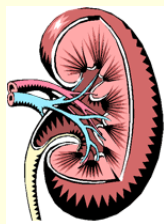


Pathophysiology of the kidney. Acute and chronic renal failure

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



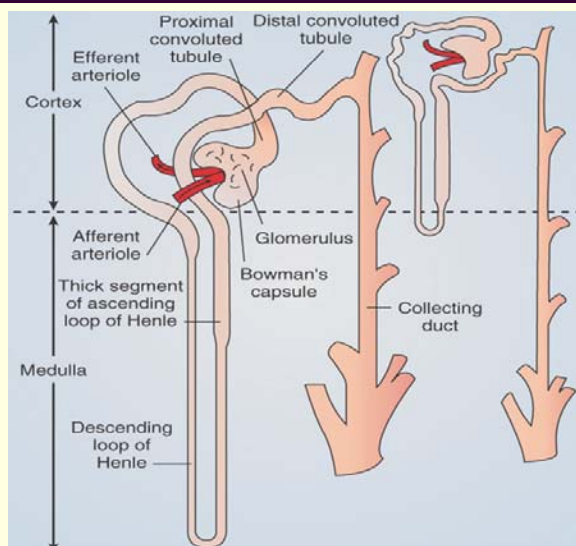
Regulation of the
blood's acid-base-
balance



Regulation of
mineral levels

Nephron

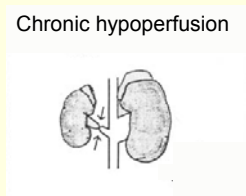
anatomy and physiology



Functional renal syndromes

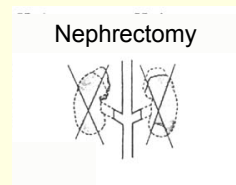
- **Hypertension** – реноваскуларна, паренхимна, ренопривна
- **Edema** – нефритни, нефрозни
- **Osteodystrophy**
- **Altered diuresis**
- **Urinary syndrome**
- **Loss of ability to concentrate/dilute urine**
- **Altered homeostasis**
- **Hyper- hypocoagulability**
- **Azotemia**
- **Lithogenesis**

Hypertension



Renovascular hypertension

↓
High Renin

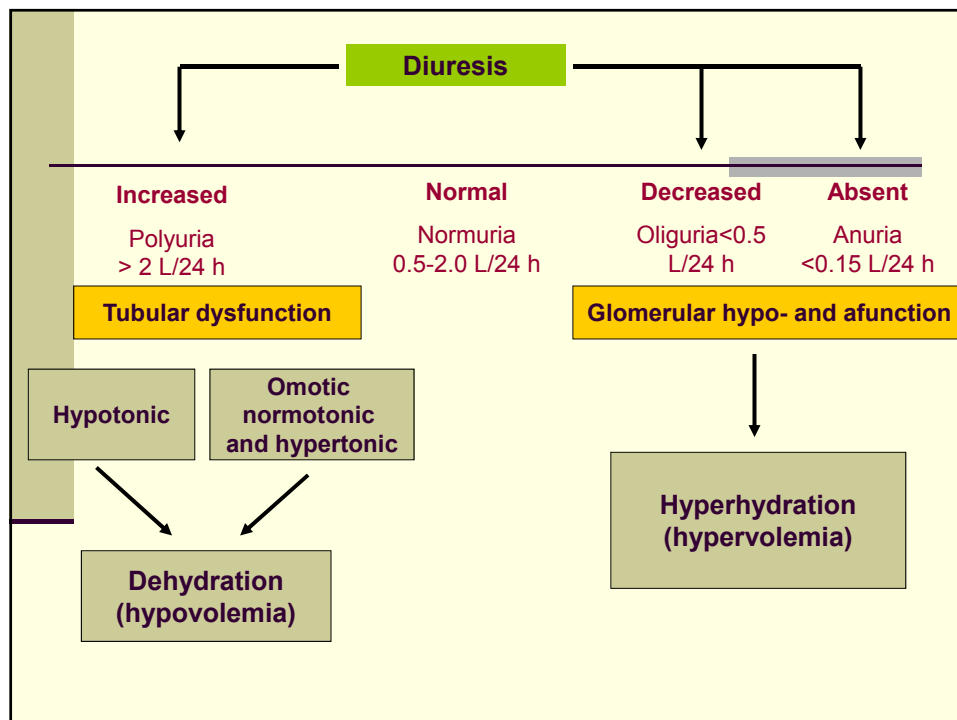
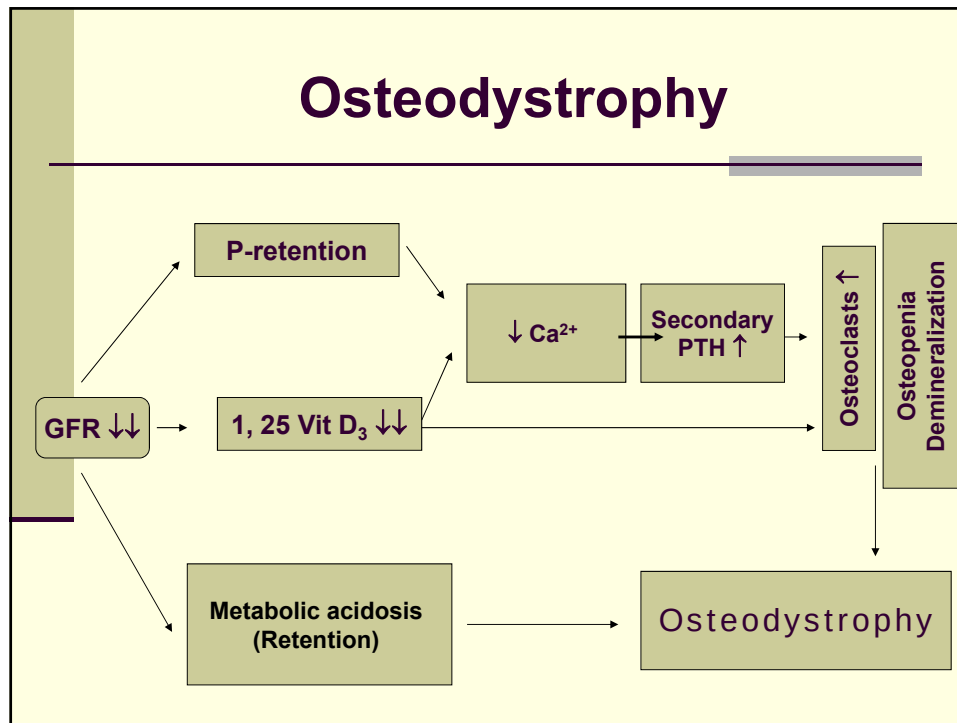


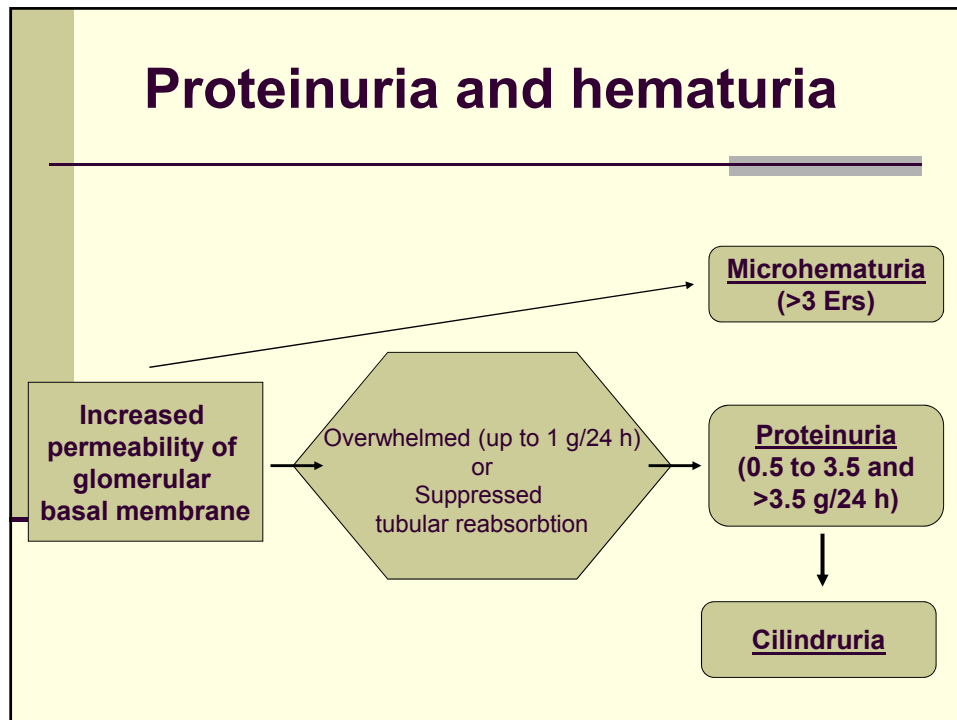
Renoprival hypertension

↓
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

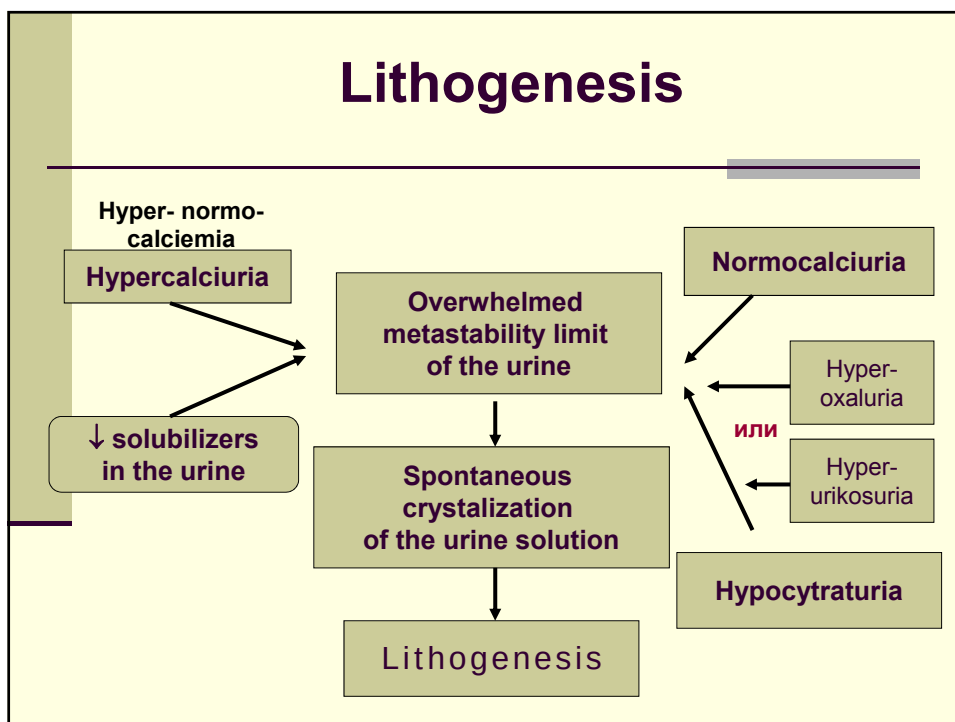
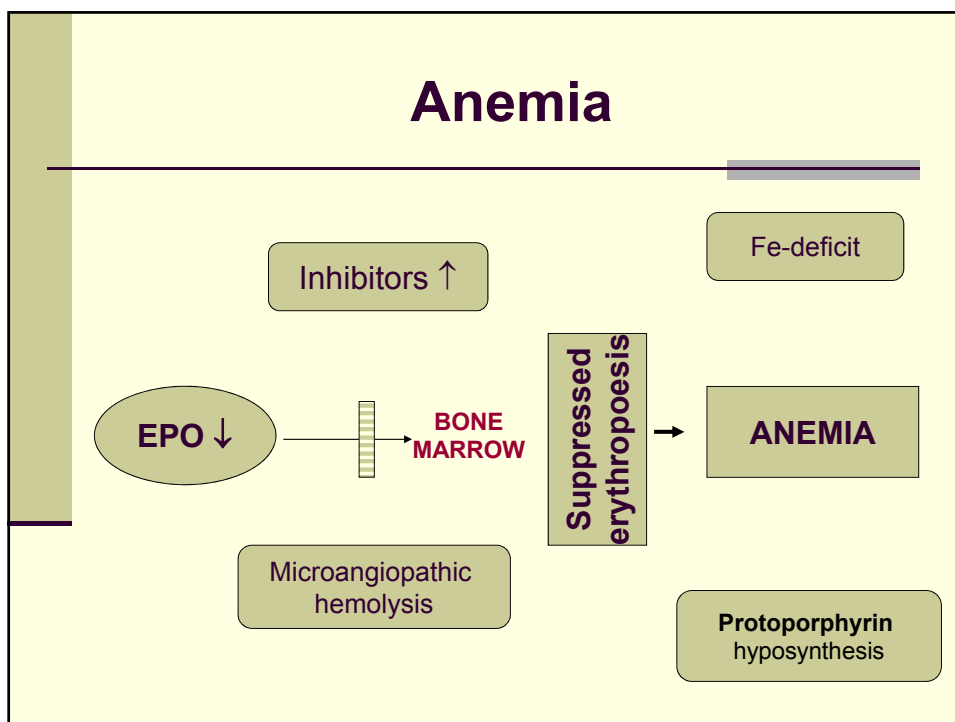




Proteinuria

- 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



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:

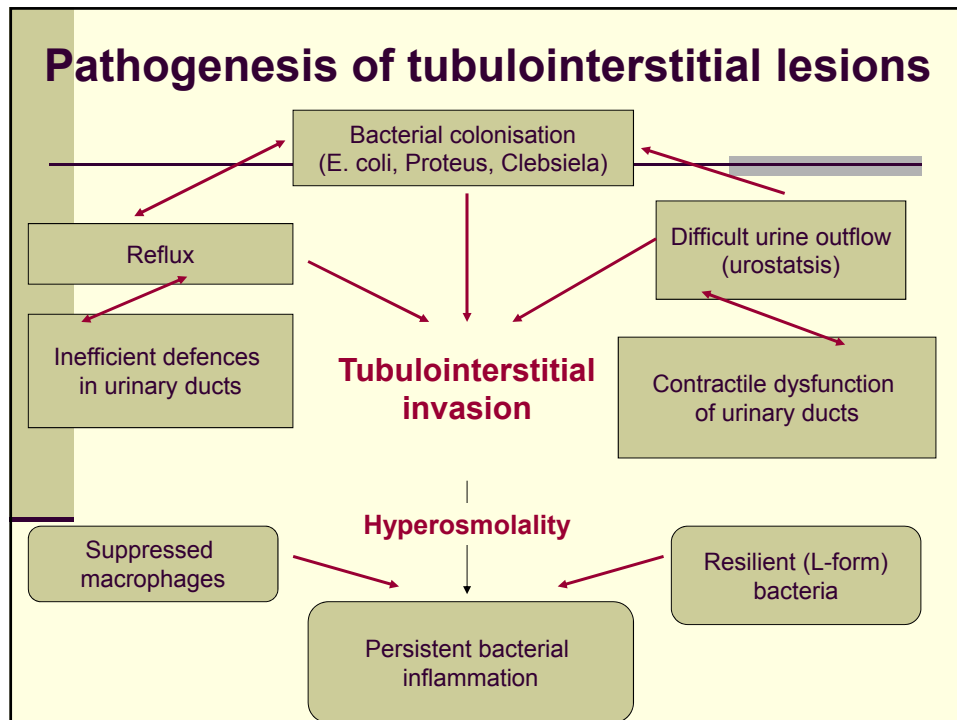
- Most common organisms:
 - Gram negative bacilli (E. Coli is the most common)
 - Proteus, Klebsiella, Enterobacter, Mycobacteria (T.B)

Predisposing factors for UTI:

- Diabetes
- Pregnant
- 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)

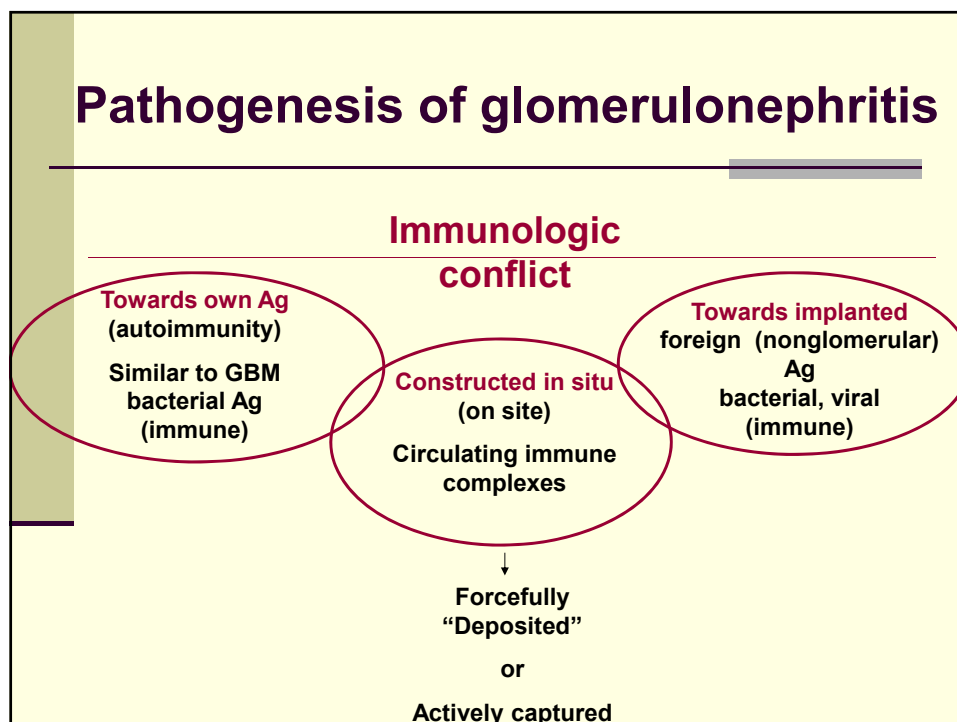
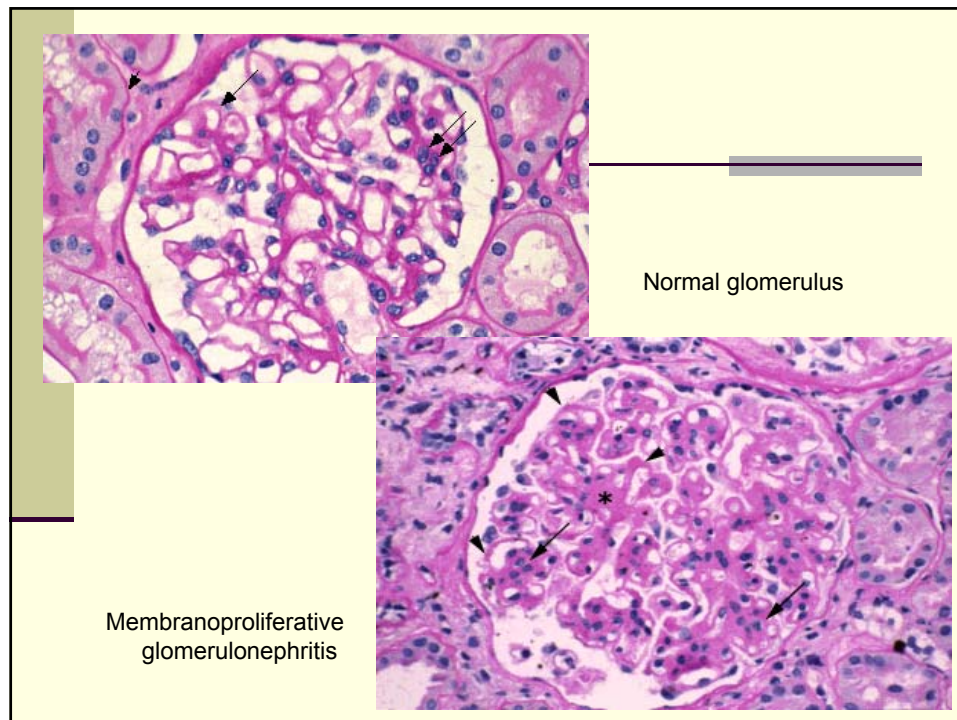


Glomerulonephritis

■ 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.



Nephrotoxicity of the complexes depends on:

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

Immune (autoimmune) inflammation

- Ab mediated complement cytotoxicity
- Ab mediated cellular cytotoxicity
- Neutrophil and/or monocyte attack
- Proliferation of cells with growth potential – monocytes, fibroblasts, mesangial cells

Signs of glomerular damage are :

- Increased permeability of glomerular basal membrane
- Drop in overall glomerular filtration rate
- Disfunction of JGA (Juxtaglomerular aparatus)
- 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 asymptotically 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)

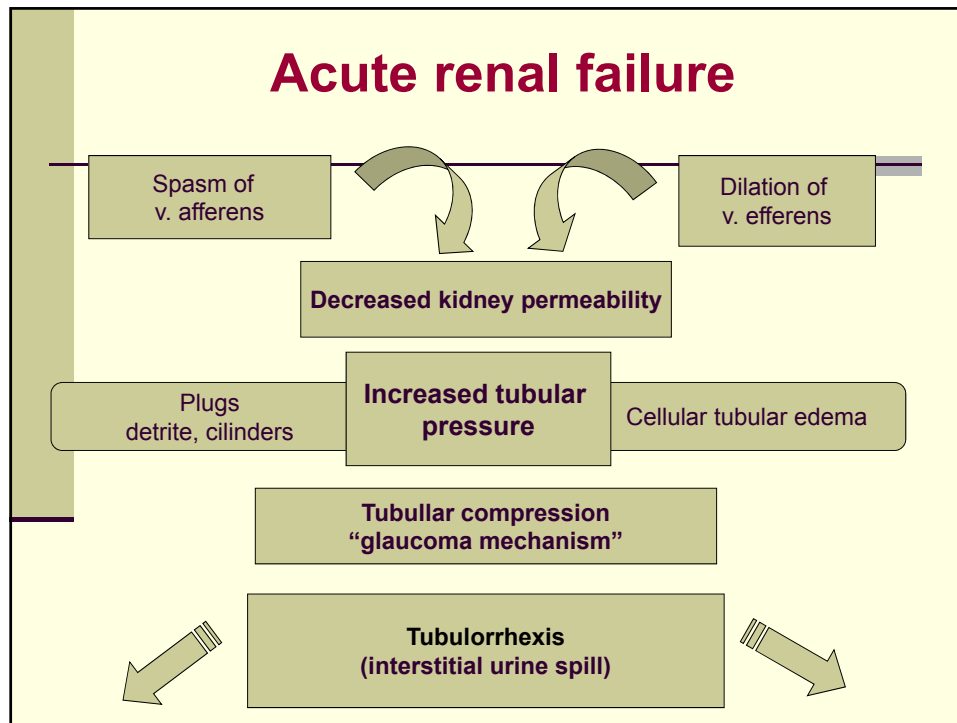
Renal failure

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.



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

Clinical 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

- **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

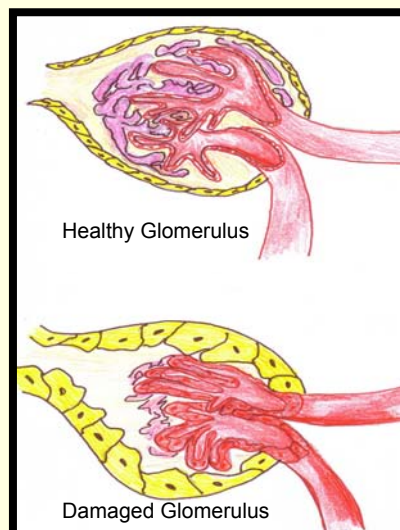
- Diabetic Nephropathy
- Hypertension
- Vascular Disease
- Polycystic Kidney Disease/Genetics
- Chronic Inflammation
- Obstruction
- Glomerular Disorders/ Glomerulonephritis

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



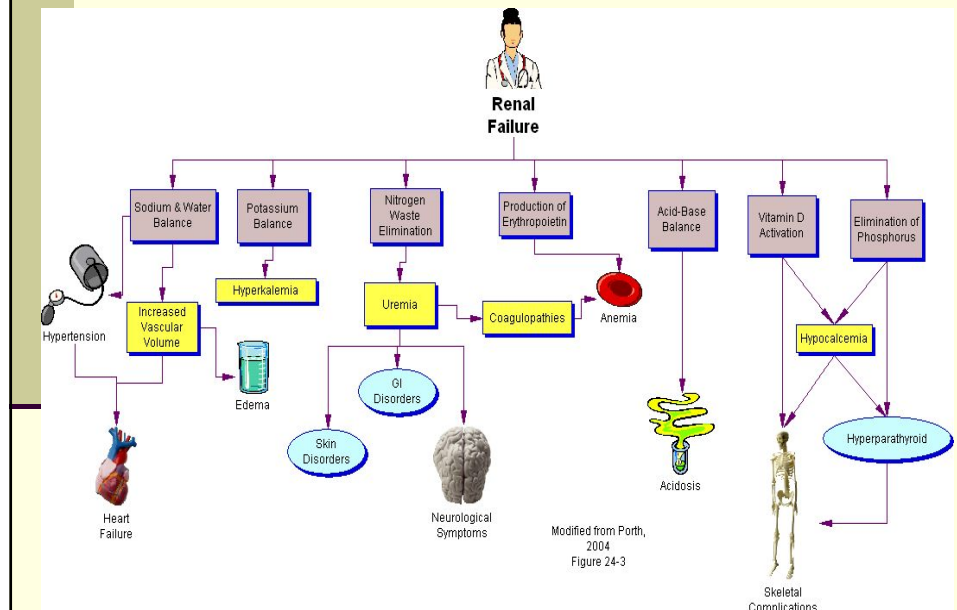
Functional Changes of CRF

- **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

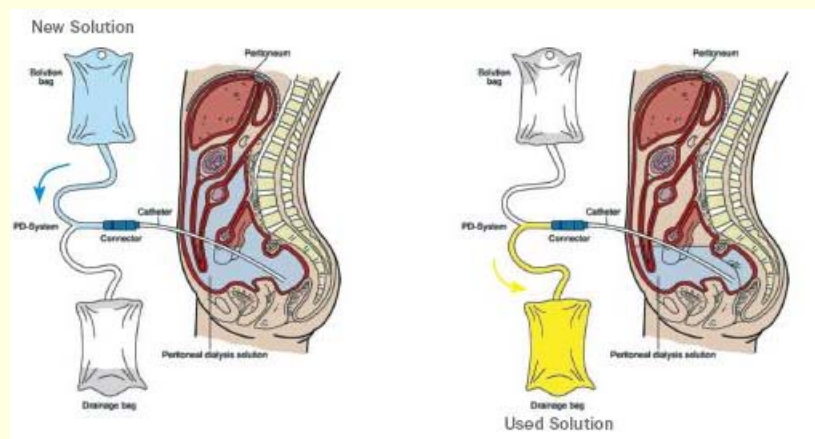
Four Stages of CRF

- **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



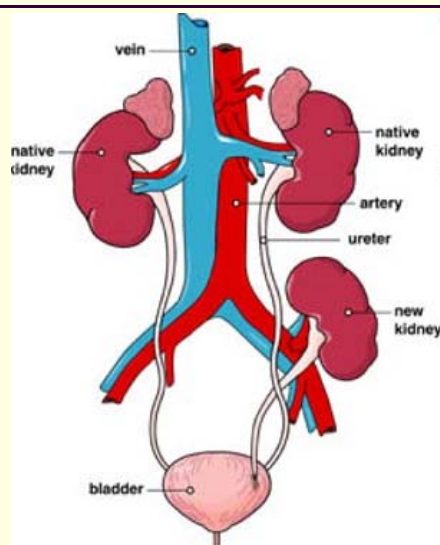
Peritoneal dialysis



Hemodialysis



Kidney transplantation



Thank you
