ACUTE AND CHRONIC TUBULOINTERSTITIAL NEPHRITIS, CYSTIC DISEASE OF KIDNEY

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TIN – TUBULOINTERSTITIAL NEPHRITIS

- TIN – encompasses a group of clinical disorders that affect principally
  - the renal tubules
  - interstitium
  - relative sparing of the glomeruli and renal vasculature

- On the basis of the rate of progression of the azotemia
  - acute interstitial nephritis (AIN)
    - rapid (days to weeks) decline in renal function
    - histologically an acute inflammatory infiltrate
  - chronic interstitial nephropathy (CHIN)
    - slowly (years) progressive azotemia
    - histologically predominantly interstitial scarring and fibrosis with a variable but less impressive amount of round – cell infiltration
AIN – ACUTE INTERSTITIAL NEPHRITIS

- **AIN – clinicopathologic syndrome characterized**
  - by the sudden onset of clinical signs of renal dysfunction
  - affection of renal tubules and prominent inflammatory cell infiltrate within the surrounding renal interstitium
  - **important cause of acute renal failure** (ARF)
    - 10-20% of ARF cases
  - **proteinuria and albuminuria is rarely > 1 g/day**
    - pyuria and sometimes haematuria are common

- **ETIOLOGY**
  - **complication of therapy with a wide variety of hypersensitivity reaction to drugs**
    - especially antibiotics (*penicillin family*)
    - nonsteroidal anti-inflammatory drugs
  - **septicemia of any cause**
    - leptospirosis, legionnaire’s disease and mononucleosis appear to have a particular predilection
  - **acute pyelonephritis (AP) is a form of AIN**
    - direct bacterial invasion of renal medulla
    - the clinical manifestations are predominantly infection, fever, chills and flank pain
    - AP only rarely causes ARF
  - **severe glomerulonephritis** (*accompanied by an interstitial inflammatory infiltrate*) is generally excluded from classifications of AIN
COMMON CAUSES OF ACUTE TUBULOINTERSTITIAL NEPHRITIS

- **DRUGS (allergic, ~70%)**
  - Penicillins
  - Sulphonamides
  - NSAID
  - Allopurinol
  - Cephalosporins
  - Rifampicin
  - Diuretics: *furosemide*, *thiazides*
  - Cimetidine
  - Phenytoin

- **SYSTEMIC INFECTION (~15%)**
  - Viruses
    - CMV
    - Hantavirus (haemorrhagic fever may be fatal)
    - EBV
  - Chlamydia
  - Legionnaires disease
  - Leptospirosis
  - Bacteria, e.g. streptococci
    - Tuberculosis

- **PRIMARY RENAL INFECTIONS**
  - Acute bacterial pyelonephritis

- **IMMUNE DISORDERS**
  - Transplant rejection

- **IDIOPATHIC (~8%)**

- **Systemic inflammatory disorders** (e.g. SLE, Sjögren’s syndrome, Wegener’s granulomatosis)

- **Toxic**
  - Myeloma light chains
  - Mushrooms
AIN – CLINICAL FEATURES

AIN

- The major clinical manifestation in the development of ARI (acute renal insufficiency)

Frequently

- Systemic manifestation of hypersensitivity reaction
- Some combination of
  - fever
  - skin rash (hypersensitivity)
  - peripheral eosinophilia
  - arthralgias (particularly in the course of AIN due to drugs)
  - the absence of any of these features is common
  - hypertension and edema are uncommon in AIN
- Signs of renal inflammation – urinary abnormalities – clue to the diagnosis
  - hematuria (seldom macroscopic)
  - sterile pyuria
  - leukocyte casts → common when AIN is caused by drugs
  - eosinophiluria is suggestive of AIN (Wright stain test of the urine)
  - RBC casts – have been found on rare occasions
  - proteinuria (mild to moderate) is present in majority of the patients (< 1g/day)
AIN – CLINICAL FEATURES

- The major clinical manifestation in the development of ARI (acute renal insufficiency)

Frequently

- Renal ultrasound
  - normal or enlarged kidneys
- Renal biopsy – can therefore made a definitive diagnosis
  - intense inflammation with polymorfonuclear leucocytes and lymphocytes surrounding tubules
    (tubulitis) and occasional eosinophils (drug induced)
- The spectrum of renal dysfunction to oliguric renal failure
  - recovery of renal function may occur over weeks to months
  - progression to ESRD has been reported with all forms of AIN
AIN – acute interstitial hypersensitive (allergic) nephritis

- AIN – allergic / hypersensitive exanthematous reaction
- AIN – hypersensitive type
  - eosinophils in the urine
- AIN – mononuclear interstitial infiltration,
  hypersensitive reaction after ampicilin
**NORMAL TUBULAR HISTOLOGY**

Normal tubular histology. The tubules are back-to-back.

**ACUTE TUBULAR NECROSIS**

There are scattered breaks (B) in tubular basement membranes, swelling and vacuolisation of tubular cells, and occasionally apoptosis and necrosis of tubular cells with shedding of cells into the lumen. The interstitium (I) is oedematous and infiltrated by inflammatory cells.

**ACUTE PYELONEPHRITIS**

Acute bacterial pyelonephritis. A widespread inflammatory infiltrate that includes many neutrophils is seen. Granulocyte casts (G) are formed within some dilated tubules (T). Other tubules are scarcely visible because of the extent of the inflammation and damage.

**ACUTE INTERSTITIAL NEPHRITIS**

Acute (allergic) interstitial nephritis. In this patient who received NSAID, an extensive mononuclear cell infiltrate (no neutrophils) involving tubules (T) is seen. This inflammation does not involve the glomeruli (not shown).
THERAPY

• Drug – induced AIN
  – discontinuing of the offending drugs
  – a short course of high-dose corticosteroids (1mg/kg/day of prednisone for 1-2 weeks) accelerate recovery in drug-induced lesions
  – steroids are not employed in infection-related AIN, but may be useful sometimes with cytotoxic agents in the treatment of nephritogenic responses in systemic immunologic disorders
  – in case of underlying infection antibiotics (ampicillin, aminoglycosides, cephalosporines, chinoline preparates)
  – high intake of watter (tea)
  – dialysis therapy in ARF

• Allograft rejection is treated with HD (pulse) – steroids, azathioprine, antithymocyte globulins

➢ Most patients have a good recovery in kidney function
  – but some may stay with significant interstitial fibrosis and persistent high serum creatinine
UTI – can be classified as uncomplicated or complicated

Uncomplicated urinary tract infection
- occurs in patients without abnormalities of the urinary tract and urological instrumentation
- evidence of infection
  - bacterinuria, pyuria, in some cases hematuria
- urinary tract infections can be divided into acute cystitis (lower tract infection) and acute pyelonephritis (upper tract infection)
- mostly in women between the age of 18 and 40, 80% are due to Escherichia coli, Staphylococcus saprophyticus causes 10-15%, also Proteus mirabilis and Klebsiella
  - E. coli migrate from the perianal skin to colonize the vaginal introit and urethra → into the bladder and to the kidney via the ureters
  - both bacterial and host factors are important, sexual intercourse appears to facilitate migration of bacteria

Clinical manifestation
- uncomplicated cystitis include
  - dysuria, frequency, urgency, voiding of small urine volumes
  - suprapubic or lower abdominal pain
  - one-third develop gross hematuria
  - on examination suprapubic tenderness
Ascending infection of the urinary tract.

Findings in reflux nephropathy compared with normal.
Treatment

Uncomplicated cystitis

- **3-day course** of thimethoprim-sulfamethoxazole or a fluoroquinolone (*ofloxacin*)
- **reccurrence** should be treated with *ampicillin, amoxicillin, first generation cephalosporins* with 7-day regimen

AP

- *in the outpatient* setting if they have no septicemia 14 days (trimethoprim – sulfamethoxazole, fluoroquinolone) are preferred
- *for inpatients* – parenteral therapy depending on the local antimicrobial sensitivity patterns
- preferred regimens are trimethoprim – sulfamethoxazole, gentamicin, fluoroquinolone or a third – generation cephalosporin until defervescence and clinical improvement
  - in 80% patients – improvement within 72 hr, oral therapy can be provided for the remaining time
- *in women with frequent recurrent episodes of cystitis* → low-dose antimicrobial prophylaxis reduces the incidence of recurrent infections and can be used safely for a long period
  - daily or twice weekly trimethoprim – sulfamethoxazole (1/2 tablet daily) or nitrofurantoin (100 mg/daily)
# Antibiotic Regimens for Treatment of Urinary Tract Infections in Adults

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Duration of course</th>
<th>Treatment of urinary tract infection</th>
<th>Dose</th>
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1 Modification of dosage is necessary when renal function is impaired.

2 Dose determined by plasma [creatinine] and [gentamicin].
Acute pyelonephritis (infection causing acute TIN)

- Presents as a classic triad of loin pain, fever and tenderness over the kidneys
  - the renal pelvis is inflamed and small abscesses are often evident in the renal parenchyma
  - histological examination shows focal infiltration by neutrophils within tubules (tubulitis) and interstitium

Pathogenesis

- renal infection is almost uniquely caused by organisms ascending from the bladder (E. coli from GIT, Proteus, Pseudomonas species, Streptococci, Klebsiella aerogenes, Enterococcus faecalis)
- rarely bacteraemia – staphylococci
- pre-existing renal damage (cyst formation) facilitates infection
  - low oxygen tension, high osmolality of renal medulla
APN – CLINICAL ASSESSMENT

• **acute onset of pain** in one or both loins
  - irradiation to the iliac fossae and suprapubic area
  - tenderness in the lumbar region, low-back or abdominal pain
• **dysuria** (30%) due to associated cystitis
• fever associated with nausea, vomiting, sweats and malaise
• **examination of urine**: neutrophils (pyuria), bakterinuria, and sometimes red cells and tubular epithelial cells
• **WBC and SER or CRP elevation**
• **renal function** is unimpaired unless complicated by urinary tract obstruction
  - rarely renal papillary necrosis – predisposition is DM, analgesic nephropathy
• **complications** – G ± septicemia, perinephritis abscess

The differential diagnosis

• acute appendicitis, diverticulitis, cholecystitis and salpingitis
AIN – Acute pyelonephritis (APN)

- **INVESTIGATION**
  - Culture of urine (*suprapubic aspiration eventually*)
  - Microscopic examination of urine (*white and red cells*)
    - dipstick examination of urine for blood, protein, glucose
  - Full blood count
  - Plasma urea, creatinine, electrolytes (K, Na)
  - Blood culture
  - Pelvic examination (*women*) and rectal examination (*men prostate*)
  - Renal ultrasound or CT (*IVU eventually*)
    - to identify obstruction, cysts, calculi
  - Cystoscopy – in hematuria or a suspected bladder lesion
  - Bacteria and neutrophils in the urine of a patient with typical clinical features confirm the diagnosis
  - Renal tract ultrasound – as soon as possible to exclude obstruction or perinephritic collection
    - if obstruction – drainage by a percutaneous nephrostomy
  - Treatment
    - Adequate fluid intake, if necessary by intravenous route
    - Antibiotics are continued for 7-14 days
      - severe cases – intravenous therapy (*cephalosporin, quinolone or gentamicin*)
    - Urine should be cultured before and after treatment
Complicated versus uncomplicated urinary tract infection.

CT scan showing a wedge-shaped area of renal cortical loss (arrow) following acute pyelonephritis.
Treatment

Uncomplicated cystitis

- 3-day course of thimethoprim-sulfamethoxazole or a fluoroquinolone (ofloxacín)
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CHTIN – CHRONIC TUBULOINTERSTITIAL NEPHRITIS

- CHTIN – is a clinicopathologic entity characterized
  - clinically by slowly progressive renal insufficiency
  - non-nephrotic-range proteinuria
  - functional tubular defects
  - pathologically by interstitial fibrosis
  - atrophy and loss of renal tubules
  - 15-30% of all end-stage renal disease (ESRD)

- Diagnosis and clinical features
  - tubular defects are disproportionately severe relative to the
    - degree of azotemia
    - RBC casts
    - or nephrotic syndrome
  - most patients have little or no clinical evidence of active renal inflammation
  - the urinalysis may show
    - modest pyuria
    - minimal haematuria
    - no cellular casts in most cases
  - affection of proximal tubule structures (MM, heavy metal toxicity)
    - proximal renal tubular acidosis (RTA)
    - glycosuria, aminoaciduria, uricosuria
  - affection of distal tubular structures (amyloidosis)
    - distal RTA
    - salt wasting
    - hyperkalemia
• Hyperchloremic metabolic acidosis
  *(not proportional to the degree of renal insufficiency)*

• Hyperkalemia
  *(not proportional to the degree of renal insufficiency)*

• Reduced maximal urinary concentrating ability
  *(polyuria, nycturia)*

• Partial or complete Fanconi’s syndrome
  - Phosphaturia
  - Bicarbonaturia
  - Aminoaciduria
  - Uricosuria
  - Glycosuria

• Urinalys
  - may be normal but may contain cellular elements
  - absence of RBC *(red blood cell)* casts

• Modest proteinuria *(< 2.0 g/day)*
  - absence of nephrotic range proteinuria
CHTIN – ASSOCIATED CONDITIONS

- **COMMON**
  - Reflux nephropathy
  - DRUGS
    - NSAID/analgesics
    - Cisplatin, cyclosporine, lithium
  - Diabetes mellitus
  - Vascular diseases
    - Nephrosclerosis
    - Ateroembolic disease
  - Metabolic disorders
    - Hypeuricemia/hyperuricosuria
    - Hypercalcemia/hypercalciuria
    - Hyperoxaluria
    - Potassium depletion
    - Cystinosis
  - Polycystic kidney disease

- **UNCOMMON**
  - Radiation nephritis
  - Immunologic diseases
    - SLE
    - Sjögren’s syndrome
    - Cryoglobulinemia
    - Goodpasture syndrome
    - Vasculitis \(\text{(Wegener’s disease…)}\)
    - Amyloidosis
    - Renal allograft rejection
  - Cadmium or lead intoxication
  - Malignancies and granulomatous diseases
    - Multiple myeloma
    - Sarcoidosis
### Causes of Chronic Interstitial Nephritis

<table>
<thead>
<tr>
<th>Category</th>
<th>Examples</th>
</tr>
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<tbody>
<tr>
<td>Acute interstitial nephritis</td>
<td>Any of the causes of AIN if persistent</td>
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<tr>
<td>Glomerulonephritis</td>
<td>Varying degrees of interstitial inflammation occur in association with most types of inflammatory glomerulonephritis</td>
</tr>
<tr>
<td>Immune/inflammatory</td>
<td>Sarcoidosis, Sjögren’s syndrome, SLE, primary autoimmune, Chronic transplant rejection</td>
</tr>
<tr>
<td>Toxic</td>
<td>Mushrooms, Lead, Chinese herbs, Balkan nephropathy</td>
</tr>
<tr>
<td>Drugs</td>
<td>All drugs causing AIN, Lithium toxicity, Analgesic nephropathy, Ciclosporin, tacrolimus</td>
</tr>
<tr>
<td>Infection</td>
<td>Consequence of severe pyelonephritis</td>
</tr>
<tr>
<td>Congenital/developmental</td>
<td>Vesico-ureteric reflux—is associated; causation not clear, Renal dysplasias—often associated with reflux, Inherited—now well recognised but mechanisms unclear, Other—Wilson’s disease, medullary sponge kidney, sickle-cell nephropathy</td>
</tr>
<tr>
<td>Metabolic and systemic diseases</td>
<td>Hypokalaemia, hypercalciuria, hyperoxaluria, Amyloidosis</td>
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ANALGESIC NEPHROPATHY (AN) (I)

- excessive consumption of certain analgesic agents
- phenacetin or acetaminophen in combination with aspirin
- NSAID (nonsteroidal anti-inflammatory drugs) → may result in CHIN

AN – occurs more frequently in women (middle aged)
- typical personality type in woman (passive-aggressive or hypochondriasis)
- large quantities (> 1-3 kg) of antipyretic – analgesic mixtures ingested (daily consumption of four tablets a 300 mg analgesic for 2-3 years)
- emotional stress, neuropsychiatric disturbances and GIT disturbances are commonly associated with AN
- anemia is present in most patients (chronic, GIT loss)
- sloughing of a necrotic papilla into the urinary tract → gross hematuria, ureteral colic (flank pain)
- mild degrees of proteinuria, pyuria and bacterinuria
- both sterile pyuria and bacteriuria are found
- rarely methemoglobinemia
ANALGESIC NEPHROPATHY (AN) (II)

- On intravenous urography or retrograde pyelography and ultrasonography
  - calyceal filling defects *(due to the sloughed papilla-ring sign)*
  - reduced renal size and bumpy contour
  - renal medullary calcification may be present
- **demonstration** of papillary necrosis suggest analgesic nephropathy
- **increased risk** of transitional cell carcinoma of the urinary tract *(renal pelvis)*
- **hematuria** – should lead to prompt evaluation to exclude a uroepithelial neoplasm
- **with cessation of analgesic use**, renal function generally stabilizes or improves

Cytotoxic / immunosuppressive agents

- cyclosporine-A, tacrolimus, cisplatin
  - more often associated with ARF → chronic TIN
- interstitial fibrosis → late renal transplant loss
Urinary tract obstruction
- is the most important cause of CHTIN

Chronic pyelonephritis (CHP) and reflux nephropathy
- CHP – the term is now specifically reserved for radiologic findings that demonstrate deformity of the pelvis and calyces in the upper and lower poles
  - *bacteriuria alone* is unlikely to result in chronic renal injury
  - the lesion of CHP results from vesicoureteral reflux, or urinary tract infection in association with obstruction
    - the development of heavy proteinuria is usually due to focal segmental sclerosis seen in association with reflux

Chinese herb nephropathy
- *Chinese herbal medicines* have been increasingly used in the West and have caused nephropathy
  - *the causal agent* – aristocholic acid produced as a result of fungal contamination of the herbal medicine
  - relentless progression to end-stage RF
  - there is a high incidence of uroepithelial tumours
Granular surface, small retracted kidney, multiple scars. Adherent capsule, thin parenchyma.

Reflux type of chronic pyelonephritis. Intravenous urogram revealing clubbing of the calyces in the right. The appearances on the left are virtually normal.

CHIN – skin pigmentation in the analgesis nephropathy  
CHIN – analgesic type  
   – papillae calcification  
IVU – obstruction uropathy. Left duplex collecting system and ureters with obstruction of the upper half/part (arrow)
HYPTERTENSIVE NEPHROSCLEROSIS

- pathological hallmark of benign nephrosclerosis is an arteriolopathy (interlobular and afferent arterioles)
- interstitial and glomerular changes appear to result from the subsequent ischemia
- tubular atrophy and interstitial scarring may precede signs of glomerular injury in arteriolar nephrosclerosis

RADIATION NEPHRITIS

- clinically evident renal injury is uncommon if less than 1000 to 2000 Gy are used
- in the early stage of radiation nephritis
  - tubular necrosis
  - medial and intimal thickening of small renal arteries
  - damage to the glomerular endothelium
- later
  - glomerulosclerosis
  - collagenous thickening of small renal arteries
  - interstitial fibrosis is prominent
- renal damage occurs several months to years after renal irradiation
- proteinuria, urinary concentrating defects
- benign hypertension with reduced GFR
- malignant hypertension with ESRF
HEAVY METALS – LEAD

- Lead exposure has declined over the past decades
- Environmental exposure to lead aerosols has markedly increased
- Lead accumulates in tubule cells and causes proximal convoluted tubule cell injury
- Glycosuria, aminoaciduria → CHTIN
- "Saturnine" gout
- EDTA (disodium ethylenediaminetetra-acetic acid) may be used to test for a lead burden

METABOLIC ABNORMALITIES

- Prolonged hyperuricemia → hyperuricaemic nephropathy renal dysfunction
- Acute hyperuricaemic nephropathy
  - Well-recognized cause of ARF in marked hyperuricaemia (lympho-/myeloproliferative disorders)
  - Most often follows cytotoxic intensive therapy → tumor lysis syndrome (increased uric acid production)
  - Intrarenal and extrarenal obstruction caused by uric acid crystals
  - Oliguria → ARF
  - S-hyperuricaemia, ultrasound demonstration of extrarenal obstruction due to stones, coexistence of intrarenal obstruction
  - Allopurinol 100-200 mg three times/day/5 days, high rate of urine flow (oral, parenteral fluids) and high rate of urine (sodium bicarbonate)

ARF – hemodialysis

- Primary hyperoxaluria, enteric hyperoxaluria may result in ESRF from CHTIN
- Chronic hypercalcemia – nephrocalcinosis and CHTIN with reduced GFR, only slowly reversible
MALIGNANCIES

- Renal involvement is common in
  - multiple myeloma → so called „myeloma kidney“ (cast nephropathy) is characterized by refractile tubular casts and tubular atrophy and interstitial fibrosis
    - in 5-15% cases of myeloma – patients develop nephrotic syndrome as a result of glomerular lesion (amyloidosis)
  - in NHL and leukemias – neoplastic infiltration of renal interstitium → renal enlargement

IMMUNE DISORDERS

- A variety of immune disorders may be associated with ATIN and CHTIN, chronic renal transplant rejection
  - Sjögren´s syndrome – CHTIN
  - The most common functional abnormalities are distal RTA and urinary concentrating defects
Renal cyst diseases are characterized by epithelium–lined cavities within the kidneys are filled with fluid or semisolid debris

- they develop primarily from renal tubular elements

**Simple or solitary cysts**

- **simple cysts** account for 65-70% of all renal masses
  - they are generally found at the outer cortex and contain fluid (*ultrafiltrate of plasma*)
- **increase in frequency with age** (*acquired cystic disease*)
- **being present** in up to 50% of the population over 50 years of age
- **most often are asymptomatic** and are discovered during imaging studies, but can become infected
- **renal ultrasonography** together with computed tomography (*CT*), permits differentiation of benign from malignant lesions, abscess, or PKD (*polycystic kidney disease*)

**Acquired cystic kidney disease**

- **development of cysts** in patients with chronic RF or ESRD who are undergoing dialysis
- **after 3-4 years on dialysis**, annual screening should be done to rule out malignancy (*carcinomas*)
- **USG and CT scan** is the diagnostic method of choice
Liver enlargement – polycystic liver and kidney.

Ultrasonography – kidney enlargement, multiple cystic.

Ultrasonography – solitary cyst of the right kidney.

Ultrasound scan of a polycystic kidney, showing an enlarged kidney with many cysts of various size.

CT in autosomal dominant polycystic kidney disease. The kidneys are enlarged and almost entirely replaced by multiple cysts. The patient required peritoneal dialysis; the dialysis catheter can be seen outside the anterior abdominal wall (arrow).
Multiple cysts in bilateral kidneys, total number depends on age

- **Adult PKD include** autosomal dominant PKD, the most common type is carried in chromosome 16 and 4
  - 3-10% of all patients on hemodialysis
  - at least three different genes: ADPKD1 on the short arm of ch.16 (85%), while ADPKD2 gene is carried on ch. 4, localization of the ADPKD3 gene has not been determined
  - defect of protein polycystin (ADPKD1) can lead to abnormal growth and cyst formation

- **family history** is compelling (75%) but not necessary
- **clinical manifestation** occur after 20-25 years
- **pain and hematuria** are the most common clinical manifestation
- **flat lumbar pain** usually occurs when the kidneys are sufficiently enlarged to be palpable on the examination of the abdomen
- **sharp, localized pain** may result from cyst rupture or infection
- **microscopic hematuria** or gross hematuria may occur
- **hypertension occurs** in 60% of patients (*ACE inhibitors*)
- **nycturia** due to a urinary concentrating defect
- **cyst and urinary tract infection** and pyelonephritis or nephrolithiasis (20%) are common
- **liver cysts** (50%), pancreatic cysts, cerebral aneurysms, mitral valve prolapse
  - subarachnoid haemorrhage after aneurysma rupture
- **progression to ESRF** is about 25% of individuals by the age of 50
- **polyglobulia** is a rare complication
The diagnosis of PKD is made on the basis of radiographic or ultrasonography evidence of multiple cysts with renal enlargement, CT scan with contrast medium is important and is more sensitive than USG.

The treatment is aimed at preventing complications and preserving renal function:
- control of hypertension and prevention and early treatment of urinary tract infections (trimethoprim – sulfamethoxazole, ciprofloxacin)
- ESRF is managed by either dialysis or transplantation
- bilateral nephrectomy may be required prior to transplantation
PKD – POLYCYSTIC KIDNEY DISEASE

Pathological - anatomic picture PKD
- multiple cysts

PKD – ultrasonography, cyst formation

CT tomographic scan
- Drawing showing cyst in right kidney
- Denotes a region of interest (the cysts), in which measurements of tissue density can be made

CT- multiple liver cysts
Malignant renal tumours

- 1-2% of all malignant tumours, M/F 2:1
  - the incidence peak between 50-70 years

Nephroblastoma (Wilms’ tumour)
- within 3 years of life only, is bilateral

Renal cell carcinoma

- The most common renal tumour in adults
- deletion of the short arm of chromosome 3 is the most consistent cytogenetic finding
  - association with von Hippel-Lindau disease (spinal and cerebellar hemangioblastomas, renal and pancreatic cysts, retinal angiomas and pheochromocytomas)
- arise from proximal tubular epithelium
  - highly vascular, expansion of the tumor into normal renal veins and even into inferior vena cava is not uncommon
  - microscopically three cell types: clear cells *(most frequent)*, granular cells, spindle cells *(poor prognosis)*
  - direct invasion of periphritic tissues is common
  - lymphatic spread occurs to para-aortic nodes
- metastatic spread – via vascular routes
  - the lungs, bone and liver are the most frequent sites of metastasis
RENAL CELL CARCINOMA

CLINICAL FEATURES

- **Classic triad** *(late feature)*: **hematuria** *(spread into the renal pelvis 60%)*, **flank pain** *(40%)*, **palpable mass** *(25%)*, **previously** *(USG positivity at this time)*
  - Large number of systemic – extrarenal manifestations
    - **fever** (~ 20%) *(“fever of unknown origin“)*
    - malaise, anorexia, weight loss (30%)
    - elevation ESR (~ 50%)
    - anemia (30%)
    - **polycythemia** *(5% secondary to increase erythropoietin)*
    - hepatic dysfunction, peripheral neuropathy
  - **ectopic hormone syndromes**: **hypercalcemia** *(PTH-like, OAF and bone metastasis)*, **Cushing’s syndrome** *(ACTH)*, **hypertension** *(renin)*

DIAGNOSIS

- **Excretion urography** – space occupying lesion of the kidney
  - 10% show calcification
- **Ultrasonography** – solid lesion *(and potency of the renal vein and inferior VC)*
  - < 3 cm tumours may be missed
- **CT scan**
- **MRI** is better than CT - for tumour staging
- **Renal arteriography** - now seldom employed
- **Urine cytology** for malignant cells - is of no value
- **ESR** is usually raised
RENAL CELL CARCINOMA

Transverse ultrasound of the right kidney, which is partly replaced by renal carcinoma (arrows).

CT after contrast in a patient with carcinoma of left kidney. Tumor thrombus can be seen in the left renal vein (arrow) and IVC.

CT after contrast, of a large carcinoma of right kidney. Spreading of tumour beyond the renal capsule (arrow) and a tumour thrombus in the IVC (small arrow).

Left renal angiogram in renal carcinoma. (a) Before embolization. (b) After embolization. There has been a significant reduction in tumor vascularity after embolization; this makes nephrectomy easier.

Renal adenocarcinoma. Pathology specimen showing typical necrosis.
<table>
<thead>
<tr>
<th>Manifestation</th>
<th>Percentage of total</th>
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<tbody>
<tr>
<td><strong>Local</strong></td>
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<tr>
<td>• Hematuria</td>
<td>60</td>
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<tr>
<td>• Abdominal mass</td>
<td>45</td>
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<tr>
<td>• Pain</td>
<td>40</td>
</tr>
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<td>• Weight loss</td>
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<tr>
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<td>• Cushing syndrome</td>
<td>&lt; 5</td>
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<tr>
<td>• Galactorrhea</td>
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TREATMENT

- Radical nephrectomy and ipsilateral lymph nodes extirpation
  - regression of metastases has been reported
  - a small, localized tumor may be removed by heminephrectomy
- Medroxyprogesterone acetate – some value in controlling metastatic disease
- Biologic agents IL-2 and INF-β produces remission in ~ 20%
- Non-myeloablative chemotherapy with ASCT support → striking regression of metastases (?)
- Mutation in tumour supression gene VHL, Raf – kinase inhibitors and VEGF → neutralizing antibody to VEGF (bevacizumab, axatimib) (slowing progression, RR ~ 40%)
  - everolimus, sunitimib, sorafenib (inhibitor mTOR)
- Tumor respond poorly to radiation and chemotherapy
- No effective chemotherapy is available for metastatic renal cell carcinoma, Vinblastine – parcial efect
- Cytoreductive nephrectomy – surgery follower by the use of systemic therapy
- Survival is related to cellular morphology, local extension and distant metastases
THANK YOU FOR YOUR ATTENTION