Pathophysiology of the kidney. Acute and chronic renal failure

Blagoi Marinov, MD, PhD
Pathophysiology Department
Medical University of Plovdiv

Kidney physiology

- Regulation of red blood cell production
- Regulation of blood pressure
- Elimination of metabolic toxins and excess water through urine
- Regulation of the blood's acid-base balance
- Regulation of mineral levels
Nephron
anatomy and physiology

![Nephron diagram]

Filtration
Reabsorption
Secretion

Functional renal syndromes

- **Hypertension** – реноваскуларна, паренхимна, ренопривна
- **Edema** – нефритни, нефрозни
- **Osteodystrophy**
- **Altered diuresis**
- **Urinary syndrome**
- **Loss of ability to concentrate/dilute urine**
- **Altered homeostasis**
- **Hyper- hypocoagulability**
- **Azotemia**
- **Lithogenesis**
Hypertension

**Chronic hypoperfusion**

- Renovascular hypertension
  - High Renin

**Nephrectomy**

- Renoprival hypertension
  - Low Renin

Edema

- Nephritic (decreased permeability)
  - Primary Na+ retention (primary hypervolemic)
    - ↓ Sympathetic tone
    - ↓RAAS
  - Secondary Na+ retention (membranogenous)

- Nephrotic (increased permeability)
  - Proteinuria
  - ↓ Oncotic pressure
  - ↑ RAAS
  - ↑ Sympathetic tone
Osteodystrophy

- GFR ↓↓
- P-retention
- ↓Ca²⁺
- Secondary PTH ↑
- Osteoclasts ↑
- Osteopenia
- Demineralization
- 1, 25 Vit D₃ ↓↓
- Metabolic acidosis (Retention)
- Osteodystrophy

Diuresis

- Increased
  - Polyuria > 2 L/24 h
- Normal
  - Normuria 0.5-2.0 L/24 h
- Decreased
  - Oliguria <0.5 L/24 h
- Absent
  - Anuria <0.15 L/24 h

- Tubular dysfunction
- Glomerular hypo- and afunction
- Hyperhydration (hypervolemia)

- Hypotonic
- Omotic normotonic and hypertonic
- Dehydration (hypovolemia)
Proteinuria and hematuria

- Increased permeability of glomerular basal membrane
- Overwhelmed (up to 1 g/24 h) or Suppressed tubular reabsorption
- Microhematuria (>3 Ers)
- Proteinuria (0.5 to 3.5 and >3.5 g/24 h)
- Cilindruria

Proteinuria

- Protein is not normally filtered at glomerulus and only trace amounts should be in urine
- Microalbuminuria-20-200 mcg/min (30-300mg/24hr)
- Proteinuria/albuminuria - >200 mcg/min (albumin is more specific for glomerular disease than protein)

Consider: Ingestion of high-protein meal and vigorous exercise -> increase protein in urine
Anemia

- Inhibitors ↑
- Fe-deficit
- Suppressed erythropoiesis
- ANEMIA
- Protoporphyrin hyposynthesis
- Microangiopathic hemolysis
- BONE MARROW

EPO ↓

Lithogenesis

- Hyper-normocalciemia
- Hypercalciuria
- ↓ solubilizers in the urine
- Overwhelmed metastability limit of the urine
- Spontaneous crystalization of the urine solution
- Lithogenesis

- Normocalciuria
- Hyper-oxaluria
- Hyper-urikosuria
- Hypocytraturia
Nosology of the kidney

- Glomerular
- Tubulointerstitial
- Toxic influences
- Neoplastic processes

The kidney is an “innocent bystander” in many systemic diseases

- Hypertension
- Hypotension
- Vasculitis
- Thrombotic diseases/DIC
- Systemic Lupus Erythematosus
- Sickle cell anemia
Tubulo-interstitial diseases:

- Cluster of abnormalities that, early on, affects the renal tubules and the interstitium
- Spares the glomeruli and the blood vessels

TIDs can be divided into the following categories:

- **Ischemic**: Acute renal failure, hypotension, blood loss, shock
- **Infections**: Acute and Chronic pyelonephritis, viruses, parasites
- **Toxins**: Drugs, analgesics, heavy metals (Pb)
- **Metabolic**: Urate, nephrocalcinosis, Oxalate
- **Neoplasms**: Multiple Myeloma
- **Immunologic reaction**: Transplant rejection
Urinary Tract Infections

- F:M ratio 8:1
  - Females 15-40 years of age
- Infecting organisms from patient’s own flora
- Bacteria reaches the kidney by:
  - Ascending route (more common)
  - Blood borne (more dangerous)

Urinary Tract infections:

- Most common organisms:
  - Gram negative bacilli (E. Coli is the most common)
  - Proteus, Klebsiella, Enterobacter, Mycobacteria (T.B)
Predisposing factors for UTI:

- Diabetes
- Pregnancy
- Obstruction (BPH, Tumors..)
- Reflux
- Immunosuppression
- Instrumentation (Catheters, surgery...)

Acute Pyelonephritis (Microscopic)

- Neutrophils in the interstitium
- Tubular damage (later)
- Microabscesses in the interstitium
- May lead to perinephric abscesses (Very painful)
Pathogenesis of tubulointerstitial lesions

- Bacterial colonisation (E. coli, Proteus, Clebsiela)
- Reflux
- Difficult urine outflow (urostasis)
- Inefficient defences in urinary ducts
- Contractile dysfunction of urinary ducts
- Suppresses macrophages
- Persistent bacterial inflammation
- Hyperosmolality
- Resilient (L-form) bacteria

Glomerulonephritis

**Definition:**

Renal disease characterized by inflammation of the glomeruli, or small blood vessels in the kidneys.

Glomerulonephrites are categorised into several different pathological patterns, which are broadly grouped into non-proliferative or proliferative types. Diagnosing the pattern of GN is important because the outcome and treatment differs in different types.
Membranoproliferative glomerulonephritis

Pathogenesis of glomerulonephritis

**Immunologic conflict**

- **Towards own Ag** (autoimmunity)
  - Similar to GBM bacterial Ag (immune)

- **Towards implanted foreign** (nonglomerular)
  - Ag bacterial, viral (immune)

- **Constructed in situ** (on site)
  - Circulating immune complexes
    - Forcefully "Deposited"
    - or
    - Actively captured
Nephrotoxicity of the complexes depends on:

- Size – small to medium;
- Ag-Ab avidity – high;
- Clearance – low;
- Electrical charge – polycationic;
- Valence - mono-, polyvalent;
- Ratio – excess of Ag

Immune (autoimmune) inflammation

- Ab mediated complement citotoxicity
- Ab mediated cellular citotoxicity
- Neutrophil and/or monocite attack
- Proliferation of cells with growth potential – monocites, fibroblasts, mesangial cells
Signs of glomerular damage are:

- Increased permeability of glomerular basal membrane
- Drop in overall glomerular filtration rate
- Disfunction of JGA (Juxtaglomerular apparatus)
- Glomerular-tubular disbalance

Acute glomerulonephritis

- Most causes are infectious
  - Follows a streptococcal infection (when taking history ask client about recent infections)
- Related to systemic diseases
  - Lupus
Signs and Symptoms

- **Hematuria**: dark brown or smoky urine
- **Oliguria**: urine output is < 400 ml/day
- **Edema**: starts in the eye lids and face then the lower and upper limbs then becomes generalized; may be migratory
- **Hypertension**: usually mild to moderate

Nephrotic Syndrome

- Condition of increased glomerular permeability that allows larger molecules to pass through the membrane into the urine and be removed from the blood
- Severe loss of protein into the urine
Clinical Manifestations Of Nephrotic Syndrome

- Severe proteinuria
- Hypoalbuminemia
- Hyperlipidemia
- Edema
- Hypertension
- Renal vein thrombosis may occur
- May progress to ESRD without tx

Chronic Glomerulonephritis

- A slow, progressive disease that can be caused by primary (Nephrotic & Nephritic Syndromes) or secondary disorders (SLE, Good pasture's)
- Typically develops asymptptomatically over many years
- Hypertension, proteinuria and hematuria exhibited with progression of disease
- Late stages display uremic symptoms of azotemia, nausea, vomiting, dyspnea and pruritis
- Leads to chronic renal failure (CRF)
Renal failure

Failure to excrete nitrogenous waste and electrolyte imbalance.

- Criteria for diagnosis (lab definition):
  - Cr increase of .5 mg / dl.
  - Increase in more than 50% over baseline Cr.
  - Decreased in calculated Cr Clearance by more than 50%.
  - Any decrease in renal function that requires dialysis.

Acute renal failure

- Acute renal failure - ARF, now increasingly called *acute kidney injury*, is a rapid loss of kidney function.
Acute renal failure

- Spasm of v. afferens
- Dilation of v. efferens
- Decreased kidney permeability
- Increased tubular pressure
- Tubular compression “glaucoma mechanism”
- Tubulorrhexis (interstitial urine spill)
- Plugs detrite, cylinders
- Cellular tubular edema

**Definition:**
Progressive tissue destruction with permanent loss of nephrons and renal function

Chronic renal failure

**Definition:**
Progressive tissue destruction with permanent loss of nephrons and renal function
Chronic renal failure

**Biology** – loss of working nephrons

**Progress** – increasing loss nephrons (%)

**Stages** – compensated, decompensated, uremic, comatous

**Clinica syndromes** – according to the main disease, complications, stage

---

Risk factors

- Age > 60 years
- Race or ethnic background
  - African-American
  - Hispanic
  - American Indian
  - Asian
- History of exposure to chemicals/toxins
  - Cigarette smoke
  - Heavy metals
- Family history of chronic kidney disease
### Chronic vs. Acute Renal Failure

<table>
<thead>
<tr>
<th><strong>Acute Renal Failure (ARF):</strong></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Abrupt onset</td>
<td></td>
</tr>
<tr>
<td>Potentially reversible</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Chronic Renal Failure (CRF):</strong></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Progresses over at least 3 months</td>
<td></td>
</tr>
<tr>
<td>Permanent- non-reversible damage to nephrons</td>
<td></td>
</tr>
</tbody>
</table>

### Causes of CRF

- Diabetic Nephropathy
- Hypertension
- Vascular Disease
- Polycystic Kidney Disease/Genetics
- Chronic Inflammation
- Obstruction
- Glomerular Disorders/ Glomerulonephritis
Pathophysiology of CRF

- Progressive destruction of nephrons leads to:
  - Decreased glomerular filtration, tubular reabsorption & renal hormone regulation
  - Remaining functional nephrons compensate
  - Functional and structural changes occur
  - Inflammatory response triggered
  - Healthy glomeruli so overburdened they become stiff, sclerotic and necrotic

Structural Changes of CRF

- Epithelial damage
- Glomerular and parietal basement membrane damage
- Vessel wall thickening
- Vessel lumen narrowing leading to stenosis of arteries and capillaries
- Sclerosis of membranes, glomeruli and tubules
- Reduced glomerular filtration rate
- Nephron destruction
Functional Changes of CRF

- The Kidneys are unable to:
  - Regulate fluids and electrolytes
  - Balance fluid volume and renin-angiotensin system
  - Control blood pressure
  - Eliminate nitrogen and other wastes
  - Synthesize erythropoietin
  - Regulate serum phosphate and calcium levels

Four Stages of CRF

- Reduced Renal Reserve (Silent): no symptoms evident- GFR up to 50ml/min

- Renal Insufficiency: ½ function of both kidneys lost- GFR 25-50 ml/min

- Renal Failure: GFR 5-25 ml/min

- End Stage Renal Disease: GFR less than 5 ml/min
Signs & Symptoms

Peritoneal dialysis
Hemodialysis

Kidney transplantation
Thank you