Baxter

Phosphate
The forgotten electrolyte

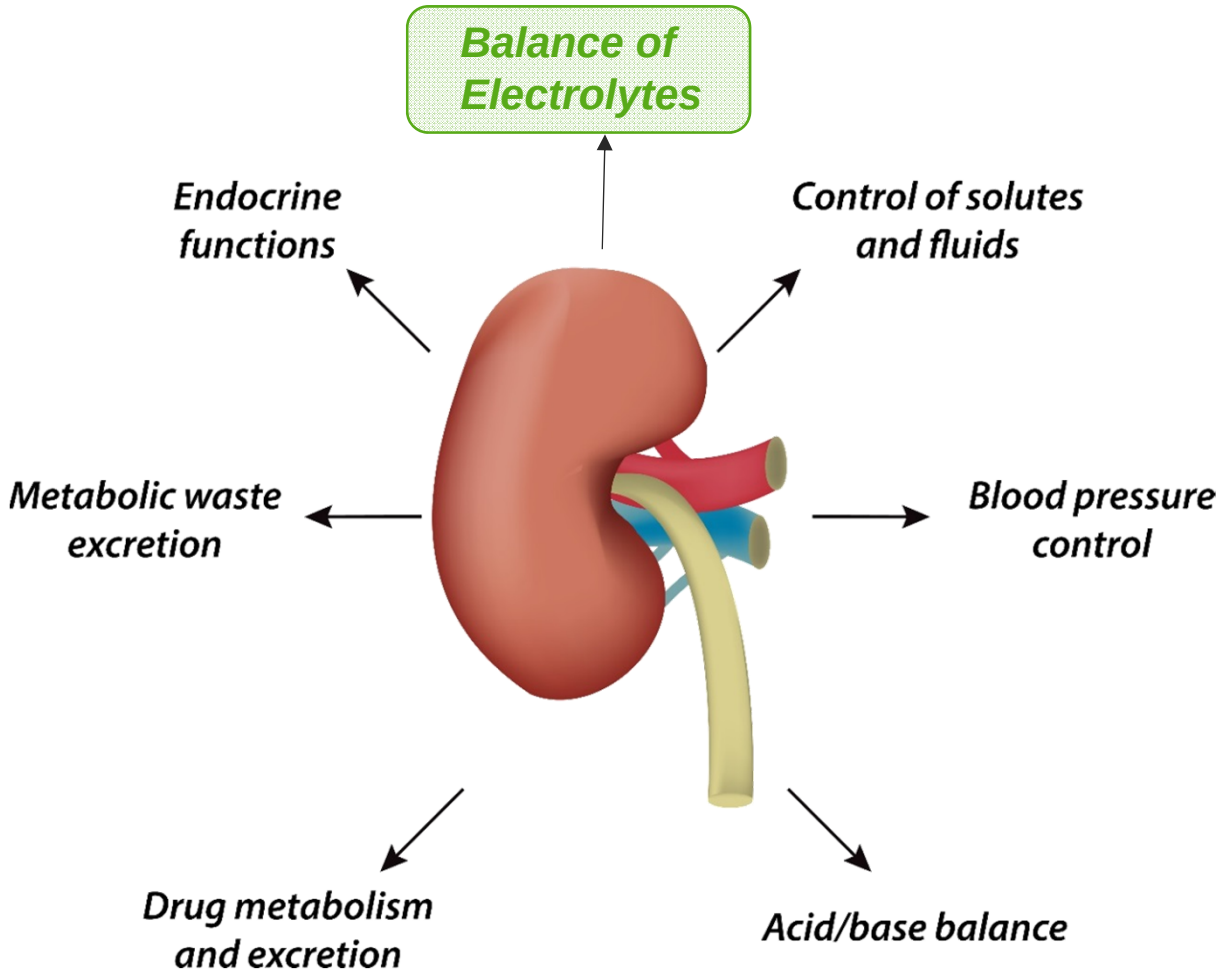
USMP/MG144/16-0004a(3) 05/18

How amazing are your kidneys?

“The kidneys are so beautifully organized; they do their work of regulation with such a miraculous--it's hard to find another word— such a positively divine precision, such knowledge and wisdom, that there is no reason why our archetypal man, whoever he is, or any one else, for that matter, should be ashamed to own a pair.”

---Aldous Huxley "Antic Hay" (1923, 1948)

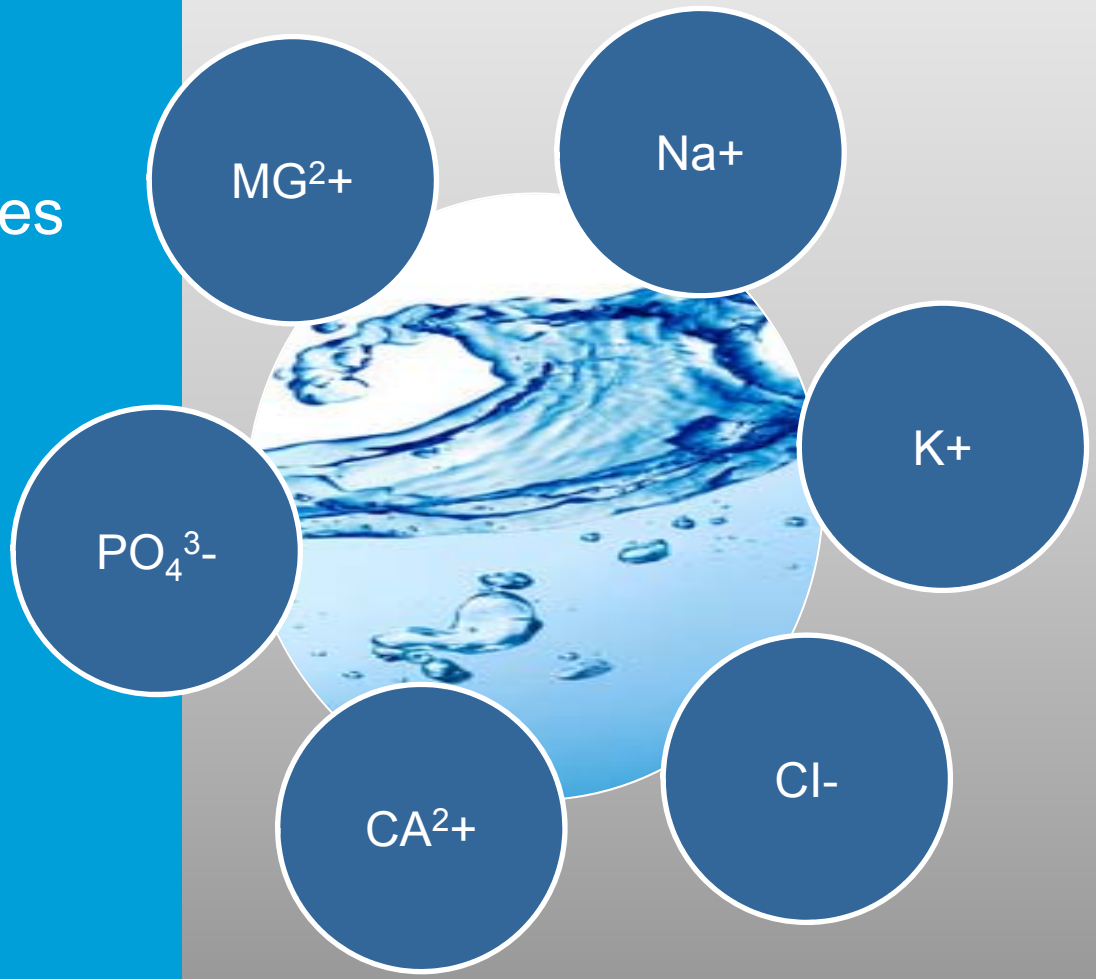
Renal responsibilities include:



NIH. National Kidney and Urologic Diseases Information Clearinghouse (NKUDIC). The Kidneys and How They Work. http://www.niddk.nih.gov/health-information/health-topics/Anatomy/kidneys-how-they-work/Pages/anatomy.aspx (Accessed 1/15/2016).

Renal function: regulation of electrolytes

- **Sodium**
- **Potassium**
- **Chloride**
- **Calcium**
- **Phosphate**
- **Magnesium**
- **And many more**



American Nephrology Nurses' Association (ANNA). Core Curriculum for Nephrology Nursing. Jannetti Pubns Inc; 4th edition (March 2001) p17

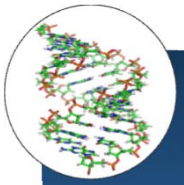
Phosphorus:

- A salt of phosphoric acid
- Nearly all the phosphorus in the body exists under the form of phosphate
- Around 85% of phosphorus in the body is found in bones and teeth, 14% in cells and 1% in extracellular fluids
- As Phosphate is the most important intracellular ion under certain acute conditions it may shift into or out of the cell causing dramatic changes in plasma phosphorus concentrations
- Expected levels in a healthy adult
  - 0.8 – 1.45 mmol/L (2.5 – 4.5 mg/dl)

Role of Phosphorus:

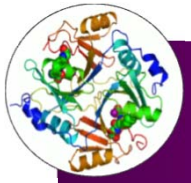
Phosphorus is involved in a wide variety of metabolic reactions and vital functions:

Formation of red blood cell 2,3 DPG (diphosphoglycerate) which facilitates oxygen delivery to tissues



Essential constituent of cell membranes and nucleic acids

Formation of energy storing substances (e.g. adenosine triphosphate ATP)

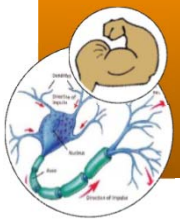


Regulates enzyme activity

Phosphorus

Acts as a buffer in the maintenance of acid-base balance

Involved in metabolism of carbohydrates, proteins and fat



Role in muscle contraction and nerve impulses

Provides structural support to bones and teeth

Phosphate: Hyperphosphatemia

Decreased urinary phosphorus excretion due to Acute Renal Failure (ARF) is the most common cause of hyperphosphatemia.

Severe hyperphosphatemia may result when AKI is associated with extensive tissue damage (e.g. rhabdomyolysis or tumor lysis syndrome)

One study, n = 99

60%+

of critically ill patients with ARF had hyperphosphatemia before starting CRRT

Even if hyperphosphatemia was present on admission, hypophosphatemia may develop during the use of (continuous) renal replacement therapy when low-phosphate replacement solution and/or dialysate are used.

Geerse et al. Critical Care 2010, 14:R147 http://ccforum.com/content/14/4/R147
Ronco, C. & Bellomo, R (eds), Critical Care Nephrology, 1998, 211-223
Ronco, C. & Bellomo, R (eds), Critical Care Nephrology, 1998, 249 - 259
Morimatsu et al. International Journal of Artificial Organs 2002, 25:6 pp 512-519

Phosphate: Hypophosphatemia

Internal redistribution is the most common cause of hypophosphatemia in ICU patients

Increased renal secretion

Decreased intestinal absorption - less common cause

Potential causes of hypophosphatemia in critically ill patients

Conditions:	Therapies:	Situations
sepsis, trauma, post operative state, diabetic ketoacidosis	Fluid therapy, glucose/insulin therapy, diuretics and CRRT	that induce intracellular shifts of phosphorus such as respiratory alkalosis or refeeding syndrome

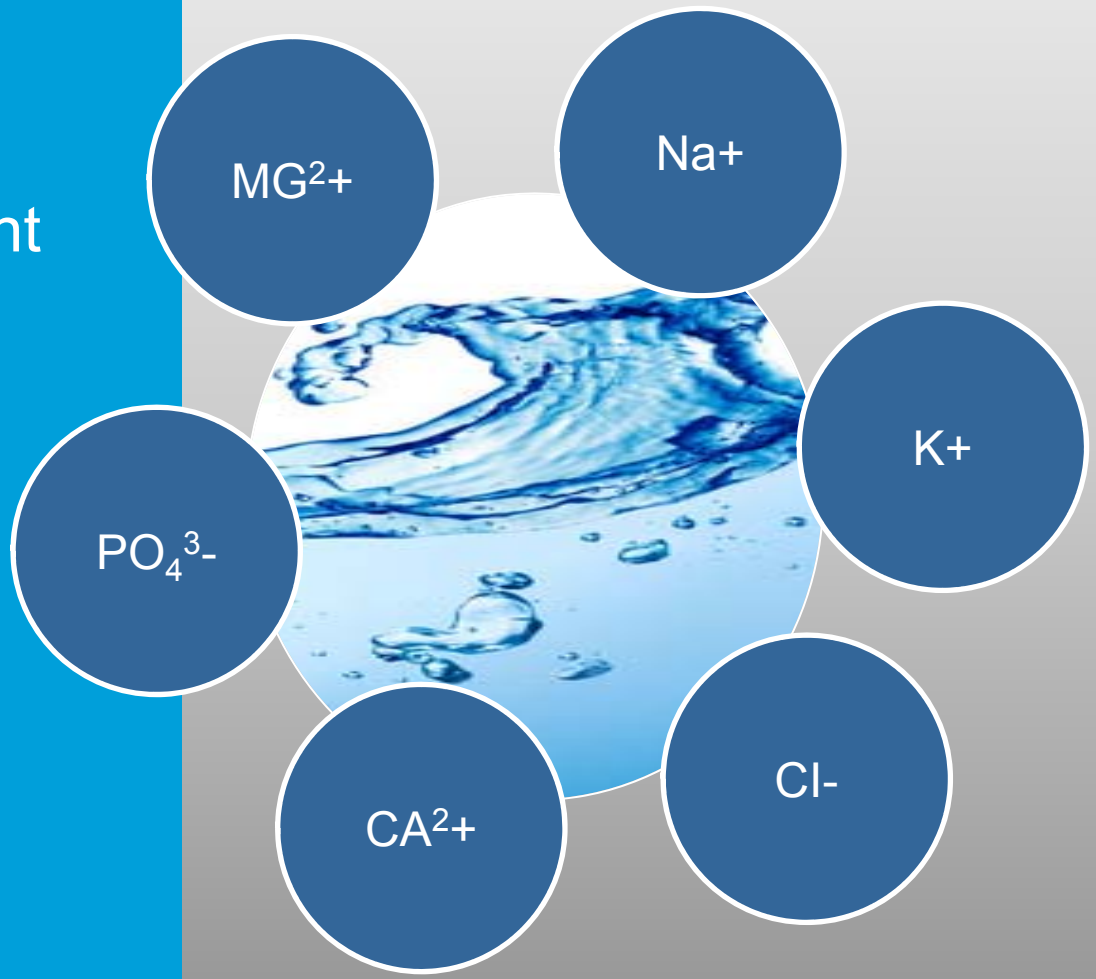
Hypophosphatemia may not always be symptomatic

Most of the clinical manifestations of hypophosphatemia result from a decreased availability of intracellular ATP (adenosine triphosphate) and impaired oxygen delivery to tissues.

Geerse et al. Critical Care 2010, 14:R147
http://ccforum.com/content/14/4/R147

What are options for Electrolyte Management in AKI patients?

- ❑ **Non-CRRT related options?**
- ❑ **CRRT related options?**



American Nephrology Nurses' Association (ANNA). Core Curriculum for Nephrology Nursing. Jannetti Pubns Inc; 4th edition (March 2001) p17

Non-CRRT related options for replacing electrolytes

- Electrolyte IV replacement as prescribed
- Electrolyte supplementation through nutrition, either via nasogastric tube or Total Parenteral Nutrition
  - If given through the GI tract consideration of Vitamin supplementation should be considered

Geerse et al. Critical Care 2010, 14:R147
http://ccforum.com/content/14/4/R147

CRRT-related options for replacing electrolytes

Guiding principle in the management of electrolytes in CRRT is that

"you get what you replace"

Kellum et al. Continuous Renal Replacement Therapy. Oxford University Press. 2010. P61

Considerations for electrolyte clearance in CRRT

The higher the intensity of the therapy, the higher the occurrence of electrolyte disturbances

Dose (ml/kg/h)	40	25
Hypophosphatemia: No. of patients/total no.	461/708 (65.1%)	396/733 (54.0%)
Hypokalemia: No. of patients/total no.	168/718 (23.4%)	180/737 (24.4%)

RENAL study (2009)

VA/NIH Acute Renal Failure Network (2008)

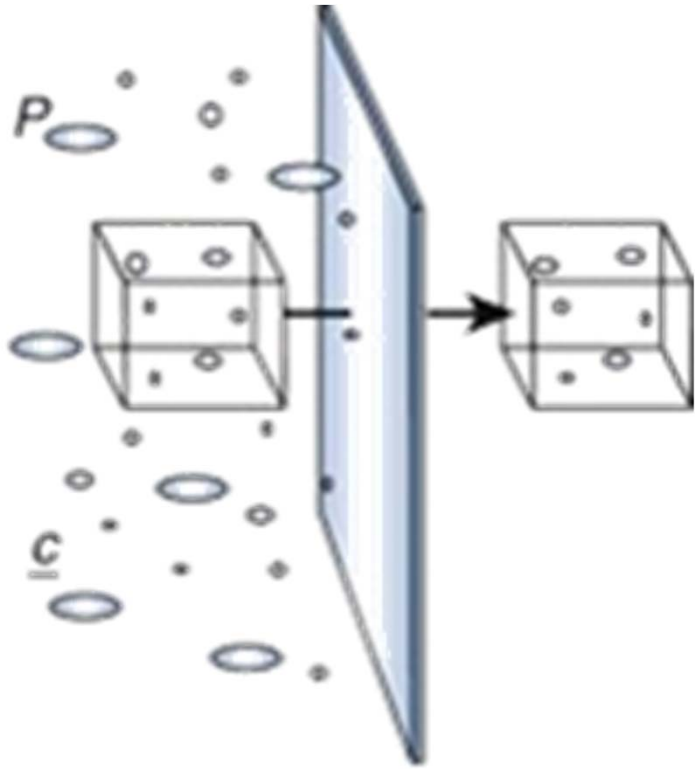
Dose (ml/kg/h)	35	20
Electrolyte disturbance No. of patients/total no.	144/563 (25.6%)	116/561 (20.7%)
Hypophosphatemia No. of patients/total no.	99/563 (17.6%)	61/561 (10.9%)
Hypokalemia No. of patients/total no.	42/563 (7.5%)	25/561 (4.5%)
Other No. of patients/total no.	99/563 (17.6%)	85/561 (15.2%)

New England Journal of Medicine 361;17 nejm.org October 22, 2009
New England Journal of Medicine 359;1 www.nejm.org July 3, 2008

Considerations for electrolyte clearance in CRRT

Convection: effectiveness less dependent on molecular size

Hemofiltration: all electrolytes are freely removed so, over time assuming no other intake or losses, plasma concentrations will approach those of the replacement fluid.



Kellum et al. Continuous Renal Replacement Therapy. Oxford University Press. 2010. P28

Considerations for electrolyte clearance in CRRT

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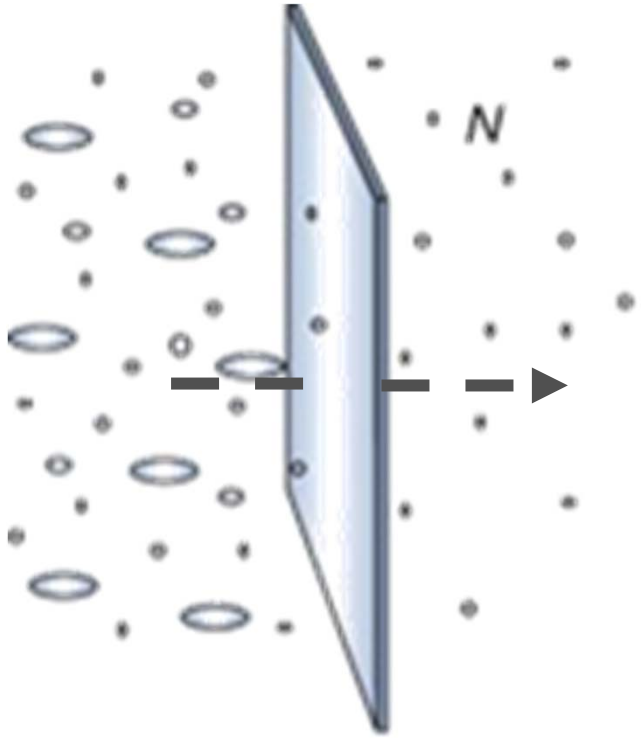
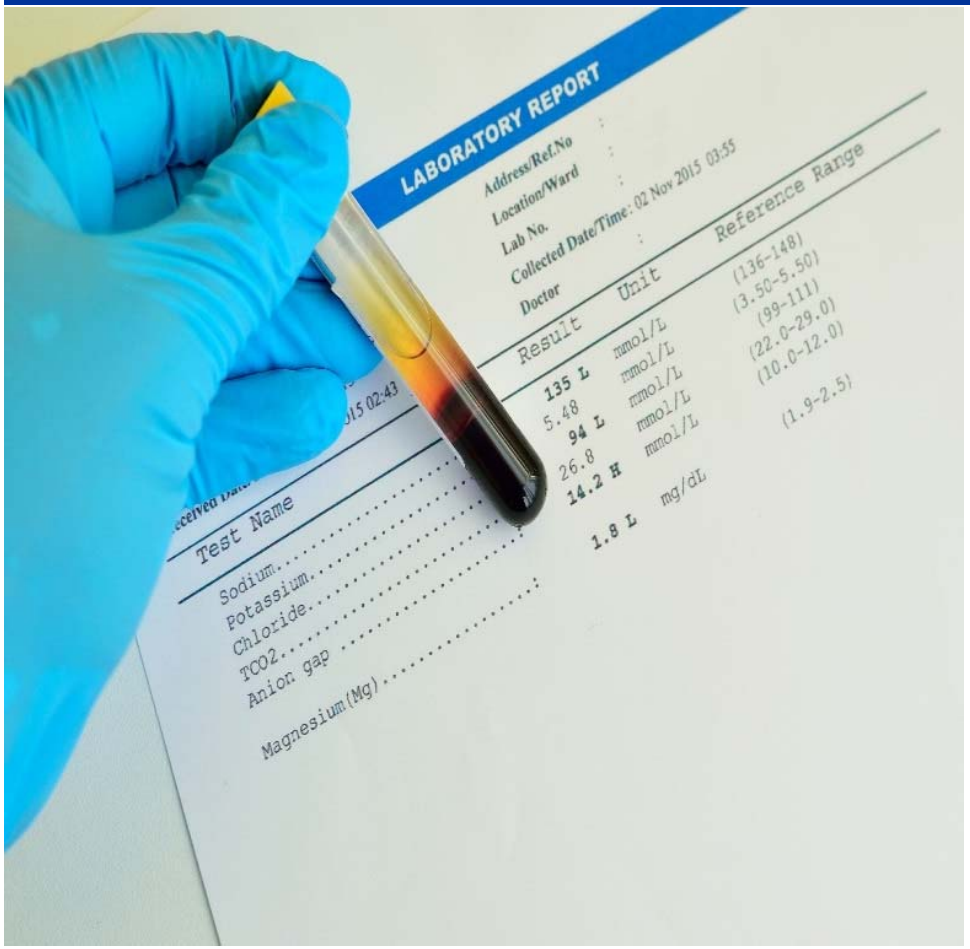
Diffusion: Best for small molecule clearance

Hemodialysis: similar to hemofiltration with one exception: **Phosphate** *although not a large molecule in size, it behaves as if it were much bigger; therefore phosphate is removed much more slowly with diffusion (dialysis) compared to convection (filtration)*



Kellum et al. Continuous Renal Replacement Therapy. Oxford University Press. 2010. P61

Precautions for electrolyte management in CRRT



- Electrolyte and Volume Abnormalities
- Hemodynamic status and fluid, electrolyte and acid-base balance are usually frequently monitored* throughout CRRT
- Electrolyte abnormalities may be corrected by changing the formulations and/or flow rates of replacement and/or dialysate solution or by supplementation
- Solutions should be changed or adjusted based on patient's needs by a registered prescriber

**Patient, hospital and prescriber specific*

Kellum et al. Continuous Renal Replacement Therapy. Oxford University Press. 2010. P61 and 73

ADQI recommendations for CRRT solutions

- **Sodium:** Generally kept isonatric with consideration of anticoagulant in use
- **Potassium / Magnesium / Chloride / anions:** should be present in replacement and/or dialysate and tailored to patient needs
- **Calcium:** presence determined in replacement and/or dialysate based on patient needs and anticoagulation in use
- **Phosphate:** loss can be reduced through replacement in either a CRRT replacement solution or as nutritional supplement; presence determined in replacement solution based on patient needs
- **Glucose:** can be present or absent, if present should be physiological

Kellum et al. Continuous Renal Replacement Therapy. Oxford University Press. 2010. P115 & 116

CRRT related options for electrolyte management

Use of an electrolyte-containing, ready-made CRRT solution

Dialysate

PrismaSATE

PRISMASATE Solution is a sterile dialysis solution intended for treatment of acute kidney disease (renal failure) using Continuous Renal Replacement Therapies, such as continuous hemodialysis and hemodiafiltration aimed at normalizing the composition of the blood.

Federal Law (USA) restricts this device to sale by or on the order of a physician.

Replacement

Phoxillum PrismaSol

PRISMASOL and PHOXILLUM Solutions are indicated in pediatric and adult patients for use as a replacement solution in Continuous Renal Replacement Therapy (CRRT) to replace plasma volume removed by ultrafiltration and to correct electrolyte and acid-base imbalances.
They may also be used in case of drug poisoning when CRRT is used to remove dialyzable substances.

For more information, please see the PHOXILLUM and PRISMASOL Solutions full Prescribing Information available on BaxterPI.com or from your Baxter representative.

CRRT related options for electrolyte management

Replacement

After mixing, additional drugs may be added to the bag via injection connector (spike connector) in large compartment B. In general, drugs other than phosphate should be administered through a different access line. When introducing drugs, use aseptic techniques and mix thoroughly.

Phoxillum

Contains Phosphate 1.0mmol/L

Additional phosphate up to 0.2 mmol/L may be added to the solution.

Use sodium phosphate if adding phosphate to bag.

The total phosphate concentration should not exceed 1.2 mmol/L.

PrismaSol

Phosphate up to 1.2 mmol/L may be added to the solution

If potassium phosphate is added, the total potassium concentration should not exceed 4 mEq/L

Requires solution and syringe

Each bag must be supplemented throughout the treatment

Potential to increase workload, risk of handling errors and contamination, etc.

For more information, please see the PHOXILLUM and PRISMASOL Solutions full Prescribing Information available on BaxterPI.com or from your Baxter representative.

PHOXILLUM Renal Replacement Solution Indications and Important Risk Information

Indications

PHOXILLUM Renal Replacement Solution is indicated in pediatric and adult patients for use as a replacement solution in Continuous Renal Replacement Therapy (CRRT) to replace plasma volume removed by ultrafiltration and to correct electrolyte and acid-base imbalances. It may also be used in case of drug poisoning when CRRT is used to remove dialyzable substances.

Important Risk Information

PHOXILLUM solution can affect electrolytes and volume and may result in hyperkalemia or hyperphosphatemia. Monitor hemodynamic status and fluid inputs and outputs, potassium, phosphorous, calcium, other electrolytes and acid-base balance throughout the procedure. Abnormalities may be corrected by changing the formulation of replacement solution and/or dialysate, supplementation, or adjusting flow rates appropriately. PHOXILLUM replacement solutions contain hydrogen phosphate, a weak acid that may increase the risk of metabolic acidosis. PHOXILLUM solution can effect blood glucose levels resulting in hypo- or hyper-glycemia depending upon the dextrose content of the replacement solution. Monitor blood glucose levels regularly. Patients may require initiation of or modification of antidiabetic therapy or other corrective measures during treatment.

For more information, please see the PHOXILLUM and PRISMASOL Solutions full Prescribing Information available on BaxterPI.com or from your Baxter representative.

PRISMASOL Renal Replacement Solution Indications and Important Risk Information

Indications

PRISMASOL Renal Replacement Solution is indicated in pediatric and adult patients for use as a replacement solution in Continuous Renal Replacement Therapy (CRRT) to replace plasma volume removed by ultrafiltration and to correct electrolytes and acid-base imbalances. PRISMASOL Solution may also be used in case of drug poisoning when CRRT is used to remove dialyzable substances.

Important Risk Information

- PRISMASOL Renal Replacement Solution is contraindicated in patients with known hypersensitivities to this product.
- PRISMASOL Solution can affect electrolytes and volume and may result in hyperkalemia or hyperphosphatemia. Monitor hemodynamic status and fluid inputs and outputs, potassium, phosphorus, other electrolytes and acid-base balance throughout the procedure. Abnormalities may be corrected by changing the formulation of replacement solution and/or dialysate, supplementation, or adjusting flow rates appropriately. The use of PRISMASOL Solutions containing dextrose may increase the risk for hyperglycemia in patients with impaired glucose tolerance. Patients may require initiation of or modification of antidiabetic therapy during treatment with PRISMASOL Solutions containing dextrose. Monitor blood glucose.

For more information, please see the PHOXILLUM and PRISMASOL Solutions full Prescribing Information available on BaxterPI.com or from your Baxter representative.

CRRT related options for replacing electrolytes

Manually Compounding Solutions by Pharmacy:

- Made to order based on patient needs
- Typically between 1 liter and 3 liter bags
- Barletta suggests that the total time spent per day compounding CRRT solutions was 40 (range, 10 to 299) minutes or 8.3 ± 3.3 minutes/bag. When multiple patients required dialysis solutions total workload reached 5 hours/day

Baxter CRRT solution and preparation for use:

- Replacement = 10 solutions / multiple formulations / 5 liter bags
- Dialysate = 9 solutions / multiple formulations / 5 liter bags

1) Immediately before use, remove the overwrap from the bag
2) Hold the small compartment with both hands and squeeze until an opening is created in the peel seal then squeeze with both hands on the large compartment (non PVC bags only) OR break red frangible pin (PVC bags only)
3) Shake gently to mix. The solution is now ready for use and can be hung on the equipment

Mixing a bag of Baxter solution takes approximately 1 minute

Barletta et al. Resource Utilization and Total Cost of Commercially-Available Versus Manually-Compounded Solutions Used for Dialysate in Continuous Renal Replacement Therapy. Hospital Pharmacy Volume 43, Number 1, pp 29–34 2008.
Phoxillum, Prismasol & Prismasate PI

Summary……

- Phosphorus is involved in a wide variety of metabolic reactions and vital functions
- Depletion of electrolytes, including phosphate, may develop during the use of (continuous) renal replacement therapy
- Phosphate can be supplemented in a variety of ways:

Non CRRT:
- IV replacement as prescribed
- Through nutrition, either via nasogastric tube or Total Parenteral Nutrition

CRRT:
- Manually compounded CRRT solutions
- Pre-mixed replacement solutions that are either:
  - Approved for phosphate addition, such as PRISMASOL Solution

  OR
  - Replacement solutions that already contain phosphate, such as PHOXILLUM Solution

THANK YOU