Pathophysiology of the kidney. Acute and chronic renal failure

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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

Functional renal syndromes

- Hypertension – реноваскулярна, 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

P-retention

GFR \downarrow \downarrow \rightarrow 1, 25 \text{ Vit D}_3 \downarrow \downarrow \rightarrow \text{Metabolic acidosis (Retention)} \rightarrow \text{Osteodystrophy}

↓ \text{Ca}^2+ \rightarrow \text{Secondary PTH} \uparrow \rightarrow \text{Osteoclasts} \rightarrow \text{Osteopenia} \rightarrow \text{Osteodystrophy} \rightarrow \text{Demineralization}

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

Hypotonic

Omotic normotonic and hypertonic

Glomerular hypo- and afunction

Dehydration (hypovolemia)

Hyperhydration (hypervolemia)
Proteinuria and hematuria

- Increased permeability of glomerular basal membrane
- Overwhelmed (up to 1 g/24 h) or Suppressed tubular reabsorption
- Proteinuria (0.5 to 3.5 and >3.5 g/24 h)
- Microhematuria (>3 Ers)
- 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/albminuria - >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
- EPO ↓
- Bone marrow
- Suppressed erythropoiesis
- Microangiopathic hemolysis
- Protoporphyrin hyposynthesis

Lithogenesis

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

Normocalciuria
- Hyper-oxaluria
- Hyper-uricosuria
- 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)
- Difficult urine outflow (urostatis)
- Contractile dysfunction of urinary ducts
- Inefficient defences in urinary ducts
- Reflux
- Suppressed macrophages
- Hyperosmolality

Tubulointerstitial invasion

- Persistent bacterial inflammation

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.
Pathogenesis of glomerulonephritis

**Immunologic conflict**

- **Towards own Ag (autoimmunity)**
  - Similar to GBM bacterial Ag (immune)
- **Towards implanted foreign (nonglomerular)**
  - Ag bacterial, viral (immune)

**Construct 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
- Plugs detrite, cylinders
- Cellular tubular edema
- Tubular compression “glaucoma mechanism”
- Tubulorrhesis (interstitial urine spill)

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

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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

- **Acute Renal Failure (ARF):**
  - Abrupt onset
  - Potentially reversible

- **Chronic Renal Failure (CRF):**
  - Progresses over at least 3 months
  - Permanent- non-reversible damage to nephrons

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