Pathology of the renal and urologic systems

V. Žampachová

I. ÚP

Signs and symptoms of renal/urinary tract problems

- Urinary frequency / urgency /nocturia
- Urinary incontinence
- Pain (shoulder, back, flank, pelvis, lower abdomen)
- Dysuria (painful urination) – usually uretritis/cystitis
- Hematuria – glomerular injury, tumors, trauma
- Pyuria - infection
- Fever and chills - infection
- Thirst, tiredness, weight gain – chronic renal failure
- Edema (facial, swollen ankles) – acute/chronic glomerular injury

Signs and symptoms of renal/urinary tract problems

- Hypertension – renal ischemia, sodium + fluid retention
- Oliguria (diminished amount of urine) – renal failure, obstruction, dehydration
- Polyuria (excessive amount of urine) – excessive fluid intake (beer), diabetes mellitus, renal tubular disorder
- Renal (ureteric) colic – passage of stone/blood clot
- Anaemia - ↓ renal production of erythropoetin
- Calcium metabolism problems – metastatic calcifications (arteries, soft tissues, inner organs), bone resorption

Signs and symptoms of renal/urinary tract problems

- Urine analysis
  - urine production rate
  - concentrating power of kidneys
  - urinary protein – glomerular / tubular lesions
  - urinary casts – hyaline casts (protein)
    granular casts (inflammatory cells)
    red cell casts (severe glomerular damage)

Signs and symptoms of renal/urinary tract problems

- Blood analysis (urea, creatinine, electrolytes) – glomerular filtration rate GFR, general integrity of renal function
- Imaging methods (X-ray, ultrasound, angiography, contrast urography)
- Cystoscopy
- Renal biopsy (histology, immunofluorescence, electron microscopy)

Signs and symptoms of renal/urinary tract problems

- Asymptomatic hematuria and/or proteinuria – mild glomerular lesion
- Polyuria + nocturia + electrolyte disorders – renal tubular defects
- Bacteriuria + pyuria – urinary tract infection (UTI)
- Renal colic + hematuria - nephrolithiasis

Signs and symptoms of renal/urinary tract problems

Uraemia

- Renal insufficiency - GFR 20-50% of normal
- Azotemia – increase of blood urea and creatinine due to decreased glomerular filtration (20-30%), or extrarenal cause
- Uraemia - azotemia together with several clinical and biochemical abnormities: metabolic, endocrine, … (uremic gastroenteritis, peripheral neuropathy, fibrinous pericarditis)
- Renal failure - GFR less than 20-25%, oedema, uraemia; causes: *prerenal, postrenal, renal (vascular, glomerular, tubulointerstitial);* acute r.f. (oliguria→anuria) chronic r.f
- End-stage renal disease - GFR less than 5% of norm

Signs and symptoms of renal glomerular problems

- Nephritic syndrome due to acute glomerular disease; hematuria + mild proteinuria + hypertension
- Rapidly progressive glomerulonephritis – very rapid (days-weeks) nephritic syndrome
- Nephrotic syndrome: usually chronic glomerular disease, severe proteinuria (>3,5 g/d) + oedema + hyperlipidemia + lipiduria

Inborn disorders

- 10% of all people
- hereditary or acquired developmental defect
- decreased volume of renal tissue (e.g. agenesis)
- disorders of differentiation (dysplasia)
- anatomical abnormalities (ectopy – abnormal site)
- metabolic disorders (cystinuria, …)

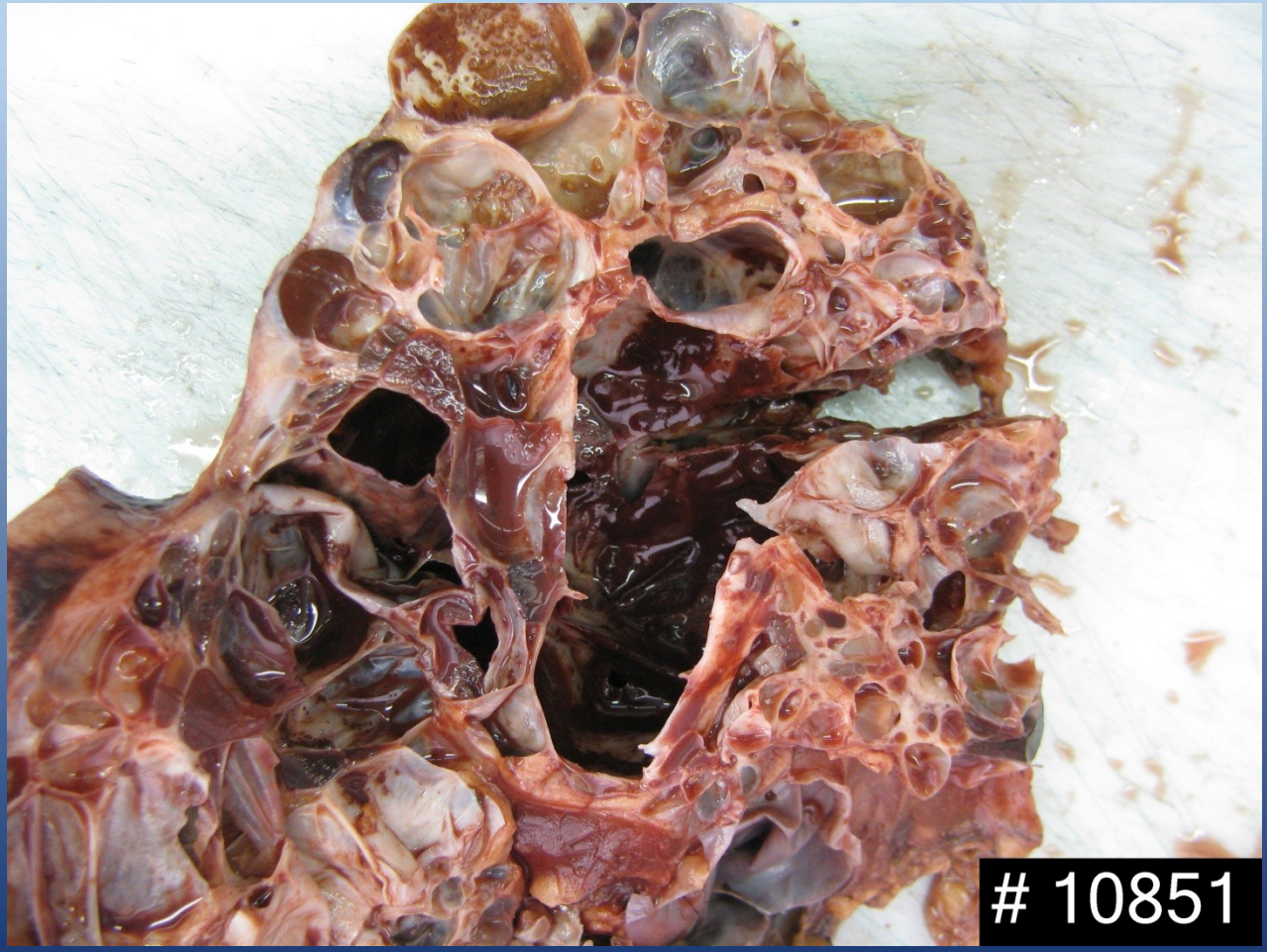
Cystic renal disease

- Hereditary, congenital nonhereditary, acquired
- Pathogenesis: primary defect of tubular epithelial cells and their growth, resulting in tubular dilatation
- Cavity filled with fluid, epithelial lining
- Multiple or solitary
- Solitary cyst may simulate a tumor
- Affects the whole kidney, or mostly cortex or medulla
- Pain, hematuria, hypertension, UTI, stones

Inborn disorders

- Adult polycystic kidney disease
  - common congenital disease, ↓of renal function in the 3.- 4. dec., autosomal dominant
  - + liver cysts, arterial berry aneurysms.
  - ↑risk of renal cancer
  - *gross:* symmetric kidney enlargement – lenght to 30 cm, weight to 8 kg, multiple cysts 0,5-50mm

Polycystic kidney



Inborn disorders - implications

- Worsening of signs/symptoms of a known disorder
- Signs/symptoms suggestive of inborn disorders
- Possible kidney enlargement – atypical findings on palpation

Urinary tract obstruction

- increased susceptibility to urolithiasis
- increased susceptibility to infection
- risk of hydronephrosis

- Combination of inborn + acquired risk factors

Vesico-ureteric reflux

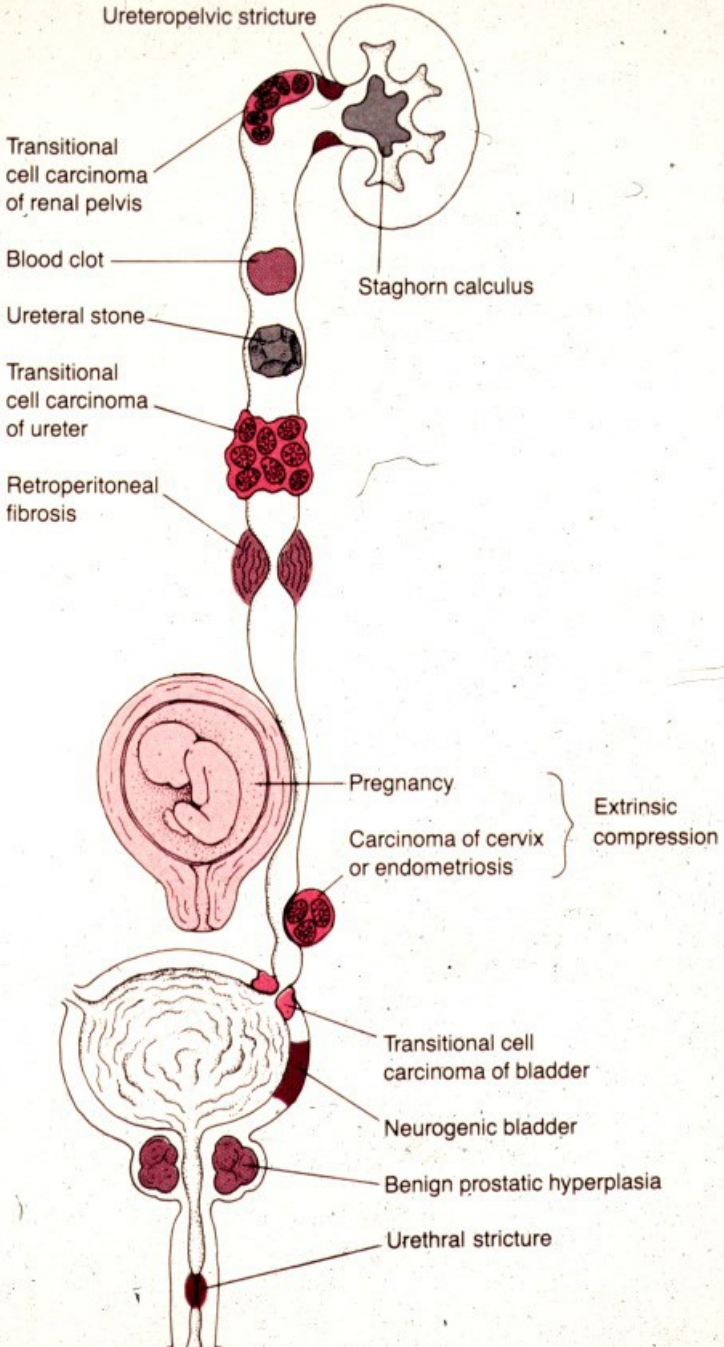
- Incompetence of the vesico-ureteral valve
- Combination of congenital defect (short intravesical part of ureter, 1-2% of children)
- ↓ ureteral contractility in infection
- acquired in bladder atony (spinal cord injury)

Obstruction causes

- Intrinsic – luminal obstruction (stone, blood clot, necrotic papilla, tumor or its part)
- Wall stenosis or dysfunction (inborn, inflammation, postinflammatory, tumor, …)
- Extrinsic – external compression, some causes common for both sexes, some different

Obstruction causes

- In males: prostatic hyperplasia, prostatic ca, urethral stenosis, phimosis + complications
- In females: pregnancy, cervical ca (+ therapy), uterine myoma, ovarian tumor, uterine prolapse
- in both: chronic inflammation/fibrosis (retroperitoneal fibrosis), tumor (colorectal ca, LN,...), aortic aneurysm


Ureteropelvic stricture
Transitional cell carcinoma of renal pelvis
Blood clot
Staghorn calculus
Ureteral stone
Transitional cell carcinoma of ureter
Retroperitoneal fibrosis
Pregnancy
Carcinoma of cervix or endometriosis
Extrinsic compression
Transitional cell carcinoma of bladder
Neurogenic bladder
Benign prostatic hyperplasia
Urethral stricture

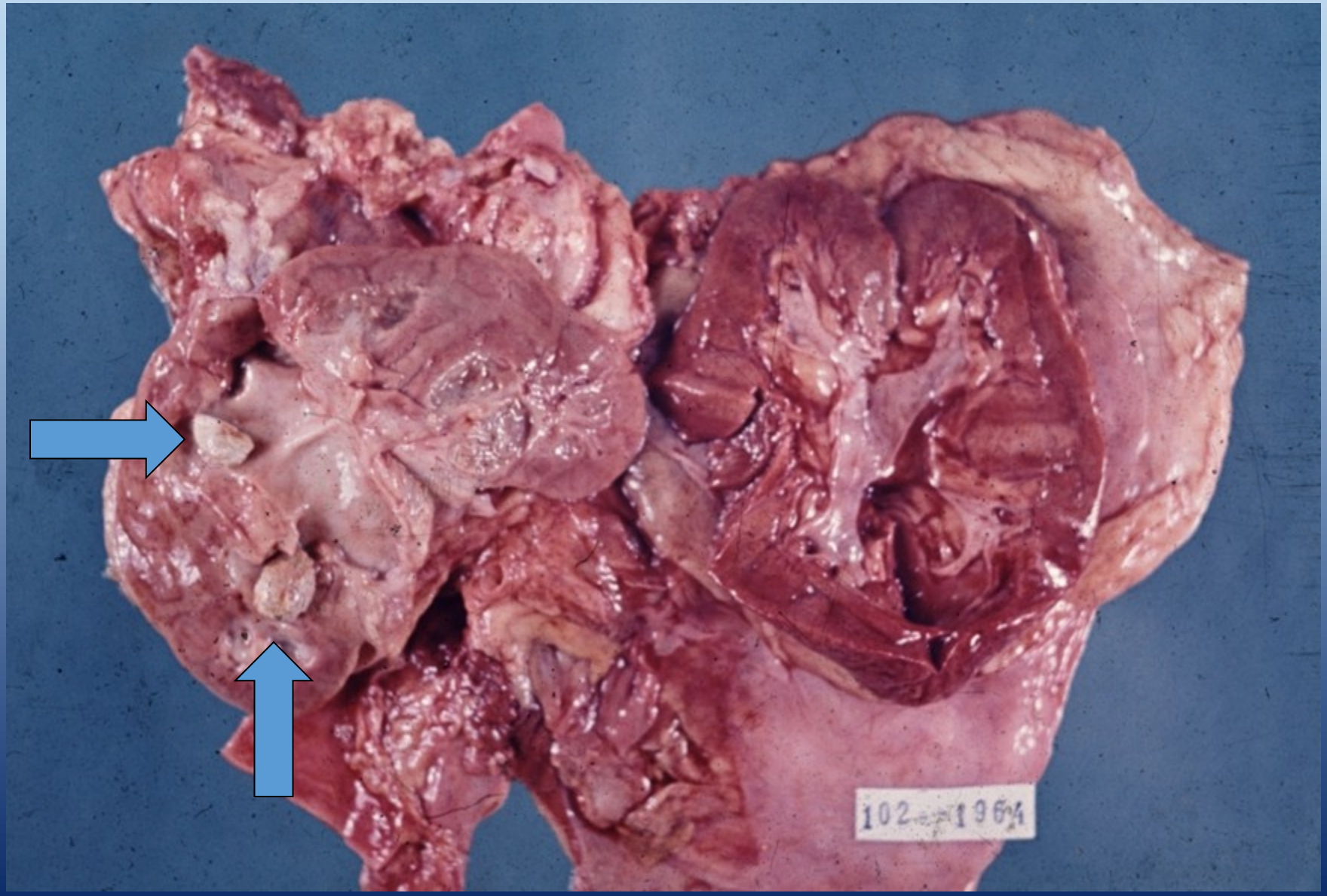
Renal – urinary calculi

- 5% of adults, recurrence common
- Usually of renal origin
- Stones $>$ 5 mm cannot pass into ureter
- Small stones - ↑ risk of obstruction
- Renal colic – pain + spasms during the passage of a stone along the ureter, hematuria
- Chronic dull pain lumbal – lower pelvic region
- Recurrent infection - possible presentation

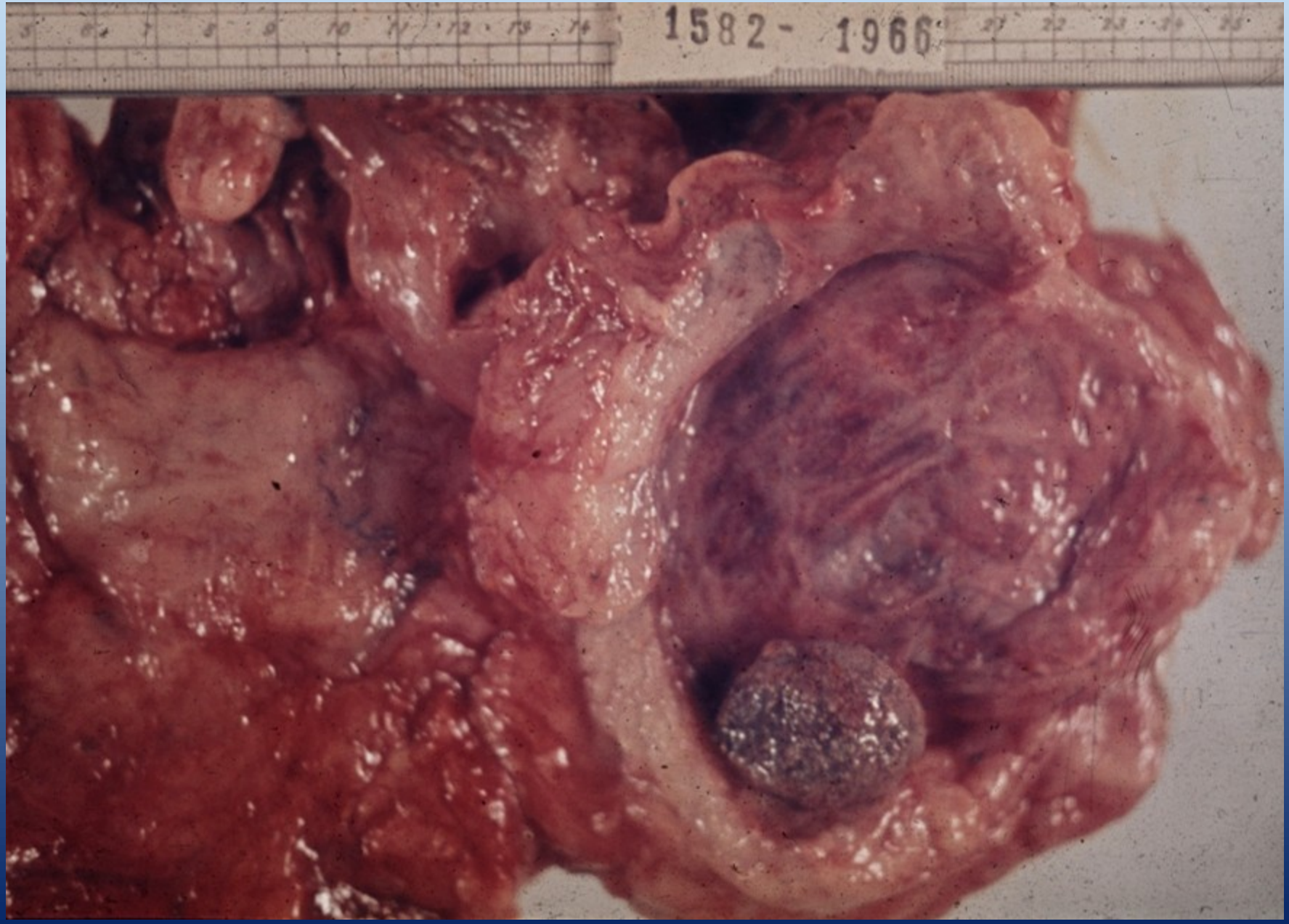
Urinary calculi

- Calcium containing stones: commonest, laid down in an acid urine.
- Complex triple phosphate stones: often associated with urinary infection, in an alkaline urine.
- Mixture of uric acid and urate-uric acid stones, 20% of patients with gout, in an acid urine.
- Cystine stones: in primary (inborn) cystinuria, important in childhood.

Pyelolithiasis in situ



Urocystolithiasis



Renal calculi - implications

- Differential diagnosis of less severe/intermittent pain x joint or muscle pain, incl. back pain
- Vigilance for signs of concurrent infection (fever, chills, sweats) necessary

Urinary tract infections

- Most commonly urethritis + cystitis
- Risk factors:
  - Females (short urethra, proximity to vagina, rectum)
  - Immobility /inactivity (impaired bladder emptying)
  - Increased sexual aktivity
  - Urinary catheter, instrumentation
  - Urinary obstruction
  - Constipation
  - Pregnancy
  - Immune deficiency

Urinary tract infections

- Mostly ascending infection
- Usually of bacterial origin (fecal – E.coli, sexually transmitted)
- Less commonly fungal (Candida), parasitic (Schistosoma)

Urinary tract infections

- Complicated – more difficult diagnosis/treatment:
  - small children (atypical signs)
  - elderly adults (less pronounced signs, confusion)
  - pregnancy (asymptomatic UTI possible)
  - patients in hospitals, long term care
  - diabetes and/or other risk factors
  - Relapse (due to low-level persisting infection) or recurrence (new infection) common
- Uncomplicated – otherwise healthy people

Urinary tract infections

- Signs:
  - Frequency
  - Urgency
  - Dysuria
  - Nocturia
  - Enuresis in children
  - Pain (suprapubic, lower abdomen, groin, lumbar)
  - Possible cloudy, bloody, foul smelling urine
  - Possible systemic signs (fever, malaise, chills)

Acute cystitis

- highly common in females (short urethra, perineal connection with anus)
- mostly fecal bacteria, mixed flora
- risk factors – urine pH, hormonal status, iatrogenic
- usually purulent (leucocytes, blood in urine), urging, pain; may have systemic signs
- complications – ureteral spread, ulcers, rare phlegmona, pseudomembranous inflammation

Chronic cystitis

- in obstruction (prostatic hyperplasia, indwelling catheter)
- acute exacerbations, stone formation
- may be risk factor for neoplasia
- diff. dg. x neoplasia

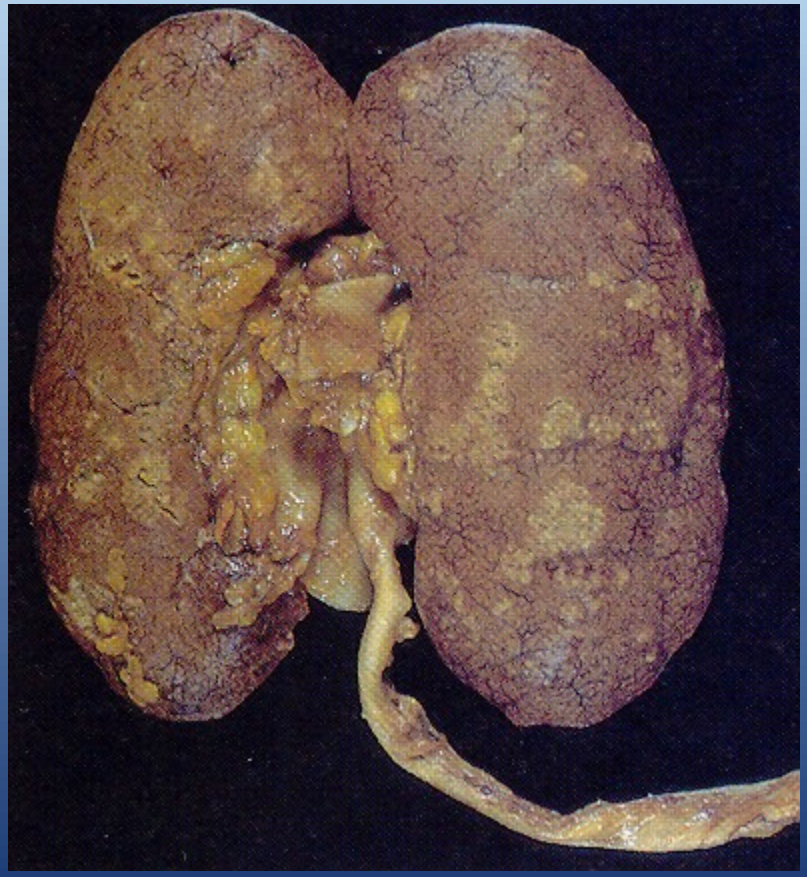
Acute pyelonephritis

- Common purulent renal inflammation, bacterial infection
- **Ascending** infection by urine reflux in urinary tract inflammation
- **Descending (haematogenous)** infection in septicaemia, rare
- Systemic signs (abrupt, high fever, chills, malaise, headache, lumbar pain, nauzea, vomiting)
- May lead to sepsis+renal failure - urosepsis

Acute pyelonephritis

- Facilitated by DM, gout, all causes of obstructive uropathy (e.g. nephrolithiasis, tumors, urinary tract anomalies incl. vesicoureteric and intrarenal reflux)
- Instrumental interventions (cathetrization, cystoscopy)
- Gross: enlarged kidney, cortical and medullary abscesses

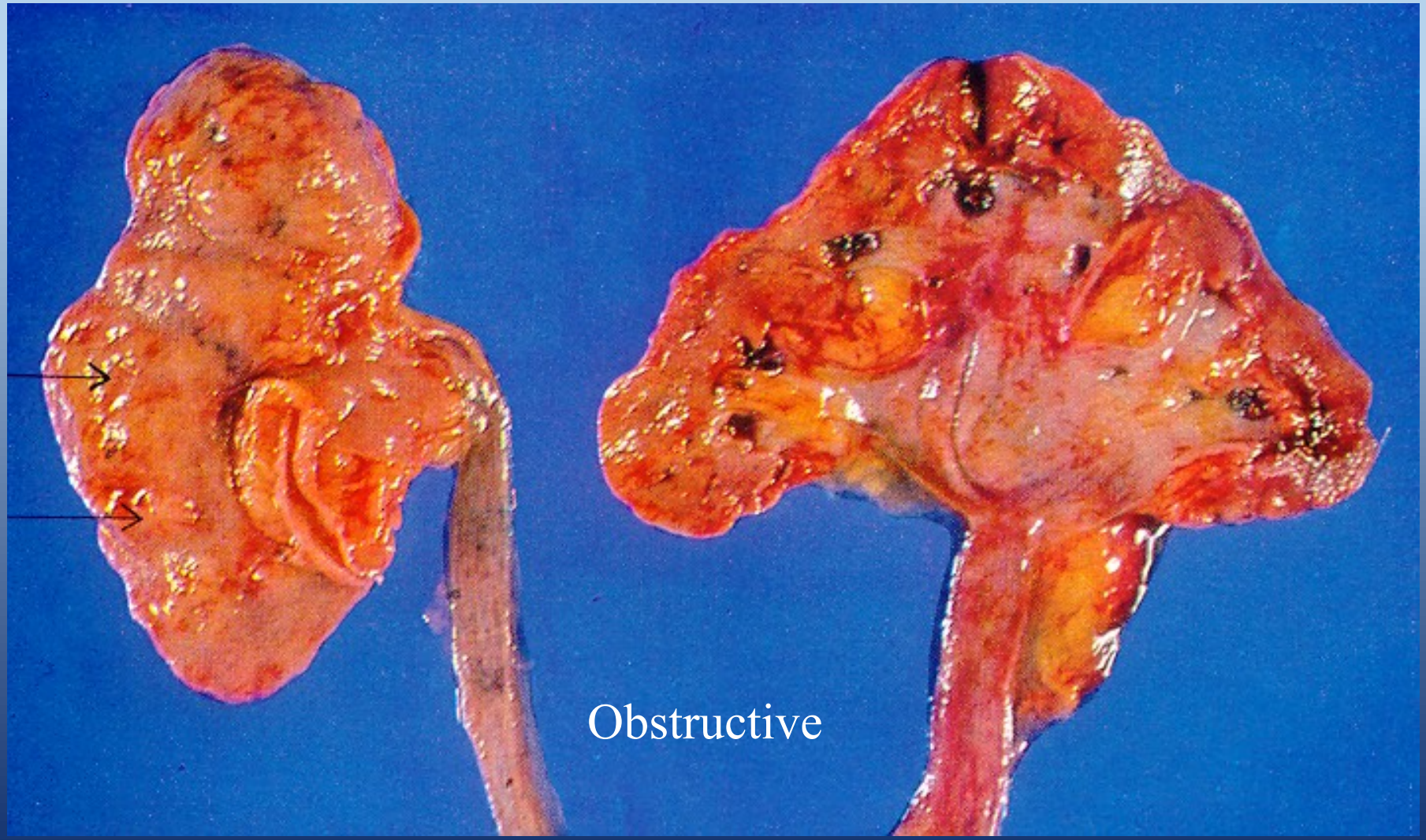
Acute pyelonephritis



Chronic pyelonephritis

- Uni- or bilateral chronic renal (tubules + interstitium) inflammation with scarring
- Progression to end-stage kidney (renal failure)
- **Obstructive PN - repeated infections**
- **Reflux nephropathy**

Chronic pyelonephritis



Urinary tract infections - implications

- Recognition of early/worsening symptoms – referral to physician – prevention of possible permanent damage
- Catheter care – diminishing risk of infections

Chronic kidney diseases (CKD)

- Alteration of kidney function/structure for ≥ 3 months
- Non-healing acute disorder (i.e. acute glomerulonephritis), or slow progression of chronic lesion
- Variable causes, most common:
  - Diabetes mellitus
  - Hypertension
  - Glomerulopathy
  - Chronic UTI
  - Cystic kidney disorders
  - Other systemic disorders (SLE)
  - Drugs (NSAIDs) – analgesic nephropathy

Chronic kidney diseases

- Common problem
- May be asymptomatic initially – incidental finding in laboratory tests
- Gradual onset of symptoms common
- Slow decrease of glomerular filtration rate
- May progress to kidney failure (GFR <5%)
- Correct diagnosis necessary
- In some types treatment possible

Chronic kidney diseases

Uremia: internal intoxication – failure of toxin excretion, maintaining the fluid, pH, electrolyte balance

Loss of important hormone secretion (renin, vitamin D, erythropoetin)

Chronic kidney diseases

Complications + consequences:

- Cardiopulmonary:
  - Coronary artery disease
  - Hypertension
  - Pulmonary edema
  - Congestive heart failure
  - Pericarditis

- Hematologic:
  - Anemia
  - Impaired platelet function

Chronic kidney diseases

Complications + consequences:

- GIT
  - Nausea and vomiting
  - Anorexia
  - Bleeding
- Central nervous system
  - Headache
  - Irritability, impaired judgment, inability to concentrate
  - Sleep disturbances
  - Seizures
  - Lethargy/coma

Chronic kidney diseases

Complications + consequences:

- Peripheral nervous system
  - Loss of deep tendon reflexes
  - Impairment of motor nerve conduction velocity
  - Burning, tingling sensations
  - Tremor
  - Muscle cramps, muscle twitching
  - weakness
- Skin
  - Itching + scratching
  - Altered skin color (pallor, brownish tint, bruises)

Chronic kidney diseases

Complications + consequences:

- Skeletal system
  - Bone demineralization
  - Joint pain / calcification
  - Myopathy

Glomerular diseases

- Variable causes (immunological x non-immunological incl. inborn)
- Variable clinical / histologic picture – variable classifications according to the changes
- Damage to the glomerular permeability → nephrotic syndrome
- Glomerular inflammation and necrosis → leakage of blood + protein into urine → nephritic syndrome
- Permanent injury → sclerosis, hyalinosis – loss of functional glomeruli, end-stage kidney with renal failure

Glomerular diseases

Glomerulonephritis

- Glomerular injury due to abnormal immune responses and/or complement system
- May be primary (antibodies against antigenes of glomerulus, SLE), secondary (postinfectious – poststreptococcal, IgA, with deposition of circulating immune complexes in the glomerulus)

Chronic kidney diseases

Diabetes mellitus

- Most common cause of end-stage kidney disease in developed countries
- Slowly progressive course (15 years) in type I DM, variable in type II DM
- Variable combination of changes
- Diabetic nephropathy – microvascular changes incl. glomeruli
- Accelerated arteriosclerosis
- UTI incl. pyelonephritis, papillary necrosis

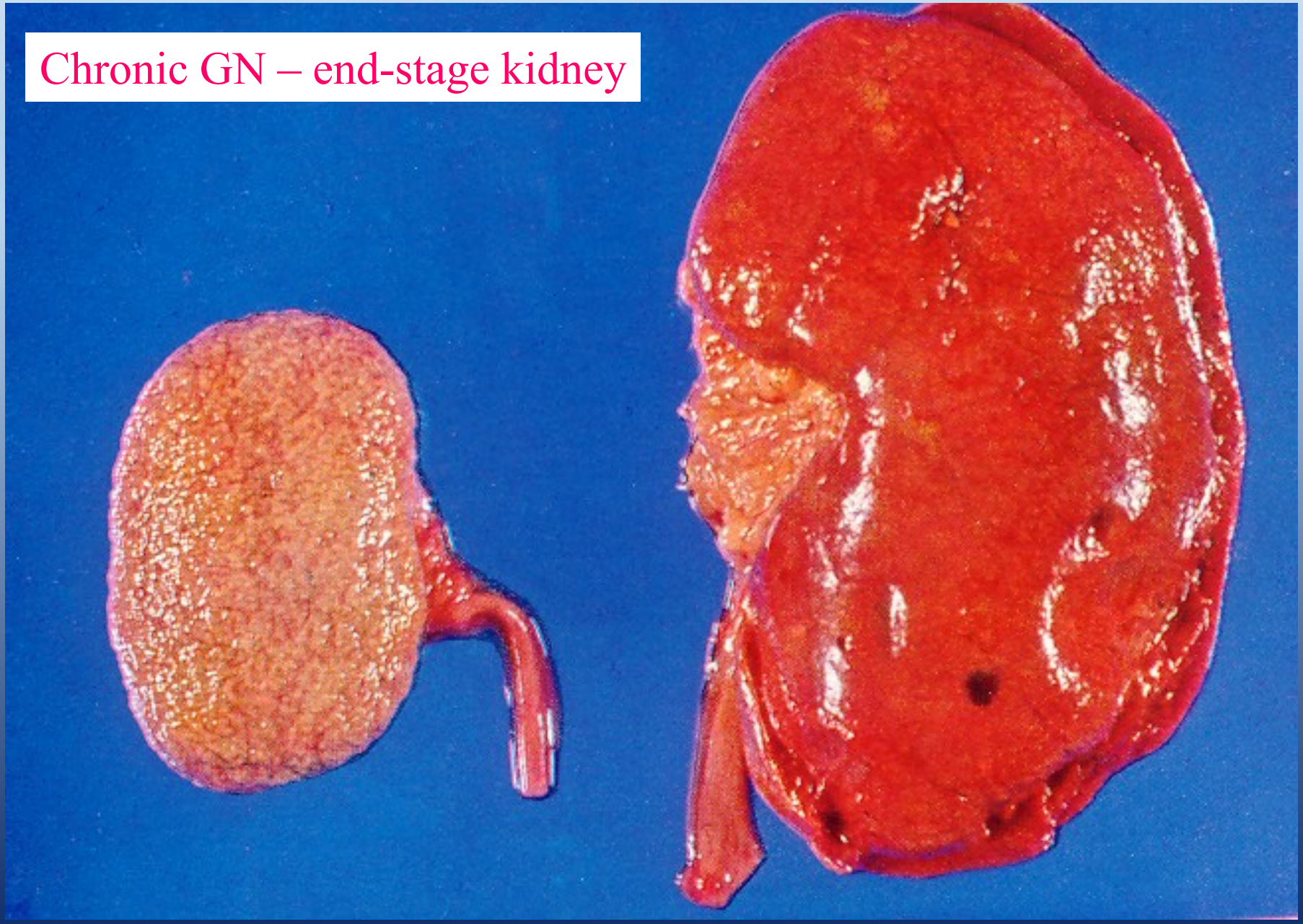
Chronic glomerulonephritis

- End stage of variable glomerular disease
- Different rate of progression in different diseases
- Focal segmental glomerulosclerosis (commonly the result of hyperfiltration in residual glomeruli due to glomerular/renal tissue loss – nephrectomy; obesity, hypertension; drugs) 50-80%
- Rapidly progressive glomerulonephritis ~ 50%
- Poststreptococcal 1-2%

Chronic glomerulonephritis

- Shrinked kidney with granular surface
- Thin cortex
- Obliterated glomeruli, arterio- and arteriolosclerosis (hypertension), tubular atrophy

Chronic GN – end-stage kidney



Chronic kidney diseases - implications

- Knowledge of association of glomerular diseases with systemic disorders – DM, hypertension, vasculitis, systemic lupus, …
- Presence of clinical signs (edema, signs of uremia, …) – referral to a physician
- Side effects of therapy (diuretics – fatigue, muscle cramps, weakness, headache, ↑frequency of urination + incontinence, depression

Chronic kidney diseases - implications

Nephrogenic systemic fibrosis

In patients with chronic kidney diseases

- Firm erythematous skin plaques, itchy
- Fibrosis +/- calcification of soft tissue incl. muscles
- Pain in joints, bones
- Muscle contracture, loss of function
- Massage, joint manipulation, exercise, swimming

Renal failure

Renal replacement therapy necessary

- Dialysis
- Renal transplantation:
  - Cheaper than long-term dialysis
  - Limited availability of organ grafts
  - Life-long immunosuppression necessary
  - Variable complications

Dialysis

- Removal/diffusion of waste products, excess fluid + electrolytes
- Peritoneal dialysis
  - Catheter implanted in the peritoneal cavity
  - Sterile dialyzing solution instilled /drained
  - Several times daily, possible during sleep
  - Independent at home procedure
  - Infectious complications, dehydration
- Hemodialysis (HD): external machine
  - Usually 3x weekly 3-4 hours
  - Rapid changes in blood constituents – severe signs possible
  - Commonly patients immobile
  - Low-intensity exercise program during the first half beneficial

Dialysis – implications for the terapist

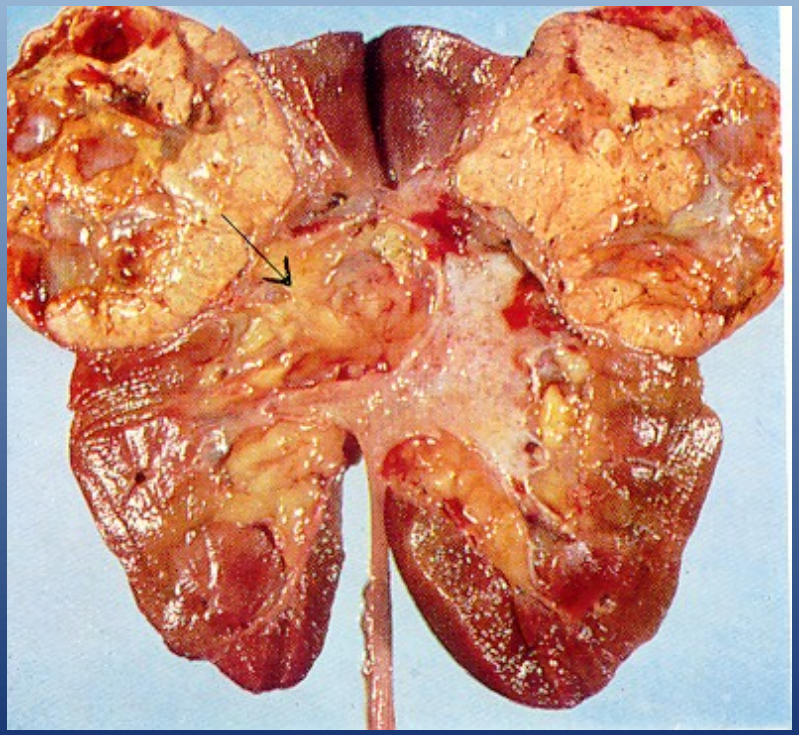
- ↑ susceptibility to infection (!hand hygiene)
- Maintaining the dialysis access site (thrombosis)
- ↑ thirst (limited fluid intake)
- Weight gain (fluid retention), but ↓ lean body mass – muscle loss
- Alternating hypertension (fluid retention) and dialysis hypotension
- Anorexia, ↑ catabolism, ↓ functional capacity (50% in CKD)
- Depression common
- Individual exercise/treatment plan

Renal cancer

- Renal cell carcinoma (RCC): most common adult renal tumor
- Transitional cell carcinoma of pelvis, ureter
- Benign tumors possible, diff. diagnosis x RCC
- Wilms tumor in children
- Metastatic cancer (primary in the lungs, breast, skin melanoma, …)

Renal cell carcinoma

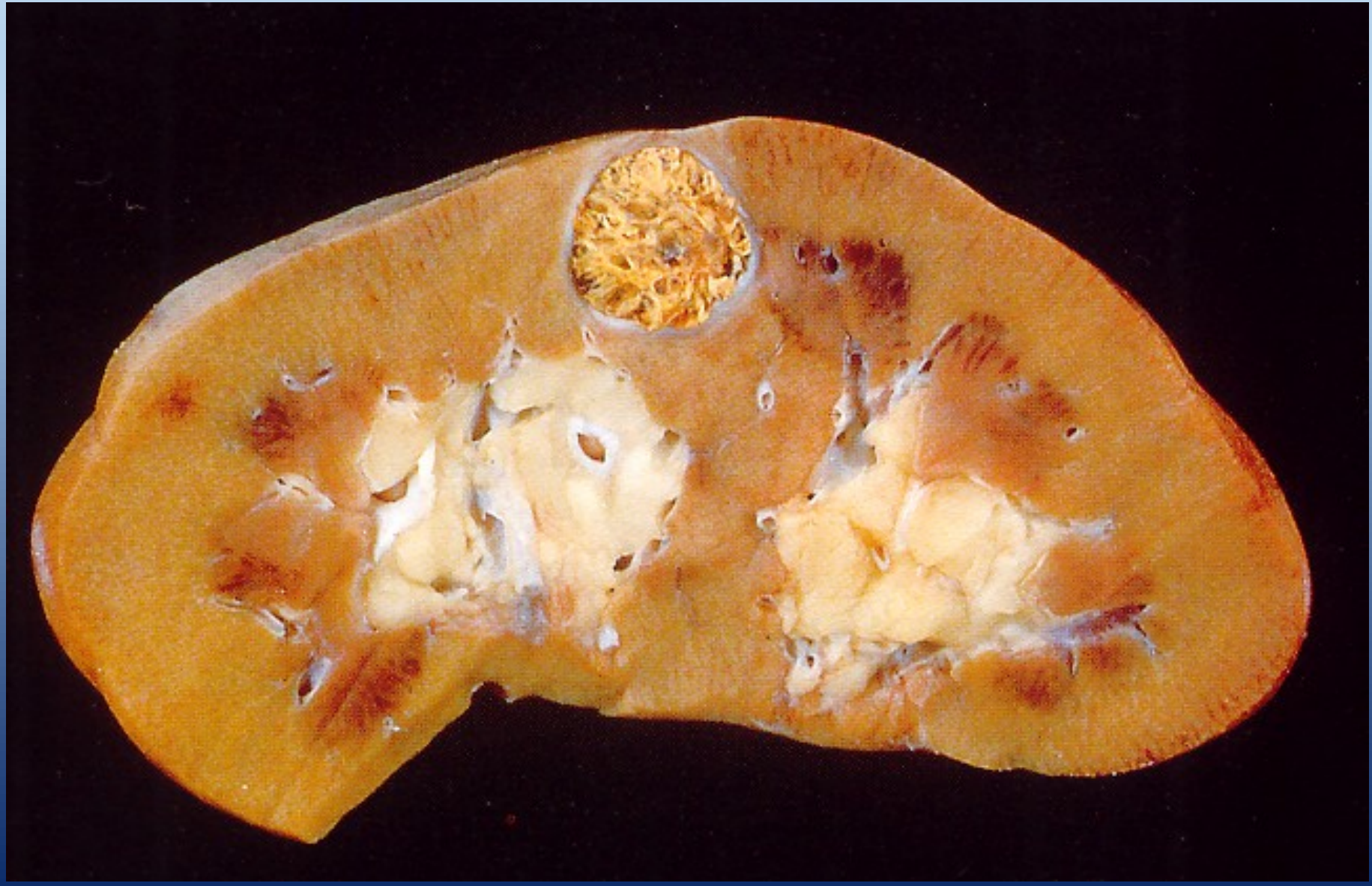
- Conventional clear cell RCC - Grawitz
- 80% of renal malignancies
- Other RCC types less common (papillary RCC)
- Metastasis mosty by hematogenous way



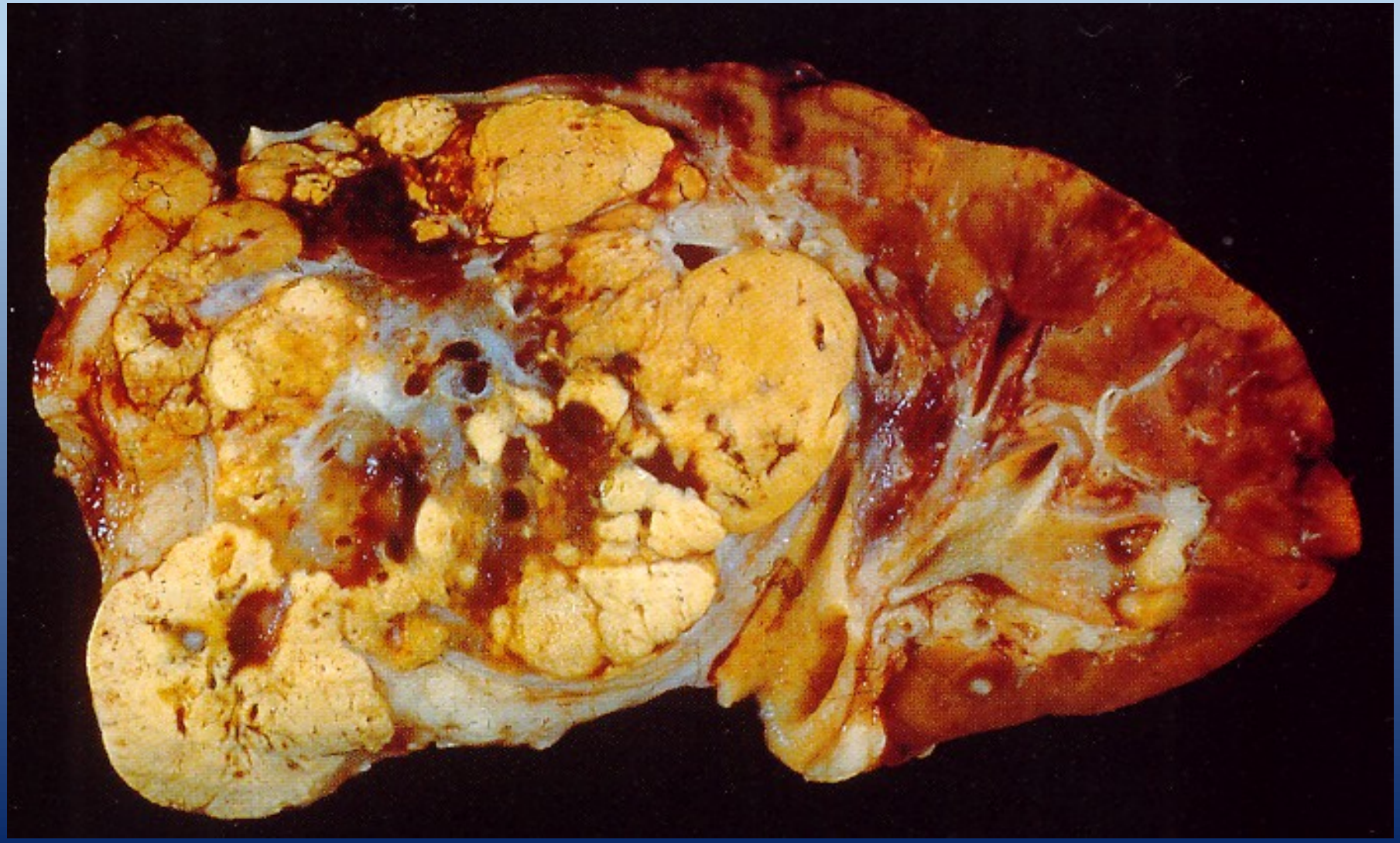
Renal cell carcinoma

- More common in males; middle-older age
- Risk factors: smoking (25% of RCC), moderate to heavy drinking, obesity (25%), familiar factors incl. cystic disease, industrial pollution, radiation treatment
- Incidental finding in imaging methods
- Hematuria (50%), may be intermittent and/or microscopic
- Flank pain, palpable mass – late sign
- Metastasis - late sign, in ¼ of patients; lung, lymph node, bone, liver
- Prognosis according to the type and stage

Renal cell carcinoma



Renal cell carcinoma



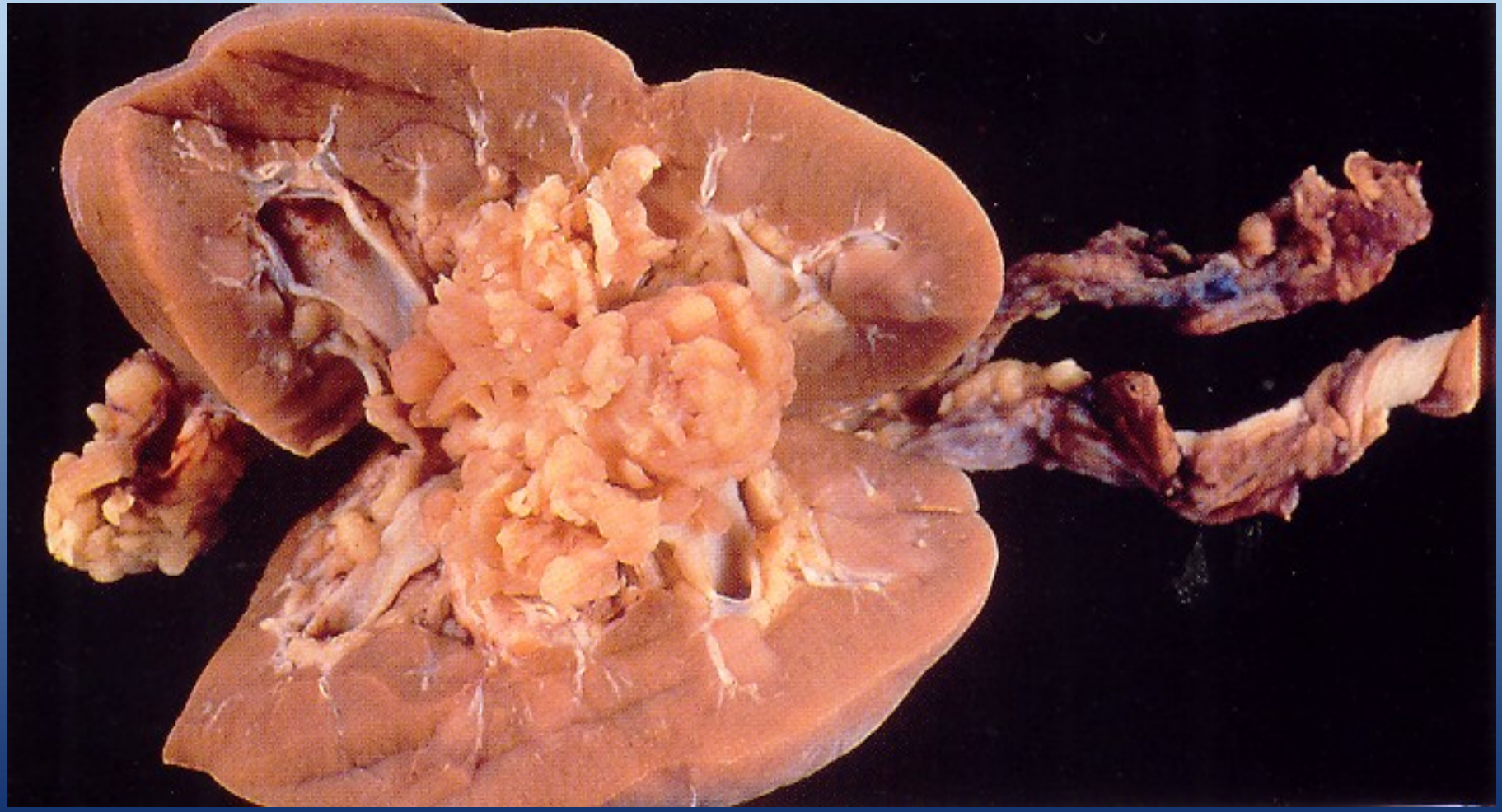
Renal cell carcinoma - implications

- Mostly in geriatric population
- Awareness/questions of possible signs
- New onset of unexplained abdominal / back pain
- Surgical treatment most important - surgical sites scarring management
- Side effects of targeted therapy

Transitional cell carcinoma

- Cca 10% of renal carcinoma
- Growth in the renal pelvis
- Early presentation with hematuria / urinary tract obstruction
- Multiple concurrent tumors in pelvis /ureter /bladder possible

Transitional cell ca of the renal pelvis



Wilms tumor

- 3rd most common malignant pediatric tumor
- Diagnosed mostly in the 1st-4th year of age
- Sporadic, or part of some syndromes
- Clinical: large tumor, palpable, complications due to compression of adjacent organs, hematuria
- Prognosis: good, chemotherapy, (radiotherapy carefully, second malignancies possible)

Disorders of the bladder and urethra

- Inflammation
  - Infections - UTI
  - Non-infective: interstitial cystitis / painful bladder syndrome: suprapubic pain related to bladder filling + ↑ urgency/frequency (day+night), without other pathology
    - Low back pain, burning, spasm possible
    - Commonly ↑ with stress, acid food, sex
    - Conservative treatment usual – symptom relief, stress management, relaxation treatment

Disorders of the bladder and urethra – neurogenic bladder

- Voiding dysfunction due to neurologic lesions
- Pelvic lesions: trauma, surgery
- Spinal cord /nerve lesions: diabetes, disc disease, injury
- Cerebral lesions
  - Stroke
  - Trauma
  - Dementia
  - Parkinson‘s
  - Multiple sclerosis
  - Tumor

Disorders of the bladder and urethra – neurogenic bladder

- Sensory – efferent nerves dysfunction (diabetes, syphilis, …), no sensation of the fullness; incontinence, no high bladder pressure
- Motor paralytic – destruction of afferent parasympathetic motor nerves (pelvic surgery, trauma) – problems in starting/maintaining urine stream, hypotonic bladder
- Reflex/spastic – spinal cord injury – loss of sensation + motoric problems – high bladder pressure, kidney injury risk
- Neurogenic detrusor overactivity – brain tumors, demyelinization, Parkinson – involuntary contractions
- Autonomous – complete separation from upper nervous centres

Disorders of the bladder and urethra – neurogenic bladder

- Complications: UTI, renal calculi, hydronephrosis
- Differential diagnosis x other lesions (bladder cancer, prostate hyperplasia, …)
- Exercise – bladder training
- Functional mobility, relaxed sitting

Disorders of the bladder and urethra - cancer

- Urothelial (transitional cell) carcinoma most common
- Middle to older age
- Manifestation: painless hematuria, frequency, dysuria
- Commonly recurrences / multiple tumors over years
- Important predisposing factors:
  - Smoking (about ½ of bladder cancer cases)
  - Occupational exposures – dyes, diesel exhaust, rubber industry, …
  - Males
  - Chronic inflammations, incl. permanent catheter, stones, parazites
  - Decreased fluid intake
  - Genetic / inborn defects

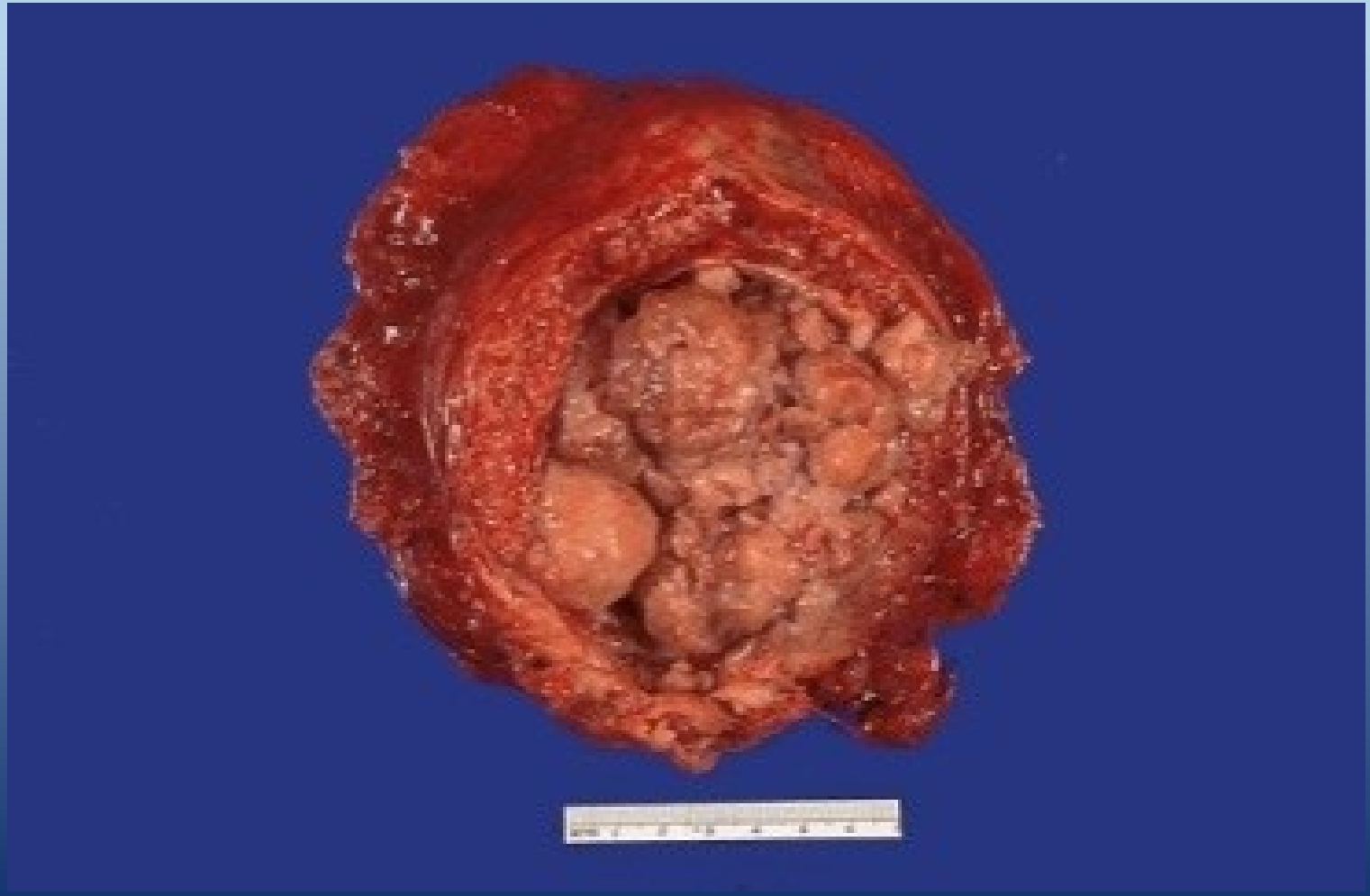
Disorders of the bladder and urethra - cancer

- Flat lesions –
  - Carcinoma in situ – confined to the epithelium
  - Invasive solid carcinoma, worse prognosis
- Mostly exophytic papillary, variable malignant potential
  - Tumor of low malignant potential – borderline malignancy, no invasion, no metastasis, good prognosis, but recurrences possible
  - Low grade carcinoma (non-invasive, invasive)
  - High grade carcinoma (non-invasive, sooner invasive)

Disorders of the bladder and urethra - cancer

- Other histologic types possible
- Secondary tumors
  - Local progression from surrounding organs not uncommon (prostate, rectum, cervix)
  - Metastasis rare

Bladder carcinoma



Disorders of the bladder and urethra – cancer - implications

- High incidence of local recurrence – signs!
- Risk of late radiation sequelae
- Sequelae of surgery (cystectomy) incl. infection, impotence
- Retraining of voiding, pelvic floor muscles

Urinary incontinence

- Complaints of involuntary urine loss
- Variable categories, commonly mixed UI
- Urgency urinary incontinence – loss of urine + urgency due to overactive bladder, variable triggers (running water, …)
- Stress urinary incontinence – during increased intraabdominal pressure
  - On effort / physical exertion – lifting weight, …
  - Coughing, sneezing

Urinary incontinence

- UI common, more prevalent in women (50%) than males (14%)
- In older adults, particularly nursing home
- Diagnosis! – not a part of the normal aging process
- Consequences:
  - depression, social isolation, limited work opportunities
  - UTI
  - Decreased exercise participation
  - Increased fracture risk (incontinence + postural hypotension → fall)

Urinary incontinence – risk factors

- Obesity, ↑ BMI
- Age
- Pregnancy (multiple)
- Pelvic surgery (prostate in males, uterus in females)
- Diabetes mellitus
- Constipation
- UTI
- Medications
- Impaired cognitive function, impaired mobility

Urinary incontinence - implications

- Rehabilitation often possible
  - Pelvic floor muscles exercises
  - Bladder training
  - Biofeedback possible
- Everyone should be asked about urinary problems
  - Esp. peri- postmenopausal women
  - Parous women (who have been pregnant)
  - People > 60 years
  - Person with multiple risk factors