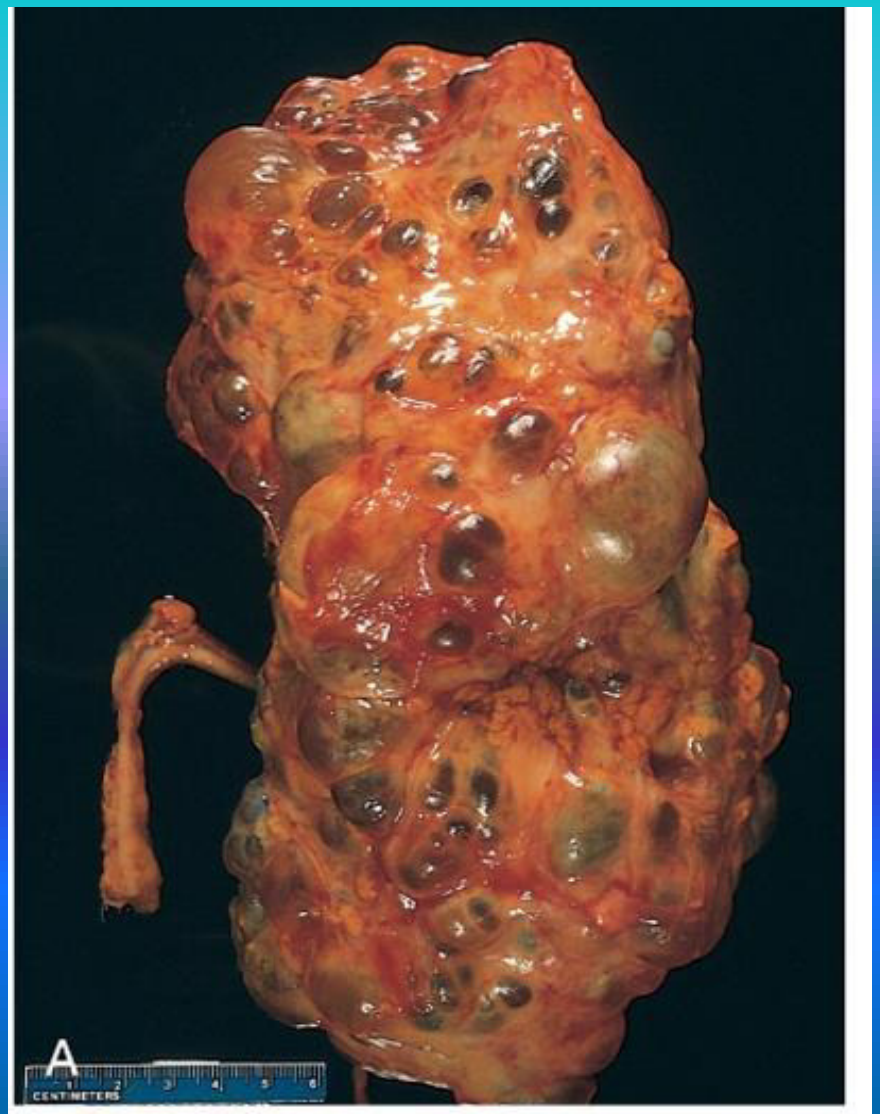
CYSTIC DISEASES OF THE KIDNEY



- **Types**

1-Simple Cysts

2-Dialysis-associated acquired cysts

3-Autosomal Dominant (Adult) Polycystic Kidney Disease

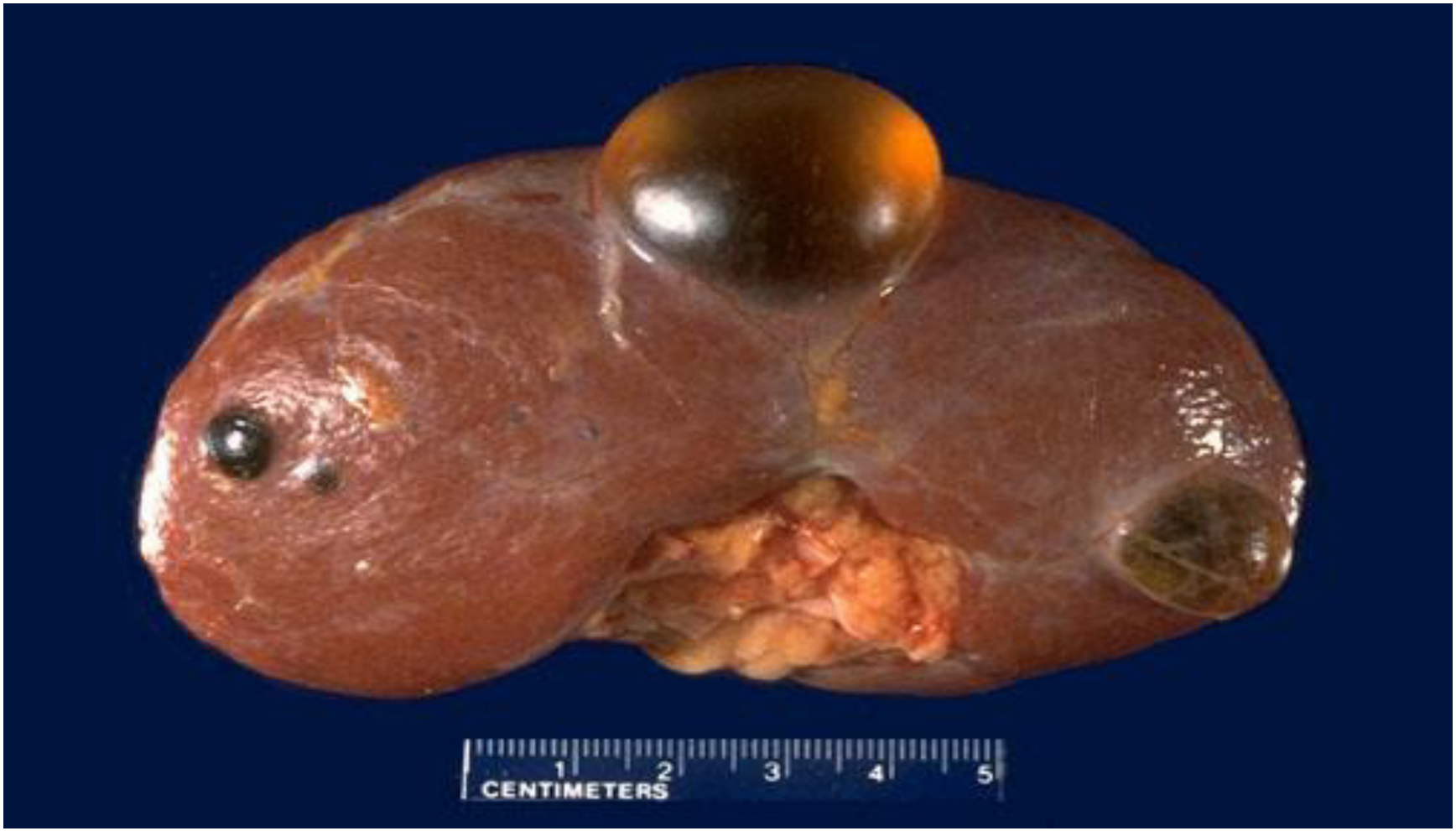
4-Autosomal Recessive (Childhood) Polycystic Kidney Disease

5-Medullary Cystic Disease

1-Simple Cysts

- **Multiple or single cystic spaces that vary widely in diameter (1-5 cm in diameter) filled with clear fluid.**
- **usually confined to the cortex.**
- **common post-mortem finding that has no clinical significance.**
- **The main importance of cysts lies in their differentiation from kidney tumors when they are discovered either incidentally or because of hemorrhage and pain**

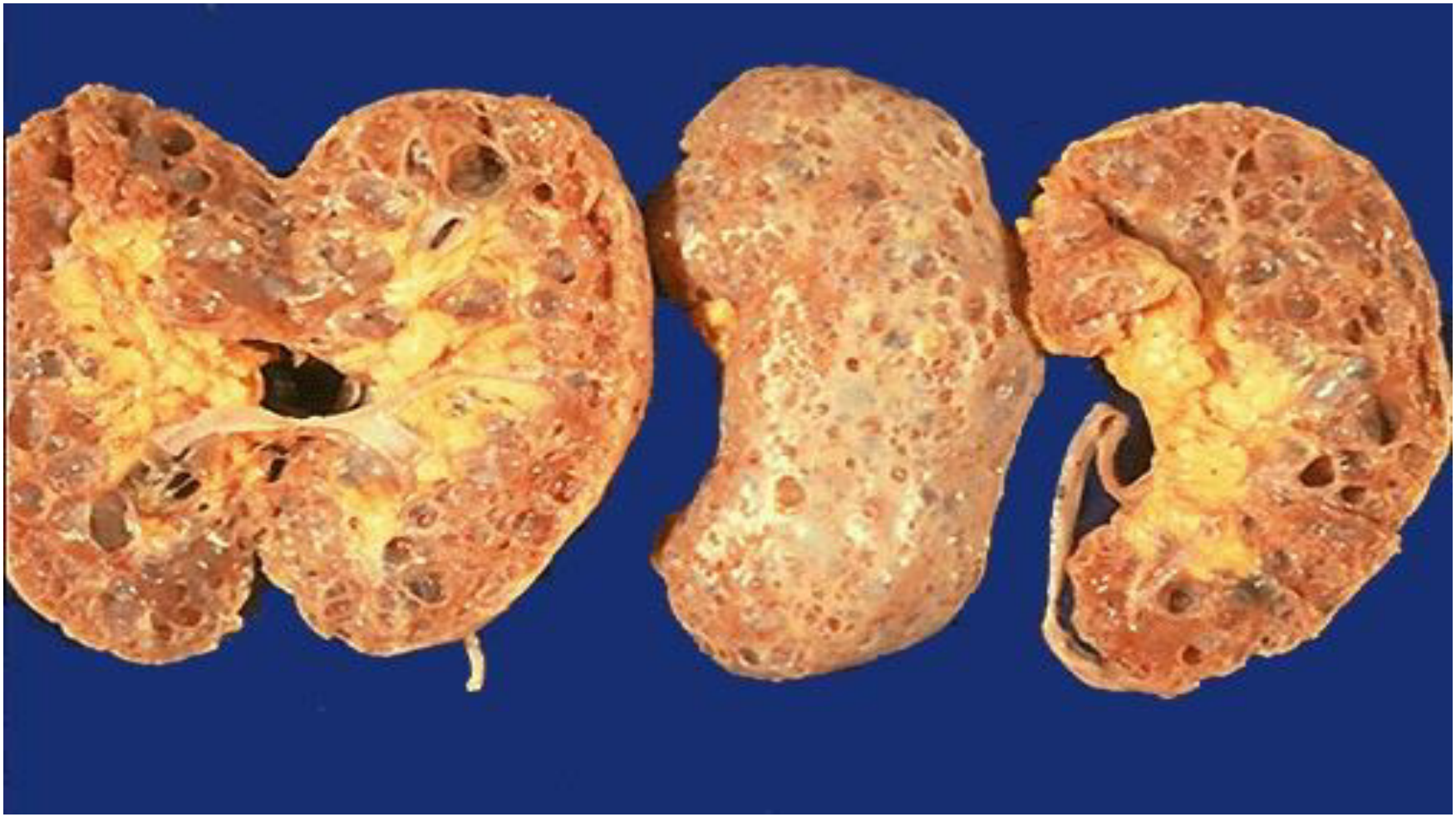
Simple renal Cysts



2-Dialysis-associated acquired cysts

- **occur in the kidneys of patients with end-stage renal disease who have undergone prolonged dialysis.**
- **They are present in both cortex and medulla and may bleed causing hematuria.**
- **renal carcinomas may arise in the walls of these cysts.**

Cystic change associated with chronic renal dialysis.



3-Autosomal Dominant (Adult) Polycystic Kidney Disease

- **Characterized by multiple expanding cysts of both kidneys that ultimately destroy the intervening parenchyma.**
- **Incidence (1: 500-1000) persons**
- **Accounts for 10% of cases of chronic renal failure.**
- **It can be caused by inheritance of one of at least 2 autosomal dominant genes of very high penetrance.**

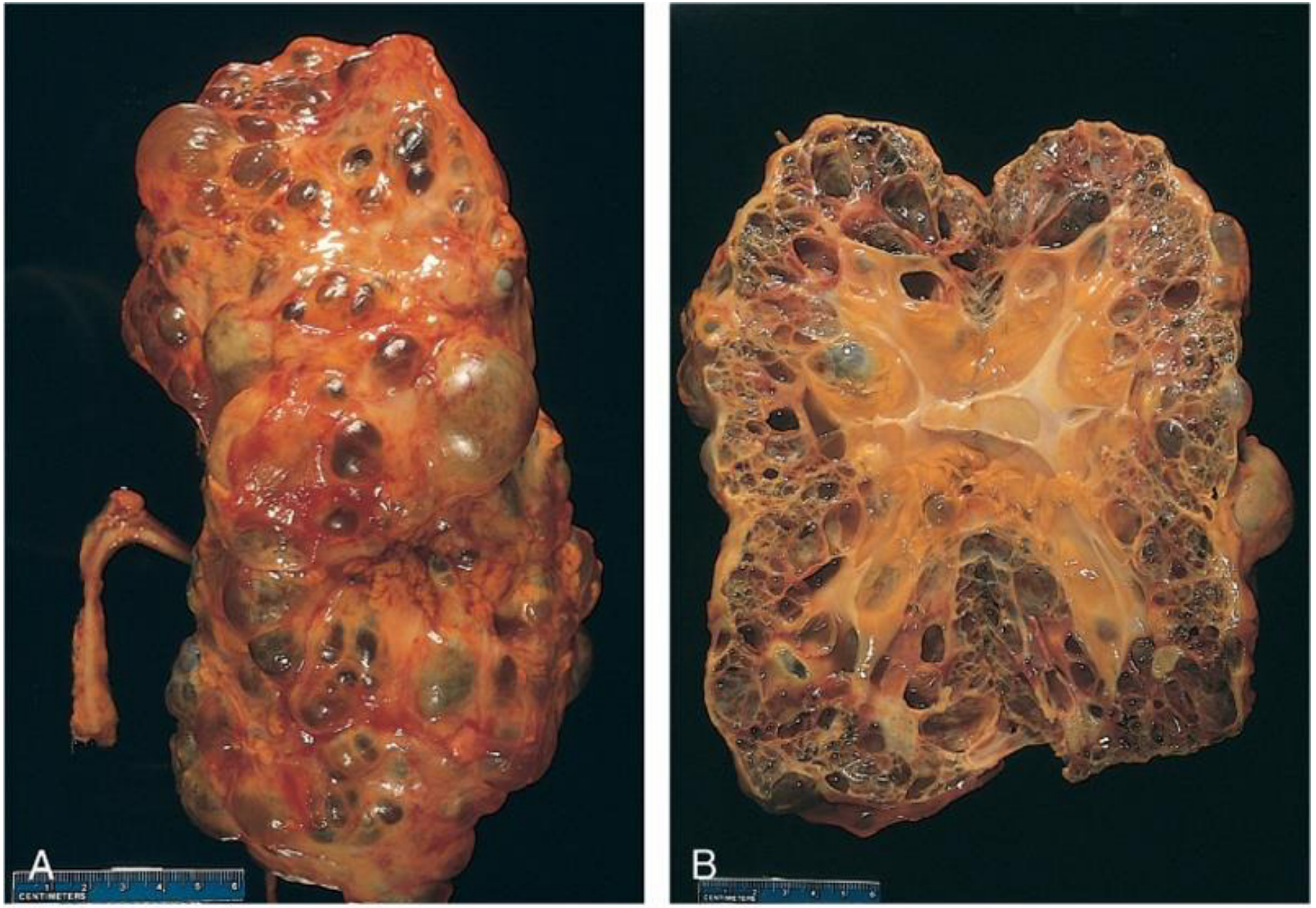
(1)- *PKD1* on the short arm of chromosome 16

- In 85-90% of families

-This gene encodes a large and complex cell membrane-associated protein called polycystin-1

(2)- *PKD2* gene (10-15% of cases) on chromosome 4:

- **encodes *polycystin 2.***
- **Polycystin 2 is thought to function as a calcium-permeable membrane channel.**
- **polycystins 1 and 2 are believed to act together by forming heterodimers.**
- **mutation in either gene gives rise to essentially the same phenotype although patients with *PKD2* mutations have a slower rate of disease progression as compared with patients with *PKD1* mutations.**



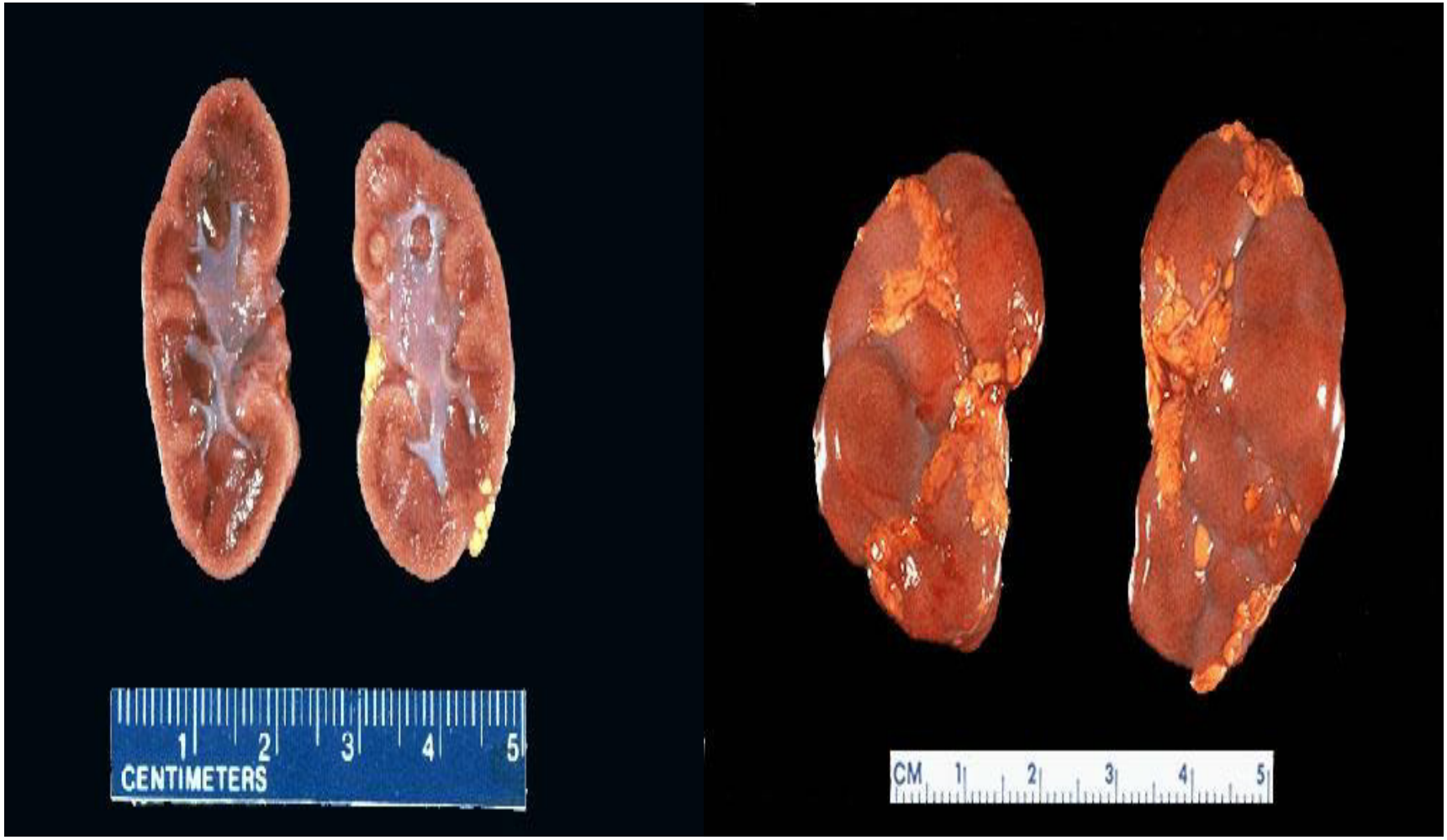
- **Clinical presentation**
- ***asymptomatic*** ***until the 4th decade*** **by which time the kidneys are quite large although small cysts start to develop in adolescence.**
- **The most common presenting complaint is *flank pain* or a heavy dragging sensation.**
- **Acute distention of a cyst either by intracystic hemorrhage or by obstruction may cause excruciating pain.**
- **palpation of an abdominal mass.**
- ***Intermittent gross hematuria*** **commonly occurs.**
- **hemorrhage.**

- **Complications**
- **1-*hypertension (75%).***
- ***2-urinary infection.***
- **3-Saccular aneurysms of the circle of Willis are present in 10% to 30% of patients (subarachnoid hemorrhage).**
- **4-end-stage renal failure occurs at about age 50 .**

4-Autosomal Recessive (Childhood) Polycystic Kidney Disease

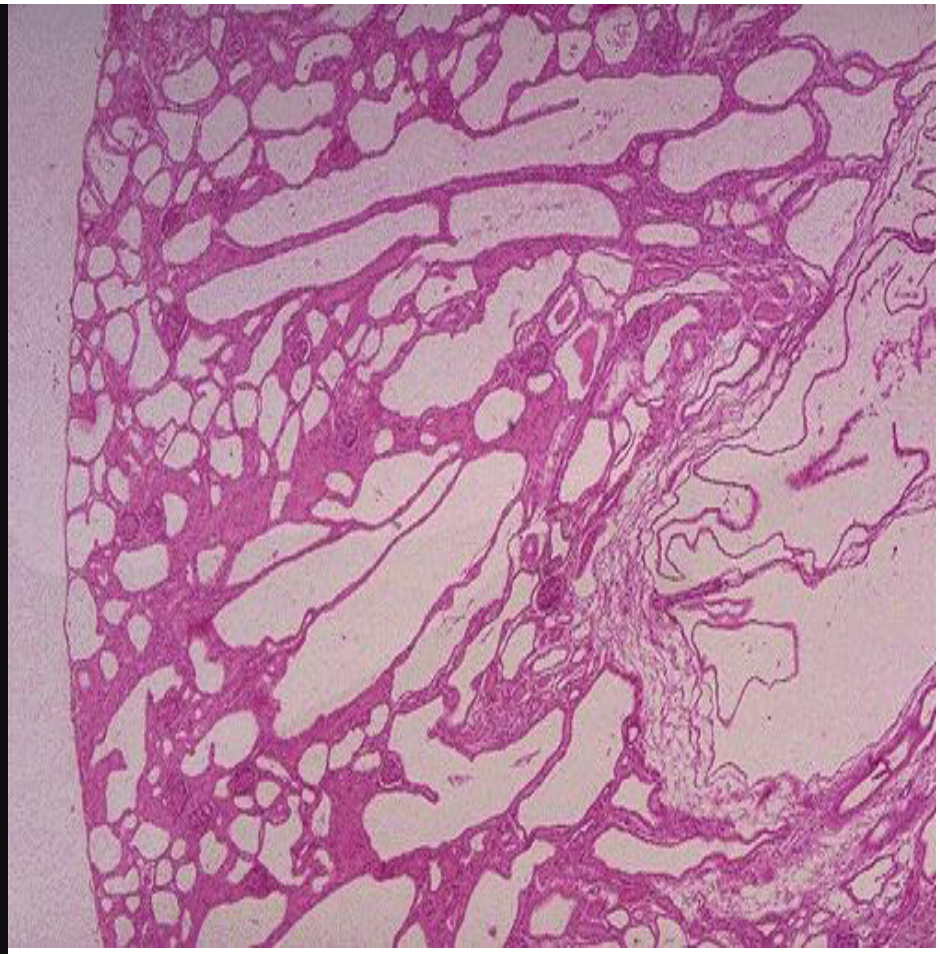
- **autosomal recessive inheritance.**
- **1:20,000 live births.**
- **Perinatal, neonatal, infantile, and juvenile subcategories have been defined, depending on time of presentation and the presence of associated hepatic lesions.**
- **Mutations in *PKHD1* gene coding for a putative membrane receptor protein called *fibrocystin*, localized to chromosome 6p.**
- **Fibrocystin may be involved in the function of cilia in tubular epithelial cells .**

Normal term infant kidneys



Cysts are fairly small but uniformly distributed throughout the parenchyma so that the disease is usually symmetrical in appearance

with both kidneys markedly enlarged.



5-Medullary Cystic Disease

- **There are 2 major types of medullary cystic disease:**
- ***1-medullary sponge kidney***
- **a relatively common and usually innocuous condition.**
- ***2-nephronophthisis-medullary cystic disease complex***
- **is almost always associated with renal dysfunction.**
- **usually begins in childhood.**
- **4 variants of this disease complex are recognized on the basis of the time of onset: infantile; juvenile (most common); adolescent; adult**

- **Clinical features**
- **polyuria and polydipsia a consequence of diminished tubular function.**
- **Progression to end-stage renal disease ensues over a 5-10-year period.**
- **The disease is difficult to diagnose, since there are no serologic markers and the cysts may be too small to be seen with radiologic imaging.**
- **cysts may not be apparent on renal biopsy if the cortico-medullary junction is not well sampled.**
- **A positive family history and unexplained chronic renal failure in young patients should lead to suspicion of medullary cystic disease.**

URINARY OUTFLOW OBSTRUCTION

- **Renal Stones (*Urolithiasis)***
- **Calculus formation at any level in the urinary collecting system.**
- **Most common arise in the kidney.**
- **(1%) of all autopsies.**
- **Symptomatic urolithiasis is more common in men than in women.**
- **Familial tendency toward stone formation**

- **Stones are unilateral in about 80% of patients.**
- **Common sites of formation are renal pelvis and calyces and the bladder.**
- **They tend to be small (average diameter 2-3 mm) and may be smooth or jagged.**
- **Progressive precipitation of salts leads to the development of branching structures known as staghorn calculi.**
- **These massive stones are usually composed of magnesium ammonium phosphate.**

- ***Pathogenesis***
- **Renal stones are composed of:**
- **1-calcium oxalate or calcium oxalate mixed with calcium phosphate(80%) .**
- **2-10% are composed of magnesium ammonium phosphate.**
- **3-6%-9% are either uric acid or cystine stones**
- **In all cases there is an organic matrix of mucoprotein that makes up about 2.5% of the stone by weight.**

- **Causes of Renal Stones**

- ***1-increased urine concentration of the stone's constituents so that it exceeds their solubility in urine (supersaturation).***
- **50% of patients who develop *calcium stones* have hypercalciuria that is not associated with hypercalcemia.**
- **Types of Hypercalciuria:**
- **A. absorptive hypercalciuria.**
- **B. renal hypercalciuria due to primary renal defect of calcium reabsorption.**
- **In 5% to 10% of persons there is hypercalcemia and consequent hypercalciuria.**

- **2-The presence of a nidus**
- **Urates provide a nidus for calcium deposition.**
- **Desquamated epithelial cells**

- **3-urine pH**
- **High urine pH favors crystallization of calcium phosphate and stone formation.**
- ***Magnesium ammonium phosphate (struvite) stones* almost always occur with a persistently alkaline urine due to UTIs.**
- **Uric acid stones formed in acidic urine (under pH 5.5).**
- ***Cystine stones* are more likely to form when the urine is relatively acidic.**

- **4-infections**
- **The urea-splitting bacteria such as *Proteus vulgaris* and the staphylococci predispose the person to urolithiasis.**

- **5-lack of substances that normally inhibit mineral precipitation.**
- **Inhibitors of crystal formation in urine include Tamm-Horsfall protein, osteopontin, pyrophosphate, mucopolysaccharides, diphosphonates, and a glycoprotein called nephrocalcin**
- **No deficiency of any of these substances has been consistently demonstrated in individuals with urolithiasis.**

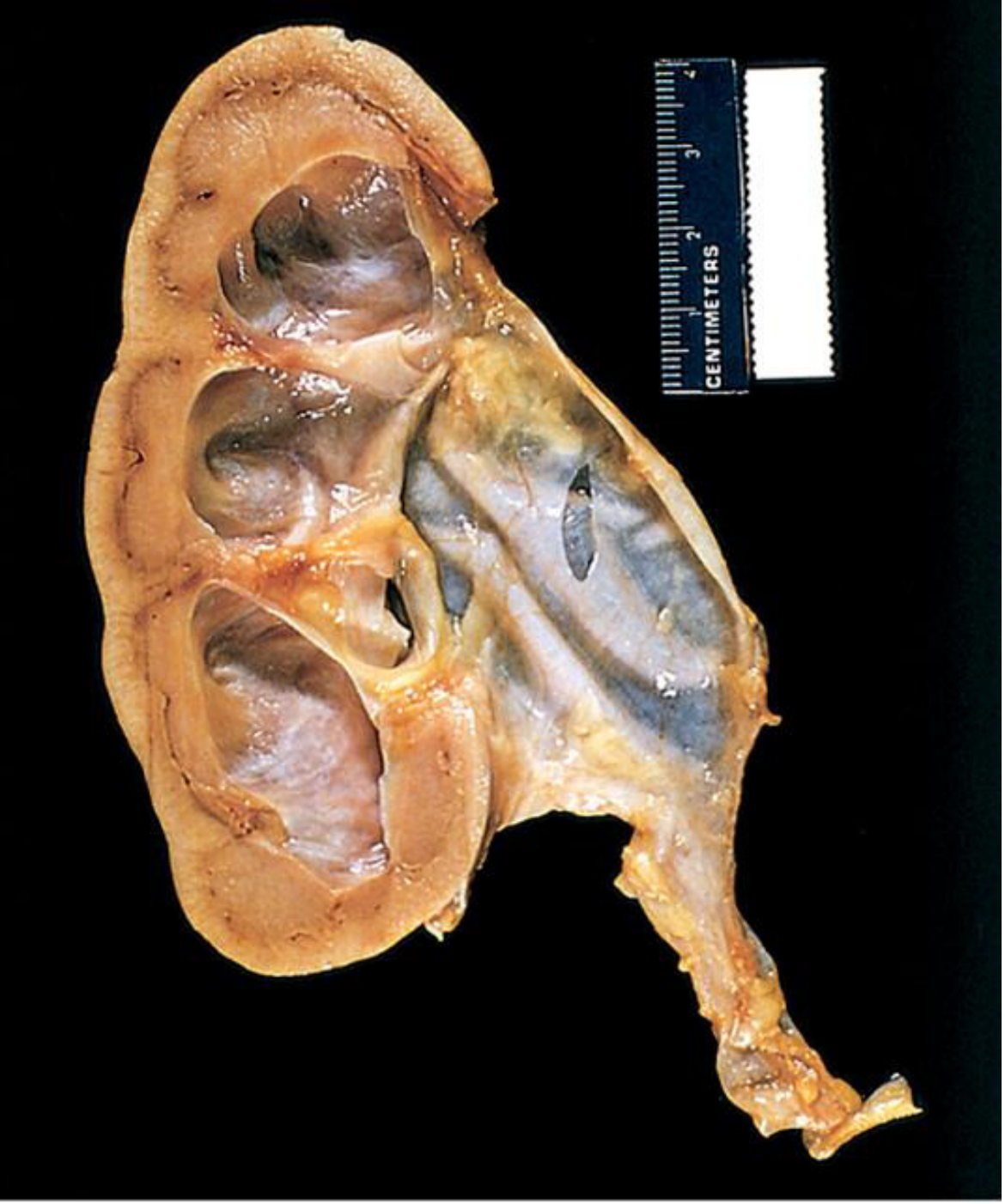
Hydronephrosis

Hydronephrosis

- **Refers to dilation of the renal pelvis and calyces, with accompanying atrophy of the parenchyma.**
- **The obstruction may be sudden or insidious and it may occur at any level of the urinary tract from the urethra to the renal pelvis.**
- **The most common causes are as follows:**

- ***1-Congenital:***
- **Atresia of the urethra**
- **Valve formations in either ureter or urethra**
- **Aberrant renal artery compressing the ureter**
- **Renal ptosis with torsion or kinking of the ureter**

- ***2-Acquired:***
- Foreign bodies: Calculi, necrotic apillae
- Tumors: Benign prostatic hyperplasia,
  carcinoma of the prostate,
  bladder tumors (papilloma and carcinoma),
  contiguous malignant disease (retroperitoneal
  lymphoma, carcinoma of the cervix or uterus
- Inflammation: Prostatitis, ureteritis, urethritis, retroperitoneal fibrosis
- Neurogenic: Spinal cord damage with paralysis of the bladder
- Normal pregnancy: Mild and reversible



Hydronephrosis of the kidney, with marked dilation of the pelvis and calyces and thinning of renal parenchyma.

DISEASES AFFECTING TUBULES AND INTERSTITIUM

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Tubulointerstitial Nephritis

- Causes :
- 1- bacterial infection.
- 2- drugs.
- 3- metabolic disorders such as hypokalemia.
- 4- physical injury such as irradiation.
- 5- viral infections.
- 6- immune reactions.
- **TIN is divided into :**
- **1-acute**
- **2-chronic**
-

Infectious : Acute Pyelonephritis

- a common suppurative inflammation of the kidney and the renal pelvis.
- **bacterial infection**.
- important manifestation of (UTI) :

1- lower UT (cystitis, prostatitis, urethritis).

2- upper UT(pyelonephritis).

3- both.

- ***Pathogenesis***
- **The principal causative organisms are :**

***1- Escherichia coli* >is the most common .**

2- *Proteus.*

3- Klebsiella.

4- Enterobacter.

5- *Pseudomonas.*

6- Staphylococci and *Streptococcus faecalis* (uncommon).

Routes of infection

- **1-hematogenous (seeding of the kidneys by bacteria in septicemia or infective endocarditis)**
- **2-ascending infection (most common): from the lower urinary tract**

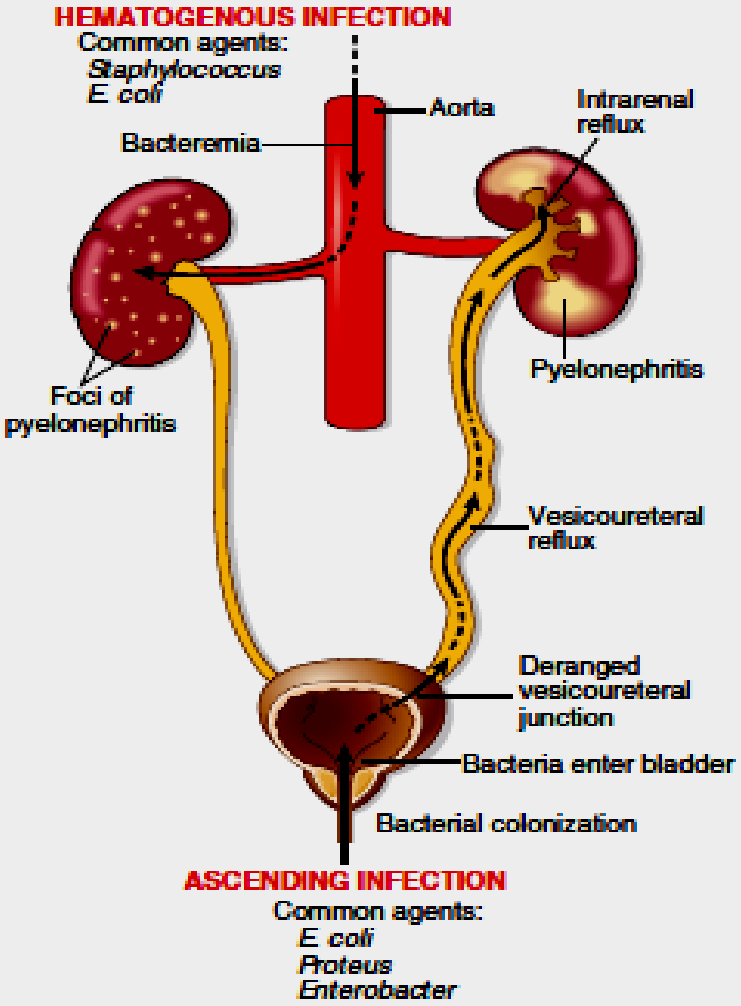


Figure 13–13 Pathways of renal infection. Hematogenous infection results from bacteremic spread. More common is ascending infection, which results from a combination of urinary bladder infection, vesicoureteral reflux, and intrarenal reflux.

- **bladder urine is sterile and remains so as a result of:**
- **1- the antimicrobial properties of the bladder mucosa.**
- **2- the flushing action associated with periodic voiding of urine.**
- **The first step is adhesion of bacteria to mucosal surfaces → colonization of the distal urethra → bladder by expansive growth of the colonies and by moving against the flow of urine.**

- **Predisposing factors**
- **1-urethral instrumentation**, including catheterization and cystoscopy
- **2-female sex** because of the close proximity of the urethra to the rectum
- **3-trauma** to the urethra
- **4-outflow obstruction or bladder dysfunction** (benign prostatic hyperplasia; uterine prolapse; neurogenic bladder dysfunction

- ***5-Pregnancy.***
- 4% to 6% of pregnant women develop bacteriuria sometime during pregnancy and 20% -40% of these eventually develop UTI.
- **6-UTI is increased in diabetes** because of the increased susceptibility to infection.
- ***7-vesicoureteral reflux***

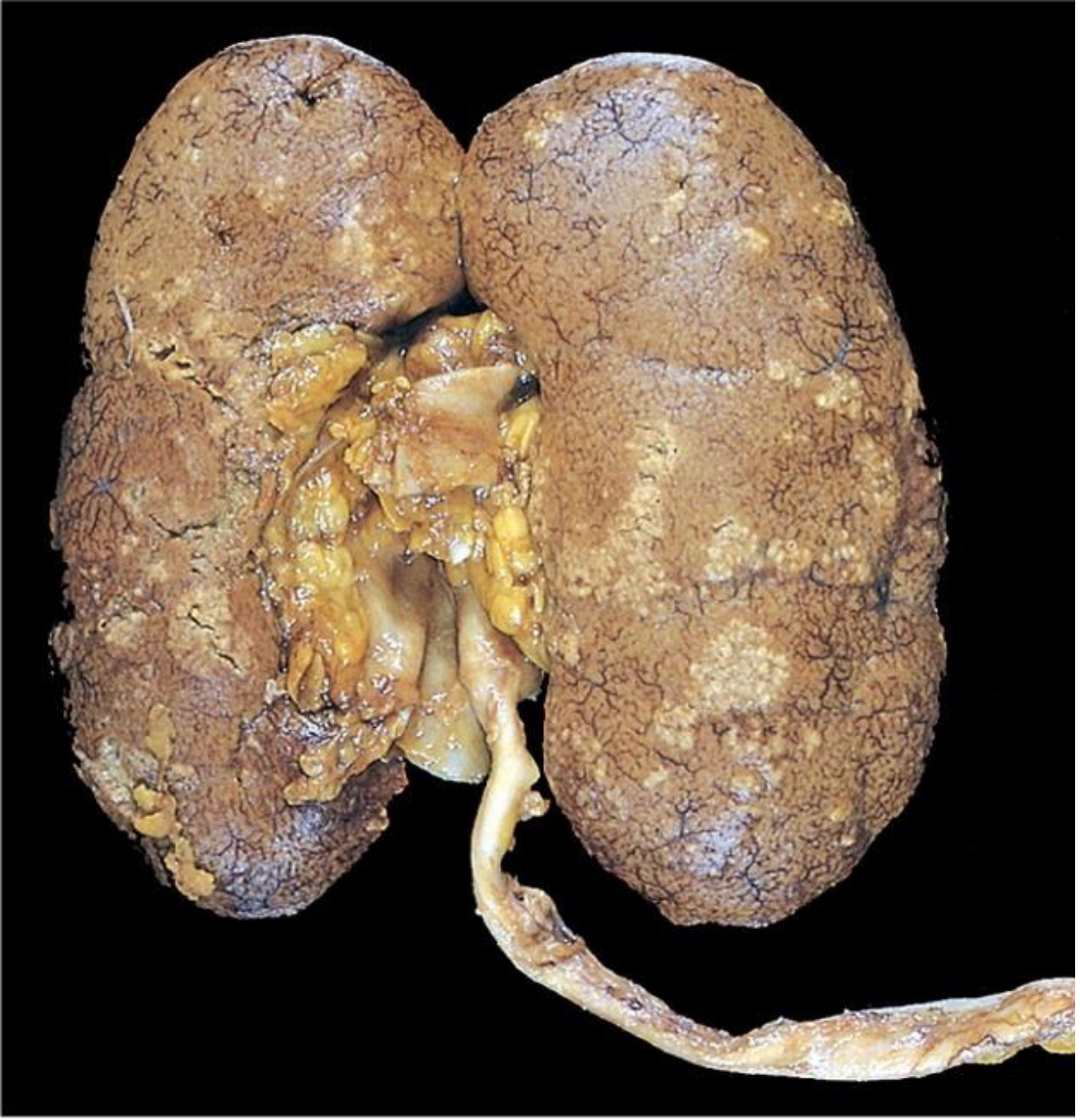
Vesicoureteral reflux

An incompetent vesicoureteral orifice allows the reflux of bladder urine into the ureters &allows bacteria to ascend the ureter into the pelvis.

- present in 20% to 40% of young children with UTI

1- congenital defect that results in incompetence of the ureterovesical valve.

2-acquired in spinal cord injury and with neurogenic bladder dysfunction secondary to diabetes



Acute pyelonephritis. The cortical surface is studded with focal pale abscesses

Drug-Induced Interstitial Nephritis

- Two forms of TIN caused by drugs are :
- 1-Acute Drug-Induced Interstitial Nephritis
- 2-Analgesic Nephropathy
- Acute TIN
- 1-most frequently occurs with synthetic penicillins (methicillin, ampicillin)
- 2- other synthetic antibiotics (rifampin), diuretics (thiazides)
- 3- nonsteroidal anti-inflammatory agents
- 4-other drugs (phenindione, cimetidine

- **Pathogenesis**
- **Many features of the disease suggest an immune mechanism.**
- **Clinical evidence of hypersensitivity is not dose related.**
- **Serum IgE levels are increased in some persons suggesting type I hypersensitivity.**
- **The mononuclear or granulomatous infiltrate, together with positive skin tests to drugs, suggests a T cell-mediated (type IV) hypersensitivity reaction.**

Morphology

- **the interstitium shows pronounced edema and infiltration by mononuclear cells, lymphocytes and macrophages .**
- **Eosinophils and neutrophils may be present, often in large numbers.**
- **With some drugs (e.g., methicillin, thiazides, rifampin), interstitial non-necrotizing granulomas with giant cells may be seen.**
- **The glomeruli are normal except in some cases caused by nonsteroidal anti-inflammatory agents.**

Clinical course

- **The disease begins about 15 days (range 2-40 days) after exposure to the drug.**
- **It is characterized by *fever*, *eosinophilia* & *rash* in about 25% of persons, and *renal abnormalities*.**
- **Renal findings include hematuria, minimal or no proteinuria, and leukocyturia (sometimes including eosinophils).**

- **A rising serum creatinine or acute renal failure with oliguria develops in about 50% of cases, particularly in older patients.**
- **It is important to recognize drug-induced renal failure, because withdrawal of the offending drug is followed by recovery although it may take several months for renal function to return to normal**

Analgesic Nephropathy: chronic drug-induced

- Consumption large quantities of analgesics may cause **chronic interstitial nephritis** *often associated with* ***renal papillary necrosis****.*
- ingestion of single types of analgesics or, most commonly people who develop this nephropathy consume mixtures containing some combination of phenacetin, aspirin, acetaminophen, caffeine, and codeine for long periods.
- **Aspirin and acetaminophen are common causes**
- **While they can cause renal disease in apparently healthy individuals preexisting renal disease seems to be a necessary precursor to analgesic-induced renal failure**

- **Pathogenesis**
- not entirely clear.
- **Papillary necrosis is the initial event**, and the interstitial nephritis in the overlying renal parenchyma is a secondary phenomenon.
- ***covalent binding* and *oxidative damage*→** Acetaminophen
- **inhibition of prostaglandin synthesis→ aspirin**

- **<u>Morphology</u>**
- The papillae show coagulative necrosis
- dystrophic calcification may occur in the necrotic areas.
- tubular atrophy, interstitial scarring, and inflammation.
- The **small vessels** in the papillae and urinary tract submucosa exhibit characteristic PAS-positive **basement membrane thickening**.

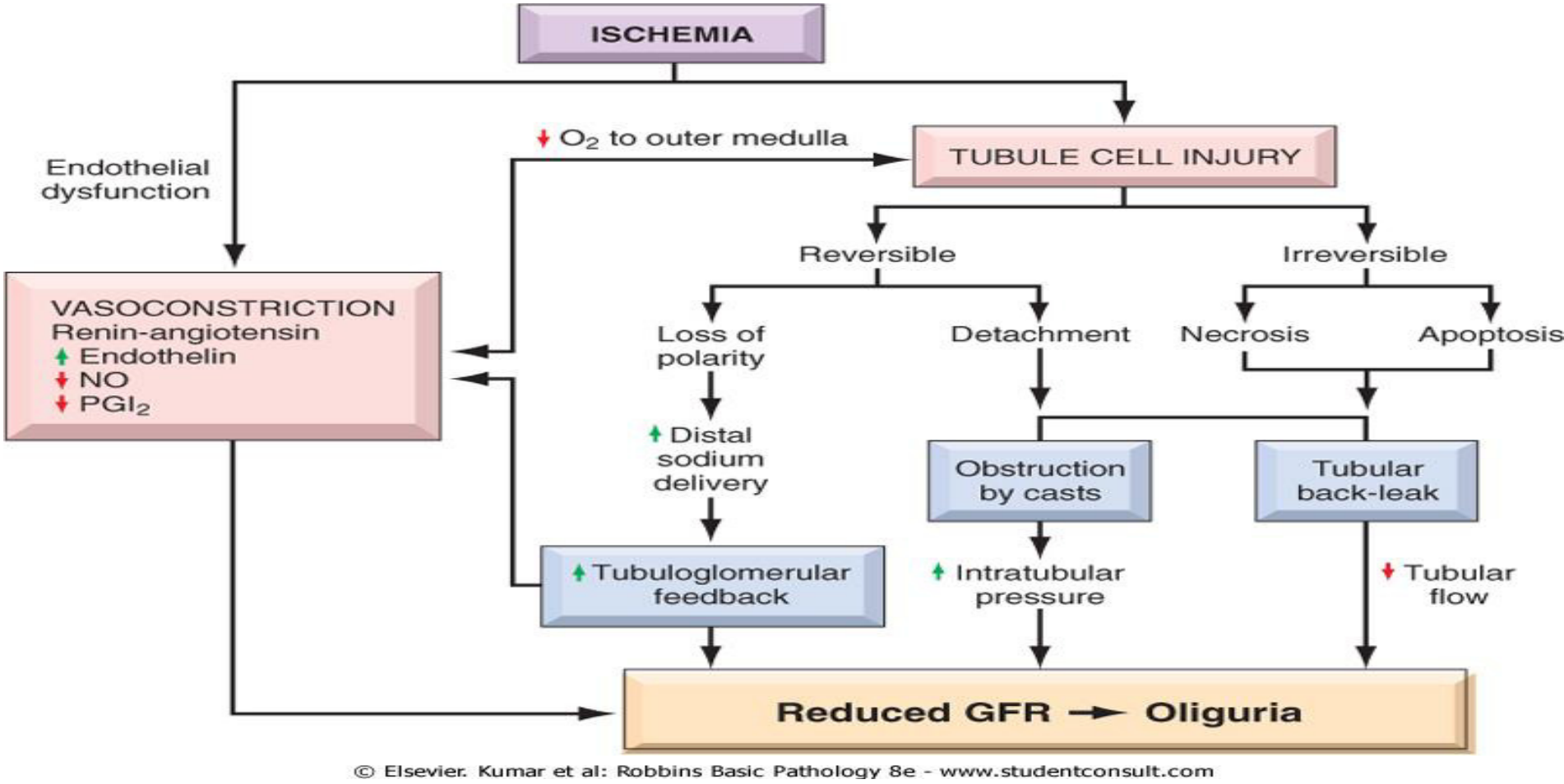
Clinical Course

- Chronic renal failure, hypertension, and anemia.
- The anemia results in part from damage to red cells by phenacetin metabolites.
- **A complication of analgesic abuse is the increased incidence of *transitional-cell carcinoma* of the renal pelvis or bladder in persons who survive the renal failure.**

Acute Tubular Necrosis (ATN)

- **ATN is a clinicopathologic entity characterized morphologically by damaged tubular epithelial cells and clinically by acute suppression of renal function.**
- ***It is the most common cause of acute renal failure.***
- **In acute renal failure, urine flow falls within 24 hours to less than 400 mL/day (oliguria).**

ATN: pathogenesis



- **ATN is a reversible renal lesion.**
- **predisposing clinical settings:**
- ***Types:***
- ***1- ischemic ATN : most common variant***
- ***is associated with shock that result from either:***
- **1- severe trauma.**
- **2- acute pancreatitis.**
- **3- septicemia.**
- **4- mismatched blood transfusions and other hemolytic crises, as well as myoglobinuria.**

- ***2- nephrotoxic ATN***
- **poisons including heavy metals (e.g., mercury)**
- **organic solvents (e.g., carbon tetrachloride)**
- **drugs such as gentamicin and other antibiotics, and radiographic contrast agents.**