Acute and Chronic Renal Failure

Last Lecture 10 (13/4/2015)

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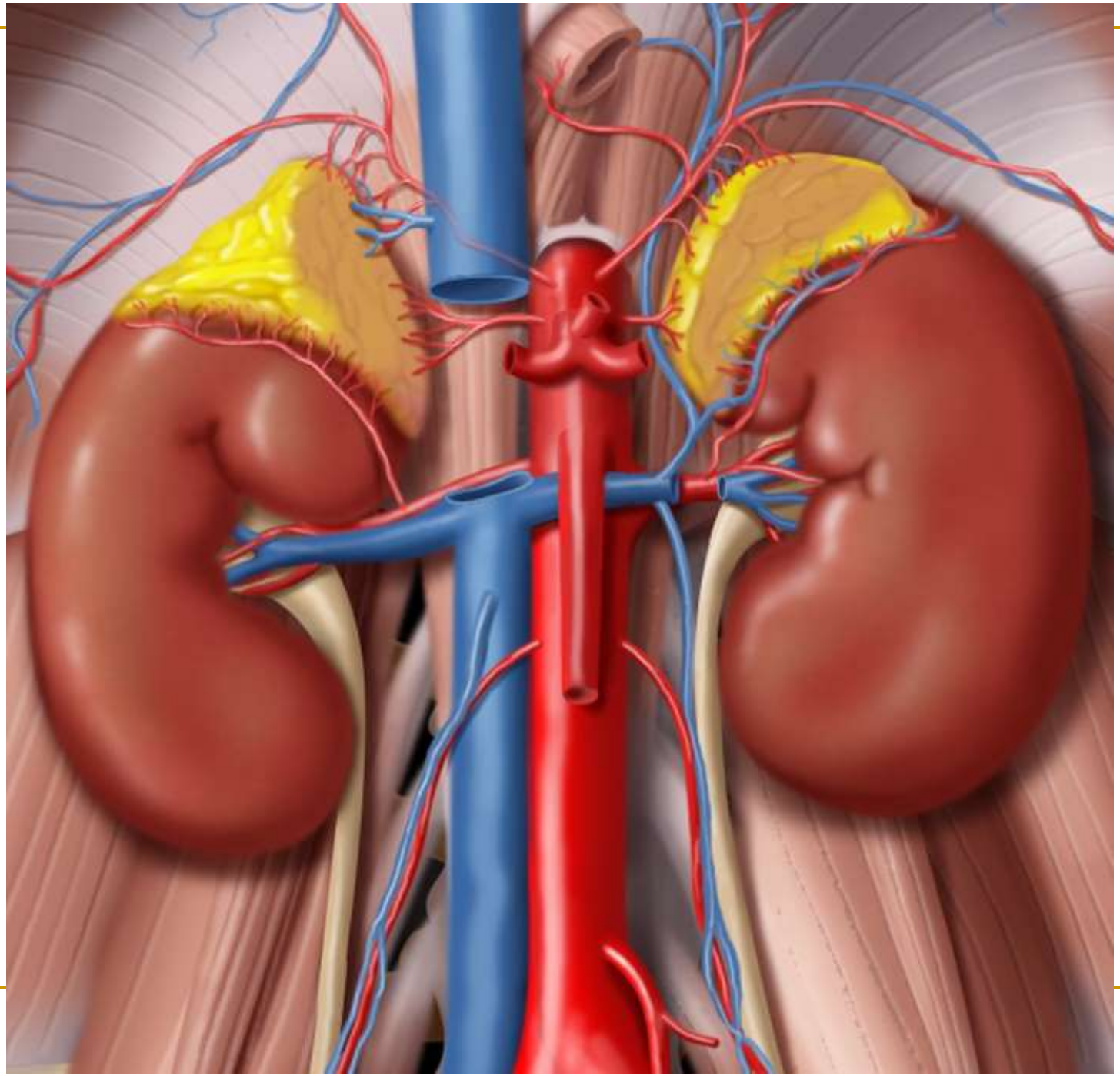

Renal failure :

Is of two types:

- **Acute RF (Acute Kidney Injury AKI) : from days → weeks.**
- **Chronic RF(CKD): months → years.**

*** Cause of AKI:**

1. Prerenal 2. intrarenal 3. postrenal

- **90% of causes are of the first two types (pre-and-intrarenal).**

***Cause of chronic Kidney Disease are:**

1. Uncontrolled hypertension 2. Uncontrolled diabetes

3. Infections

Acute Kidney Injury AKI

- **Epidemiology of AKI:**
- 0.1% population **good prognosis (85% recovery)**
- 3-7%hospitalized
- 25-30% ICU **poor prognosis (**mortality can reach 45-75%**)**

- *Pre-renal* (causes reside in the decrease in RBF):
-
  - Hypovolemeia: Fluid loss or blood loss →Shock: (excessive diuretics use, vomiting diarrhea, bleeding)
  - hepatorenal syndrome in which renal perfusion is compromised in liver failure
  - vascular problems, such as atheroembolic disease and renal vein thrombosis

- *Intrarenal* (damage to the kidney itself):

- Prerenal can be converted to intra-renal if not treated properly. The most common cause is acute tubular necrosis ATN. Less common is pyelonephritis and glomerulonephritis. In ATN: causes can be prolonged ischemia, heavy metals, or nephrotoxic drugs etc. Usually the tubular injury in ATN is reversible.
- Toxins or medications (e.g. NSAIDs, aminoglycoside antibiotics, iodinated contrast, lithium, etc.
- rhabdomyolysis (breakdown of muscle tissue) - the resultant release of myoglobin in the blood affects the kidney; it can be caused by injury (especially crush injury and extensive blunt trauma), etc.
- hemolysis - the hemoglobin damages the tubules; acute glomerulonephritis

- *Post-renal* (obstructive causes in the urinary tract) due to:
  - medication interfering with normal bladder emptying.
  - benign prostatic hypertrophy or prostate cancer.
  - kidney stones.
  - due to abdominal malignancy (e.g. ovarian cancer, colorectal cancer).
  - obstructed urinary catheter.

Staging Of AKI

- Risk: GFR decrease >25%, serum creatinine increased 1.5 times or urine production of < 0.5 ml/kg/h for 6 hours

- Injury: GFR decrease > 50%, doubling of creatinine or urine production < 0.5 ml/kg/h for 12 hours

- Failure: GFR decrease > 75%, tripling of creatinine (> 4 mg/dl) OR urine output below 0.3 ml/kg/h for 24 hours or anuria for 12 hours.
- Loss: persistent AKI or complete loss of kidney function for more than 4 weeks
- End stage renal disease: need for renal replacement therapy (RRT) for more than 3 months

Classic laboratory findings in AKI

Type	U_{Osm}	U_{Na}	Fe_{Na}	BUN/Cr
Prerenal	>500	<10	<1%	>20
Intrinsic	<350	>20	>2%	<15
Postrenal	<350	>40	>4%	>15

BUN:Cr Ratio as a tool

Location	BUN:Cr	Urea:Cr	Mechanism
Prerenal	>20:1	>100:1	BUN reabsorption is increased. BUN is disproportionately elevated relative to creatinine in serum. Dehydration is suspected.
Intrarenal	<10:1	<40:1	Renal damage causes reduced reabsorption of BUN, therefore lowering the BUN:Cr ratio.
Normal or Postrenal	10-20:1	40-100:1	Normal range. Can also be postrenal disease. BUN reabsorption is within normal limits.

MAJOR CONSEQUENCES OF AKI.

(Problems we might face in AKI):

1. Daily increase in creatinine and urea.

Plasma Urea : In complete renal shutdown

Urea: it rises by about 5 mmol/L per day.

Creatinine rises by 1 mg/dl daily.

2- Hyperkalemia…might need dialysis

3- M. Acidosis

4- Extracellular volume expansion → Malignant hypertension, pulmonary edema (can be fatal)

Prevention Of Acute Renal Failure

Why should we prevent ARF ?

- The kidneys are susceptible to the adverse effects of medications because the kidneys are repeatedly exposed to substances in the blood
- The kidneys receive a large blood flow (23% of the cardiac output at rest ; the entire blood volume circulates through the kidneys about 14 times/minute)
- The kidney is the major excretory organ for many toxic substances & during the normal urine concentration process, these substances increase in concentration & can be toxic to the kidneys

How to prevent ARF ?

- In patients taking nephrotoxic medications (gentamicin, vancomycin), renal function should be monitored closely
- Serum BUN & creatinine levels should be obtained for 24 hours after initiation of these medications & at least twice a week while the patient is receiving them
- Closely monitor dosage & Duration of use
- Provide adequate hydration to patients at risk for dehydration:
- Pre- intra- post- operative patients
- Patients with neoplastic disorders or those receiving chemotherapy
- Treat hypotension
- Continually assess renal function (urine output, laboratory values) when appropriate
- Prevent & treat infections (infections can produce progressive renal damage)
- Give meticulous care to patients with indwelling catheters to prevent infections of urinary tract. Remove catheters as soon as possible

Chronic Renal Failure: Chronic kidney disease (CKD)

Introduction-

- Chronic kidney disease (CKD), is a progressive loss in renal function over a period of months or years.
- Chronic kidney disease is diagnosed as a result of screening of people known to be at risk of kidney problems, such as those with **high blood pressure or diabetes .**
- It is differentiated from acute kidney disease in that the reduction in kidney function must be present for over **3 months**.
- Chronic kidney disease is identified by a blood test for **creatinine**.
- Higher levels of **creatinine** indicate a lower GFR and as a result a decreased capability of the kidneys to excrete waste products.

Pathophysiology

- In CKD, reduced clearance of certain solutes principally excreted by the kidney results in their retention in the body fluids .

- CKD leads to progressive decline in renal function.
- Reduction in renal mass leads to **hypertrophy** of the remaining nephrons with **hyperfiltration**, and the GFR in these nephrons is transiently increased, placing a burden on remaining nephrons.
- leading to progressive **glomerular sclerosis and interstitial fibrosis**

- The **hyperfiltration and hypertrophy** of residual nephrons, although beneficial it is major cause of progressive renal dysfunction (this is an example of positive feed back…destruction breeds more destruction).

- The increased glomerular capillary pressure may damage the capillaries, leading to **glumeriolosclerosis**

Etiology Of CRF

Causes of chronic kidney disease (CKD) include the following:

- Diabetic kidney disease.
- Hypertension.
- Vascular disease (Angina & MI).
- Glomerular disease .
- Tubulointerstitial disease (nephritis affecting the interstitium of the kidneys)
- Urinary tract obstruction or dysfunction
- Recurrent kidney stone

Pathophysiology of diabetic nephropathy

- When the level of **blood glucose rises** beyond the kidney's capacity to reabsorb glucose from the renal ultrafiltrate
- glucose remains diluted in the fluid, raising its **osmotic pressure** and causing more water to be carried out, thus, increasing the excreted urine volume.
- The increased volume dilutes the sodium chloride in the urine, signalling the release of more **renin** causing **vasoconstriction >>** passing less blood through the kidneys. Because the kidney is **nurtured** exclusively by the blood it filters, the vasoconstriction also reduces the nutrients supplied to it, causing **infarct** of its tissues and reduction of renal function which results in
- Glumerular **sclerosis**.

MAJOR CONSEQUENCES OF CKD

- **Metabolic acidosis**
- **Salt and water retention**
- **Anemia**
- **Uremia**
- **Endocrine disorder**
- **Disorder of mineral metabolism**

Chronic Failure:

With 4 phases:

Described earlier as an example of using GFR as a tool to stage CRF (Lecture 1 or 2):

1st phase: **Decrease renal reserve:**
in which 50% of GFR is only there.
Homeostasis is perfectly maintained
Urea and creatinine levels are within normal range.

2nd phase: **Renal insufficiency:**
20-50 % of GFR is maintained only.
The earliest sings is isosthenuria or polyuria with isotonic urine. Azotemia, anemia, and hypertension appear too.

3rd phase: **Chronic RF:**
20-5% of GFR.
All signs and symptoms of uremia
Pt may enter a viscous circle, less functional nephrons → more pressure on already working so on and so forth.

4th phase: **End-stage Renal Failure**
Can't survive without dialysis or kidney transplantation

Another Classification for CKD

- **Stage 1** Slightly diminished function; kidney damage with normal or relatively high GFR (≥90 ml/min/1.73 m^2): Kidney damage is defined as pathological abnormalities or markers of damage, including abnormalities in blood or urine test or imaging studies.
- **Stage 2** Mild reduction in GFR (60–89 ml/min/1.73 m^2)
- **Stage 3** Moderate reduction in GFR (30–59 ml/min/1.73 m^2)
- **Stage 4** Severe reduction in GFR (15–29 ml/min/1.73 m^2) Preparation for renal replacement therapy.
- **Stage 5** Established kidney failure (GFR <15 ml/min/1.73 m^2) permanent renal replacement therapy, or end-stage renal disease.

Dialysis

- **Dialysis is primarily used to provide an artificial replacement for lost kidney function. It aims to restore the composition of the body's fluid environment toward normal**
- 1) **Hemodialysis**: In this type the patient's blood is pumped through the blood compartment of a dialyzer, exposing it to a semipermeable membrane. The cleansed blood is then returned via the circuit back to the body; **all in all it is a complicated procedure done for(4-6) hours, 3 times per week and needs an A-V shunt**

Dialysis

- 2) **Peritoneal dialysis: In this procedure a sterile solution containing minerals (even potassium at LOW concentrations) and glucose is run through a tube into the peritoneal cavity, the abdominal body cavity around the intestine, where the peritoneal membrane acts as a semipermeable membrane. The dialysate is left there for a period of time to absorb waste products, and then it is drained out through the tube and discarded…*this procedure needs a long time (may reach 24 hours).***

Hemodialysis

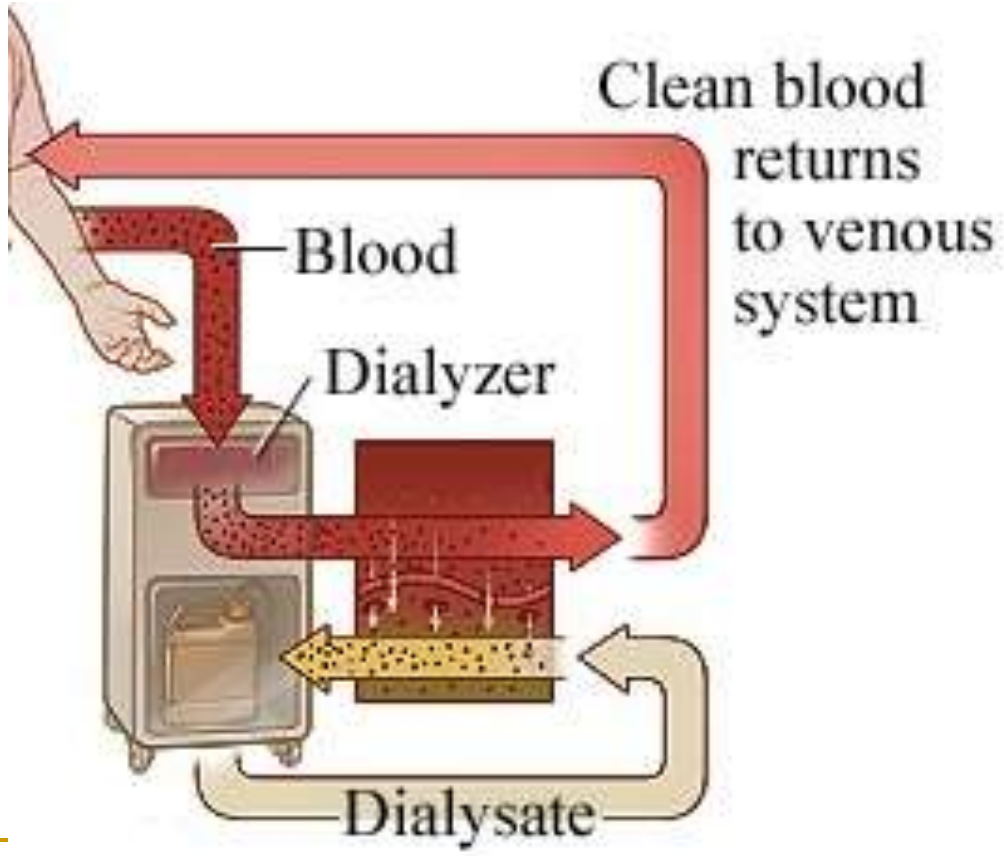

Table 31-7

Comparison of Dialyzing Fluid with Normal and Uremic Plasma			
Constituent	Normal Plasma	Dialyzing Fluid	Uremic Plasma
Electrolytes (mEq/l)			
Na^+	142	133	142
K^+	5	1	7
Ca^{++}	3	3	2
Mg^{++}	1.5	1.5	1.5
Cl^-	107	105	107
HCO_3^-	24	36	14
Lactate			
HPO4-			
Urate			
Sulfate			
Nonelectrolytes			
Glucose	100	125	100
Urea	26	0	200
Creatinine	1	0	6

Good Luck