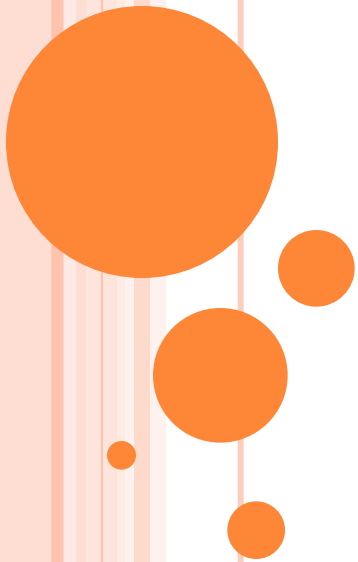


PATHOPHYSIOLOGY OF THE URINARY SYSTEM



LECTURE CONTENT

- Disorders of kidney function disorders
- Disorder of glomerular function - glomerulonephritis
- Poststreptococcal glomerulonephritis
- Nephrotic syndrome
- Renal hypertension
- Tubulointerstitial diseases
- Acute tubular necrosis
- Selective disorders of tubular functions
- Pyelonephritis
- Acute renal failure
- Chronic renal failure
- Nephrolithiasis

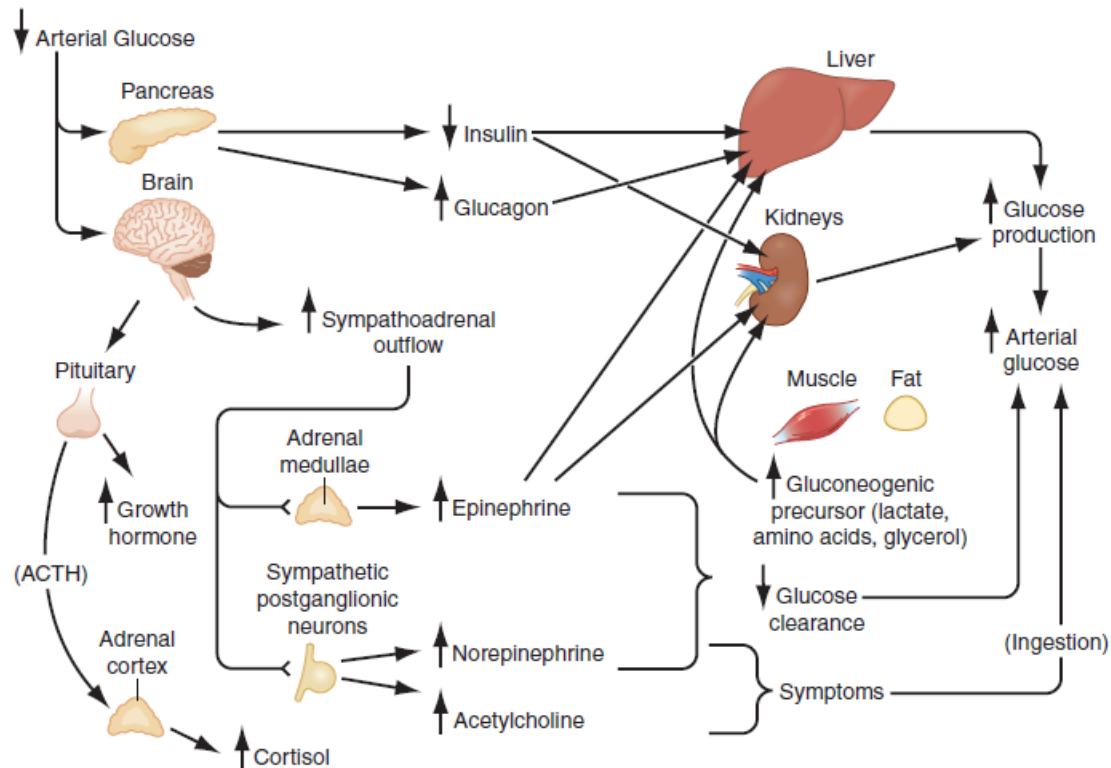


KIDNEY (REN) FUNCTION

- Elimination of harmful substances
- Endocrine (3 hormones)
- Regulation of acid-base balance
- Maintenance of fluid and electrolyte homeostasis
- Role in glucose metabolism (gluconeogenesis and glucose storage)
- Hormone metabolism (the elimination rate of hormones from the body)



GLUCONEOGENESIS AND GLUCOSE STORAGE

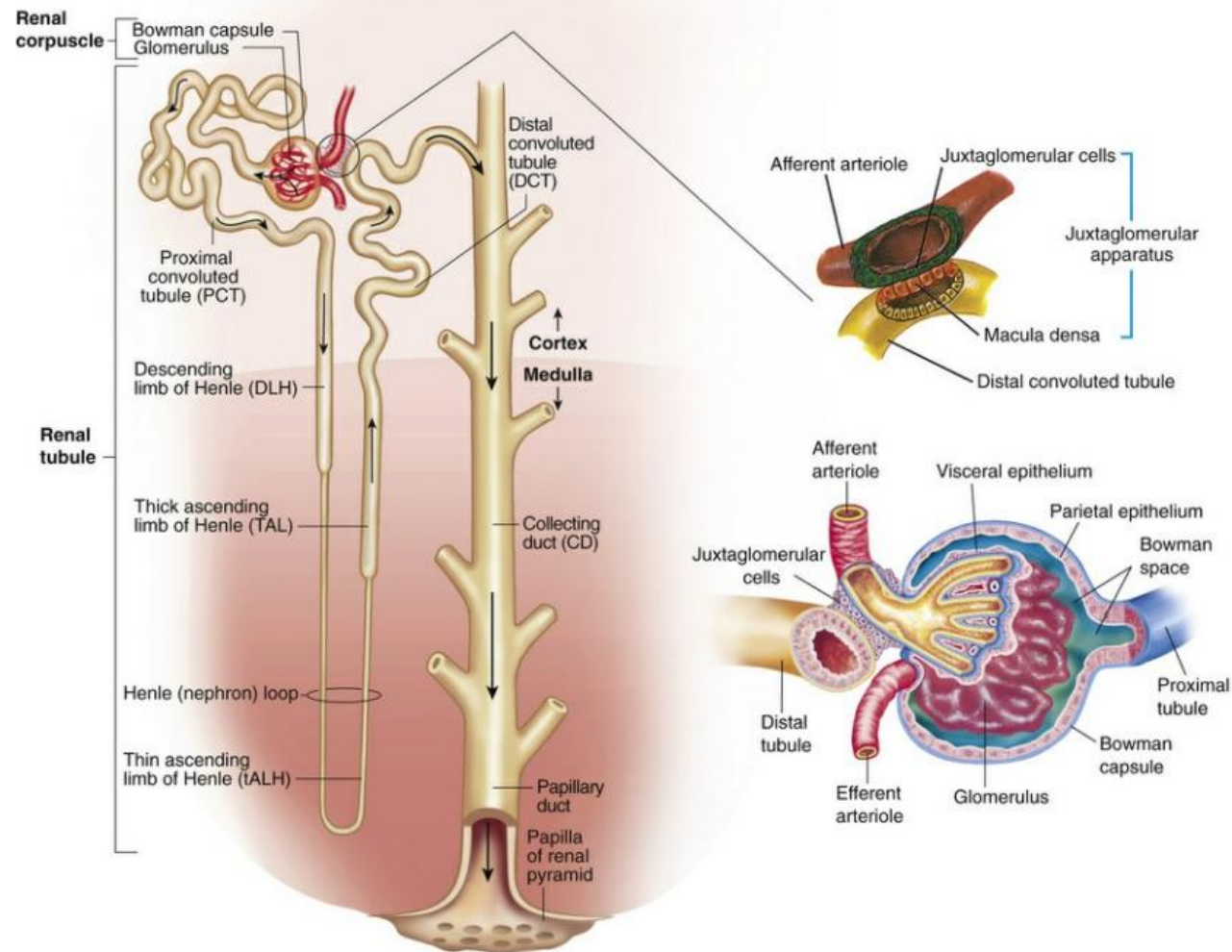


STRUCTURE OF THE KIDNEY

- Two diferente organs
- Anatomically
 1. Cortex
 2. Medulla
- Basic unit of kidney structure – NEFRON
- The structure of the nephron
 1. Glomerul
 2. Tubule



NEPHRON



Patton KT, Thibodeau GA, Douglas MM.
Essentials of anatomy & physiology. in 2012

DISORDERS OF KIDNEY FUNCTION

- **Prerenal - there is a problem before the kidney** (caused by renal hypoperfusion)
- **Renal - problem is at the kidney level**
 - Glomerular (nephritic and nephrotic Sy)
 - Non-glomerular (vascular diseases, tubular diseases, interstitial diseases)
- **Postrenal - there is a problem after the kidney** (urinary tract obstruction)



PRERENAL DISORDERS

○ As a consequence of:

1. **Blood vessel (A. renalis) disorders/diseases**

- Blood vessel embolism, obstruction by thrombus or damage by hypertension, immune factors)

2. **Disorders in systemic circulation**

- Disorders of cardiac output and BP considering that 20% of cardiac output go through the kidneys (hypovolemia, transfer of fluid into the intercellular spaces, severe dehydration)

Disruption of systemic blood flow leads to a decrease in capillary pressure in the glomerulus and further to a drop in glomerular filtration rate and kidney failure.



RENAL DISORDERS

○ GLOMERULAR FUNCTION DISORDERS

1. Primary - damage of glomerular structures of the nephron
 2. Secondary - damage of the glomerular structures of the nephron (as a consequence of another disease)
-
- Glomerulonephritis is an inflammatory kidney disease accompanied by proteinuria and hematuria (NEPHRITIC SYNDROME)
 - Proteinuria over 150 mg/day but below 3g/day
 - Hematuria over 3 erythrocytes per visual field



TYPES OF GLOMERULONEPHRITIS

- Depending on the distribution of the pathological process:
 1. Diffuse (involves all glomeruli)
 2. Focal (involving only some glomeruli)
 3. Segmental (involving only some parts of one glomeruli (larger number of glomeruli))
- Based on immunopathogenetic mechanisms:
 1. Immunocomplex (III type of hypersensitive reactions)
 2. Cytotoxic (II type of hypersensitive reactions)
- According to pathomorphological changes and proliferation:
 1. Non-proliferative
 2. Proliferative
- Based on the clinical picture and duration :
 1. Acute
 2. Subacute
 3. Chronic



BASIC MECHANISMS OF GLOMERULUS DAMAGE

Mechanism	Cause	Disease
Immunological	Specific antibodies	Immunocomplex and cytotoxic glomerulonephritis
Metabolic	Hyperglycemia	Diabetes nephropathy
Hemodynamic	Hypertension	Hypertensive nephropathy
Toxic	NSAIDs (Brufen)	Thrombotic microangiopathy
Deposition disease	Amyloid fibers	Amyloid nephropathy
Hereditary	Gene deficiency for some parts of collagen structure	Alport syndrome
Infectious	Viruses, bacteria, protozoa	Glomerulonephritis



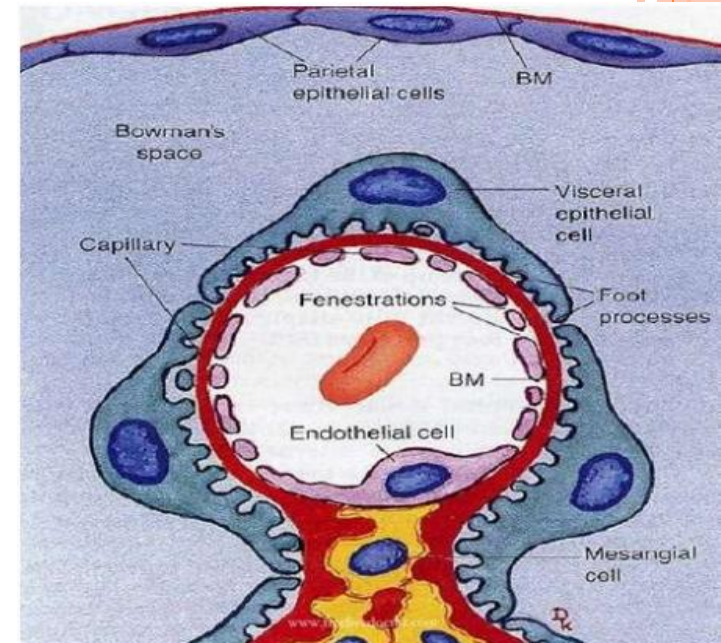
TYPES OF GLOMERULONEPHRITIS

- Based on immunopathogenetic mechanisms
- 1. Antibody-mediated glomerulonephritis (in which antibodies play a significant role in the development)
 - Immunocomplex (III type of hypersensitive reactions)
 - Cytotoxic (II type of hypersensitive reactions)
- 2. Glomerulonephritis mediated by lymphocytes



GLOMERULONEPHRITIS MEDIATED BY CIRCULATING IMMUNOCOMPLEXES

- The most common type of glomerulonephritis
- The most important stimuli for production of antibodies are antigens of microbes (exogenous) or parts of DNA, tumor proteins (endogenous)
- Specific histological structure and changes of glomeruli
- Immune complexes can be deposited in several places:
 - Subendothelial
(between capillary endothelium and GBM)
 - Intramembranous (in GBM)
 - Subepithelial (between epithelium and GBM)
 - In the mesangium
- Followed by the activation of effector mechanisms (Complement or neutrophils)



ACUTE POSTSTREPTOCOCCAL GLOMERULONEPHRITIS

- It manifests usually 2-4 weeks after a streptococcal throat infection or 4-6 weeks after a skin infection
- **Aseptic inflammation** of glomeruly that occurs after the streptococcal infection, usually of the throat (pharyngitis) or skin
- Group A beta hemolytic streptococcus (rarely other strains) that has a nephrogenic M protein in the wall (type M1, M4, M12 in angina and M49 in skin infection)
- Most often appears before the age of ten



ACUTE POSTSTREPTOCOCCAL GLOMERULONEPHRITIS

- PATHOGENESIS
- Molecular mimicry between streptococcal and glomerular antigens
- This is followed by complement activation with damage to the glomerular basement membrane
- Damage and thickening of the basement membrane with reduced glomerular filtration rate
- Subepithelial deposition of immune complexes in the glomerulus
- In some situations it is also possible to create antibodies against glomerular basement membrane antigens



ACUTE POSTSTREPTOCOCCAL GLOMERULONEPHRITIS

○ CLINICAL MANIFESTATIONS

1. Hematuria with proteinuria
2. Oliguria
3. Fluid retention in the body and the formation of edema
4. Development of moderate hypertension
5. High levels of urea and creatinine

○ In childhood, it is mostly reversible

○ In adults only in 50% of cases

○ It can progress to chronic glomerulonephritis



GLOMERULONEPHRITIS MEDIATED BY ANTIBODIES TO BASAL MEMBRANE

- Forming of antibodies against glomerular basale membrane proteins
- A less common type of glomerulonephritis (about 5%)
- After labeling cells of the basal membrane with antibodies, effector mechanisms are activated that lead to the destruction of the basal membrane



GLOMERULONEPHRITIS MEDIATED BY LYMPHOCYTES

- Cell (lymphocyte) mediated damage
- Cytotoxic T lymphocytes CD8⁺ independently (from activation of T helper CD4⁺ lymphocytes) damage basement membrane cells
- With the activation of T lymphocytes by antigen-presenting cells or MHC I class that activate CD8⁺ cells



NEPHROTIC SYNDROME

- It is defined as a significant increase in the permeability of GBM for proteins due to damage of epithelial layer of the wall of glomerular capillaries (deposition of relatively small immunocomplexes in the subepithelial space).

- Features:
 - Massive proteinuria (> 3.5 g/24h)
 - Hypoalbuminemia
 - Edema
 - Hyperlipidemia (compensatory increased synthesis of triglycerides in the liver in response to hypoalbuminemia)
 - Blood hypercoagulability (increased synthesis of fibrinogen, increased loss of antithrombin III in urine).



NEPHROTIC SYNDROME

- ETIOLOGY

- Primary: in primary glomerular diseases (for ex. In some types of glomerulonephritis)

- Secondary:

1. Systemic diseases (Systemic lupus erythematosus, Henoch-Schönlein purpura, Wegener's granulomatosis)
2. Metabolic diseases (Diabetes)
3. Infections (Hepatitis B, hepatitis C, Cytomegalovirus, etc.)
4. Toxins and drugs (penicillamine, nonsteroid anti-inflammatory drugs)



RENAL HYPERTENSION

- A condition of elevated blood pressure caused by damage to the kidney and/or its vascular structures

- Types:
 1. Renoparenchymal
(caused by diseases of the renal parenchyma)
 2. Renovascular
(caused by disruption of blood flow through a. renalis)



RENOPARENCHYMAL HYPERTENSION

ETIOLOGY

- Acute diseases
 - Glomerulonephritis (thickening GBM)
 - Acute urinary obstruction
- Chronic diseases
 - Chronic renal failure
 - Chronic pyelonephritis
 - Diabetic nephropathy
 - Polycystic kidneys (alone or as part of polycystic disease)



RENOPARENCHYMAL HYPERTENSION

- Why does hypertension occur ???
- $TA = MV \times PR$
- A physiological kidney creates **180 liters of primary urine per day**
- After damage to the glomerulus, there is a **reduction in the total filtration surface/area**, which leads to reduced primary urine production and fluid retention in the body
- On the other side, due to **reduced production of nitric oxide and prostacyclin (vasodilatory effect)** and **increased sympathetic** and angiotensin activity (**vasoconstrictory effect**), there is an increase in peripheral vascular resistance

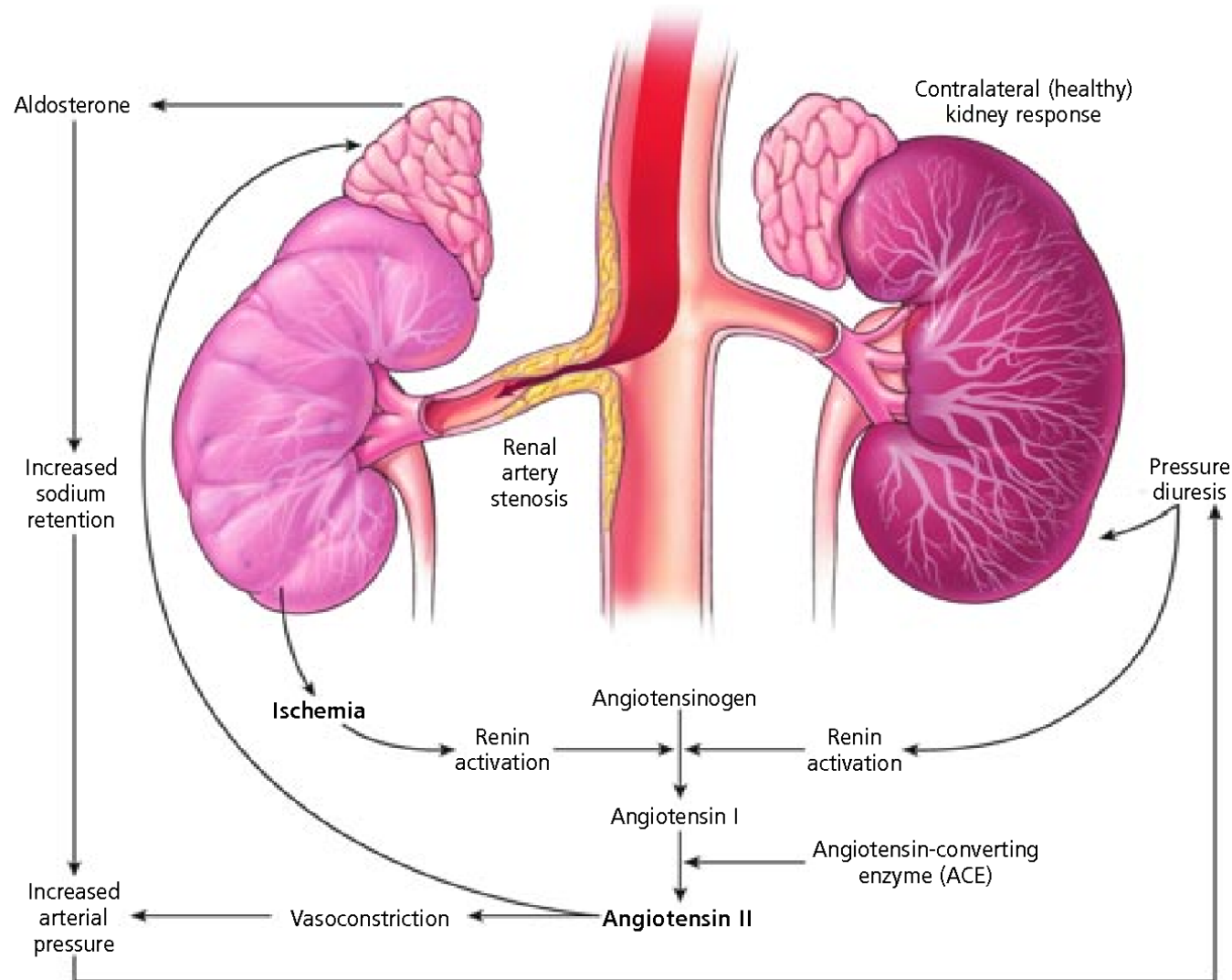


RENOVASCULAR HYPERTENSION

- The state of elevated blood pressure due to disturbed blood flow through a. renalis
- ETIOLOGY
 - Atherosclerosis 75-90% (elderly)
 - Fibromuscular dysplasia 10-25% (younger people)
 - The other causes
 - Aorto-renal dissection
 - Takayasi's arteritis
 - Thrombosis and fat embolism
 - Post-transplant stenosis
 - Post-radiation stenosis



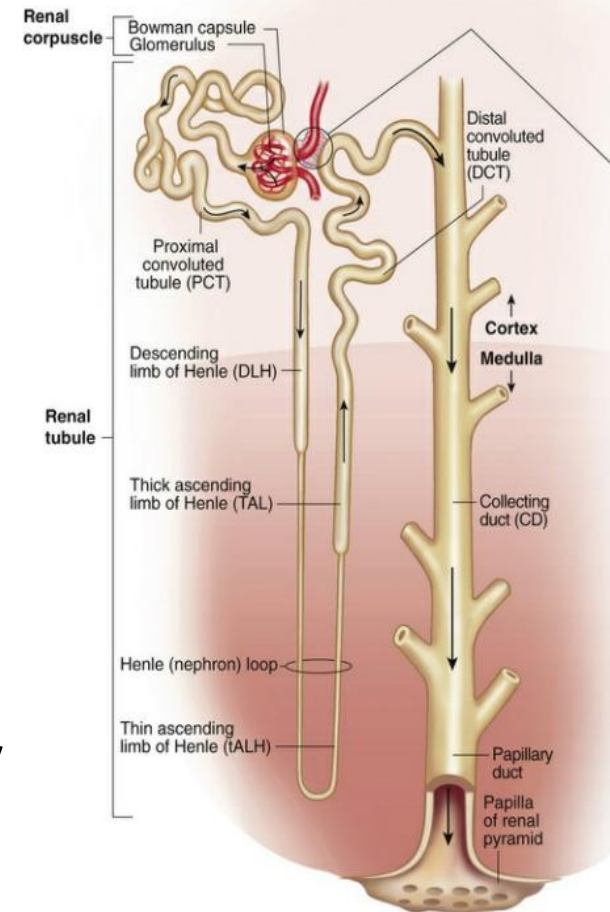
PATHOGENESIS OF RENOVASCULAR HYPERTENSION



Garovic VD, Kane GC, Schwartz GL. Renovascular hypertension: balancing the controversies in diagnosis and treatment. Cleve Clin J Med. in 2005

TUBULOINTERSTITIAL KIDNEY DISEASES

- A group of diseases in which the tubular segment of the nephron and the associated interstitium are primarily damaged (**glomerul is normal**)
- Physiology of tubules:
 - Water reabsorption and urine concentration
 - Reabsorption of ions, proteins and glucose
 - Secretion
 - Excretion
- Dominant resorptive capacity disorder
- New term - Isosthenuria
urine osmolarity is equal to blood osmolarity



TUBULOINTERSTITIAL KIDNEY DISEASES

1. Tubulointerstitial nephritis (non-specific inflammatory reaction affecting the tubule and/or interstitium)
 - Acute
 - Chronic (fibrosis processes dominate with the development of secondary glomerulosclerosis and renal insufficiency)
2. Acute tubular necrosis (ischemic or toxic damage to tubular cells)



TUBULOINTERSTITIAL NEPHRITIS

- Division according to etiology
 1. Primary (**inflammatory damage to tubules and interstitium, glomeruli and blood vessels are normal - undamaged**)
 2. Secondary (**result of primary damage to glomeruli, blood vessels or systemic diseases**)
 3. Reactive (as part of systemic infections where the kidneys are sterile – specific autoimmune Ab)
 4. Infectious (presence of microorganisms in the kidneys)
 5. Idiopathic



ACUTE

TUBULOINTERSTITIAL NEPHRITIS

ETIOLOGY

- **Drug - induced nephropathy (>75%)**
 - **Antibiotics:** ampicillin, cephalosporins, ciprofloxacin, penicillin, methicillin, sulfonamides, rifampicin, vancomycin.
 - **NSAIDs**
 - **Others:** acyclovir, allopurinol, furosemide, famotidine....
- **Infections (5-10%):**
 - Bacteria (brucella, campylobacter, legionella, salmonella, streptococcus, staphylococcus, E. coli, yersinia)
 - Viruses (CMV, EBV, HIV, HCV...)
 - Others: mycobacterium TB, leptospira, mycoplasma, rickettsia..
- **Systemic diseases (10-15%):**
 - Sarcoidosis, SLE, Sjogren's syndrome
- **Idiopathic (5%):** Tubulointerstitial nephritis with tubular basement membrane antibodies



CHRONIC

TUBULOINTERSTITIAL NEPHRITIS

ETIOLOGY

- Medicines during **chronic use** (analgesics, cytostatics, immunosuppressive therapy...)
- Heavy metals (mercury)
- Obstructive uropathy, nephrolithiasis
- Cystic kidney disease
- Immune diseases (amyloidosis, SLE, Sjögren's disease , sarcoidosis)
- Metabolic diseases (hypercalcemia, hyperuricemia, hyperoxaluria, chronic hypokalemia, cystinosis)
- Granulomatous diseases (sarcoidosis, TB...)
- Hematological diseases (multiple myeloma, leukemia, lymphomas, sickle cell disease)
- Radiation nephritis
- Idiopathic



DISORDER OF TUBULAR FUNCTION IN NEPHRITIS

- **Decrease in the concentration capacity of the kidneys with the occurrence of polyuria**
- **Initially, glomeruli are not affected** and moderate proteinuria occurs (< 1.5 g/24 h)
- Tubular epithelial cells, leukocyturia (pyuria) and granular casts can be found in the urine
- **Secondary damage to the glomerulus can occur** if the damaged tubule cells (get into the lumen) and close the lumen of the tubule
- Acute renal failure
- **In 30 to 70% of patients, complete recovery of kidney functions does not occur** (due to the specificity of tubulocytes and the onset of rapid fibrosis)



ACUTE TUBULAR NECROSIS

- **Necrosis of renal tubules** caused as a result of **kidney ischemia** or the **toxic effect** of various substances
- Types:
 - Ischemic - **Segmental necrosis** along the entire nephron with damage to the tubule basal membrane
 - Nephrotoxic - **Diffuse necrosis of tubular cells** with preserved basement membrane
- Acute tubular necrosis - the most common cause of renal ARF



TOXINS AS A CAUSE OF ACUTE TUBULAR NECROSIS

ENDOGENOUS

- Hemolysis
- Rhabdomyolysis
- Uric acid
- Oxalates
- Multiple myeloma (light chains of Ab)

EXOGENES

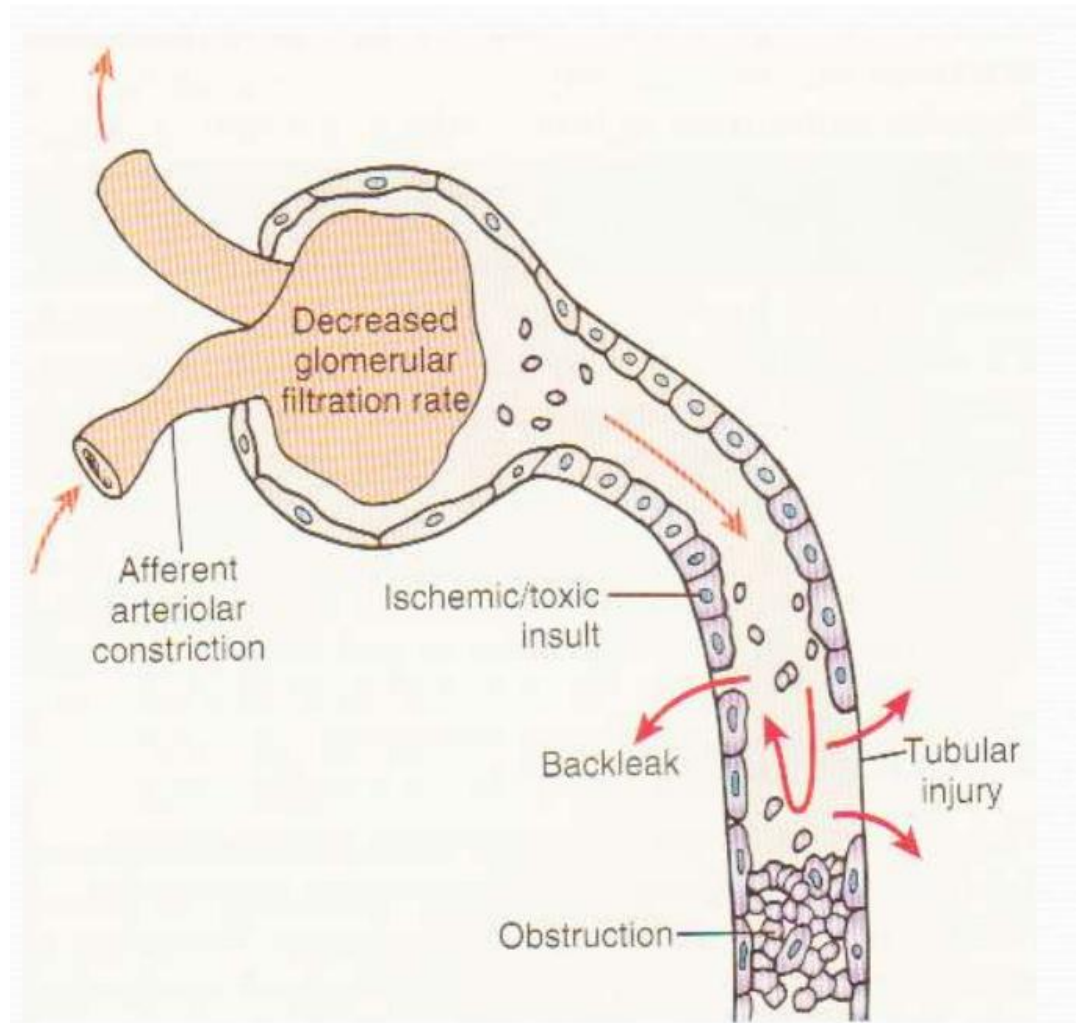
- Antibiotics (aminoglycosides)
- Radiocontrast agents
- Cyclosporine (cisplatin)
- Chemotherapy
- Organic solvents



ACUTE TUBULAR NECROSIS

PATHOGENESIS

- An increase
 - RAA system
 - Endothelin
- Reduction
 - Nitrous oxide
 - PGI_2



LECTURE CONTENT

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- Acute tubular necrosis



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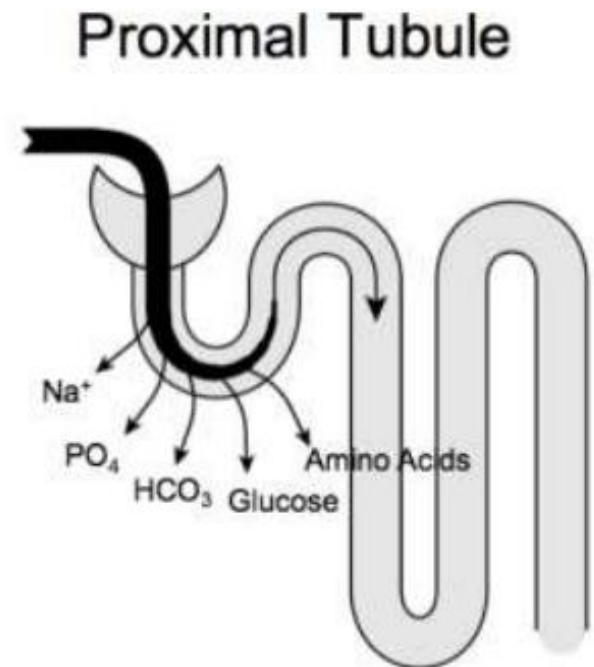
SELECTIVE DISORDERS OF RENAL FUNCTION

- Disturbance of one or more then one tubular functions with preserved glomerular function
- Most disorders are hereditary
- **Gene disorders that control the synthesis of specific carriers or enzymes needed for transport**
 - Electrolyte
 - Glucose
 - Amino acid



DISORDERS OF PROXIMAL TUBULES

- Fanconi syndrome
- Aminoaciduria (cystinuria)
- Nephrogenic diabetes mellitus (glucose reabsorption transporter defect)
- Renal hypophosphatemic rachitis (phosphate reabsorption disorder)
- Proximal tubular acidosis (decreased bicarbonate reabsorption)



DISORDER OF DISTAL TUBULES

- Pseudohypoaldosteronism (disorder of sodium channel or aldosterone receptor gene)
- Nephrogenic diabetes insipidus (disorder at the level of the ADH receptor)
- Distal tubular acidosis (decreased secretion of hydrogen ions)



URINARY INFECTIONS

- The presence of microorganisms in the previously sterile urinary system (bacteriuria over 100,000 bacteria/ml of urine)
- According to localization, they are divided into:
 1. infections of the lower parts of the urinary system (cystitis, urethritis, prostatitis)
 2. upper parts of the urinary system (abscess and pyelonephritis).
- According to the course, they are divided into
 1. acute
 2. chronic
- After the presence of symptoms on:
 1. asymptomatic
 2. symptomatic urinary infections



ACUTE PYELONEPHRITIS

- Tubulointerstitial diseases caused by infection
- The most common causes of acute pyelonephritis are gram-negative bacteria (*Escherichia coli*, *Proteus*, *Klebsiella*...); but also certain gram-positive ones such as staphylococci and streptococci
- Ascending spread of infection from the lower urinary tract, less often due to hematogenous/lymphogenous spread
- The presence of leukocyturia, leukocyte cylinders and significant bacteriuria is an important diagnostic criterion



ACUTE PYELONEPHRITIS

- Factors that potentiate the occurrence of infection:
 - Anatomical features of the urethra (female)
 - Obstruction of urine flow due to obstruction (narrowing of the urethra, tumors, hypertrophy of the prostate)
 - Neurogenic dysfunction
 - Pregnancy
 - Vesicoureteral reflux
 - Catheterization
 - Immunodeficiency



CHRONIC PYELONEPHRITIS

- The consequence of many repeated infections of the urinary system, which leads to atrophy and fibrosis of the nephron with a decrease in kidney function and renal failure
- Etiology:
 1. vesicoureteral reflux
 2. urinary tract obstruction caused by stones
 3. neurogenic bladder



RENAL INSUFFICIENCY

- Renal failure or renal insufficiency is a condition in which the kidneys fail to maintain their functions.

1. **Acute renal failure** is defined as a **sudden decrease in renal function** - glomerular filtration (GF) with accumulation of nitrogenous substances (urea and creatinine).

Recovery of function may occur

2. **Chronic renal failure** is defined as a **gradual, irreversible and permanent deterioration of renal function**, ie nephrons.



ACUTE RENAL INSUFFICIENCY

- A syndrome characterized by a sudden drop in the strength of glomerular filtration (within 48 hours), retention of nitrogenous substances, changes in the volume of extracellular fluid, electrolytes and acid-base status
- Can be potentially reversible
- Frequency: 5% of hospitalized patients, 15-30% in intensive care unit (severe patients)
- It is often accompanied by oliguria, although normal diuresis does NOT rule out ABI



ACUTE RENAL INSUFFICIENCY

- Division into three large groups:
 - Prerenal (circulatory) - 55%
(circulation disorders)
 - Renal (parenchymal) - 40%
 - Acute tubular necrosis - 85%
 - Interstitial nephritis - 10%
 - Acute glomerulonephritis - 5%
 - Postrenal (obstructive) - 5%



PRERENAL ACUTE RENAL INSUFFICIENCY

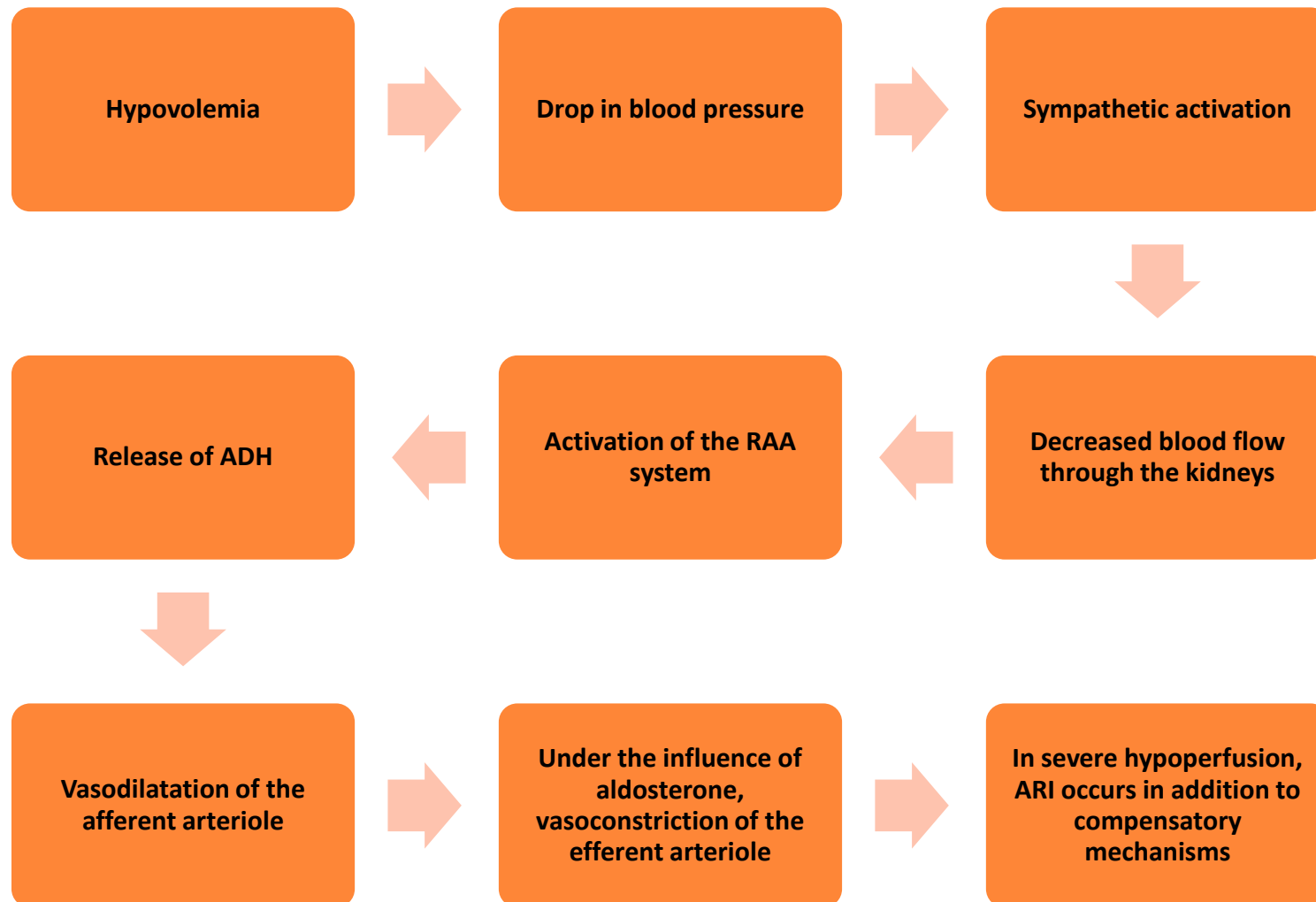
- As a consequence of renal hypoperfusion

ETIOLOGY:

- Systemic blood flow disorders:
 - hypovolemia,
 - hemorrhage
 - severe dehydration,
 - vomiting, diarrhea, burns
 - decreased cardiac output,
 - myocardial diseases, heart defects
 - systemic vasodilatation
 - sepsis, anaphylaxis
- Diseases of blood vessels of the kidneys
 - Embolism a. renalis



PRERENAL ACUTE RENAL INSUFFICIENCY



PRERENAL ACUTE RENAL INSUFFICIENCY

- The flow of ischemic ARI (3 phases):
 1. Initial phase
 - Hypoperfusion leads to ischemic damage and the fall of the GFR
 2. Maintenance phase
 - Decreased GFR, oliguria, and disorder of ion homeostasis
 3. Recovery phase
 - Recovery of glomerular functions along with the delay of recovery of tubules with appearance of polyuria



ACUTE RENAL INSUFFICIENCY

- A consequence of damage to the renal parenchyma

ETIOLOGY:

- Acute tubular necrosis
- Glomerular and microvasculature diseases
- Interstitial nephritis



POSTRENAL ACUTE RENAL INSUFFICIENCY

- Inability to eliminate urine due to obstruction of the urinary tract

ETIOLOGY:

- At the level of the ureter:
 - Calculus, blood clots, compression
- At the level of the bladder neck:
 - prostate hypertrophy, calculus, cancer
- At the level of the urethra
 - strictures, congenital valve, phimosis
- Above the site of obstruction, there is an increase in pressure that reduces GFR, in long-term cases, post-renal changes to renal ARI



PATHOPHYSIOLOGICAL CONSEQUENCES OF ACUTE RENAL INSUFFICIENCY

- **Development of uremic syndrome** (due to ↓ excretory function of the kidneys, ↑ concentration of urea, creatinine, uric acid and other nitrogen-containing metabolites occurs)
- **Disturbance of homeostasis of water , electrolytes and acid-base balance**
- Disorder of organic systems



DISORDER OF HOMEOSTASIS OF WATER, ELECTROLYTES AND ACID-BASE BALANCE

- **Oliguria/anuria** with **hyperhydration** and edema
- **Hyponatremia** (effect of excess fluid; inability to reabsorb by damaged tubule cells in parenchymal ABI)
- **Hyperkalemia and hyperphosphatemia** (↓ secretion and release from damaged cells, hypoxia and acidosis)
- **Hypocalcemia** (deposition of calcium phosphate in tissues and ↓ release of calcium from bones due to parathyroid hormone resistance)
- **Metabolic acidosis with an increased anion gap** (↓ excretion of hydrogen ions due to damage to cells of the proximal tubules, ↓ exchange of hydrogen and filtered sodium; ↓ excretion of anions)



CHRONIC RENAL INSUFFICIENCY

- It represents the progressive and irreversible deterioration of the nephron, followed by the insufficiency of all renal functions
- Physiologically, after the age of 30, GFR decreases by 1 ml/min (per year)
- Chronic renal failure and as reduction of GFR during several years or decades
- Dialysis or transplantation is necessary



CREATININE CLEARANCE

- Volume of purified blood per unit of time (ml/s or ml/min)
- $\text{Clearance} = \frac{U \text{ (conc in urine)} \times V \text{ (volume of urine in 24h)}}{P \text{ (conc in plasma)}}$
- Creatinine clearance is always slightly higher than GFR because creatinine is additionally secreted at the tubule level
- A convenient parameter for the clinical analysis of GFR
- Inulin clearance would be the best to estimate GFR



DETERMINATION OF THE ESTIMATED LEVEL OF THE STRENGTH OF GLOMERULAR FILTRATION

- eGFR
- Quick assessment based on a couple of parameters
- Can be very useful for clinical use
- You get the result immediately
- <https://www.mdcalc.com/calc/76/mdrd-gfr-equation>
- Do not work with acute renal failure




PATHOGENESIS OF CHRONIC KIDNEY INSUFFICIENCIES

ETIOLOGY



- The 2 most common causes of HRI:
 - Arterial hypertension
 - Diabetes
 - Other causes of HRI:
 - Glomerulonephritis
 - Polycystic kidneys
 - Tubulointerstitial diseases
 - Reflux nephropathy
 - Obstructive uropathy



CHRONIC RENAL INSUFFICIENCY

- 
- Reduction in the number of nephrons
 - Adaptive hyperfiltration (Bricker theory)

- 
- Increased permeability of glomeruli
 - Increased filtration of proteins and macromolecules

- 
- Nephrotoxic remodeling/inflammation
 - Segmental glomerulosclerosis and tubulointerstitial fibrosis with a decrease in GFR and diuresis
- 

CHRONIC RENAL INSUFFICIENCY

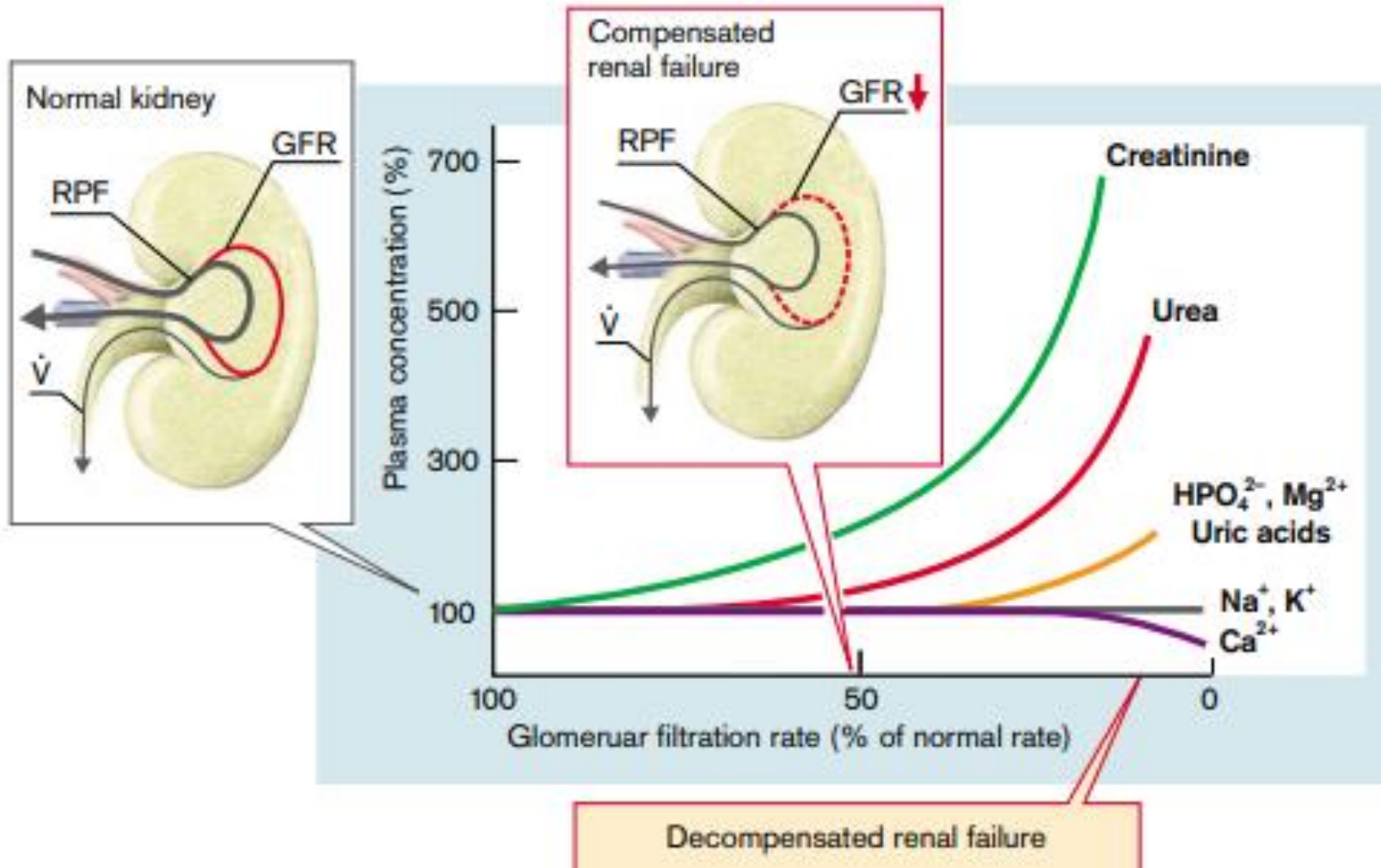
PATHOGENESIS

- Brick's theory of intact nephrons
- „We suggest that an alteration in glomerular permselectivity is an integral part of the adaptive changes which occur when nephron mass is reduced, that this change permits an increased passage of plasma proteins across the glomerular barrier, and that this results in the increased proteinuria observed from remaining nephrons when total renal mass is reduced .

Robson AM, Mor J, Root ER, Jager BV, Shankel SW, Ingelfinger JR, Kienstra RA, Bricker NS. Mechanism of proteinuria in nonglomerular renal disease. Kidney Int. in 1979



CHRONIC RENAL INSUFFICIENCY



CHRONIC RENAL INSUFFICIENCY

- UREMIC SYNDROME
- A set of disorders of organs and organ systems , which occur in more severe stages of renal failure as a result of retention of breakdown products of metabolism (mainly protein metabolism).
- Urea, xanthine, hypoxanthine, uric acid, tryptophan, phenol...



CHRONIC RENAL INSUFFICIENCY

- Disturbance of body fluids and electrolytes:
 1. Loss of concentration and dilution ability of the kidneys
 2. Isosthenuria
 3. Retention of Na^{+1} and water in the terminal stage ; hypervolemia and hypertension
 4. Hyperkalemia
 5. Hypocalcemia and hyperphosphatemia
- Metabolic acidosis with increased anion gap (increased loss of bicarbonate, retention of hydrogen ions)




CHRONIC RENAL INSUFFICIENCY

- Disorder of the metabolism of organic substances:
- Decreased excretion of products of protein metabolism
- Decreased activity of lipoprotein lipase - hypertriglyceridemia
- Decreased sensitivity of peripheral tissues to insulin (direct effect of uremic toxins)
- Disturbed insulin metabolism - hyperinsulinemia



CHRONIC RENAL INSUFFICIENCY

- Disorder of other organ systems:
 - Hematopoietic system
 - Anemia
 - Due to erythropoietin deficiency (normocytic normochromic)
 - Hemolytic anemia (effect of uremic toxins)
 - Immunodeficiencies
 - Disorder of cellular immunity
 - Thrombocytopenia
 - KVS
 - Hypertension , myocardial hypertrophy to failure , pericarditis
 - GIT
 - Nausea, vomiting, loss of appetite, weight loss , mouth sores, bad breath (uremic fetor)
- 

CHRONIC RENAL INSUFFICIENCY

- Disorder of other organ systems:
 - CNS
 - **Neuropathy** (disorders of sensitivity and motor skills), **loss of concentration, changes in behavior and reasoning , disorder of the state** of consciousness up to coma,
 - Skeletal system
 - **Disorder of vitamin D metabolism** (due to reduced production)
 - **Secondary hyperparathyroidism**
- Renal osteodystrophy
- Endocrine
 - Decreased T3 concentration, prolonged cortisol half-life, impaired glucose tolerance



CHRONIC RENAL INSUFFICIENCY

- Clinical stages according to the strength of glomerular filtration

stadium	description	GFR (ml/min)
1.	Kidney disease with normal or increased GFR	>90
2.	Kidney disease with mild reduction in GFR	60-89
3.	Moderate reduction in GFR	30-59
4.	Heavy reduction in GFR	15-29
5.	Renal insufficiency	<15 (dialysis)



CHRONIC RENAL INSUFFICIENCY

- Stages according to the severity of GFR damage

Phases of retention	GFR (% of reduction)	Concentration ability	Azotemia
I renal hypofunction	Up to 50%	Normal or mildly reduced	Nitrogen matter normal
II compensated retention	50-70%	Reduced, polyuria, 500-450 mOsm	Nitrogen matter mildly elevated
III decompensated retention	75-90%	Very reduced 350-300 mOsm	Significant increase of H, K, PO ₄ , SO ₄
IV terminal HRI-uremia	>90%	Izostenuria, oliguria	Heavy retention of toxins, Na, H ₂ O



UROLITHIASIS

- Physiology:

The role of the kidneys is to excrete unnecessary substances in a certain amount of water (which varies in relation to the intake and the state of the organism)

- When there is **an increase in the excretion of unnecessary substances, along with the need to retain water** in the body and/or the absence of crystallization inhibitors (disturbance of balance), favorable conditions for the development of urolithiasis - **nephrolithiasis occur**.
- Nephrocalcinosis - deposition of calcium salts in the collecting ducts and papillae of the kidney or renal parenchyma.



UROLITHIASIS

- Localization of stones
 - In the kidney (at the level of the renal cups and pelvis)
 - At the level of the ureter
 - At the level of the bladder
- Acute - increase in pressure with gradual decrease in GFR, renal ABI can occur
- Chronic - there is an expansion of the urinary tract and the excretory system of the kidneys with a significant decrease in kidney function and its atrophy



FACTORS THAT PROMOTE UROLITHIASIS

- Age
- Gender
- Race
- Heritage
- Nutrition
- Urine track
- Infections
- Kidney morphology disorder
- Metabolic disorders



CRYSTALLIZATION INHIBITORS AND PROMOTERS

Inhibitors

Promoters

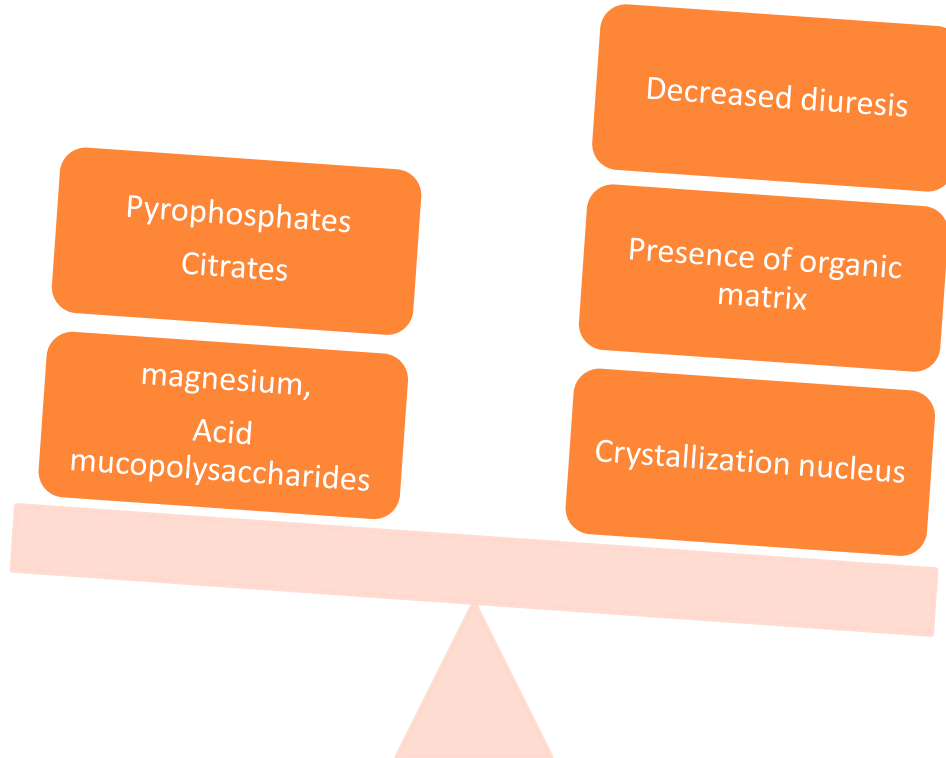
Pyrophosphates
Citrates

magnesium,
Acid
mucopolysaccharides

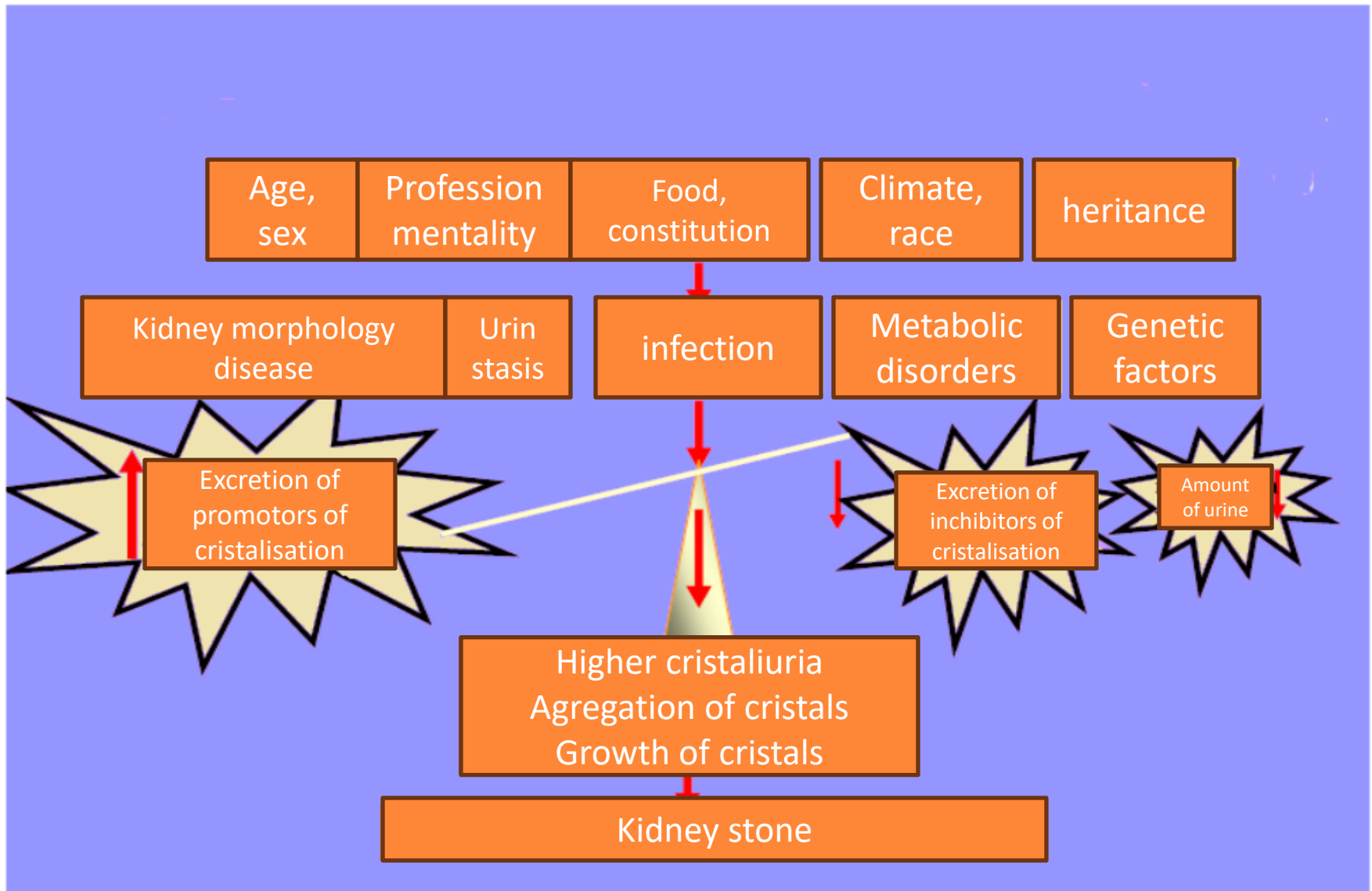
Decreased diuresis

Presence of organic
matrix

Crystallization nucleus



UROLITHIASIS



TYPES OF STONES

Types of stones	Percentage	Cause
Oxalat	75-85%	Hypercalciuria, dehydration Ingredients-Ca oxalate or Ca oxalate with Ca phosphate
Struvit	10-15%	Chronic UTI by bacteria that dissolve urea Ingredients-Mg-NH ₃ -phosphate
Urate	5-8%	Gout Ingredients-uric acid
Cystin	1-2%	Cystinuria Ingredients: cystin
Xanthin	<1%	Xanthinuria Ingredients- 2,8-dyhydroxyadenin, xanthin, different drug metabolites (sulphonamides)

UROLITHIASIS

- Clinical consequences:

1. Obstruction
2. Colic-like pains
3. Hematuria
4. Infections
5. Renal insufficiency



LECTURE CONTENT

- Division of kidney function disorders
- Disorder of glomerular function - glomerulonephritis
- Poststreptococcal glomerulonephritis
- Nephrotic syndrome
- Renal hypertension
- Tubulointerstitial diseases
- Acute tubular necrosis
- Selective disorders of tubular functions
- Pyelonephritis
- Acute renal failure
- Chronic renal failure
- Nephrolithiasis



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