Urinary tract infection (UTI)
Cystic diseases of the kidney
Renal neoplasms

Dr. András Tislér
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Urinary tract infections (UTI)

E. coli
Introduction

- UTI – most frequent bacterial infections
- Occurs in all ages, wide clinical spectrum
- Annual incidence 12%/year in females
- Incidence 0.7/1py in college women, 0.07 in postmenopausal women
- by the age 32 50% of females had at least 1 episode
- Needs special attention in children, males, diabetics, pregnant woman, elderly, those with indwelling catheter
Some definitions

- **Colonization**
  - Bacterial attachment to skin, mucosal surfaces
- **Contamination**
  - Bacteria entering the urine during sample collection
- **Sterile leukocyturia**
  - Leucocyturia with no bacterial growth in the sample
- **Asymptomatic bacteriuria**
  - Significant bacteriuria without symptoms
- **Relapse**
  - Recurrent infection with same organism
- **Reinfection**
  - Recurrent infection with an other organisms
Classification

Complicated

Uncomplicated

Upper UTI:
- Pyelonephritis

Lower UTI:
- Cystitis
- Urethritis
Classification

- **Uncomplicated UTI**
  - acute cystitis and pyelonephritis occurring in healthy premenopausal, nonpregnant women with no history suggestive of an abnormal urinary tract
    - Better prognosis
    - No need for culture/sensitivity
    - Empiric treatment

- **Complicated:** otherwise
Classification of UTI: Non-complicated vs. complicated

- Male sex
- Age
  - <15 years, >65y
- Diabetes
- Pregnancy
- Immunocompromised patient
  - Steroids, chemotherapy, transplanted
- Urinary tract abnormalities
  - Structural: stone, stricture, obstruction, cysts, prostate hypertrophy
  - Functional: neurogenic bladder, vesicoureteral reflux, dialyzed
- Urological procedure within 14 days
- Risk for resistant strains
  - Hospital acquired
  - ABx within 30 days
  - Symptoms more than 7 days
Pathogenesis: bacterial colonization

- **Virulence factors**
  - Fimbriae
  - Flagellae
  - Urease synthesis

- **Defence mechanisms**
  - Normal vaginal flora (lactobacillus)
  - Glycocalyx
  - Tamm-Horsfall protein
  - Uroepithelial cell shedding
  - ABO non-secretor (increased risk)
  - P1 genotype (increased risk)
Risk factors for UTI

• Bacterial virulence and host defence mechanisms

• Uncomplicated UTI (usually young female)
  – Genetic factors
  – Sexual intercourse
  – Spermicide use
  – Previous UTI, family Hx of UTI

• Complicated UTI
Diagnosis

• Typical signs and symptoms
• Urine dipstic: leukocyte estherase +, nitrit+
• Urinary sediment:
  – WBCs, WBC casts in pyelonephritis
  – RBCs
• Urinary culture and sensitivity
  – Complicated UTI
  – Atypical signs/symptoms
  – No improvement on empiric therapy in uncomplicated UTI
  – Recurrent infection,
• Urine sample:
  – Best first morning void
  – Local desinfection (nonfoaming antiseptic), drying
  – Spreading the labia - pulling back foreskin
  – Midstream sample
  – Immediate culturing or store on +4 degrees
  – Use of dip-slide
### Main Microbial Strains Responsible for Urinary Tract Infection

<table>
<thead>
<tr>
<th>Microbial Strain</th>
<th>First Episode or Delayed Relapse</th>
<th>Relapse Due to Early Reinfection</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Escherichia coli</em></td>
<td>71%–79%</td>
<td>60%</td>
</tr>
<tr>
<td><em>Proteus mirabilis</em></td>
<td>1.1%–9.7%</td>
<td>15%</td>
</tr>
<tr>
<td><em>Klebsiella</em></td>
<td>—</td>
<td>20%</td>
</tr>
<tr>
<td><em>Enterobacter</em></td>
<td>1.0%–9.2%</td>
<td>—</td>
</tr>
<tr>
<td><em>Enterococcus</em></td>
<td>1.0%–3.2%</td>
<td>—</td>
</tr>
<tr>
<td><em>Staphylococcus saprophyticus</em></td>
<td>3%–7%</td>
<td>—</td>
</tr>
<tr>
<td>Other species</td>
<td>2%–6%</td>
<td>5%</td>
</tr>
</tbody>
</table>

Diagnosing UTI: definition of positive culture

- Classically significant bacteriuria $10^5$ CFU/ml
- If typical symptoms then lower counts are diagnostic (as low as $10^3$ CFU/ml)
- Consider already treated patients with lower counts

- Urine culture typically grows monoflora unless
  - Contamination during sampling
  - Fecal contamination of the bladder
Asymptomatic bacteriuria

- Positive culture in a asymptomatic person (>10^5 CFU/ml)
- To be screened for and to be treated in:
  - Pregnancy
  - Vesico-ureteral reflux (VUR)
  - before urological procedures
  - struvite (staghorn) stone disease

Treatment is not indicated in:
- Diabetes
- non pregnant women
- elderly
- spinal cord injury
Sterile pyuria

CAUSES OF ASEPTIC LEUKOCYTURIA

Self-medication before urine culture
Sample contamination by cleansing solution
Vaginal discharge
Urinary stone
Urinary tract tumor
Chronic interstitial nephritis (especially due to analgesics)
Fastidious microorganisms requiring special culture medium (Ureaplasma urealyticum, Chlamydia, Candida)
tuberculosis
Examples for abnormalities rendering an UTI "complicated"
Examples for abnormalities rendering an UTI „complicated”

**Staghorn calculi** Plain film of the abdomen (no contrast) showing bilateral radiopaque branched, staghorn calculi filling the collecting systems (arrows). (From Rose, BD, Pathophysiology of Renal Disease, 1st ed, McGraw-Hill, New York, 1981.)
Acute urethritis

- **Pathogens:**
  - Chlamydia trachomatis, N. gonorrhoeae (STD)

- **Signs/symptoms**
  - Dysuria, leucocyturia, usually no hematuria
  - Urethral dyscharge

- **Complication**
  - Cervicitis, pelvic inflammation, urethral stricture

- **Treatment**
  - Macrolid ABx, doxycyclin, partner needs treatment
**Acute cystitis in adults**

- In otherwise healthy adult woman: non complicated
- 50-60 % of adult women had at least one episode
- In men less cystitis
  - Longer urethra
  - Less frequent colonization
  - Antibacterial substance in the prostatic fluid
- **Microbiology**
  - *E. coli, S saprophyticus*
- **Signs/symptoms**
  - Dysuria, frequency, hematuria, no fever
  - Suprapubic tenderness
- **Dx**
  - Pyuria, culture not necessary if typical clinical picture
  - Dipstick: false negatives!
- **DDx**
  - Urethritis, vaginal discharge, pyelonephritis, pelvic inflammation
Acute pyelonephritis

- Only in young females may be considered uncomplicated
- Pathology:
  - Acute tubulointerstitial nephritis
  - Tissue invasion!
- Microbiology
  - E. coli, Proteus, Klebsiella, Enterococcus, Enterobacter
  - Usually no S. saprophyticus
- Signs symptoms
  - Dysuria, hematuria, fever, lumbal pain, loin pain, nausea, vomiting
  - Bacteriemia: 30%
  - Pyuria,
  - WBC casts
  - infection: either ascending or hematogen spreading
  - Susceptibility increased: nephrolithiasis, obstruction, vesicoureteral reflux, developmental defects, immunosuppression, diabetes, iatrogeny
Acute pyelonephritis

- Needs culture/sensitivity (unless uncomplicated)
- Needs hospitalisation if:
  - Inability to take in enough fluid
  - Non-compliance
  - Progressive clinical picture
  - Uncertain diagnosis

Infection with
- Citrobacter, Staph aureus, Pseudomonas, fungi

Complications
- renal abscess
- Perirenal abscess
- Sepsis
- Papilla necrosis
- Chr pyelonephritis
## E. coli antibiogramok urine - 2008, OEK

<table>
<thead>
<tr>
<th>Antibiotikum</th>
<th>Ampicillin</th>
<th>Amoxicillin/ clav. sav</th>
<th>Piperacillin/ Tazobac</th>
<th>Imipenem</th>
<th>Meropenem</th>
<th>po/iv</th>
<th>Cefuroxim</th>
<th>Cefotaxim</th>
<th>Ceftriaxon</th>
<th>Cefazidim</th>
<th>po</th>
<th>po</th>
<th>Ceftibuten</th>
<th>Cefepine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Érzékeny (%)</td>
<td>50,4</td>
<td>78,4</td>
<td>91,7</td>
<td>100,0</td>
<td>99,9</td>
<td>94,3</td>
<td>95,8</td>
<td>96,2</td>
<td>96,4</td>
<td>96,8</td>
<td>97,5</td>
<td>95,5</td>
<td></td>
<td></td>
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<tr>
<td>Mérsékelt (%)</td>
<td>1,7</td>
<td>6,8</td>
<td>3,5</td>
<td>0,0</td>
<td>0,0</td>
<td>1,3</td>
<td>0,3</td>
<td>0,1</td>
<td>0,2</td>
<td>0,2</td>
<td>0,1</td>
<td>0,2</td>
<td></td>
<td></td>
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<tr>
<td>Rezisztens (%)</td>
<td>47,9</td>
<td>14,8</td>
<td>4,8</td>
<td>0,0</td>
<td>0,1</td>
<td>4,4</td>
<td>3,9</td>
<td>3,7</td>
<td>3,4</td>
<td>3,0</td>
<td>2,4</td>
<td>4,3</td>
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<table>
<thead>
<tr>
<th>Antibiotikum</th>
<th>Nitrofurantoin</th>
<th>Ofloxacin</th>
<th>Ciprofloxacin</th>
<th>Levofloxacin</th>
<th>Norfloxacin</th>
<th>Gentamicin</th>
<th>Tobramycin</th>
<th>Amikacin</th>
<th>Tetracyclin</th>
<th>Sumetrolim</th>
</tr>
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<tr>
<td>Érzékeny (%)</td>
<td>96,0</td>
<td>80,7</td>
<td>80,6</td>
<td>80,1</td>
<td>80,7</td>
<td>94,9</td>
<td>92,3</td>
<td>97,0</td>
<td>66,9</td>
<td>75,4</td>
</tr>
<tr>
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<td>1,6</td>
<td>0,6</td>
<td>0,3</td>
<td>0,2</td>
<td>0,4</td>
<td>0,4</td>
<td>1,7</td>
<td>2,1</td>
<td>1,7</td>
<td>0,5</td>
</tr>
<tr>
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<td>2,4</td>
<td>18,7</td>
<td>19,1</td>
<td>19,7</td>
<td>18,9</td>
<td>4,7</td>
<td>6,0</td>
<td>0,9</td>
<td>31,4</td>
<td>24,1</td>
</tr>
</tbody>
</table>
UTI: empiric treatment

- INCREASE FLUID INTAKE (>2000cc/day urine)

**Cystitis:** First line
- Nitrofurantoin (5d)
- Cefuroxime
- Fosfomycin (1 dose)
- TMP/STX (Sumetrolim) (3d)

Second line
- Amoxicillin/clav. (3-5d)
- Fluorokinolones (3-5d)

**Acute pyelonephritis (usually 10-14 d)**
- Fluorokinolones, TMP/STX (Sumetrolim), oral beta lactams
- 3. generation cephalosporin iv - then po
  - cefotaxim, ceftriaxon - cefixim, ceftibuten

- Urosepsis: ICU, "penem"
Profilaxis recurrent UTI in women

- Avoid spermicides, postcoital voiding - fluid intake
- Cranberry juice
- Wipe front-to back after defecation
- Postmenopausal: estrogen cream

• According to culture and sensitivity

• Profilaxis
  - Continuous: daily bedtime, or fosfomycine q10d
  - Self-treatment: postcoital, TMP/SMX, nitrofurantoin cephalexine
# Principal Cystic Diseases of the Kidney

<table>
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<td><strong>Autosomal-dominant</strong></td>
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<tr>
<td>Simple renal cysts (solitary or multiple)</td>
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<tr>
<td>Cysts of the renal sinus (or peripelvic lymphangiectasis)</td>
<td><strong>Tuberous sclerosis complex</strong></td>
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<td>Orofaciodigital syndrome, type I</td>
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Simple renal cysts

- Most common renal masses
  - Solitary, multiple, bilateral
- Typically no symptoms
- Complication: infection

### PREVALENCE OF SIMPLE RENAL CYSTS DETECTED BY ULTRASONOGRAPHY

<table>
<thead>
<tr>
<th>Age group, y</th>
<th>≥1 Cyst</th>
<th>≥2 Cysts*</th>
<th>≥3 Cysts*</th>
<th>≥1 Cyst in Each Kidney</th>
</tr>
</thead>
<tbody>
<tr>
<td>M</td>
<td>F</td>
<td>M</td>
<td>F</td>
<td>M</td>
</tr>
<tr>
<td>15–29</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>30–49</td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>50–69</td>
<td>15</td>
<td>7</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>≥70</td>
<td>32</td>
<td>15</td>
<td>17</td>
<td>8</td>
</tr>
</tbody>
</table>

*Unilateral or bilateral. M—male; F—female.
Simple renal cysts: diagnosis

- **US:**
  - Round, sharply demarcated, smooth walls
  - No echoes
  - Strong posterior echo
Simple renal cysts: diagnosis

- CT:
  - sharply demarcated, smooth-thin walls
  - Fluid homogenous, <20HU
  - No contrast enhancement
Simple renal cysts: differential Dx

- APKD
- Localized cystic disease
- Malignancy
  - Thickened, irregular walls
  - Septae
  - Contrast enhancement
  - Multilocular
# PRINCIPAL CYSTIC DISEASES OF THE KIDNEY

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</table>
Acquired cystic disease

- Typically seen in patients on renal replacement therapy
- May begin prior to dialysis and progresses thereafter
- Usually asymptomatic
- Pathogenesis
  - Activation of proto-oncogenes, growth factors
- Complications
  - Bleeding, associates with size
  - Infection
  - Renal cell carcinoma
    - (8-10 y after dialysis commencement)
    - Mutations in tumor suppressor genes (VHL)
- Screening
  - US 3-5 years, if positive CT
Acquired cystic disease
Medullary sponge kidney

*Medullary sponge kidney* Intravenous pyelogram with tomography in medullary sponge kidney. All of the calyces are abnormal (seen best in the left kidney), showing a brushlike appearance radiating outward from the calyces (arrows). (From Rose, BD, Pathophysiology of Renal Disease, 2d ed, McGraw-Hill, New York, 1987.)

Calcifications in medullary sponge kidney
Medullary sponge kidney
Medullary sponge kidney: multidetector CT
Medullary sponge kidney: clinical picture

Nephrolithiasis, hypercalciuria, hyperuricosuria

Hematuria

Distal RTA

Urinary tract infection

Decreased concentrating ability

Good prognosis

Treatment:

Similar to Ca nephrolithiasis
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Autosomal dominant polycystic kidney disease (APKD)

- Common – 1:400-1000 live births
- Leads to end stage renal failure
- One half may remain undiagnosed
<table>
<thead>
<tr>
<th>Disease (OMIM)</th>
<th>Mode of Inheritance</th>
<th>Locus</th>
<th>Gene</th>
<th>Protein</th>
<th>Renal Abnormalities</th>
<th>Extrarenal Abnormalities</th>
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</thead>
<tbody>
<tr>
<td>Autosomal dominant polycystic kidney disease (601313, 173910)</td>
<td>AD</td>
<td>16p13</td>
<td>PKD1</td>
<td>Polycystin-1</td>
<td>Cortical and medullary cysts</td>
<td>Cerebral aneurysms; liver cysts, other²</td>
</tr>
<tr>
<td></td>
<td>AD</td>
<td>4q21</td>
<td>PKD2</td>
<td>Polycystin-2</td>
<td>Cortical and medullary cysts</td>
<td>Cerebral aneurysms; liver cysts, other²</td>
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<tr>
<td>Autosomal recessive polycystic kidney disease (263200)</td>
<td>AR</td>
<td>6p21</td>
<td>PKHD1</td>
<td>Fibrocystin (polycystin)</td>
<td>Distal tubule and collecting duct cysts</td>
<td>Hepatic fibrosis; Caroli’s disease</td>
</tr>
<tr>
<td>Nephronophthisis I (juvenile/adolescent, 256100)b</td>
<td>AR</td>
<td>2q13</td>
<td>NPHP1</td>
<td>Nephrocystin</td>
<td>Small fibrotic kidneys; medullary cysts</td>
<td>Retinitis pigmentosa</td>
</tr>
<tr>
<td>Nephronophthisis II (infantile, 602088)b</td>
<td>AR</td>
<td>9q31</td>
<td>NPHP2(INVS)</td>
<td>Inversin</td>
<td>Large kidneys; widespread cysts</td>
<td>Situs inversus</td>
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<td>Nephronophthisis III (juvenile/adolescent, 604387)b</td>
<td>AR</td>
<td>3q22</td>
<td>NPHP3</td>
<td>Nephrocystin-3</td>
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<td>Retinitis pigmentosa; hepatic fibrosis</td>
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<td>Medullary cystic kidney disease (174000, 603860)</td>
<td>AD</td>
<td>1q21</td>
<td>MCKD1</td>
<td>Unknown</td>
<td>Small fibrotic kidneys; medullary cysts</td>
<td>None</td>
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<td>16p12</td>
<td>MCKD2(UMOD)</td>
<td>Uromodulin (Tamm-Horsfall protein)</td>
<td>Small fibrotic kidneys; medullary cysts</td>
<td>Hyperuricemia and gout</td>
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<td>Tuberous sclerosis (191100)</td>
<td>AD</td>
<td>9q34</td>
<td>TSC1</td>
<td>Hamartin</td>
<td>Renal cysts; angiomyolipomas; renal cell carcinoma</td>
<td>Facial angiofibromas; CNS hamartomas</td>
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<tr>
<td></td>
<td>AD</td>
<td>16p13</td>
<td>TSC2</td>
<td>Tuberin</td>
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<td>Facial angiofibromas; CNS hamartomas</td>
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<td>Von Hippel-Lindau disease (608537)</td>
<td>AD</td>
<td>3p26-</td>
<td>VHL</td>
<td>pVHL</td>
<td>Renal cysts; renal cell carcinoma</td>
<td>Retinal angiomas; CNS hemangioblastomas; pheochromocytomas</td>
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<tr>
<td></td>
<td>p25</td>
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</table>
• „second hit” hypothesis
  – Fewer than 10% of the nephrons affected
• PKD1-polycystin 1
  – Renal tubular epithelia, hepatic bile ducts, pancreatic ducts
  – Integral membrane protein
  – More abundant in fetal epithelia
  – Protein-cell-matrix interaction
• PKD-2 Polycystin 2
  – Cell Ca signaling
  – Expressed in tubular cells
Polycytins

- Interaction between polycystin 1 and 2
  - Interaction on C-terminal domains
  - Abnormal cilia function
  - Unregulated epithelial cell growth

- Cyst development and growth
  - Epithelial proliferation
  - Fluid secretion into the cyst (cAMP mediated)
  - Fibrosis
APKD: cyst growth

Normal tubule with germinal PKD1 mutation in each cell → Occurrence of somatic mutation of the normal PKD1 allele in one tubular cell (the "second hit") → Monoclonal proliferation leading to cyst formation → Isolated cyst disconnected from its tubule of origin

Thickened tubular basement membrane

Fluid Accumulation

APKD: cyst growth
APKD: cyst growth

APKD – cystogenesis

Microdissected single nephron from 35 yo F


1. Loop of Henle
2. PCT
3. Arrow indicating direction
APKD – manifestations

APKD – renal manifestations

- Progressive renal failure
- Flank and abdominal pain
  - Renal cyst bleeding, infection, stone
- Gross hematuria (50%)
- UTI (20 male-80% female)
- Nephrolithiasis (20%, uric acid)
- Proteinuria (usually mild, <1g/day)
- Anemia usually not seen due to erythropoietin production
APKD – extrarenal manifestations

- Cerebral aneurisms (4-10%)
  - Risk increases with positive family Hx
  - Progressive disease
  - Rupture: Risk increases with size, hypertension, family Hx
  - Screening
    - Previous rupture, high risk occupation, warning symptoms, family history

- Coronary aneurisms, aortic dissection - rare

- Valvular abnormalities – 25-30%
  - Mitral prolapse, Ao insuff

- Hepatic cysts (10-60%)

- Pancreatic cysts

- Diverticulas, hernias
**Polycystic kidney disease**

An excretory phase radiograph of the left kidney demonstrates multiple cysts throughout the parenchyma of the left kidney in a patient with autosomal dominant polycystic kidney disease. Courtesy of Jonathan Kruskal, MD.

**Polycystic kidney disease**

Abdominal CT scan in a patient with polycystic kidney disease shows extensive cysts in both kidneys; the cysts have almost completely replaced the renal parenchyma. Courtesy of Jonathan Kruskal, MD, PhD.
APKD
APKD: hepatic cysts
APKD: cyst infection
APKD: cerebral aneurisms
APKD – progression
APKD – progression

Concentrating defect, Hypertension, Proteinuria

Pain, Hematuria, Stones, Infections

Kidney function (%) vs. Age (years)
APKD – risk factors for progression

- Young age at diagnosis
- Afro-American race
- Male
- PKD2 mutation
- Macroscopic hematuria
- Hypertension
- Progressive kidney and cyst growth
- Speed of progression in relatives
Objective: to decrease progression and avoid complications

- Blood pressure management: ACEI, CCB
- Cyst punction, if needed antibiotics
- if needed: renal replacement therapy (HD, PD, Transplantion)
- avoid coffee (increases cAMP level)
- Vasopressin V2 receptor antagonist – tolvaptan: decreased cAMP and cyst growth
- High fluid intake (decreases ADH release)
- Somatostatin: decreases fluid accumulation and cyst growth
- mTor inhibitors (sirolimus, everolimus): decreased tubular cell proliferation
- EGF receptor tirozin kinase inhibitor
APKD – screening

- **US/CT**

- **Genetic**
  - Flanking DNA probes (linkage studies)
  - Sequencing
  - Potential donor
  - Differentiation PKD1-2
  - At-risk fetus

**ADPKD: ULTRASONOGRAPHIC DIAGNOSTIC CRITERIA**

<table>
<thead>
<tr>
<th>Age</th>
<th>Cysts</th>
</tr>
</thead>
<tbody>
<tr>
<td>15–29</td>
<td>2, uni- or bilateral</td>
</tr>
<tr>
<td>30–59</td>
<td>2 in each kidney</td>
</tr>
<tr>
<td>≥60</td>
<td>4 in each kidney</td>
</tr>
</tbody>
</table>

Minimal number of cysts to establish a diagnosis of ADPKD in PKD1 families at risk.

### Principal Cystic Diseases of the Kidney

<table>
<thead>
<tr>
<th>Nongenetic</th>
<th>Genetic</th>
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</thead>
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<td><strong>Autosomal-dominant</strong></td>
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<td><em>X-linked</em></td>
</tr>
<tr>
<td></td>
<td><em>Orofaciodyndrome, type 1</em></td>
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</table>
### Table 284-1 Inherited Cystic Kidney Diseases

<table>
<thead>
<tr>
<th>Disease (OMIM)</th>
<th>Mode of Inheritance</th>
<th>Locus</th>
<th>Gene</th>
<th>Protein</th>
<th>Renal Abnormalities</th>
<th>Extrarenal Abnormalities</th>
</tr>
</thead>
<tbody>
<tr>
<td>Autosomal dominant polycystic kidney disease (601313, 173910)</td>
<td>AD, AD</td>
<td>16p13</td>
<td>PKD1</td>
<td>Polycystin-1</td>
<td>Cortical and medullary cysts</td>
<td>Cerebral aneurysms; liver cysts, other⁴</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4q21</td>
<td>PKD2</td>
<td>Polycystin-2</td>
<td>Cortical and medullary cysts</td>
<td>Cerebral aneurysms; liver cysts, other⁴</td>
</tr>
<tr>
<td>Autosomal recessive polycystic kidney disease (263200)</td>
<td>AR</td>
<td>6p21</td>
<td>PKHD1</td>
<td>Fibrocystin (polycystin)</td>
<td>Distal tubule and collecting duct cysts</td>
<td>Hepatic fibrosis; Caroli’s disease</td>
</tr>
<tr>
<td>Nephronophthisis I (juvenile/adolescent, 256100)¹</td>
<td>AR</td>
<td>2q13</td>
<td>NPHP1</td>
<td>Nephrocystin</td>
<td>Small fibrotic kidneys; medullary cysts</td>
<td>Retinitis pigmentosa</td>
</tr>
<tr>
<td>Nephronophthisis II (infantile, 602088)¹</td>
<td>AR</td>
<td>9q31</td>
<td>NPHP2 (INVS)</td>
<td>Inversin</td>
<td>Large kidneys; widespread cysts</td>
<td>Situs inversus</td>
</tr>
<tr>
<td>Nephronophthisis III (juvenile/adolescent, 604387)¹</td>
<td>AR</td>
<td>3q22</td>
<td>NPHP3</td>
<td>Nephrocystin-3</td>
<td>Small fibrotic kidneys; medullary cysts</td>
<td>Retinitis pigmentosa; hepatic fibrosis</td>
</tr>
<tr>
<td>Medullary cystic kidney disease (174000, 603860)</td>
<td>AD</td>
<td>1q21</td>
<td>MCKD1</td>
<td>Unknown</td>
<td>Small fibrotic kidneys; medullary cysts</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td>AD</td>
<td>16p12</td>
<td>MCKD2 (UMOD)</td>
<td>Uromodulin (Tamm-Horsfall protein)</td>
<td>Small fibrotic kidneys; medullary cysts</td>
<td>Hyperuricemia and gout</td>
</tr>
<tr>
<td>Tuberous sclerosis (191100)</td>
<td>AD</td>
<td>9q34</td>
<td>TSC1</td>
<td>Hamartin</td>
<td>Renal cysts; angiomyolipomas; renal cell carcinoma</td>
<td>Facial angiofibromas; CNS hamartomas</td>
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<tr>
<td>Von Hippel-Lindau disease (608537)</td>
<td>AD</td>
<td>3p26-p25</td>
<td>VHL</td>
<td>pVHL</td>
<td>Renal cysts; renal cell carcinoma</td>
<td>Retinal angiomas; CNS hemangioblastomas; pheochromocytomas</td>
</tr>
</tbody>
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Nephronophytosis, medullary cystic kidney complex
Different Clinical Forms of the Nephronophthisis-MCKD Complex, with Age at Diagnosis, Mode of Transmission, and Known Genetic Localization

Nephronophthisis (NPHP)
- Infantile
- Juvenile
- Adolescent

MCKD (Medullary cystic kidney disease)
- MCKD1 (1q21)
- MCKD2 (16p12)

Genetic Localization:
- NPHP1: 2q13
- NPHP2: 9q22
- NPHP3: 3q22
- NPHP4: 1p36

Iversin nephrocytisin

Uromodulin (Tam-Horfall protein)

Recessive Dominant
Histologic aspect of nephronophthisis. Tubular basement membranes are thickened in certain areas, and thin in other areas. Tubular atrophy and interstitial fibrosis develop.
Clinical picture

**Nephronophytysis**
- Decreased concentrating ability
- Na loss
- Progressive renal failure
- Tapetoretinal degeneration (Senior-Loken sy)
- Cerebellar ataxia
- Mental retardation
- Congenital amaurosis, retinitis pigmentosa (Leber)
- Hepatosplenomegaly

**Medullary cystic kidney disease**
- Slowly progressive renal failure
- Hyperuricemia, gout
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<td>Orofaciodigital syndrome, type I</td>
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Renal cell carcinoma (RCC)

- **Risk factors**
  - Smoking
  - Occupational exposure
    - Cadmium, asbestos, petroleum py-products
  - Obesity
  - Acquired cystic disease
  - Analgetic abuse
- **Genetic factors**
  - VHL
  - C-met oncogene mutations
  - Hereditary leiomyoma RCC (Reed syndrome)
  - Birt-Hogg-Dube syndrome (spontaneous RCC, RCC)
RCC pathology

- **Clear cell**
  - proximal tubule, most frequent, associates with 3p deletion – VHL
- **Chromophilic**
  - Papillary
- **Chromophobe**
  - Intercalated cells, several somatic mutations
- **Oncocytic**
  - Eosinophilic cells, collecting duct, benign course
- **Bellini’s duct tumor**
  - More aggressive
RCC medical therapy

- **Chemotherapy**
  - Single agents usually not effective
  - Vinblastin, floxuridine, 5-FU
  - Non clear cell – carboplatin

- **Immunotherapy**
  - Interferon alpha, gamma
  - Combination with chemotherapy, debulking nephrectomy
  - Interleukin-2

- **Anti angiogenesis therapy**