Summer Pathophysiology course 2005

KIDNEY DISORDERS
PART 2

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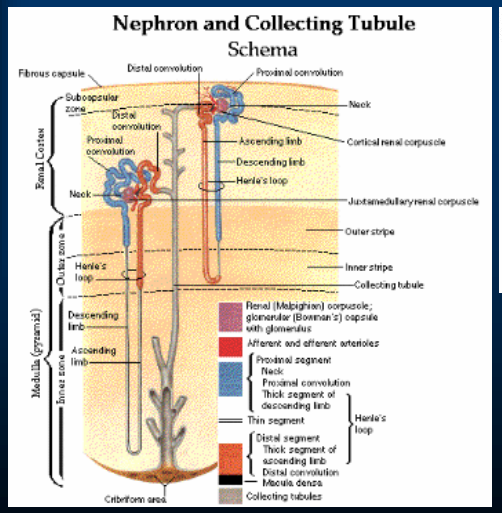
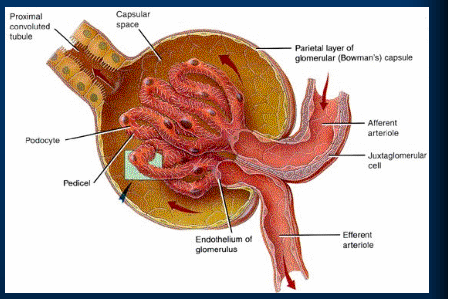
Kidney disorders – according to locus





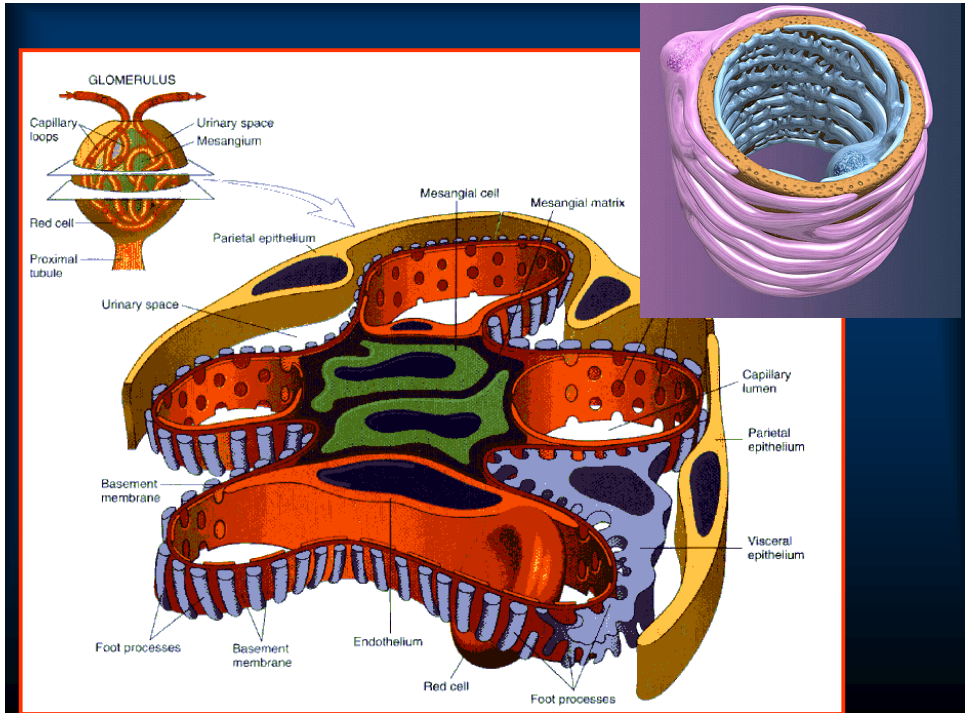
1. Glomerulopathies
2. Tubulopathies
3. Tubulointerstial disorders
4. Renovascular vasculopaties
5. Destructive laesions

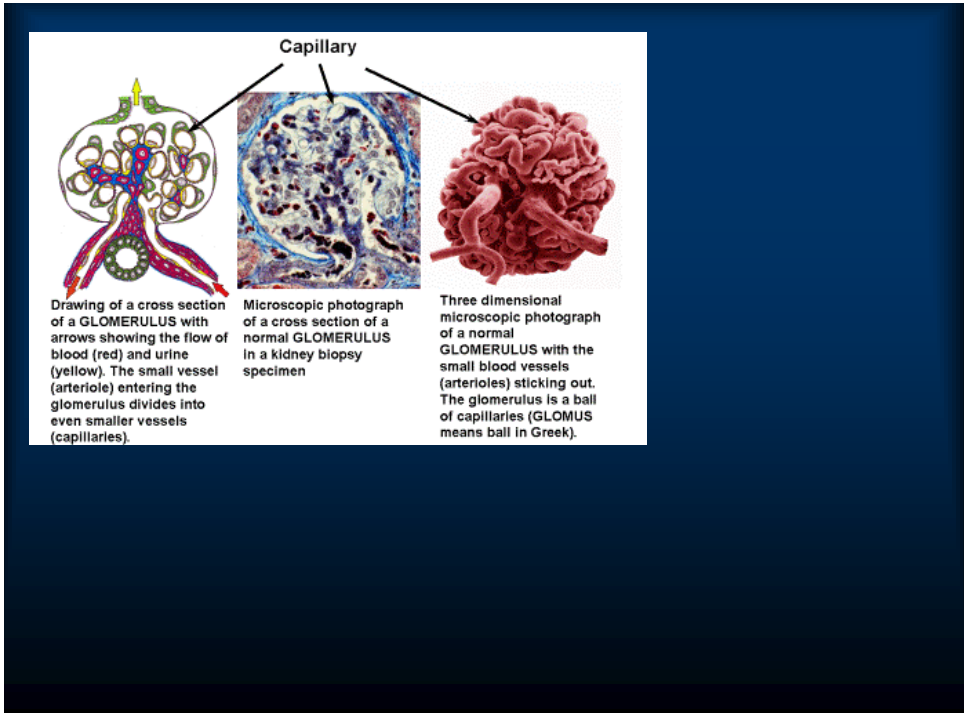
Functions:
- Excretion of waste products
- Regulation of water and salt
- Maintenance of acid balance
- Secretion of hormones and by-products

Syndromes:
- Acute Nephritic syndrome
- Nephrotic syndrome
- Asymptomatic hematuria
- Asymptomatic proteinuria
- Acute renal failure
- Chronic renal failure
- Urinary tract infection (UTI)
- Nephrolitiasis
- Tumors

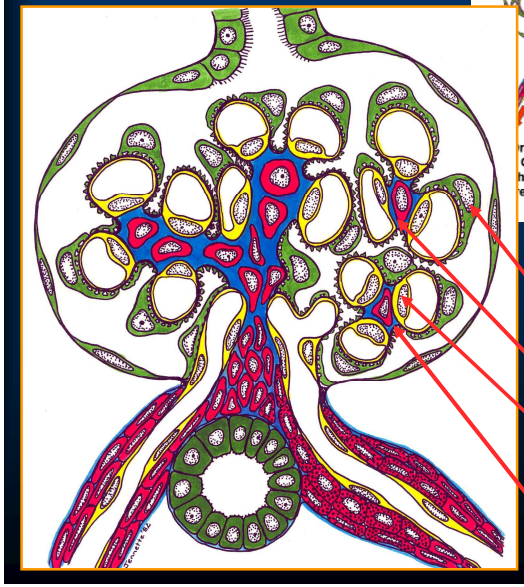
1

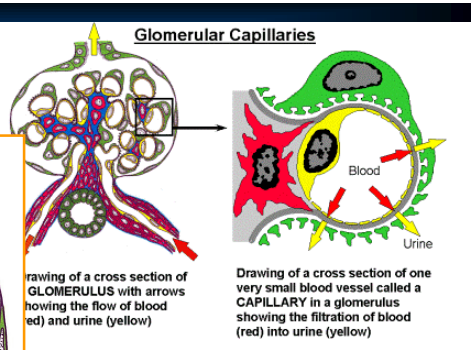
Glomerulopathies



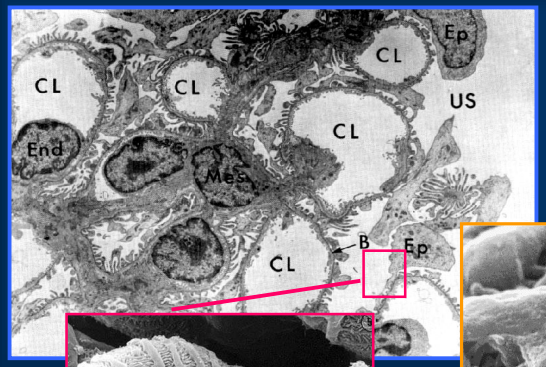


Zmeny štruktúry glomerulu

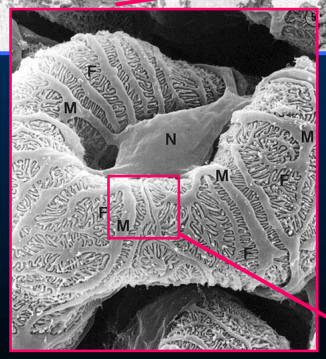


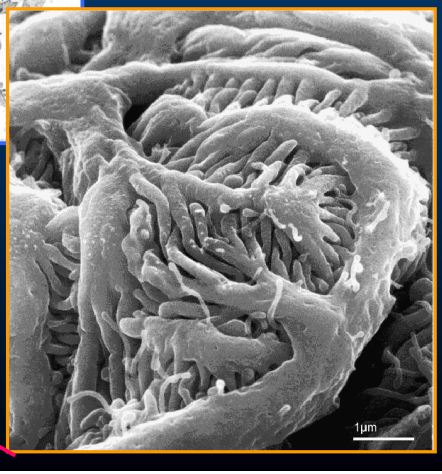


- Podocytes
- Mesangium)
- Endothel
- Basement membrane



Low-power electron micrograph of glomerulus: CL, capillary lumen; End, endothelium Mes, mesangium; B, basement membrane; Ep, visceral epithel with foot processes; US, urinary space.





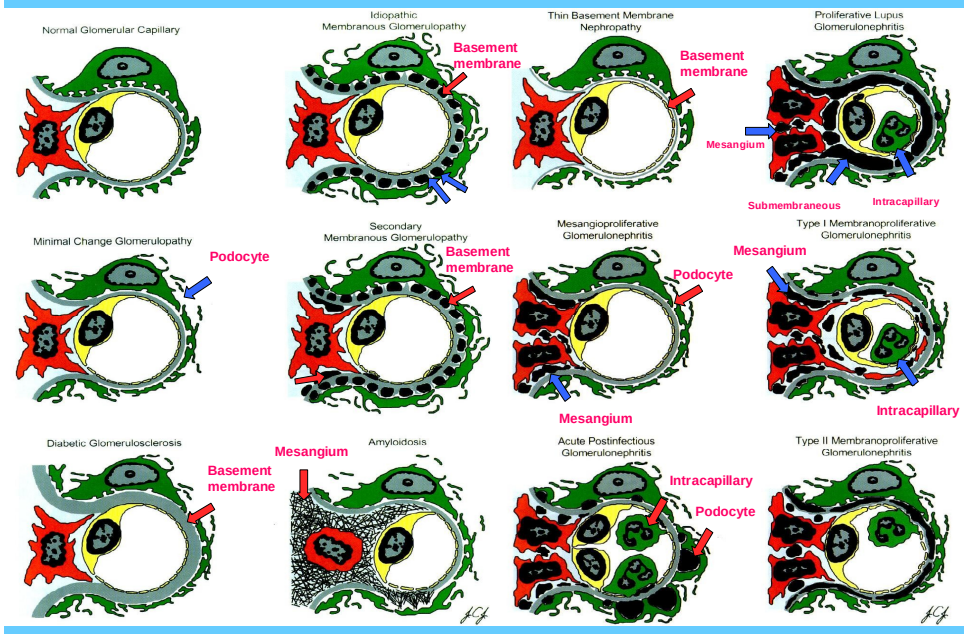
Glomerulopathies - Forms

Primary Glomerulonephritis
- Acute diffuse proliferative GN
- Rapidly progressive GN
- Membranous GN
- Lipoid nephrosis (minimal change disease)
- Focal segmental glomerulosclerosis
- Membranoproliferative GN
- IgA Nephropathy
- Chronic GN

Secondary (Systemic) Diseases
- Systemic lupus erythematosus
- Diabetes mellitus
- Amyloidosis
- Goodpasture's syndrome
- Polyarteritis nodosa
- Wagener's granulomatosis
- Henoch-Scholein purpura
- Bacterial endocarditis

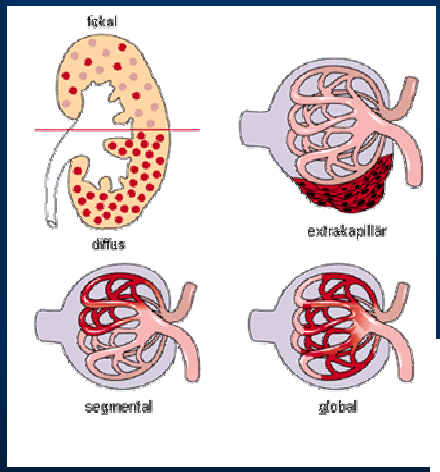
Hereditary Disorders
- Alport's syndrome
- Fabry's disease

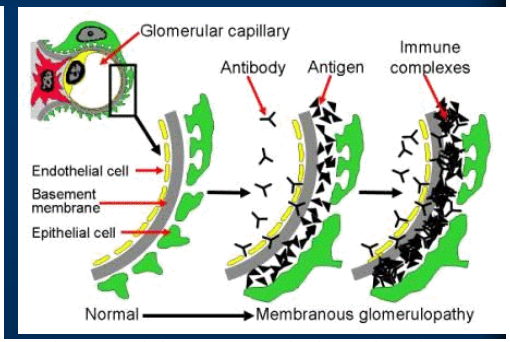
Various histologic glomerulopathies

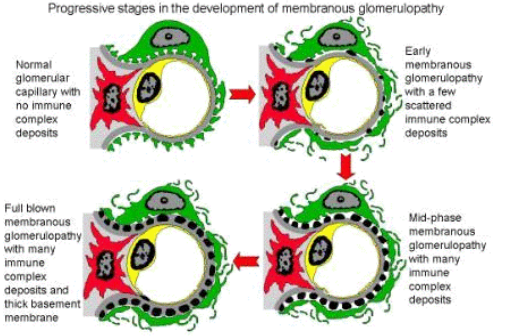


Glomerulopathies - Manifestations

1. asymptomatic proteinuria
2. nephrotic syndrome
   (proteinuria, hypoproteinemia, lyperlipidemia, edema)
3. asymptomatic hematuria
4. glomerulonephritis
   (hematuria, proteinuria, hypertension, renal failure)
5. acute glomerulonephritis
   (neprhitis with short term renal failure)
6. crescentic glomerulonephritis
   (nephritis with rapidly progressive renal failure)
7. chronic glomerulonephritis
   (chronic progression of renal failure)
8. End Stage Renal Disease
   (irreversible renal failure)





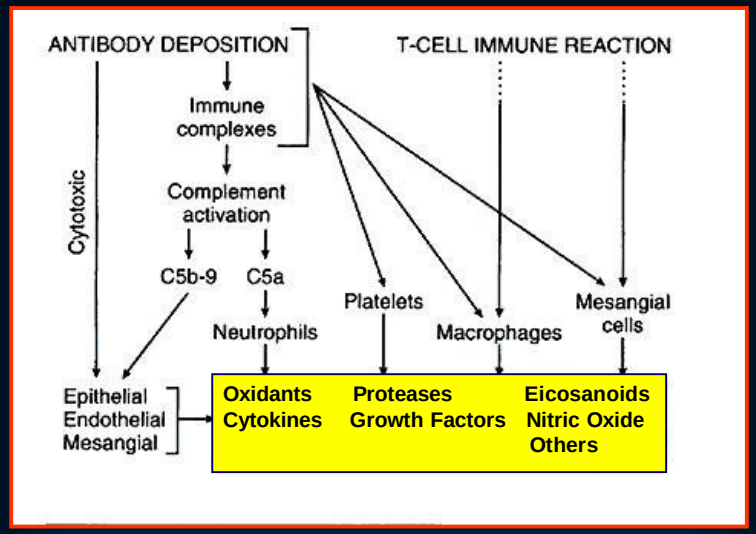


1. Nefritic syndrome

Definition: finding and laboratory data indicating glomerular damage in kidney; mainly **haematuria + hypertension**

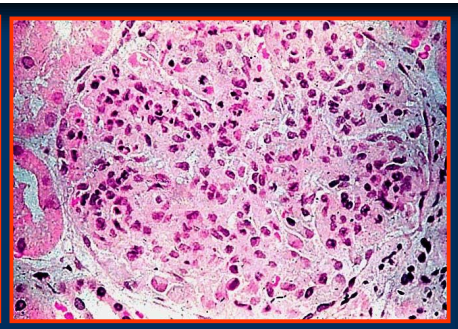
Symptoms:

- **hematuria** – failure of barrier; casts of haemolyzed erytrocytes (erytrocyturia), or haemoglobin, or hem (hemoglobinuria) → often precipitates and plugs tubuli → loss of filtration pressure, anuria
- **proteinuria** (mild to moderate) – both low-molecular and high molecular proteins are lost ň
- **oliguria** – decrease of water filtration → cummulation of water in vssels
- **hypervolemia – hypertension** – due to decreased GFR; if loss of solutes is normal → **hypoosmolalitay** in plasma develops

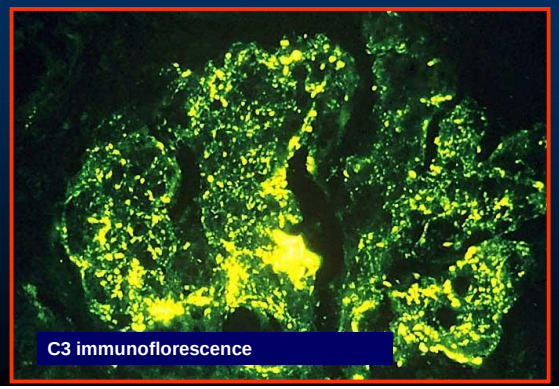


Mediators of immune glomerular injury.

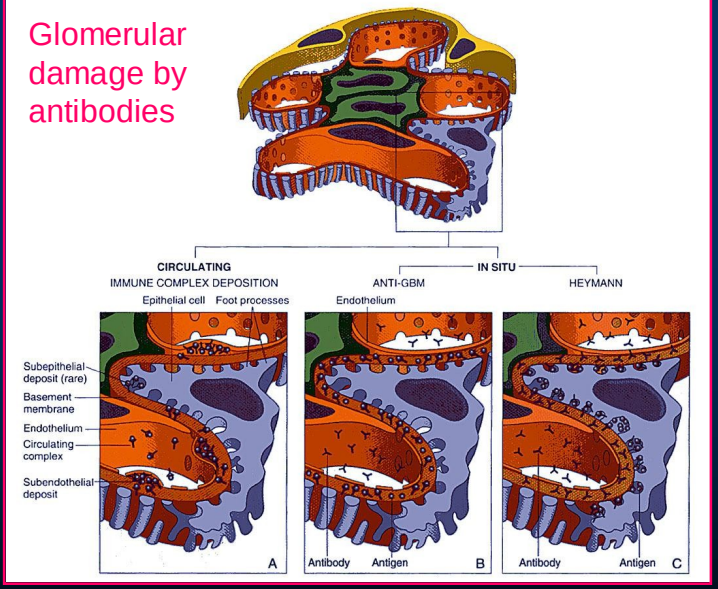

Erytrocytes in cast



Acute Nephritic Syndrome

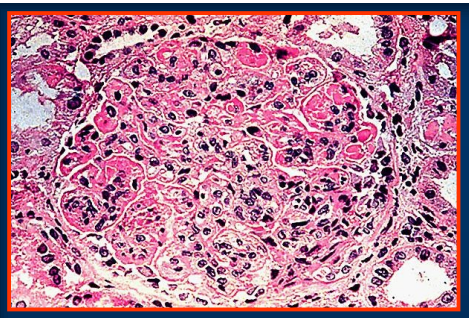

C3 immunoflorescence

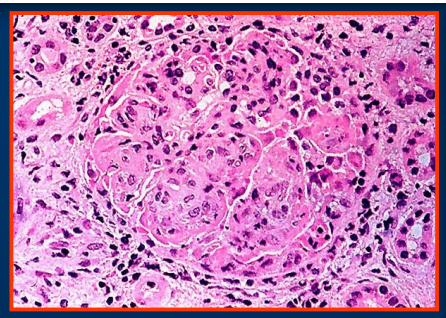
Glomerular damage by antibodies

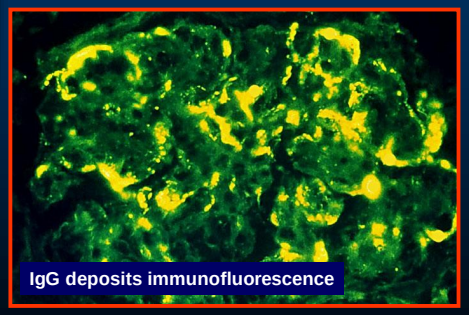


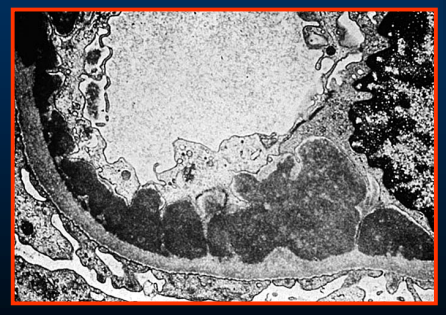
(A) Circulating Ab-Ag complexes, (C) Ab-Ag complexes created in situ
(B) Antibodies against basement membrane

From: Kumar, Robins:2004



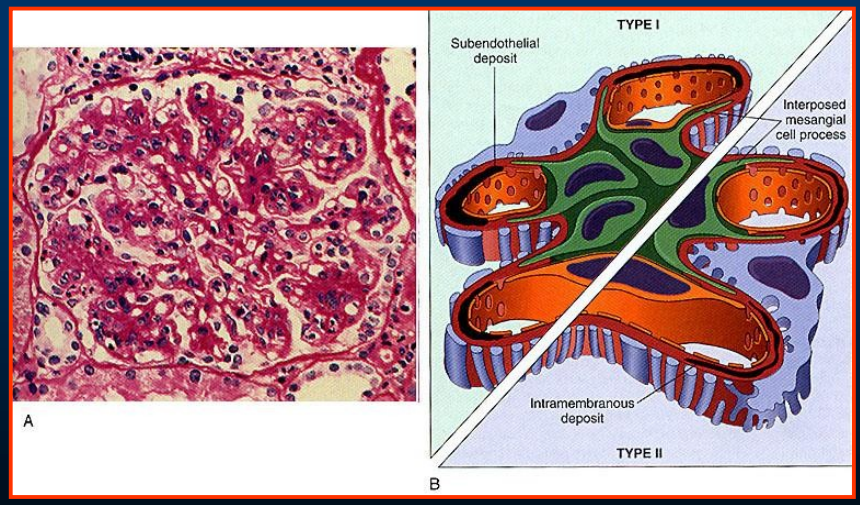






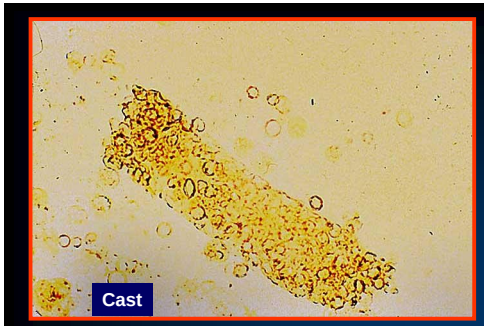
Proliferative Glomerulonephritis - Systemic Lupus

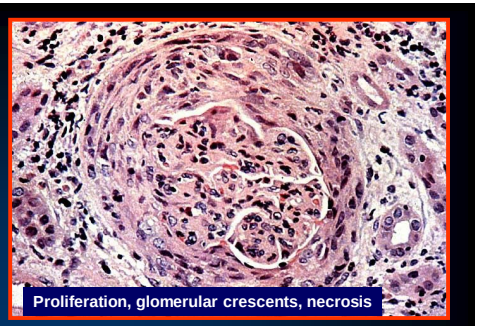
Membranoproliferative Glomerulonephritis

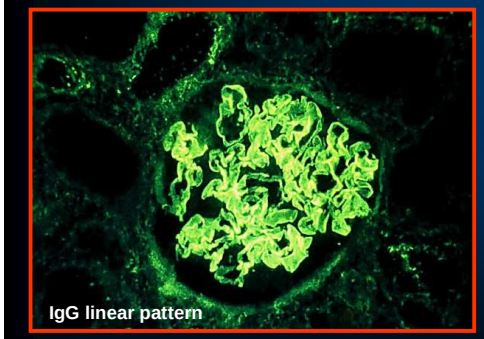


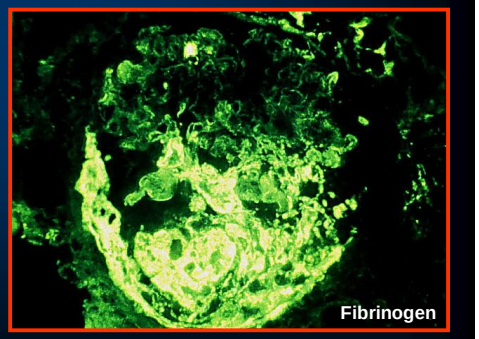
Mesangial proliferation,basement membrane thickening, leukocyte infiltration and accentuation of lobular architecture.Type I and Type II MGN .

From: Kumar, Robins:2004









Acute nephritic syndrome Goodpasture's syndrome

2. Nephrotic syndrome (Nephrosis)

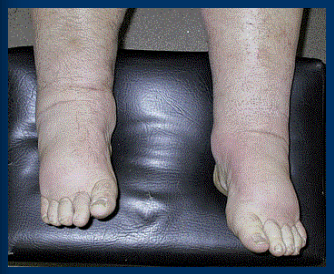
Definition: manifestations and lab. findings evidences for heavy damage in glomerular filtration barrier; main features: **proteinuria + edemas**

Symptoms:

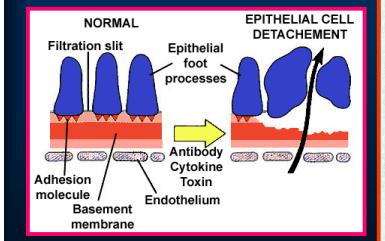
- **heavy proteinuria** (> 3,5 g/d) foamy urine; selective proteinuria (low-molecular – loss of Albumin) or non-selective
- **hypoalbuminemia** (< 3 g/d) → ↓ oncotic blood pressure → leak of liquide into interstitium → **hypovolemia** → hyperaldosteronism → reapsorption of NaCl + water
- **generalized edemas** – face, periorbit, ev. ascites (kids, young adults), ankle swelling (adults)
- **hyperlipidemia** – liver compensated losses of proteins by overproduction; they are mostly lost in urine except lipoprotein particles leading to relative abundance of LDL → atherosclerosis
- **recurrent infections** – are due to losses of immunoglobulins (Ig) and complement in urine
- **oliguria** (rarely anuria) – is due to capillary and basemesnt mambrane thickening

Nephrotic syndrome - Causes

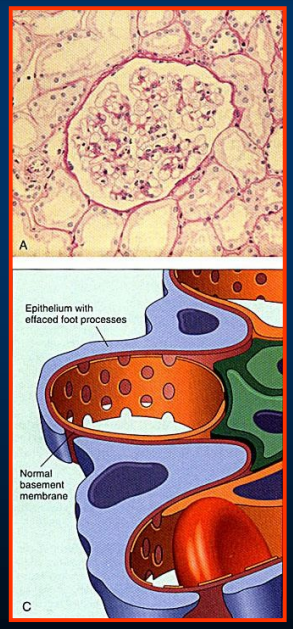
	Children	Adults
Primary Glomerular Disease	95%	60%
• Membranous glomerulonephritis (GN)	5	30 – 40
• Minimal change disease	65	10 – 15
• Focal segmental glomerulosclerosis	10	15 – 35
• Membranoproliferative glomerulonephritides	10	7 – 10
• Other proliferative glomerulonephritis (focal, "pure mesangial," IgA nephropathy)	10	15 - 25
Systemic Diseases	5%	40%
• Diabetes mellitus, Amyloidosis, Systemic lupus erythematosus		35%
• Drugs (nonsteroidal anti-inflammatory, penicillamine, "street heroin")		
• Malignant disease (carcinoma, lymphoma)		5%
• Infections (malaria, syphilis, hepatitis B and C, acquired immunodeficiency syndrome)		
• Miscellaneous (bee-sting allergy, hereditary nephritis)		



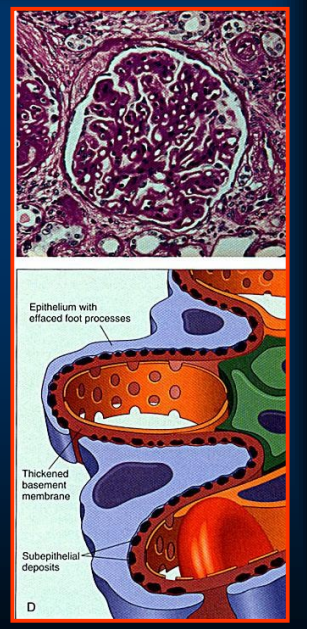
Edema around ankles



Normally, the base-ment cell membrane does not filter large molecules such as albumin (70,000 kD).

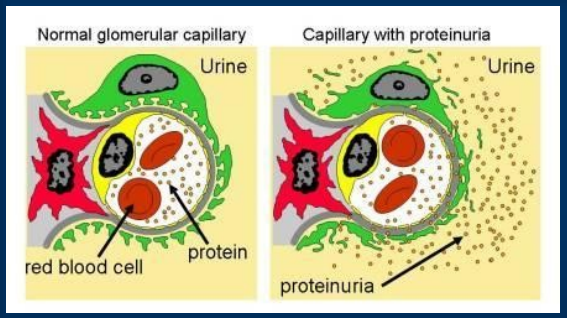


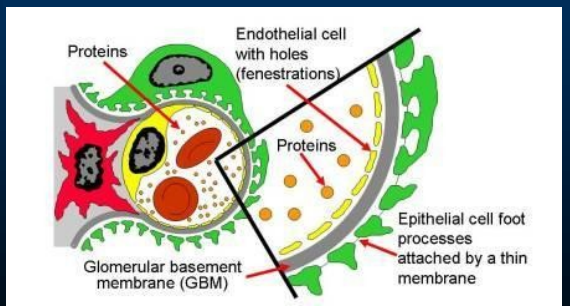
Lipoid nefrosis



Membrane GN

From: Kumar, Robins:2004





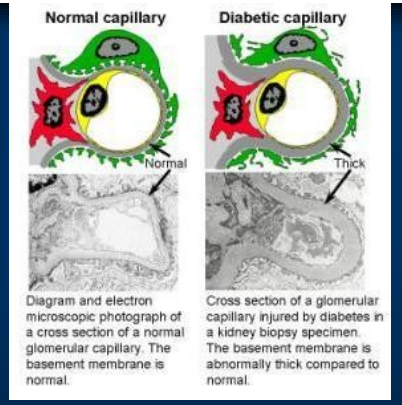
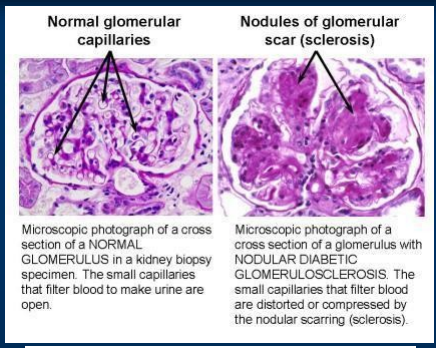


Diagram and electron microscopic photograph of a cross section of a normal glomerular capillary. The basement membrane is normal.

Cross section of a glomerular capillary injured by diabetes in a kidney biopsy specimen. The basement membrane is abnormally thick compared to normal.

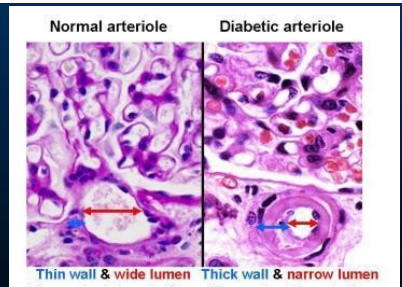
Diabetic Glomerulosclerosis

- thickening of the basement membrane; nodules of scars (sclerosis) in the glomeruli
- sclerosis in the walls of arteries (arteriosclerosis) and arterioles (arteriolosclerosis) in the kidneys and other tissues



Microscopic photograph of a cross section of a NORMAL GLOMERULUS in a kidney biopsy specimen. The small capillaries that filter blood to make urine are open.

Microscopic photograph of a cross section of a glomerulus with NODULAR DIABETIC GLOMERULOSCLEROSIS. The small capillaries that filter blood are distorted or compressed by the nodular scarring (sclerosis).



Microscopic photograph of a cross section of a normal arteriole next to a glomerulus. The lumen is wide open to allow normal flow of blood.

Microscopic photograph of a cross section of an arteriole with diabetic arteriolosclerosis. The lumen is narrowed by the thick wall thus reducing flow of blood.

2

Tubulointerstitial disorders

Tubulointerstitial Nephritis
Acute pyelonephritis
Chronic pyelonephritis
Drug-Induced interstitial nephritis

Acute tubular necrosis

Acute interstitial nephritis (AIN)

Mechanisms

- Renal interstitial inflammation
- T-Cell mediated Hypersensitivity Reaction

Causes

Infection

Diphtheria (classic), Group A beta hemolytic Streptococcus (classic) Legionella Yersinia Staphylococcus or Streptococcus infection

Mycobacterium , Toxoplasmosis , Mycoplasma Leptospira, Rickettsia Syphilis

Herpes viruses (e.g. CMV, EBV, HSV) , Human Immuno-deficiency Virus (HIV), Hantavirus Hepatitis C Mumps

Medications
(AIN occurs >2 weeks after drug started)

Penicillins, Cephalosporins, Sulfonamides, Vasculitis reaction
NSAIDs Nephrotic Syndrome type reaction
Rifampin Diuretics, Allopurinol
Other medications have caused AIN to a lesser extent

Miscellaneous conditions

Glomerulonephritis
Necrotizing Vasculitis
Systemic Lupus Erythematosus
Acute kidney transplant rejection

Tubulointestitial disorders - Causes

Infections

Acute bacterial pyelonephritis
Chronic pyelonephritis (including reflux nephropathy)
Other infections (e.g., viruses, parasites)

Toxins

Drugs, Analgesics
Acute hypersensitivity interstitial nephritis
Heavy metals Lead, cadmium

Metabolic Diseases

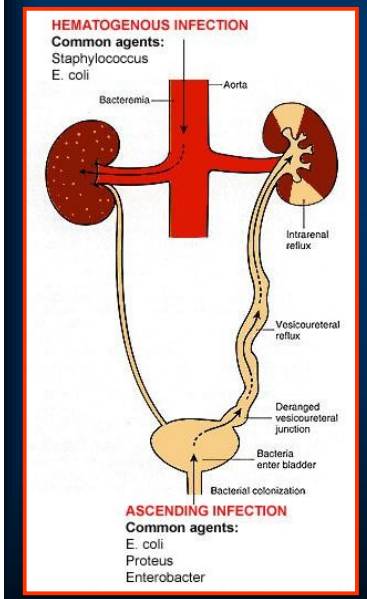
Urate nephropathy
Nephrocalcinosis (hypercalcemic nephropathy)
Hypokalemic nephropathy
Oxalate nephropathy

Physical Factors

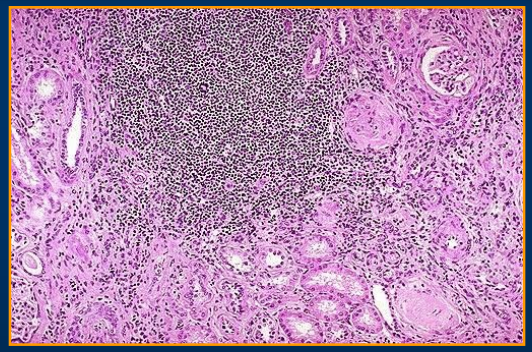
Chronic urinary tract obstruction
Radiation nephropathy

Neoplasms

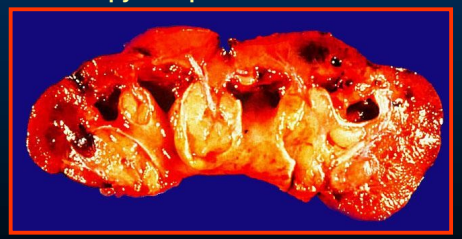
Multiple myeloma (cast nephropathy)



Spread of infection



Chronic pyelonephritis



Hydronephrosis and chronic obstructive pyelonephritis

Acute interstitial nephritis (AIN)

Symptoms and Signs

- Classic triad
  - § Low grade fever (>70% of cases)
  - § Rash (>30% of cases)
  - § Arthralgia (>15% of cases)
- Acute renal failure (15% of cases)
  - § Oliguria, Malaise, vomiting
- Recovery in weeks if cause eliminated within 2 weeks
- Poor prognosis in interstitial fibrosis

Laboratory findings

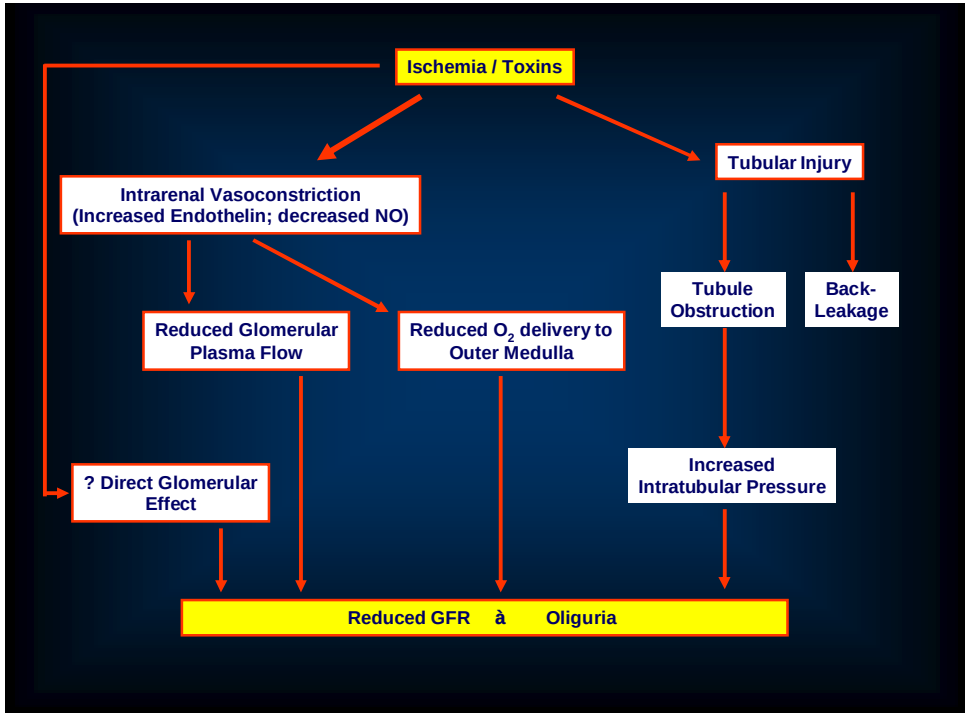
- Urine
  - § Eosinophiluria, Proteinuria,
  - § Creatinine increased
  - § Uremia
  - § Hyperchloremic metabolic acidosis

Renal biopsy

- Inflammation of renal interstitium
  - § Mononuclears, T-Lymphocytes
- Glomerular and vascular sparing

Management

- Corticosteroids Prednisone 1 mg/kg/day for 2 weeks, Cyclophosphamide in steroid non-responders
- Optimization of fluid status, electrolyte abnormalities and hyperkalaemia
- Symptomatic relief of fever and arthralgias



Acute Tubular Necrosis

Characterisation:

- destruction of epithelial tubular cells, cells "slough off" from the BM; casts plug the tubules; BM may be destroyed too
- fail to excrete urine even when renal blood flow is restored
- If the BM remains intact, new epithelia grow along BM within 10 to 20 days.

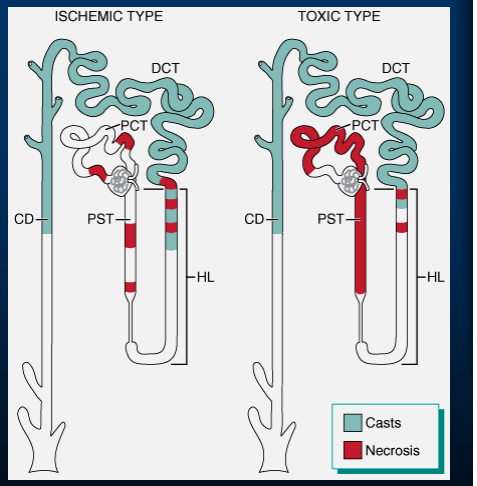
Causes:

Severe ischemia (shock kidney)

- circulatory shock - inadequate supply of oxygen and nutrients to the tubular epithel

Renal poisons - specific toxins to epithel

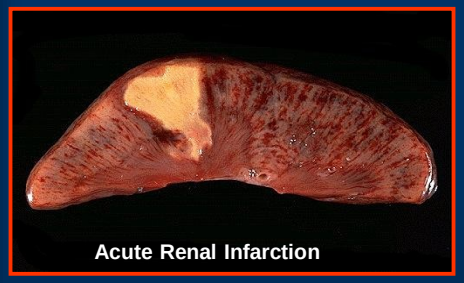
- carbon tetrachloride, Hg, Cd, Pb, ethylene glycol (antifreeze), insecticides, medications (tetracyclines), cis-platinum



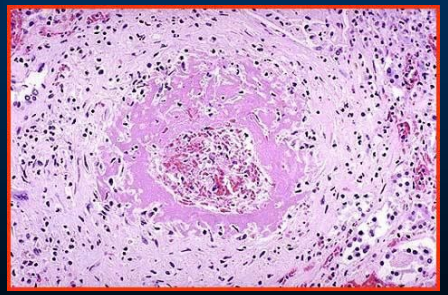
3

Renovascular disorders

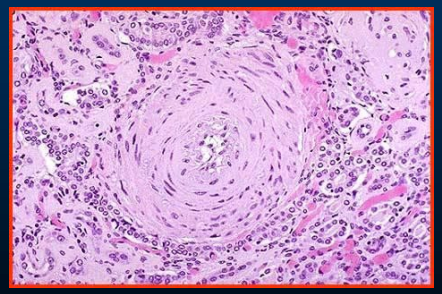
Benign nephrosclerosis
Malignant hypertension
Malignant nephrosclerosis
Thrombotic microangiopathies



Acute Renal Infarction



Malignant hypertension → fibrinoid necrosis of small arteries = formation of pink fibrin



Thickening of arterial wall with hyperplastic arteriolitis "onion skin"appearance

Cystic Diseases of the Kidney

Definition:

- heterogeneous group comprising hereditary, developmental but nonhereditary, and acquired disorders.
- common and often represent diagnostic problems for clinicians, radiologists, and pathologists;
- some forms, such as adult polycystic disease, are major causes of chronic renal failure
- can occasionally be confused with malignant tumors

Classification

1. Cystic renal dysplasia
2. Polycystic kidney disease

a. Autosomal-dominant (adult) polycystic disease
b. Autosomal-recessive (childhood) polycystic disease

3. Medullary cystic disease

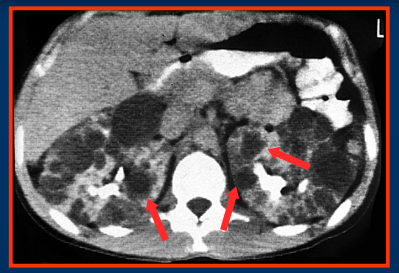
a. Medullary sponge kidney
b. Nephronophthisis

4. Acquired (dialysis-associated) cystic disease
5. Localized (simple) renal cysts
6. Renal cysts in hereditary malformation syndromes (e.g., tuberous sclerosis)
7. Glomerulocystic disease
8. Extraparenchymal renal cysts (pyelocalyceal cysts, hilar lymphangitic cysts)

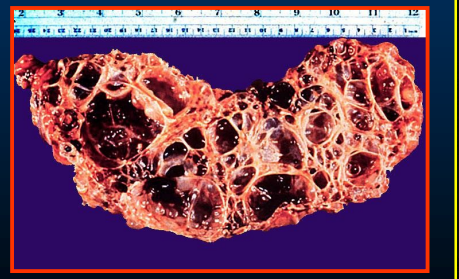
4

Cystic diseases of kidney

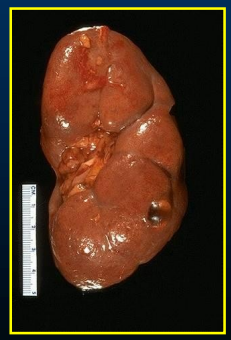
Autosomal Recessive Polycystic Kidney Disease (infant)

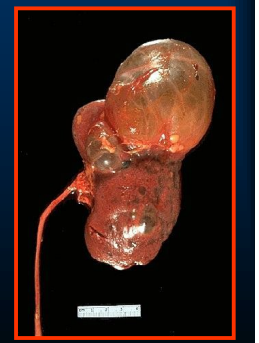


Autosomal Dominant Polycystic Kidney Disease (adults)



Polycystic Kidney Disease (adults)





Simple Cysts

Autosomal Dominant Polycystic Kidney Disease (ADPKD)

- mutation in one of two kidney building block proteins - polycystin 1 and polycystin 2 (genes PKD1 and PKD2).
- Children can be born with severely enlarged kidneys (the size of normal adult kidneys) and can have immediate kidney failure at birth

Autosomal Recessant Polycystic Kidney Disease (ARPKD)

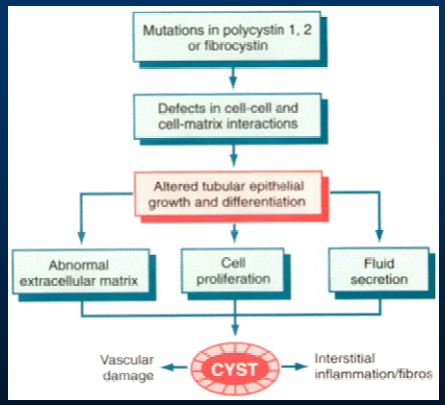
- mutation in a kidney building block protein called fibrocystin (gene PKHD1) found in up to 90% of people
- born with severely enlarged kidneys, high blood pressure, cysts and scarring of the liver

5

Kidney stones

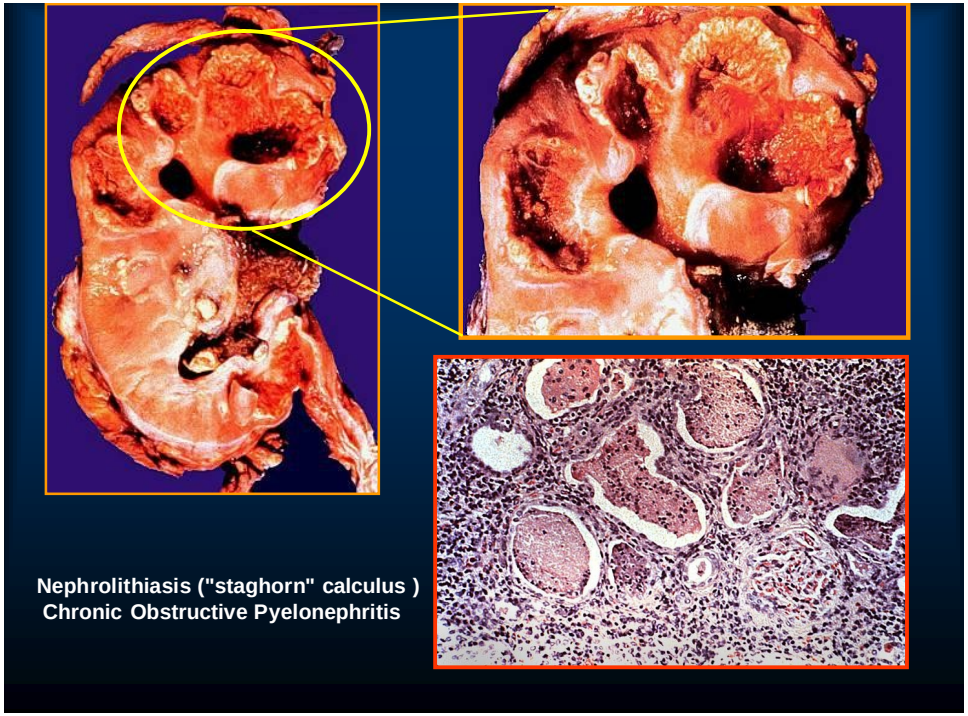
CYSTIC RENAL DYSPLASIA

- Occure unilaterally or bilaterally; kidney is usually enlarged, extremely irregular, and multicystic cysts vary microscopic several centimeter
- Abnormal lobar organization. immature collecting ductules, islands of undifferentiated mesenchyme, often with cartilage
- Most cases are associated with ureteropelvic obstruction, ureteral agenesis or atresia, and other anomalies of the lower urinary tract.



Possible mechanisms of cyst formation in polycystic kidney disease

Types	Frequency
Calcium oxalate (or phosphate)	75%
Magnesium ammonium phosphate (struvite, or "triple phosphate")	12%
Uric acid	6%
Cystine	1%
Other	6%



Nephrolithiasis ("staghorn" calculus)
Chronic Obstructive Pyelonephritis