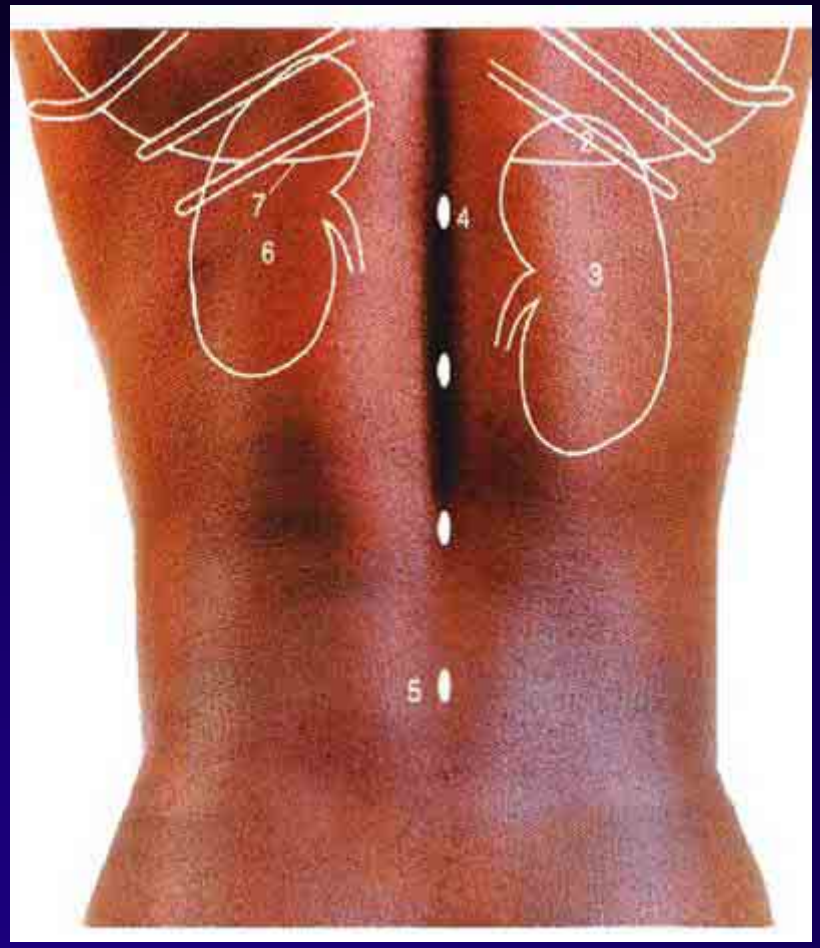
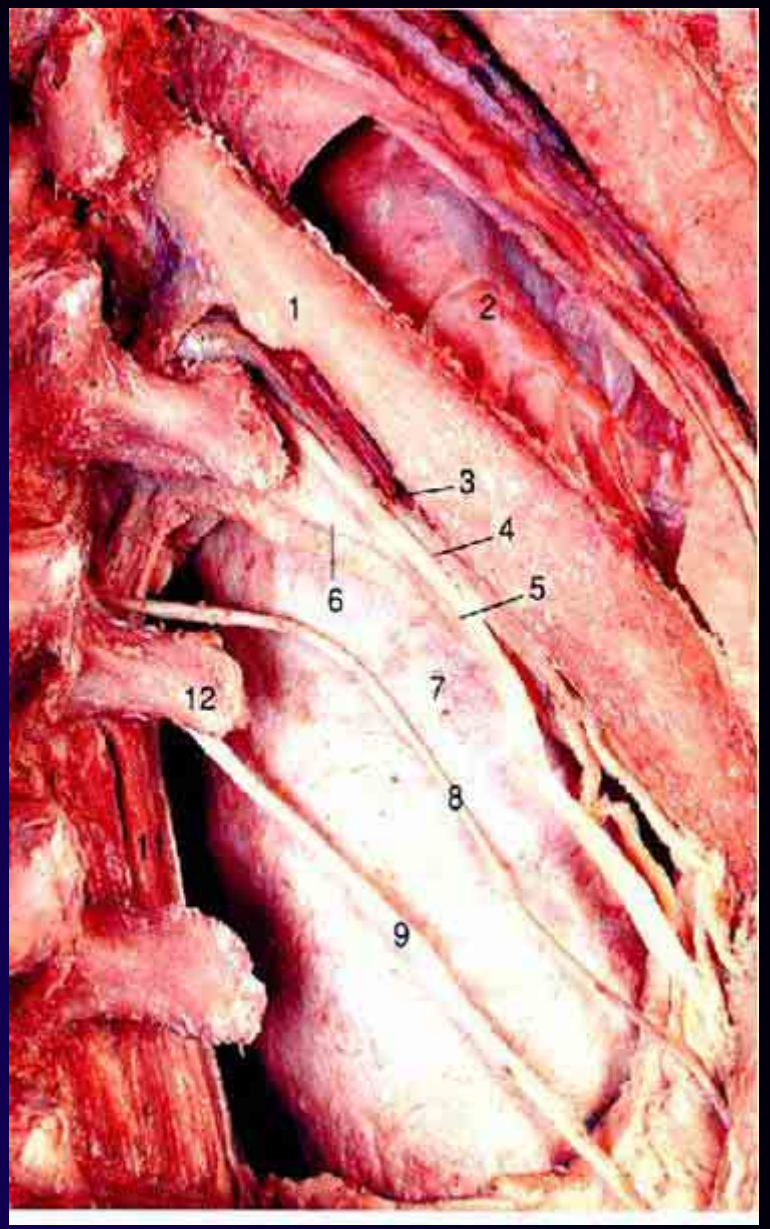
Pathology of Kidney Disorders

Anatomy-Kidney

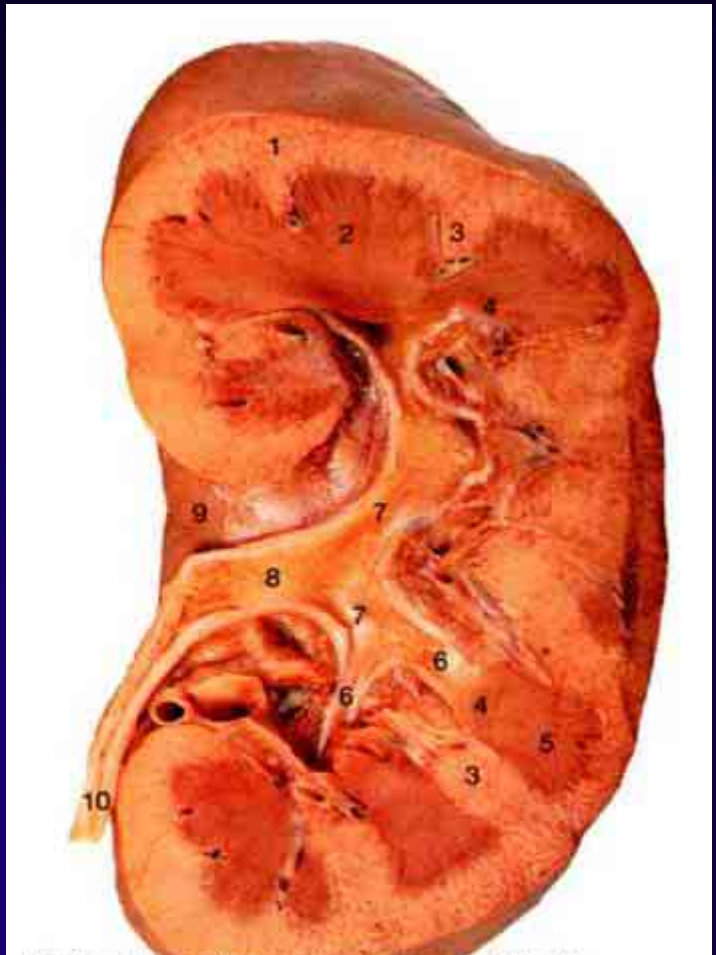




Components of Glomerulus:

- Capillary basement membrane
- Mesangium
- Bowman capsule
- Cells
  - Endothelial
  - Epithelial
  - Mesangial

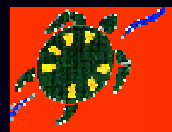
Anatomy of Kidney



Color Atlas of Human Anatomy, 3rd Ed.
McMinn, RMH, et al editors
Mosby Year Book Co.,
St. Louis, 1993

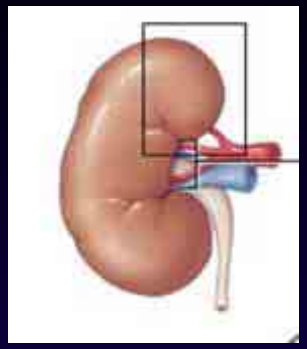
Anatomic Compartments

- Glomerulus
- Tubules
- Blood vessels
- Interstitium
- Collecting system
- (Callices & Pelvis)

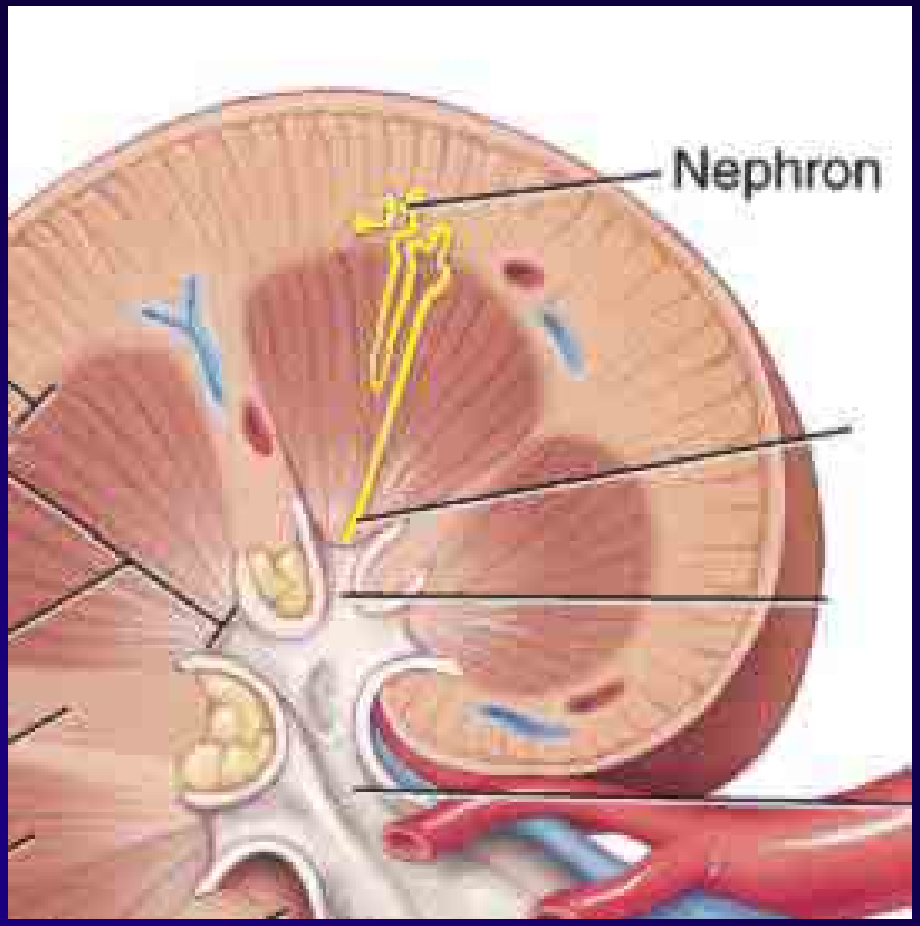


Kidney Functions:

- Excretion metabolic waste/drugs.
- Water/fluid balance.
- Electrolyte balance.
- Acid-base balance.
- Blood pressure.
- Erythropoietin secretion.



Anatomy of Kidney



Note the positions of

Glomerulus

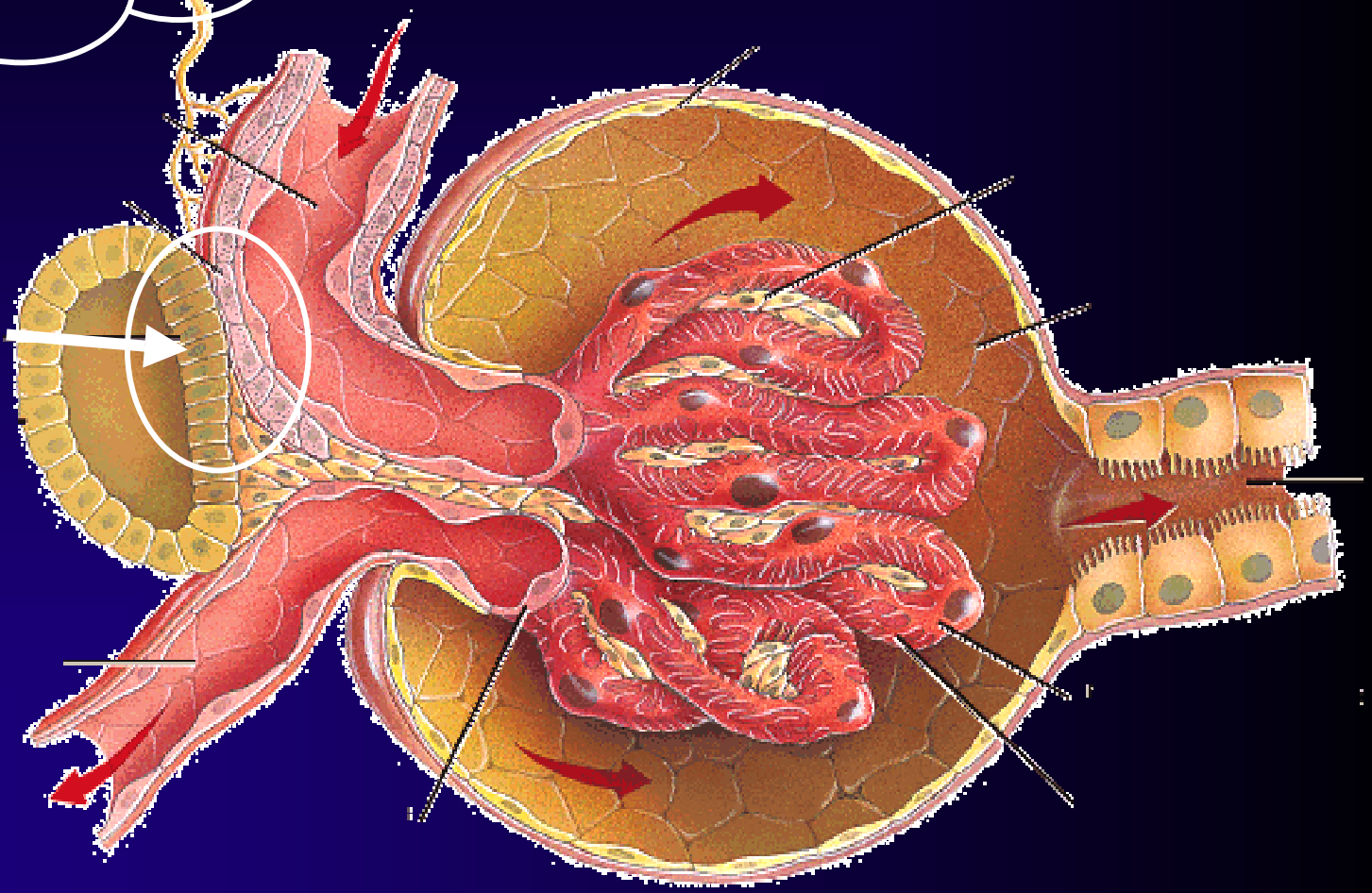
Loop of Henley

PCT, DCT, CT

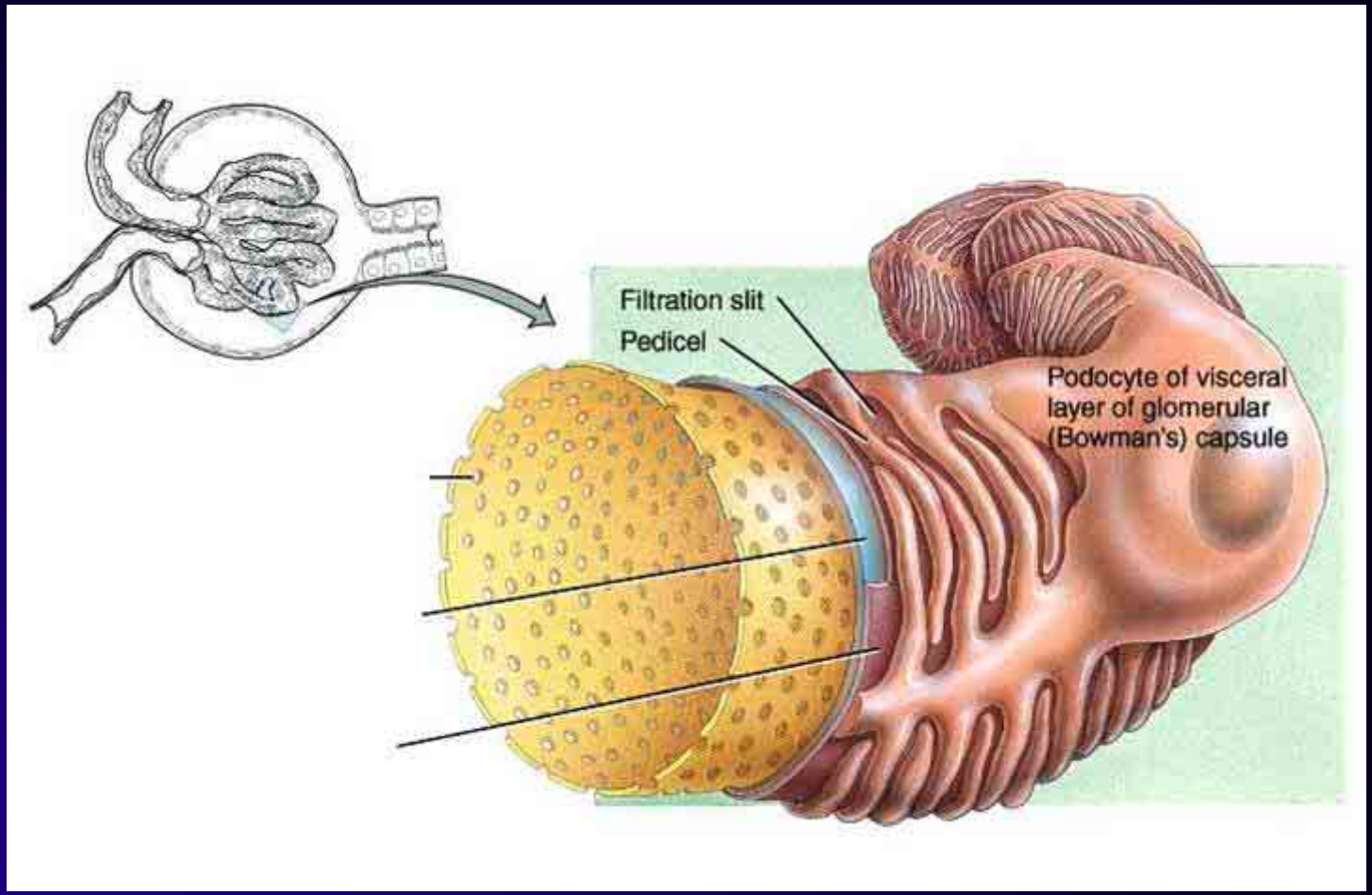
Cortex, Medulla, Pelvis.

GFR → Renin
→Angiotensin
Blood Pressure

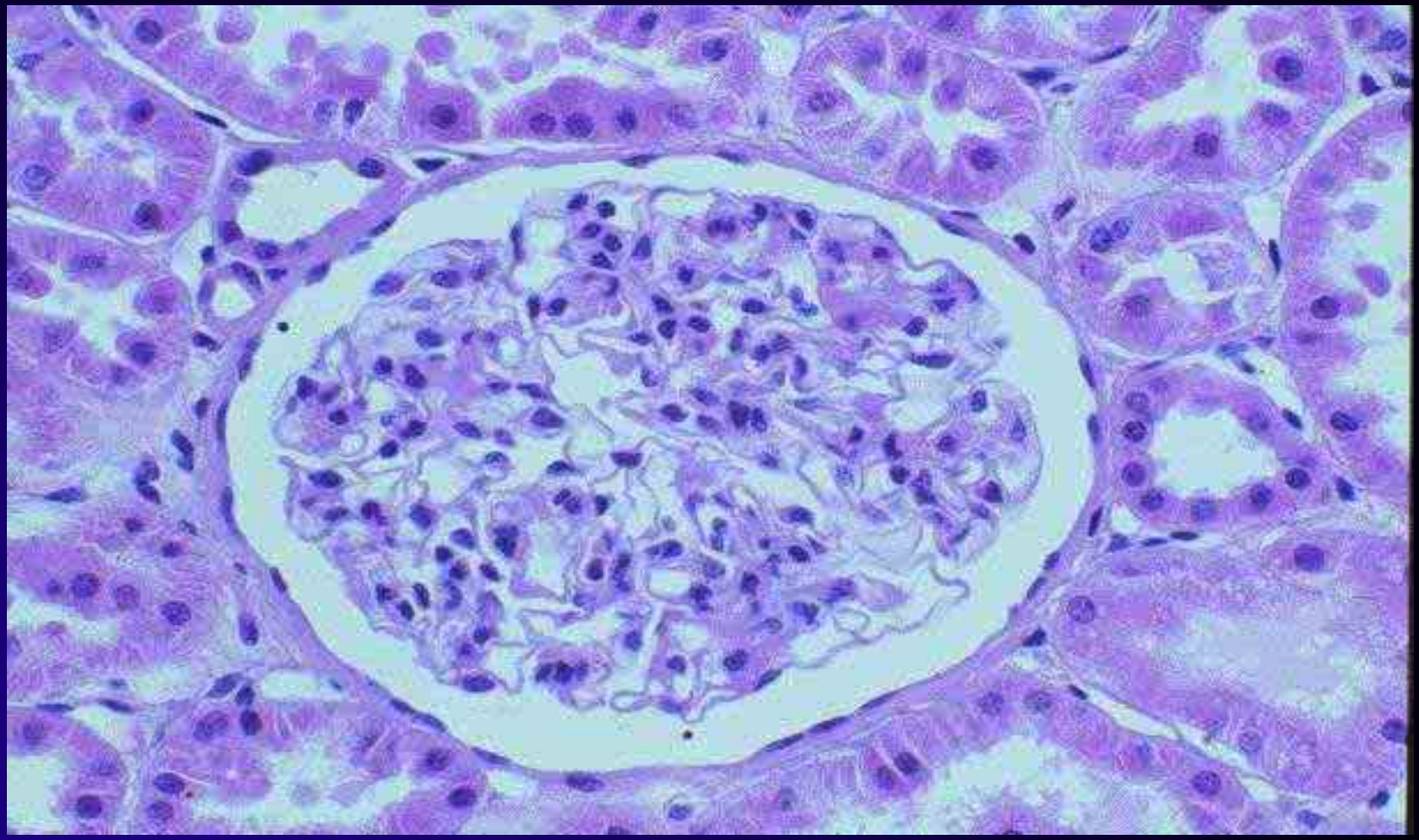
JGA



Filtration Membrane:



Normal Kidney:



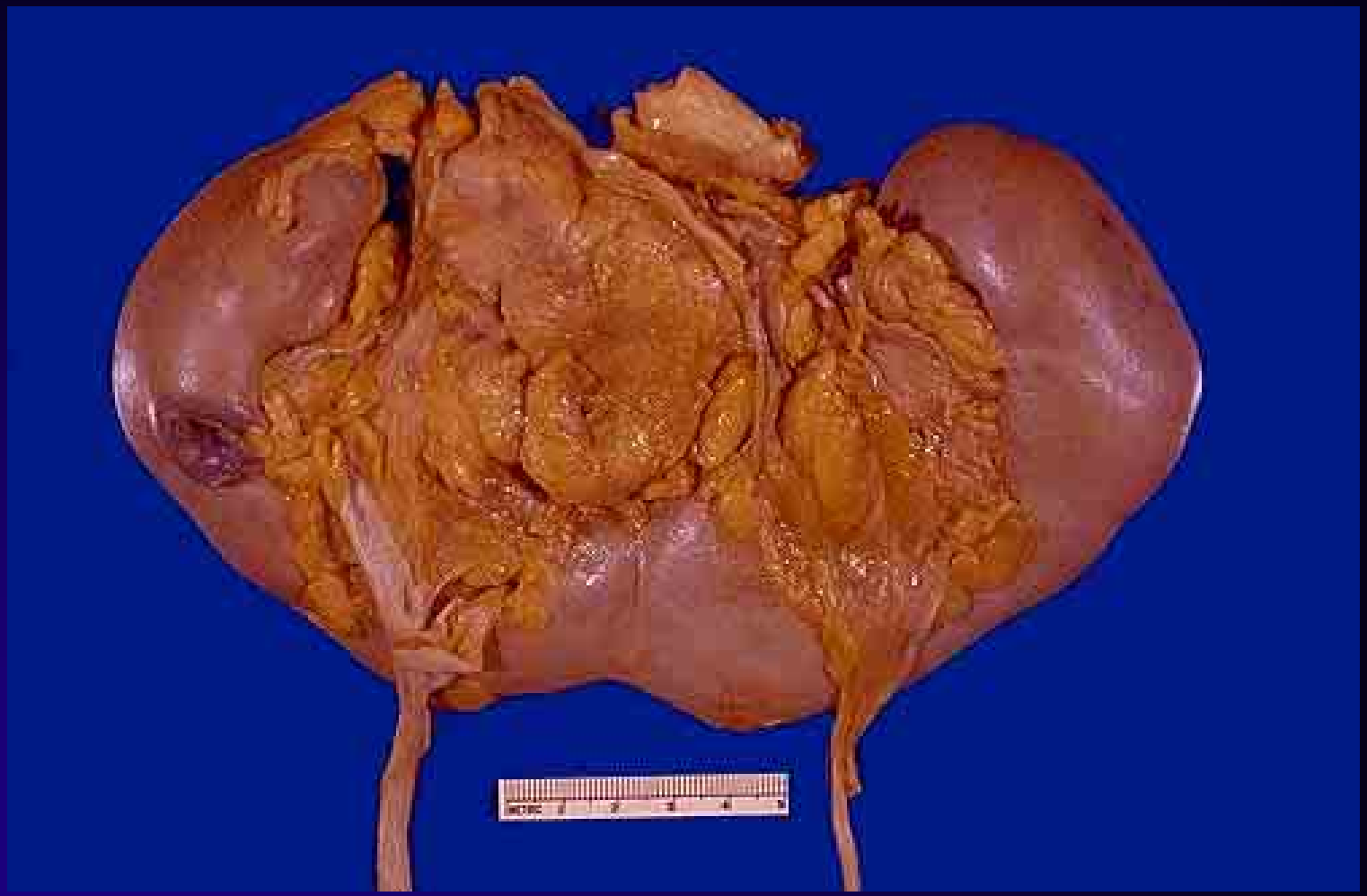
Kidney Diseases

- Developmental disorders
- Glomerular diseases
- Tubulo-interstitial diseases
- Urinary stones
- Obstructive uropathy
- Tumors

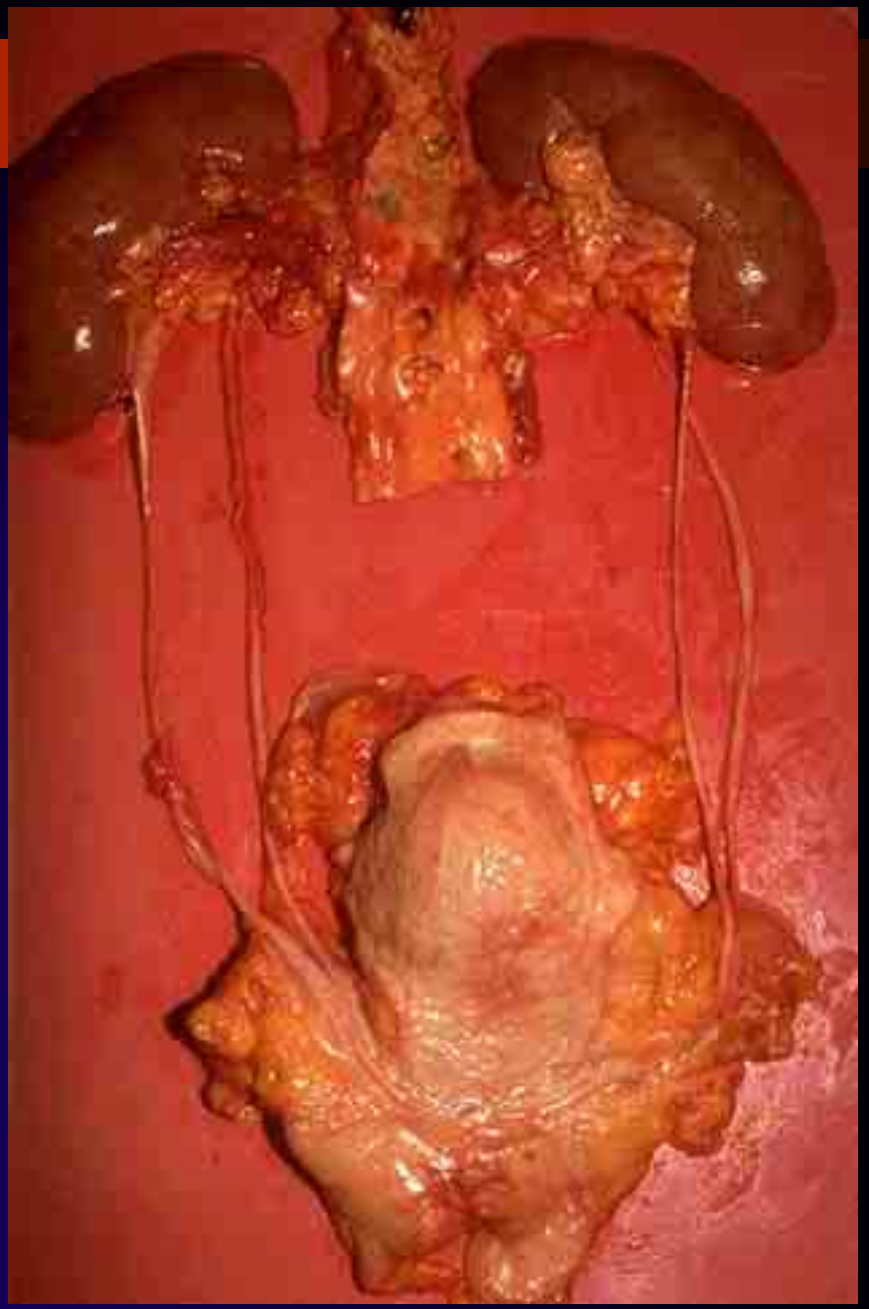
Congenital Anomalies:

- Agenesis – Potter syndrome
- Ectopia
- Fusion
- Dysplasia
- Simple cysts
- Polycystic kidney disease

Horse Shoe Kidney

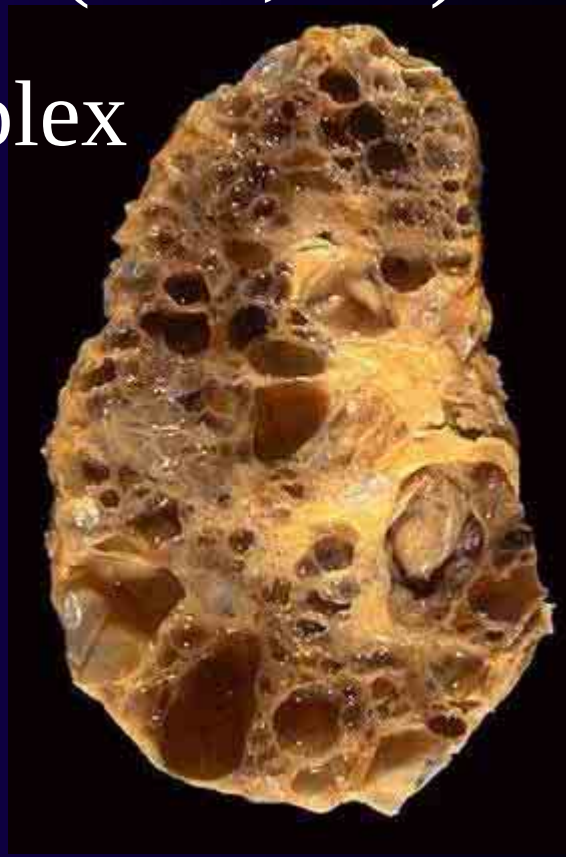


Double Ureter:



Polycystic kidney disease

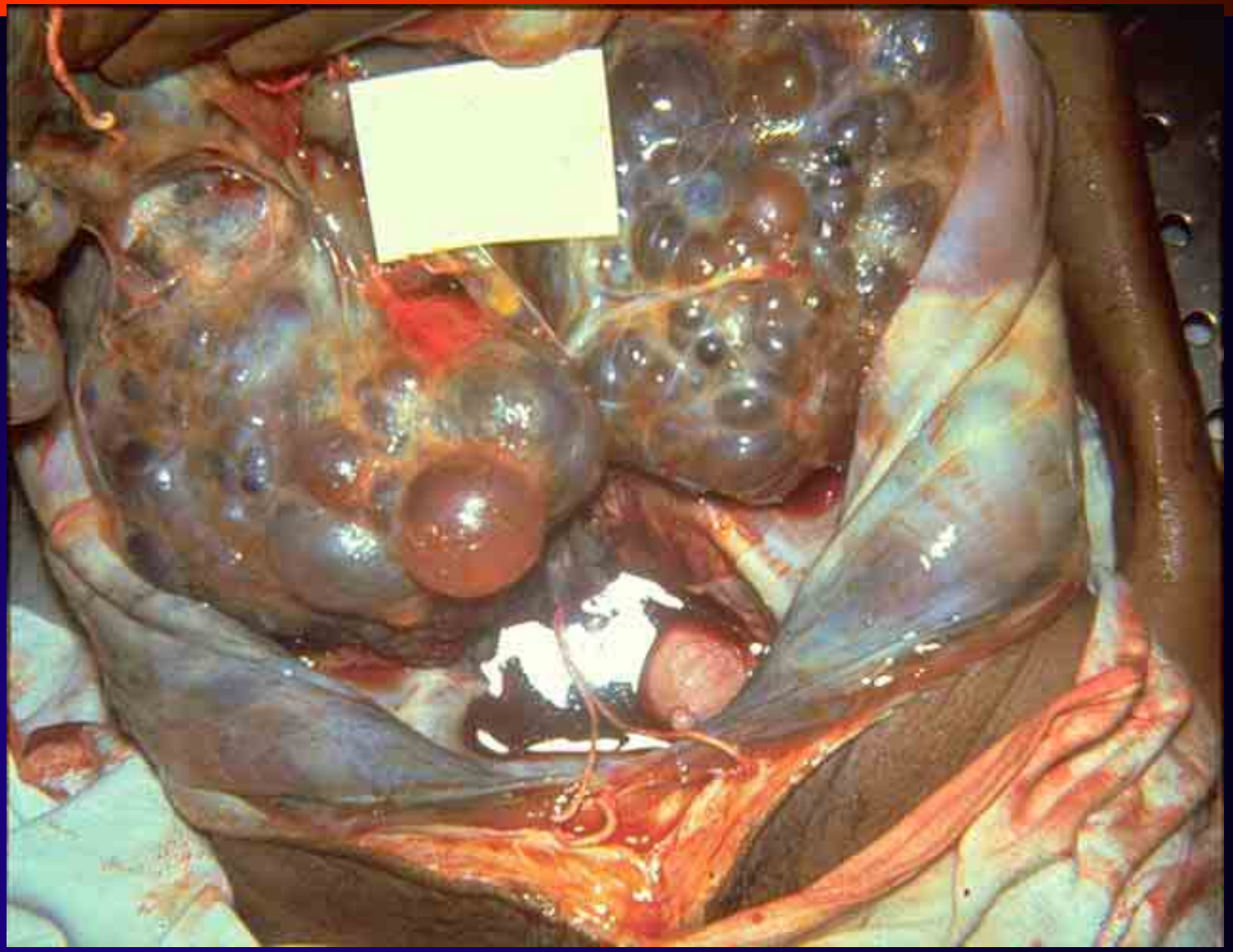
- Autosomal dominant (adult) (1:1,000)
- Autosomal recessive (infantile (1:30,000)
- Medullary cystic disease complex (1:10,000)
- Medullary sponge kidney
- Acquired cystic renal disease



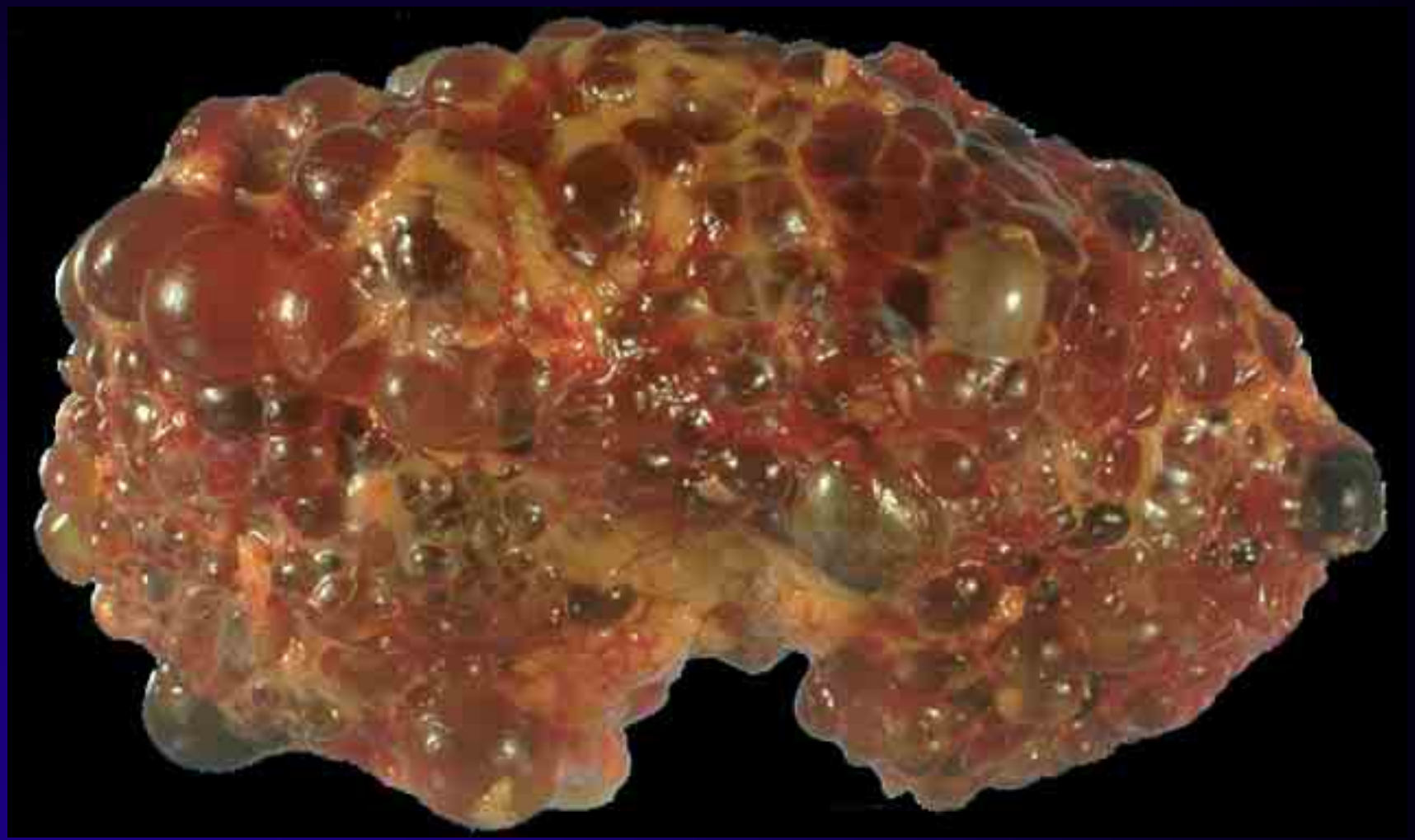
Autosomal Dominant PKD

- Common kidney disease (1:1,000)
- 10% of all transplant/dialysis patients
- ADPKD-1 gene (polycystin) mutation 85%
- Bilaterally enlarged kidneys (>3,000g)
- Symptoms appear in adult life
- Renal failure 5-10 years thereafter

ADPKD:



ADPKD:



ADPKD Associated Conditions

- Liver cysts (30%)
- Splenic cysts (10%)
- Pancreatic cysts (5%)
- Cerebral aneurysms (20%)
- Diverticulosis coli

Kidney Disorders – clinical.

A	Asymptomatic hematuria/proteinuria
N	Nephrotic syndrome
N	Nephritic syndrome
U	Urolithiasis
R	Rapidly progressive glomerulonephritis
I	Interstitial and tubular diseases
C	Chronic renal disease

“To be a great champion you must believe you are the best. If you’re not, pretend you are.”

– Muhammad Ali

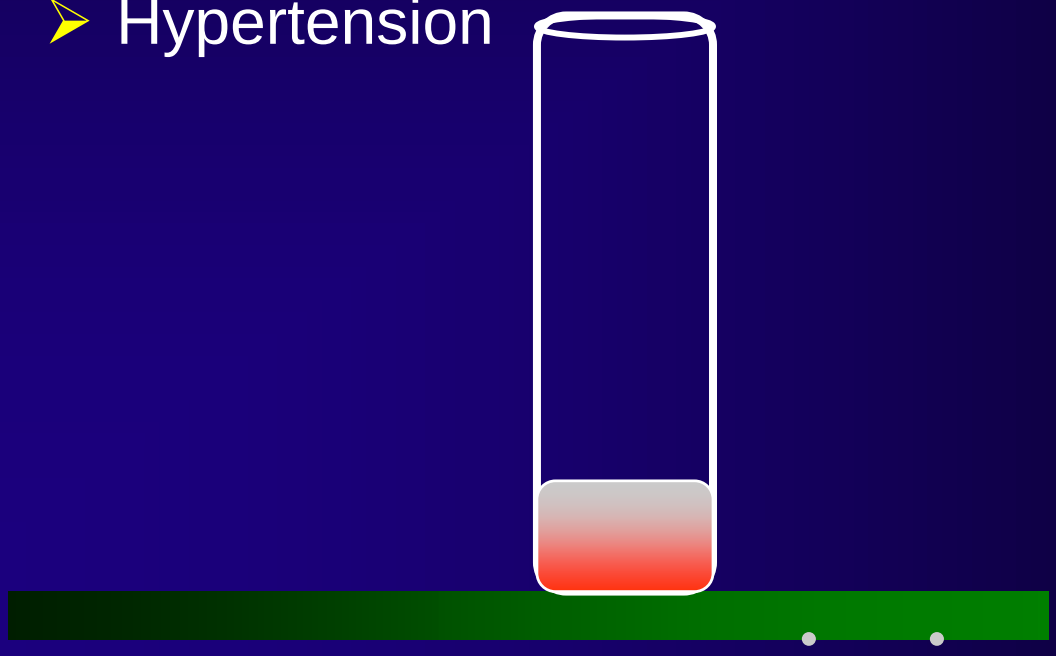
Glomerular Disorders:

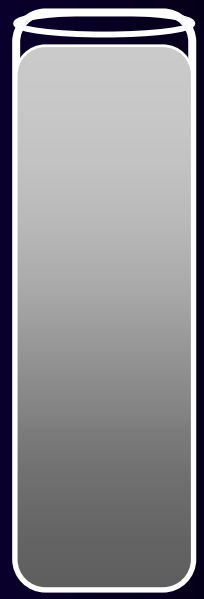
Nephritic

- Hematuria
- Proteinuria
- Hypoalbuminemia
- Oliguria (GFR↓, Cr↑, BUN↑)
- Edema (salt and water retention)
- Hypertension

Nephrotic

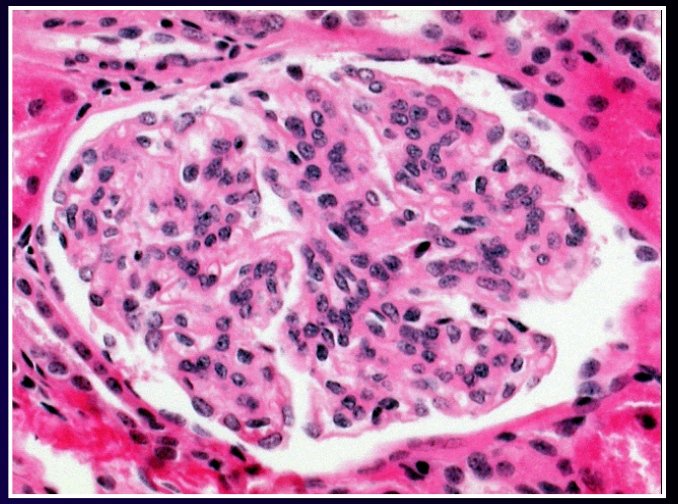
- Proteinuria (“nephrotic range” >3.5g/24h)
- Hypoalbumimenia
- Edema
- Hyperlipidemia
- Lipiduria

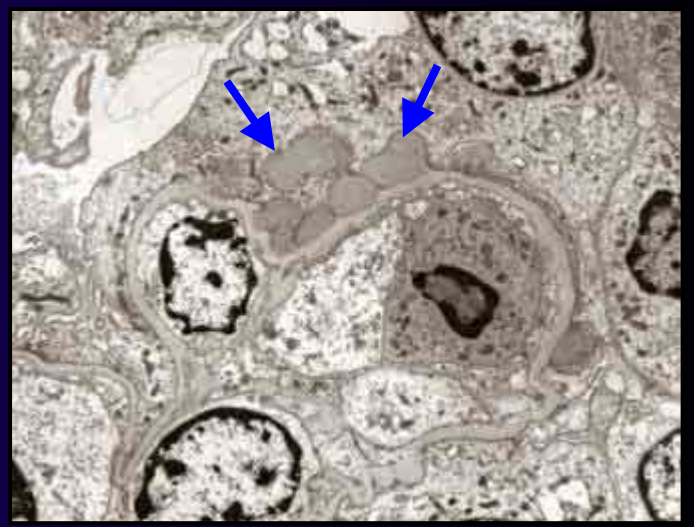




Acute Post Strepto. GN:

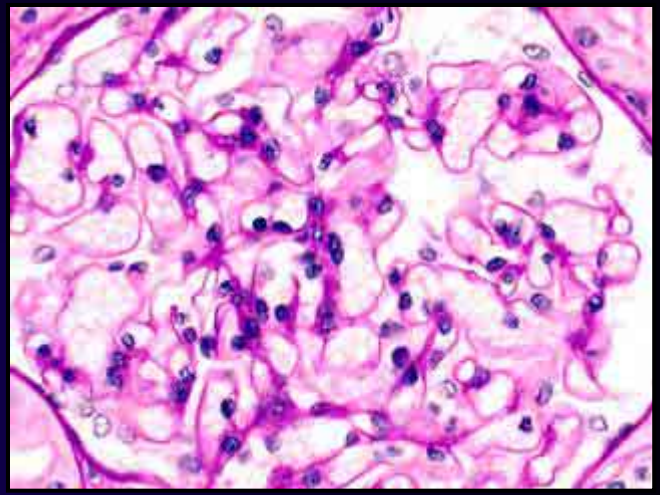
Synonyms:	Acute proliferative glomerulonephritis, acute post-infectious GN.
Incidence:	Peak incidence in children (3-14). Sporatic, mostly winter and spring.
Etiology:	Glomerular trapping of circulating anti-streptococcal immune complexes. Group A, B-hemolytic streptococci, type 12.
Clinical:	Acute nephritic syndrome post-strept pharyngitis or pyoderma. Other infections.
Lab:	Nephritic urine with RBC casts. Evidence of streptococcal infection or serologic evidence of recent infection. Decreased serum complement.
Path:	Enlarged, hypercellular glomeruli with endothelial and mesangial cell proliferation. Acute inflammation. IgG and C3 in very coarsely granular pattern along GBMs. Discrete, subepithelial “hump-like” deposits.
Clinical Course:	Children - Excellent prognosis. Adults - Worse prognosis, some develop progressive disease.

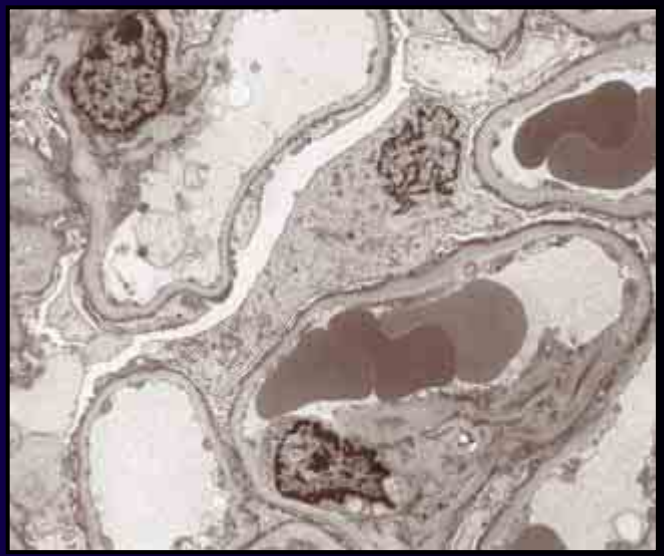




Minimal Change GN:

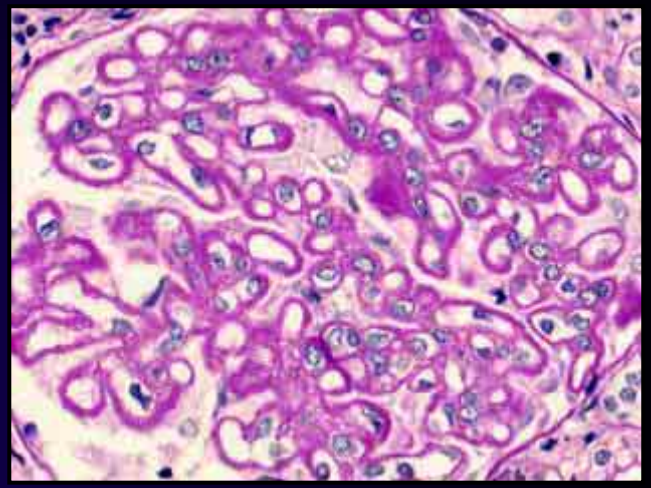
Synonyms:	Nil disease, lipoid nephrosis, foot process disease
Incidence:	80% of nephrotic syndrome in children (1-8 yrs.), mostly male. Adults in 2nd-3rd decade.
Etiology:	Idiopathic. Loss of net negative charge on capillary basement membrane.
Clinical Features:	Nephrotic syndrome. History of recent URI in 30%. Association with Hodgkin's lymphoma. Overlap with FSGS patients.
Lab Features:	Selective proteinuria. No specific laboratory findings.
Pathology	LM - Normal. IF - Negative. EM - Focal fusion/loss of foot processes.
Clinical Course:	Spontaneous remission in 25-40%. Complete remission in 65-70% of patients. Steroid resistant patients may progress to FSGS.

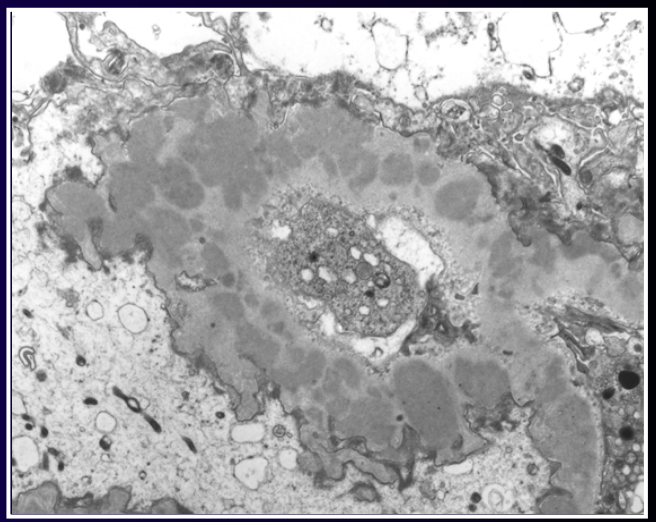




Membranous GN:

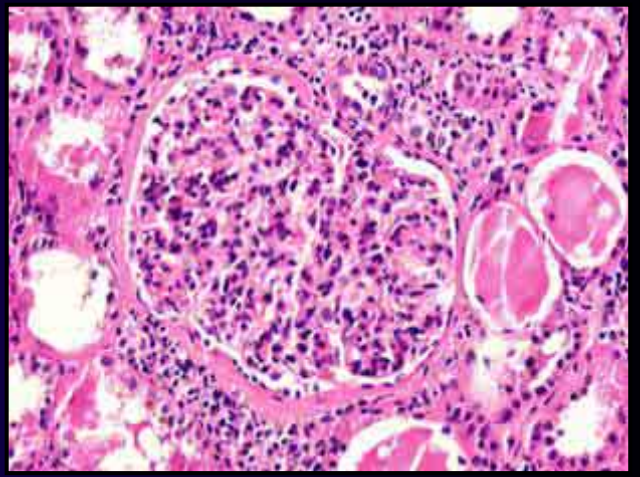
Synonyms:	Epimembranous, extramembranous GN
Incidence:	40-60 Years, 50% of adult nephrotic syndrome.
Etiology:	Immune complex disease. Idiopathic in most patients, associated with infections, drugs, carcinomas, and heavy metals.
Clinical:	Nephrotic syndrome in 80%, asymptomatic proteinuria in 20%. Microscopic hematuria.
Lab:	Non-selective proteinuria ± hematuria.
Path:	Diffuse, uniform BM thickening with subepithelial projections (“spikes”). Diffuse, coarsely granular IgG and C3 deposits along basement membranes. Electron-dense subepithelial deposits.
Clinical Course:	Excellent prognosis in children. Some adults develop ESRD. Exclusion of other diseases is required.

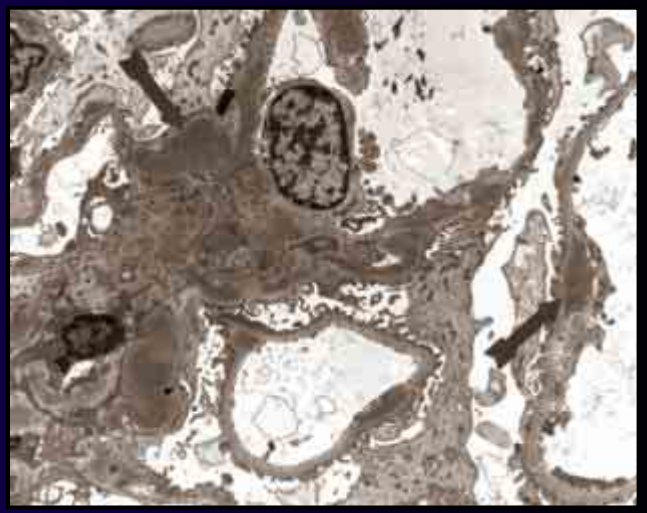




Membranoproliferative GN

Incidence:	Children and young adults (5-25 years).
Etiology:	Chronic immune complex GN. Associated with chronic infections, SLE, cancer, cirrhosis, heroin abuse, etc.
Clinical:	Nephrotic syndrome in 50%, acute nephritic syndrome in 20%. Recent history of URI in 50%. Hypertension and/or renal insufficiency.
Lab:	Hypocomplementemia of classic and alternate pathways. C3 nephritic factor (C3NEF). Circulating immune complexes.
Path:	Diffuse proliferative GN with thickening of the glomerular capillary walls,, and GBM splitting (“tram-tracking”). Diffuse, coarsely granular C3 and IgG deposits along GBMs. Electron-dense subendothelial deposits.
Clinical Course:	Progressive deterioration of renal function ± short remissions. ESRD within 10 years in 50% of children and 80% of adults.





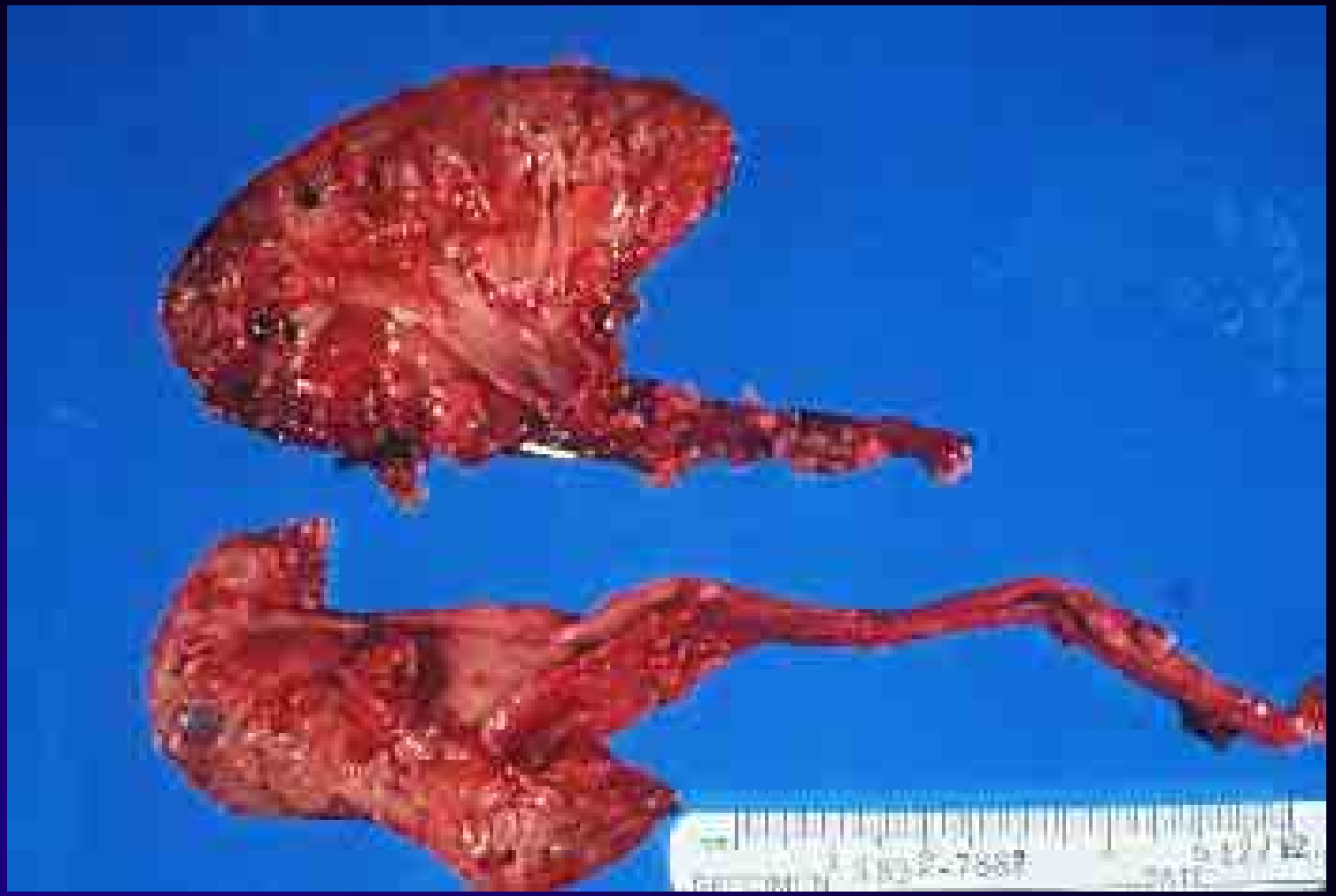
Causes of nephrotic syndrome

Disease	Children(%)	Adults(%)
Minimal change GN	**75**	20
Membanous GN	**5**	**40**
MPGN I	5	5
Other GN	5	20

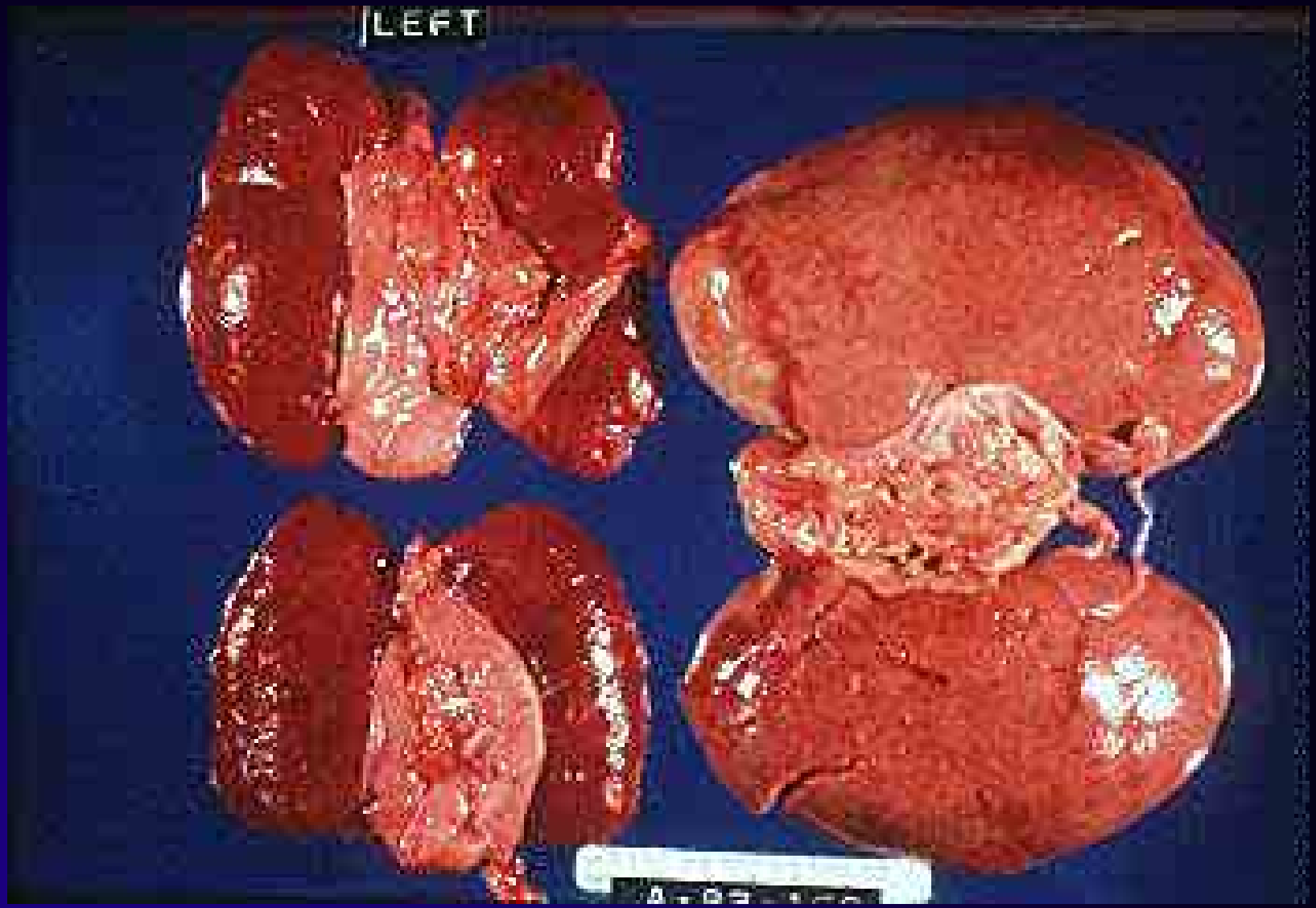
Chronic renal failure (uremia)

- General symptoms – weakness, fatigue
- Cardiovascular – hypertension, pericarditis
- G.I. – nausea, vomiting, diarrhea
- CNS – lethargy, confusion, coma
- Muscles – twitching, weakness
- Bones – osteodystrophy
- Metabolic – acidosis, P↑K↑, BUN↑, Cr↑.
- Endocrine - parathyroids↑

Chronic Renal Failure: ESKD



CRF- ESKD with transplant:



Diabetic kidney diseases

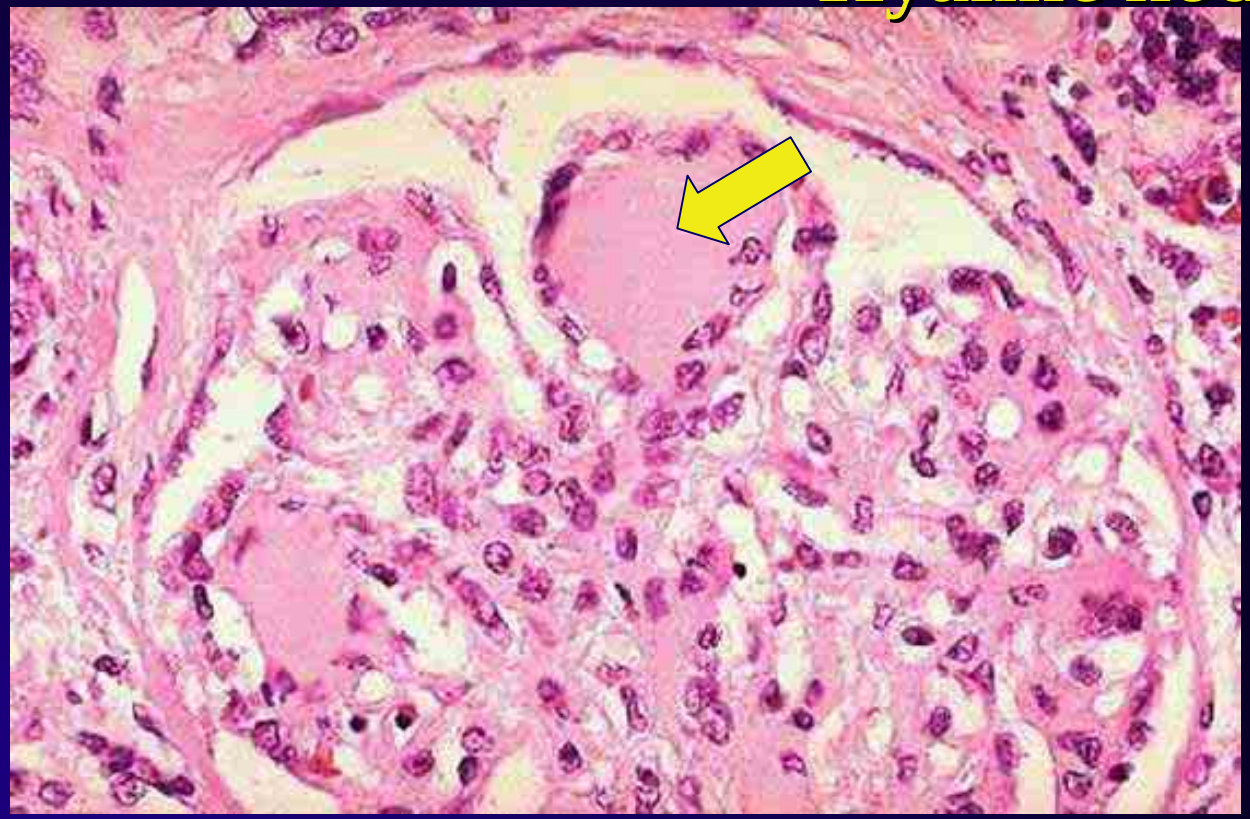
- Glomerulosclerosis
- Arteriolosclerosis → Hypertension
- Pyelonephritis
- Papillary necrosis

Diabetic glomerulosclerosis

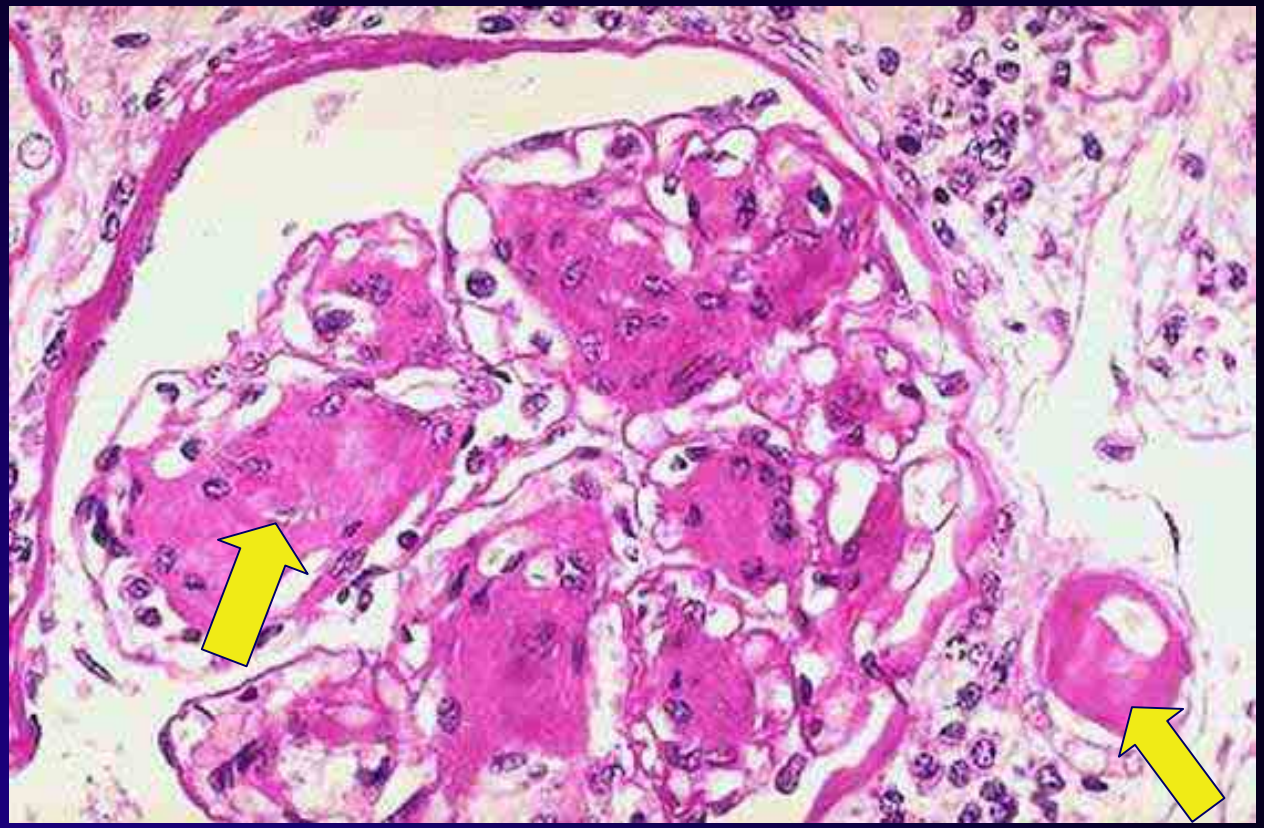
- Diabetes BM thickening Proteinuria→ renal failure (leading cause of mortality in DM)
- nonenzymatic glycation (?), BM synthesis ↑, leaky.
- Pathology:
  - Diffuse global thickening of BM
  - Nodular sclerosis (K-W)
  - Arteriolosclerosis
  - Trapping of serum proteins
- Clin: Proteinuria (in 50% diabetics)
- ESKD (30%)

Diabetic Glomerulosclerosis

Hyaline nodules



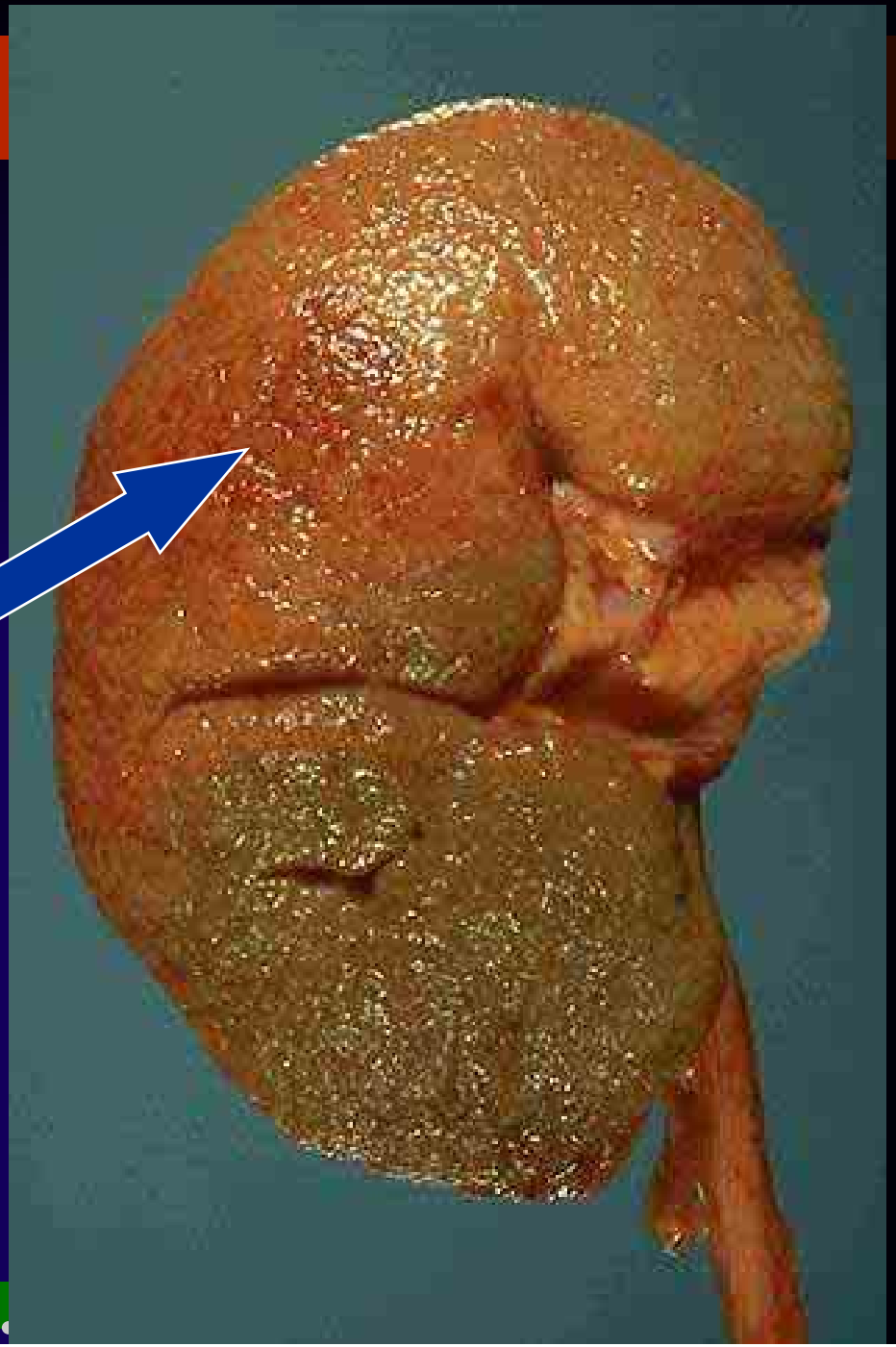
Diabetic Glomerulosclerosis



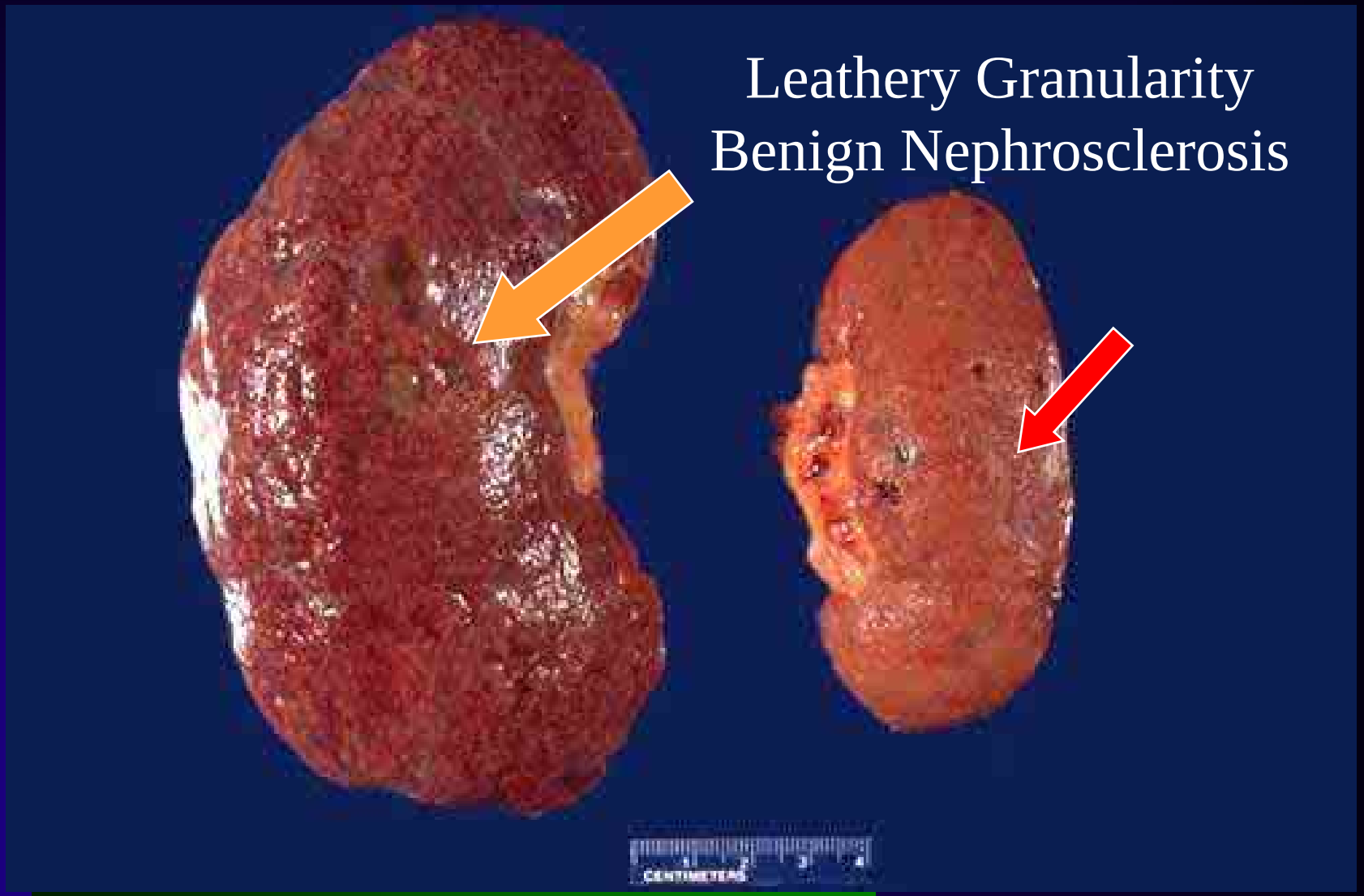
KW lesion…

Benign Nephrosclerosis:

Leathery Granularity
due to minute scarring



Renal Artery stenosis - Atrophy



IgA Nephropathy (berger)

- Most common form of GN
- Young adults (15-30 years)
- IgA deposits in mesangium, varied severity
- Asymptomatic microscopic hematuria (40%)
- Bouts of macro hematuria (40%)
- Nephrotic syndrome (10%)
- Renal failure (10%)

Nephrosclerosis - Hypertension

Benign

- sustained mild hypertension.
- hyaline arteriolosclerosis
- arterial fibrosis
- glomerular hyalinization, tubular atrophy

Malignant

- BP>125 mm/Hg, retinal hemorrhage, papilledema, renal dysfunction
- fibrinoid necrosis of arterioles
- microthrombi

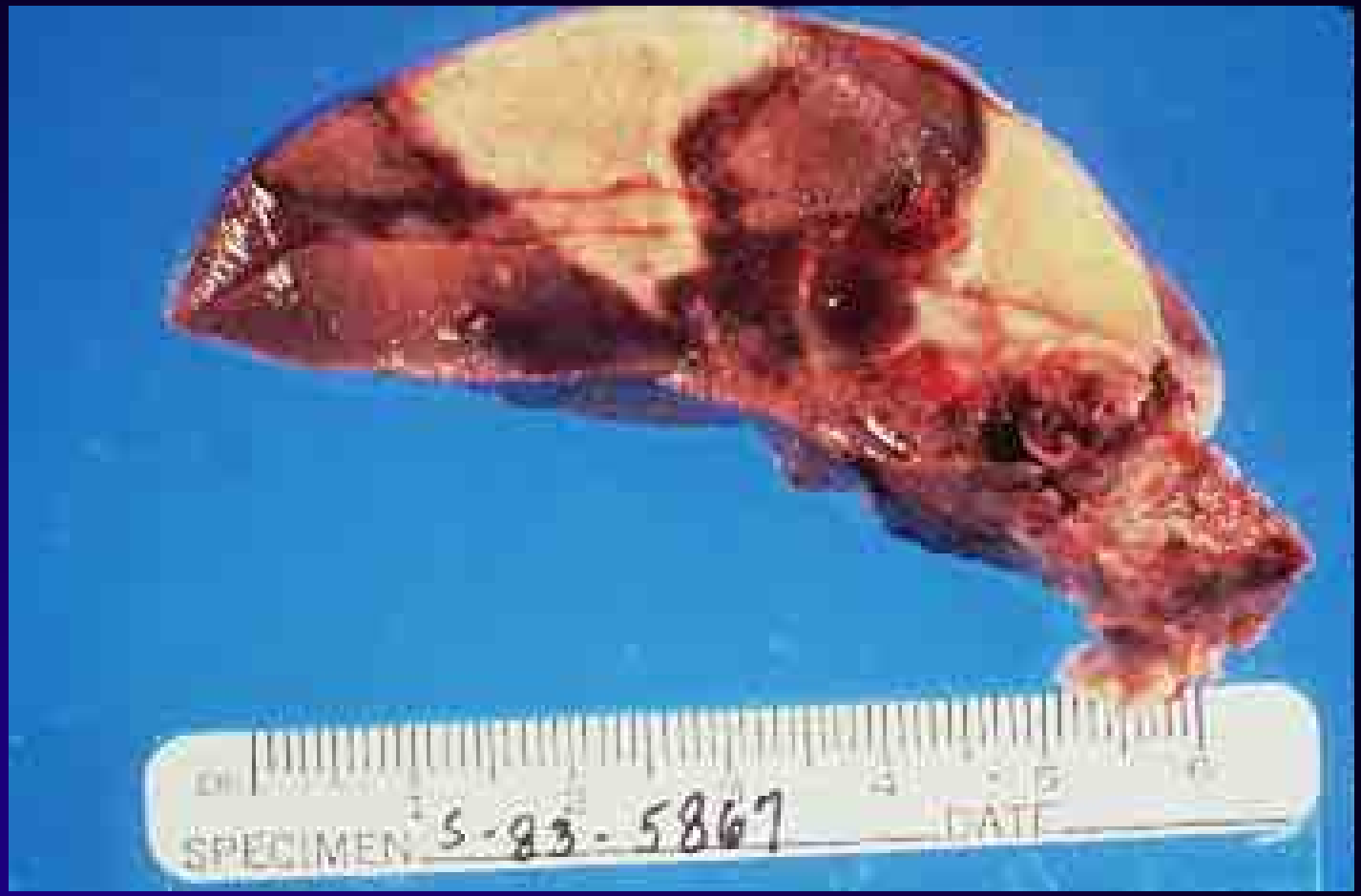
Thrombotic microangiopathy

- Morphologic finding in several diseases
- microangiopathic hemolytic anemia
- HUS, TTP, Malignant nephrosclerosis
- Systemic sclerosis

Renal infarcts

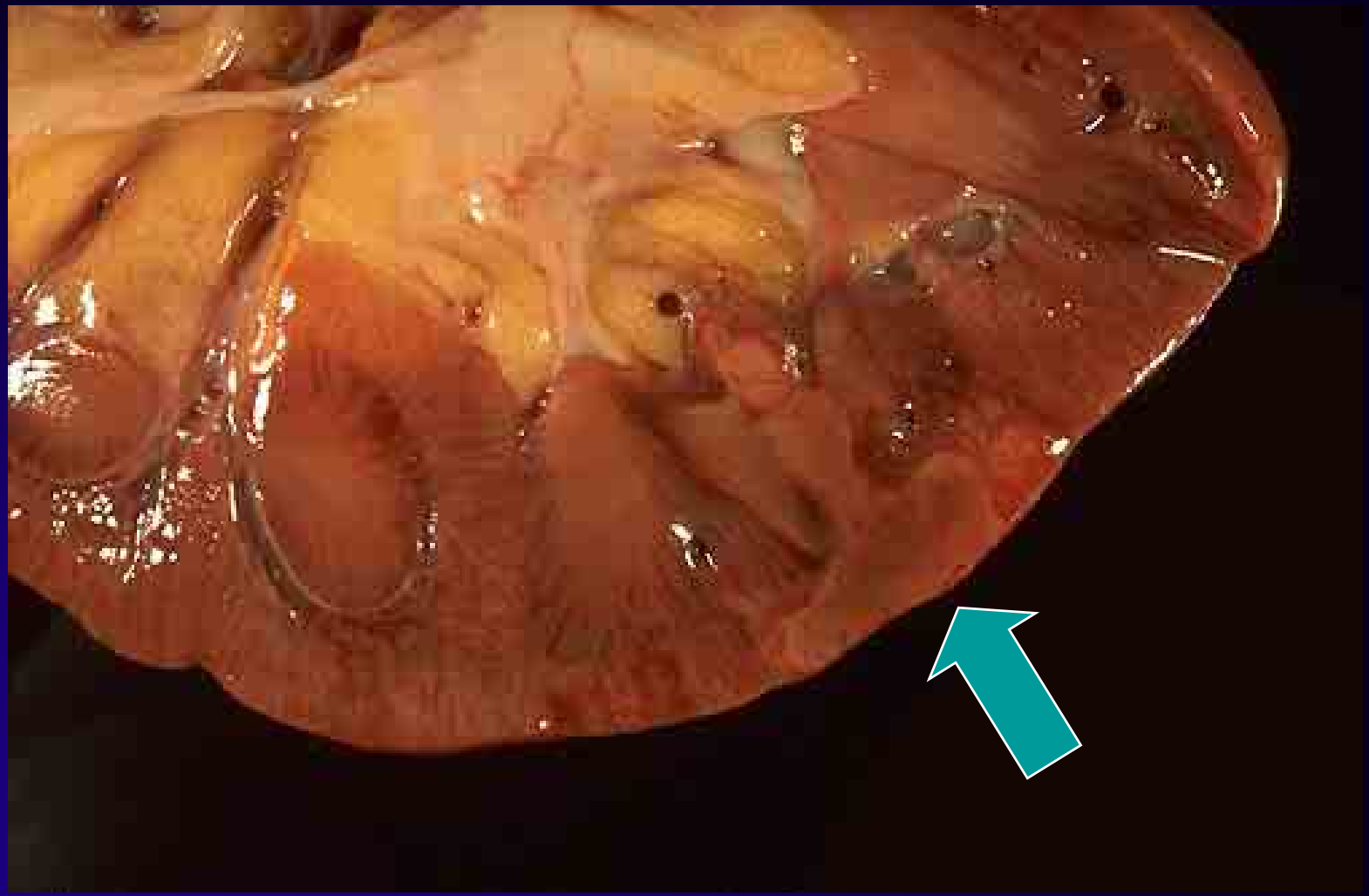
- Thromboemboli
- Mural thrombi
- (M.I., atrial fibrillation)
- Endocarditis
- Aortic thrombi (atherosclerosis)
- Cholesterol emboli

Renal Infarcts:



Renal Infarct:

Renal Infarct:



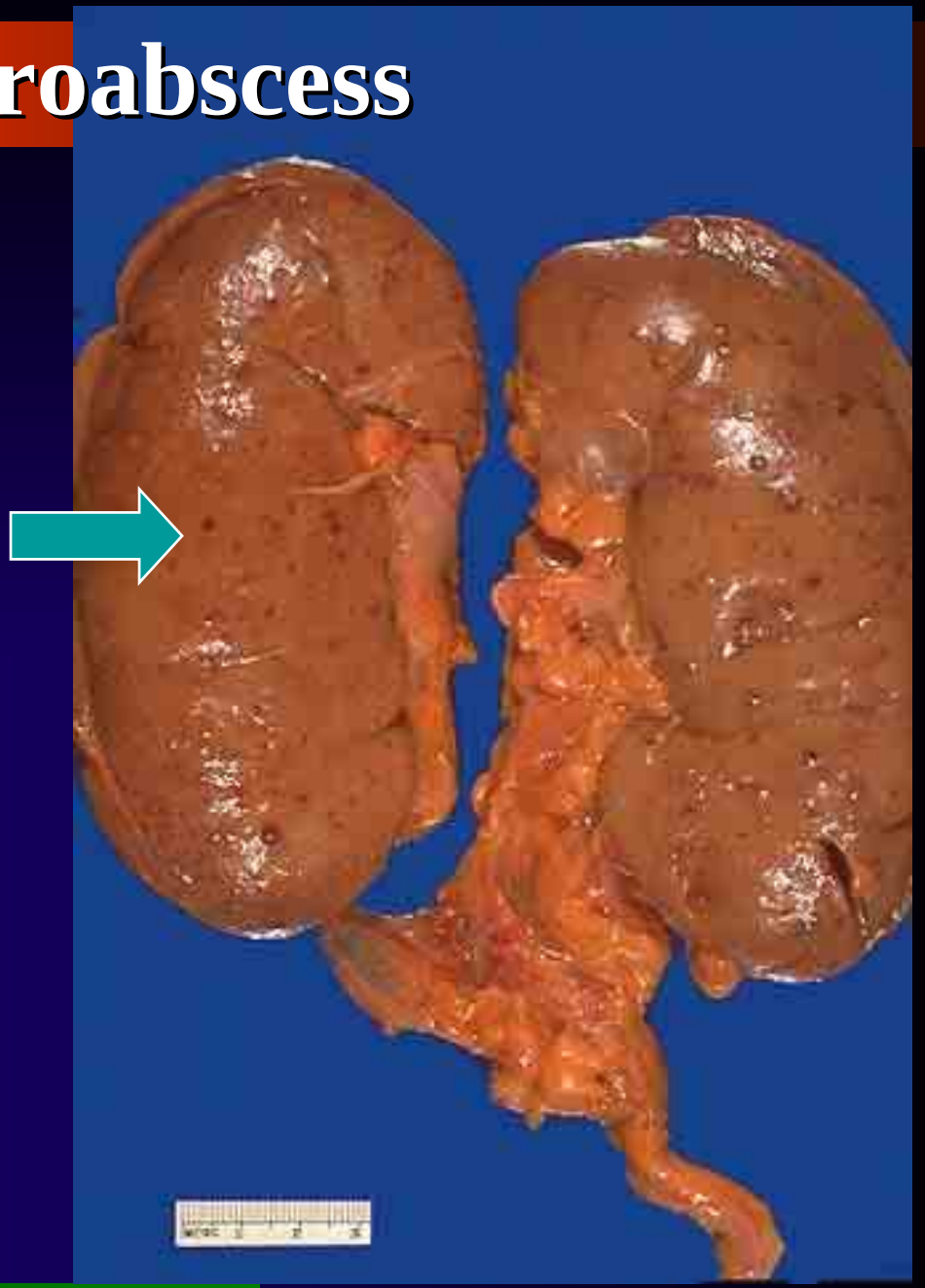
Acute Tubular Necrosis:

- Common cause of acute renal failure
- “Dirty” brown casts in urine
- Oliguria→ anuria→ polyuria
  - Azotemia
  - Acidosis, K↑
  - Fluid retention
- Recovery 1-2 weeks

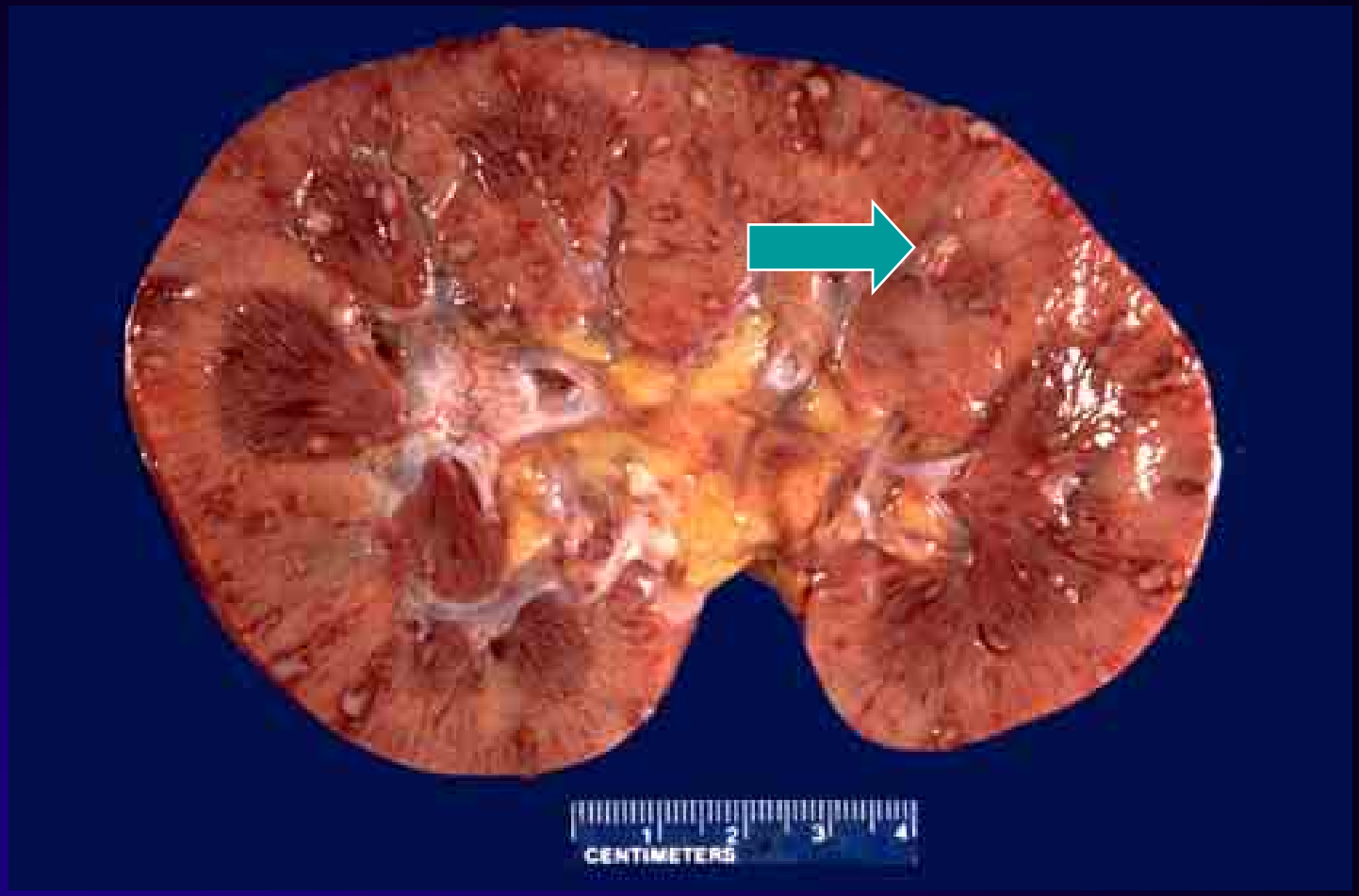
Acute Pyelonephritis

- Bacterial infection (E. coli 80%)
- Ascending / hematogenous
- Lower UTI precedes renal infection
- Fever, flank pain, neutrophilia
- Leukocyte casts in urine
- Healing - recurrence→ chronic pyelonephritis

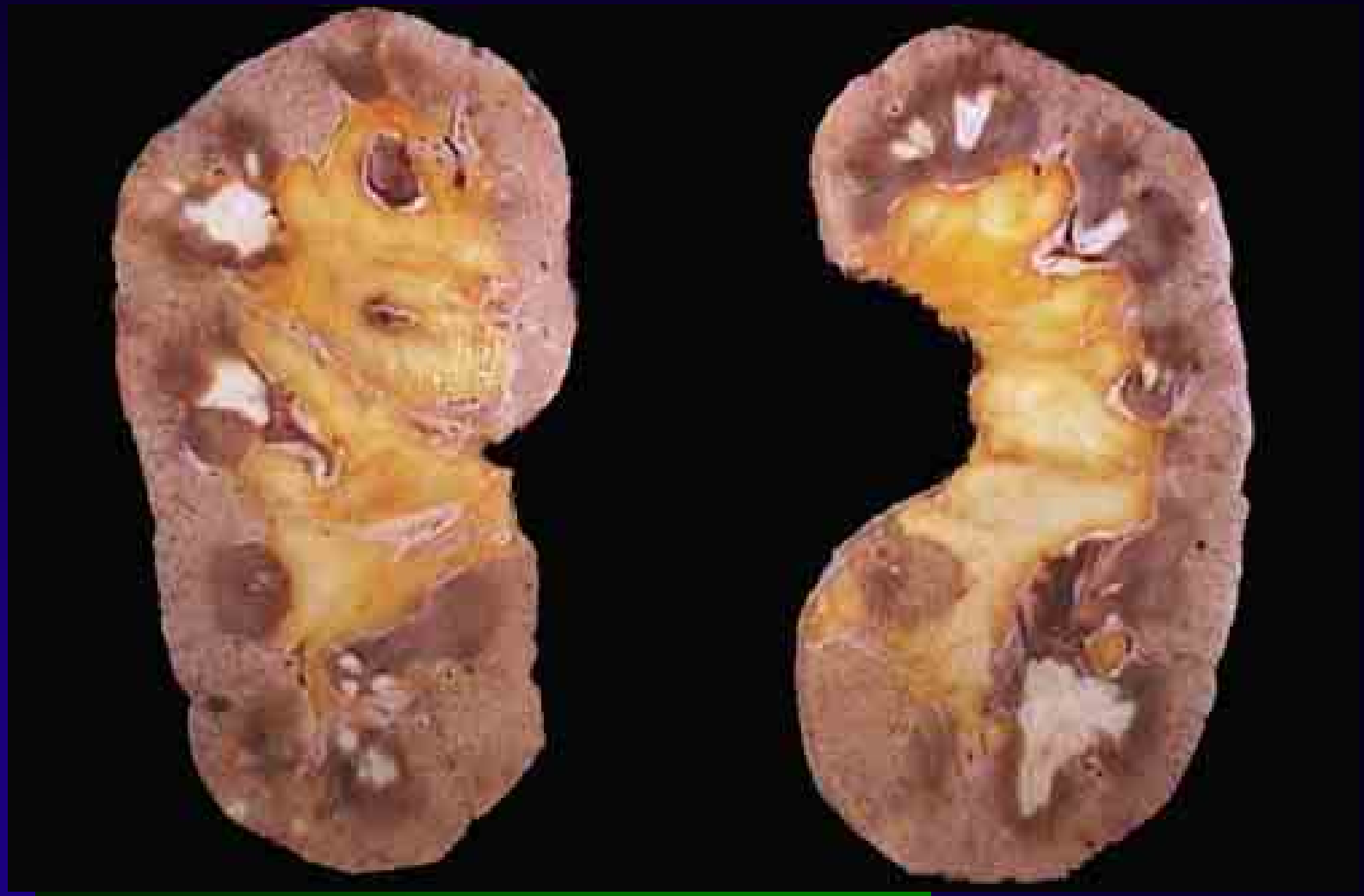
Septicemia-Microabscess



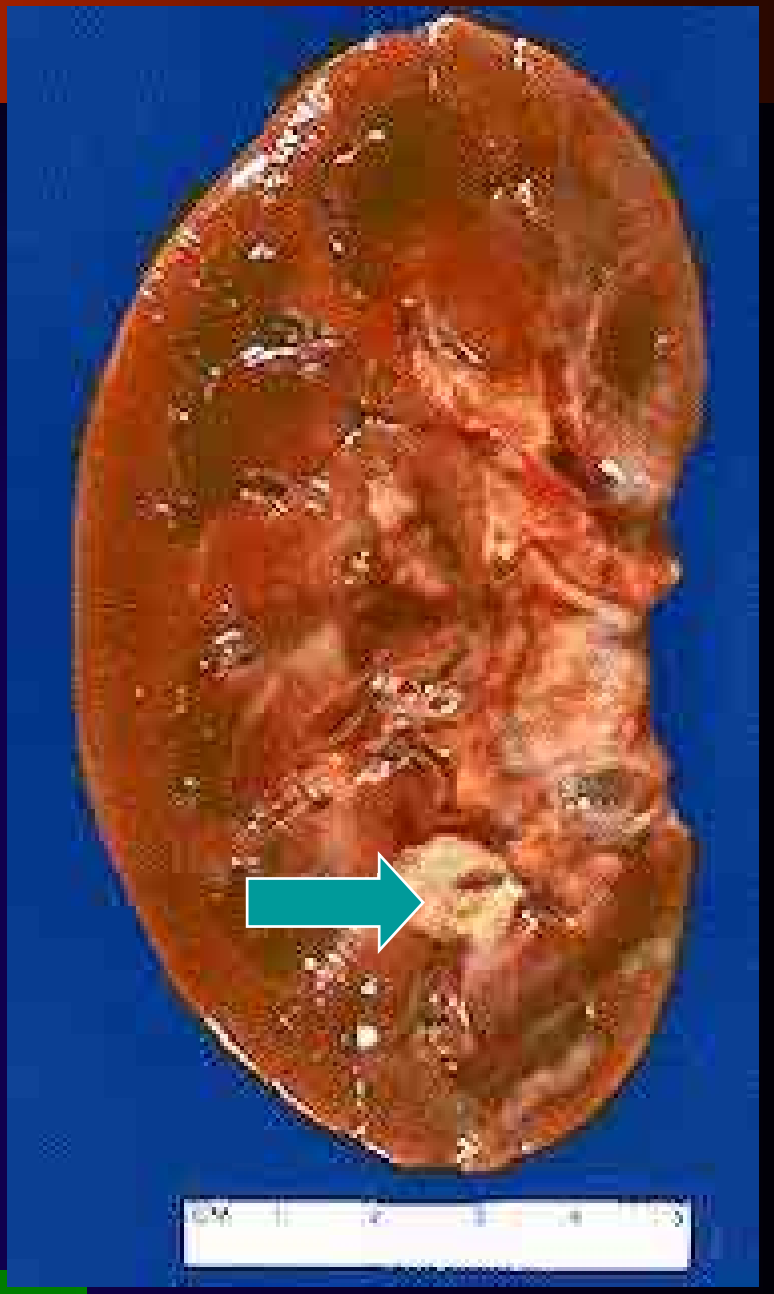
Septicemia-Microabscess



Acute Pyelonephritis with papillary necrosis (diabetes)



Septicemia-abscess



Pyelonephritis – Predisposing Cond.

U Urolithiasis

R Reflux (vesico-ureteric)

I Infections of lower UT

N Neoplasms (ureteric, vesical, prostatic)

E External compression (e.g.) pregnancy retroperitoneal fibrosis

Chronic Pyelonephritis Pathology

- Destruction of renal tissue and fibrosis
  - Cortical scars
  - Loss of papillae
  - Ectasia of calices
  - Hydronephrosis
- Irregularly shrunken small kidney
- Chronic inflammatory infiltrates
- Tubular atrophy with casts (“thyroidization”)

Drug induced renal disorders:

1. Acute tubular necrosis(toxic)
   Gentamycin, mercury, contrast agents.
2. Acute tubulointerstitial nephritis (allergic)
   – methicillin, thiazides.
3. Analgesic nepropathy (Phenacetin)
   chronic tubulointerstitial nephritis with
   papillary necrosis.

Urolithiasis – Stones:

Urolithiasis:

- 1-5%, environment, males, pelvis
- Renal colic, dull ache in loins
- Urinary tract infection recurrent.
- Factors affecting:
- Urine pH, Infection, Metabolic,
- Pyrophosphates and citrate inhibit.

Urolithiasis – stones:

Infection

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

Hypercalcemia / Hypercalciuria

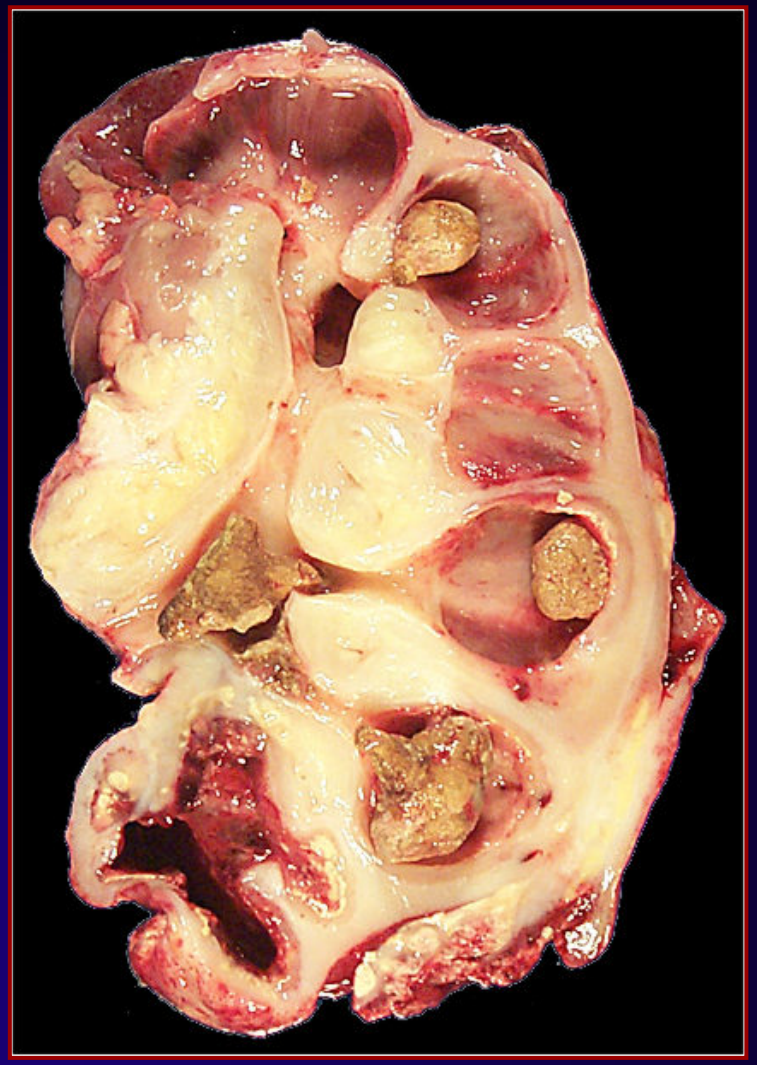
Primary (increased intestinal absorption of Ca)

- Idiopathic (most common)
- Milk-alkali syndrome
- Vitamin D excess
- Sarcoidosis

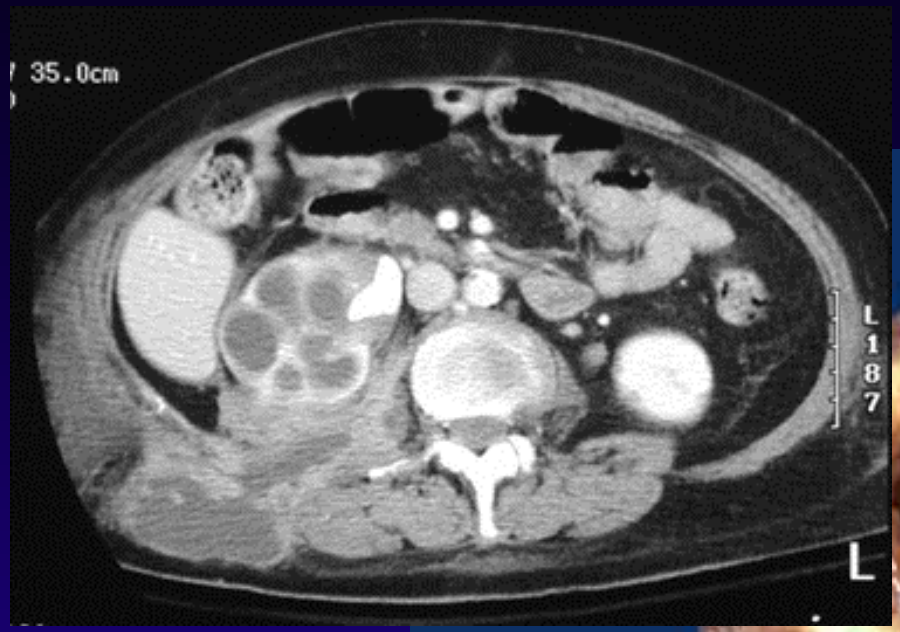
Secondary (release of Ca from bones)

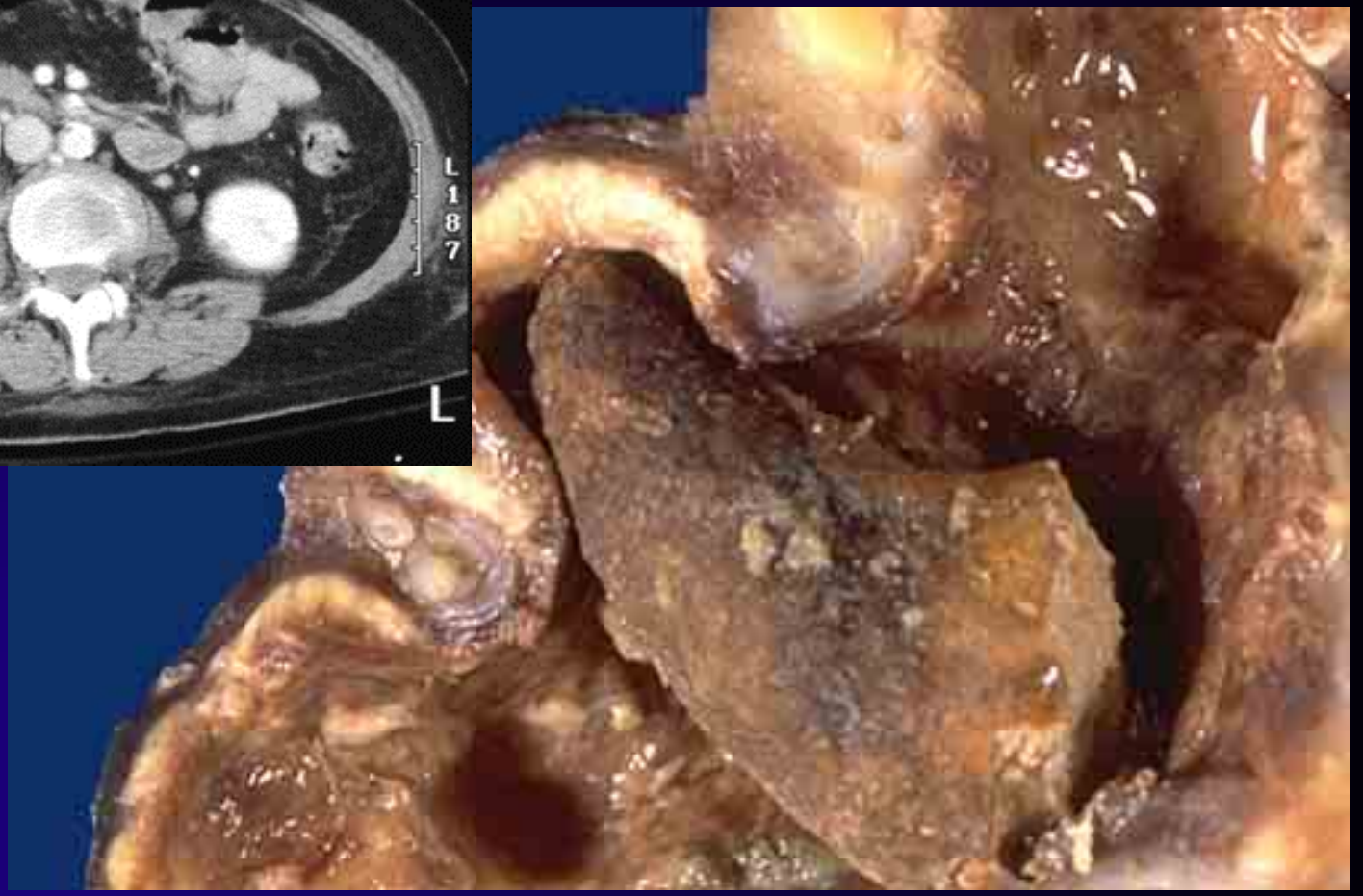
- Renal osteodystrophy
- Hyperparathyroidism
- Osteolytic metastases (e.g. breast cancer)
- Paraneoplastic syndromes (PTrP)

Urolithiasis:

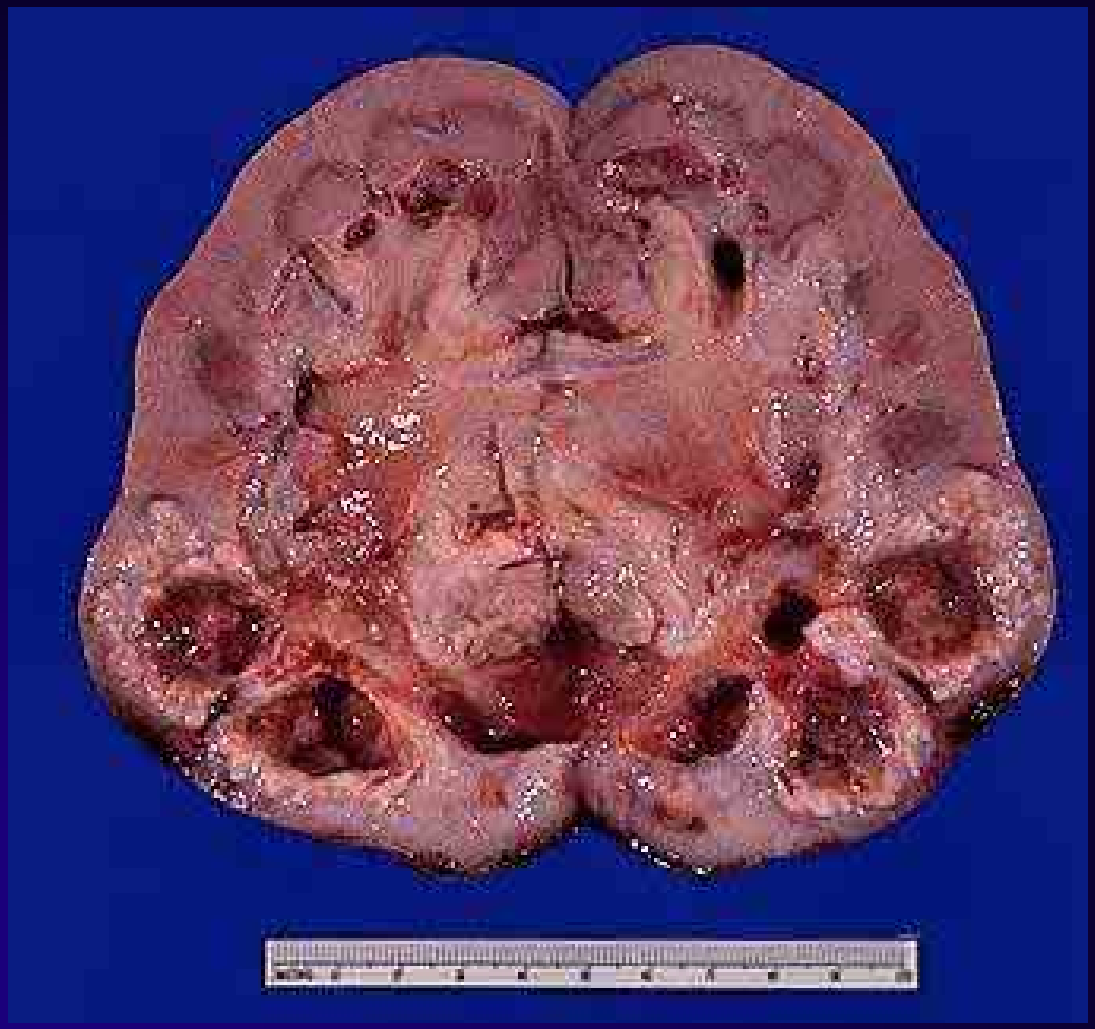


Staghorn Calculus:

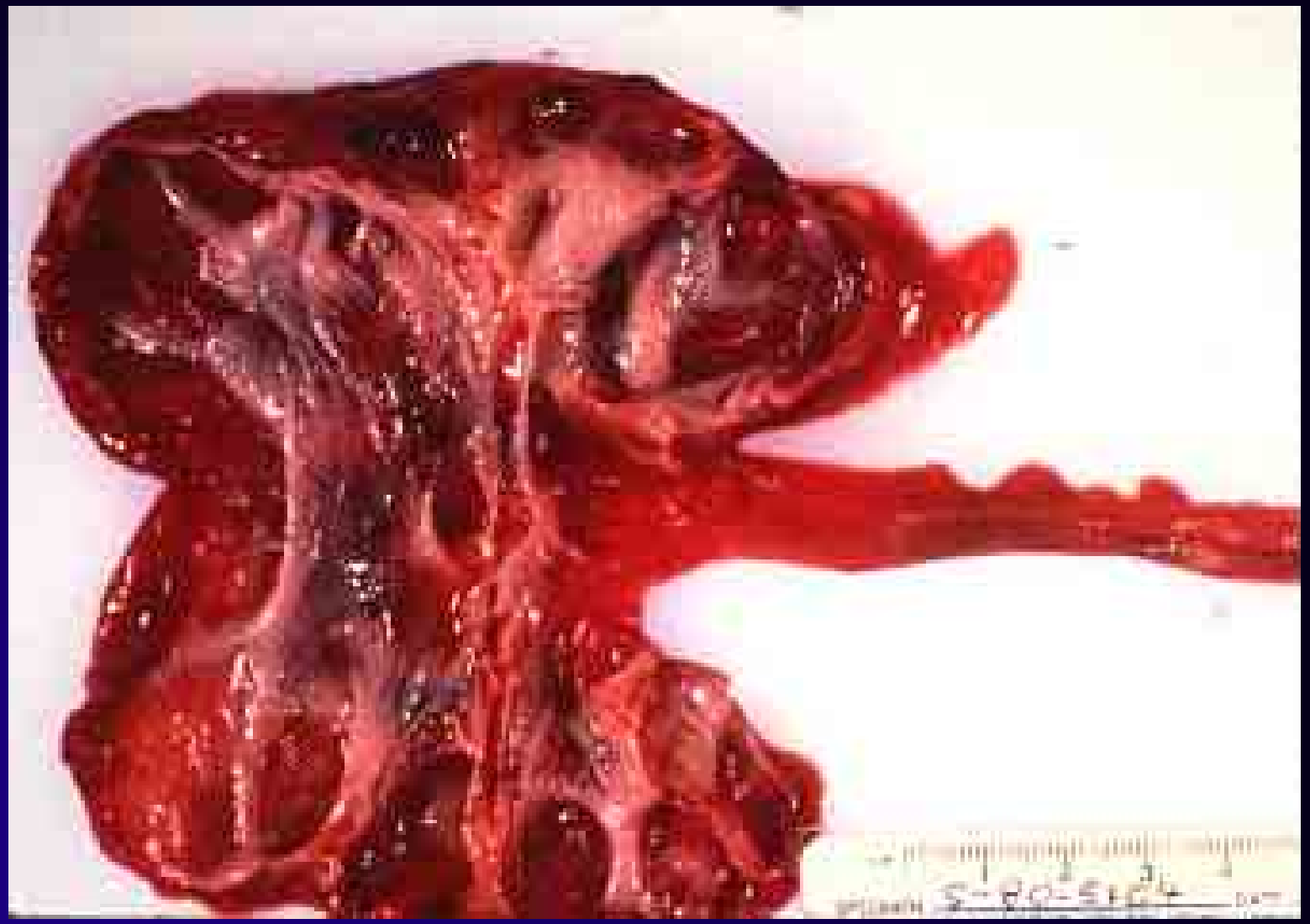




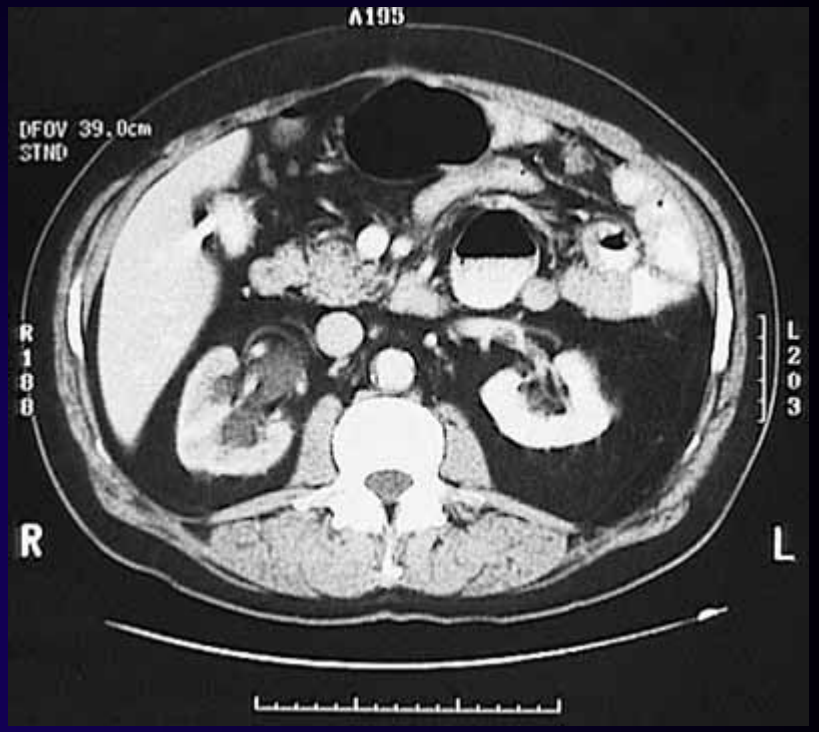
Urolithiasis with hydronephrosis:



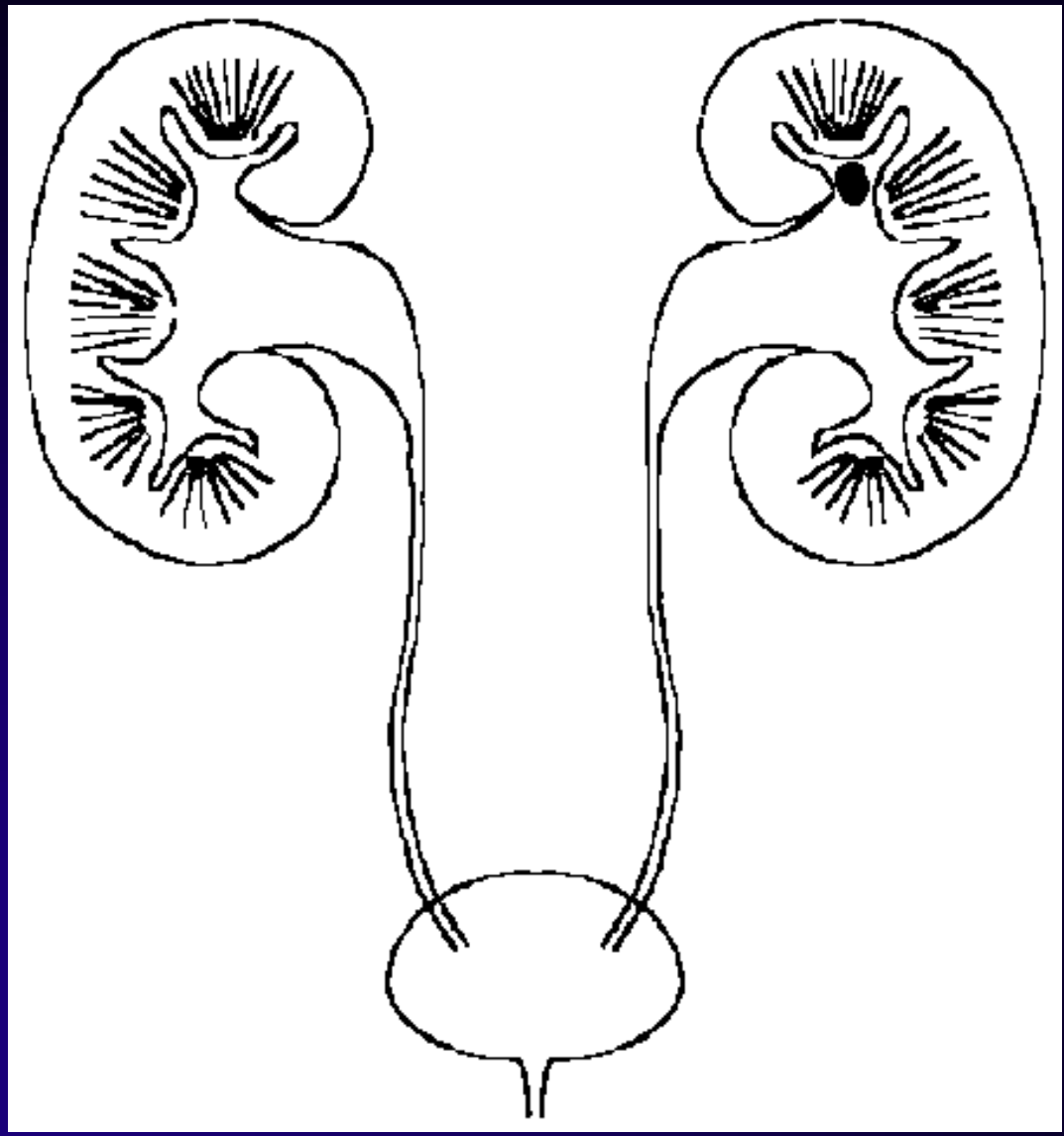
Hydronephrosis:



Hydronephrosis:

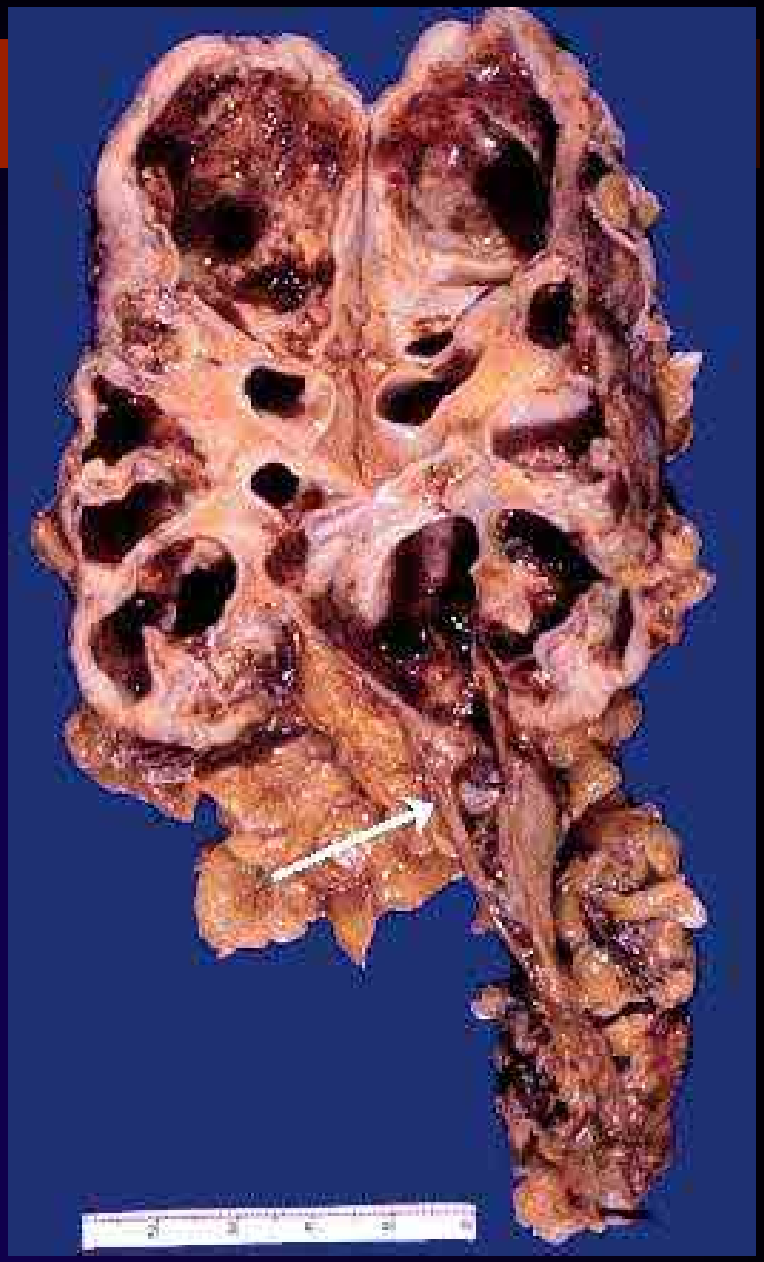


Urolithiasis – sites of impaction

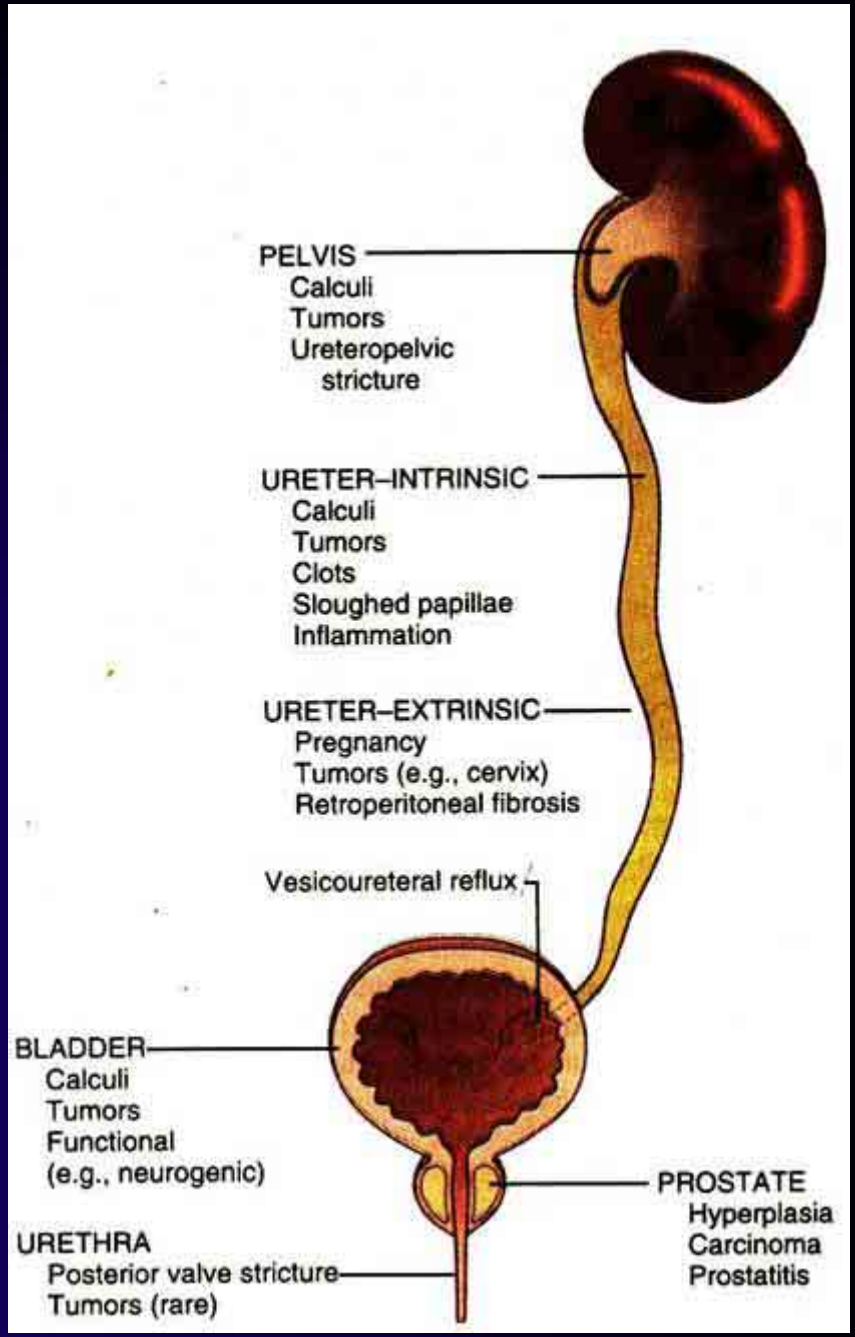


Hydronephrosis

- Urolithiasis

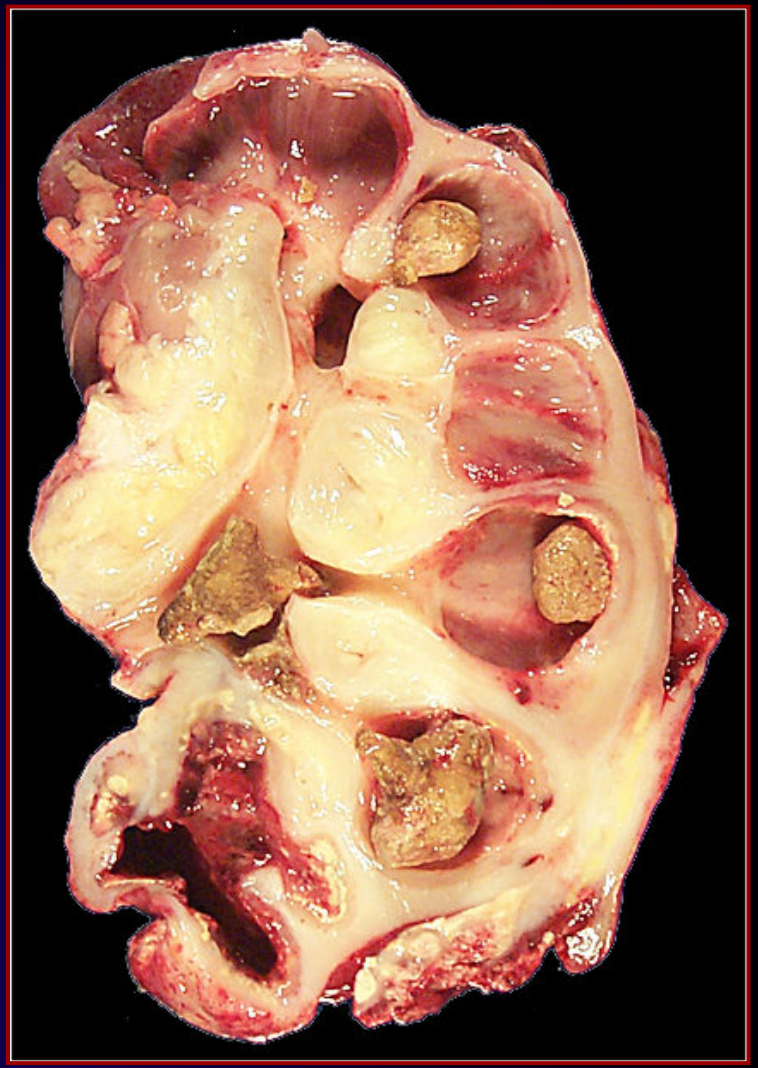


Causes of Obstructive Uropathy



Urolithiasis:

Incidence:	Common, male predominance.
Etiology:	Environmental, metabolic, infectious.
Clinical Features:	Develop silently until episode of renal colic. Cause obstruction, pain, infection, hydronephrosis, and hydroureter.
Lab:	Gross or mcroscopic hematuria. Chemical analysis to identify type of stone. Characteristic radiographic findings.
Path:	Calcium phosphate or oxalate - Hard, sharp. Uric acid - Smooth. Staghorn - Cast of calyceal system.
Clinical Course:	May recur. Complications are the problem.
Treatment:	Surgery, lithotomy, or ultrasonic lithotripsy to remove stone. Treatment of metabolic process, if indicated. Adequate hydration.



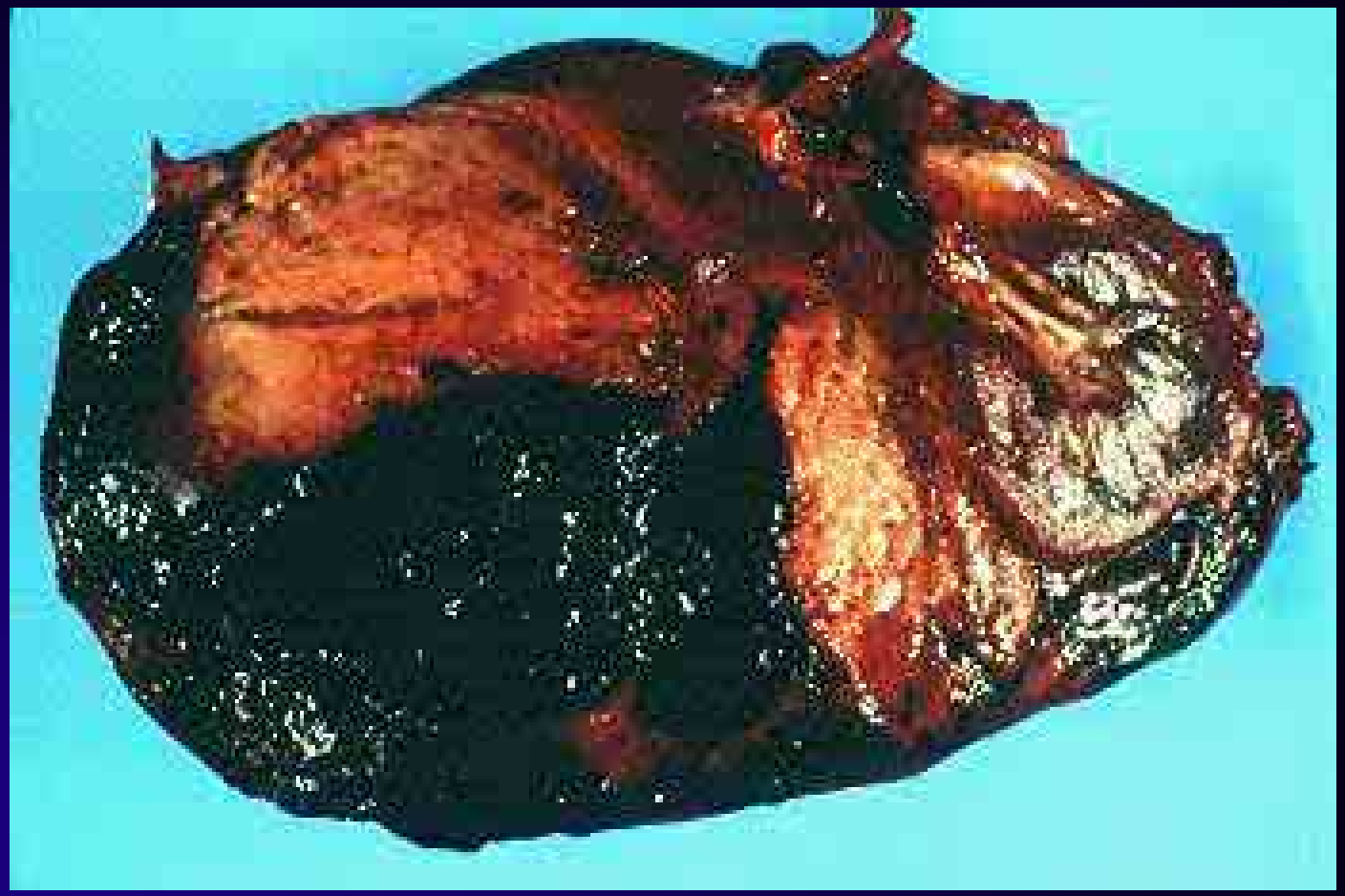
“The weak can never forgive. Forgiveness is the attribute of the strong.”

–Mohandas Gandhi

Renal tumors

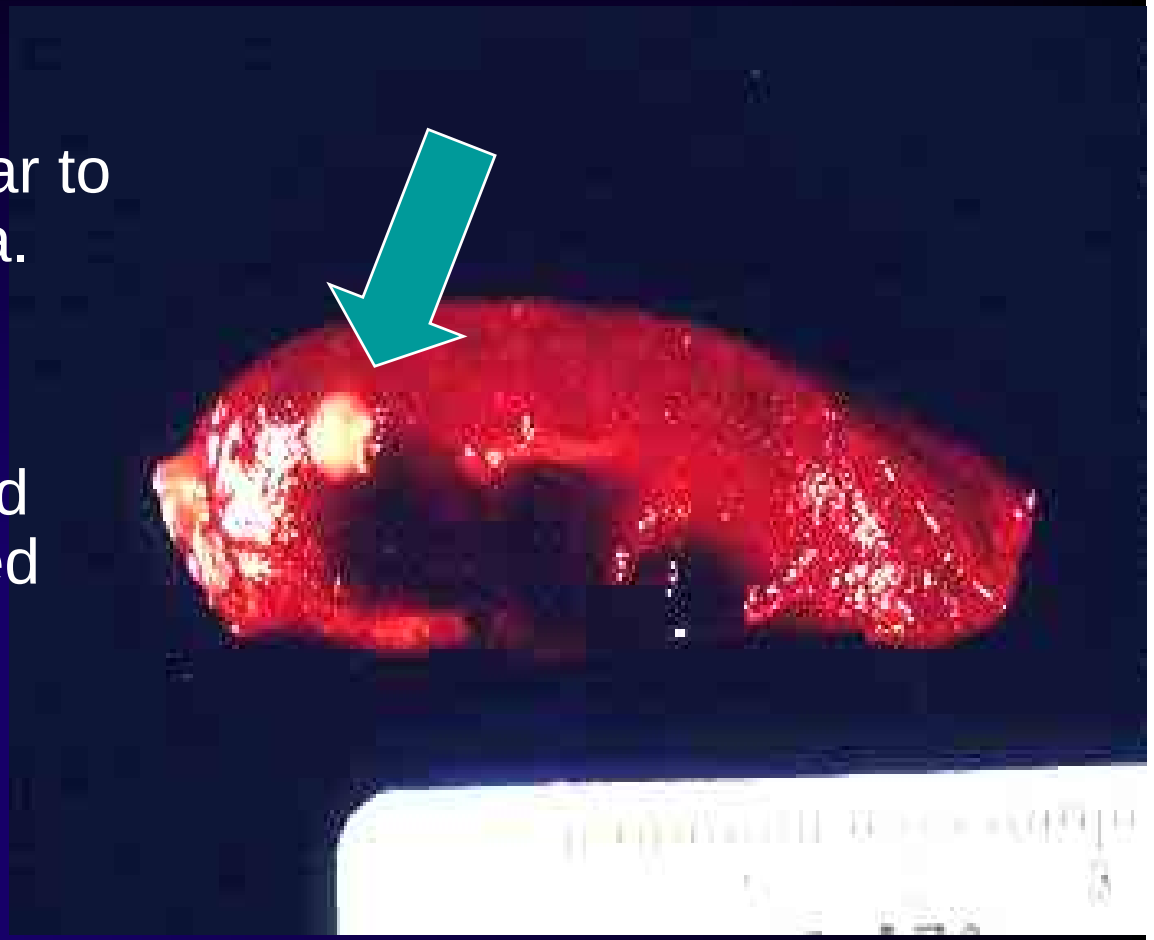
- **Benign**
  - Adenoma, oncocytoma, angiomyolipoma, fibroma (rare!)
- **Malignant:**
  - Renal cell carcinoma (common – adults)
  - Wilms tumor (childhood)
  - Transitional cell carcinoma of renal pelvis

Angiomyolipoma (Benign)

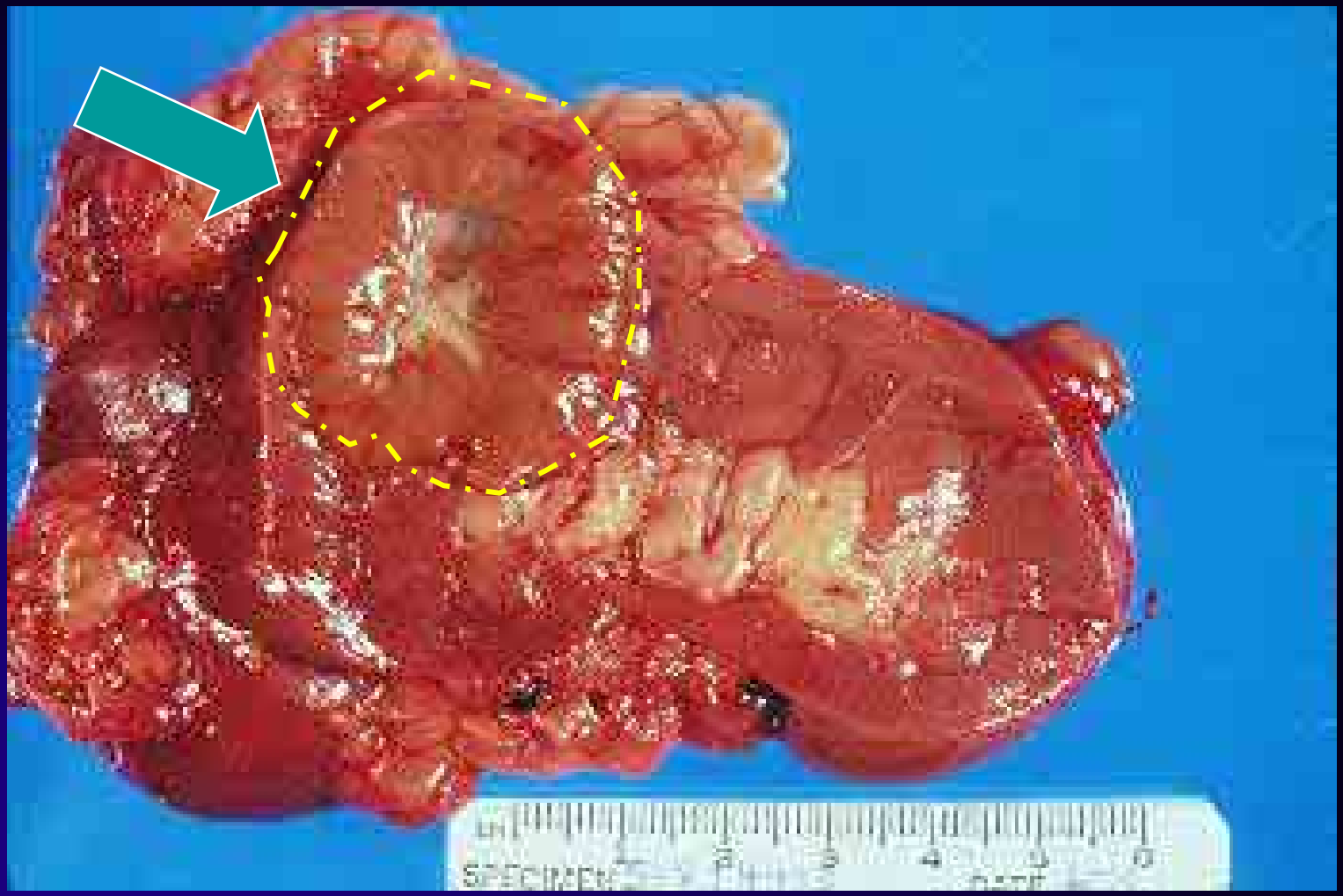


Renal Papillary Adenoma

- Papillary
- Common
- Histopathology similar to renal Cell Carcinoma.
- < 3cm – benign
- > 3cm - malignant
- All tumors considered malignant until proved otherwise.

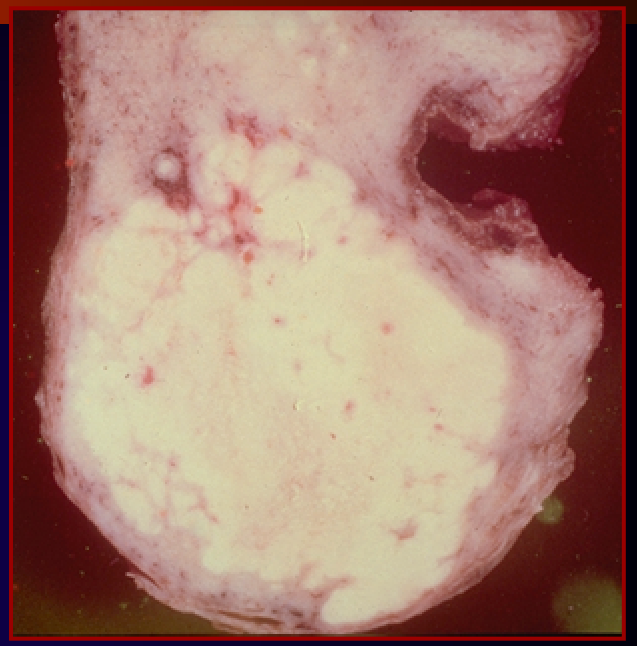


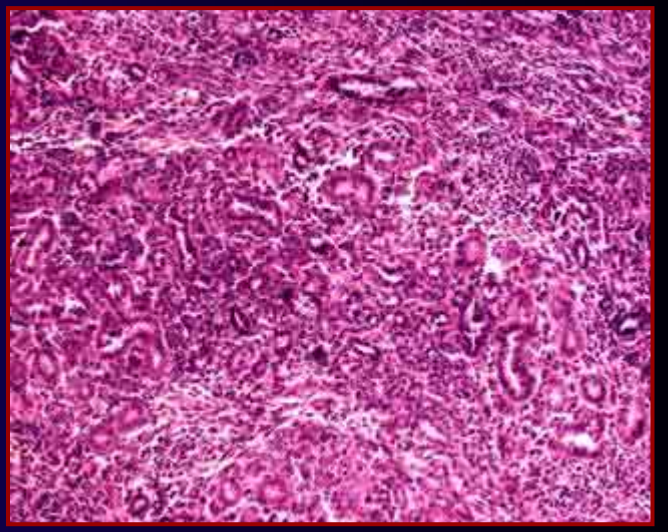
Oncocytoma (DCT epithelia, benign)



Wilm's Tumor

Synonyms:	Nephroblastoma.
Incidence:	Most common renal tumor of childhood. Peak age - 2.5 - 3.5 years.
Etiology:	Embryonic renal tissue (metanephric blastema). Genetic abnormalities.
Clinical Features:	Palpable abdominal mass. Abdominal pain, fever, anorexia, nausea/vomiting. Hematuria.
Lab:	No specific clinical laboratory findings. Diagnosis by radiographic techniques.
Path:	Gross: Solitary/multiple cystic mass, sharply delineated. Soft, bulging, gray-white with focal hemorrhage and necrosis. Micro: Triphasic mesenchymal stroma, tubules, and solid areas (blastema). Primitive glomeruli, skeletal muscle, cartilage, bone, etc. (embryonic tissues)
Clinical Course:	5-yr. Survival 80%. Metastases to lung, liver, bone, brain.
Treatment:	Prompt resection with chemotherapy ± radiotherapy.





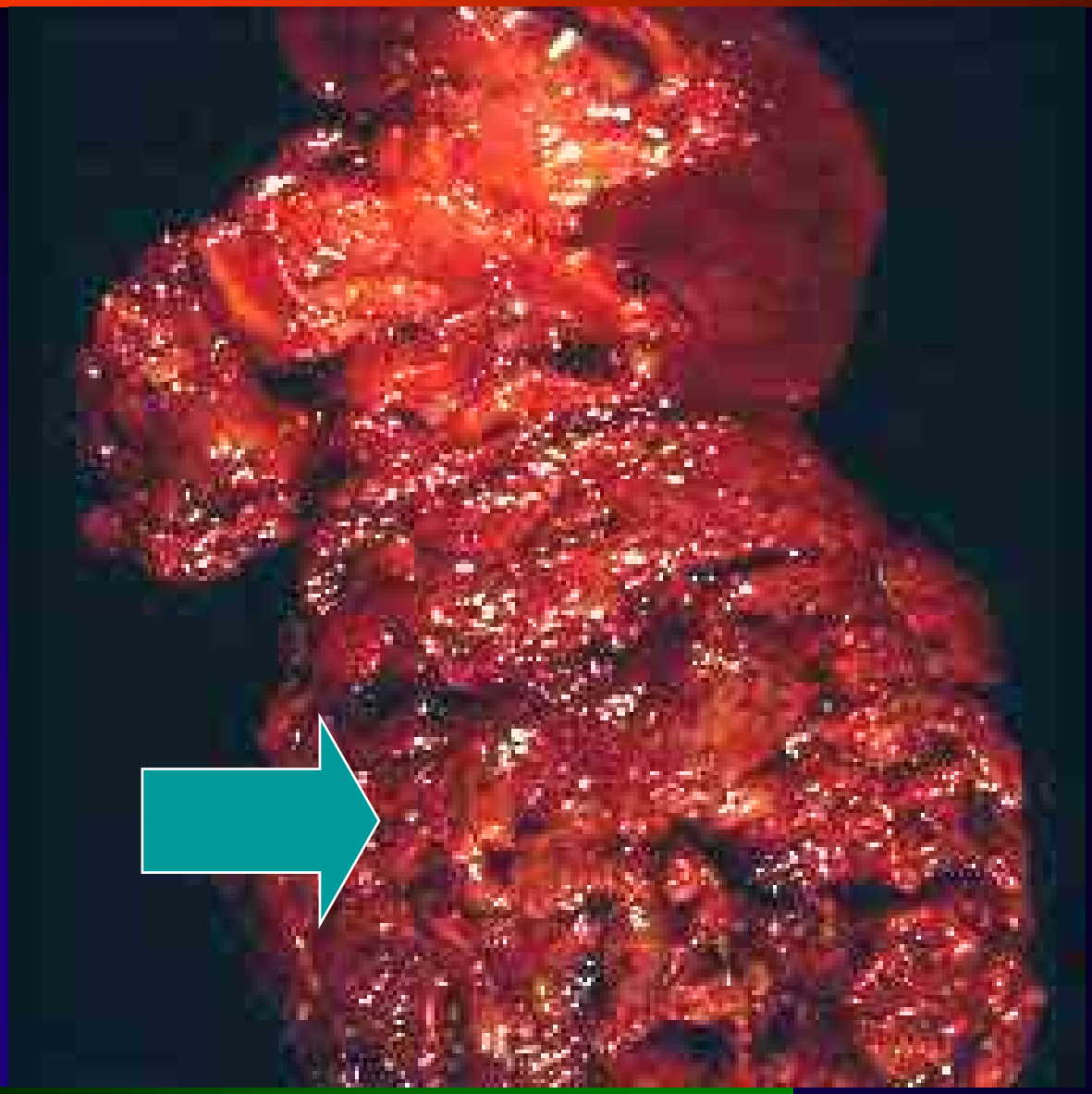
Renal Cell Carcinoma

- Most common renal tumor
- Peak age – 60y M:F = 3:1
- Incidence increasing world wide
- Tobacco; Obesity, genetics (VHLgene, familial cases)
- Von Hippel-Lindau syndrome
  - Hemangioblastoma cerebellum retina
  - Bilateral renal cysts,
  - Clear cell type RCC – common.

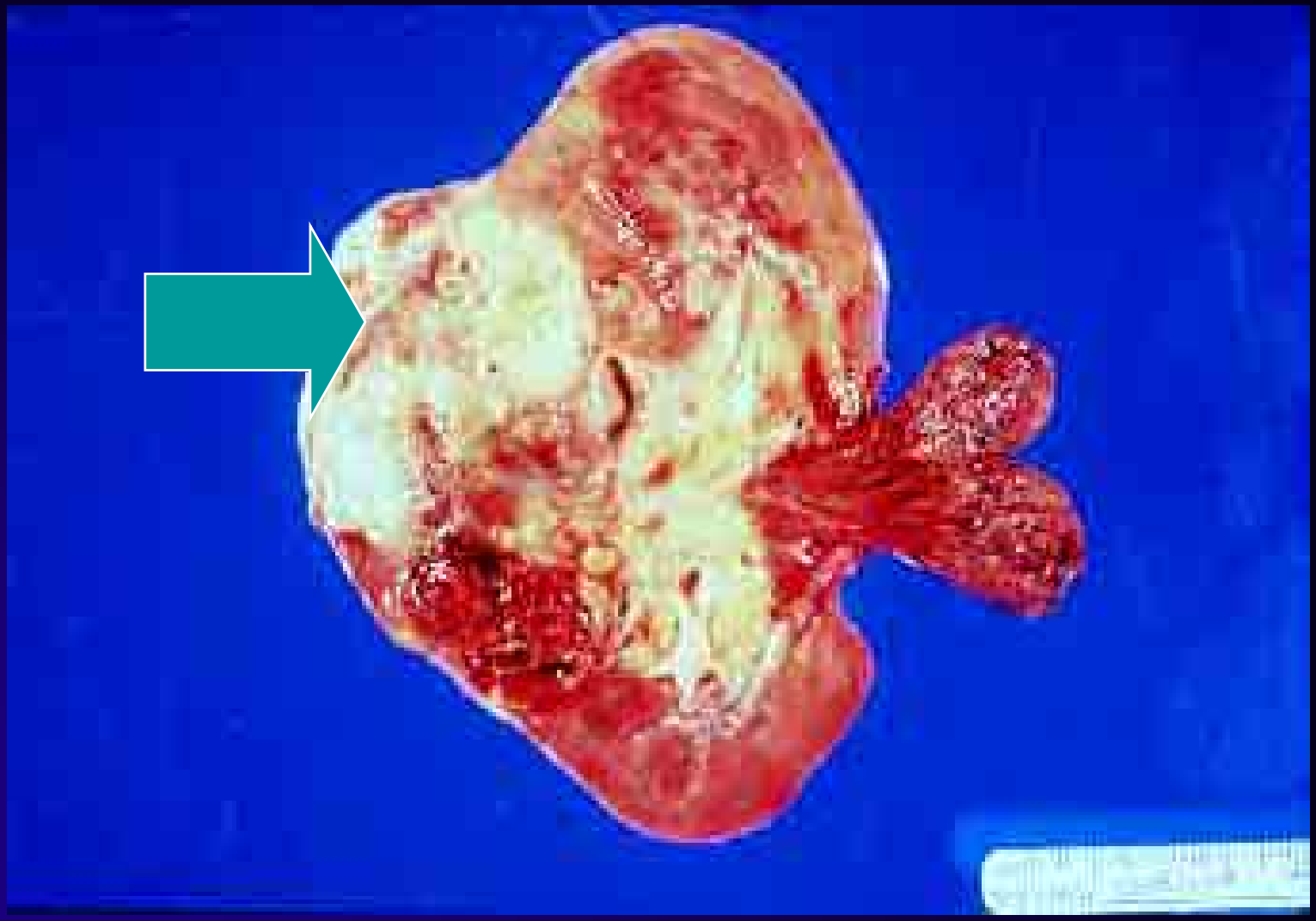
RCC - Pathology

- Yellow orange tumor –Hypernephroma.
- Partially encapsulated
- Extends into renal vein
  - tubular clear cell (77%)
  - papillary (15%)
  - granular, chromophobe, sarcomatoid (5%)

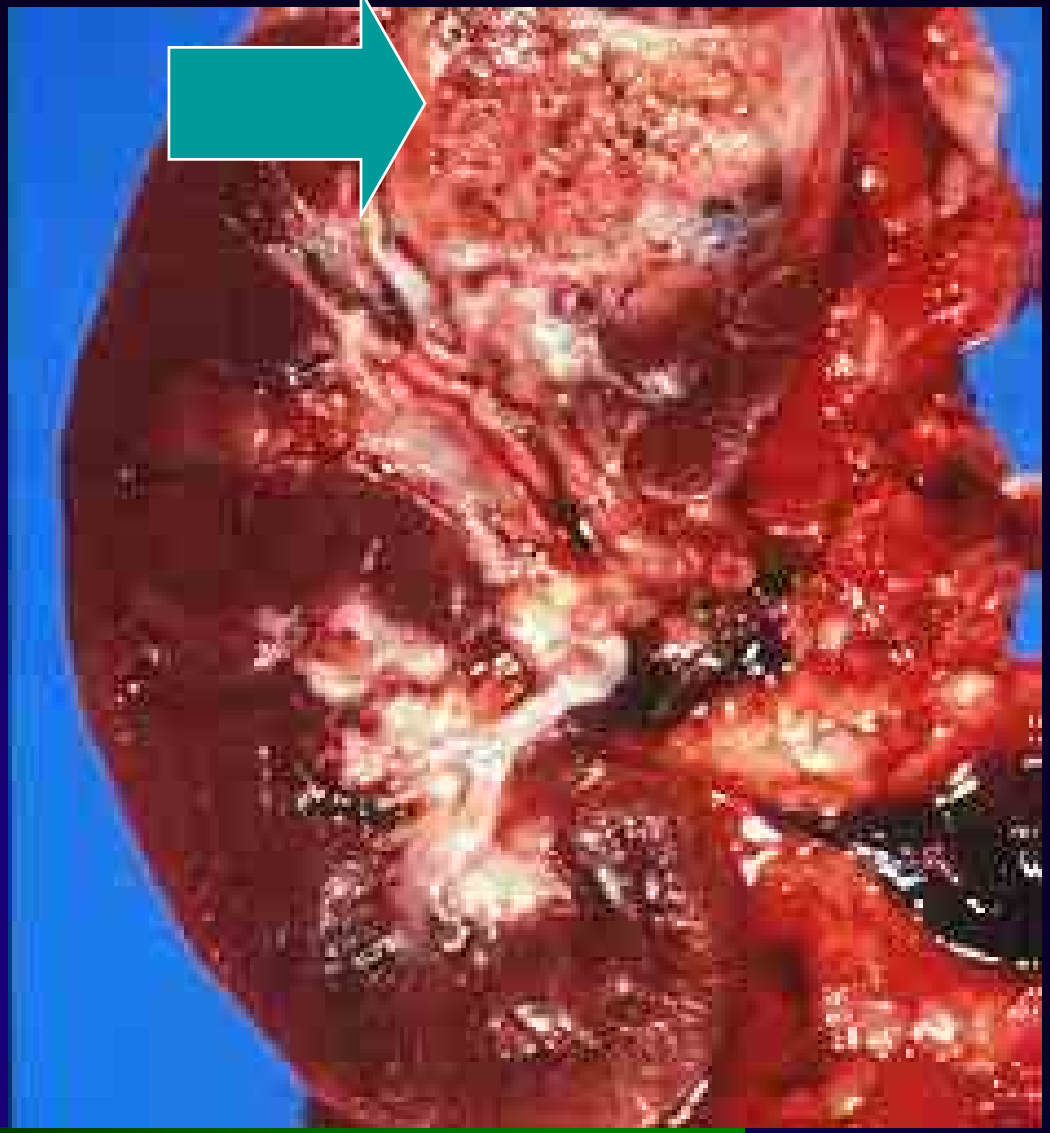
Renal Cell Carcinoma:



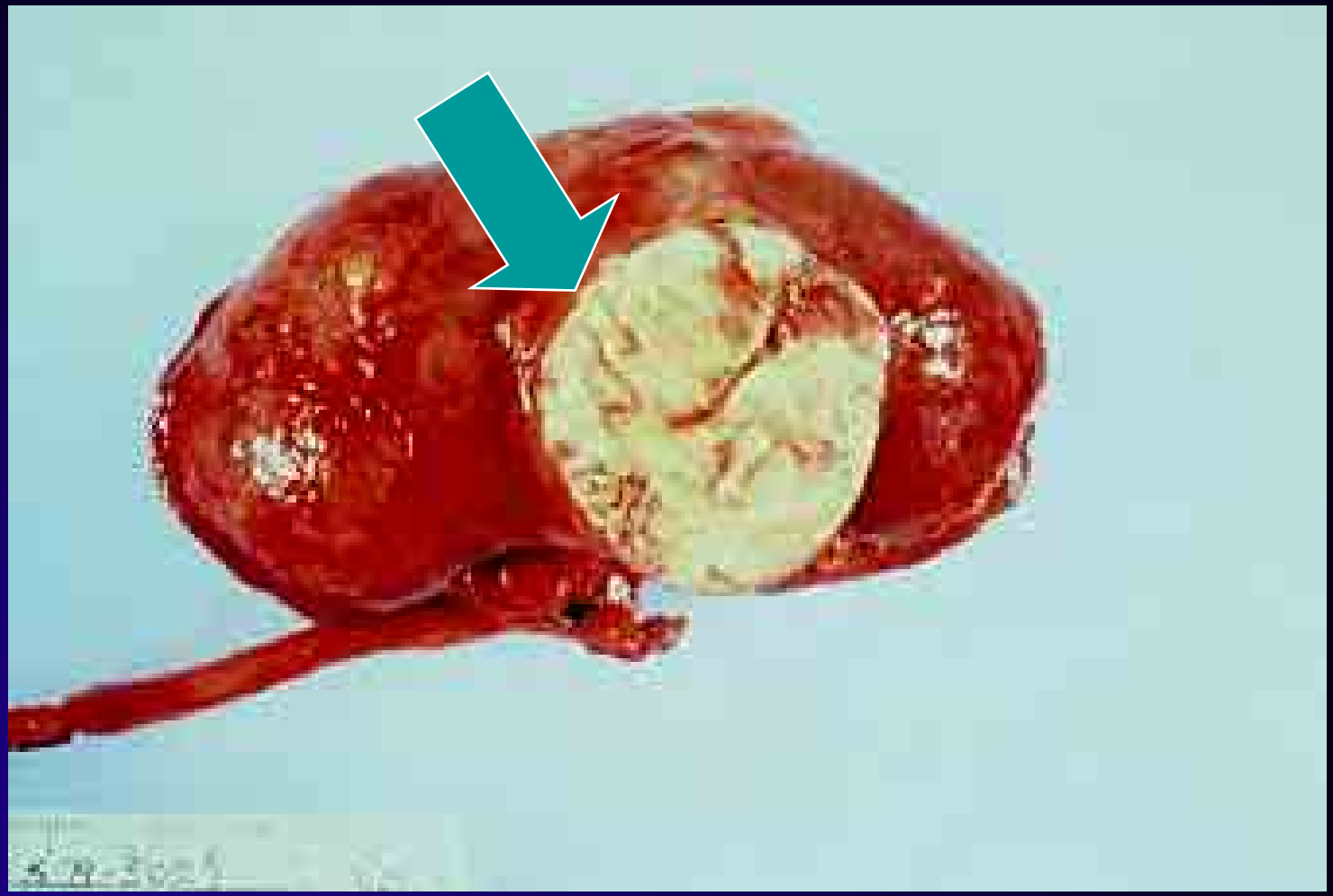
Renal Cell Carcinoma:



Renal Cell Carcinoma:



Renal Cell Carcinoma:

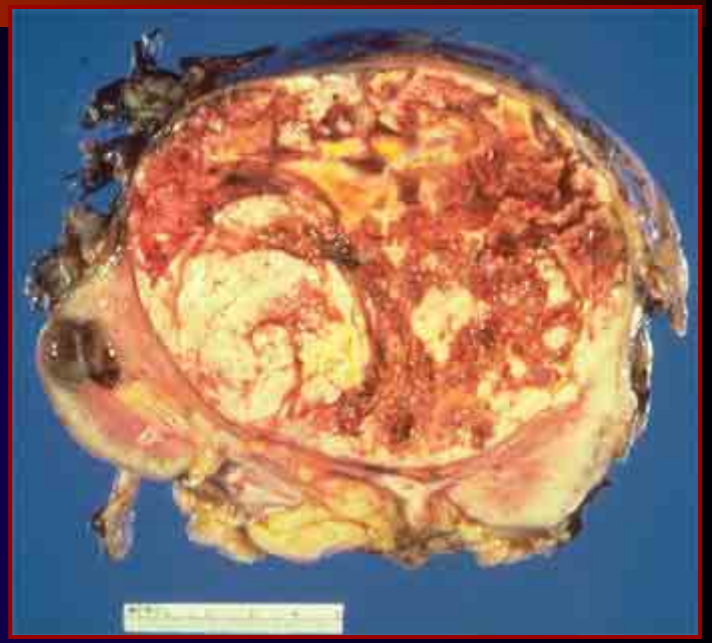


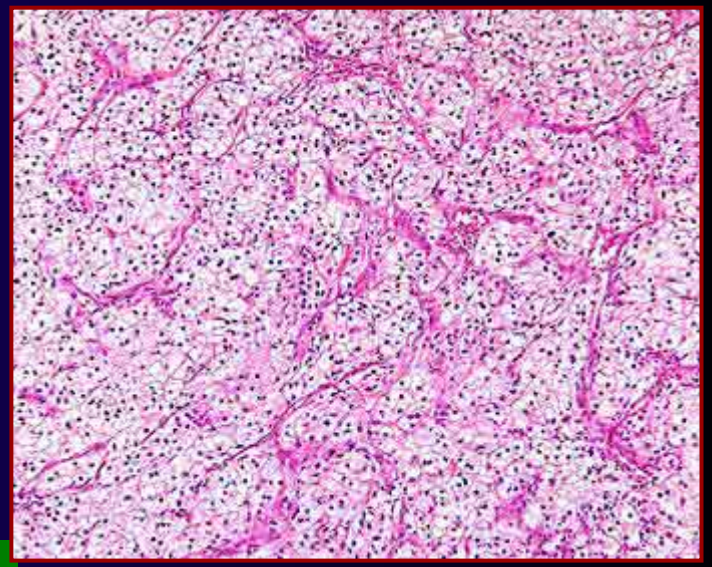
RCC – Clinical Features:

- Classical triad (hematuria, flank pain, mass) (<10%)
- Hematuria (50%) most common symptom
- Metastases-hematogenous and local abdominal
- Paraneoplastic syndromes (PTH, Epo, amyloid)
- 5 year survival = 40%

Renal Cell Carcinoma:

Synonyms:	Hypernephroma, clear cell carcinoma.
Incidence:	5th and 6th decades, most common primary renal malignancy.
Etiology:	Cells of proximal convoluted tubule. Risk factors are smoking, obesity, analgesic abuse, APCKD.
Clinical Features:	Hematuria*, flank pain, palpable mass. Frequently metastasize (lungs, bone, skin, liver, brain).
Lab:	Gross or microscopic hematuria. Specific Dx by radiographic techniques.
Path:	Gross: Large yellow mass with hemorrhage and necrosis. Invade renal vein. Micro: Usually clear or granular cells with little anaplasia. Other histologic variants (“great mimicker”).
Clinical Course:	5-yr. survival 40%. Poor prognosis with metastases.
Treatment:	Chemotherapy, surgery, immunotherapy.

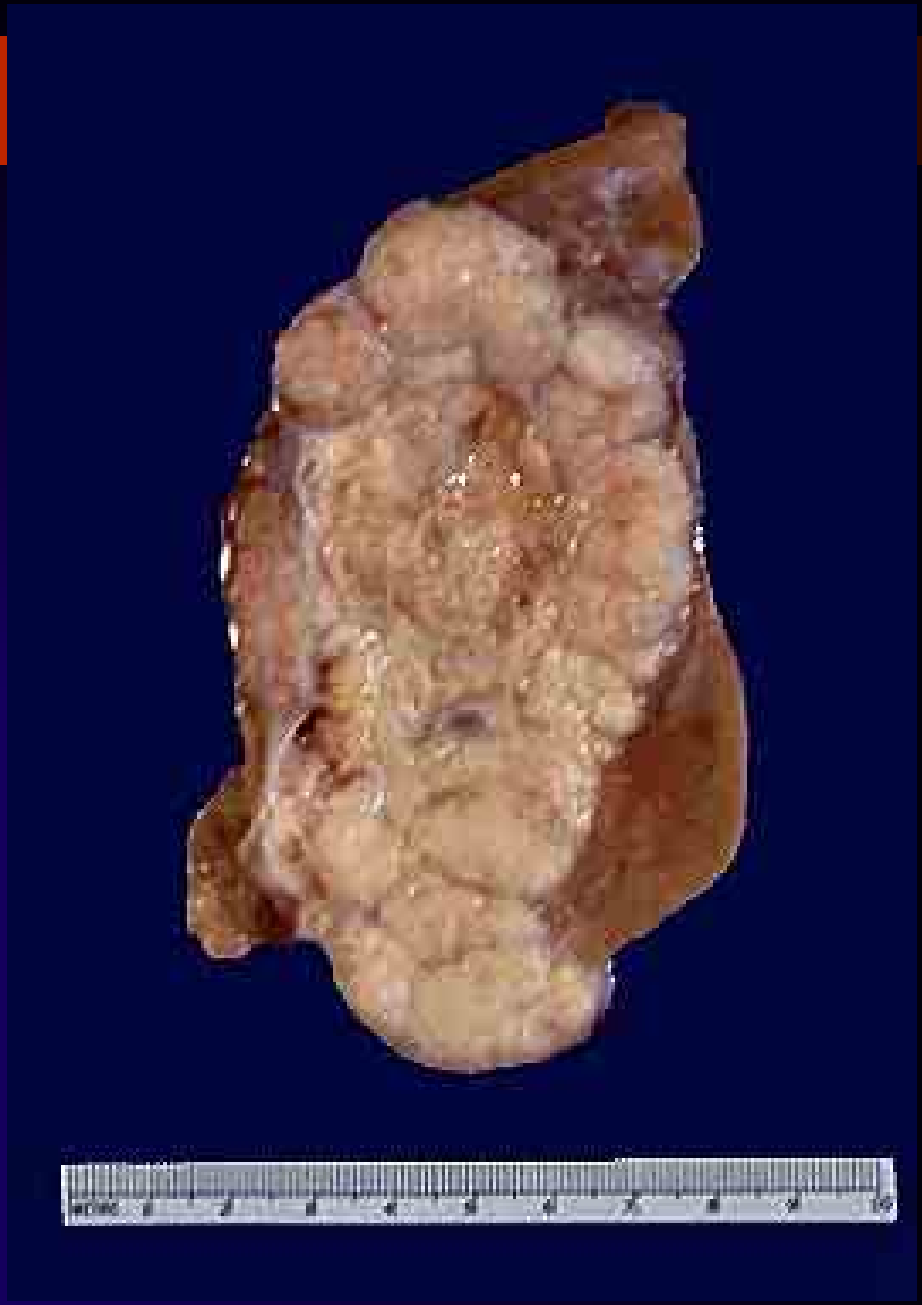




Wilms tumor

- Childhood tumor (2-5y) 98%< 10 years
- Most common tumor in childhood
- Sporadic, unilateral (90%)
- Bilateral more common in familial cases (20%)
- Familial syndromic (5%), nonsyndromic (5%)
- WAGR sy – Aniridia, genital abn, Mental Ret. WT1
- Beckwith Wiedemann sy - Hemihypertrophy – WT2

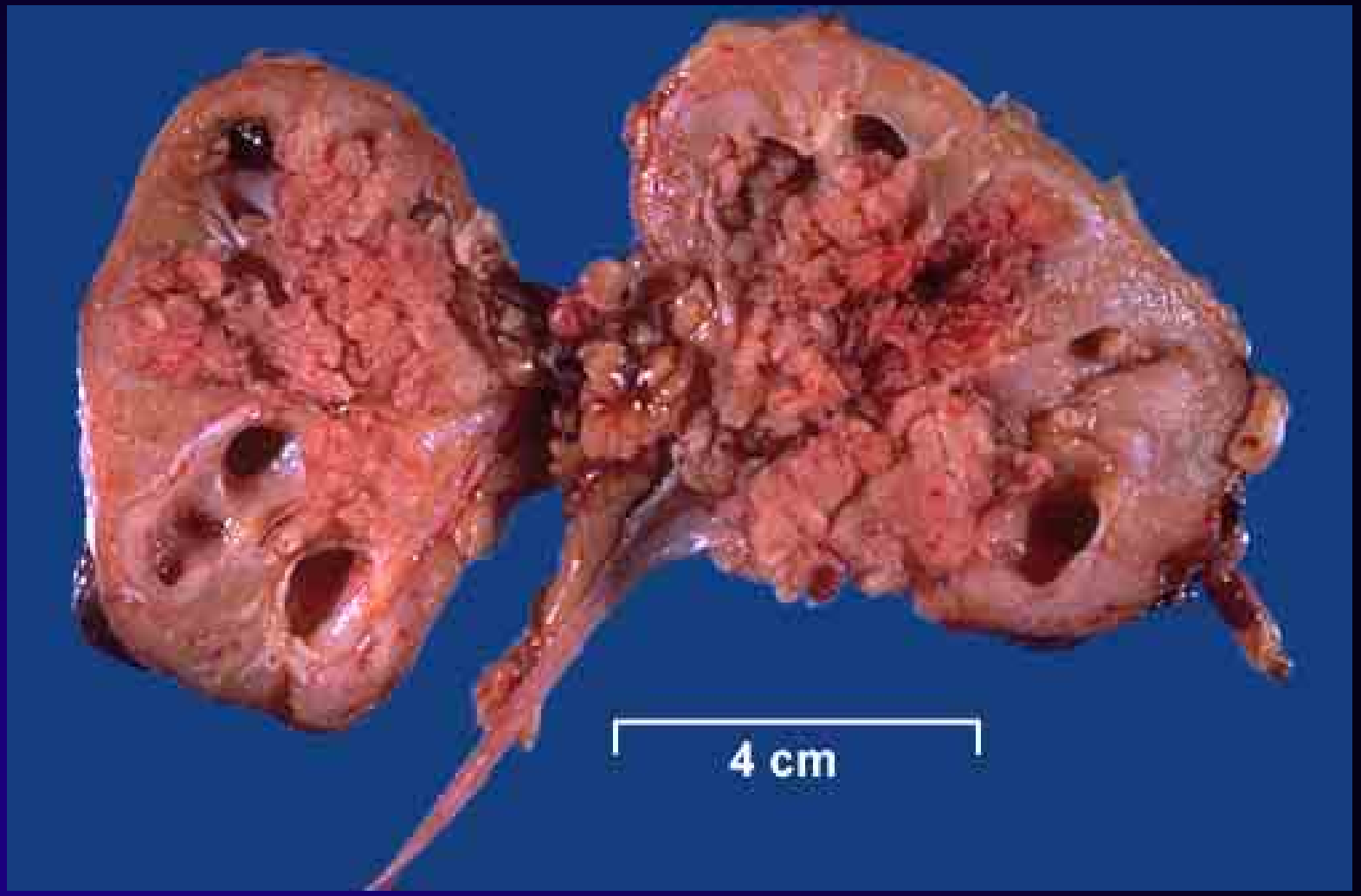
Wilms Tumor:



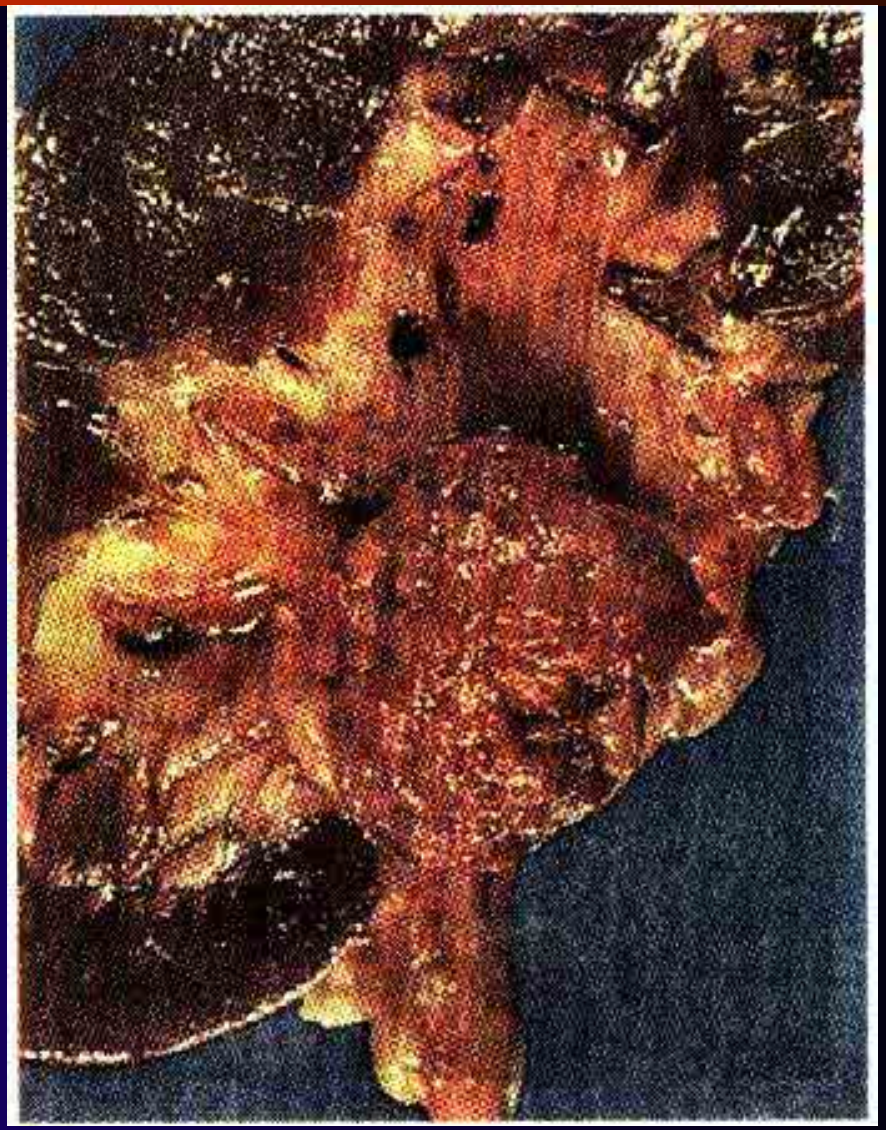
Transitional Cell Carcinoma:

- 5-10% of adult renal ca.
- Etiology: Analgesic abuse, dye, rubber etc..
- Multiple common.
- Malignant cells in urine
- Desquamated tissue may cause obstruction.
- Hematuria & pain.

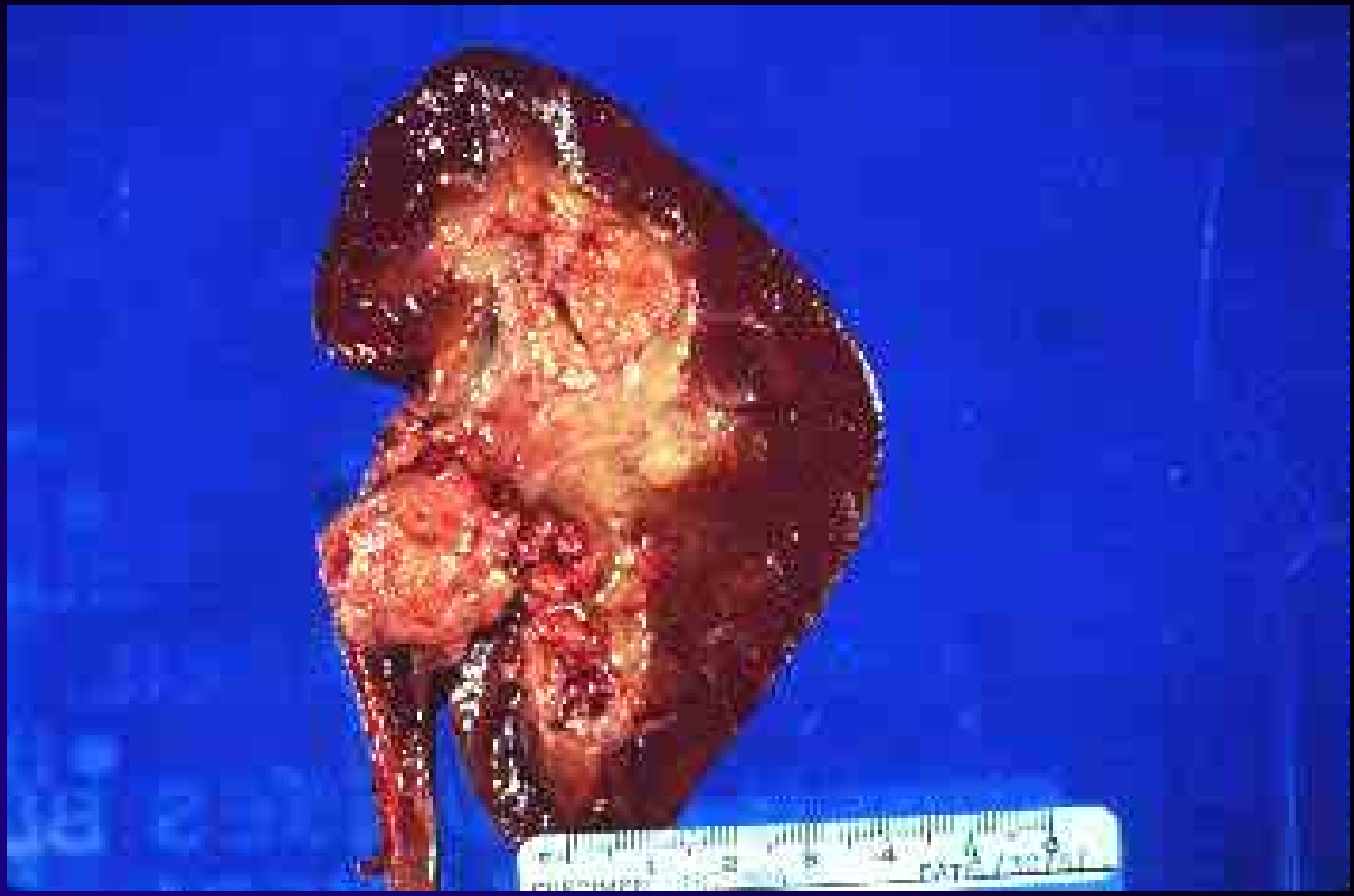
Transitional cell Carcinoma:



Transitional cell Carcinoma:



Transitional cell Carcinoma:



Wilms Tumor Features:

- Lobulated tumors mass –encapsulated
- Histology: mixture of immature cells metanephric, stromal, tubular
- Chemotherapy + surgery = 5 years = 90%
- Children < 2 years better prognosis

“When you develop the habits of success, success will become a habit.”

http://SuccessNet.org