Investigation Of kidney and Urinary tract

Dept. pathological physiology

By Pavel Maruna

Functional tests

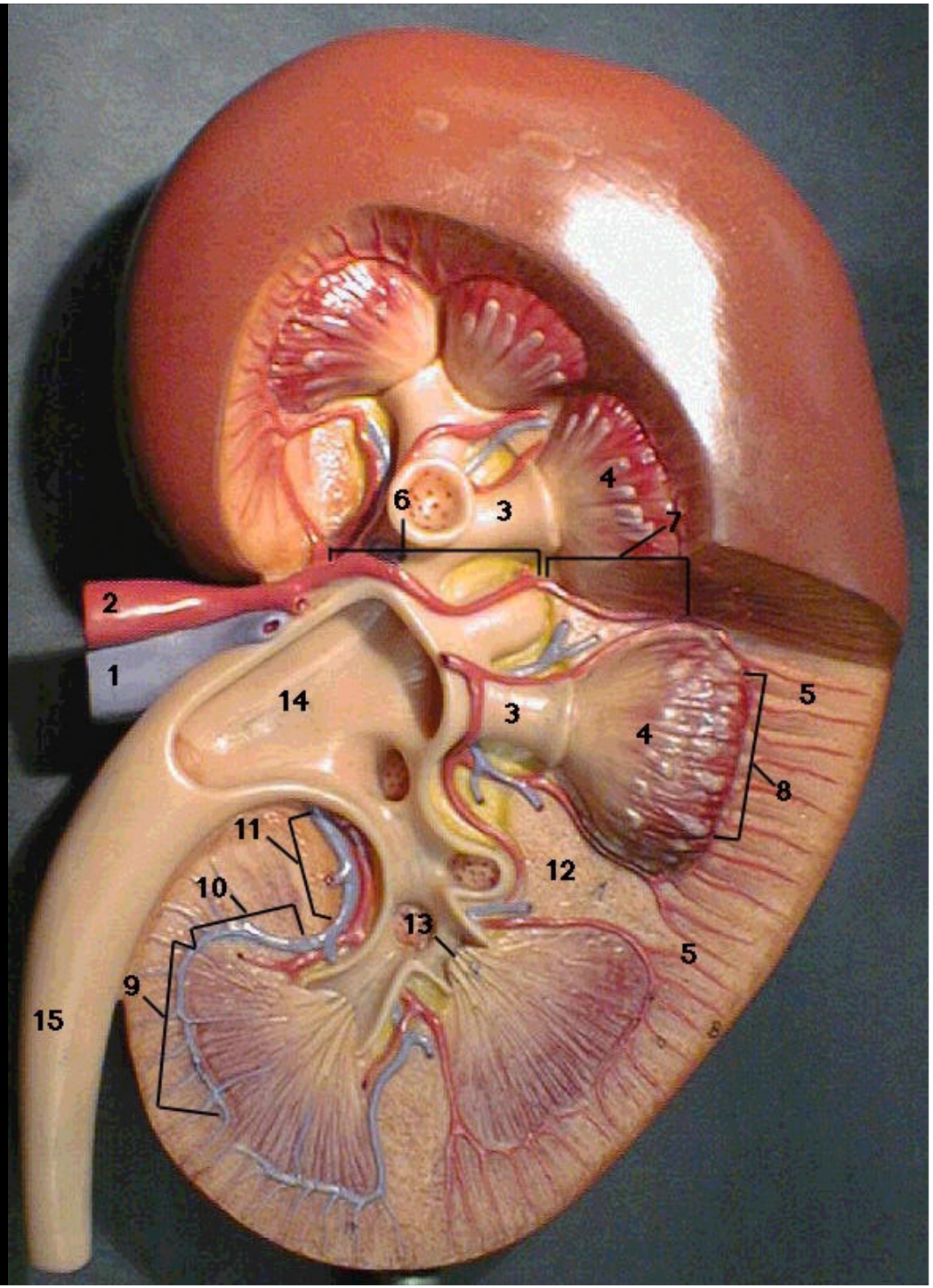
Glomerular filtration
Tubular resorption
Concentration test
Acidification test
Blood gases

Imaging methods

Native X-ray
scintigraphy
angiography
Ultra-sonography
MRI

Endoscopy/ laparoscopy

Laboratory tests



Definitions

Renal insuficiency

Kidneys are able to maintain homeostasis of the inner milieu under normal conditions, but unable to do so in a stress conditions (infection, surgery, overlod by water and electrolytes).

Renal failure

Kidneys are unable to maintain homeostasis of the inner milieu even under basic conditions.

Uremia

Syndrome of higher level of nitrogen metabolites in inner milieu, which can develop as a consequence of (mostly chronic) renal failure.

Chronic renal failure/ uremic syndrome

1. Retention of
   - water
   - electrolytes
   - small molecules
   - medium size molecules (500 - 3000 D)

2. Losses of
   - water, electrolytes
   - amino acids, proteins, vitamines (soluble in water)

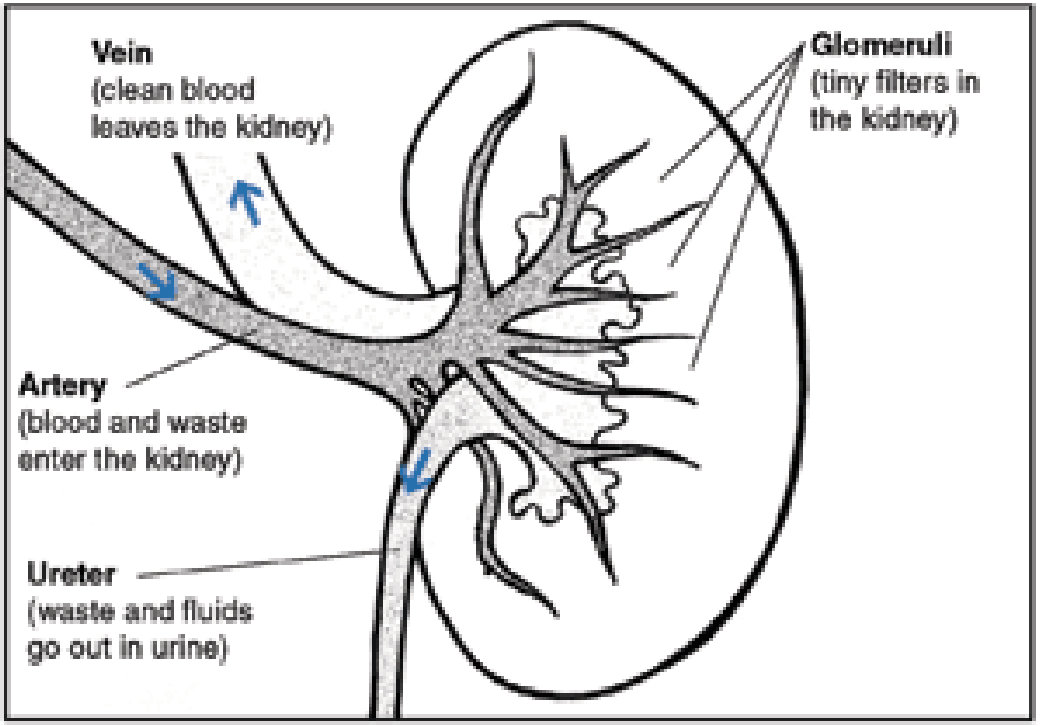
3. Lower production of
   - Erythropoietin
   - 1,25-OH-D3 (vitamin D)

4. Trade off hypothesis
   = picture develops due to compensatory mechanisms

Acute renal failure

According to site/ causes

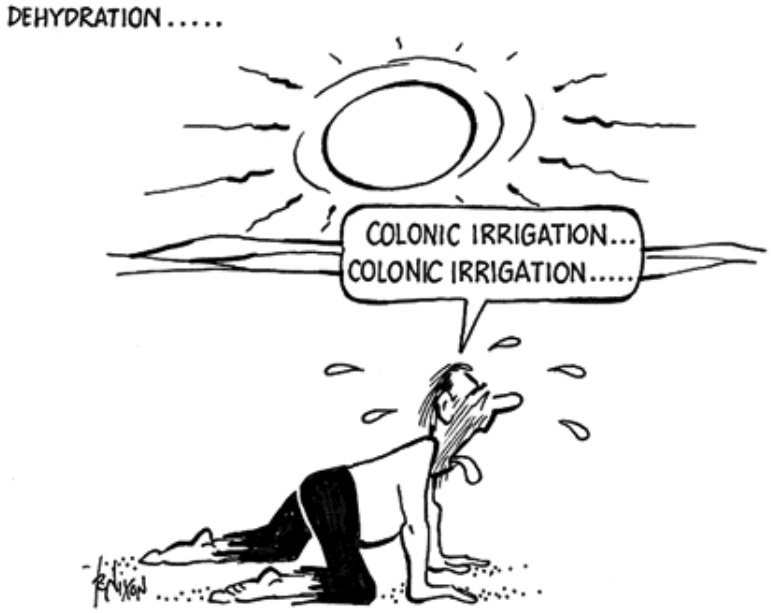
1. Pre-renal
2. Renal (parenchymatous)
3. Post-renal (obstructive)



Acute renal failure

Causes

1. Prerenal → **Changes in haemodynamics Circulation shock, (Losses of blood, water and electrolytes)**



Acute renal failure

Causes

2. Renal (parenchymatous) – mostly defects of tubules

- TIN (tubulo-interstitial nephritis)
- Glomerulo-nephritis (streptococcus, SLE, Goodpast. sy)
- Nefrotoxic drugs (CCl4, etylenglykol, propylenglykol, Hg, Au,Bi,
- nefrotox. substances (SFA, gentamycin, cefaloridin), amanita phal.
- hemolysis (incompatible TRF)
- crush syndrom
- burns (dehydration, sepsis, toxemia)
- toxo-infectious insult (sepsis)
- childbirth, abortion, surgery
- acute pancreatitis
- Vascular disorders (occlusion a. renalis, thrombosis of kidney veins, hypertension)

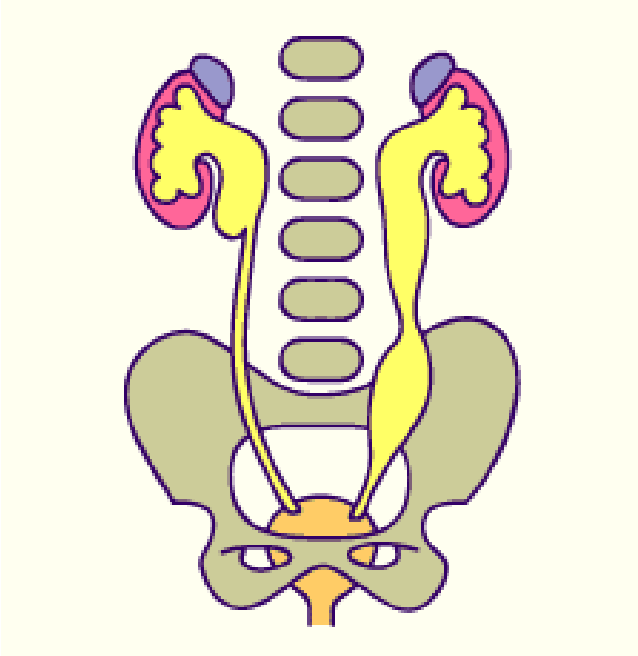
Acute renal failure

Causes

Obstruction of urinary tract

3. Post-renal →

- urolithiasis, blood clots
- tumours
- prostatic hypetrophy
- retro-peritoneal fibrosis
- surgical fixation of ureters
- atonia of urinary bladder



Acute renal failure

Parameter	Pre-renal f.	Renal f.
Natriuria	< 20	> 40 mM
U-osmolarity	> 500	< 350 mosm / kg
conc. index creatinin	> 40	< 20 (U-cr / P – cr)
conc. index of urea	> 8	< 3 (U-urea / P-urea)
excretion fraction of Na	< 1	> 2

Holds only in a condition before cure (by diuretics and/or infusion).

Acute renal failure

Stages

1. Initial ... Dominated by its cause/ primary disease
2. Anuric / oliguric phase
3. Diuretic ... Polyuric phase (up to 5-6 l / 24 h)
4. Convalescence ... Sanatio ad integrum can take 1 year

Oliguria < 500 ml / 24 h

Anuria < 100 ml / 24 h

Chronic renal insuficiency

Final stage of various kidney ailments

44 %	glomerulonephritis, glomerulopathy
25 %	TIN (tubulo-interstitial nephritis)
10 %	kidney polycystosis

Staging

I. Fully compensated (cr. < 300)

II. Compensated retention (cr. = 300-700)

III. De-compensated retention (cr. > 700) ... Haemo-dialisys

IV. Uremia

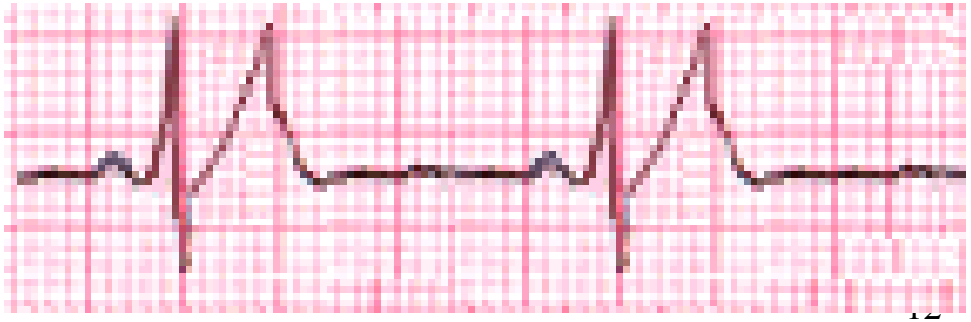
Uremia

Water and electrolyte dysbalance

- losses / retention of water
- ↓ Na (dilution, distribution, depletion)
- ↑ K (retention)

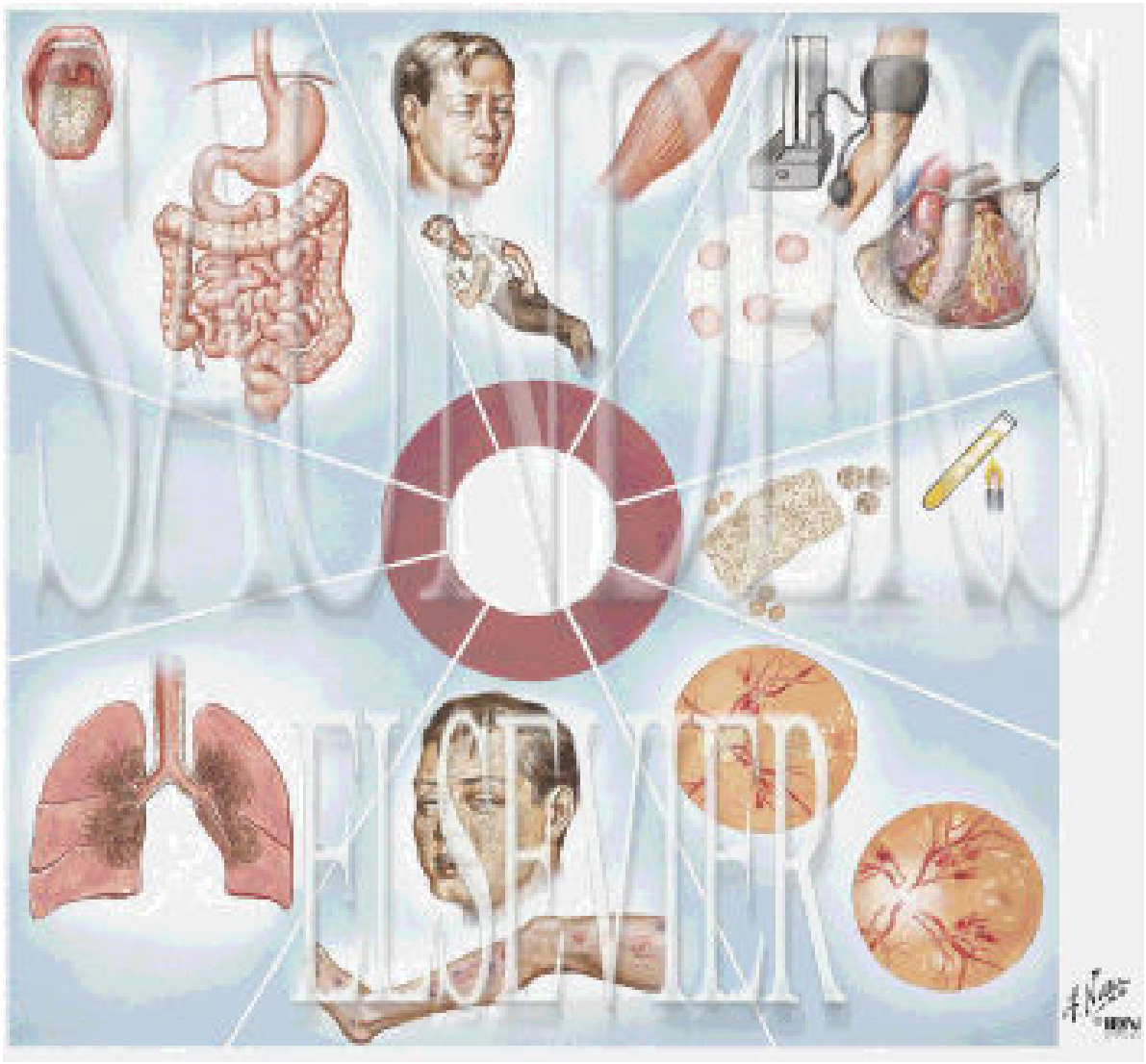
oedemas± dehydration

weakness, tiredness
dyspepsia (anorexia, morning nausea, vomiting, diarrhea)
arrythmia, perikarditis



Uremia

Bleeding
Secondary gout
Poly-neuropathy



Uremia

Renal (reno-parenchymatous) hypertension

Factors:

- **presoric (kidney hypoperfusion → renin)**
- **depresoric (kallikrein/kinins, PG E)**
- **excretion of Na, H_2O**

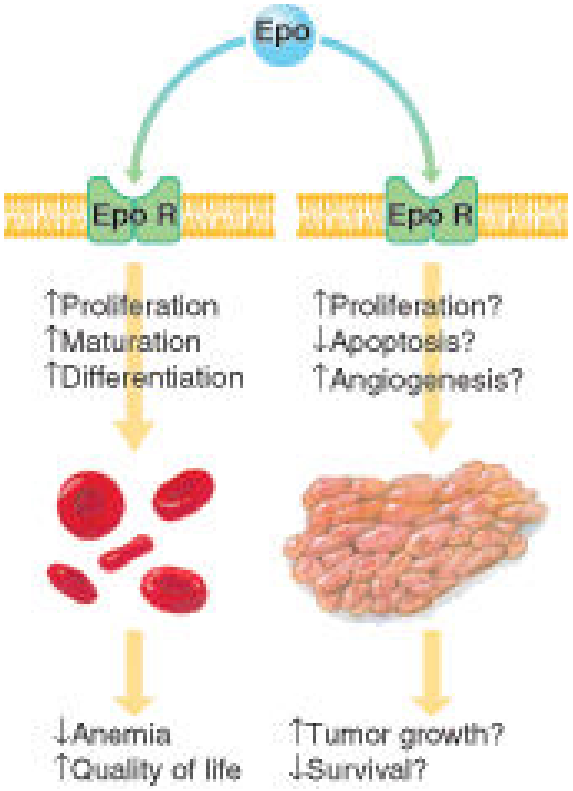
x

Renovascular hypertension

Renal presoric mechanisms (renin) only

Hypo-perfusion in renal artery stenosis

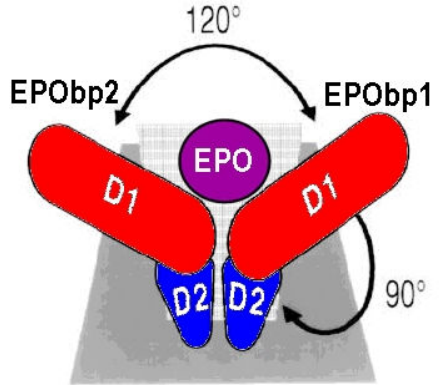
Uremia



Anemia

Factors:

- **Epo**
- **vitamin losses, protein losses (proteinuria)**
- **blood losses (hematuria)**
- **low iron (inflammation, ↓ Trf)**
- **toxic suppression of bone marrow**
- **inflammatory inhibition of erythropoiesis**



Uremia

Renal osteodystrophy

Factors:

- ↑ PO_4
- ↓ 1,25-0H-vit. D3 ... Lower production
- ↓ Ca ... losses, ↓ intestinal resorption
- secondary, ↑ PTH ... bone resorption

decreased production by the proximal convoluted tubule

retention

↓ 1,25-0H-vit. D3

↑ PO_4

↓ gut uptake of Ca

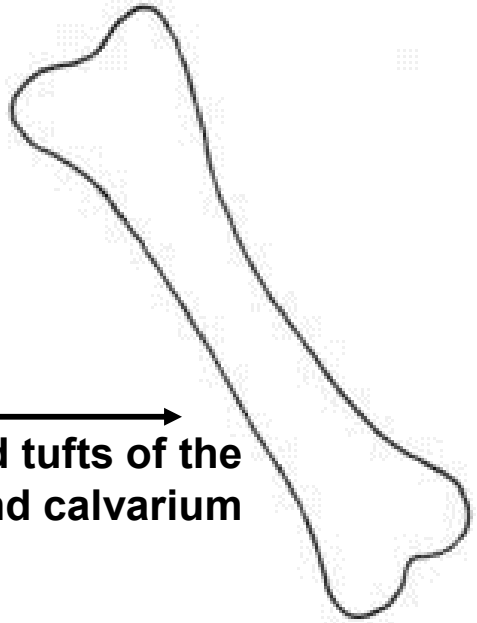
renal loss

binding of serum Ca

↓ Ca

secondary hyperparatyreodidism

↑ PTH



bone resorption, commonly from subperiosteal regions and tufts of the phalanges, proximal humerus, tibia and femur, and calvarium

Uremia

Renal osteodystrophy

"Salt and pepper" skull

Higher para-thyroid activity causing characteristic subperiostal resorption

Uremia

Renal osteodystrophy

Bone changes are partially reversible
snapshots of the same finger before and 6 months
after therapy of secondary hyper-parathyreosis

Uremia

Secondary infections

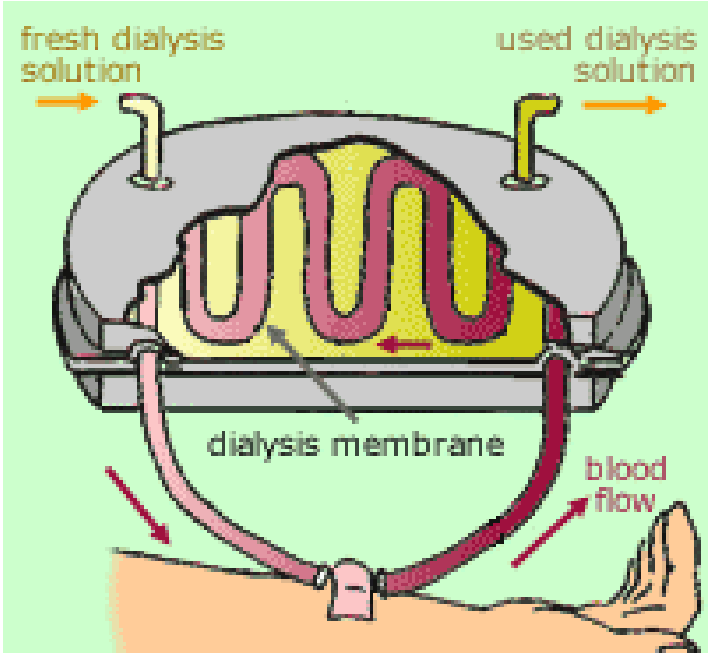
Bronchitis, broncho-pneumonia
Hepatitis
Sepsis

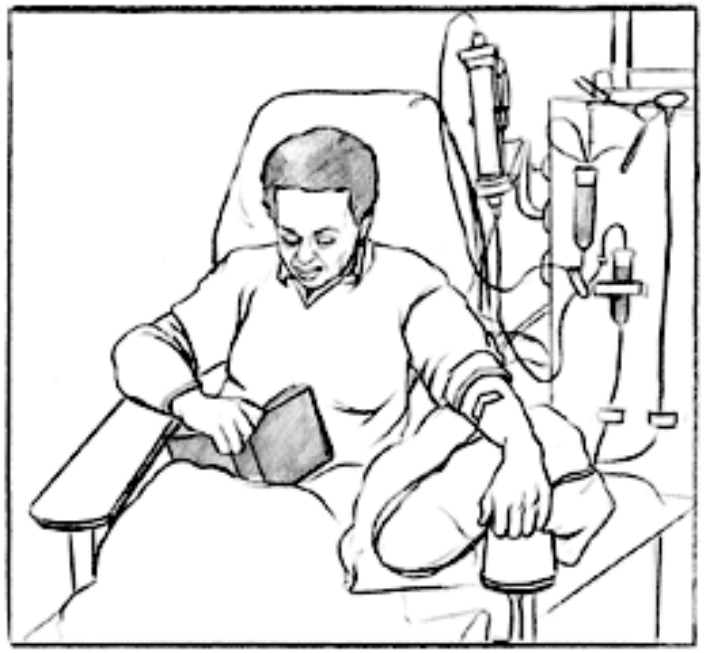
Cheyne - Stokes breathing pattern

Acute dialysis

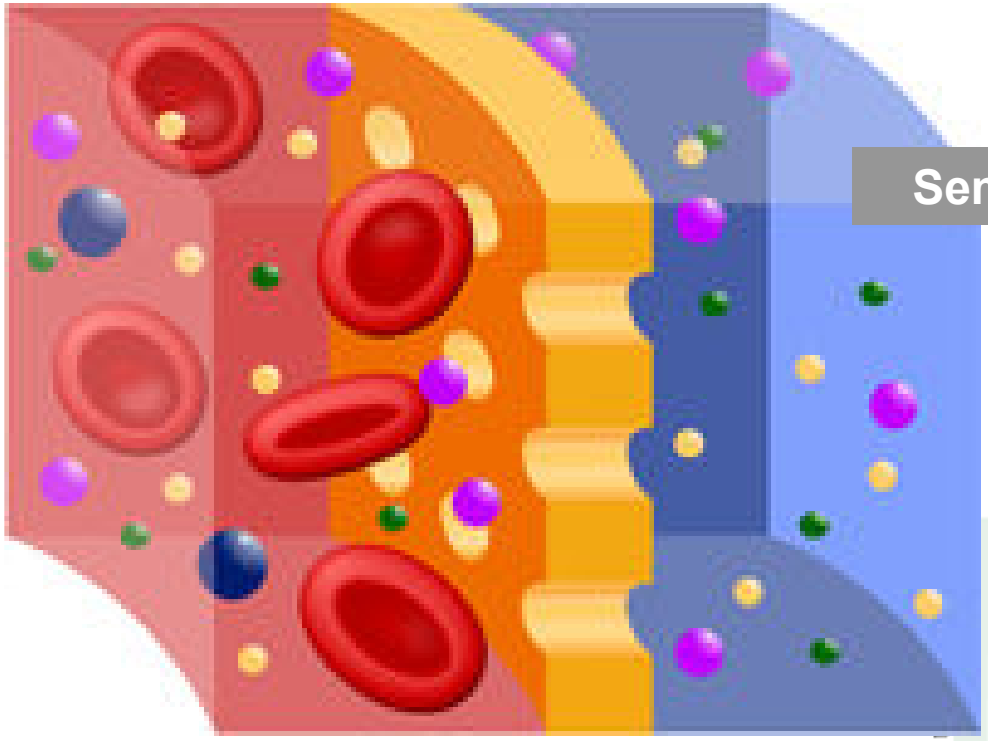
Principle

The dialysis membrane allows to exchange of low molecular substances to dialysis solution in accordance of its concentration (x molecules bound on plasma proteins)

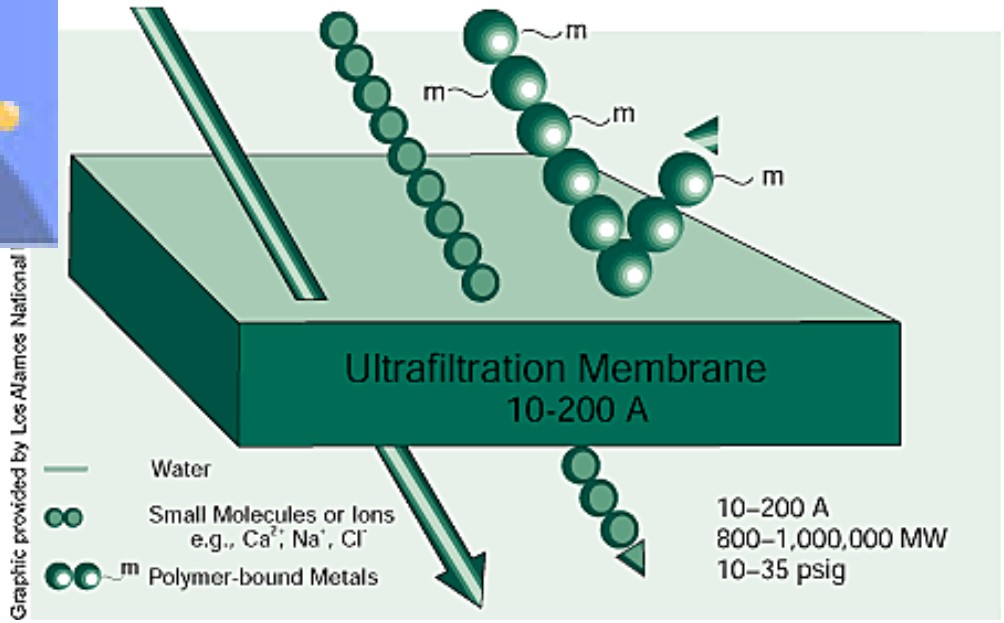




Acute dialysis



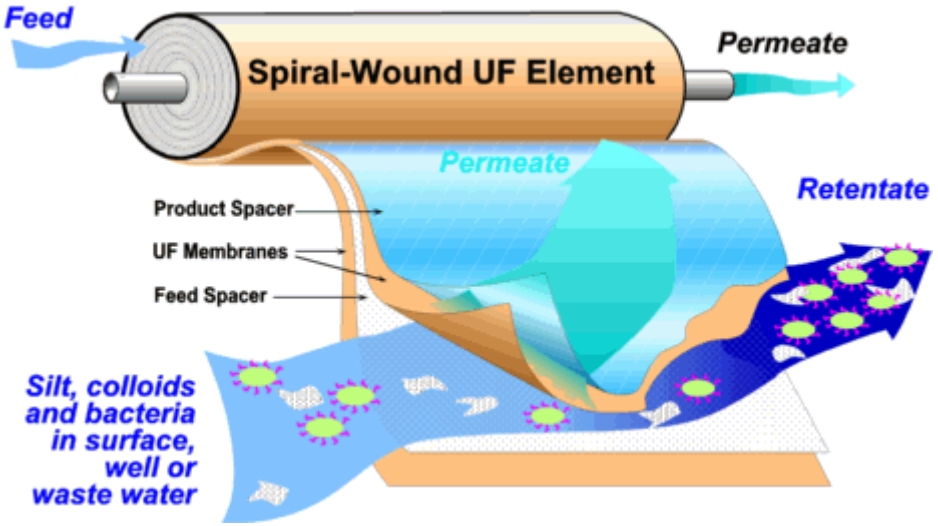
Semipermeable dialysis membrane



Acute dialysis

The possible combination with ultrafiltration

(in hyperhydratation, pulmonary edema)



Utrafiltration

The membrane process that uses moderate hydraulic pressure to transfer water and low molecular weight species through a membrane while retaining colloids and large organic molecules

Acute dialysis

Indications

1. Renal failure

- uremia
- anuria / oliguria > 3 days
- creatinine > 700 umol / l
- urea > 30 mmol / l
- ↑ urea > 10 mmol / l / day
- K > 6,5 mmol / l
- acidosis
- hyperhydration (conservatively immedicable)

Acute dialysis

Indications

1. Renal failure
2. Intoxication ... drugs non-bound on proteins

psychiatric drugs
fridex (coolant fluid)

Acute dialysis

Indications

1. Renal failure
2. Intoxication
3. ↑ Ca
4. ↑ urikemia ... e.g. after cytostatic therapy of leukemia
5. Hypotermia
6. Alcalosis ... rarely (not in CZ)

Acute dialysis

Contraindications:

Only terminal stage of malignancy

Not age or diagnosis

All patients with creatinine > 300 nmol / L have to be followed in predialysis centers

Peritoneal dialysis

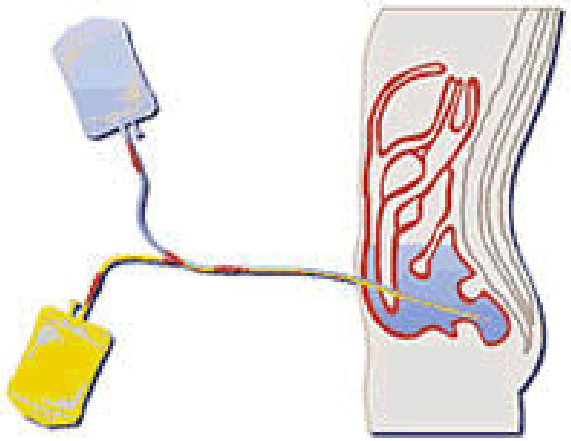
Principle

Peritoneum is used as a dialysis membrane.

The abdominal cavity is filled by a dialyze liquid.

The liquid (artificial ascites) is get out after some interval.

CAPD = Continual ambulatory peritoneal dialysis

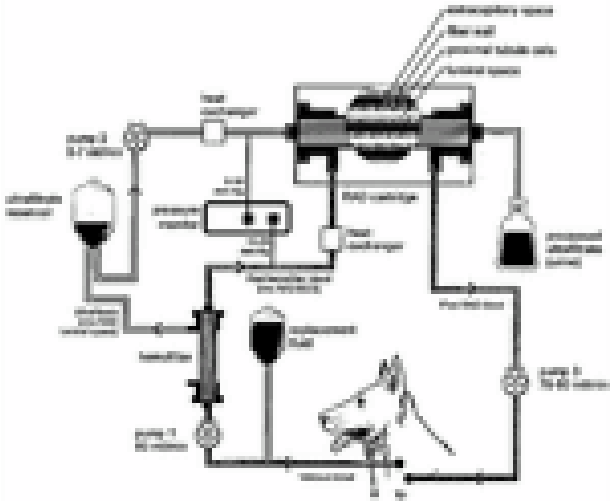


Hemoperfusion

Principle

The blood flows in hemoperfusion capsules through an absorbent.

Elimination method of toxins bound on proteins



hemoperfusion capsule

Dialysis

Complications

Sy of insufficient dialysis

Sy of excessive dialysis ... a loss of AA, vitamins, enzymes, hormones, hypotension due to hypovolemia

Sy of disequilibrium ... a brain edema duo a quick dialysis

Sy of hard water ... Ca in dialyse fluid → hypertension, vomiting, fatigue, headache

Infectious complication ... hepatitis B

Urine biochemistry

U-Na ... 100 - 200 mmol / 24 h
U-K ... 30 - 80 mmol / 24 h

U-Na : U-K < 1 ... Na/K exchange in distal tubuli (aldosterone)

Pathology: primary kidney dis.
renin / angiotensin / aldosterone

Urine biochemistry

Excretion fraction (EF)

= The fraction of its glomerular filtration flux, which passes to and is excreted in the urine

$EF = J_{excr}/J_{filtr}$

$J_{excr} = (C_u \times V°_u)$ and $J_{filtr} = (GFR \times C_{filtr})$. It follows that:
$EF = (C_u \times V°_u) / (GFR \times C_{filtr})$
C_{filtr} = the concentration of the substance in the ultrafiltrate.

Inulin EF = 1.
Substances with an EF > 1 are subject to net secretion.
Substances with an EF < 1 are subject to net reabsorption.

Urine biochemistry

Proteinuria

Physiol.	< 150 mg / 24 h
Pathol.	> 500 mg / 24 h
Haevy	> 3500 mg / 24 h
Nephrotic sy	> 5000 mg / 24 h

Methods of quantifying proteinuria:

- urine dipstick test
- sulfosalicylic acid tests

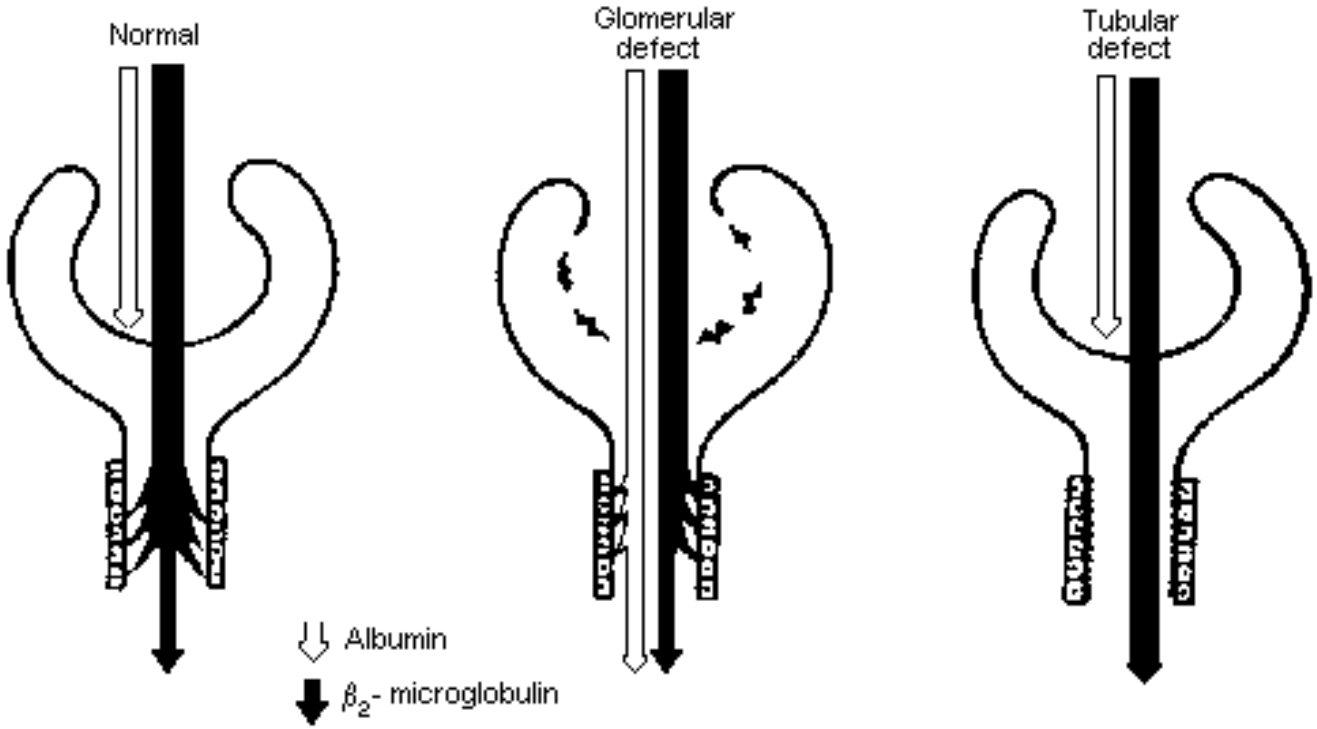
Protein urinary excretion of > 2 g per 24 h is usually a result of glomerular disease.

Young men with proteinuria < 2 g per 24 h and who have a normal creatinine clearance should be tested for orthostatic proteinuria

Urine biochemistry

Proteinuria

Glomerular x Tubular



Urine biochemistry

Proteinuria

Glomerular	**Increased glomerular capillary permeability to protein** **Primary or secondary glomerulopathy**
Tubular	**Decreased tubular reabsorption of proteins in glomerular filtrate** **Tubular or interstitial disease**
Overflow	**Increased production of low- molecular-weight proteins** **Monoclonal gammopathy, leukemia**

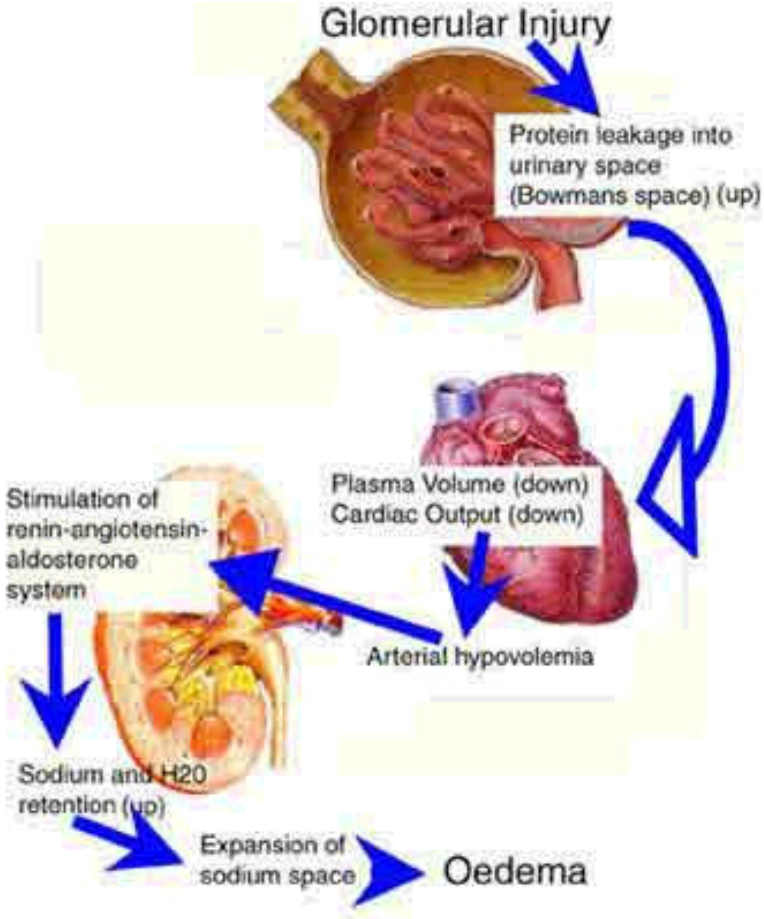
Urine biochemistry

Proteinuria

Nephrotic syndrome

Diagnostic criteria:

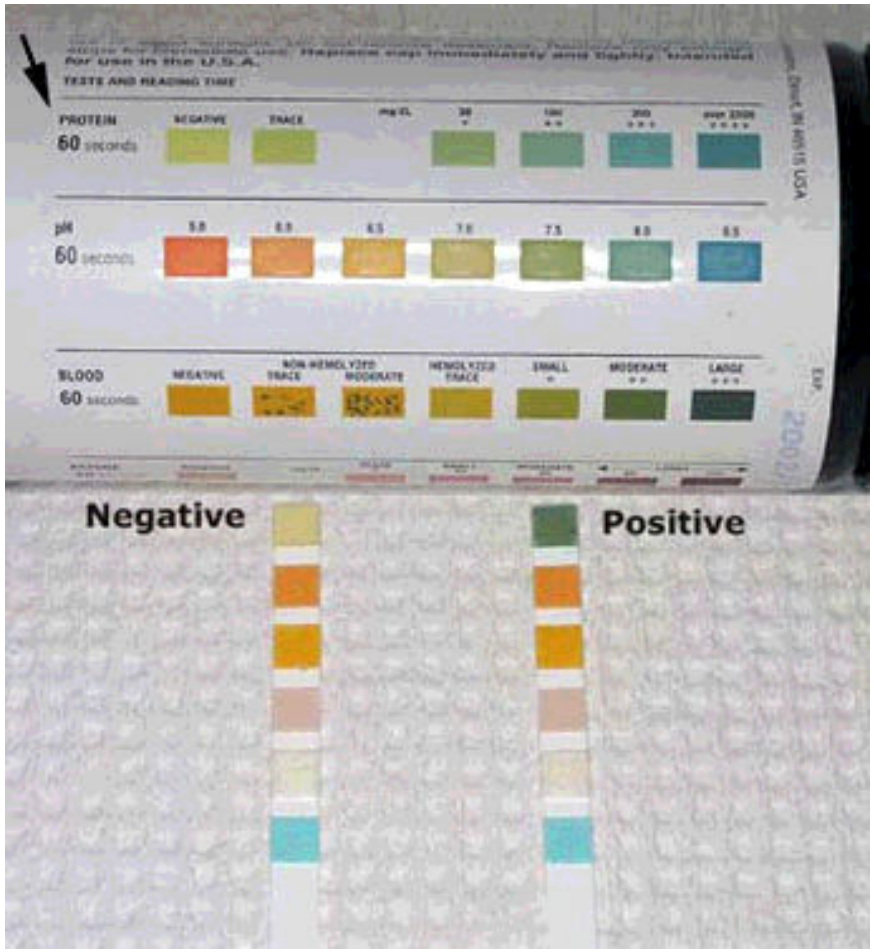
- **heavy proteinuria (>3500 g / 24 h)**
- **hypoalbuminemia**
- **edema**
- **hyperlipidemia**
- **lipiduria**



Urine biochemistry

Dipstick strip tests

pH
Glucose
Protein
Blood
Bilirubin
Urobilinogen
Ketones
Nitrite
Leukocytes



Urine sediment

Addis:	**RBC < 2 mil.**	**WBC < 4 mil.**	**casts < 100 000**	**/ 24 h**
Hamburger:	**RBC < 2000**	**WBC < 4000**	**casts < 60 - 70**	**/ min.**

Phase-contrast RBC microscopy

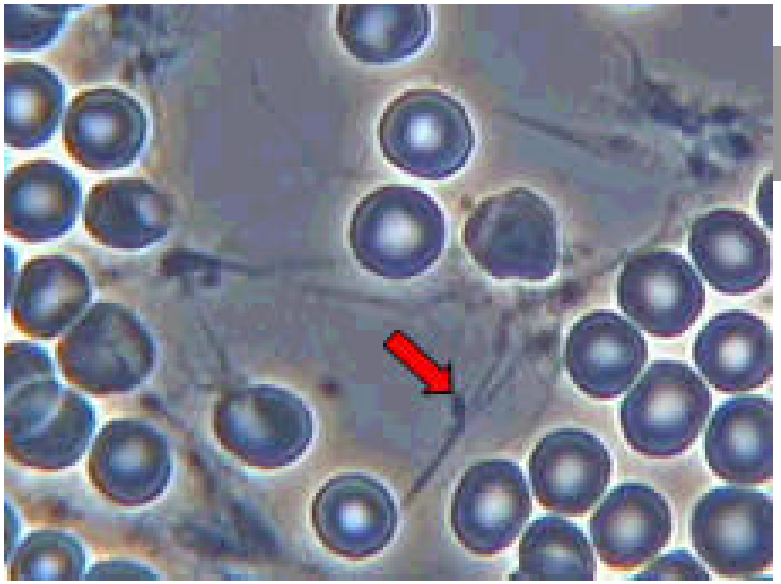
... to determine an origin of RBC

RBC from glomeruli ... deformation

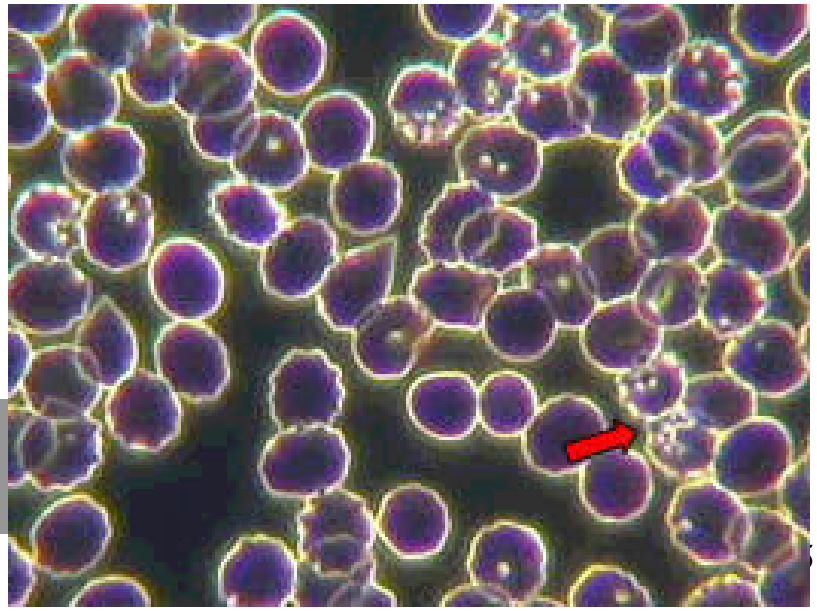
RBC from urinary trct ... intact, smooth cells

Urine sediment

Phase-contrast RBC microscopy

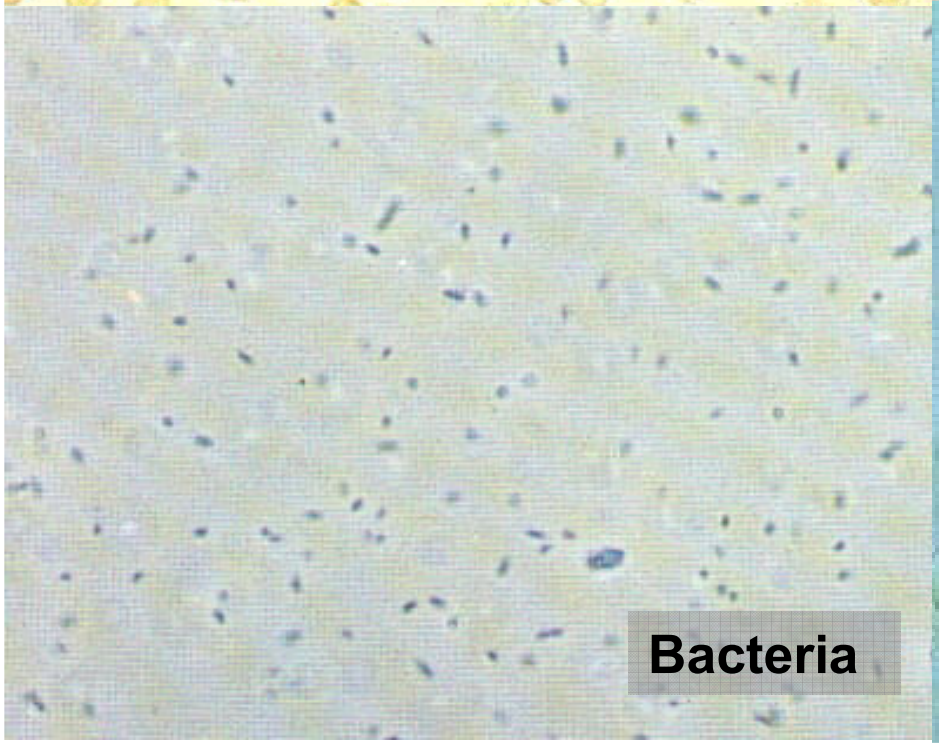


Intact RBC
(extraglomerular origin)

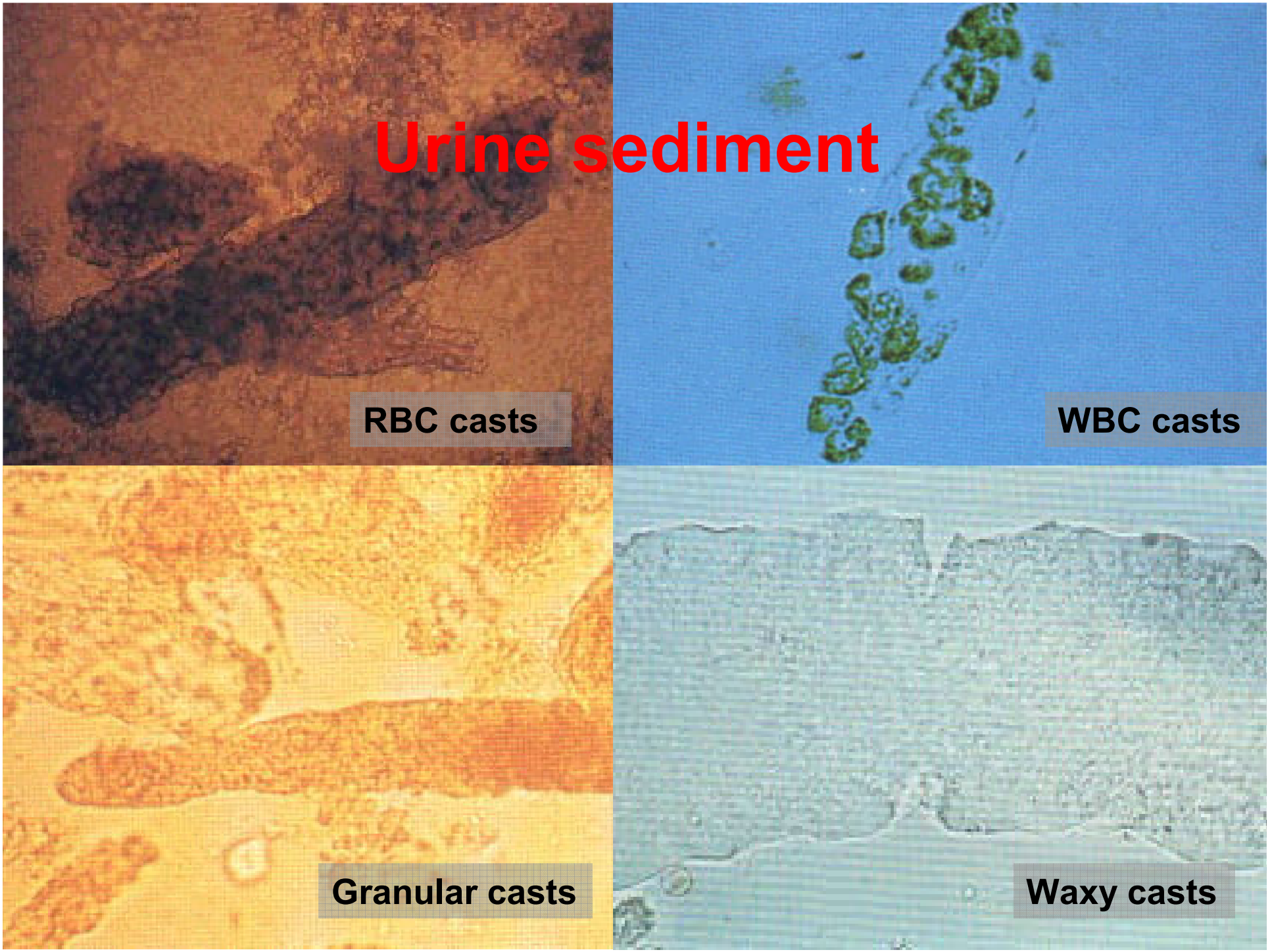


Marginal deformation
(RBC from glomeruli)

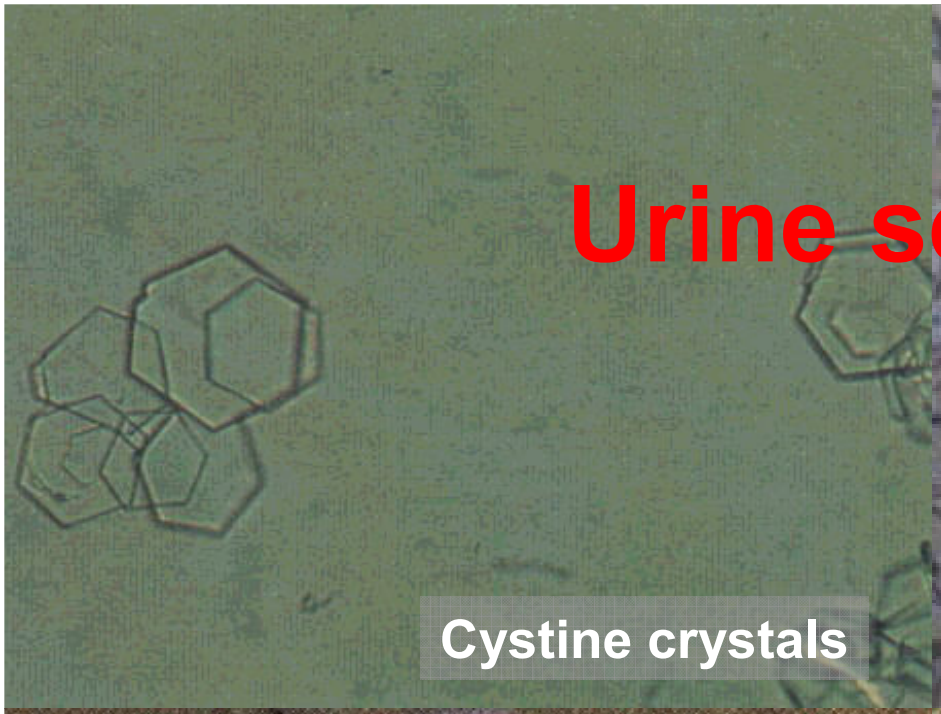
Urine sediment



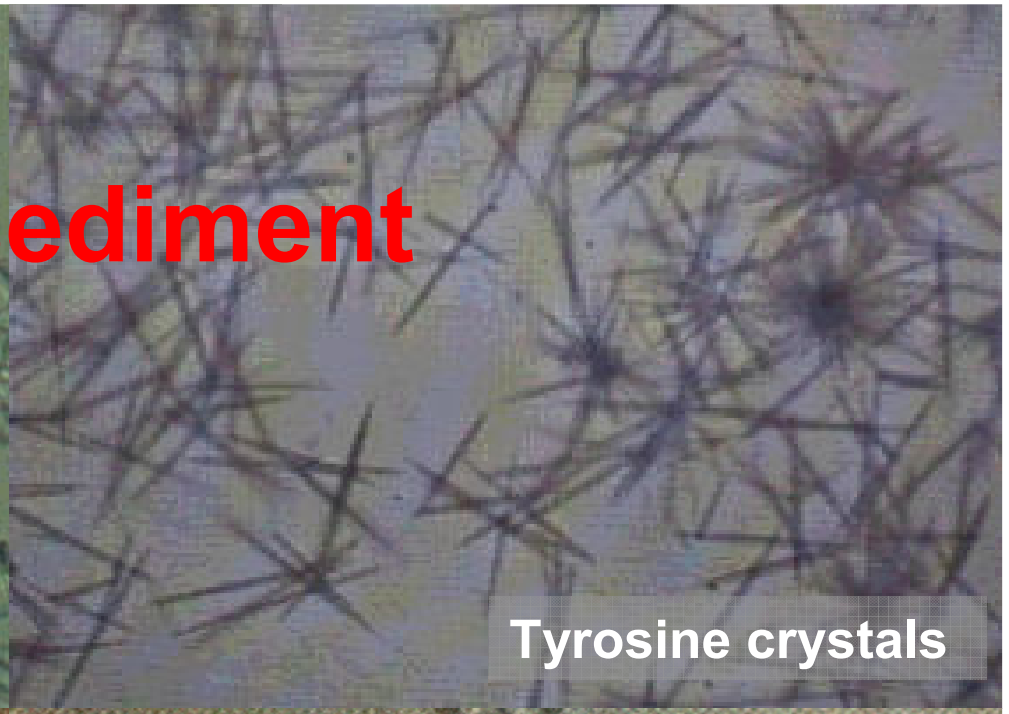
Urine sediment



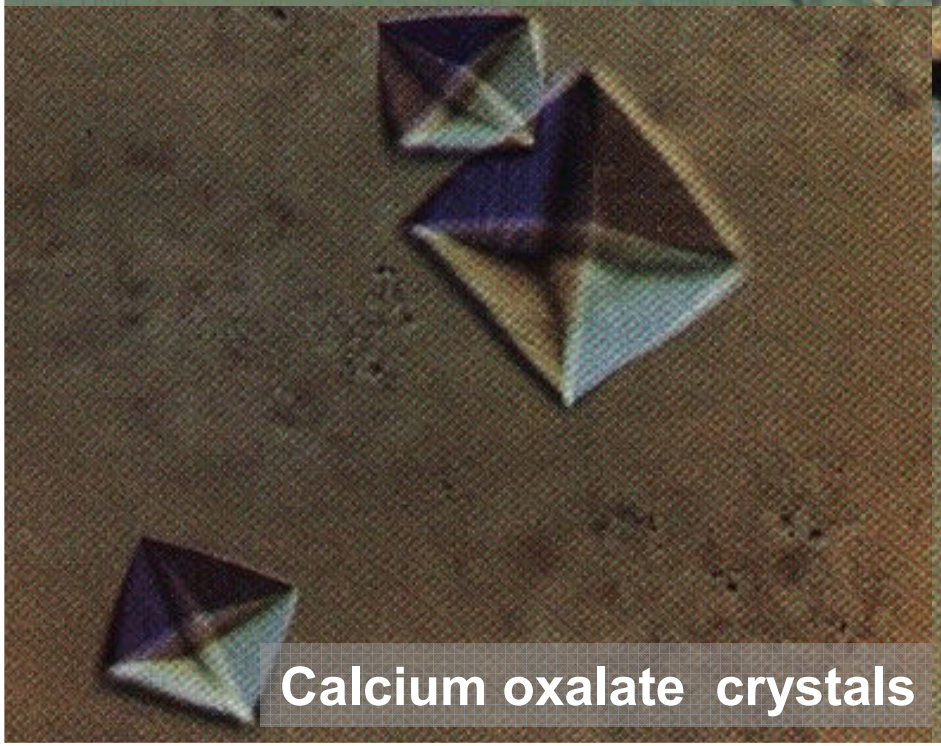
Urine sediment



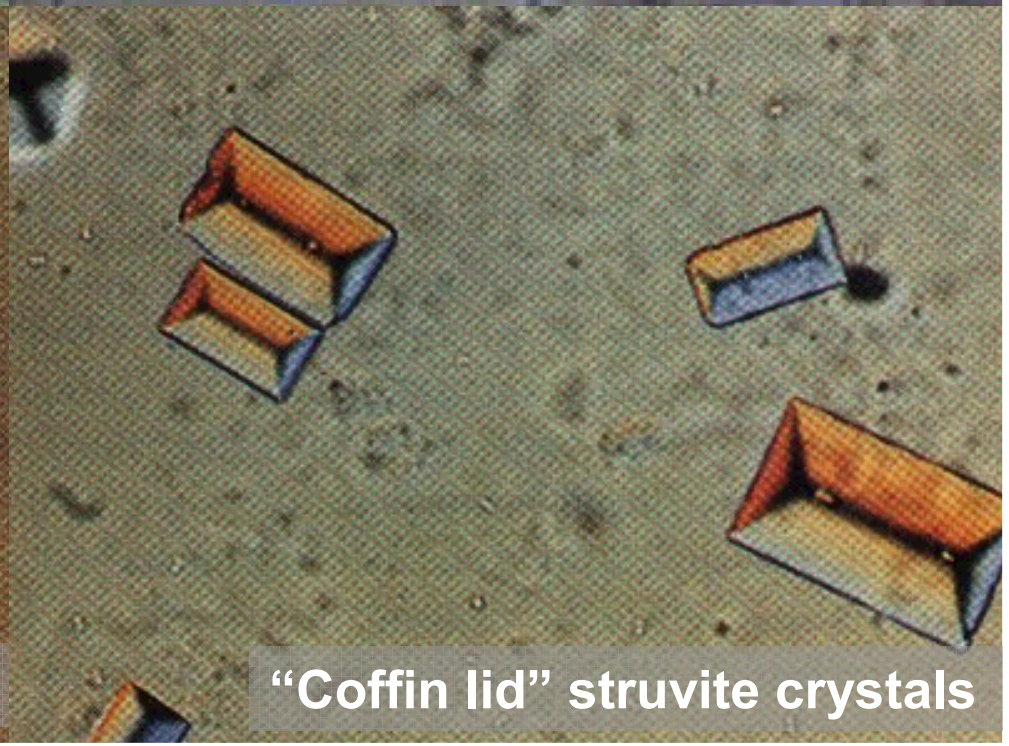
Cystine crystals



Tyrosine crystals



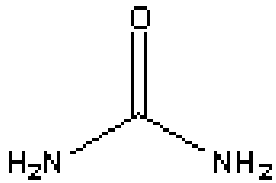
Calcium oxalate crystals



“Coffin lid” struvite crystals

Serum biochemistry

Urea



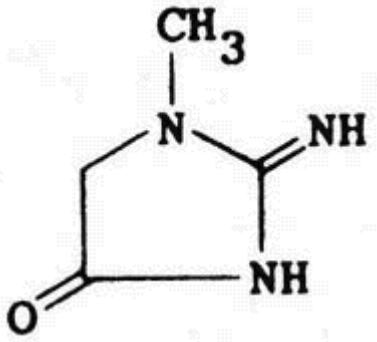
= A breakdown product of proteocatabolism
Serum urea depends upon both protein turnover and kidney function

Normal values: < 7,5 mmol / l

↑ ... ↓ glomerular filtration rate (orient. parameter)
dehydration
↑ proteocatabolism

Serum biochemistry

Creatinine



= A breakdown product of creatine, which is an important part of muscle

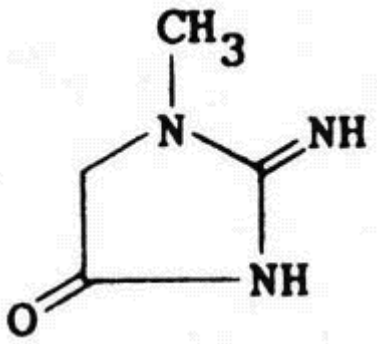
Orientation parameter of GF

Normal values:

- male < 124 umol / l
- female < 115 umol / l (because of less muscle mass)

Serum biochemistry

Creatinine



Creatinine x urea:
- **Stabile 24-h concentration**
- **Independent on protein income**
- **Independent on physical activity**

Pathology:

↑ ... ↓ glomerular filtration rate
muscular dystrophy, rhabdomyolysis

↓ ... muscular dystrophy (late stage), myasthenia gravis

Functional tests

Creatinine clearance

= GFR; Glomerular filtration rate

GFR = ($C_u \times V°_u$) / C_p [(mg/ml)×(ml/min)/(mg/ml)= ml/min].
= (U-creatinine x U-volume) / P-creatinine
= cca 2 ml / s (120 ml / min.)

Normal values:

- **male: 97 - 137 ml / min.**
- **female: 88 - 128 ml / min.**

Functional tests

Creatinine clearance

Test compares the level of creatinine in urine with the creatinine level in the blood, usually based on measurements of

- **24-h urine sample and**
- **blood sample drawn at the end of the 24-h period**

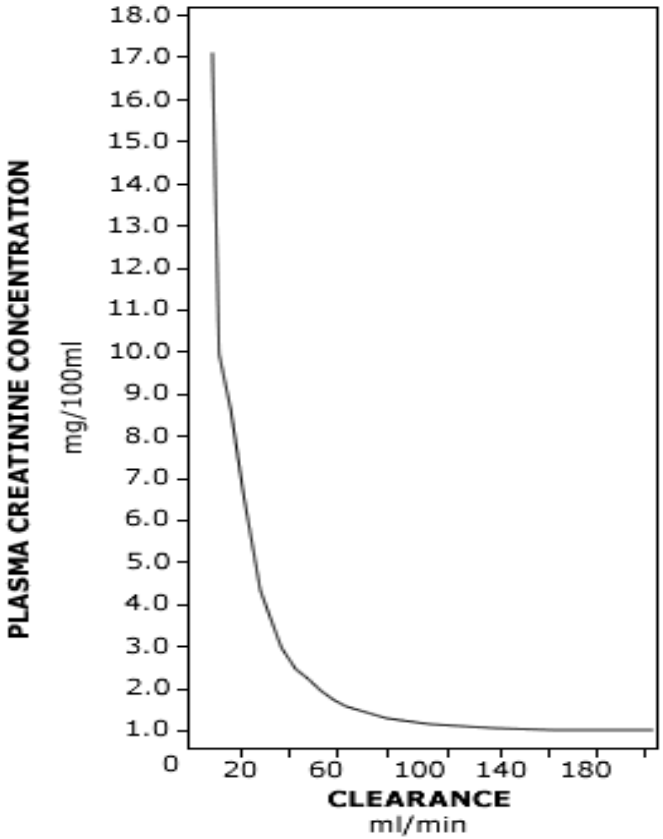
Functional tests

Creatinine clearance

Pathology:

↓ ... nephron damage
acute hemodynamic changes

↑ ... ↓ oncotic pressure
↑ glomerular membrane permeability
(incip. DM nephropathy)

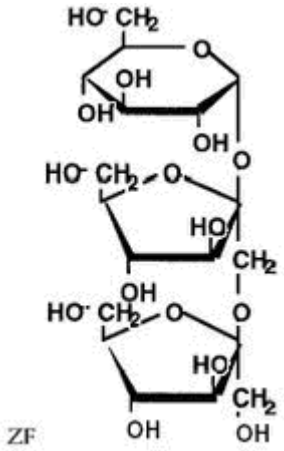


Functional tests

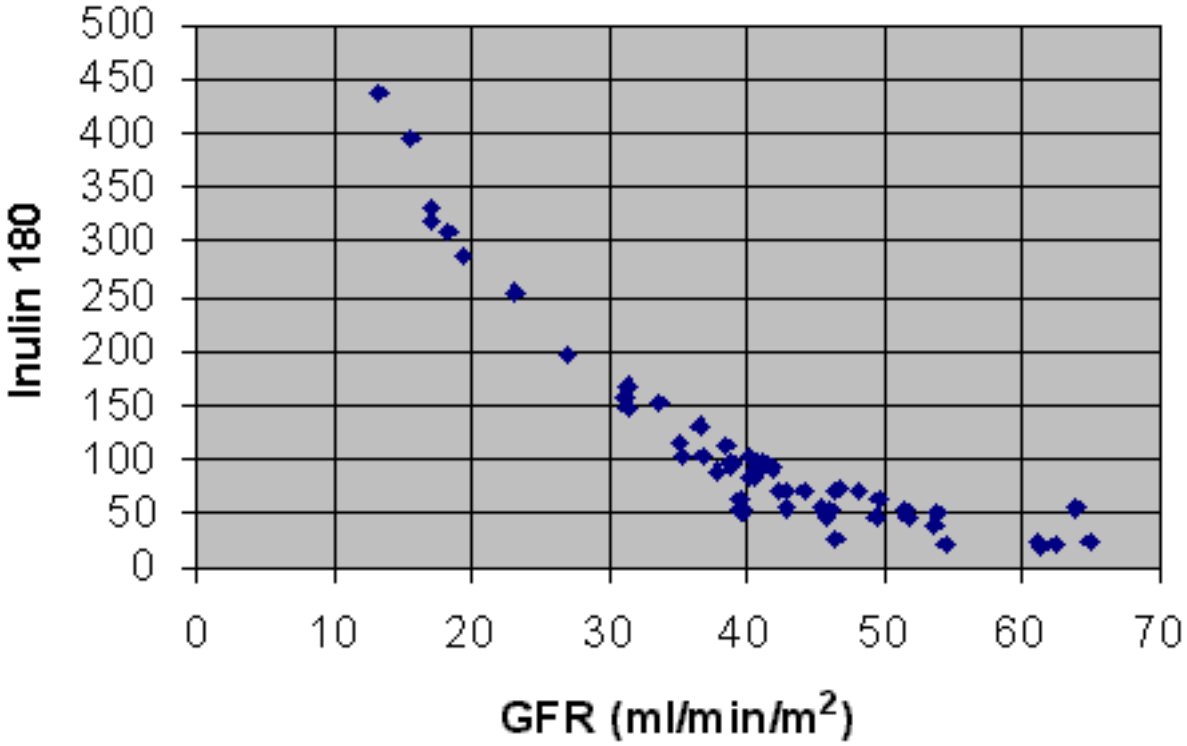
Inulin clearance

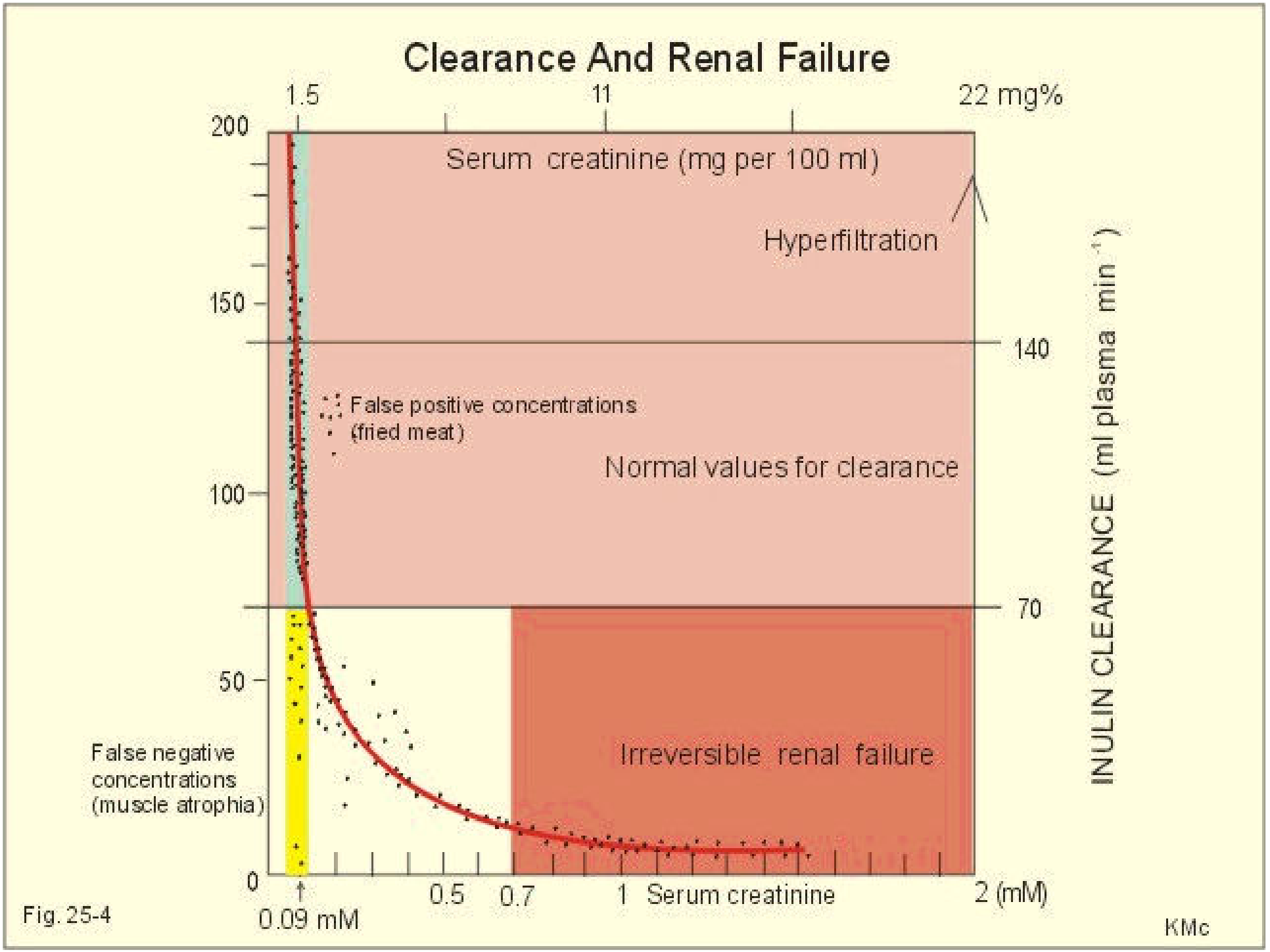
= The flux of inulin filtered through the glomerular barrier per min

= GFR × C_p/0.94



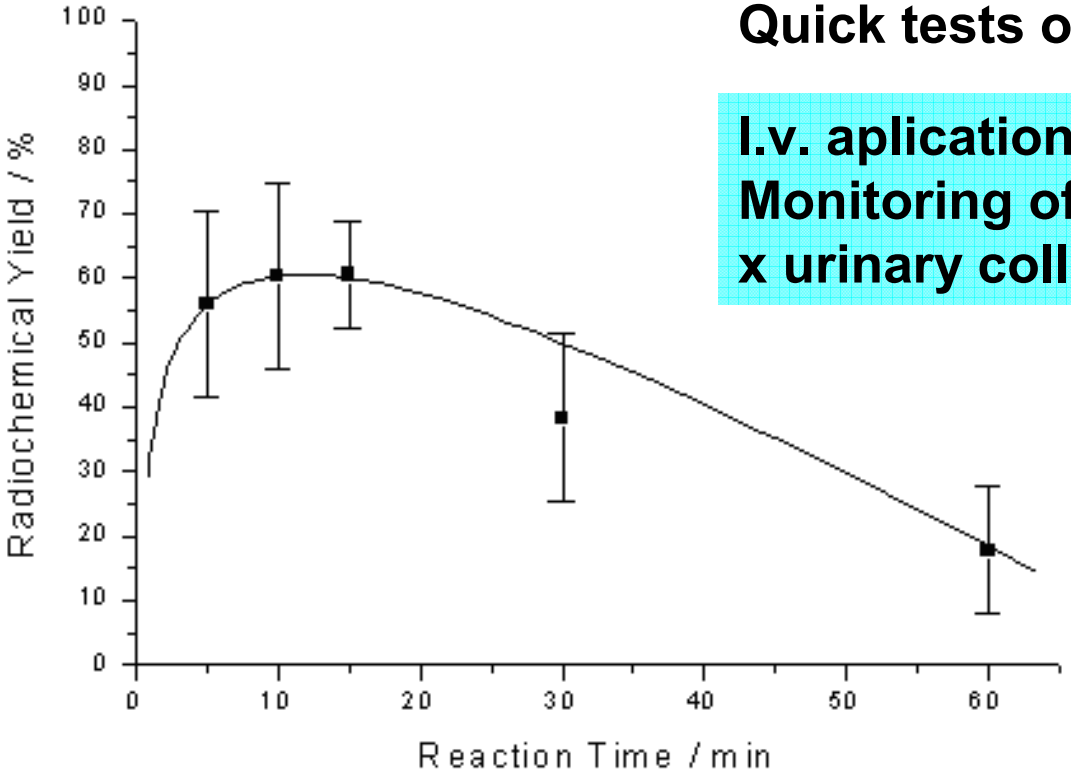
Fructan molecule of the inulin




Clearance And Renal Failure
1.5
11
22 mg%
200
150
100
50
0
Serum creatinine (mg per 100 ml)
Hyperfiltration
140
70
False positive concentrations
(fried meat)
Normal values for clearance
Irreversible renal failure
False negative
concentrations
(muscle atrophia)
0.09 mM
0.5
0.7
1 Serum creatinine
2 (mM)
INULIN CLEARANCE (ml plasma min-1)
Fig. 25-4
KMc

Functional tests

^{51}Cr - EDTA clearance
^{99m}Tc - DTPA clearance



Quick tests on glomerular filtration rate

I.v. aplication of isotope,
Monitoring of decreased plasma activity,
x urinary collection.

Functional tests

Concentration test

Stimulatory test on ADH production / kidney function
Test measures the ability of the kidneys to conserve or excrete water appropriately.

Changes - diabetes insipidus = inability of the kidneys to conserve water, which leads to frequent urination and pronounced thirst.

- **central (hypothalamic) = a lack of ADH**
- **peripheral (nephrogenic) = a defect of the kidneys**

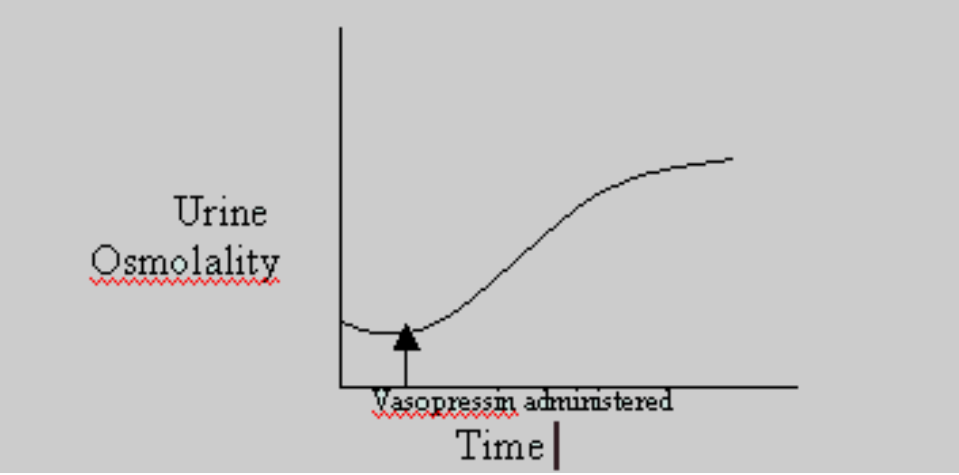
Functional tests

Concentration test

Test variants:

The specific gravity of urine is measured

- **before and after water loading (urine should become dilute),**
- **water deprivation (urine should become concentrated),**
- **water deprivation and administration of ADH**



Functional tests

Acidification test

Urine pH = 5-6
Changes:

- **infection**
- **congenital / acquired abnormalities ... RTA**

NH_4Cl overload (0,1 g/kg p.o.) ... urine collection á 1 h intervals
normally: ↓ U-pH < 5,4
CI: metabolic acidosis, liver failure, GI dis.

↑ U-pH + metabolic acidosis = susp. renal acidification dis.

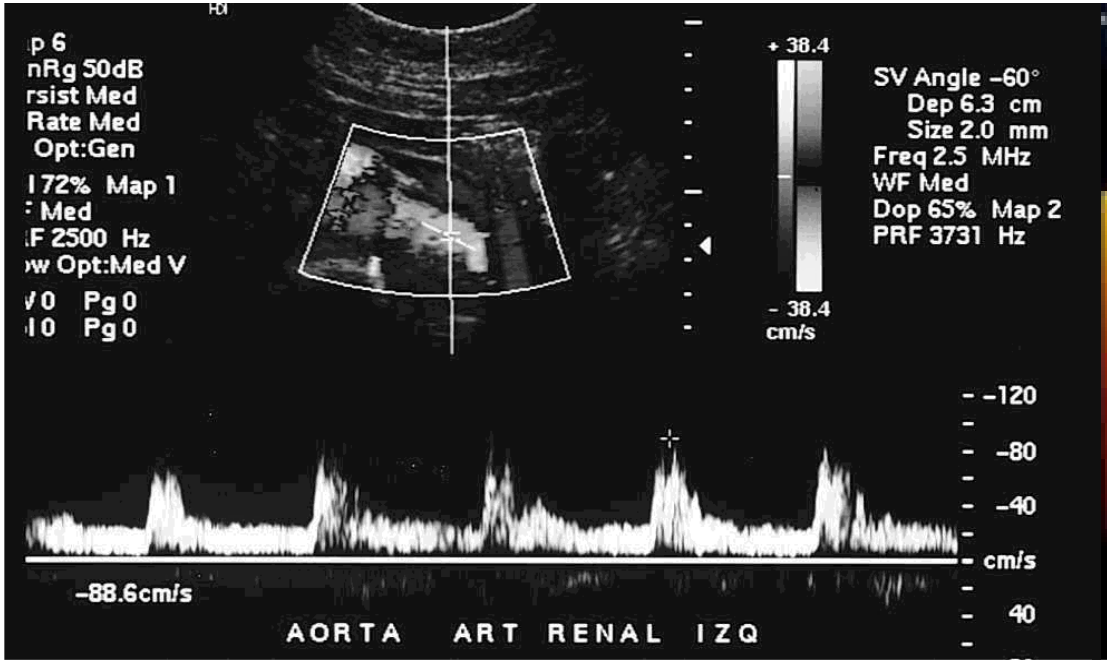
Imaging procedures

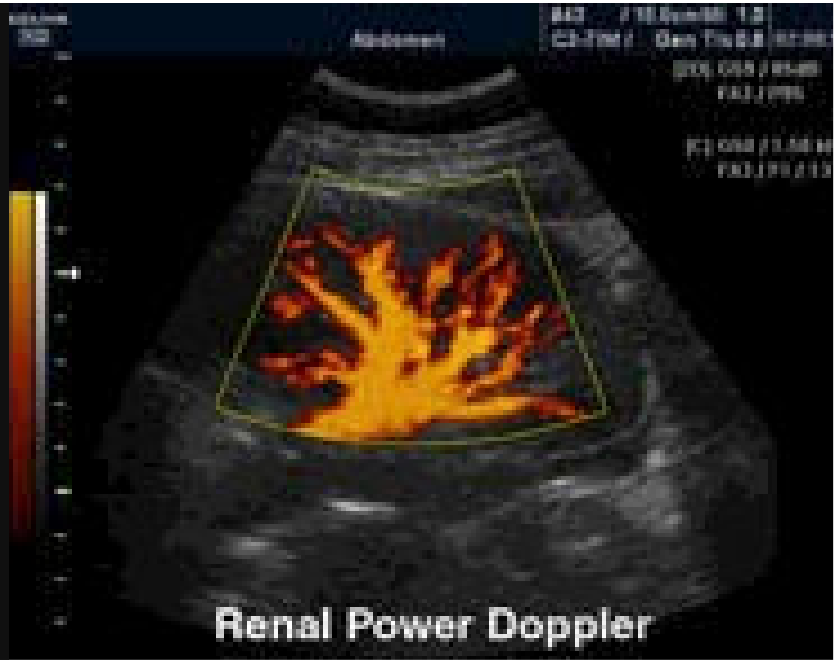
1. Ultrasonography

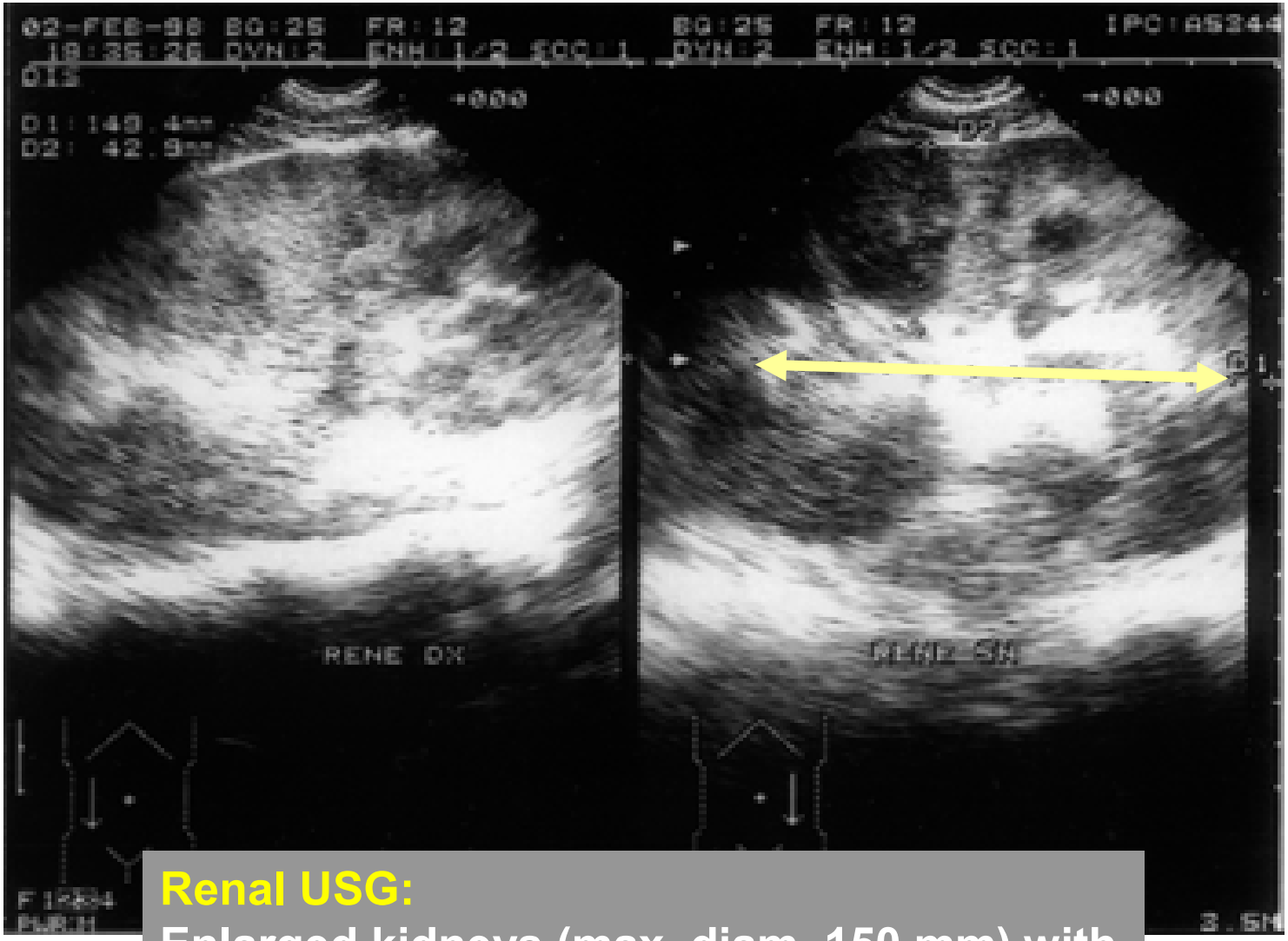
Basic graphic examination

2D USG: Size, shape, localization, symmetry, tumors, lymphonodi...)

Doppler / Color Doppler: aa. renalis (stenosis)







Renal USG:
Enlarged kidneys (max. diam. 150 mm) with no evidence of urinary obstruction

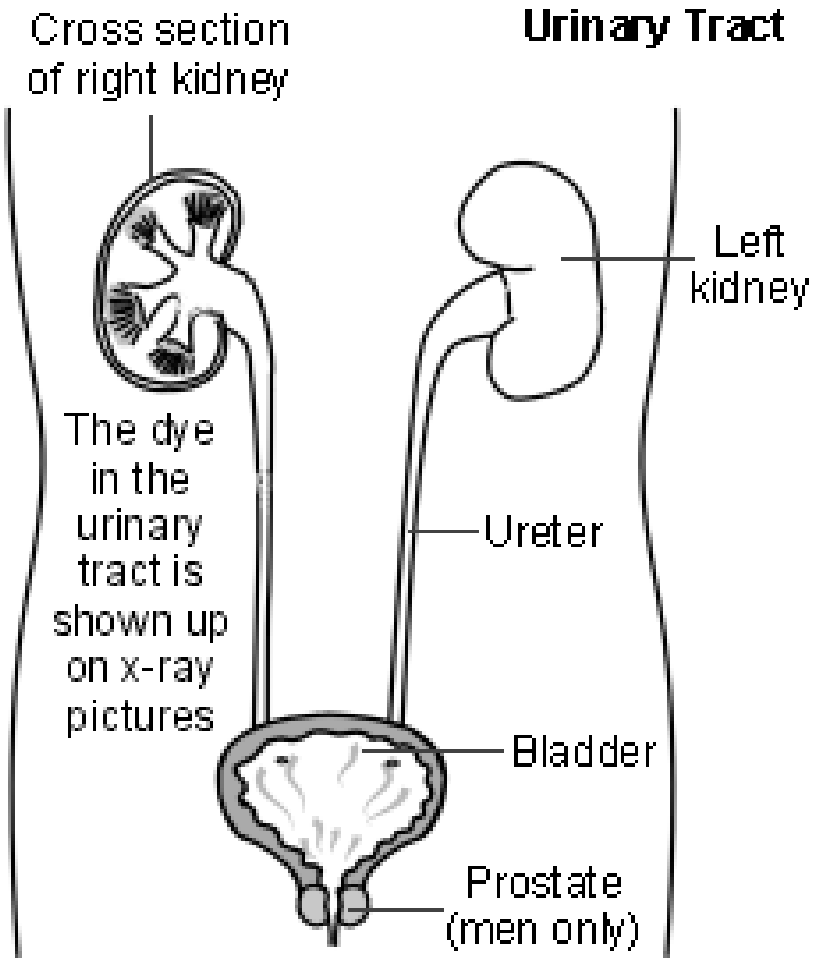
Imaging procedures

2. X-ray examination

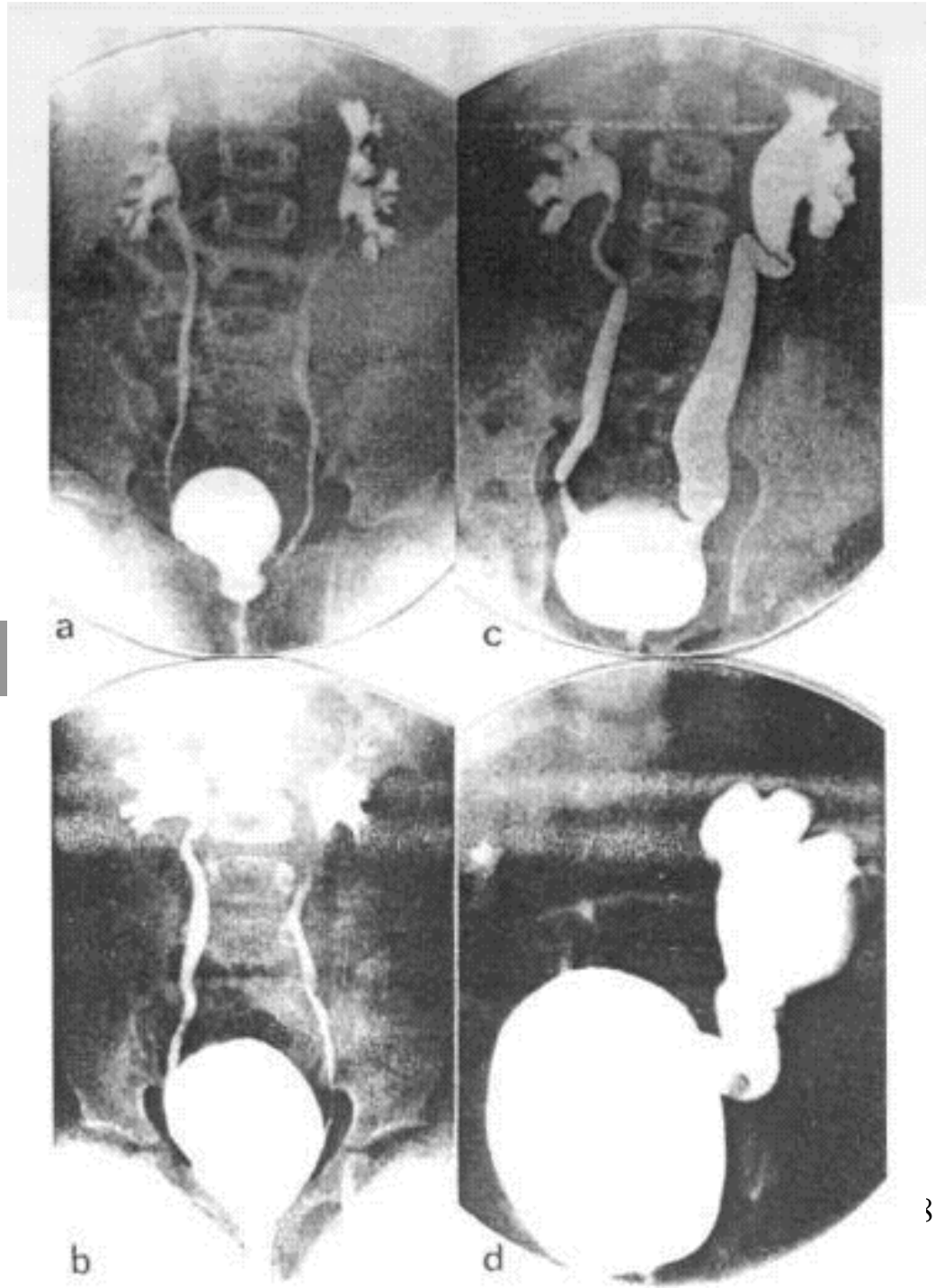
I.v. urography (IVU)
(Ascendant) pyelography
/ cystouretherography

Indications

- **Kidney stones**
- **Infections**
- **Hematuria**
- **Obstruction**



Cystouretherography



Imaging procedures

3. Computed tomography (CT)

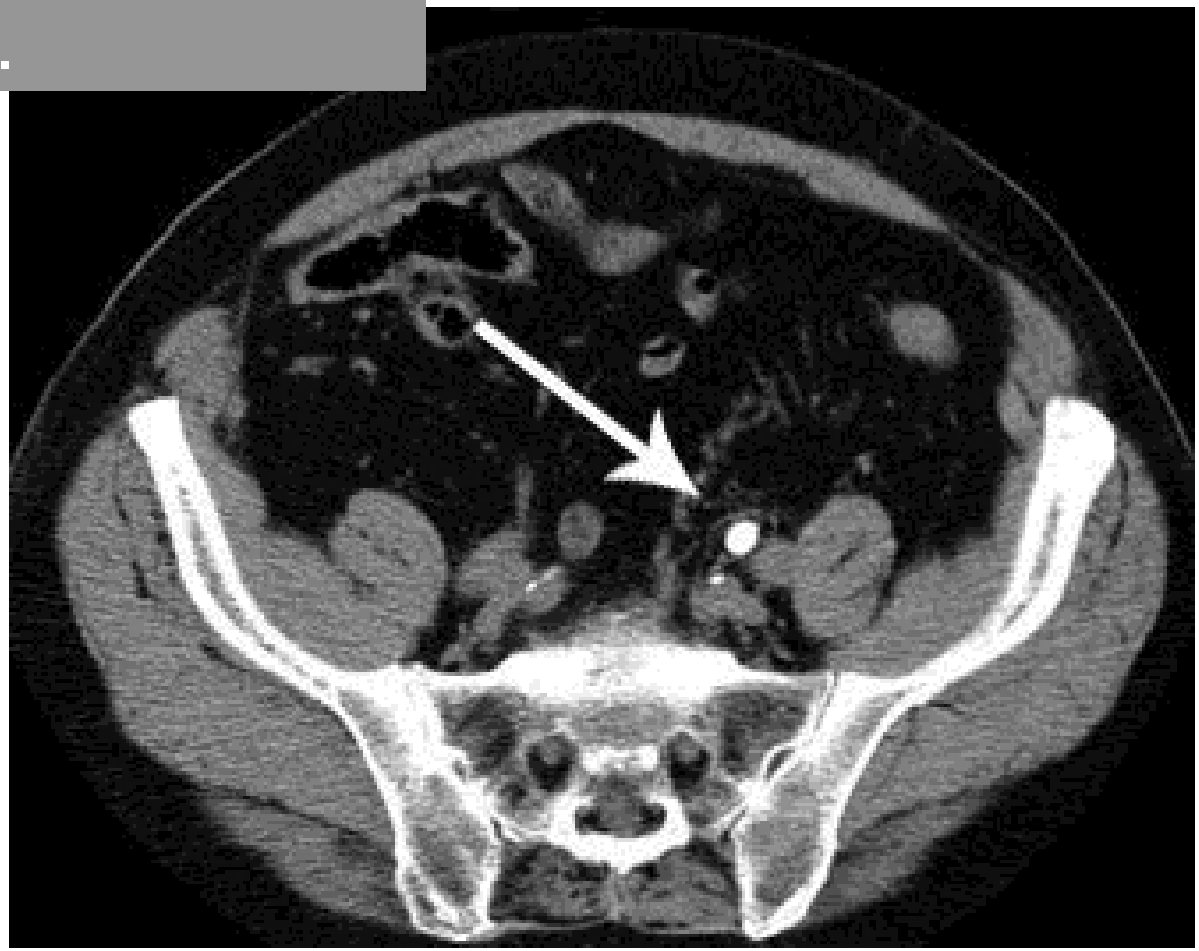
4. Nuclear Magnetic Resonance (MRI)

MRI: The same effectiveness as CT in cancer staging

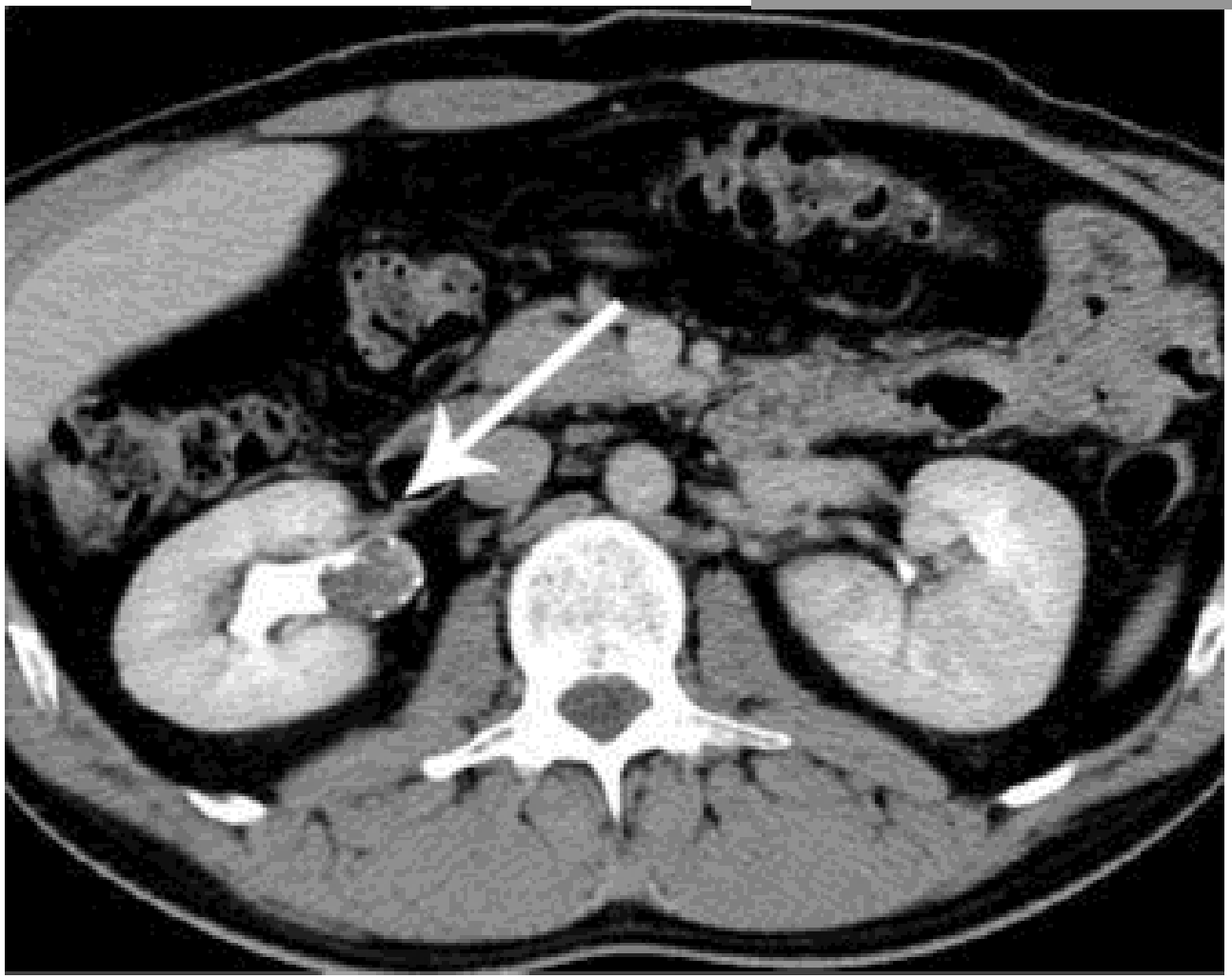
CT renal protocols:

1. **Stone protocol** ... Non-contrast CT imaging from kidney to bladder
2. **Hematuria Protocol** (CT Uurography) ... non-contrast followed by contrast CT imaging from kidney to bladder
3. **Renal Mass Protocol** ... non-contrast followed by contrast CT imaging of kidneys only.

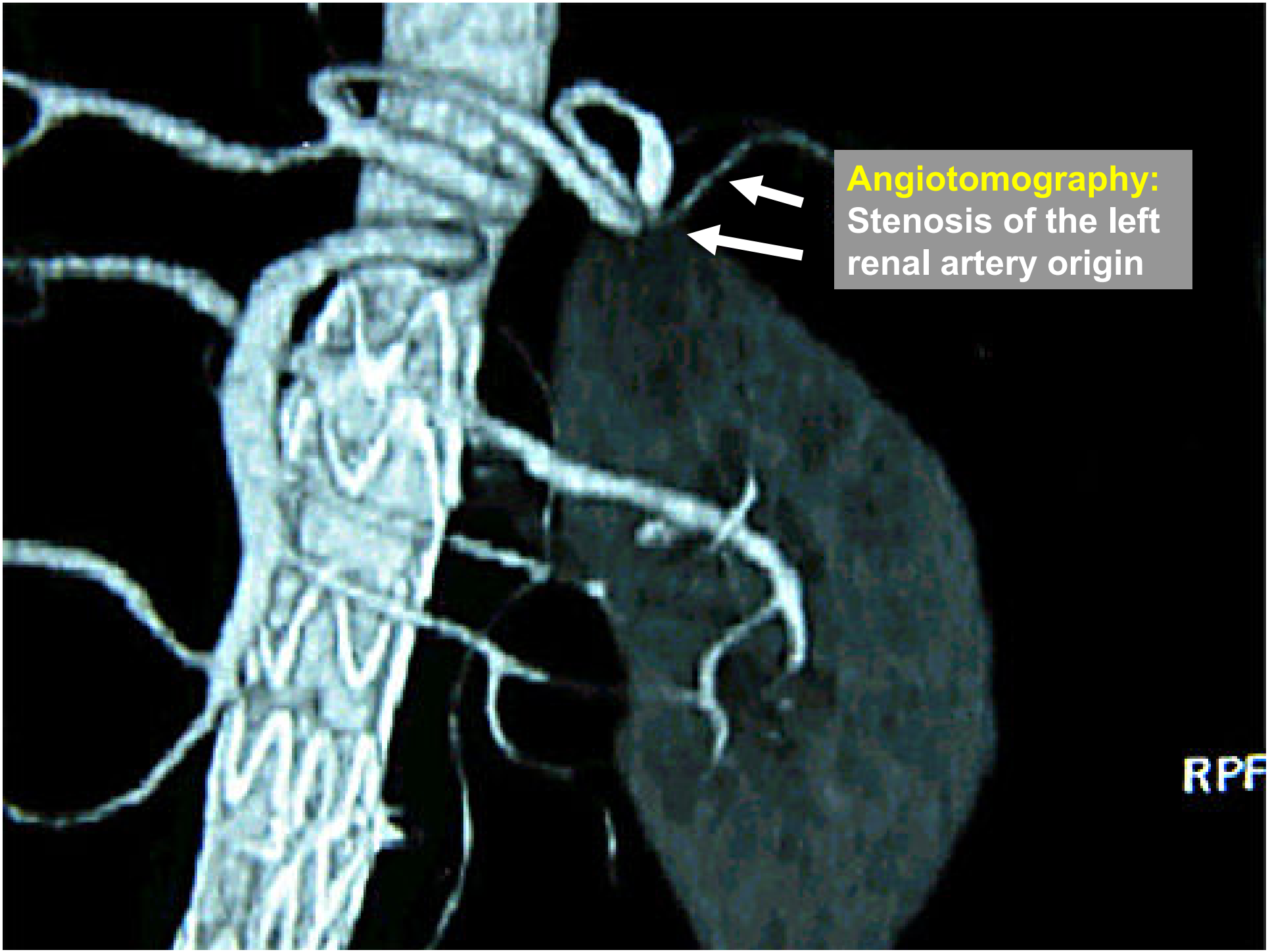
Non-contrast CT examination:
(Stone protocol)
Left ureteral stone.

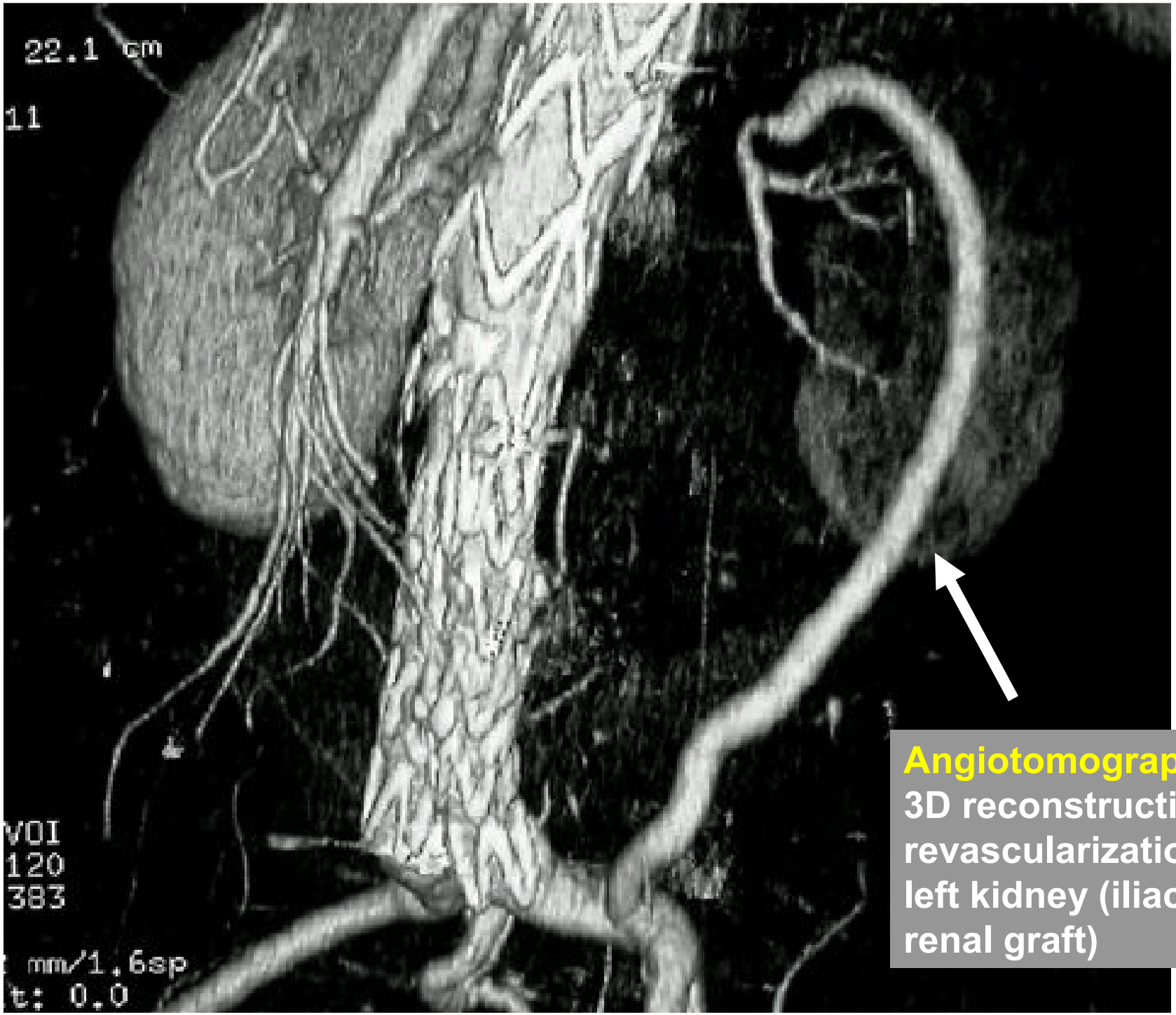


CT examination:
(Renal Mass Protocol)
A filling defect in the right renal pelvis = a large urothelial tumor



CT i.v. urography:
The reduction in the left kidney size and a. renalis without contrast imaging


Angiotomography:
Stenosis of the left
renal artery origin
RPF



Angiotomography:
3D reconstruction with revascularization of the left kidney (iliac and renal graft)

Imaging procedures

5. Scintigraphy (isotope nephrography)

^{99m}Tc - DTPA (diethylentriaminpentaacetate)

Indications

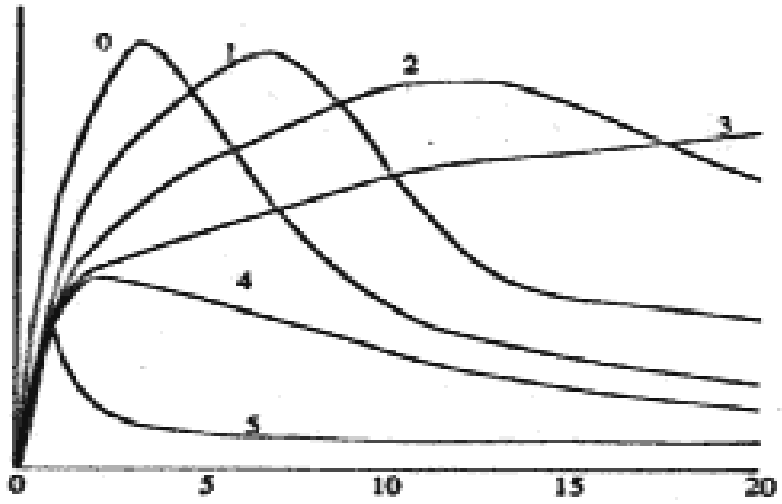
- **TIN (pyelonephritis)**
- **Determine relative (differential) renal function in the left and right kidneys**
- **Acute renal failure**
- **Multicystic dysplastic kidneys**
- **Trauma**
- **Renal ectopia**
- **Infarction**
- **Hypertension**
- **Horseshoe kidney**

Information relating to renal vascularity, renal function and excretion.

Imaging procedures

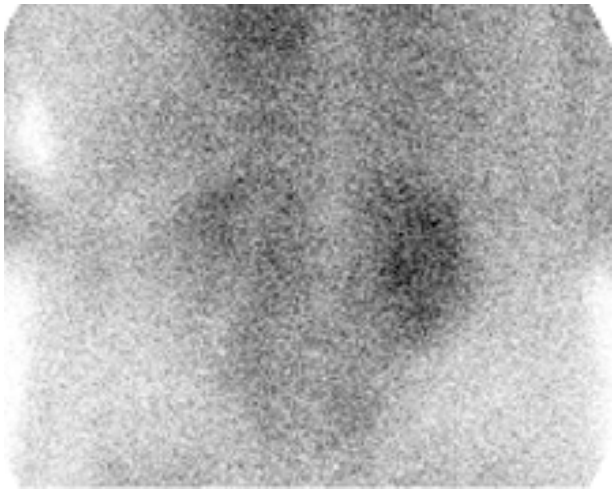
5. Scintigraphy (isotope nephrography)

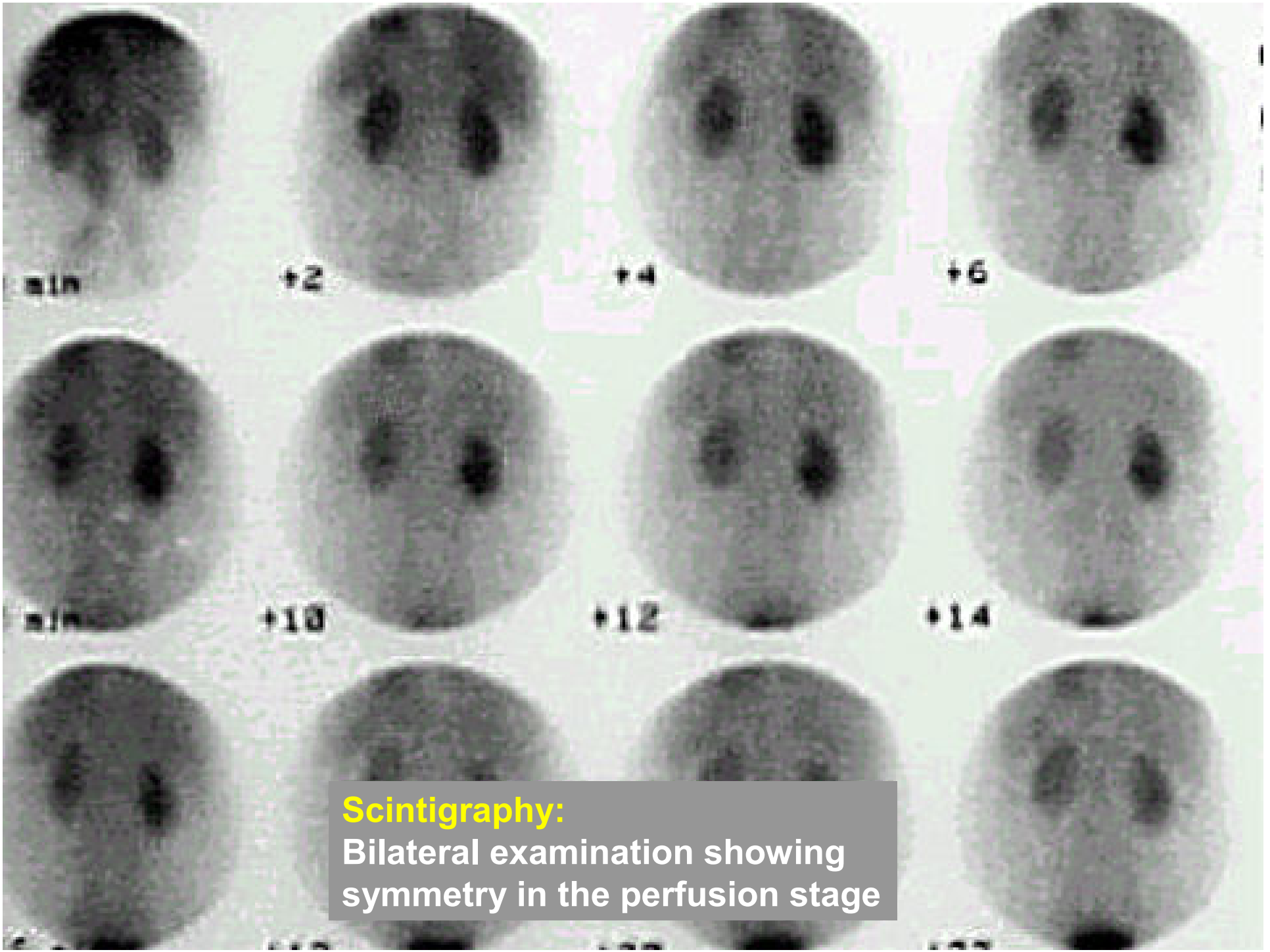
^{99m}Tc - DTPA (diethylentriaminpentaacetate)



0 ... normal curve of activity
5 ... renal failure without accumulation

assymetric ^{99m}Tc DTPA accumulation in acute renal failure



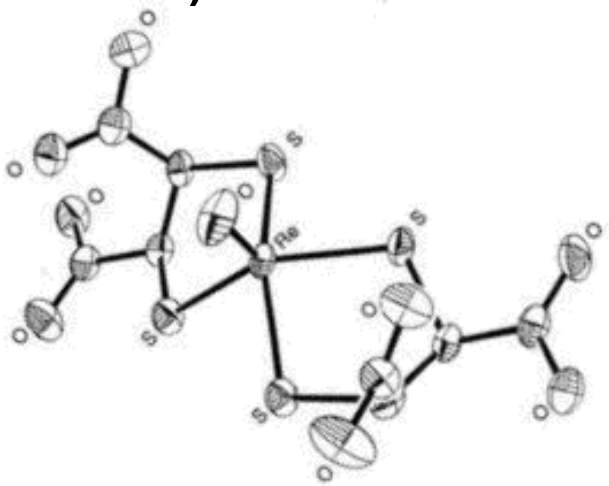


Scintigraphy:
Bilateral examination showing symmetry in the perfusion stage

Imaging procedures

5. Scintigraphy (isotope nephrography)

^{99m}Tc - DMSA (*meso*-2,3-dimercaptosuccinic acid)



Indications

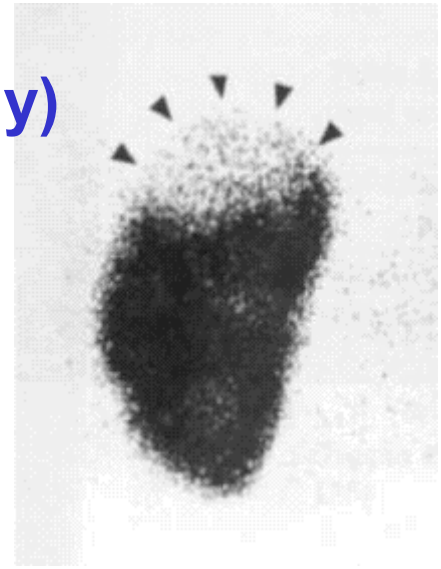
- Recent TIN (pyelonephritis)
- Assess relative function of each kidney
- Check for renal scarring
- Evaluation of congenital abnormalities

Uptake in functional renal parenchyma

Imaging procedures

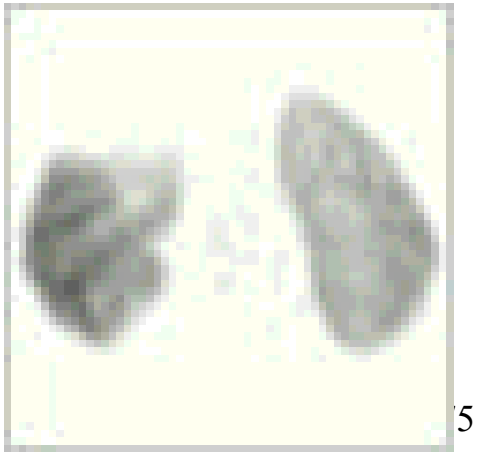
5. Scintigraphy (isotope nephrography)

^{99m}Tc - DMSA



DMSA application:

1. i.v. application of ^{99m}Tc - DMSA
2. Imaging after 3 - 4 h aprox. 30-60 min.
   This delay allows the kidneys to absorb the DMSA.

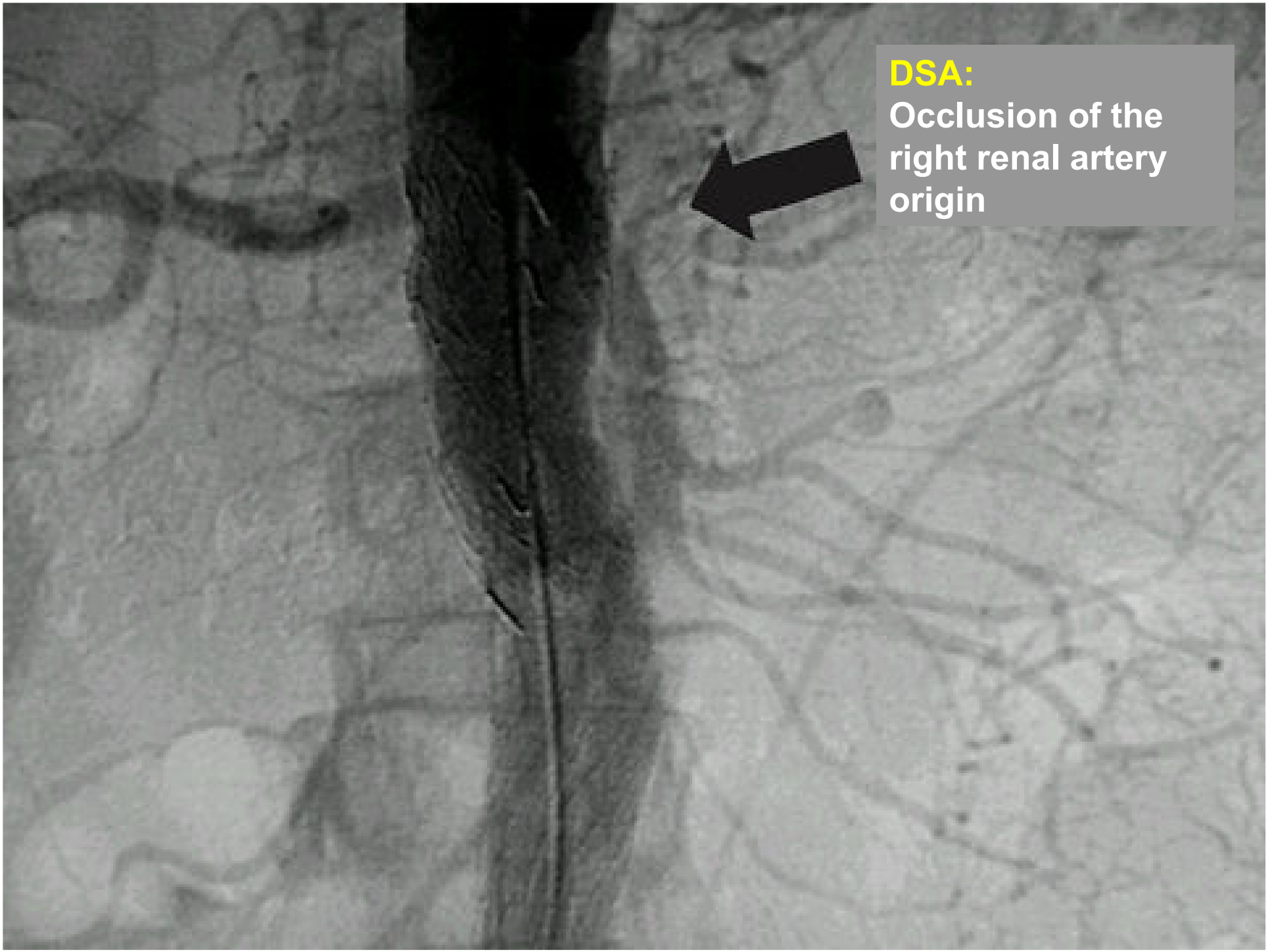


Imaging procedures

6. Angiography / DSA (Digital subtraction angiography)

Injection of radiopaque material into abdominal aorta / aa. renalis.

Dg.: stenosis / oclusion of a. renalis
susp. renovascular hypertension
tumor vascularisation


DSA:
Occlusion of the right renal artery origin

Microbiology

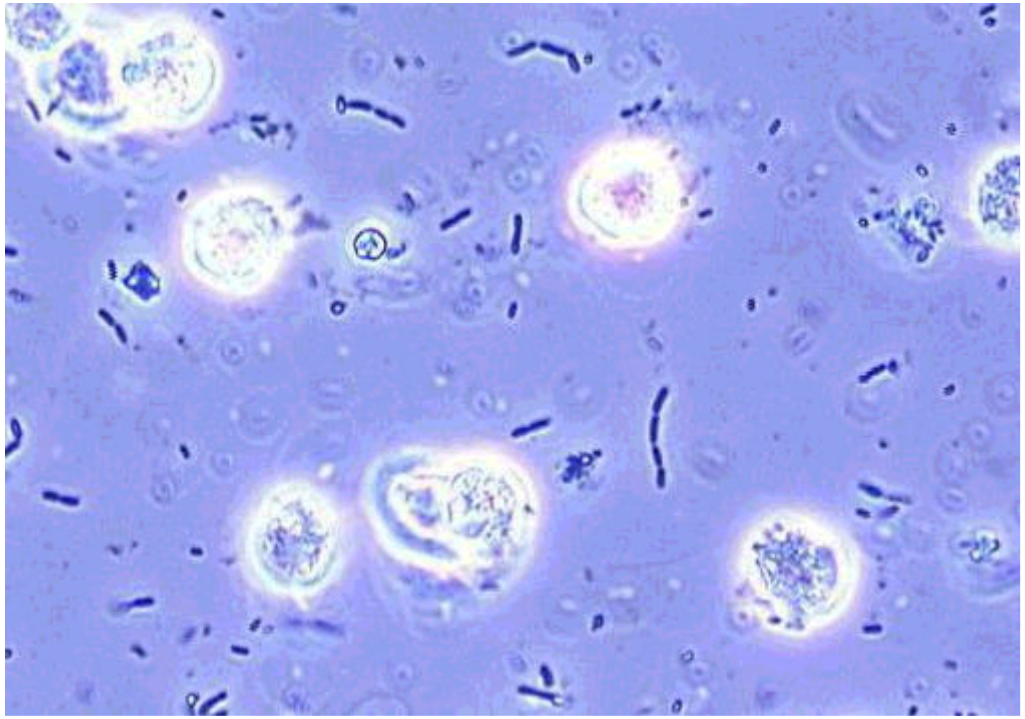
Bacteriology examination

Urine culture (aerobic, anaerobic)

Microscopy

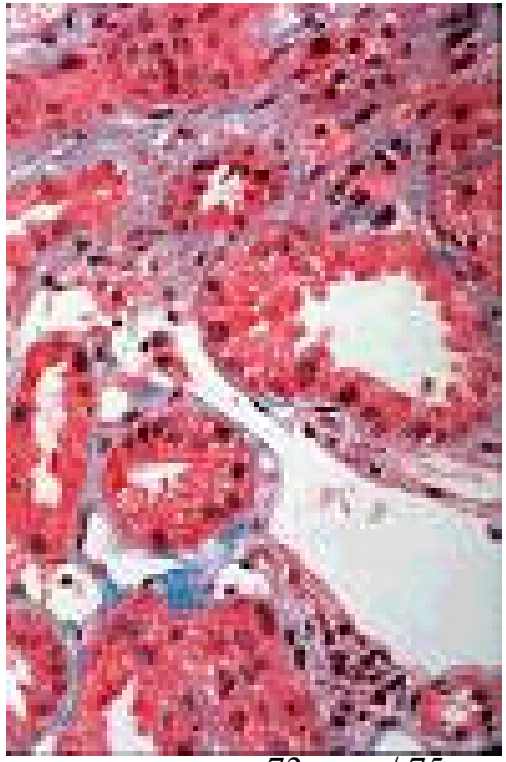
Molecular tests (PCR)

Elements in urinary sediment



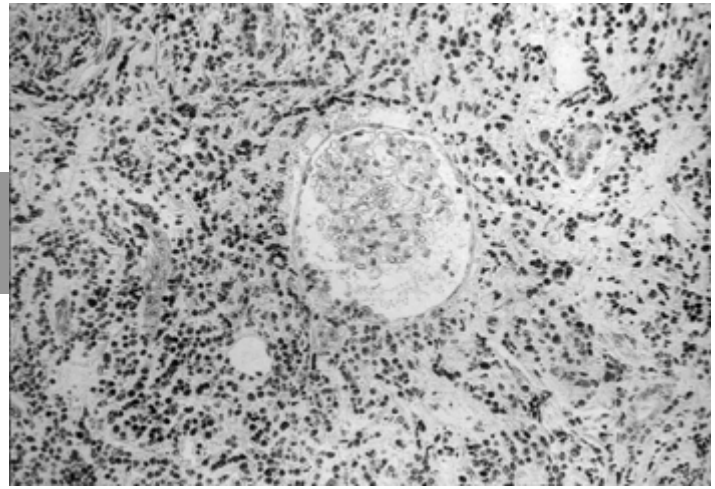
Biopsy

Percutaneous renal biopsy

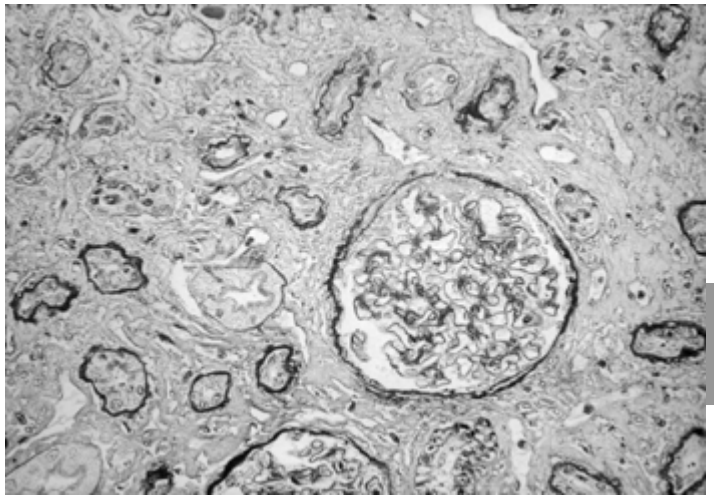


Biopsy

Percutaneous renal biopsy

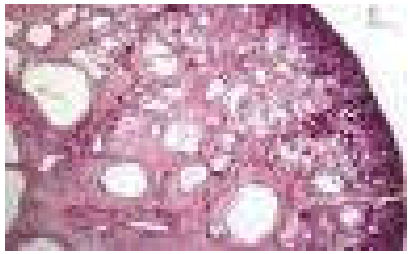


Massive infiltration of parenchymal mononuclear cells



Diffuse interstitial fibrosis and tubular atrophy

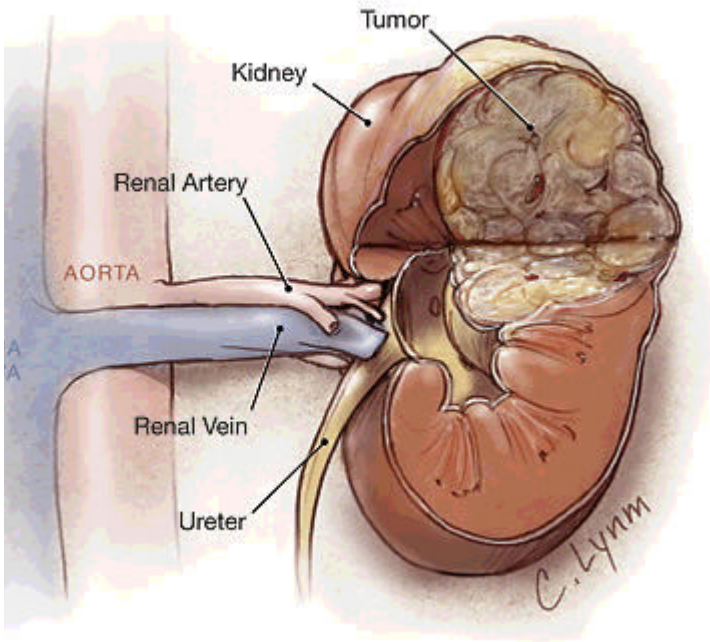
Genetics



Polycystic kidney disease

- AR, AD

Hereditery risk factors of kidney cancer



- Hippel-Lindau (VHL) syndrome
- Tuberous sclerosis
- Birt-Hogg-Dube syndrome
- Hereditary non-VHL clear cell renal cell cancer
- Hereditary papillary renal cell cancer