropriate and would welcome any feedback deemed appropriate. My educational partner in this endeavor, Dr. Guillamondegui, will send his outline and questions under separate cover.

Best regards,

Lewis J. Kaplan, MD

Objectives:

1) Provide an overview of basic principles and current controversies regarding:
   a) fluid resuscitation
   b) maintenance fluids
   c) common electrolyte problems
2) Review definitions and diagnostic modalities for:
   a) Acute kidney injury
   b) Acute Renal failure
   c) Chronic renal failure
3) Explore basic modalities, outcomes and timing for
   a) Intermittent dialysis
   b) Ultrafiltration
   c) Continuous renal support techniques

Fluids and Electrolytes

1) Resuscitation fluids (FDA approved)
   a) Goal is to restore effective circulating volume to reestablish DO2 and VO2
   b) Operating characteristics
      i) Normotonic and without dextrose – crystalloids predominate in the US
         (1) Lactated Ringer's
         (2) 0.9% saline solution (NSS)
         (3) many variations with electrolytes more close to plasma that NSS
         (4) lack of dextrose is to avoid overwhelming renal glucose transport and establishing an osmotic diuresis and an artificially high Uop
      ii) Colloids – purported to be three times as potent as crystalloids but data demonstrates only 1.4 x's as effective in the ICU
         (1) Starch based colloids (potato or maize based) in the US
         (2) Characterized by both molecular weight (average) and degree of substitution (# hydroxyethyl groups per 100 glucose groups)
            (a) Higher MW and DS = longer t ½
            (b) Thought to be a design flaw due to potential association of starches with renal dysfunction in sepsis
               (i) Not demonstrated in other patient populations
         (3) Current US starches
            (a) 6% HES in NSS (Hespan; 670 kda/0.7)
            (b) 6% HES in balanced salt solution (Hextend; 670/0.7)
            (c) 6% HES in NSS (Voluven; 130/0.4)
               (i) design is based on known gap junction size during capillary leak (larger size theoretically impedes passage through openings and increases retention)
      iii) Biologically active colloids
         (1) Albumin (60 kda), as safe as NSS in all but TBI patients
         (2) FFP lacks specific guidelines and is associated with TRALI/TACO
         (3) Fresh whole blood – principally a militarily relevant product

(4) Massive transfusion protocol 1:1:1 ratio transfusion
(a) Unclear if this is the best ratio, but is a reasonable approximation of FWB and may have its major benefits in reduced time to transfusion and reductions in crystalloid transfusion volume
(b) Well supported by having a performance improvement team evaluating the damage control resuscitation process on a regular basis

2) Maintenance Fluids
a) Common accompaniment of hospital admission and generally appropriate for resuscitated patients
b) Common features of maintenance fluids
i) Hypotonic, dextrose containing, ± additives (i.e. KCl)
ii) Targeted to actual body weight (BW) in the non-obese
(1) Adjusted body weight (ABW) in the obese
(a) ABW = IBW + $^{1}/_{3}$(actual – IBW)
iii) Multiple guides to selecting the appropriate rate
(1) All are approximations and require adjustment based on response
c) Fluid prescription is related to baseline needs and solute handling ability of the kidney
i) Na: 1-2 mEq/kg/day
ii) K: 0.5 mEq/kg/day
iii) Cations generally are paired with Cl as their anion
d) Dietary intake of oral elements is generally in grams
i) Regular diet: 9 gm NaCl (the same as one liter of 0.9% NSS)
(1) Patients are generally not salt deficient after surgery or resuscitaiton as a result (see hyponatremia below)
ii) No added salt: 4 gm
iii) Salt restricted (cardiac): 2 gm

3) Common Electrolyte Problems
a) Hyperchloremic metabolic acidosis
i) More rapidly occurring with NSS than LR
(1) Related to NSS 154 mEq/L Na and Cl compared to LR's composition
(a) More normal but hyponatremic Na and less hyperchloremic Cl
ii) Results in elevated Cl relative to Na as [Cl] < [Na] → more rapid change in concentration, despite identical change in total ions
iii) Low pH out of proportion to lactate or anion gap
iv) Small increase in mortality on ICU admission relative to no acidosis, but less than having a lactic acidosis
v) Repaired by providing less chloride in fluids, as well as using fluids with nearly normal electrolyte contents
b) Disorders of Na
i) Hyponatremia
(1) More common than hyperNa

(2) Generally related to free water excess and NOT salt deficiency in surgical patients
(a) See resuscitation fluids and grams of salt above
(b) Each liter of fluid comes with a liter of free water
(c) Dilutional hypoNa
(i) Low Na but nearly normal Cl; U_{Na} not low
(ii) Treat with free water restriction
(iii) May add diuretic such as furosemide
(iv) Aquaporin is useful (V_2 receptor antagonist)
1. Clears free water and not salt
(v) Rate of repair should parallel rate of acquisition
1. Excessive rate leads to dehydration of cellular space
2. Reduce Na no greater than 0.5 mEq/L per hour and no more than 10 mEq/L per 24 hour period to avoid cell dehydration, myelin sheath destruction and central pontine myelinolysis
a. Irreversible
(d) HyperNa
(i) Generally related to induced diuresis for brain injury management
(ii) Occasionally noted with diuresis after acute kidney injury
1. Kidney clears water > solute
2. Compounded by intake without free water such as tube feeds
(iii) Therapy is provision of free water
1. Multiple formulae
2. Reduce Na no greater than 0.5 mEq/L per hour and no more than 10 mEq/L per 24 hour period to avoid induced edema and cell swelling and central pontine myelinolysis
a. Irreversible
b. Occurs less commonly than with hypoNa therapy

ii) Disorders of potassium (K)
(1) HypoK
(a) Extremely common in post-operative surgical patients
(b) Related to provision of K-free solutions as well as diuretics and GI track losses (diarrhea in particular)
(c) Complications include proarrhythmogenicity (cardiac)
(d) Therapy is K provision
(i) K < 3.0 mEq/L is nonlinear with regard to repletion
1. Generally needs at least 100 mEq and may need > 200 mEq to replete concentration
a. Need to restore intracellular K as well as extracellular
b. Requires cardiac monitoring and central access is ideal
2. Assess Mg as K and Mg cotransport (renal)
a. May be unable to restore K with hypoMg

(2) HyperK
  (a) Three goals: displacement of plasma K, support of myocardial conduction, total body reduction in K
  (b) If the plasma space is overloaded, so too is the cellular space
  (c) Major complications is dysrhythmia and then death (similar to diastolic arrest with cardioplegia)
  (d) Displacement
    (i) Drive K intracellularly (unfavorable gradient)
    (ii) Insulin (similar to insulin-like growth hormone) drives K against its gradient
      1. also happens to drive glucose as well
        a. provide $D_{50}W$ to avoid iatrogenic hypoglycemia
        b. temporary repair strategy
  (e) Support of myocardial conduction
    (i) $CaCl_2$ (not Ca gluconate – requires hepatic processing to remove the gluconate)
    (ii) Supplemental $MgSO_4$ as membrane stabilizer
    (iii) NaHCO3 – most are acidotic and chemomechanical coupling for myocardial contraction is supported by a normal pH based on the pK_a of the involved enzymes
      1. Many have acute kidney injury or acute renal failure and are metabolically acidotic
  (f) Reduction in total body K
    (i) Forced diuresis
      1. 1000 cc NSS, Furosemide (dose adjusted for renal function) and then another 1000 cc NSS
        a. clears K in the urine
        b. requires renal function and ability to tolerate volume
        c. NSS is acidifying and furosemide is alkalinizing
          i. Balanced acid-base effects
    (ii) Cation exchange resin
      1. Kayexelate
        a. Exchanges a Na from the resin for a K from body fluid
        b. Requires access to body fluid
          i. Preparation is mixed in sorbitol (osmotic cathartic)
          ii. Goal is diarrhea
        c. PO route is preferred (needs gastric access)
          i. PR may be used
    (iii) Dialysis
      1. Direct concentration gradient removal of excess K
        a. Requires venous access and dialysis nurse
          i. May be done with an ICU nurse if done as CRRT
        b. May be accompanied by fluid removal and management of pH as needed
        c. Use is not precluded by utilizing any or all of the above management modalities

iii) Disorders of Mg
    (1) Most common is hypoMg
        (a) Associated with fluid resuscitation and diuresis
        (b) Recall cotransportation with K → look for hypoK
        (c) More common to under-replete
            (i) Need to replete the intracellular domain and the extracellular
            (ii) Very low risk of inducing hyperMg
                1. Different from tocolysis (has a bolus and continuous infusion)
        (d) Generally asymptomatic
    (2) HyperMg
        (a) Associated with excessive repletion and renal failure
        (b) Hyporeflexia and if severe → respiratory compromise
        (c) Therapy is similar to hyperK
            (i) Volume expansion
            (ii) Forced diuresis
            (iii) Acute dialysis if severe (rare)
iv) Disorders of Ca
    (1) Most common is hypoCa
        (a) Neural hyperexcitability (Chvostek and Tinel signs)
        (b) Associated with resuscitation, diuresis and parathyroid >> thyroid surgery
        (c) Most commonly asymptomatic
        (d) Check for hypoalbuminemia in the asymptomatic patient when Ca is low
            (i) Corrected Ca = Measured Ca + [(Normal – measure albumin) x 0.8]
                1. Principally bound to albumin
        (e) Alternatively, check ionized Ca (denoted Ca^{2+})
            (i) Biologically active and unbound portion
                1. Would like to do the same for Mg but not practical
    (2) HyperCa
        (a) Plethora of causes (PTH versus non-PTH mediated)
        (b) Primarily associated with malignancy or primary hyperprathyroidism
            (i) Bone destruction (malignancy >> primary hyperparathyroid)
        (c) Emergency management is similar to hyperK
            (i) May benefit from calcitonin as well
            (ii) Long-term management generally involves control of the underlying process, including pharmacologic manipulation of calcium metabolism
                1. Cinacalcet (decreases PTH secretion)
                2. Pamidronate (inhibits osteoclasts)
                3. Glucocorticoids less commonly
        (d) Hypercalcemic crisis

(i) Tachycardia, Hypertension, high Ca, lethargy, altered mental status, weakness, polyuria, polydipsia, nausea, abdominal pain
1. Ca generally > 14
2. Relatively rare

v) Disorders of PO4
(1) Most common is hypoPO4
(a) Associated with resuscitation of diuresis
(i) Some association specifically with hepatic resection
(ii) Strongly associated with refeeding syndrome
1. Incorporation into phospholipid membranes
(b) Generally asymptomatic until PO4 < 1
(i) Spontaneous respiratory arrest may occur
(c) Therapy is repletion of PO4 as Na or K salt
(2) HyperPO4
(a) Associated with renal failure or excessive repletion
(b) Generally asymptomatic
(i) When high, and Ca is high → concern re: extramedullary Ca-PO4 deposition via precipitation
1. Ca x PO4 > 55 (in general)
(c) Therapy is PO4 binding, reduction is intake, plasma volume expansion and forced diuresis
(i) Dialysis may be required in those unable to generate urine or tolerate additional volume

4) Fluid Excess
a) Excess crystalloid volume is associated with
i) Organ edema
ii) Tissue edema
iii) Secondary ACS
iv) Acidosis
v) ALI/ARDS
vi) Coagulopathy
vii) Impaired mobility
viii) Anastomotic failure
ix) Electrolyte abnormalities
x) Prolonged ICU LOS
b) Some data that MTPs using 1:1:1 ratios enjoy some of their benefit from crystalloid reduction
i) Confounded by earlier time to transfusion

5) Renal Dysfunction
a) Acute Kidney Injury versus Acute Renal Failure
i) AKI is a relatively new diagnosis
(1) Often included in older definitions of ARF
(2) Specific criteria articulated by ADQI and AKIN

(3) Overlap with ATN, hyperchloremia and reduced renal blood flow, BUT, AKI is a toxic phenomenon – not a plasma volume or blood flow issue
(4) Important overlap with hyperoncoticity, esp. in published research trials
(a) Lack of free water when assessing test article
(b) Will be clarified, in part, by CHEST and 6S trials wrt starch
(i) Association of starch, sepsis and AKI

b) ARF generally has loose definitions in most studies
i) Scr or Uop based but not very specific
c) AKI definition (abrupt and occurring within 48 hours)
i) Scr increase by 0.3; Scr increase by 50%, Uop < 0.5 cc/kg/hr for > 6 hours
d) AKI May be divided into 3 stages (Uop and Scr exist)
i) Stage 1
(1) Uop: < 0.5 cc/kg/hour for > 6 hours
(2) Scr: absolute increase > 0.3; 50-100% increase in Scr
ii) Stage 2
(1) Uop: < 0.5 cc/kg/hour for > 12 hours
(2) Scr: 200-300% increase in Scr
iii) Stage 3
(1) Uop: < 0.3 cc/kg/hour for 24 hours OR anuria for 12 hours
(2) Scr: > 300% increase or absolute Scr > 4 with acute increase of at least 0.5
(3) Special note: if patient is on CRRT they have Stage 3 by definition
e) ARF definition is related to lack of recovery of renal function over time
i) Risk Injury Failure Loss End-stage (RIFLE)
(1) ADQI foundation for AKIN AKI staging
(2) RIFLE stage correlates with mortality
(a) “Worst” RIFLE (RIFLE max)
ii) Index event mortality = 30-50%
iii) If survive, 10% mortality on average per year → 70% over 7 years

6) Dialysis
a) Intermittent vs extended vs continuous
i) Relates to resource utilization, timing, hemodynamic appropriateness
b) Fluid removal
c) Solute removal
d) Inflammatory mediator clearance
i) Not reliably related to outcome

7) Timing
a) Some data on enhanced outcome in post-traumatic ARF with early initiation
b) Indications for initiation not clearly defined in all others
i) Overlap of chronic HD with acute care HD
(1) New specialty emerging

c) Cessation of IHD is also not as clear unless graded by creatinine clearance
    i) Generally, if clearance is > 25 → HD not as helpful
d) Cessation of CRRT is abrupt, not well timed wrt criteria and is unlike most other therapies that are weaned off
    i) Outcome data lacking on weaning vs abrupt cessation

8) Intermittent Dialysis
    a) Venous, two stage cannula
        i) Recirculation less with subclavian or IJV versus femoral
            (1) 4 vs 16%
    b) Several hour course of therapy
        i) Daily vs other schedule
    c) Extended IHD has longer courses of therapy to increase intensity
        i) Fluid and solute clearance and pH management
9) Continuous techniques
    a) CVVH, CVVH-D, CVVH-DF
    b) Techniques are all continuous, and differ slightly in what they clear and how effectively they do so
        i) Two stage venous cannula
        ii) May be less relevant given back-leak rates across current filters
    c) SCUF: slow continuous ultrafiltration
        i) Arterio-venous circuit
            (1) Water > solute clearance
10) General Mechanisms of dialysis
    a) Convection – ultrafiltrate
        i) Larger molecules
        ii) Water movement carries other molecules
            (1) Middle molecules cleared more efficiently
    b) Diffusion – dialysate
        i) Smaller molecules
        ii) Concentration gradient based transfer
    c) Pre vs post-dilution
        i) Pre: decreased filtration fraction due to dilution of blood reaching filter
        ii) Post: increased filtration fraction as blood concentration is unchanged until after filtration
11) Outcomes
    a) Major issue: most trials include patients who are sufficiently stable to be acceptably randomized to either IHD or CRRT
        i) NOT the septic shock patient who is unstable on two pressors
            (1) CRRT designed for this patient
        ii) When comparing STABLE patients, there is no outcome difference
            (1) No trial comparing unstable patients
                (a) Lack of clinical equipoise wrt CRRT in those patients
    b) BEST Kidney – improved recovery from dialysis dependence with CRRT vs IHD (2005)
    c) Early data that dialysis dose influenced outcome (2000)

d) ATN Trial (2008)
    i) Stable = IHD while unstable = CRRT
    ii) Sorted within groups into intensive versus less intensive dialysis
    iii) Intensive renal support in critically ill patients with acute kidney injury did not decrease mortality, improve recovery of kidney function, or reduce the rate of non-renal organ failure as compared with less-intensive therapy involving a defined dose of intermittent hemodialysis three times per week and continuous renal-replacement therapy at 20 ml per kilogram per hour.
e) Outcomes and recovery from AKI/ARF may be significantly influenced by the following major factors:
    i) Initiation of therapy (timing, definition, indications)
    ii) Duration of therapy
    iii) Hemodynamic stability
    iv) Use of diuretic agents
    v) Use of starch (septic patients only)
    vi) Pre-existing renal dysfunction
f) Country based differences
    i) Australia – predominantly CRRT
    ii) US – predominantly IHD
    iii) EU/UK – mixed with significant inter-country variation

12) Conclusions
a) Fluids, electrolytes and renal function are readily understandable
b) Therapy for perturbations in physiology may have both salutary and undesirable consequences
    i) Clinician should be able to anticipate and compensate for untoward effects
c) Indications, timing, and duration of renal support are not uniform
    i) Definition of AKI and ARF have been refined
d) Outcomes in stable patients are not influenced by choice of dialysis technique
e) No clear data on outcomes comparing mode for unstable patients
f) Renal recovery may be influenced by factors other than intensity of dialysis and warrants further study