Urolithiasis

Types of stones in the urinary tract

I. Calcium oxalate stones

1in 5% of patients are associated with *hypercalcemia* and *hypercalciuria*, such as occurs

a. Hyperparathyroidism,
b. Sasarcoidosis, and other hypercalcemic states.

2. In About 55% have *hypercalciuria without hypercalcemia*. And this is caused by several factors, including

a. Hyperabsorption of calcium from the intestine (absorptive hypercalciuria),

b. Intrinsic impairment in renal tubular reabsorption of calcium (renal hypercalciuria)

3. 20% of calcium oxalate stones are associated with increased uric acid secretion *(*hyperuricosuric calcium nephrolithiasis*)* with or without hypercalciuria.

Note:

- The mechanism of stone formation in this setting involves “nucleation” of calcium oxalate by uric acid crystals in the collecting ducts.

4. 5% are associated with Hyperoxaluria, either

a. Hereditary (primary oxaluria) or,

b. More commonly, acquired by intestinal over absorption s called enteric hyperoxaluria, especially in vegetarians, because much of their diet is rich in oxalates.).

II. Magnesium ammonium phosphate stones

- *A*re formed largely after infections by bacteria (e.g., *Proteus*) that convert urea to ammonia.
- The resultant alkaline urine causes the precipitation of magnesium ammonium phosphate salts.
- These are the largest type of stones called staghorn stones calculi that occupy large portions of the renal pelvis .

Staghorn stones

III. Uric acid stones

- Are common in individuals with hyperuricemia, such as

a. Gout,
b. Diseases involving rapid cell turnover, such as the leukemias.
c. More than half of all patients with uric acid calculi have neither hyperuricemia nor increased urinary excretion of uric acid.

Note: In this group, it is thought that an unexplained tendency to excrete urine of pH below 5.5 may predispose to uric acid stones, because uric acid is insoluble in acidic urine

IV. Cystine stones

- Are caused by genetic defects in the renal reabsorption of amino acids, including cystine, leading to cystinuria.

- It can therefore be appreciated that

a. Increased concentration of stone constituents,

b. Changes in urinary pH,

c. Decreased urine volume,

d. and the presence of bacteria influence the formation of calculi.

- Many individuals with hypercalciuria, hyperoxaluria, and hyperuricosuria often do not form stones.
- It has therefore been postulated that stone formation is enhanced by a deficiency in inhibitors of crystal formation in urine.

- The inhibitors is long, include

a. Pyrophosphate,
b. Diphosphonate,
c. Citrate,
d. and a glycoprotein called *nephrocalcin*.

Cystic diseases of the kidney

1.Simple cysts

- Are single or multiple, usually cortically
- Size is between 1-5 cm
- Are common postmorteum findings without clinical significance

2.Autosomal Dominant (Adult) Polycystic Kidney Disease

- Is an autosomal dominant disease
- Account for about 5% to 10% of cases of end-stage renal disease requiring transplantation or dialysis.
- The predisposition to develop the diseases is inherited as an autosomal dominant

- One mutant allele is inherited, the other allele shows acquired mutation
- Both alleles of the involved genes have to be nonfunctional for development of the disease.

- It results from mutations in *PKD1* and *PKD2*

1. The *PKD1* gene is located on ch16

- Mutations in *PKD1* account for about 85% of cases.

- It encodes a large integral membrane protein named ***polycystin-1***,

Note

- In individuals with these mutations, the likelihood of developing renal failure is less than 5% by 40 years of age, rising to more than 35% by 50 years, more than 70% at 60 years of age, and more than 95% by 70 years of age.

2. The *PKD2* gene, located on chromosome 4

- Accounts for most of the remaining cases of polycystic disease.
- Its product, ***polycystin-2***,
- The is less severe than that associated with *PKD1* mutations

- Renal failure occurs in less than 5% of patients with *PKD2* mutations at 50 years of age, but this rises to 15% at 60 years of age, and 45% at 70 years of age.

Morphology

Gross

- The kidneys are bilaterally enlarged and may achieve enormous sizes; weights may reach as much as 4 kg for each kidney
- The external surface appears to be composed solely of a mass of cysts, up to 3 to 4 cm in diameter, with no intervening parenchyma.

Microscopic examination

- Reveals functioning nephrons dispersed between the cysts.
- The cysts may be filled with a clear, serous fluid or with hemorrhagic fluid
- As these cysts enlarge, they may encroach on the calyces and pelvis to produce pressure effects.

- The disease is bilateral;
- The cysts initially involve a minority of the nephrons, so renal function is retained until about the fourth or fifth decade of life.

-The cysts arise from the tubules throughout the nephron and therefore have variable lining epithelia.

Clinical Features.

1. Many patients remain asymptomatic until renal insufficiency announces the presence of the disease.
2. In others, hemorrhage or progressive dilation of cysts may produce pain.
3. Excretion of blood clots causes renal colic.

4. The disease occasionally begins with the insidious onset of hematuria, followed by other features of progressive chronic kidney disease, with **hypertension.**

Note: Patients with *PKD2* mutations tend to have an older age at onset and later development of renal failure.

Note:

Individuals with polycystic kidney disease also tend to have extrarenal congenital anomalies.

a. About 40% have one to several cysts derived from biliary epithelium in the liver (polycystic liver disease) that are usually asymptomatic.

b. Intracranial berry aneurysms, presumably from altered expression of polycystin in vascular smooth muscle, arise in the circle of Willis

c. Mitral valve prolapse

- About 40% of adult patients die of hypertensive heart disease,
- 15% of a ruptured berry aneurysm or hypertensive intracerebral hemorrhage, and the rest of other causes.

3.Autosomal Recessive (Childhood) Polycystic Kidney Disease

- Is genetically distinct from adult polycystic kidney disease.
- *Categories* depending on the time of presentation and presence of associated hepatic lesions

1.Perinatal,

2. Neonatal,

3. infantile, and

4. *juvenile*,.

Note:

- The first two are the most common; serious manifestations are usually present at birth, and the young infant might develop renal failure early and dies of the disease.

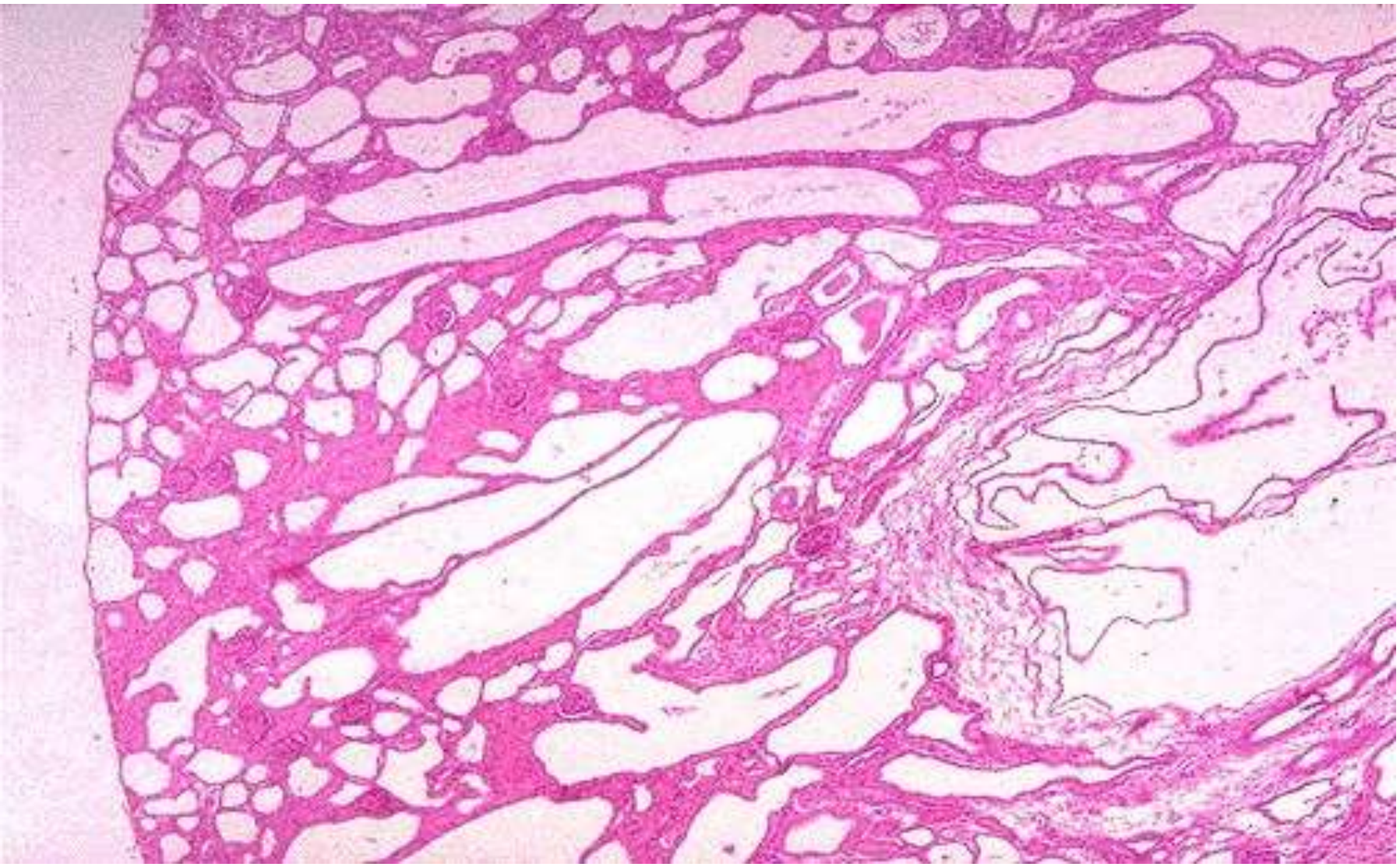
Genetics and Pathogenesis.

- In most cases, the disease is caused by mutations of the *PKHD1* gene, on ch 6
- The gene is highly expressed in adult and fetal kidney and also in liver and pancreas.
- It encodes ***fibrocystin***

Morphology

- Kidneys are enlarged with smooth external surface
- The cysts are in the form of ilated delongated channels at right angle to the cortex
- Completely replacing the cortex and medulla
- Have uniform lining of cuboidal cells reflecting their origin from the collecting ducts

ARPKD



- Patients who survive the infancy may develop congenital hepatic fibrosis
- In older children, the hepatic diseases is the predominant form

4. Acquired cysts in kidneys on dialysis

- These patients may develop renal cell carcinoma as a complication
- Carcinoma of papillary type

Renal tumors

I. Benign tumors

- Papillary adenoma
- Angiomyolipma
- Oncocytoma

II. Renal cell carcinoma

I. Risk factors

- Tobacco is the most significant risk factor.,.
- Exposure to asbestos, and petroleum products, and heavy metals.
- There is also an increased incidence in patients with acquired cystic disease from dialysis

1. Most renal cancers are sporadic,
2. Unusual forms of autosomal dominant familial cancers occur, usually in younger individuals and account for 4% of renal cell carcinomas

A. <u>Von Hippel-Lindau (VHL) syndrome</u>:

- *Half to two thirds of individuals with VHL (nearly all, if they live long enough)will develop renal cysts and renal cell carcinomas.*

2. Hereditary (familial) clear cell carcinoma, without the other manifestations of

Clear cell renal carcinoma

- This is the most common type, accounting for 70% to 80% of renal cell cancers.
- The tumors are made up of cells with clear cytoplasm and are nonpapillary.
- They can be familial, but in most cases (95%) are sporadic.

- **Clinical Features.**

- The three classic diagnostic features of renal cell carcinoma are

a. Costovertebral pain,

b. Palpable mass, and

c. Hematuria,

Note: These are seen in only 10% of cases

- The most reliable of the three is hematuria, but it is usually intermittent and may be microscopic; thus, the tumor may remain silent until it attains a large size.

- At this time it is often associated with generalized constitutional symptoms, such as fever, malaise, weakness, and weight loss.
- Due to this pattern of asymptomatic growth occurs in many patients, the tumor may have reached a diameter of more than 10 cm when it is discovered.

- *One of the common characteristics of this tumor is its tendency to metastasize widely before giving rise to any local symptoms and metastsis is the early manifestaion in 25% of cases*

- The most common locations of metastasis are

1. The lungs (more than 50%)
2. Bones (33%),
3. Followed in frequency by the regional lymph nodes, liver, adrenal, and brain.

prognosis

- The average 5-year survival rate of persons with renal cell carcinoma is about 45% and as high as 70% in the absence of distant metastases.
- With renal vein invasion or extension into the perinephric fat, the figure is reduced to approximately 15% to 20%.