JOINT TRAUMA SYSTEM CLINICAL PRACTICE GUIDELINE (JTS CPG)

Hyperkalemia and Dialysis in the Deployed Setting (CPG ID: 52)

Provides recommendations for the management of patients with, or at risk for, acute kidney injury and hyperkalemia in the austere deployed environment.

Contributors

MAJ Ian Stewart, USAF, MC
LCDR Jonathan Bolanos, MC, USN
MAJ Dustin Little, MC USA
LTC Kevin Chung, MC, USA
LtCol Jonathan Sosnov, USAF, MC
LCDR Nancy Miller, MC, USN
MAJ Mark Poirier, MC, USAR
LtCol Kristin Saenz, USAF, MC
LCol Vivian McAlister, RCMS
LCol Soraya Moghadam, RCMS
CAPT Ray Kao, RCMS
CAPT Zsolt Stockinger, MC, USN

Publication Date: 24 January 2017

TABLE OF CONTENTS

BACKGROUND

Acute kidney injury (AKI) is a recognized complication of combat trauma. The complications associated with acute kidney injury, such as life threatening hyperkalemia, are usually delayed in onset. In the recent conflicts, rapid evacuation of U.S. and coalition personnel generally resulted in these complications occurring at higher echelons of care where renal replacement therapies were available. In the future however, deployed providers may not have this luxury and should be prepared to temporize patients while they await transport.

RECOMMENDATIONS

These recommendations are intended to temporize patients until the patient can be evacuated to a higher echelon of care with the full range of renal replacement therapy capabilities.

MONITORING

Monitor patients at risk for acute kidney injury and hyperkalemia. Specifically, hourly urine output, serum creatinine and serum potassium.

Acute kidney injury after combat trauma occurs in up to 34.3% of the most critically injured patients, usually within the first 2 days after injury.[1] In the recent conflicts in Iraq and Afghanistan, rapid evacuation out of theater ensured that the complications of AKI (including hyperkalemia) occurred further up the evacuation chain (Role 3-4), where renal replacement therapy (RRT) was often available.[2] As a consequence, there are no recent data on the frequency of hyperkalemia following AKI in theater when evacuation is delayed. However, evidence from prior conflicts suggests that up to one-third of combat casualties with oliguric renal failure develop severe hyperkalemia within four days of injury.[3] In future operations, military providers should be prepared for prolonged evacuation times.[4] As a consequence, AKI and life threatening hyperkalemia may be encountered at Role 1-3 facilities more frequently, where RRT is limited or non-existent. AKI is classified by relative changes in creatinine or a decrease in urine output and can be diagnosed with as little as a 0.3mg/dL increase in creatinine over a 48 hour period.[5] While mild AKI can generally be managed with supportive care; more severe AKI (characterized by oliguria or a doubling of serum creatinine) may require RRT. Therefore, providers caring for patients in austere or deployed environments should monitor patients for AKI and be prepared to expedite evacuation to a higher echelon of care, when necessary. We recommend closely monitoring urine output and, when possible, serum creatinine and potassium concentrations in trauma patients.

MEDICAL MANAGEMENT

The first step in the management of AKI with hyperkalemia is medical therapy. This includes cardiac membrane stabilization (with intravenous calcium chloride or calcium gluconate) and/or shifting potassium intracellularly (with insulin, a β-2-adrenergic agonist or sodium bicarbonate). Maneuvers to remove potassium may also be considered, with diuretics and potassium binding resins, but use may be limited by hemodynamic status, anuria and bowel injuries. We suggest shifting potassium intracellularly when the potassium is greater than 5.5meq/L [with intravenous insulin and 50 percent dextrose (D50), with or without albuterol]. Calcium should be given if there is evidence of altered conduction on electrocardiogram (peaked T waves, widened QRS, flattened P waves). Calcium can also be considered empirically for a potassium concentration >6meq/L. See Appendix A for a list of medications, routes of administration and recommended treatment order.

FAILURE OF MEDICAL MANAGEMENT

In the experience of the authors, the most common reason for starting RRT for patients with AKI in the deployed setting is hyperkalemia that is resistant to medical management. A level greater than 6 meq/L, despite medical management, should prompt consideration of RRT with either the NxStage® System One™ or acute peritoneal

dialysis (PD). Occasionally, patients may require RRT in theater for other indications, such as acidemia or severe volume overload. The methods detailed below can effectively temporize patients with these indications as well.

SEVERE HYPERKALEMIA & NXSTAGE® SYSTEM ONE™

If available, the NxStage® System One™ should be used for severe hyperkalemia that does not respond to medical management.

Since 2010, the NxStage® System One™ (NxStage Medical, Lawrence, MA) has been deployed to Craig Joint Theater Hospital, Bagram Airfield, Afghanistan.[6] To utilize this system, the patient must have central venous access with a dialysis catheter, the machine must be setup and the prescription must be entered. There are five components to a CRRT prescription: mode, blood flow rate, replacement fluid, replacement fluid rate and ultrafiltration rate. See Appendix B for a suggested initial prescription.

- **Central Venous Access**

Prior to initiation, a hemodialysis catheter must be placed. In terms of location, we concur with current guidelines[5] that suggest the first choice of access is the right internal jugular vein (with a 12-14 French, 15cm catheter) because this location has been associated with the lowest rates of catheter dysfunction.[7] The second choice is the femoral vein (with a 20-25cm catheter). The last choice is the left internal jugular vein (with a 20cm catheter) because it is associated with the highest rates of catheter dysfunction.[7] If possible, the subclavian veins should be avoided. Lines in this location often result in subclavian stenosis, which can complicate or preclude future dialysis access in patients at risk for the development of end stage renal disease.[8,9]

- **Setup**

The "SIMPLE" (Set up – Initiate – Make connections – Program – Launch treatment – End) instructions are displayed on the NxStage® computer screen once the machine is turned on. These instructions are quite detailed and, if followed closely step-by-step, will guide the provider through priming the cartridge, putting the patient on the machine, entering the prescription and ending the treatment once it is complete. Ideally, providers that deploy to a location with a NxStage® System One™ should be trained on the setup and use of the system prior to deployment. However, in our experience the instructions are straightforward enough to allow an inexperienced physician or nurse to perform a treatment.

- **Mode**

The NxStage® System One™ can provide continuous venovenous hemofiltration (CVVH) or continuous venovenous hemodialysis (CVVHD), both of which are forms of continuous renal replacement therapy (CRRT). Out of the packaging, it is ready for CVVH mode and, for the sake of simplicity, we suggest that this be used if providers are unfamiliar with the machine. If the provider is familiar with the machine, we suggest that CVVHD be considered, as this mode provides slightly more efficient clearance.[10] This can be done by connecting the two green ports as specified in the step-by-step priming instructions.

- **Blood Flow Rate**

The minimum blood flow rate is 200ml/min and should be increased to 400ml/min if possible. A faster blood flow rate will decrease the likelihood of blood clotting the filter. The most common limitation for increasing the blood flow rate is the pressure required to draw blood out of the dialysis catheter. If this pressure becomes too negative, the machine will alarm and stop the treatment. This alarm is often due to catheter port suction against the vessel wall. If this occurs, decrease the blood flow rate until the machine no longer alarms. Catheter manipulation, line reversal or line relocation may solve this issue. To manipulate the catheter, using sterile technique, grasp the catheter proximal to the sutured/secured hub and twist it 180 degrees. This may move the blood flow ports away from a vessel wall. To reverse the lines, first stop the

machine and clamp both the blood lines and both the dialysis catheter ports. Then disconnect the blood lines and re-connect them to the dialysis catheter ports opposite of how they were previously connected. If these efforts fail, an alternate insertion site for the catheter should be considered.

- **Replacement Fluid**

Several commercially made replacement fluids have been stocked at Craig Joint Theater Hospital. Regardless of the specific brand available, there will be 0meq/L potassium (0K) and 4meq/L potassium (4K) options. Since CRRT in the deployed environment is usually initiated for hyperkalemia, we suggest starting with the 0K fluid and following the potassium concentration every 2-4 hours. Once the potassium decreases to <5.5 meq/L, the patient can be transitioned to the 4K replacement fluid. It is important to note that the replacement fluid bags have two separate compartments, to avoid precipitation of calcium and bicarbonate. It is vital that the seal between the two compartments is broken in the manner detailed in the step-by-step instructions on the NxStage® System One™ display screen. If commercial solutions are not available, replacement fluids can be made in a similar manner as improvised PD fluids. (See Appendix C.) However, dextrose should not be added if these solutions are to be used as replacement fluids. If a non-commercial fluid is used, calcium and magnesium should be closely monitored and replaced as needed.

- **Replacement Fluid Rate**

The replacement fluid rate is the rate at which the machine infuses replacement fluid and it is the primary determinant of clearance. Initially, we suggest starting with a replacement fluid rate of 3L/hour with close monitoring. If the potassium fails to improve, the replacement fluid rate should be increased. With the NxStage® System One™, the maximum replacement fluid rate is dependent on the blood flow rate. Therefore, if high clearances are needed, the blood flow rate should be increased to 400ml/min and the replacement fluid rate should be set as high as the machine allows (8.4L per hour). If this fails, the patient likely has severe ongoing tissue necrosis and surgical re-evaluation for debridement should be considered. As a final measure, a second line can be placed and a second CRRT circuit set up.

- **Ultrafiltration Rate**

This is the rate at which the machine removes volume from the patient. For example, if this is set at 100ml/hr, 2.4L will be removed from the patient over the next 24 hours. In the absence of overt hypervolemia, we suggest initially setting the ultrafiltration rate to 0 or equal to all of the patient's hourly fluid input (IV fluids, antibiotics, etc.). However, if the patient has significant volume overload (e.g., pulmonary edema), this can be titrated to achieve a net negative fluid balance of 1-2L per day (all quantifiable inputs minus all quantifiable outputs).

Since these patients will have had recent trauma, often with associated coagulopathy, and citrate anticoagulation is not available in the deployed setting, we suggest not anticoagulating patients for the sole purpose of CRRT. Should filter clotting become an issue, the following maneuvers may be useful: 1) increase blood flow rate, 2) change to pre-filter CVVH (if in CVVHD mode), 3) increase replacement fluid rate (if in CVVH mode). If needed, and the patient is not a bleeding risk, 500 units per hour of heparin can be given. This should be infused into the blood line coming out of the patient and going to the NxStage® System One™.

ACUTE PD

If patients do not respond to medical management, and an NxStage® System One™ is not available, acute PD should be considered.

While its use in has been supplanted by CRRT in most developed nations, PD is an established treatment for AKI with electrolyte disturbances such as hyperkalemia.[11] PD relies on the diffusion and convection of solutes from the blood into a fluid across the peritoneal membrane. For the purposes of potassium clearance, a fluid that is low in potassium is infused into the peritoneal space. Potassium then flows down its concentration gradient from the blood and extracellular space into this fluid. Once equilibration is achieved (i.e. the concentration in the blood and fluid are equal) no further potassium goes into the fluid. Therefore, the fluid must be exchanged periodically to maintain clearance.

Because recent abdominal surgery is considered a relative contraindication to PD[12], the efficacy of PD and the complications associated with PD in trauma patients that have undergone laparotomy and/or have bowel in discontinuity are largely unknown. However, there are case reports of PD being used in combat casualties with recent laparotomy.[13] Therefore, if no other forms of renal replacement therapy are available and the patient cannot be evacuated to a higher echelon of care, it can be considered even in patients without an intact peritoneal lining.

In order to perform PD, access to the peritoneal space is needed. Once access is established, there are three components to a PD prescription: fluid type, exchange volume and dwell time.

- **Catheter Placement**

Under normal circumstances, specialized catheters are used for PD. However, these are not usually available in the deployed setting, requiring that available supplies be repurposed. Jackson-Pratt (JP) abdominal drains and pediatric chest tubes have both been used as improvised PD catheters in theater.[13] Nasogastric tubes have also been recommended as improvised catheters.[11] While catheters can be placed via a variety of methods (including modified Seldinger and laparoscopic techniques), most patients in the forward deployed environment will require open surgical approaches.[13] Under ideal circumstances, PD catheters should be tunneled in order to decrease the risk of peritonitis.[11] However, this may not be an option in the austere, forward deployed environment where the use of stoma appliances as a protective dressing to prevent infections has been described.[13]

- **Fluid Type**

While specialized PD fluids are made commercially, they are not normally available in deployed locations. However, a variety of fluids can be used for field expedient PD. (Refer to Appendix C for this section.). If the indication is hyperkalemia, a solution with a potassium concentration of 0 should be used at the initiation of PD. The patient's potassium level should be monitored and, once it is normalized, the fluid should be changed to a concentration of ~4meq/L by using one of the alternate fluids. Note that in the setting of shock or liver failure, a solution with bicarbonate (not lactate) will reverse acidemia more rapidly.[14] If acidemia persists after correction of potassium in patients in shock, ~4meq/L of potassium should be added to the "potassium free solution" of choice to avoid using lactate as a buffer. The amount of fluid removed by PD is determined by two factors: 1) the amount of time the fluid is in the abdomen and 2) the concentration of dextrose in the solution. As others have recommended [11], we suggest that a concentration of ~1.5% dextrose be used for patients that are euvolemic or hypovolemic. For patients that are moderately or severely volume overloaded, we suggest ~2.5% and ~4.5% dextrose concentrations, respectively. Note that a 4.5% dextrose fluid can remove volume very quickly (up to 1L in 4 hours)[11], therefore its use should be limited to hemodynamically stable patients with severe, life-threatening pulmonary edema.

- **Exchange Volume**

The volume of fluid infused into the peritoneal space is known as the "exchange volume." Removing the fluid after the dwell and instilling fresh fluid is referred to as an "exchange." We recommend starting with a volume of 1L per exchange and then increasing to 2L per exchange if tolerated. The volume infused may be

limited by fluid leakage around the surgical site, especially in patients with large laparotomy incisions or open abdomens. Patients should be kept in the supine position during PD to avoid leakage.

- **Dwell Time**

The length of time that the fluid is allowed to sit in the peritoneal space between exchanges is known as the "dwell time." We recommend an initial dwell time of 2 hours. Exchanges should be done every 2 hours until the initial therapeutic goal has been achieved (e.g. potassium normalized or acidemia reversed) at which point the dwell time can be extended to every 4 hours with close monitoring.

In the forward deployed setting, the use of PD can be complicated by fluid leakage (especially if the abdomen must be left open) and also by the development of abdominal compartment syndrome with fluid infusion. These may severely limit the volume of fluid that can be infused and allowed to dwell. In this case, the fluid can be continuously exchanged.[13] In practice, this means instilling fluid into the peritoneum from one site (e.g. from a pediatric chest tube or JP drain) while simultaneously removing fluid from another site (e.g. a different drain, or wound vac if available.) If continuous exchange of fluid is utilized, the inflow and outflow ports in the peritoneal space should be physically separated as much as possible to maximize the surface area that the fluid passes by as it goes from the inflow catheter to the outflow catheter.

While improvised PD can improve hyperkalemia, acidemia and hypervolemia, it does not significantly improve azotemia or uremia.[13] Therefore, patients should be transferred for definitive care as soon as possible. For more information on the treatment of AKI with PD, the reader is encouraged to review recently published guidelines[11] by the International Society for Peritoneal Dialysis available on line at http://ispd.org/ispd-guidelines/.

PERFORMANCE IMPROVEMENT (PI) MONITORING

INTENT (EXPECTED OUTCOMES)

- Rapidly institute medical management for patients with AKI and/or serum potassium >5.5 meq/L and/or EKG changes consistent with hyperkalemia
- Consider prompt initiation of RRT for patients with AKI and serum potassium values persistently greater than 6meq/L, despite medical management. To include prompt initiation of evacuation to a facility with RRT capability.

PERFORMANCE/ADHERENCE MEASURES

- Rapidly institute medical management for patients with AKI and/or serum potassium >5.5 meq/L and/or EKG changes consistent with hyperkalemia
- Consider prompt initiation of RRT for patients with AKI and serum potassium values persistently greater than 6meq/L, despite medical management. To include prompt initiation of evacuation to a facility with RRT capability.

DATA SOURCE

- Patient Record
- Department of Defense Trauma Registry (DoDTR)

SYSTEM REPORTING & FREQUENCY

The above constitutes the minimum criteria for PI monitoring of this CPG. System reporting will be performed biannually; additional PI monitoring and system reporting may be performed as needed.

The system review and data analysis will be performed by the Joint Trauma System (JTS) Director and the JTS Performance Improvement Branch.

RESPONSIBILITIES

The trauma team leader, along with his or her infection control team, will ensure familiarity, appropriate compliance and PI monitoring at the local level with this CPG.

REFERENCES

1. Heegard KD, Stewart IJ, Cap AP, et al. Early acute kidney injury in military casualties. J Trauma Acute Care Surg. 2015; 78: 988-993.
2. Bolanos JA, Yuan CM, Little DJ, et al. Outcomes after post-traumatic AKI requiring RRT in United States Military service members. Clin J Am Soc Nephrol. 2015 (Epub ahead of print).
3. Teschan PE. Acute renal failure during the Korean War. Ren Fail. 1992; 14: 237-239.
4. Rasmussen TE, Baer DG, Doll BA, Caravalho J. In the Golden Hour. Army AL&T Magazine 2015; January-March: 80-85.
5. Kidney Disease: Improving Global Outcomes (KDIGO) Acute Kidney Injury Work Group. KDIGO Clinical Practice Guideline for Acute Kidney Injury. Kidney Inter., Suppl. 2012; 2: 1–138.
6. Zonies D, DuBose J, Elterman J, et al. Early implementation of continuous renal replacement therapy optimizes casualty evacuation for combat-related acute kidney injury. J Trauma Acute Care Surg. 2013; 75 (2 Suppl 2): S210-4.
7. Parienti JJ, Mégarbane B, Fischer MO, et al. Catheter dysfunction and dialysis performance according to vascular access among 736 critically ill adults requiring renal replacement therapy: a randomized controlled study. Crit Care Med. 2010; 38: 1118-1125.
8. Schillinger F, Schillinger D, Montagnac R, Milcent T. Post catheterisation vein stenosis in haemodialysis: comparative angiographic study of 50 subclavian and 50 internal jugular accesses. Nephrol Dial Transplant. 1991; 6: 722-724.
9. Cimochowski GE, Worley E, Rutherford WE, Sartain J, Blondin J, Harter H. Superiority of the internal jugular over the subclavian access for temporary dialysis. Nephron. 1990; 54: 154-161.
10. Brunet S, Leblanc M, Geadah D, et al. Diffusive and convective solute clearances during continuous renal replacement therapy at various dialysate and ultrafiltration flow rates. Am J Kidney Dis. 1999; 34: 486-492.
11. Cullis B, Abdelraheem M, Abrahams G, et al. Peritoneal dialysis for acute kidney injury. Perit Dial Int. 2014; 34: 494-517.
12. Burdmann EA, Chakravarthi R. Peritoneal dialysis in acute kidney injury: lessons learned and applied. Semin Dial. 2011; 24: 149-156.

13. Pina JS, Moghadam S, Cushner HM, Beilman GJ, McAlister VC. In-theater peritoneal dialysis for combat-related renal failure. J Trauma. 2010; 68: 1253-1256.

14. Bai ZG, Yang K, Tian J, et al. Bicarbonate versus lactate solutions for acute peritoneal dialysis. Cochrane Database Syst Rev. 2010; 9: CD007034

APPENDIX A: INITIAL MEDICAL MANAGEMENT FOR HYPERKALEMIA

Drug/ Treatment	Dose & Route of Administration	Mechanism of Action	Time to Onset	Duration of Effect	Caution/Contraindication	Other Comments
Stabilize Cardiac Membranes						
Calcium gluconate	1000mg=one 10ml "amp" of 10% (100mg/mL) solution; infused IV over 2-3 mins	Stabilizes myocyte membrane electrical activity	Immediate	30-60 mins	Caution if pre-existing hypercalcemia	Can be administered via peripheral IV; repeat in 5 mins for persistent EKG changes
Calcium chloride	1000mg=one 10ml "amp" of 10% (100mg/mL) solution; infused IV over 2-3 mins	Stabilizes myocyte membrane electrical activity	Immeditate	30-60 mins	Administration via central line preferred (can damage small vessels, cause tissue necrosis); caution if pre-existing hypercalcemia	Repeat in 5 mins for persistent EKG changes
Shift Potassium Intracellularly						
Insulin, regular	10 units by IV bolus; if blood glucose <250 mg/dL give 50 mL 50% dextrose immediately after insulin	Shifts potassium intracellularly by way of Na-K ATPase pump	10-20 mins	4-6 hr	Caution if hypoglycemia	Check blood glucose within one hour of administration
Albuterol	10 mg nebulized, over 10 mins	Shifts potassium intracellularly by way of Na-K ATPase pump	20-30 mins	1-2 hr	Can cause tachycardia	Has additive effect with insulin tx
Sodium Bicarbonate	150 meq in 1L of D5W over 2-4 hr	Shifts potassium intracellularly by increasing blood pH	~4 hr	Variable	Can decrease ionized calcium and destabilize cardiac membranes; caution in setting of volume overload	Minimally effective and should not be used unless pH<7.2
Remove Potassium						
Sodium polystyrene sulfonate (Kayexalate®)	30 grams PO	Exchanges sodium for potassium in the large intestine	>2 hours	Variable	Case reports of colonic necrosis; avoid in setting of bowel obstruction or following bowel injury or surgery; may be of limited utility in setting of severe hyperkalemia	Can repeat every 4-6 hours; consider initial dose of 45-60 grams in body weight >80 kg
Furosemide	40mg IV	Impairs renal potassium reabsorption	5 mins	2 hours	Avoid if sulfa allergy; caution in volume depletion, hypotension	May require larger does (up to 200mg) or be ineffective in setting of acute kidney injury

APPENDIX B: CONTINUOUS RENAL REPLACEMENT THERAPY USING THE NXSTAGE SYSTEM ONE

NOTE: *Suggested starting prescriptions and dosage*

	Recommendation	Notes
Mode	CVVH	If hospital personnel are familiar with the machine, CVVHD should be considered because it is more efficient per liter of volume infused.
Blood Flow Rate	200-400 ml/min	The blood flow rate should be increased as much as tolerated by the access pressures and machine alarms to avoid clotting. We suggest maintaining flows of at least 200 cc/min
Replacement Fluid Type	0K	For use with hyperkalemia. Change to 4K when potassium <5.5 meq/L. If neither of these fluids are available, CRRT can be performed using lactated ringer, Plasmalyte or the improvised solutions for peritoneal dialysis (Table 3). Note that if a solution with 0 Ca is used, the ionized calcium should be closely monitored and replaced as needed.
Replacement Fluid Rate	3L per hour	Increase if needed for further clearance of potassium.
Ultrafiltrate Rate	0 ml/min	If desired, fluid can be removed via ultrafiltration. In the acute setting, barring overt hypervolemia, fluid removal should be avoided. However, consider setting the ultrafiltration rate to the patient's hourly "In's" to avoid hypervolemia.

APPENDIX C: IMPROVISED SOLUTIONS FOR PERITONEAL DIALYSIS

Starting Fluid	Addition(s)	Ending Concentrations
Potassium Free Solutions		
1 Liter ½ Normal Saline Na 77, Cl 77	40ml of 8.4% Bicarbonate 35ml of 50% Dextrose 60ml of 3% Saline	Na 130, K 0, Ca 0, Cl 95, bicarbonate 35, Osm 338, Dextrose 1.54%
1 Liter ½ Normal Saline Na 77, Cl 77	40ml of 8.4% Bicarbonate 60ml of 50% Dextrose 65ml of 3% Saline	Na 129, K 0, Ca 0, Cl 95, bicarbonate 34, Osm 388, Dextrose 2.57%
1 Liter ½ Normal Saline Na 77, Cl 77	43ml of 8.4% Bicarbonate 105ml of 50% Dextrose 75ml of 3% Saline	Na 130, K 0, Ca 0, Cl 94, bicarbonate 35, Osm 476, Dextrose 4.29%
Potassium Containing Solutions		
1Liter Lactated Ringers Na 130, K 4, Ca 2.7, Cl 109, Lactate 28, Osm 273	30ml 50% Dextrose	Na 126, K 3.9, Ca 2.6, Cl 106, Lactate 27, Osm 339, Dextrose 1.46%
1Liter Lactated Ringers Na 130, K 4, Ca 2.7, Cl 109, Lactate 28, Osm 273	53ml of 50% Dextrose 10ml of 3% Saline	Na 127, K 3.8, Ca 2.5, Cl 107, Lactate 26, Osm 392, Dextrose 2.49%
1Liter Lactated Ringers Na 130, K 4, Ca 2.7, Cl 109, Lactate 28, Osm 273	95ml of 50% Dextrose 25ml of 3% Saline	Na 128, K 3.6, Ca 2.4, Cl 109, Lactate 25, Osm 481, Dextrose 4.24%

*1L fluid bags may contain extra fluid (40-60ml), this additional volume is not included in these calculations as it will not make a significant clinical difference.

These suggested fluids are based on what is likely to be available in the forward deployed setting. In case other fluids need to be improvised, an example of how these solutions were derived may be instructive. These calculations are based on the total amount of the substance divided by the total volume. For example, the Na concentration in the first fluid in the table:

1. Total amount of Na: amount in ½ NS (77meq/L x 1L=77meq) plus amount in 8.4% bicarbonate (1000meq/L x 0.04L= 40meq) plus amount in 3% saline (513meq/L x 0.06L= 30.78meq). Therefore, total amount is 77+40+30.78=147.78. Note that there is no Na in 50% dextrose.
2. Total volume: Volume of ½ NS plus volume of 8.4% bicarbonate plus volume of 50% Dextrose plus volume of 3% saline. 1+0.04+0.035+0.06=1.135 L.
3. Dividing the total amount of Na (147.78 meq) by the total volume (1.135L) equals 130.20264 or about 130 meq/L.

APPENDIX D: ADDITIONAL INFORMATION REGARDING OFF-LABEL USES IN CPGS

PURPOSE

The purpose of this Appendix is to ensure an understanding of DoD policy and practice regarding inclusion in CPGs of "off-label" uses of U.S. Food and Drug Administration (FDA)–approved products. This applies to off-label uses with patients who are armed forces members.

BACKGROUND

Unapproved (i.e., "off-label") uses of FDA-approved products are extremely common in American medicine and are usually not subject to any special regulations. However, under Federal law, in some circumstances, unapproved uses of approved drugs are subject to FDA regulations governing "investigational new drugs." These circumstances include such uses as part of clinical trials, and in the military context, command required, unapproved uses. Some command requested unapproved uses may also be subject to special regulations.

ADDITIONAL INFORMATION REGARDING OFF-LABEL USES IN CPGS

The inclusion in CPGs of off-label uses is not a clinical trial, nor is it a command request or requirement. Further, it does not imply that the Military Health System requires that use by DoD health care practitioners or considers it to be the "standard of care." Rather, the inclusion in CPGs of off-label uses is to inform the clinical judgment of the responsible health care practitioner by providing information regarding potential risks and benefits of treatment alternatives. The decision is for the clinical judgment of the responsible health care practitioner within the practitioner-patient relationship.

ADDITIONAL PROCEDURES

Balanced Discussion

Consistent with this purpose, CPG discussions of off-label uses specifically state that they are uses not approved by the FDA. Further, such discussions are balanced in the presentation of appropriate clinical study data, including any such data that suggest caution in the use of the product and specifically including any FDA-issued warnings.

Quality Assurance Monitoring

With respect to such off-label uses, DoD procedure is to maintain a regular system of quality assurance monitoring of outcomes and known potential adverse events. For this reason, the importance of accurate clinical records is underscored.

Information to Patients

Good clinical practice includes the provision of appropriate information to patients. Each CPG discussing an unusual off-label use will address the issue of information to patients. When practicable, consideration will be given to including in an appendix an appropriate information sheet for distribution to patients, whether before or after use of the product. Information to patients should address in plain language: a) that the use is not approved by the FDA; b) the reasons why a DoD health care practitioner would decide to use the product for this purpose; and c) the potential risks associated with such use.