Module 1: CRRT Overview

CRITICAL CARE NEPHROLOGY | alliance

Edwards

(page intentionally blank)

CRRT OVERVIEW

TABLE OF CONTENTS

Lesson 1. Renal Anatomy & Physiology

Lesson 2. Acute Renal Failure

Lesson 3. What is CRRT?

Lesson 4. Delivery of CRRT

Lesson 5. CRRT Considerations

These materials were created by Baxter Healthcare Corporation and Edwards Lifesciences Corporation as part of the Critical Care Nephrology Alliance. Seeking to provide CRRT professionals with the highest caliber of multidisciplinary expertise, products and services, the Alliance brings together the unique strengths of Baxter, an expert in renal therapies, and Edwards Lifesciences Corporation, a leader in critical care.

Baxter

CRITICAL CARE NEPHROLOGY | alliance

Edwards LIFESCIENCES

Notes:

(page intentionally blank)

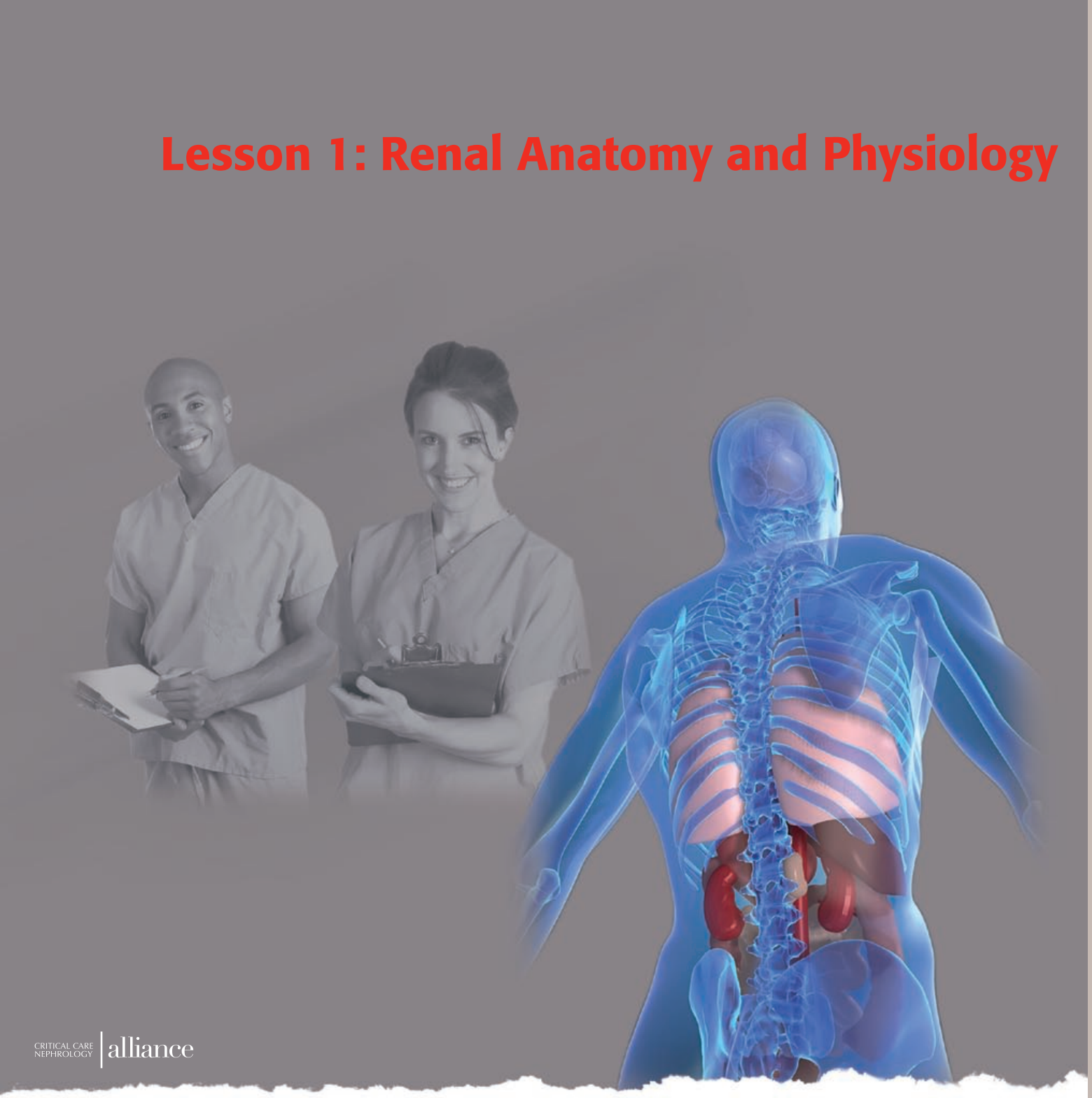
LEARNING OBJECTIVES

- Recognize the role of the kidney in maintaining balance in the body
- Understand the causes and phases of acute renal failure (ARF)
- Understand the principles of fluid and solute management in continuous renal replacement therapy (CRRT): diffusion, convection, adsorption, ultrafiltration
- Understand the rationale for using each CRRT modality
  - Slow continuous ultrafiltration (SCUF)
  - Continuous veno-venous hemofiltration (CVVH)
  - Continuous veno-venous hemodialysis (CVVHD)
  - Continuous veno-venous hemodiafiltration (CVVHDF)
- Discuss the importance of vascular access and anticoagulation in successful CRRT usage
- Understand the rationale for using substitution and dialysate fluids in CRRT
- Recognize all the components needed to perform a successful CRRT treatment
- Recognize advantages, limitations and special requirements when performing CRRT

Notes:

(page intentionally blank)

Lesson 1: Renal Anatomy and Physiology



CRITICAL CARE NEPHROLOGY | alliance

Edwards

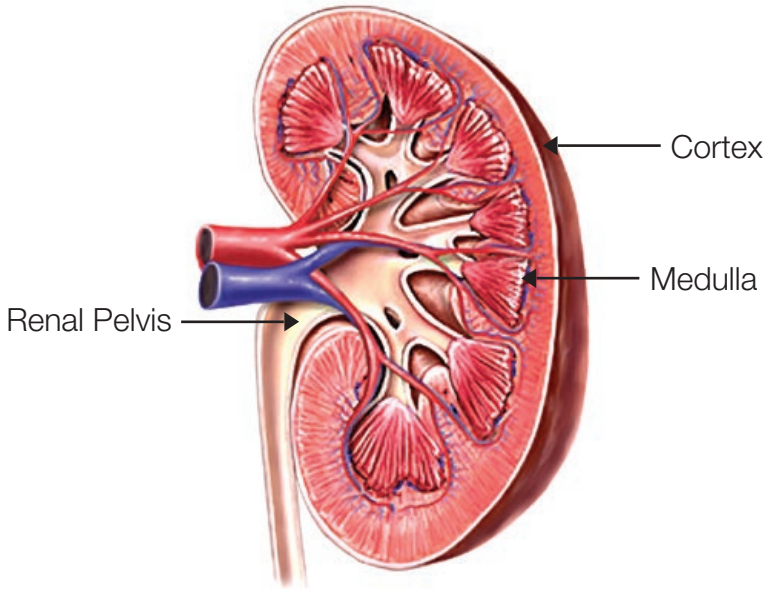
(page intentionally blank)

RENAL ANATOMY AND PHYSIOLOGY

Every time the heart beats, 25% of the cardiac output is sent to the kidneys.

THE KIDNEY

- The kidney functions using three principles: ultrafiltration, excretion and reabsorption
- The kidney consists of three parts:



Notes:

COMPONENTS OF THE KIDNEY

1. The cortex (outer layer) contains 80% of the nephrons. These nephrons filter the blood continuously to maintain balance.

2. The medulla (inner layer) contains 20% of the nephrons. These nephrons also filter the blood, but have the added responsibility to concentrate urine. This becomes an important diagnostic tool.

3. The renal pelvis is the start of the collecting system, containing the collecting tubules and the ureter.

Additionally, ureters carry urine into the bladder where it is stored until it is eliminated from the body through the urethra.

RESIDUAL KIDNEY FUNCTION

- The kidney is capable of maintaining the body's equilibrium until about 50% of the nephrons are damaged

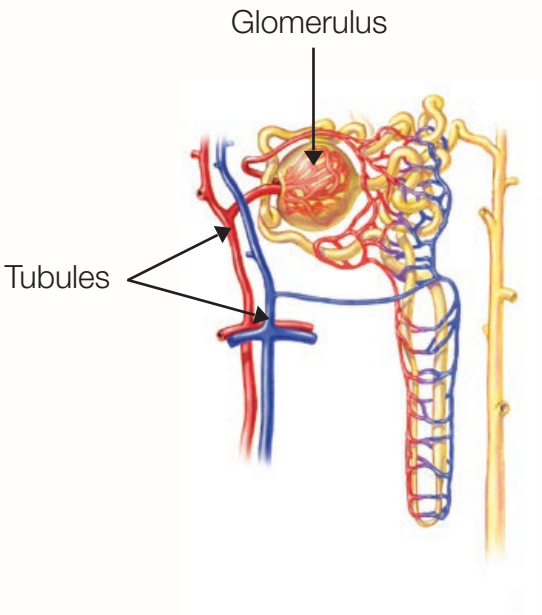
- After 50% loss of kidney function, the body begins to make trade-offs to maintain homeostasis. For example, parathyroid hormone (PTH) increases to compensate for increased excretion of phosphorus. The patient will likely remain asymptomatic

- After 90% loss of kidney function, some form of renal replacement therapy is necessary to preserve life

Notes:

THE NEPHRON

The functional unit of the kidney is called a nephron. Each kidney has about one million nephrons. Each nephron contains a glomerulus, which functions as an individual filtering unit. It also contains tubules for secretion and absorption of substances.



THE BLOOD PATHWAYS

Blood leaves the heart, enters the abdominal aorta and enters the kidney through the renal artery. The renal artery divides into seven branches of arterioles until it becomes the afferent arteriole.

The afferent arteriole carries blood to the glomerulus, where it is filtered. It then leaves the glomerulus through the efferent arteriole, and is returned to the venous system. This system branches into many larger vessels until it becomes the renal vein.

Blood leaves the kidney via the renal vein, and is returned to the heart via the inferior vena cava.

Notes:

THE GLOMERULUS

The glomerulus consists of a group of cells with selective permeability. It is a semi-permeable membrane.

Selective permeability means that certain substances will cross the membrane and others will not be allowed to cross. Through selective permeability, the kidney regulates fluid and electrolyte balance. The tea filter is a sample of a membrane with selective permeability.

The kidneys produce approximately 180 liters of filtrate per day. Only 1.5 - 2 liters are excreted as urine. The remaining 178 liters remain in the body. This is simply recycled body water.

THE AFFERENT AND EFFERENT ARTERIOLES

The afferent arteriole has a larger lumen than the efferent arteriole. Therefore, blood flows into the glomerulus faster than it flows out, which creates a pooling of blood in the Bowman's capsule.

Hydrostatic pressure on the blood will force fluid to cross the glomerular membrane and enter the tubules. This is ultrafiltration.

As filtrate flows through the tubular network, special cells will respond to the need for reabsorption and secretion.

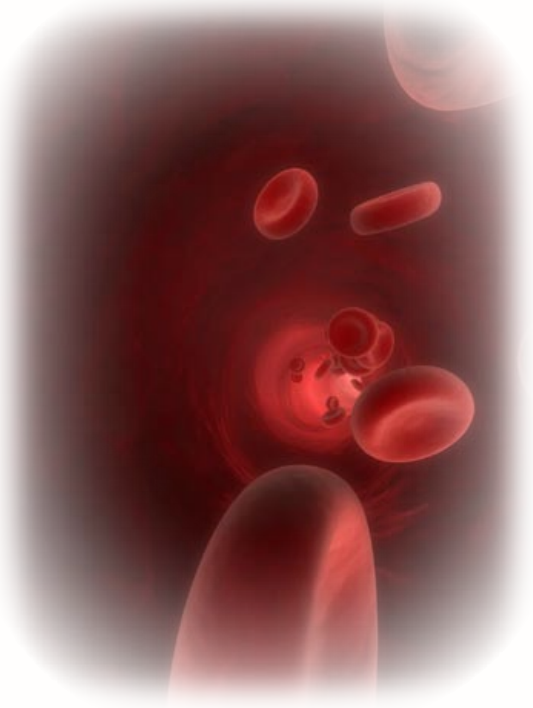
Notes:

The end product of this filtrate is urine. In the normal kidney, this urine will be the right color, have the right osmolality and contain the right substances.

The urine color is light to dark yellow depending on volume, and the color is provided by solutes. Osmolality is used because it measures particles independently of their molecular weight. Substances including urea, creatinine, phosphorus, potassium acids etc. are cleaned and filtered to keep the blood values normal.

The goal of the kidney is to maintain a normal balance of fluids, electrolytes, minerals and acid-base. It works continuously to preserve equilibrium and homeostasis.

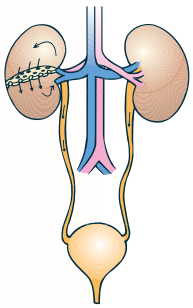
The kidneys also produce hormones like renin, vitamin D and erythropoietin. Renin promotes sodium retention and it also causes vasoconstriction. Vitamin D stimulates calcium and phosphate absorption. Erythropoietin promotes production of red blood cells in the bone marrow.



Notes:

In summary:

- With every heartbeat, 25% of the cardiac output goes to the kidneys
- Blood enters the abdominal aorta and flows into the renal artery
- The renal artery branches until it becomes the afferent (entering) arteriole
- The afferent arteriole takes the blood into the glomerulus (the filtering unit located in Bowman's capsule of the nephron)
  - Because blood flows into Bowman's capsule faster than it flows out, a resulting increase in pressure facilitates filtration
- The efferent (leaving) arteriole takes the blood coming out of the glomerulus and returns it to the venous system. The venous system branches into larger vessels to become the renal vein
- The renal vein carries blood to the vena cava and returns it to the heart
- This process is continuous



Notes:

KIDNEY FUNCTIONS

The kidney has several functions (CRRT deals with the first four functions):

1. Fluid balance
   - Through ultrafiltration and reabsorption

2. Electrolyte balance
   - Through reabsorption and excretion

3. Acid-base balance
   - Through reabsorption and excretion

4. Excretion of drugs and by-products of metabolism
   - Nitrogen
   - Urea
   - Creatinine

5. Synthesis of erythropoietin
   - Stimulates the bone marrow to produce healthy red blood cells and help them mature

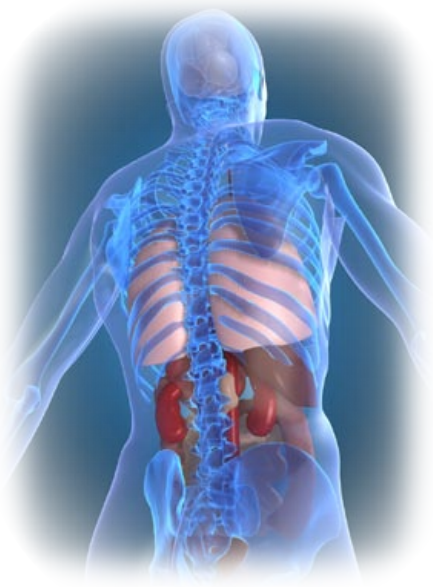
6. Regulation of blood pressure
   - Secretes renin to help regulate blood pressure

7. Maintenance of calcium:phosphorus balance
   - A normal ratio is 2:1
   - The kidneys produce the active vitamin D and regulate calcium
   - The kidney also is the major excretor of phosphorus. If the kidney does not function properly, phosphorus builds up in the blood stream. As the body struggles to maintain the 2:1 calcium:phosphorus ratio, it will steal calcium from the bones by increasing parathyroid hormone (PTH) production

Notes:

KIDNEY FACTS

- The kidneys are two bean shaped organs, located just below the inferior boundary of the rib cage
- Each kidney can function independently of the other
- Each kidney weighs approximately 110 – 170 grams and is about the size of a human fist
- The kidneys receive 1,200 milliliters of blood (25% of cardiac output) every minute. That is 72 liters per hour or 1,728 liters per day
- Normal kidney function is measured in terms of glomerular filtration rate (GFR). Normal GFR is 125 milliliters per minute. That is 7,500 milliliters per hour or 180 liters per day



Notes:

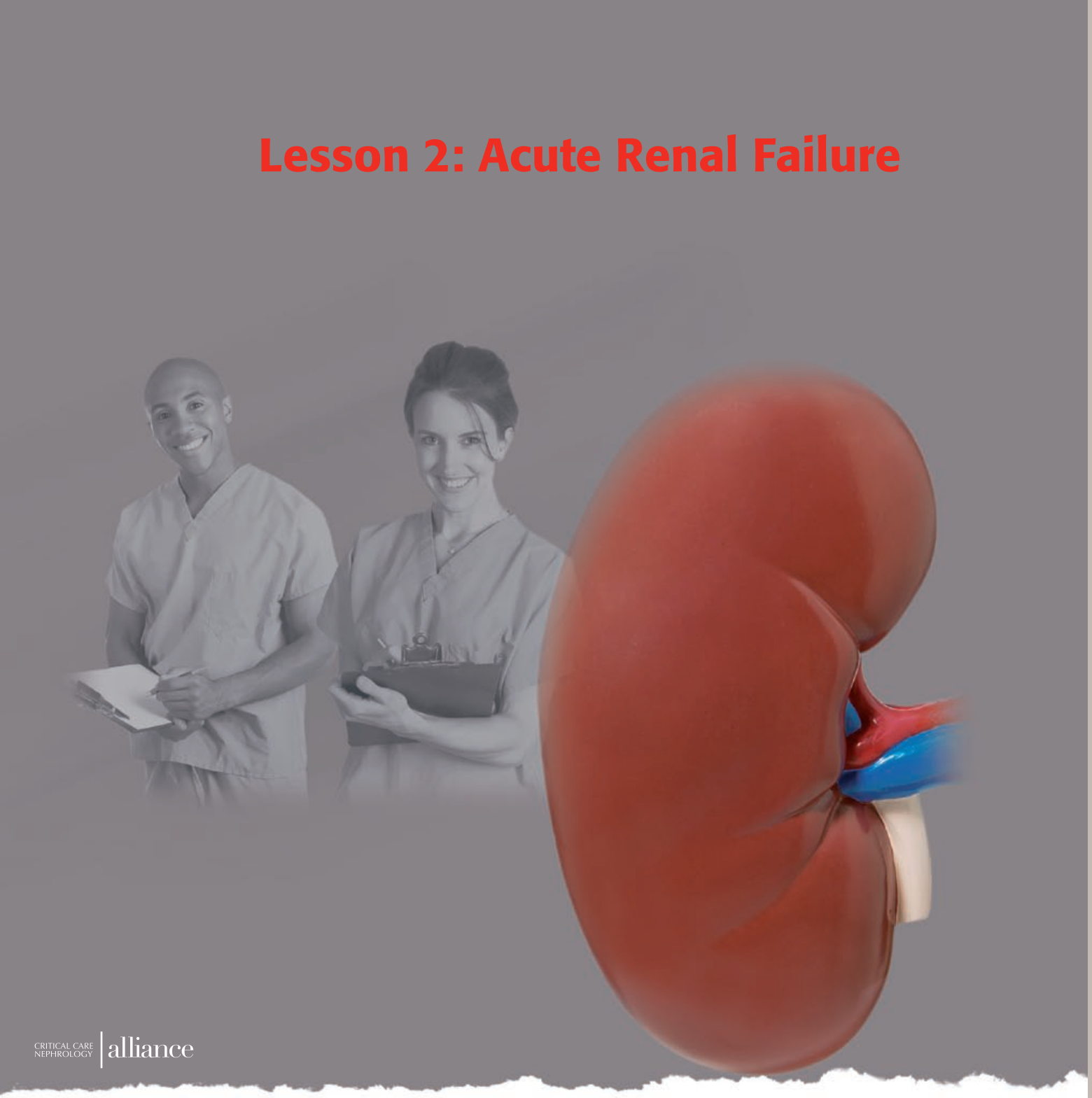
- The kidney is divided into three parts: the cortex, the medulla and the renal pelvis
- The functional unit of the kidney is called a nephron
- Each kidney contains approximately one million nephrons
- Each nephron has a glomerulus, which functions as an individual filtering unit. It also contains the tubules which are responsible for reabsorption and secretion
- The kidney will maintain homeostasis in the body until less than 50% of the nephrons are functioning
- The kidney has several roles:

    - Fluid balance
    - Electrolyte balance
    - Acid-base balance
    - Excretion of drugs and by-products of metabolism
    - Synthesis of erythropoietin
    - Regulation of blood pressure
    - Maintenance of calcium:phosphorus balance

Notes:

(page intentionally blank)

Lesson 2: Acute Renal Failure



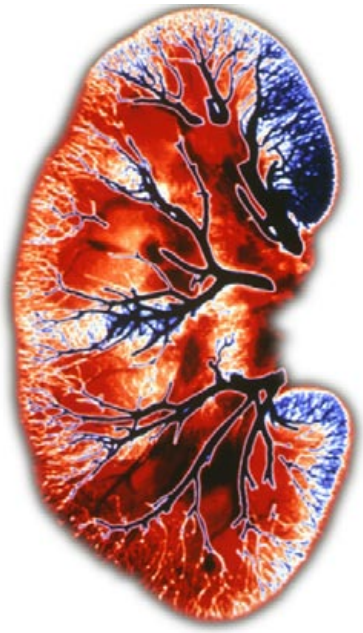
CRITICAL CARE NEPHROLOGY | alliance

Edwards

(page intentionally blank)

ACUTE RENAL FAILURE / ACUTE RENAL INJURY

Acute renal failure (ARF) results from the sudden loss of kidney function. Acute renal failure in the setting of critical care patients is defined as an abrupt decline in glomerular filtration rate resulting from ischemic or toxic injury to the kidney.[1]



- Waste products that are usually excreted by the kidney accumulate in the blood
- ARF may be accompanied by metabolic, acid-base and electrolyte disturbances and fluid overload
- ARF may affect many other organ systems
- ARF often requires immediate treatment

Notes:

[1] AR Nissenson: Acute Renal Failure: Definition and pathogenesis. Kidney Int Suppl. 1998 May; 66:S7-10

Acute renal failure can be classified as:

A. PRE-RENAL

Pre-renal failure typically results from decreased blood flow to the kidneys. The reduction in glomerular filtration enables the solutes in the blood to accumulate but does not cause any structural damage to the kidney itself. Examples of situations leading to pre-renal failure may include dehydration, hemorrhage, congestive heart failure, sepsis, and embolism/thrombosis.

B. RENAL (INTRA-RENAL)

Intra-renal failure typically involves direct injury to the kidney itself. The most common cause is acute tubular necrosis (ATN). Some causes of ATN are ischemia, hypertension, nephrotoxin and some systemic vascular diseases such as lupus.

C. POST-RENAL

In post-renal failure, the underlying cause is typically a bilateral obstruction below the level of the renal pelvis and may be due to tumor development, thrombi, urinary tract obstruction, or hyperthrophic prostate.

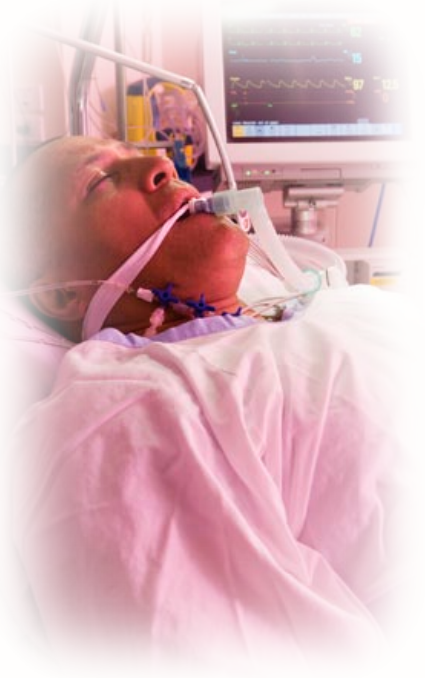
Notes:

PHASES OF ACUTE RENAL FAILURE

In most cases of acute renal failure, patients will progress through distinct phases as outlined below.

- **Oliguric phase**

  - Can last anywhere from five days to 21 days
  - Low urine output (less than 400 mL/24 hrs)
  - Protein in the urine
  - Electrolyte imbalances
  - Metabolic acidosis



- **Diuretic phase**

  - Begins when urine output begins to rise
  - Has variable time frames, sometimes occurring as little as 24 hours after the onset of renal failure
  - Associated with potassium and sodium loss in the urine
  - Enhanced urine output may not reflect restored kidney function but rather may be the result of accumulating serum urea and creatinine, which have an osmotic diuretic effect

- **Recovery phase**

  - May last several months following the onset of the acute renal failure
  - During this period, kidney function gradually returns to normal and proper urine concentrations and volumes are achieved

Notes:

(page intentionally blank)

Lesson 3: What is CRRT?

CRITICAL CARE NEPHROLOGY | alliance

Edwards

(page intentionally blank)

CRRT: DEFINITION

Continuous renal replacement therapy (CRRT) is a therapy indicated for continuous solute removal and/or fluid removal in the critically ill patient. It allows for slow and isotonic fluid removal that results in better hemodynamic tolerance even in unstable patients with shock and severe fluid overload. This process can be applied to both adults and children.

CRRT can be modified at any time of the day and night to allow adaptation to the rapidly changing hemodynamic situation of critically ill patients.

CRRT therapy indications may be renal, non-renal, or a combination of both. It is the treatment of choice for the critically ill patient needing renal support and/or fluid management.

HISTORY OF CRRT

'The history of CRRT is relatively short. Its beginning was in 1977 when Kramer, while introducing a catheter into the femoral vein before hemodialysis, accidentally inserted the catheter into the femoral artery. He realized the possibility of using the arteriovenous gradient for filtration of blood and fluid elimination. He replaced the excessive losses by continuous infusion of substituting solutions. He used for the method the term continuous arteriovenous hemofiltration (CAVH). This was the first step in CRRT.'[2] Over the past thirty years CRRT has continued to develop and has emerged as a front line therapy for treatment of critically ill patients with acute renal failure.

Notes:

[2] Hladik M, Tymonova J, Kadicik M, Adamkova M: Treatment by continuous renal replacement therapy in patients with burn injuries. Burn Centre and Centre for Child Dialysis and Nephrology, University Hospital Ostrava, Czech Republic J. Tymonova Burn Centre 17.listopadu 1790 708 52 Ostrava Czech Republic.

CRRT GOALS[3,4]

- Removal of waste products
- Restoration of acid-base balance
- Correction of electrolyte abnormalities
- Hemodynamic stabilization
- Fluid balance
- Nutritional support
- Removal and/or modulation of septic mediators

CRRT INDICATIONS[5]

Accepted indications are acute renal failure combined with:

- Hemodynamic instability (cardiovascular)
- Severe fluid overload unresponsive to diuretics
- Hypercatabolic states/trauma - rhabdomyolysis
- High fluid requirements (nutrition, blood products)

Less established (non-renal) indications:

- Sepsis, lactic acidosis, acute respiratory distress syndrome (ARDS), multiple organ dysfunction score (MODS)
- Chronic congestive heart failure (CHF), or decompensated CHF
- Pre- and post-cardiovascular surgery / coronary artery bypass graft (CABG)
- During extracorporeal membrane oxygenation (ECMO) for fluid management

Notes:

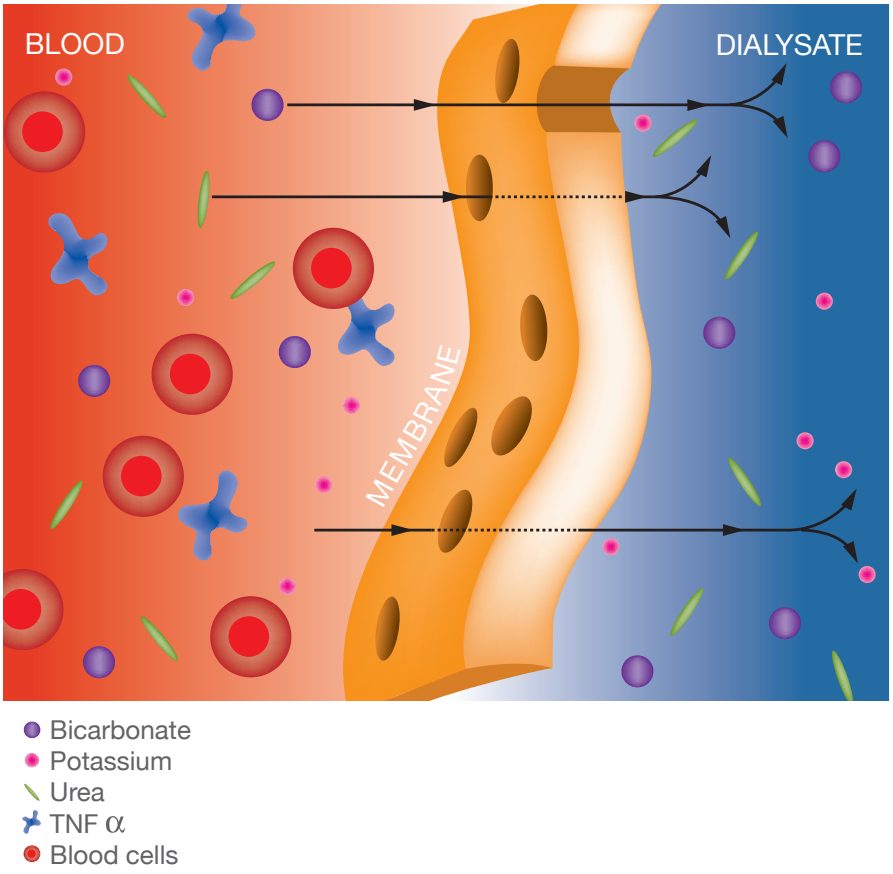
[3] Bellomo R, Ronco C, Mehta R: Nomenclature for continuous renal replacement therapies. AJKA, Vol 28, No.5, pages S1-S7, November 1996.
[4] Honore, et al: The big bang of hemofiltration: The beginning of a new era in the third millenium for extra-corporeal blood purification. IJAO/Vol29/no 7, 2006/pp649-659.
[5] Schetz, M: Non-Renal Indications for Continuous Renal Replacement Therapy. Kidney Intern Vol 53, Suppl 66 (1998).

PRINCIPLES OF CRRT / SOLUTE MANAGEMENT

DIFFUSION

Diffusion is the movement of solutes through a semi-permeable membrane from an area of higher concentration to an area of lower concentration until equilibrium has been established.

- Solutes move from a higher concentration to a lower concentration
- In CRRT, diffusion occurs when blood flows on one side of the membrane, and dialysate solution flows counter-current on the other side
- The dialysate does not mix with the blood
- Efficient for removing small molecules but not large molecules
- Molecular size and membrane type can affect clearances
- Diffusion occurs during hemodialysis

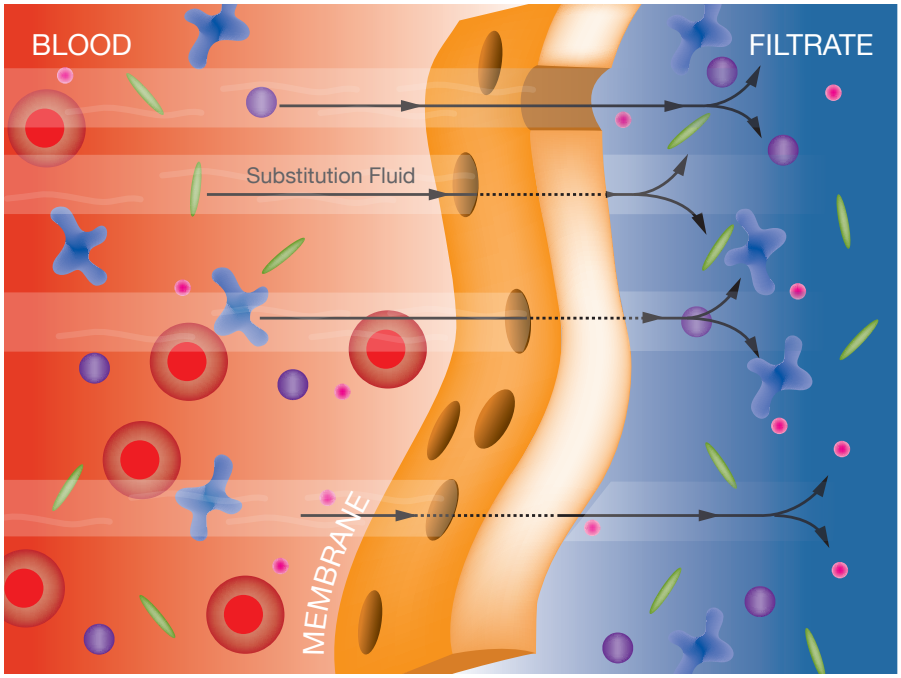


Notes:

CONVECTION

Convection is the one-way movement of solutes through a semi-permeable membrane with a water flow. Sometimes it is referred to as solvent drag.

- Efficient for both larger and smaller molecules
- The faster the substitution flow rate, the higher the clearance
- Pressure difference between the blood and ultrafiltrate causes plasma water to be filtered across. This causes solvent drag for small and large molecules across the membrane leading to removal from the blood. The ultrafiltrate containing the solute should be replaced by substitution solutions
- Substitution solutions must have near physiological levels of electrolytes and buffer, and be sterile



- Solute molecular size and membrane type can affect clearances
- Convection is a hemofiltration principle

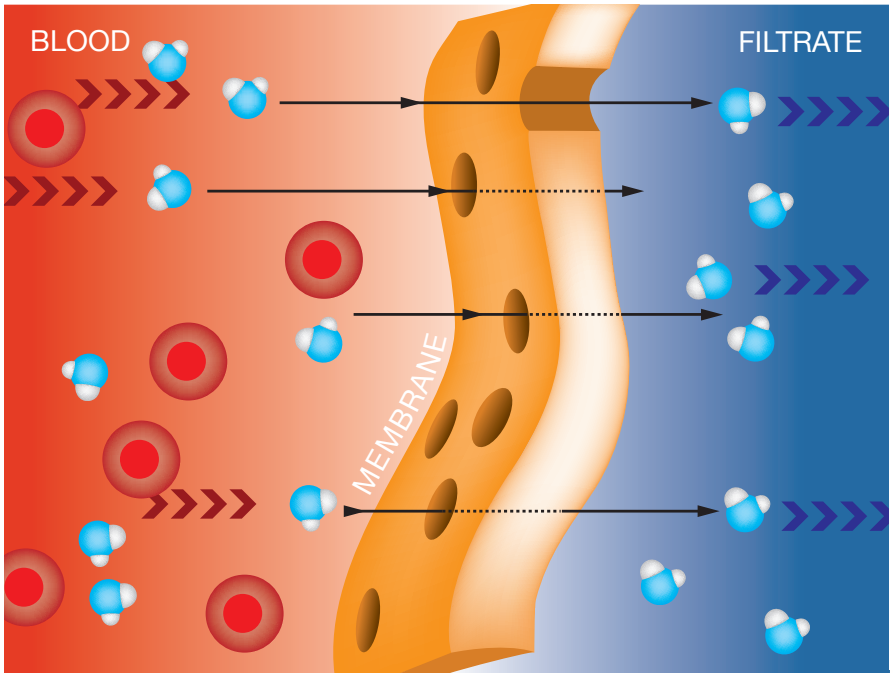
Notes:

PRINCIPLES OF CRRT / FLUID MANAGEMENT

ULTRAFILTRATION

Ultrafiltration is the movement of fluid through a semi-permeable membrane along a pressure gradient.

- Positive and negative pressures affect ultrafiltration
- Positive pressure is generated on the blood side of the membrane and negative pressure is generated on the fluid side
- This gradient, positive to negative, influences the movement of fluid from the blood side to the fluid side, resulting in a net removal of fluid from the patient
- The ultrafiltration rate depends on the pressure applied to the filter, inside and outside the fibers
- Minimal solute clearance happens by convection during ultrafiltration

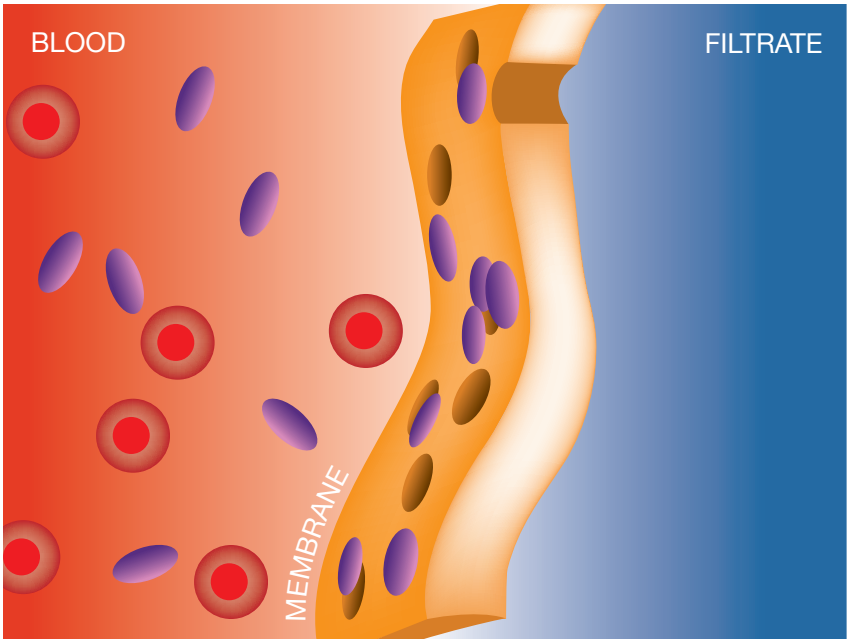


Notes:

ADSORPTION

Adsorption is the adherence of solutes and biological matter to the surface of a membrane.

- High levels of adsorption can cause certain filters to clog and become ineffective
- Membrane type affects adsorptive tendencies /effectiveness
- Adsorption may also cause limited removal of some solutes (e.g., ß2 microglobulins) from the blood

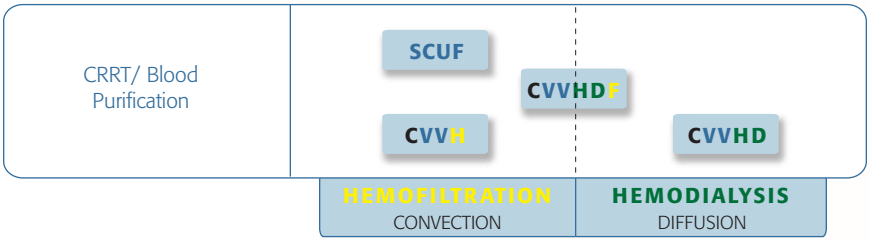


In summary:

Principles used in all CRRT/blood purification therapies are:

- Diffusion (hemodialysis)
- Convection (hemofiltration)
- Diffusion & convection (hemodiafiltration)
- Ultrafiltration (all therapies)
- Adsorption (all therapies)

Notes:



CRRT includes several treatment modalities that use a veno-venous access. The choice will depend on the needs of the patient and on the preference of the physician.

Slow **C**ontinuous **U**ltra**F**iltration (SCUF)
Removal of ultrafiltrate at low rates without administration of a substitution solution. The purpose is to prevent or treat volume overload when waste product removal or pH correction isn't necessary.

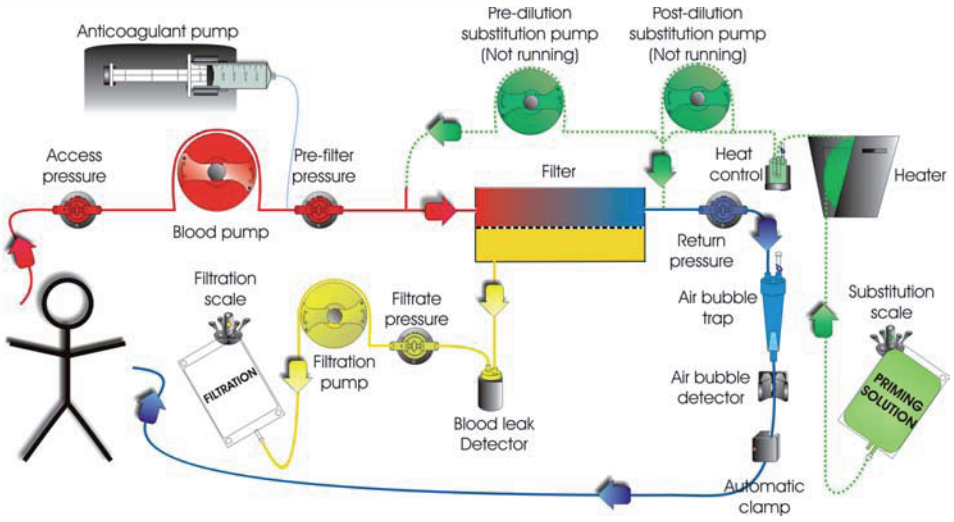
Continuous **V**eno-**V**enous **H**emofiltration (CVVH)
Continuous convective removal of waste products (small and large molecules) utilizing a substitution solution. pH is affected with the buffer contained in the substitution solution.

Continuous **V**eno-**V**enous **H**emo**D**ialysis (CVVHD)
Continuous diffusive removal of waste products (small molecules) utilizing a dialysis solution. pH is also affected with the buffer contained in the dialysate.

Continuous **V**eno-**V**enous **H**emo**D**ia**F**iltration (CVVHDF)
Continuous diffusive and convective removal of waste products (small and large molecules) utilizing both dialysate and substitution solution. pH is also affected with the buffer contained in the dialysate and substitution solution.

Notes:

SLOW CONTINUOUS ULTRAFILTRATION[6] (SCUF)



Primary therapeutic goal:
- Safe management of fluid removal

Primary indications:
- Fluid overload without significant electrolyte imbalance

Principle used: ultrafiltration

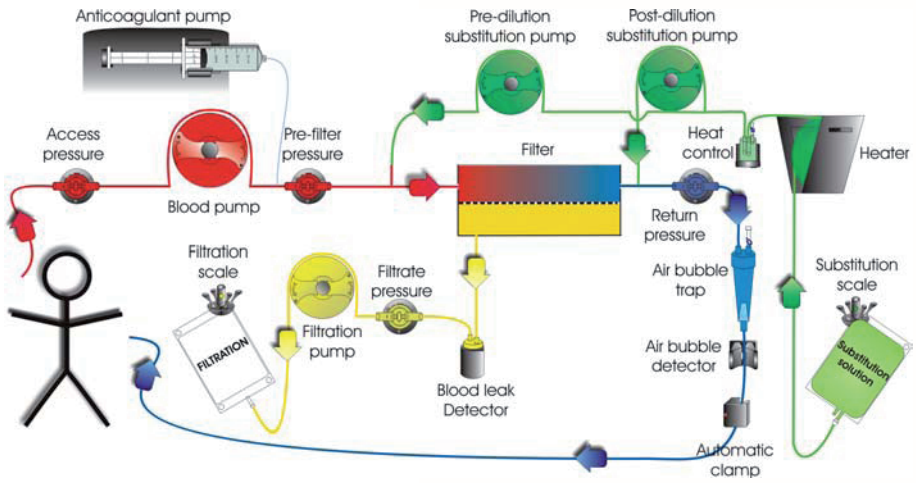
Therapy characteristics:
- No dialysate or substitution solutions
- Fluid removal only

NOTE: The colors of text in this Module indicate its correlation to elements of Figures 4-7 in the Operator's Manual (p. 19-20)

Notes:

[6] Operator's Manual, Automated Fluid Balance Monitor, Aquarius for Platinum software version 6 U.S. Page 19.

CONTINUOUS VENO-VENOUS HEMOFILTRATION[7] (CVVH)



Primary therapeutic goal:
- Solute removal and safe management of fluid volume

Primary indications:
- Uremia, severe acid/base or electrolyte imbalance
- When removal of larger molecular weight substances is required

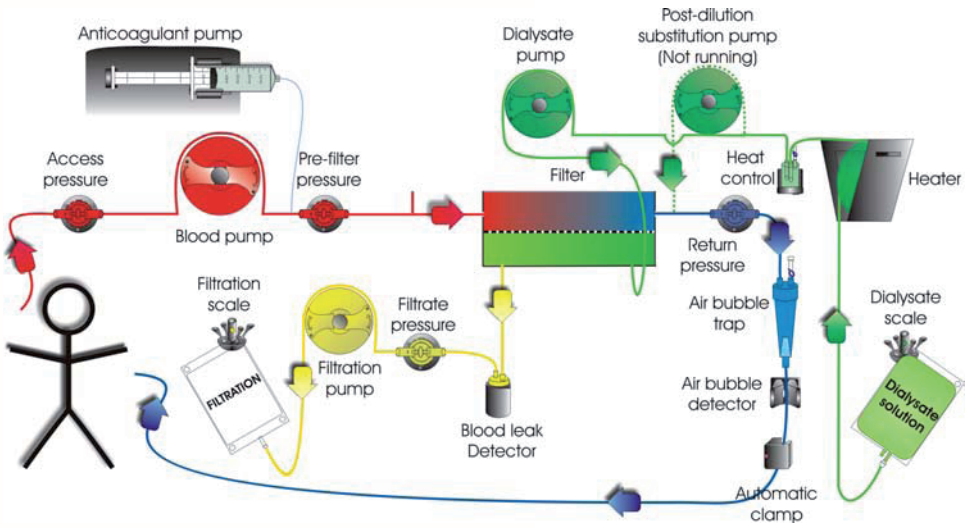
Principle used: convection

Therapy characteristics:
- Requires substitution solution to drive convection
- No dialysate solution
- Effective at removing small and large molecules

Notes:

[7] Operator's Manual, Automated Fluid Balance Monitor, Aquarius for Platinum software version 6 U.S. Page 19.

CONTINUOUS VENO-VENOUS HEMODIALYSIS[8] (CVVHD)



Primary therapeutic goal:
- Solute removal and safe management of fluid volume

Primary indications:
- Uremia, severe acid/base or electrolyte imbalance

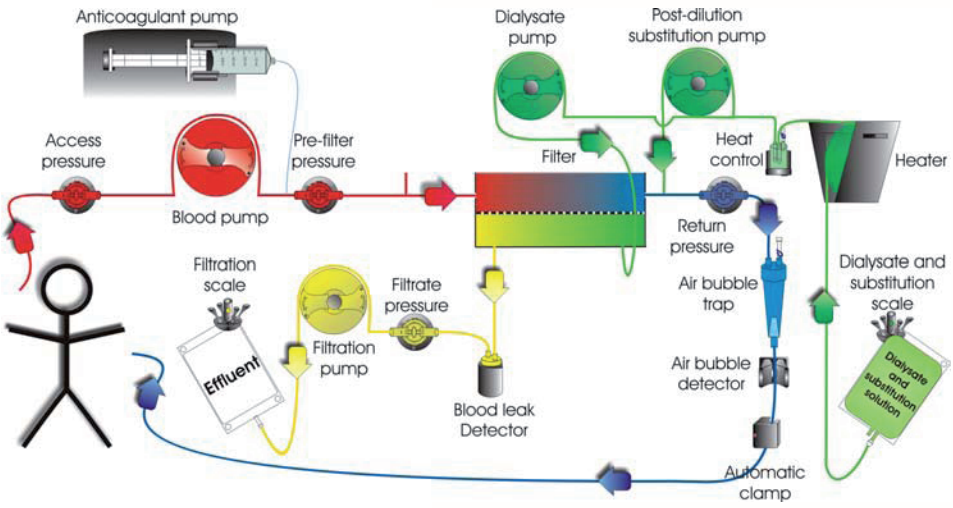
Principle used: diffusion

Therapy characteristics:
- Requires dialysate solution to drive diffusion
- No substitution solution
- Effective at removing small to medium molecules

Notes:

[8] Operator's Manual, Automated Fluid Balance Monitor, Aquarius for Platinum software version 6 U.S. Page 20.

CONTINUOUS VENO-VENOUS HEMODIAFILTRATION[9] (CVVHDF)



Primary therapeutic goal:
- Solute removal and safe management of fluid volume

Primary indications:
- Uremia, severe acid/base or electrolyte imbalance
- When removal of large molecular weight substances is required

Principle used: diffusion and convection

Therapy characteristics:
- Requires dialysate fluid and substitution solution to drive diffusion and convection
- Effective at removing small, medium and large molecules

Notes:

[9] Operator's Manual, Automated Fluid Balance Monitor, Aquarius for Platinum software version 6 U.S. Page 20.

(page intentionally blank)

Lesson 4: Delivery of CRRT

CRITICAL CARE NEPHROLOGY | alliance

Edwards

(page intentionally blank)

COMPONENTS OF A CRRT PROGRAM

- Vascular access
- Anticoagulation
- CRRT system (machine, hemofilters, line sets, accessories)
- Fluid management
- Team

VASCULAR ACCESS

NOTE: In this training guide, all references are to veno-venous vascular access. When inserting vascular access for CRRT, please follow the manufacturer's instructions and your hospital's protocols for insertion of central lines.

Vascular access is a basic prerequisite to perform any type of extracorporeal therapy. Access is particularly important in CRRT where catheter performance is tested 24 hours a day. In dialysis therapies, central venous catheters provide rapid and easy access permitting immediate use in critically ill patients[10]. The most common catheter now in use is the large-bore, double-lumen catheter. The primary sites for insertion include the femoral vein, internal jugular vein, and, less commonly, the subclavian vein.

WARNING: To have an effective CRRT treatment, it is absolutely crucial to have functional access. Failure to have functional access will result in a less than optimal treatment.

Using a blood pump, the patient's blood is removed via the red coded line typically connected to the red port of the catheter and delivered through the hemofilter back to the patient via the blue coded line typically connected to the blue port.

Notes:

[10] Ronco C, Bellomo R, LaGreca, (eds): Blood Purification in Intensive Care. Contrib Nephrol. Basel, Karger, vol 132, pp 266-282.

Many factors affect the functioning of a CRRT access[11, 12, 13]

- Type and size of catheter
  - Polyurethane or silicone
  - French size
- Length and placement site of catheter

To ensure proper flow, it is important that the appropriate catheter is placed in the appropriate vessel. The following are suggestions.

  - For jugular placement, it's usually 12.5 cm on the right side and 15 cm on the left side (check each manufacturer's recommendations)
  - For subclavian placement, it's usually 15 cm on the right side and 20 cm on the left side (check each manufacturer's recommendations)
  - The femoral vein should have an extra long catheter (24 cm) (check each manufacturer's recommendations)
  - Right side is anatomically easier to cannulate for jugular & subclavian
  - As a rule, the left side needs the longer catheter (Left-Long)

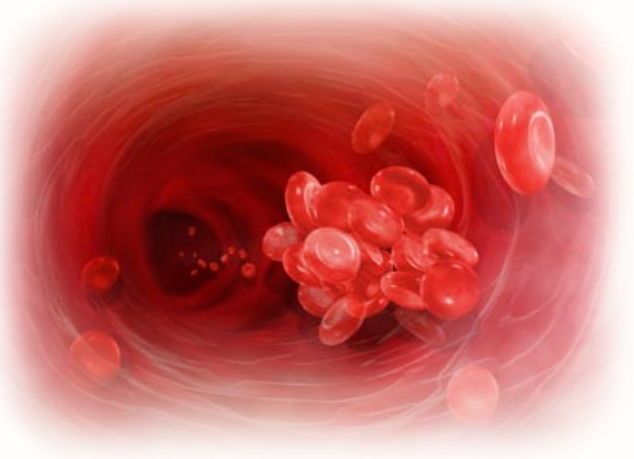
- The patient's disease processes and fluid status. (If the patient has hypercoagulopathies and/or is dehydrated, it will be more difficult to maintain patency and proper flow)

Notes:

[11] Canaud, et al.: Vascular access for extracorporeal renal replacement therapies in ICU. In: Ronco C, Bellomo R, LaGreca G, (eds): Blood Purification in Intensive Care. Contrib Nephrol. Basel, Karger, vol 132, pp 266-282.
[12] Kelber, et al.: Factors affecting delivery of high-efficiency dialysis using temporary vascular access. Am J Kidney Dis 1993; 22:24-9.
[13] McGee WT, Ackerman BL, Rouben LR, Prasad VP, Bandi V, Mallory DL: Accurate placement of central venous catheters: A prospective, randomized, multicenter trial. Crit Care Med 1993;21:1118-1123.

ANTICOAGULATION

Anticoagulants are used to prevent the blood from clotting within the extracorporeal circuit during the CRRT procedure. In many critically ill patients undergoing CRRT, anticoagulation is typically achieved through the use of low-dose heparin administered into the blood, before the hemofilter. The remaining patients may have underlying conditions, which put them at high risk of bleeding, and therefore heparin anticoagulation is not used.



All types of anticoagulation have risks. It is a constant challenge to find a balance between the risk of filter clotting and the risk of patient bleeding.

The formation of clots in the blood is primarily the result of platelet activation and subsequent obstruction of coagulation cascade. Therefore the majority of anticoagulation therapies are designed to interfere with the coagulation pathway. Both the patient and the circuit should be monitored to determine the effect of anticoagulation delivered, keeping in mind that preventing patient bleeding takes priority over preventing filter clotting.

CRRT uses various anticoagulants, the most common of them are heparin and citrate.

⚠ WARNING: The use of citrate with CRRT is not FDA approved within the US.

Notes:

HEPARIN

Heparin is the most frequently used anticoagulant. It is commonly used during the priming of the hemofilters and is infused into the CRRT circuit after the blood pump and before the filter. The effects of heparin are systemic and both the patient and the CRRT circuit are anticoagulated. All types of heparin carry the risk of heparin-induced thrombocytopenia (HIT) and platelet counts must be monitored. If HIT is suspected, heparin must be discontinued immediately.

HEPARIN DELIVERY

- Typical low-dose pre-filter heparin
  - Approximately 5-10 units/kg/hr
  - Delivered into the CRRT circuit post-pump, pre-filter
  - Mildly elevates the activated partial thromboplastin time (aPTT)
- Typical medium-dose pre-filter heparin
  - Approximately 8-10 units/kg/hr
  - Delivered into the CRRT circuit post-pump, pre-filter
  - Mildly elevates the aPTT
- Therapeutic systemic heparin
  - Adjusted to achieve required aPTT as prescribed by physician
  - Administered via a volumetric infusion pump
  - Most commonly used for patients with systemic anticoagulation requirements, other than CRRT needs
  - Rarely used to prolong filter life
  - If possible, infuse heparin pre-filter—however, remember to continue the infusion if CRRT is stopped since its main indication is another need—i.e. deep vein thrombosis (DVT), Atrial fibrillation, etc.
- Regional heparin
  - Rarely used
  - Heparin is infused pre-filter and protamine infused post-filter to reverse effects of heparin
  - Goal is to anticoagulate the circuit without anticoagulating the patient

Notes:

- Low-molecular weight heparin
  - Less likely to cause HIT
  - Contra-indicated for patients who have developed HIT
  - Difficult to monitor and difficult to reverse
  - More expensive

⚠ WARNING: Precaution should be taken to monitor patient closely for excessive anticoagulation due to heparin

OTHER ANTICOAGULANTS[14, 15]

Other, less frequently used anticoagulants mentioned in the literature, include:

- Prostacyclin
- Nafamostat mesilate
- Hirudin
- Agatroban

NO ANTICOAGULATION

In some circumstances, risks to the patient complicates the use of any anticoagulant. These circumstances may include, but are not limited to:

- Active bleeding
- Increased aPTT
- Increased international normalized ratio (INR)
- Liver failure
- Low platelet count

Notes:

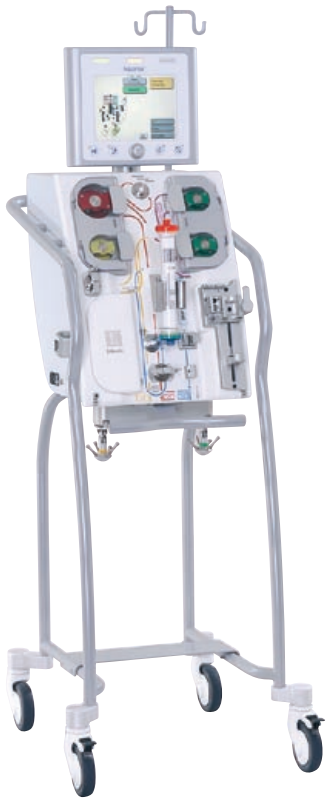
[14] Davenport A: Anticoagulation in continuous renal replacement therapy. In: Ronco C, Bellomo R, LaGreca G (eds): Blood Purification in Intensive Care. Contrib Nephrol, Basel, Karger, 2001, vol 132, pp 283-303.

[15] Matsuo T, Kario K, Kodama K, Okamoto S: Clinical application of the synthetic thrombin inhibitor, Agatroban (MD-805) Semin Thromb Hemost, 1992;18:155-60

THE CRRT SYSTEM

Delivering CRRT requires an integrated system consisting of:

- Machine
- Hemofilter
- Line sets
- Solutions
- Accessories



CRRT MACHINE

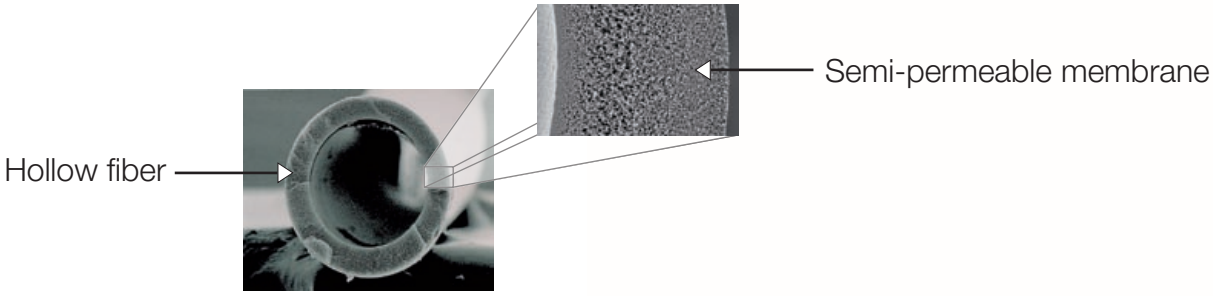
The **Aquarius** is an instrument designed to deliver CRRT. It consists of blood and fluid pumps, user-friendly interface, scales and integrated safeguards (see section Getting Started with **Aquarius** of the Operator's Manual).

Notes:

HEMOFILTER

The hemofilter (often referred to as an artificial kidney) is a requirement of any CRRT system. The hemofilter contains a semi-permeable membrane in a hollow-fiber design.

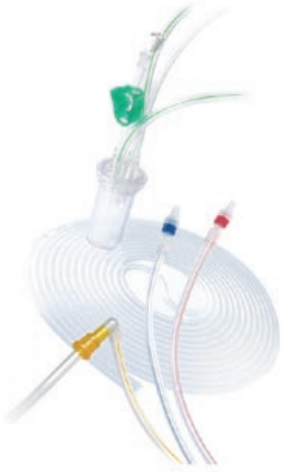
- Blood flows inside of the hollow fibers
- Dialysate flows on the outside of the fibers
- Solute and fluid removal will be determined by the type of membrane and the surface area (see Module 3 for available surfaces)
- Hemofilters are usually synthetic



Notes:

LINE SETS

The line set is used to transport blood and fluids through the hemofilter and the CRRT circuit (see Module 3 for detailed description)



ACCESSORIES

Other accessory products may be used in the CRRT settings. They include:

- Drainage bags
- Three-way or four-way adaptor (manifold)
- Stop cocks
- Syringes
- Anticoagulant
- Priming solution
- Dual-lumen catheters

Notes:

FLUID MANAGEMENT

The goals of fluid management in CRRT are typically to achieve two important functions:

- Solute removal
- Fluid removal

Substitution and dialysate solutions are used to facilitate the removal of solutes from the patient's blood using the principles of convection (substitution) and/or diffusion (dialysate). Fluids for this purpose are simultaneously removed by the CRRT machine as delivered, and do not affect the patient's circulating volumes. Substitution solutions can be infused before the filter (pre-dilution) and after the filter (post-dilution).

To manage the patient's circulating volume, it is often necessary to remove fluid from the patient. This is Patient Fluid Removal. When calculating Patient Fluid Removal, it is necessary to consider the non-CRRT intakes and outputs of the patient. Fluids removed from the patient (substitution solutions and dialysate solutions) are collected, as filtrate, in the drainage bag.

Notes:

SUBSTITUTION SOLUTION

- Primary function: removal of solutes via convection (small, medium, large)
- Does not affect the patient's intravascular volume
- Must be physiological from an electrolyte standpoint and sterile
- They must be labeled for IV use
- Can be pharmacy-prepared
- Infused into the patient's blood pre-dilution, post-dilution or both
- Formulation, volume, and infusion method (pre- or post-dilution) are prescribed by a physician
- Substitution solution allows convective clearance
- The volume of substitution solutions infused is automatically removed by the machine
- Sometimes referred to as 'replacement fluid'

DIALYSATE SOLUTION

- Primary function: removal of solutes via diffusion (small)
- Does not affect the patient's intravascular volume
- Must be physiological and should be sterile
- Commercially available (see Module 3 for codes and formulations available)
- Prescribed by a physician
- Dialysate solution allows diffusive clearance
- Infused into the external dialysate port of the hemofilter counter-current to the blood flow
- The volume of dialysate solutions infused is automatically removed by the machine
- Buffers include lactate and bicarbonate (see Module 3 for codes and formulations available)
- Formulation is usually calcium-free when used with citrate anticoagulation

⚠ WARNING: The use of citrate with CRRT is not FDA approved within the US.

Notes:

PATIENT FLUID REMOVAL

- Fluid removed directly from the patient's intravascular compartment
- Hourly rate of removal is prescribed by the physician
- Non-CRRT intakes and outputs must be calculated and considered
- Fluid removal occurs by ultrafiltration
- Fluid removed contains components of plasma water

FILTRATE

- Filtrate is a combination of the substitution fluid, dialysate fluid and fluid removed from the patient
- Components of filtrate include water, electrolytes, waste products, immune mediators, drugs, vitamins and amino acids
- Filtrate is removed from the filtrate port of the hemofilter into a drainage bag
- Filtrate is a biological waste substance, hospital protocols should be followed

TEAM

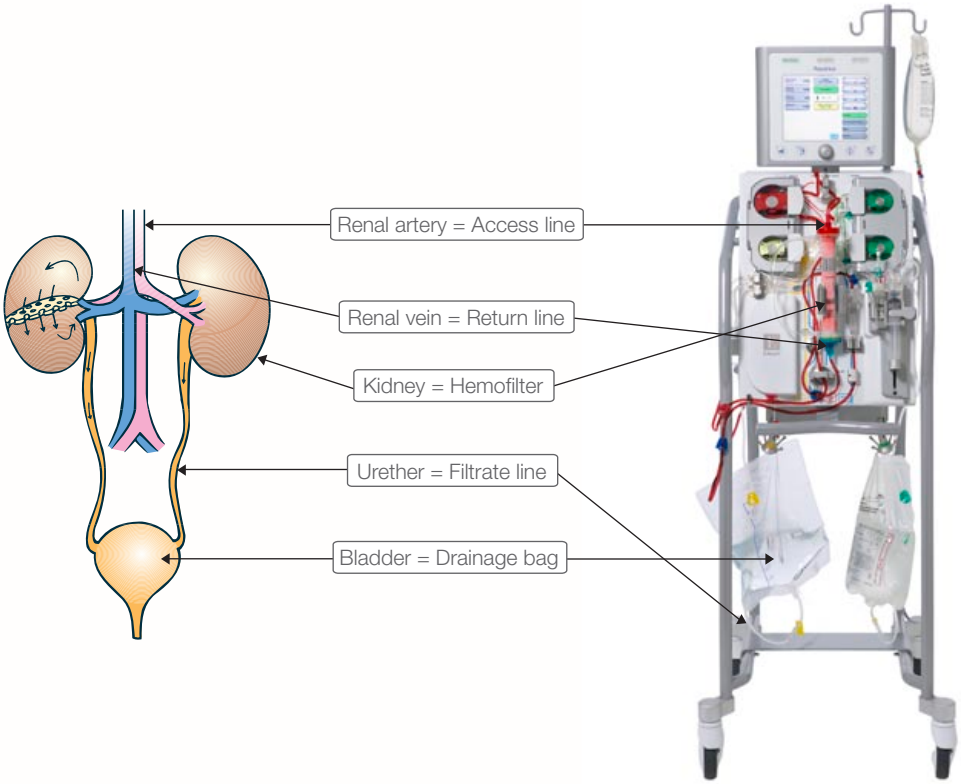
The addition of CRRT to the critically ill patient's care requires the expertise, cooperation and focus of a cross-functional team, which may include:

- Intensivist
- Nephrologist
- Critical care nurse
- Nephrology nurse
- Pharmacist
- Dietician

Notes:

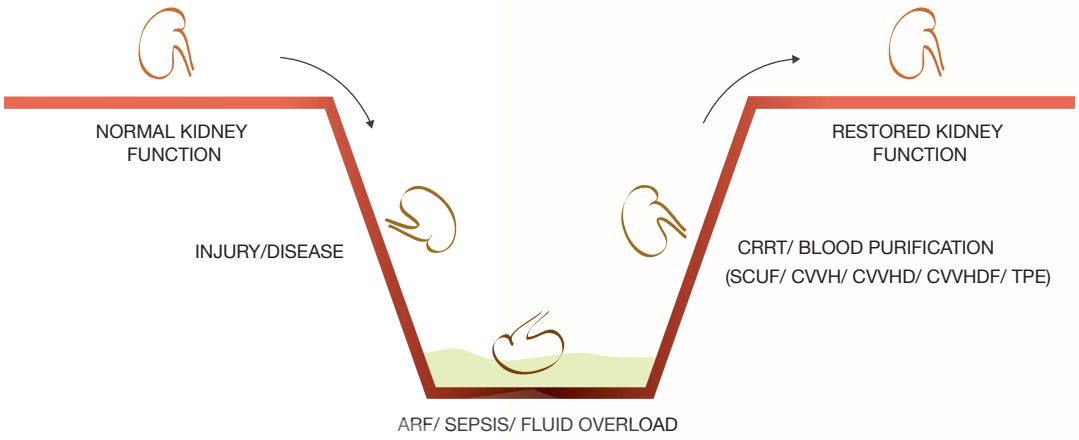
SUMMARY

In summary, the main goals of CRRT are removal of waste products, restoration of acid/base balance, and correction of fluid and electrolyte abnormalities, while maintaining hemodynamic stability. The goal of any continuous renal replacement therapy is to replace, as best as possible, the lost function of the native kidney. While CRRT provides a good option for a patient with ARF, nothing will replace the complete function of a healthy kidney. The illustration below demonstrates how the CRRT system attempts to mimic the function of the native kidney.



Notes:

Some studies[16,17] suggest that recovery from acute renal failure is better when patients are treated with CRRT. When normal kidney function can be restored, freedom from the need for chronic dialysis can provide the patient with a better quality of life. The following illustration depicts kidney function from a healthy kidney, to failure, to treatment, to recovery.



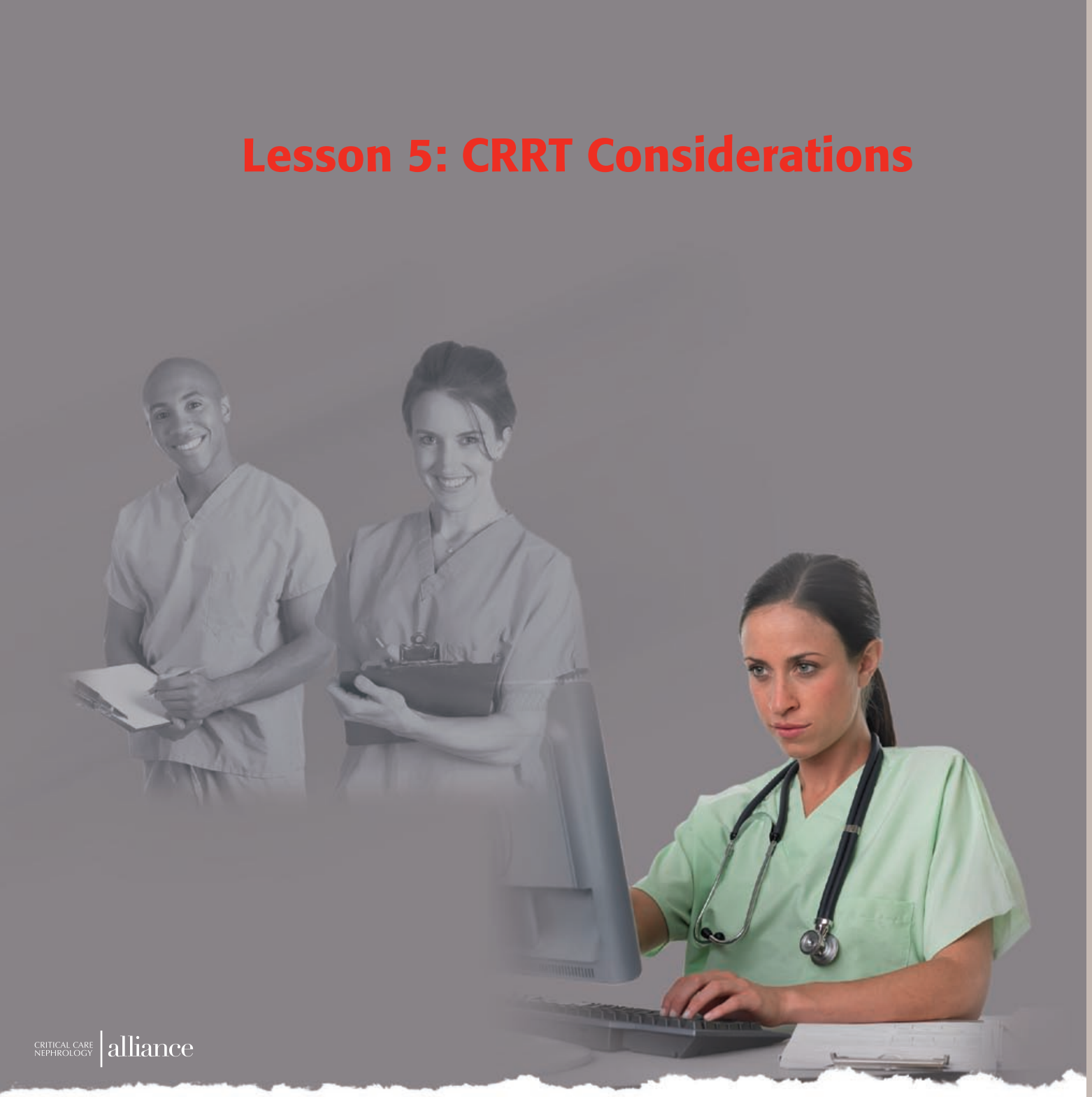
Notes:

[16] Mehta RL, McDonald B, Gabbai FB, et al.: A Randomized clinical Trial of Continuous versus Intermittent dialysis for Acute Renal Failure. Kidney Int 2001; 6: 1154-63.

[17] Michael J. Jacka et al.: Continuous renal replacement therapy improves renal recovery from acute renal failure. Can J Anesth 2005; 52:3 pp 327- 332.

(page intentionally blank)

Lesson 5: CRRT Considerations



CRITICAL CARE NEPHROLOGY | alliance

Edwards

(page intentionally blank)

ADVANTAGES

- Compared to standard hemodialysis applied for a short period of time, CRRT provides improved hemodynamic stability (slow, gentle and continuous)
- Provides continuous fluid and electrolyte management (avoidance of rapid fluid and electrolyte shifts)
- May facilitate removal of cytokines and mediators[18]
- Adapted to the needs of the critically ill

LIMITATIONS

- Requires a large-bore central vascular access
- Typically requires continuous anticoagulation
- Requires immobilization of the patient for prolonged periods

Notes:

[18] Bellomo, et al.: Extracorporeal blood purification therapy for sepsis and systemic inflammation: Its biological rationale. In: Ronco C, Bellomo R, La Greca G (eds): Blood Purification in Intensive Care. Contrib Nephrol, Basel, Karger, 2001, vol 132, pp 367-374.

SPECIAL CONSIDERATIONS

CRRT is used to treat critically ill patients, typically suffering from acute renal failure accompanied by hemodynamic instability. While CRRT offers some advantages, certain parameters may require special monitoring.

DRUG MANAGEMENT

Drug removal in CRRT techniques is dependent upon the molecular weight of the drug, the sieving coefficient and the degree of protein binding. Drugs with significant protein binding are removed minimally. Additionally, some drugs may be removed by adsorption to the membrane. Most of the commonly used drugs require adjustments in dose to reflect the continuous removal during CRRT[19].

ACID/BASE AND ELECTROLYTE BALANCES

During CRRT, acid/base and electrolyte balances are continually modified, and should be watched closely.

BLEEDING

Patients receiving continuous anticoagulation may be at risk of bleeding. The patient should be monitored for bleeding. Patient's clotting parameters and access site should be closely monitored.

Notes:

[19] Mehta RL: Supportive Therapies: Intermittent Hemodialysis, Continuous Renal Replacement Therapies, and Peritoneal Dialysis. Atlas of Diseases of the Kidney (editor Schrier RW) Chapter 19, February 1999.

HYPOTHERMIA[20]

CRRT patients are prone to hypothermia due to the significant volume of blood that is circulated outside of the body, and the significant volumes of the substitution and dialysate fluid used. During CRRT significant thermal energy is lost. There is little published on thermal energy exchange during CRRT, but some potential effects of cooling could be:

- May improve cardiovascular stability
- May affect nutritional requirements
- May affect immune function
- May increase risk of circuit clotting

Warming both dialysate and substitution fluids to 37° C (98.6° F) still leads to thermal energy losses, and these losses will be increased when larger volumes of substitution and dialysate are used[12].

Notes:

[20] Davenport A: Dialysate and substitution fluids for patients treated by continuous forms of renal replacement therapy. In: Ronco C, Bellomo R, La Greca G (eds): Blood Purification in Intensive Care, Contrib Nephrol, Basel, Karger, 2001, vol 132, pp 313-322.

Edwards Lifesciences