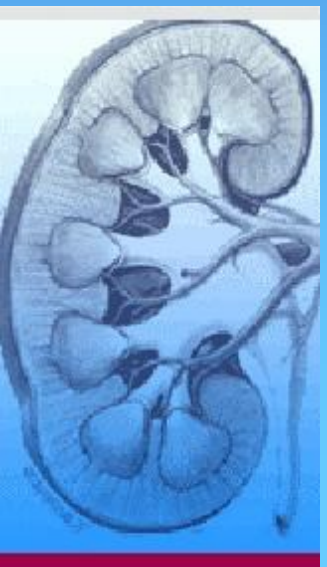
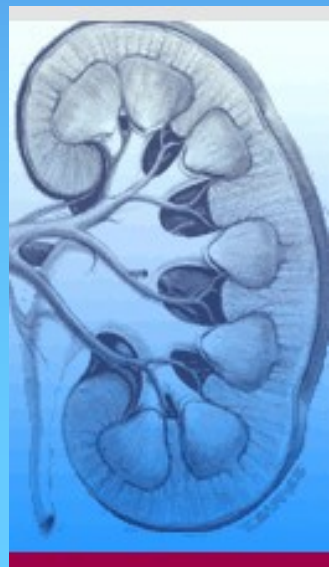
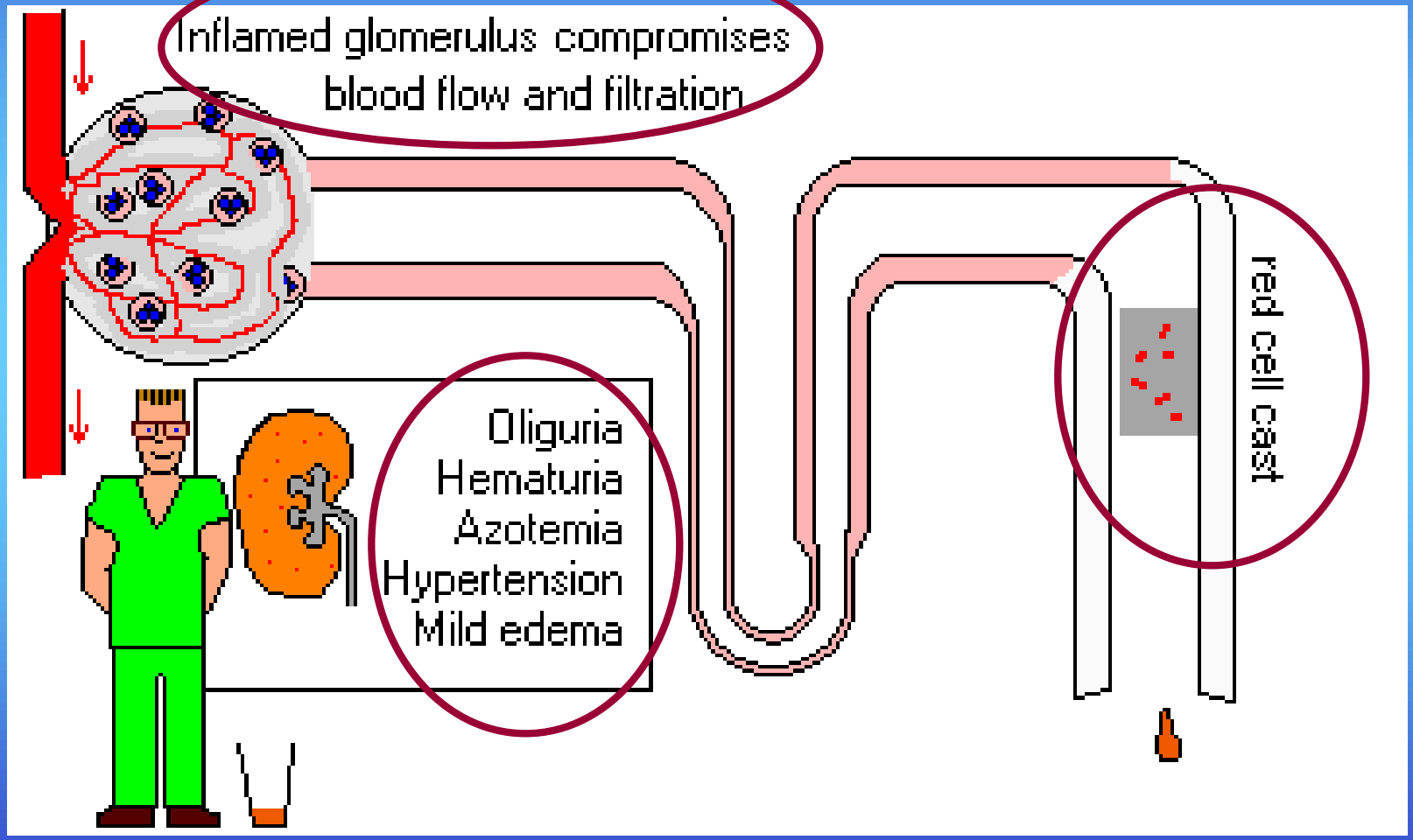
PATHOPHYSIOLOGY OF RENAL DISORDERS (III)

Dr. Pavel Maruna





Nephritic syndrome



Nephritic syndrome

Glomerulonephritis

Pathological changes in glomeruli caused by immune processes.

Glomerulopathy

Similar clinical image as GN, but inflammation is not clearly expressed.

Glomerulonephritis

Classification

diffuse x focal

acute x rapidly progressive x chronic

immunocomplex x auto-Ab against basal membrane

Glomerulonephritis

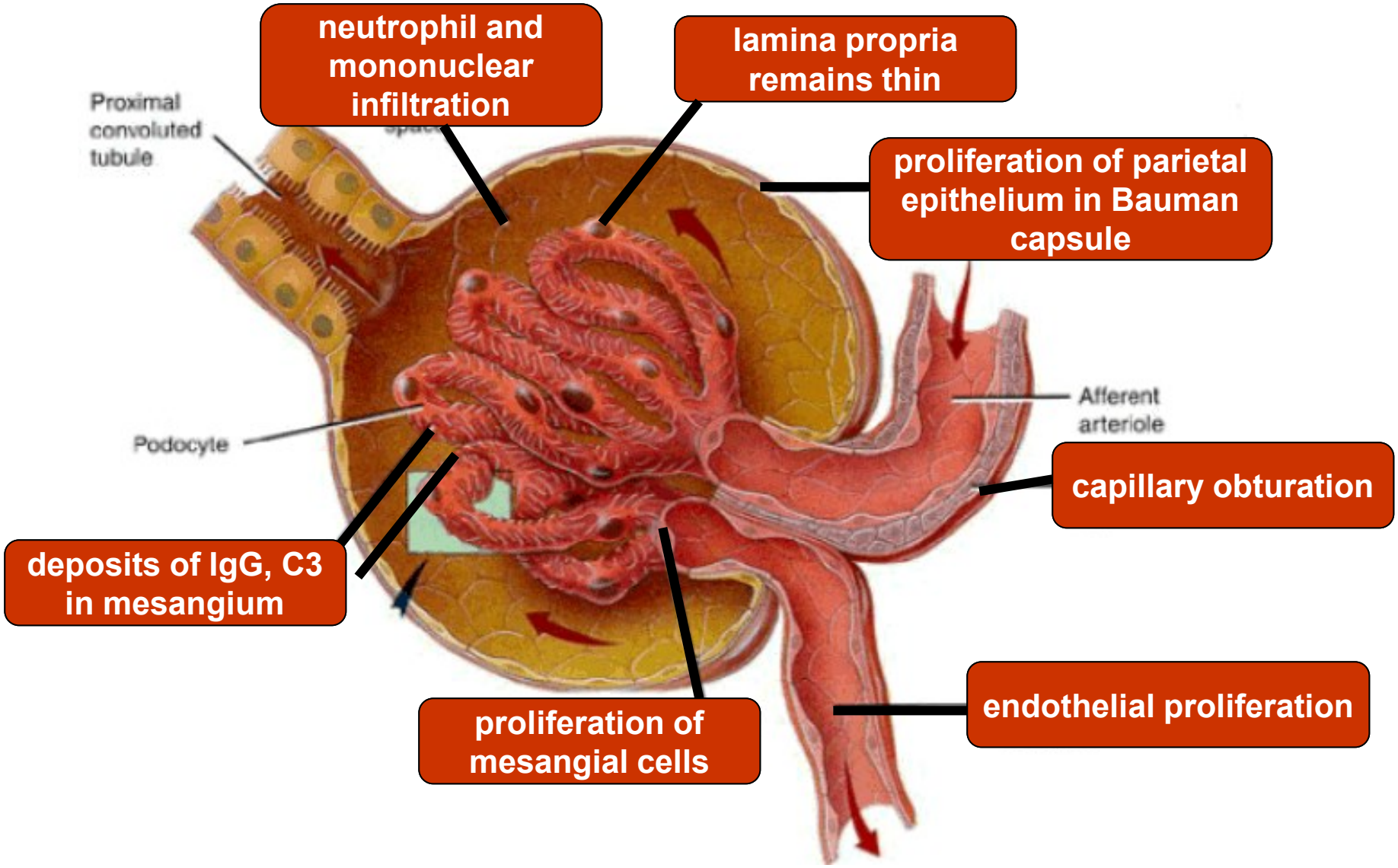
Acute GN

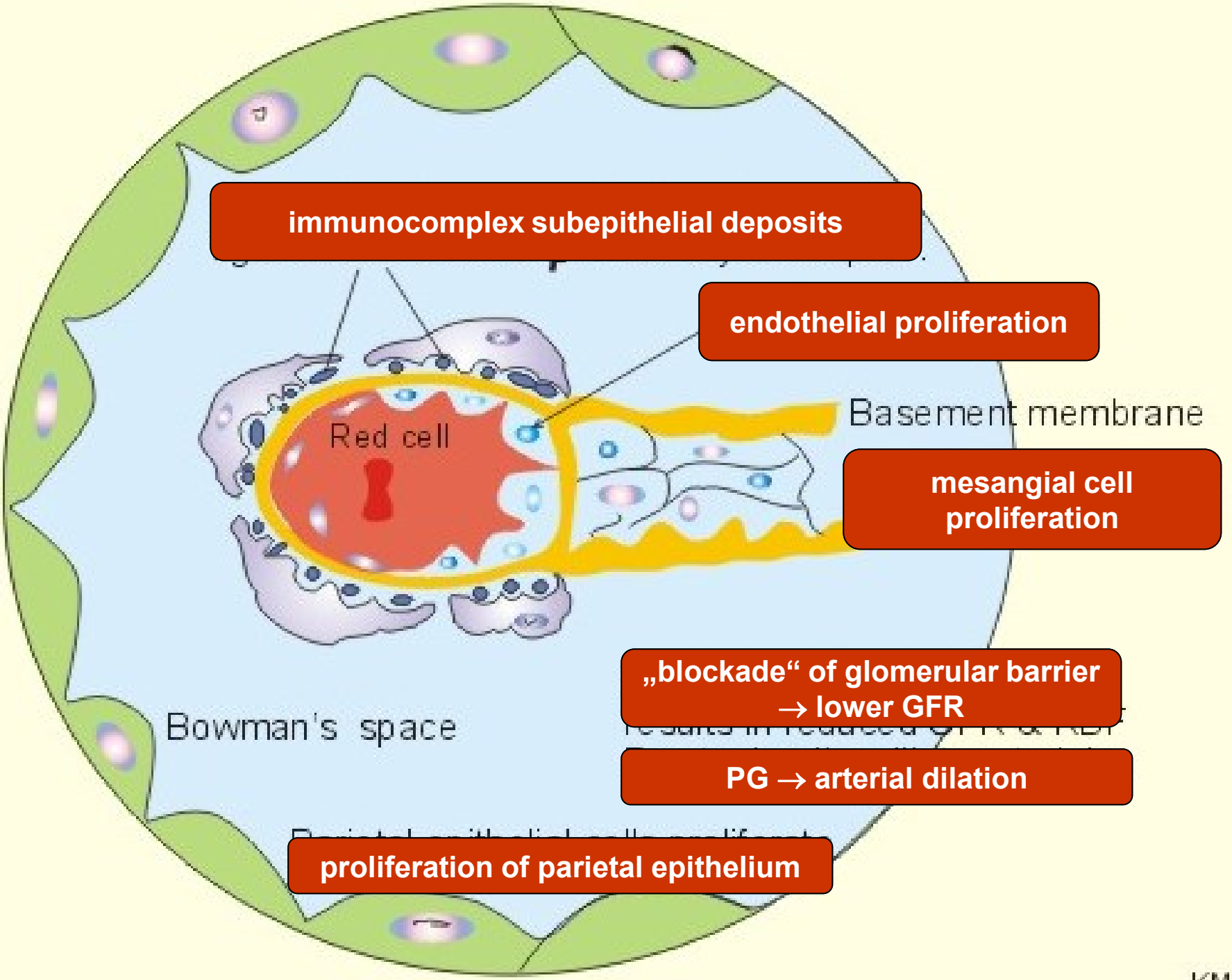
post-streptococcal GN

commonly type 12 of hemolyt. streptococcus, primary infection usually in pharynx

related to other infection

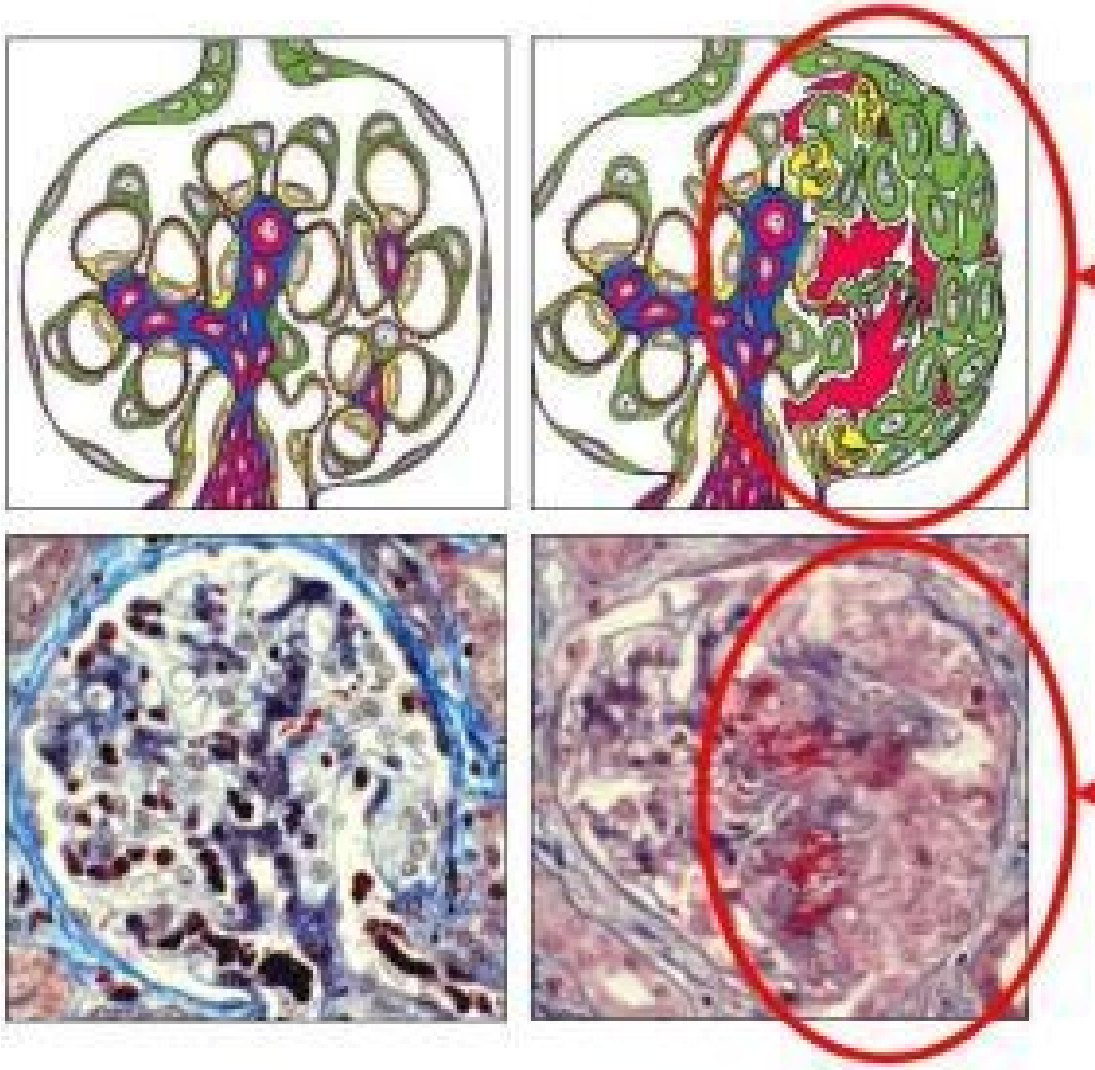
- Str. viridans (bact. endocarditis)
- Str. pneumoniae (pneumonia)
- typhus, syphilis, brucelosis, leptospirosis
- hepatitis, inf. mono, varicella, parotitis
- toxoplasma, malaria


neutrophil and mononuclear infiltration
lamina propria remains thin
Proximal convoluted tubule
proliferation of parietal epithelium in Bauman capsule
Afferent arteriole
Podocyte
capillary obturation
deposits of IgG, C3 in mesangium
endothelial proliferation
proliferation of mesangial cells


immunocomplex subepithelial deposits
endothelial proliferation
Red cell
Basement membrane
mesangial cell proliferation
„blockade“ of glomerular barrier → lower GFR
Bowman's space
PG → arterial dilation
proliferation of parietal epithelium

Normal glomerulus

ANCA-positive GN

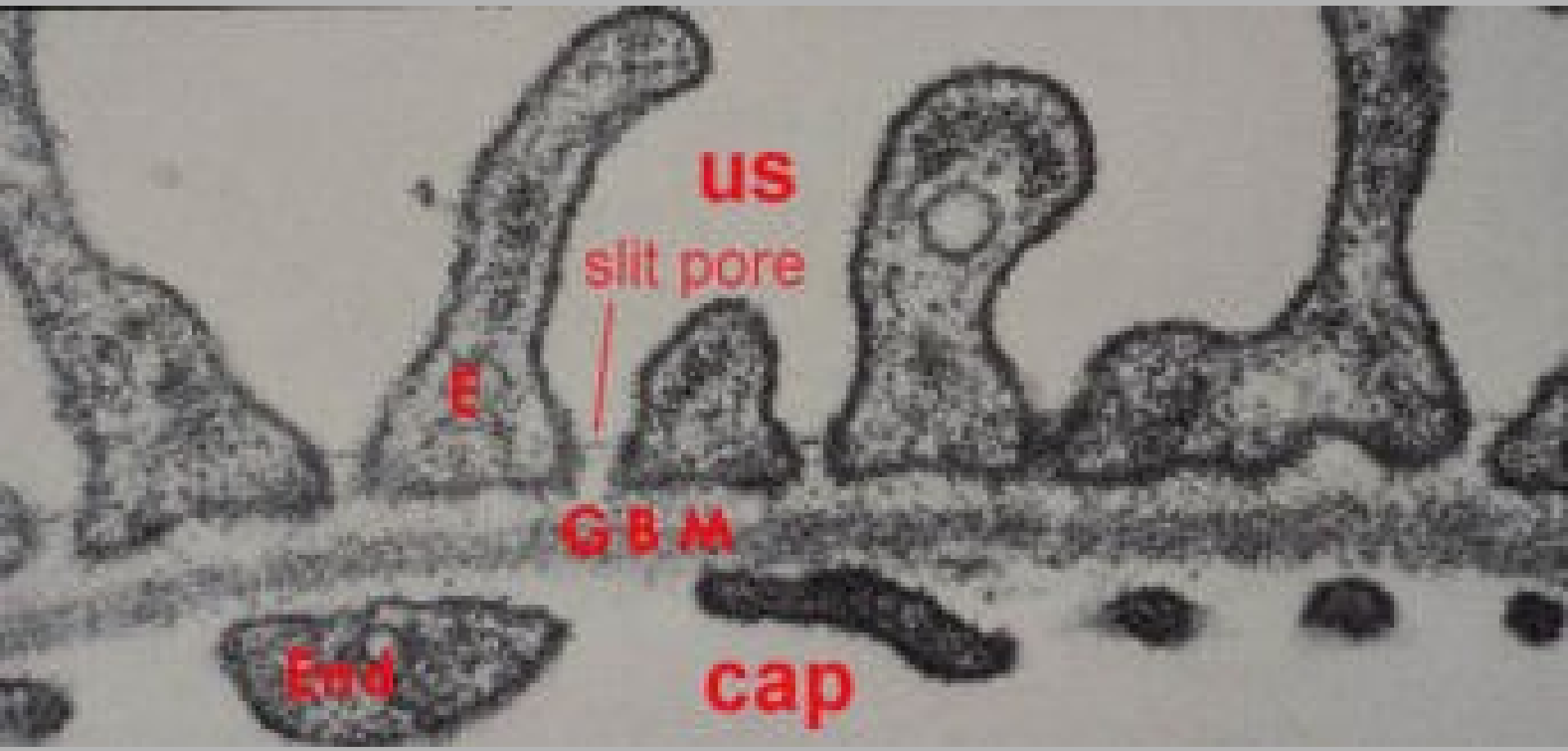


endothelial proliferation

mesangial cell proliferation

Schematic section

Biopsy


us
slit pore
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GBM
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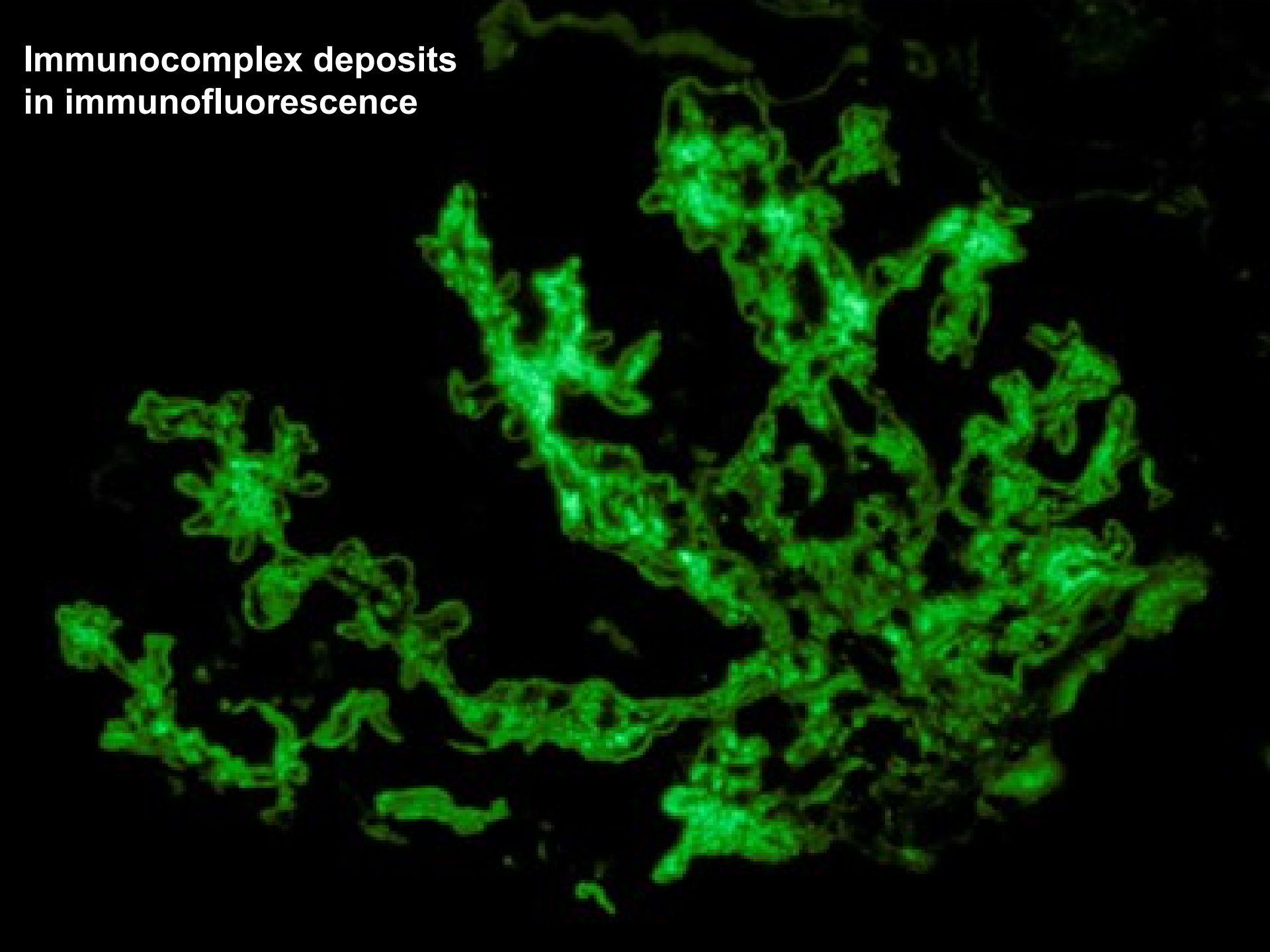
cap

Immunocomplex deposits in immunofluorescence



Glomerulonephritis

Acute GN

Clinical course

- young patient (commonly 3-7 yr. - better prognosis in children)
- onset 1-2 weeks after infection disease
- fatigue, poorness, loin pain from kidney distension
- macroscopic hematuria, proteinuria
- leukocytosis, FW
- oliguria to anuria
- nephrotic sy, swelling
- arter. hypertension
- extrarenal symptoms disappear during several weeks
- normalization of urine parameters and renal functions after months to 1 years

Glomerulonephritis

Acute GN

Clinical course

recovery in 95% of children, in 80-90% of adults

progression to renal insufficiency + extrarenal symptoms mean switch to chronic phase

rarely fatal course

Glomerulonephritis

Rapidly progressive GN

Quick and irreversible damage of glomeruli

mechanism

- **immunocomplex** — granular deposits
- **antirenal Ab** — linear subendothelial deposits in immunofluorescence

etiology

- **idiopatic**
- **systemic disease** — = syndrome lung - kidney; hemoptysis due to alveolar damage foreruns hematuria
  - **Goodpasture sy**

Glomerulonephritis

Rapidly progressive GN

Clinical course

- rapid onset (fatigue, loin pain)
- oliguria / anuria
- progressive renal failure during several weeks to months
- previously unambiguously malign course
- now: high dose corticoids, IS, cytostatics allow stabilization

Indication to renal biopsy (x in acute GN)

Glomerulonephritis

Chronic GN

Etiology

- **Idiopatic**
- **Secondary**

= secondary to systemic disease, colagenoses

Commonly immunocomplex mechanism

Glomerulonephritis

Chronic GN

Classification

An exact classifications is based on renal biopsy only.
Clinical image of different forms is not always characteristic.

Glomerulonephritis

Chronic GN

- mesangio-proliferative
- membrano-proliferative
- membranous
- lipoid nephrosis
- focal segmental glomerulosclerosis

Glomerulonephritis

Chronic GN

- **mesangio-proliferative**
- membrano-proliferative
- membranous
- lipoid nephrosis
- focal segmental glomerulosclerosis

proliferation of mesangial cells, ↑ mesangial matrix

usually benign course to recovery, or change to nephrotic syndrome

Glomerulonephritis

Chronic GN

- mesangio-proliferative
- **membrano-proliferative**
- membranous
- lipoid nephrosis
- focal segmental glomerulosclerosis

- **thickening of basement membrane**
- **nephrotic sy**
- **progression to renal failure**

Glomerulonephritis

Chronic GN

- mesangio-proliferative
- membrano-proliferative
- **membranous**
- lipoid nephrosis
- focal segmental

- granular epimembranous deposits
- come after infection (hepatitis B), intoxication (Hg, Au), SLE, tumors
- variable prognosis:
  - recovery after removal of an origin
  - long benign course
  - progression to renal failure

Glomerulonephritis

Chronic GN

- mesangio-proliferative
- membrano-proliferative
- membranous
- **lipoid nephrosis**
- focal segmental glo

- „minimal change disease“
- fusion of pedicels in podocytes
- mainly in children
- benign course, but frequent relapses
- dominant sign: proteinuria

...nephrotic syndrome

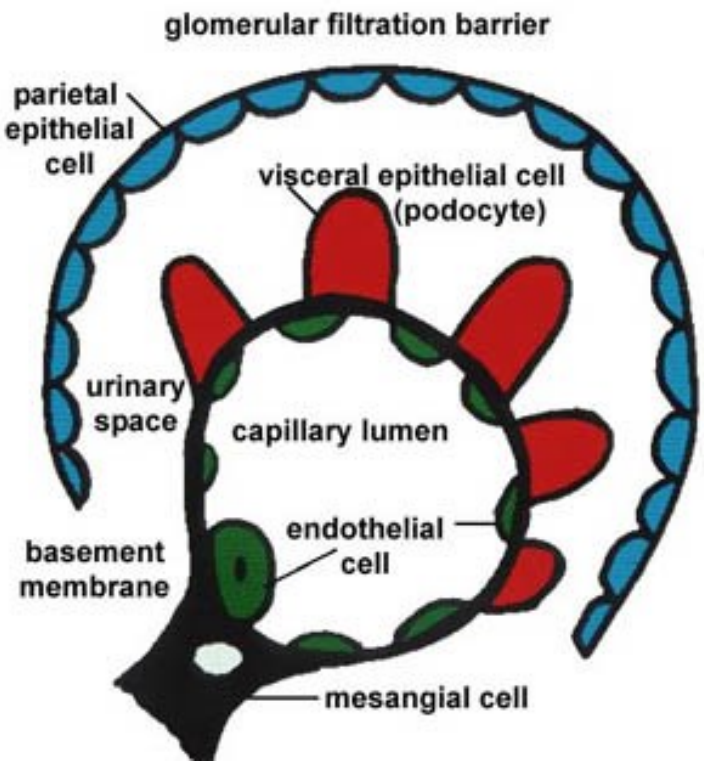
Glomerulonephritis

Chronic GN

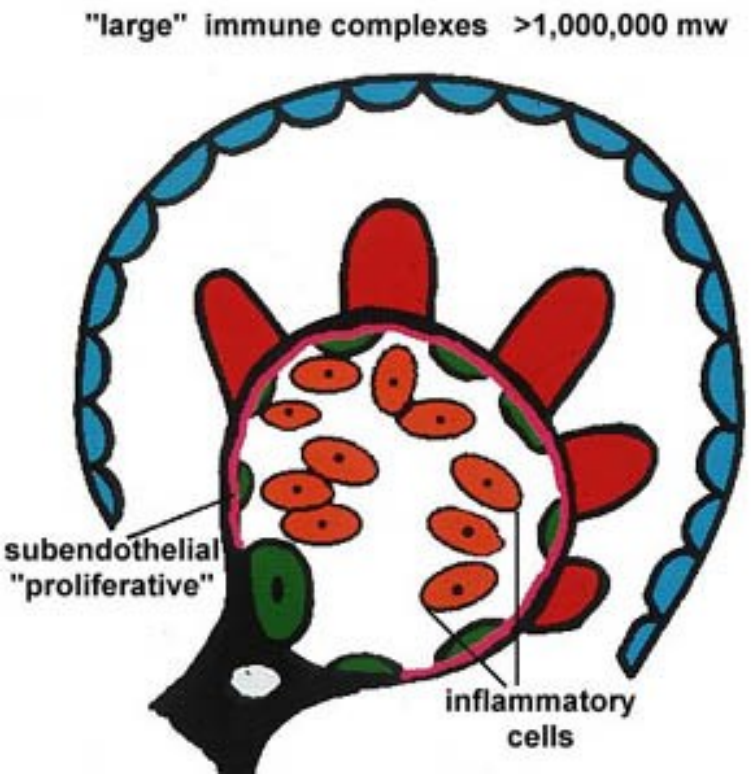
- mesangio-proliferative
- membrano-proliferative
- membranous
- lipoid nephrosis
- **focal (segmental) glomerulosclerosis**

segmental changes of glomerulus, mainly juxtaglomerular

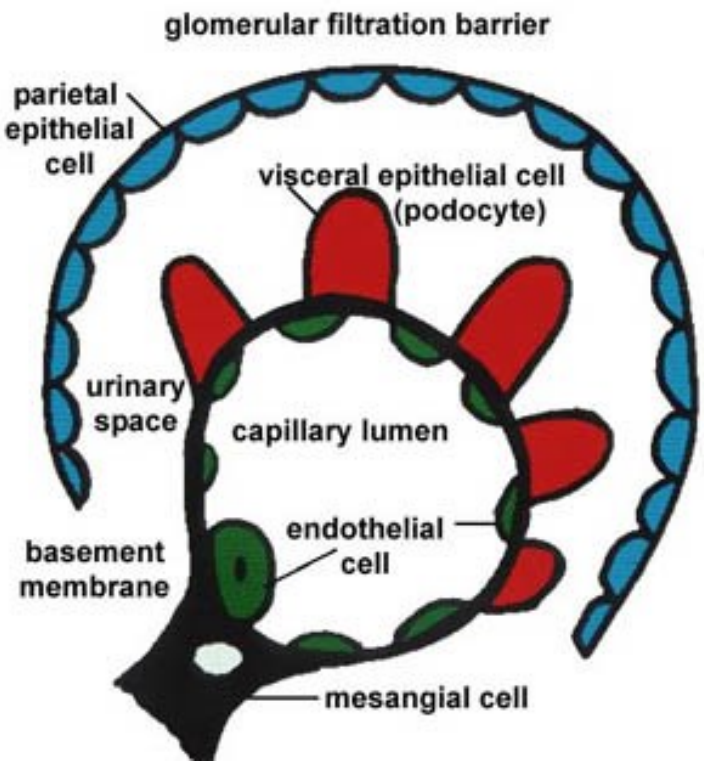
normal glomerulus



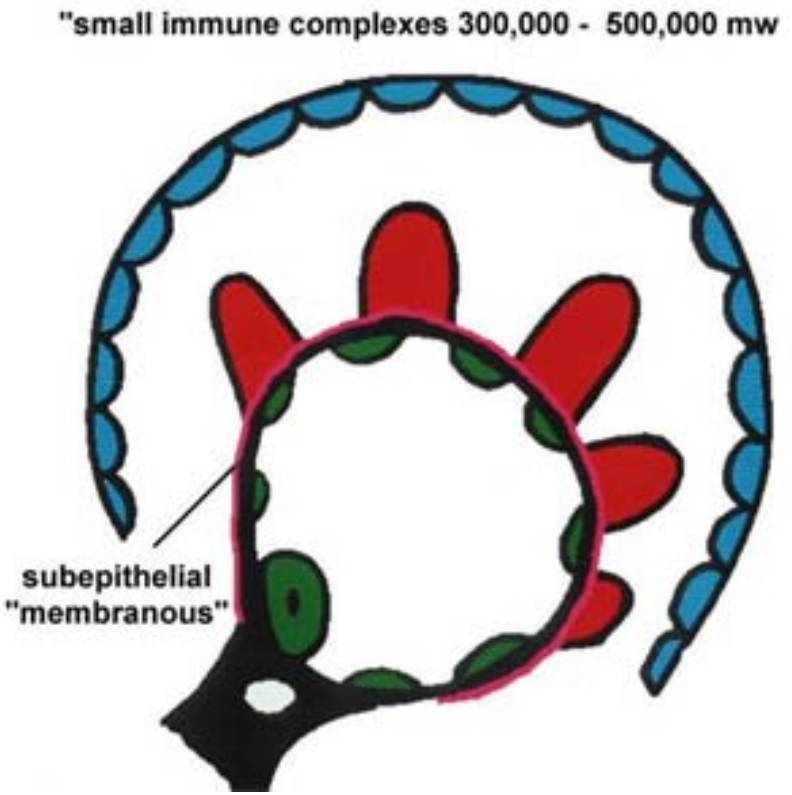
membranous immunocomplex GN



normal glomerulus



membrano-proliferative GN



Laboratory urine findings in GN

Proteinuria (g)	Hematuria (mil.)	Description	Examples
+	-	isolated selective proteinuria	lipoid nephrosis
-	+	selective hematuria	IgA nefropathy tumors, lithiasis
0,5 – 1,0	5 - 10	mild proportional failure	mesangioproliferative GN
2,5	25	middle proportional failure	mesangioproliferative GN
> 4	> 40	heavy proportional failure	membranose-prolifer. GN RPGN immunocomplex. type
5	15	dominant non-selective proteinuria	membranous GN focal segmental GN

Urolithiasis

= Formation of stones in kidneys and urinary tract ducts

x **Crystaluria** = the presence of crystals in urine (= in urine sediment, microscopic finding)

Crystaluria may be physiological,

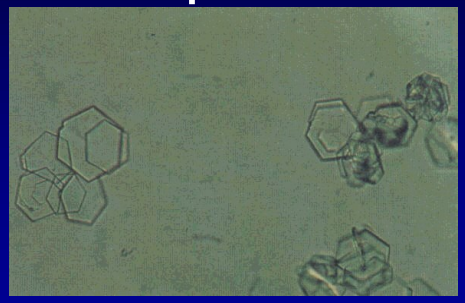
The current crystaluria in patient with urolithiasis may be useful for diff. diagnosis - type of stones

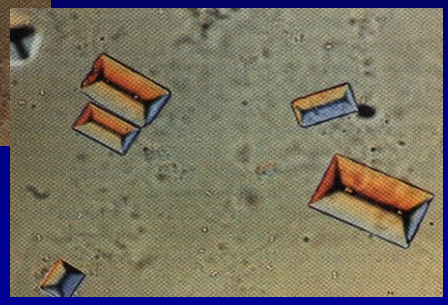
Urolithiasis

Crystaluria / urolithiasis

- $CaCO_3$, Ca-oxalate, Ca-phosphate (60 %)
- urate (uric acid, 10 %)
- struvite (ammonium Mg phosphate, 10 %)
- cystine (1 %)

...

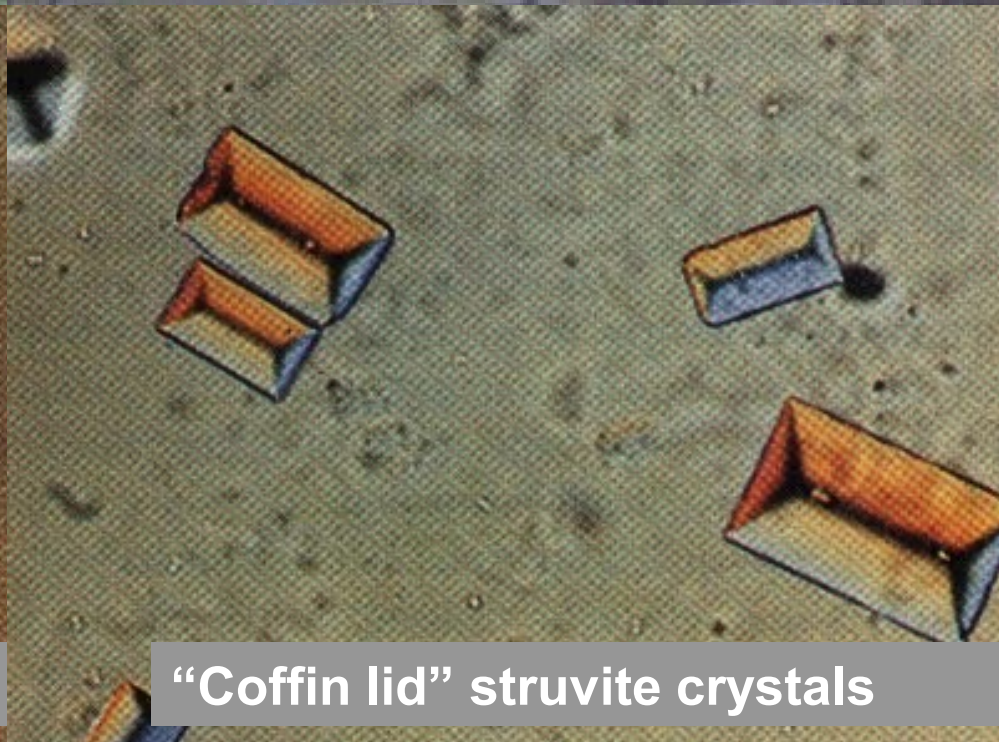





Cystine crystals


Thyrosin crystals


Ca oxalate crystals


“Coffin lid” struvite crystals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Urolithiasis

Pathogenesis:

1. Nidus (nest)

= the base of a stone, consists of organic compounds (epithelium, proteins, erythrocytes, uromucoids...)

2. Urine is saturated with minerals

(Ca, uric acid...)

Urolithiasis

Pathogenesis:

3. Lack of inhibitory factors
(protective colloids produced by epithelial cells of urinary tract, with anti-precipitation effect)

4. Stasis of urine
(prosthetic hyperplasia, hydronephrosis)

5. Low diuresis

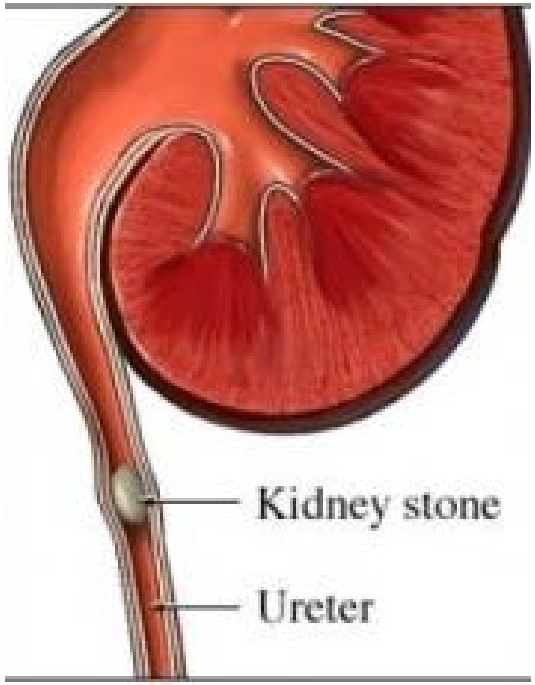
6. pH

7. Infection

Urolithiasis

Symptoms:

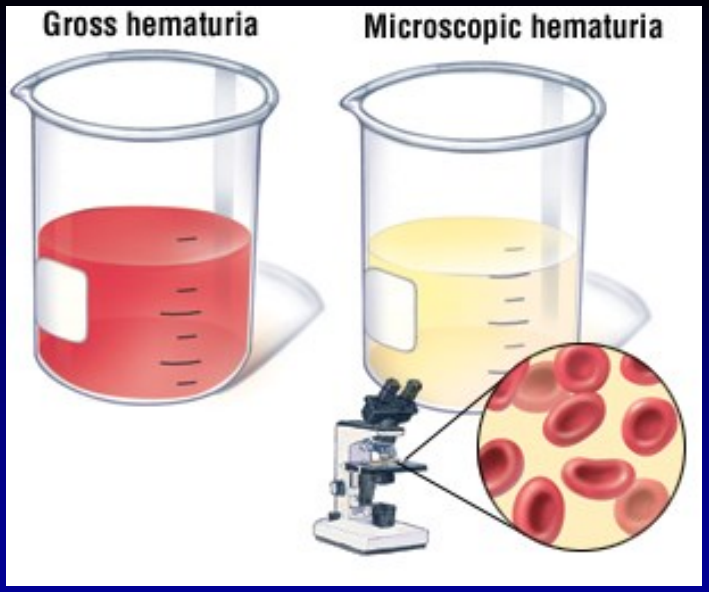
1. Renal colic



Urolithiasis

Symptoms:

2. Hematuria ... macroscopic or microscopic (phase contrast)

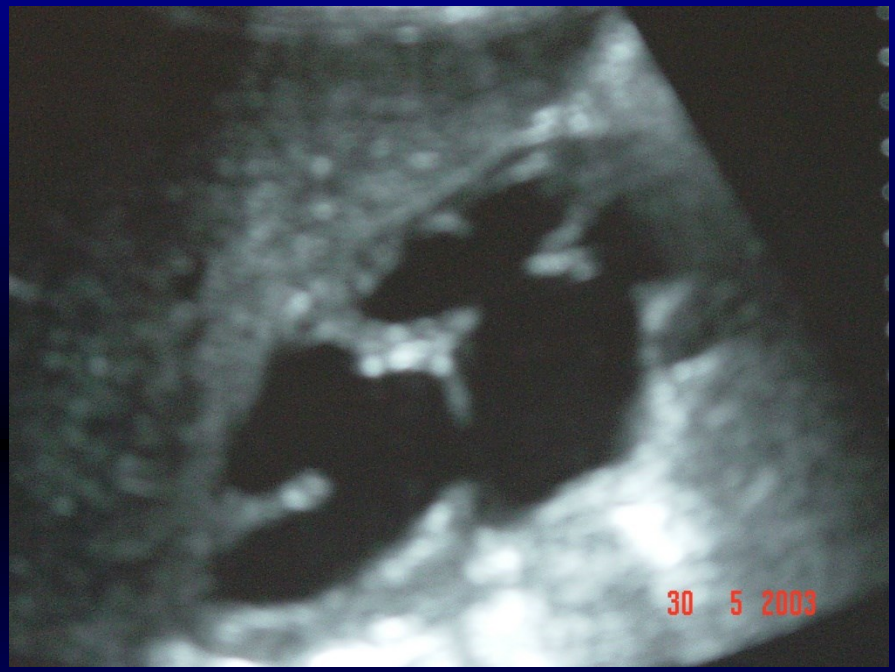


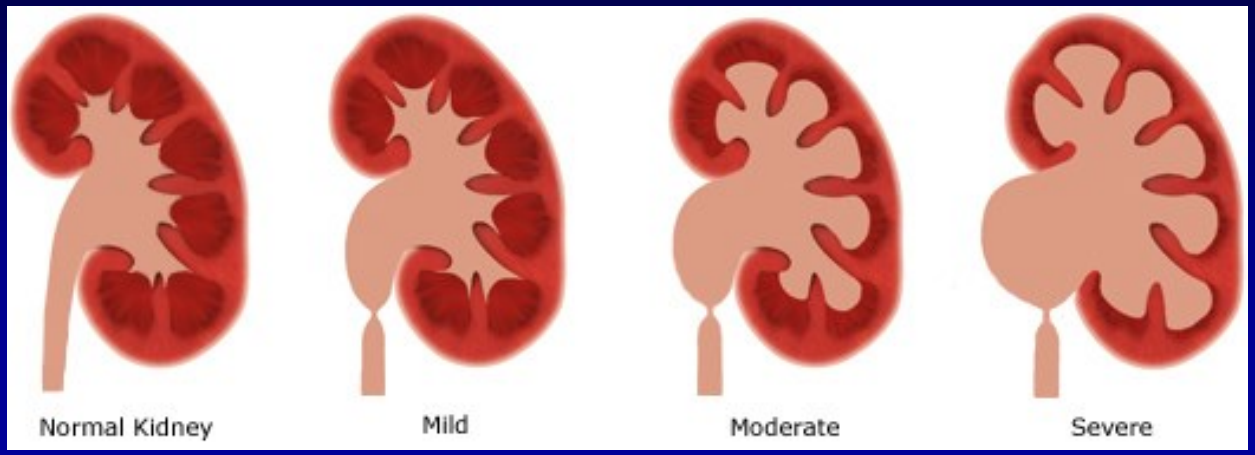
Urolithiasis

Symptoms:

3. Hydronephrosis

... urine stasis due to obstruction



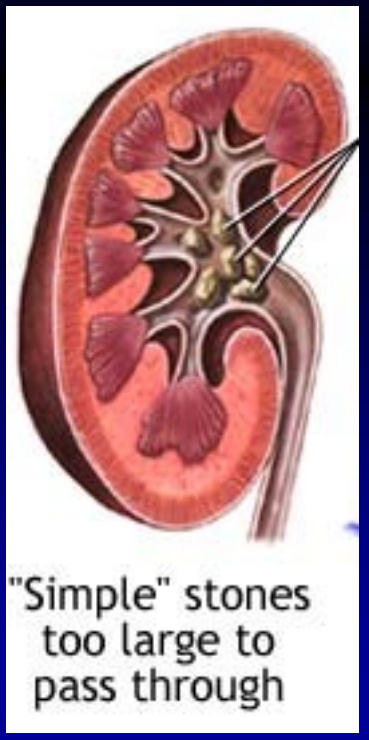


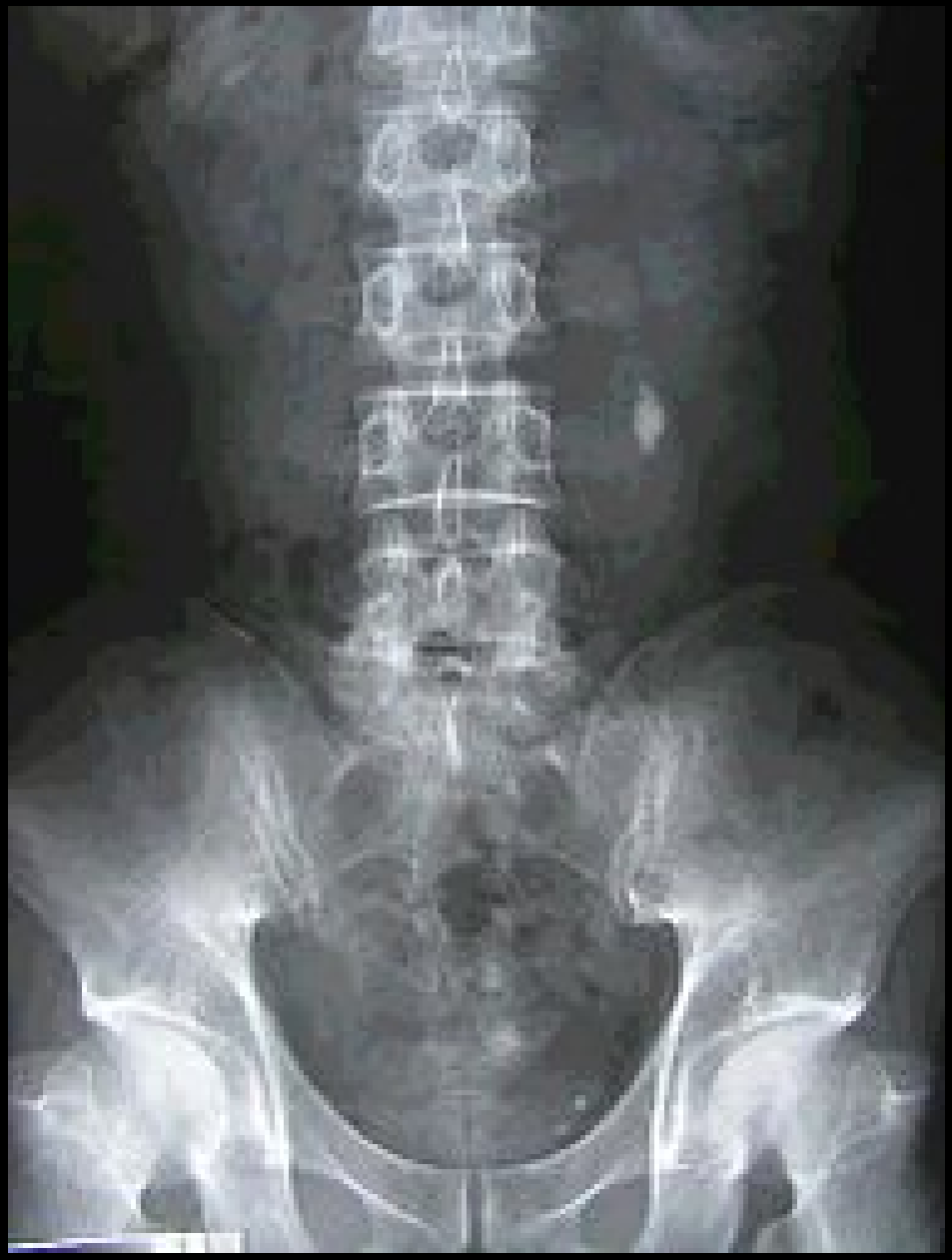
Urolithiasis

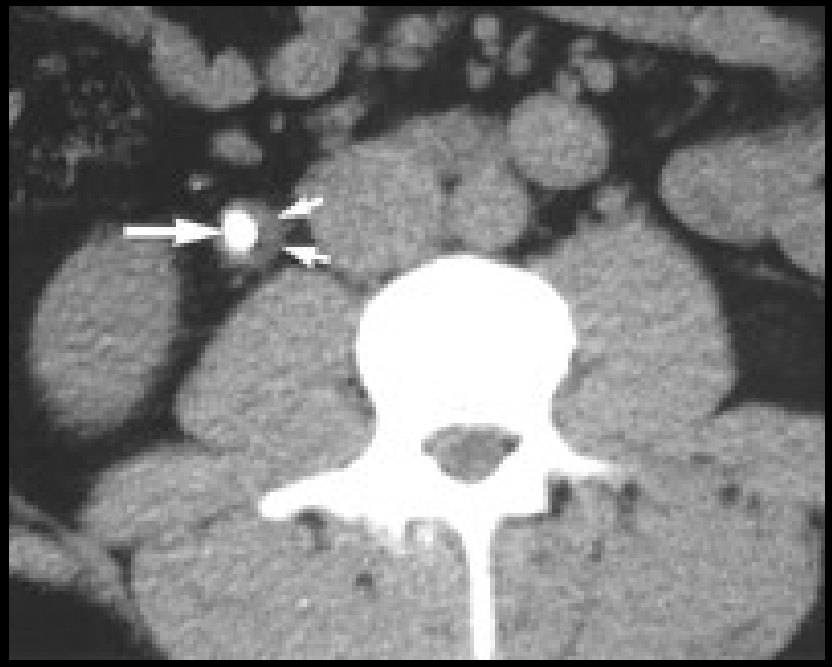
Symptoms:

4. Ascendent infection ... recidiv. inflammation, even pyonephros

5. Latent course ... mainly in big stones

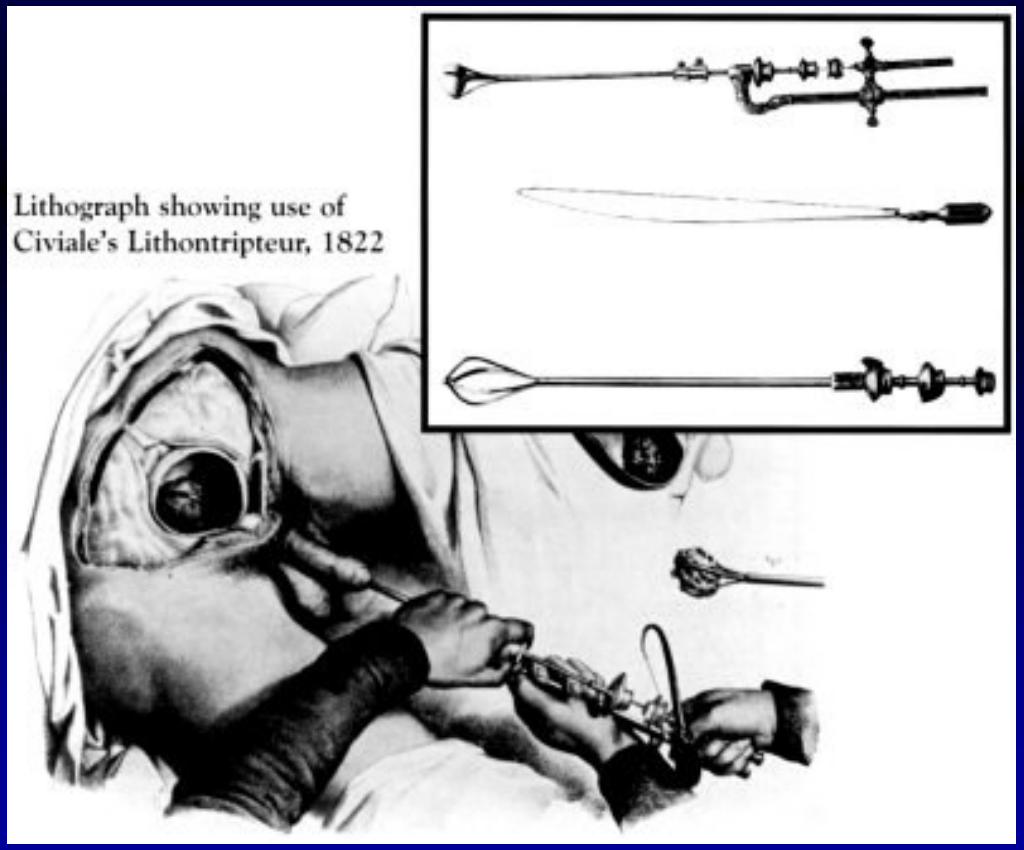






Urolithiasis

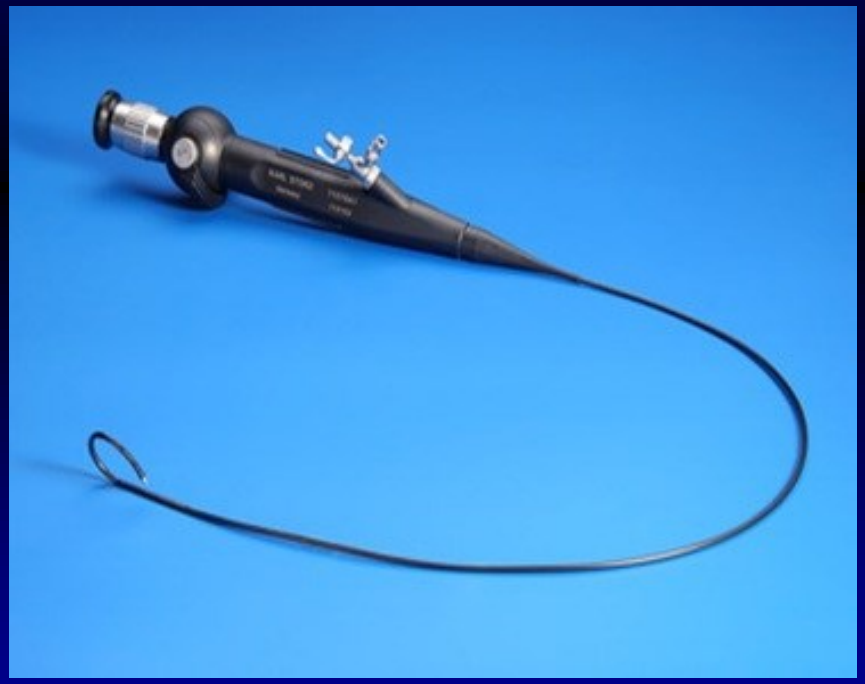
Surgical treatment of urolithiasis in 1822

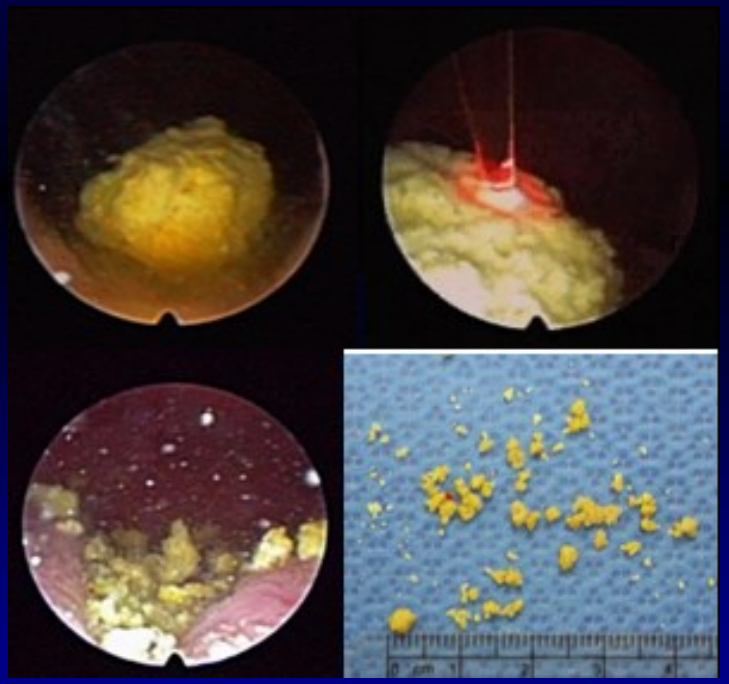


Lithograph showing use of
Civiale's Lithontripteur, 1822

Urolithiasis

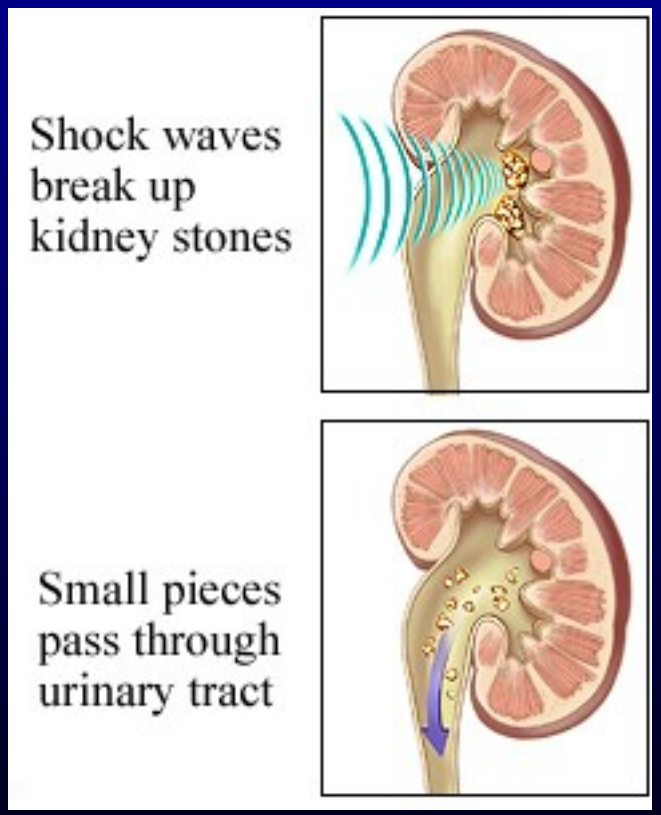
Cystoscopy and laser treatment of lithiasis





Urolithiasis

Lithotripsy using shock waves



Case report (2)

42-year old man was admitted to the emergency department with a history of sudden loss of consciousness while waiting to board an aircraft.

Prior to admission the patient was said to be complaining of bilateral loin pain, poor appetite, lethargy and generalized weakness for which he attended different hospital casualty departments.

Case report (2)

In past history without chronic diseases
Smoker for about 25 years.
Without chronic medication

Case report (2)

Physical examination:

- acidotic breathing,
- blood pressure 140/80 mmHg
- tachycardia 108 / minute
- temperature 38ºC
- consciousness level according to the Glasgow scale was 5/15

He was intubated immediately and mechanically ventilated

Case report (2)

Laboratory findings:

• hemoglobin	89 g / L
• platelets	286 × 10^9 / L
• K^+	10.3 mmol / L
• creatinine	3581 µmol/L
• urea	59.9 mmol/L
• pH	6.8
• ECG	peak T wave, SV tachycardia

Case report (2)

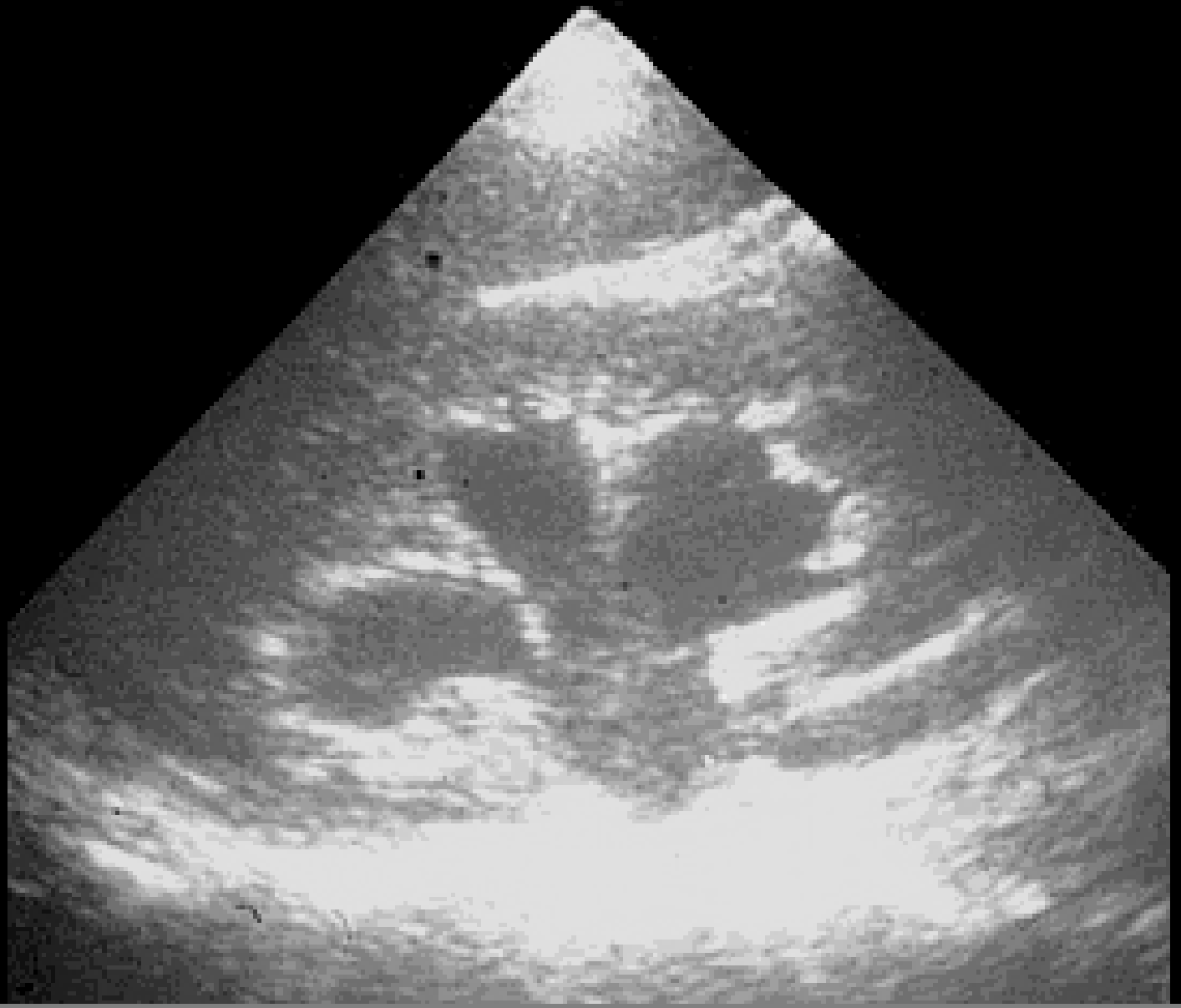
The patient was put on fluid therapy, i.v. antibiotics (Rocephine 2g). Emergency haemodialysis was carried out.

Haemodialysis resulted in rapid lowering of K^+ from 9.9 to 5.9 mmol/L within a 12 hour period.

Case report (2)

Biochemistry profile

	Day 1	Day 1	Day 1	Day 1	Day 2	Day 3	Day 6	Day 32
Urea (mmol/L)	59.9	44.8	42.9	29.7	31.7	33.7	7.6	6.5
Creatinine (umol/L)	3581	3236	2387	2043	1776	1839	170	170
K+ (mmol/L)	10.3	9.9	6.2	5.9	4.6	4.8	4.5	4.3

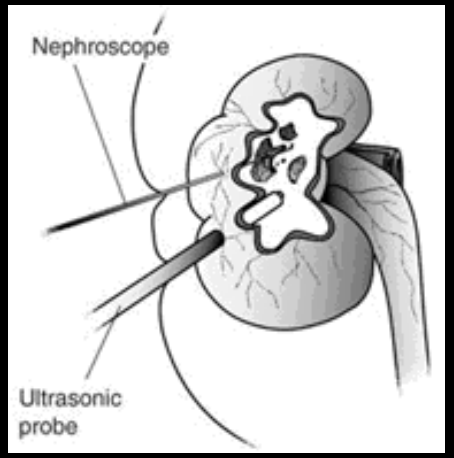


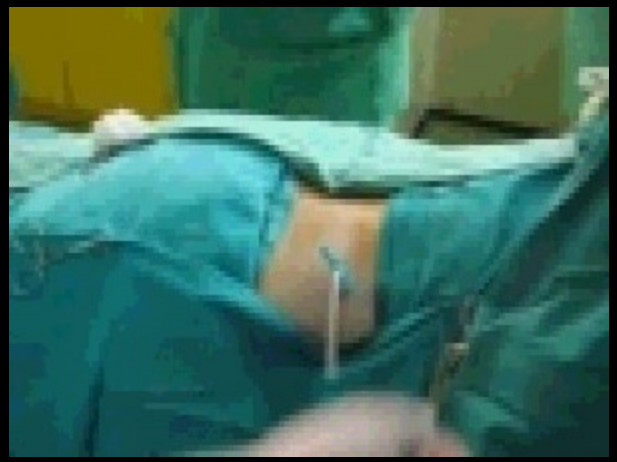
USG of the abdomen: Bilateral huge hydronephrosis with loss of parenchyma (left > right), thickened bladder wall and a mass in the bladder.

Case report (2)

... After biochemistry was improved, on the third post admission day...

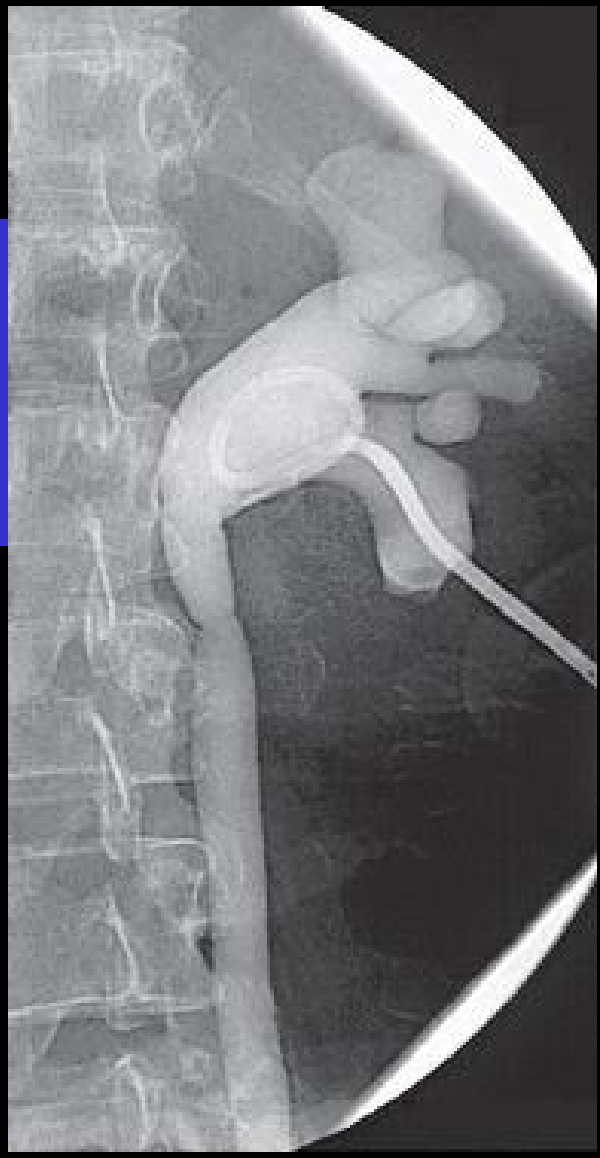
Bilateral percutaneous nephrostomy tubes were inserted.
Following it, the patient had post obstructive diuresis.
After 7 days, the serum creatinine had stabilized at 170 umol / L and K+ at 4.3 mmol / L.





Case report (2)

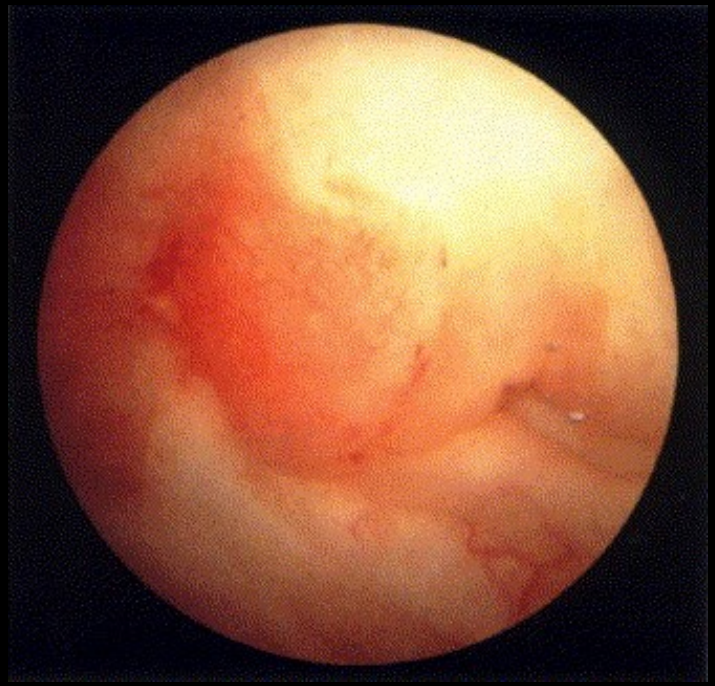
Bilateral antegrade pyelography
through the nephrostomic tubes showed complete bilateral ureteric obstruction at the level of the sacro-iliac joints.

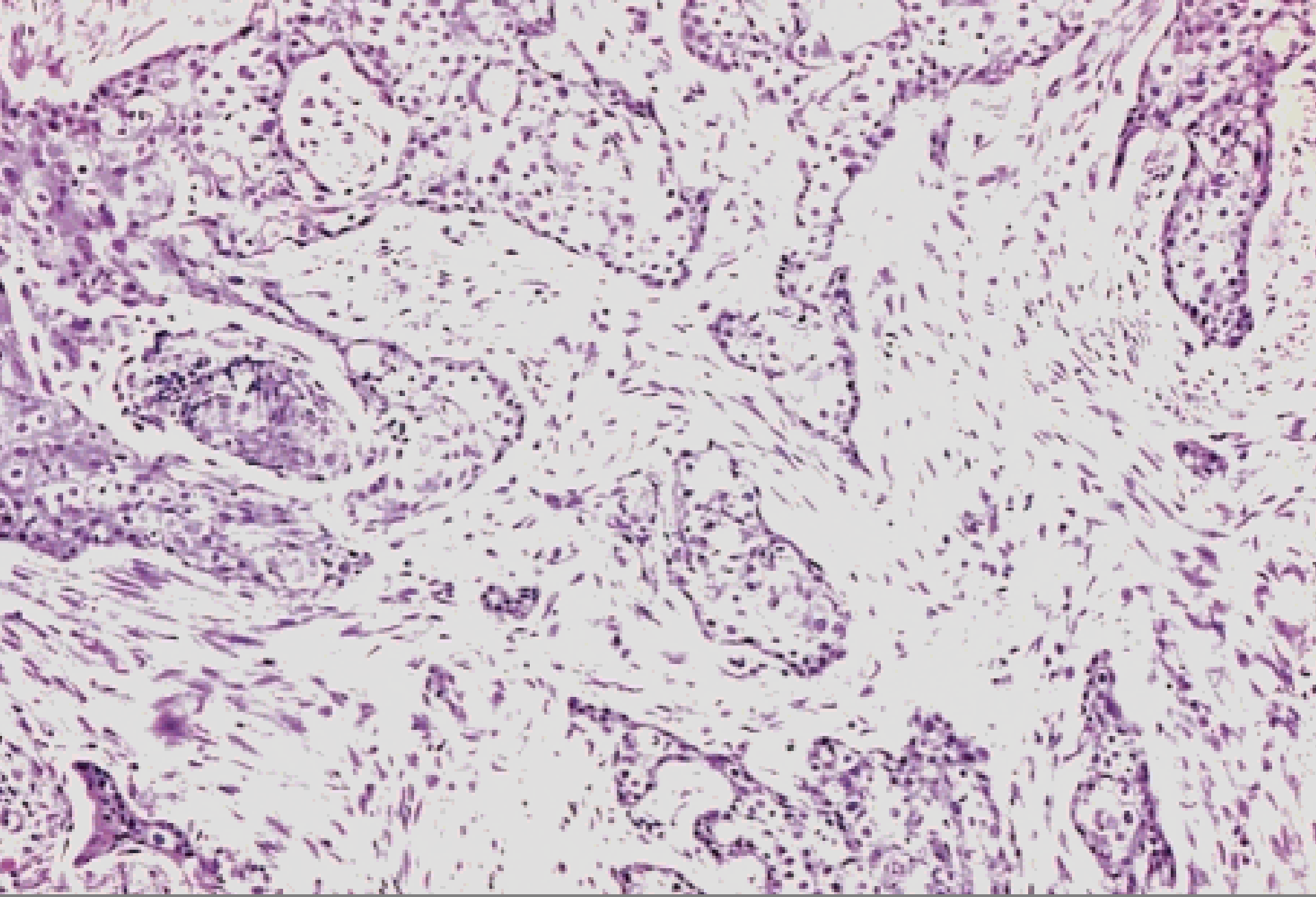


Case report (2)

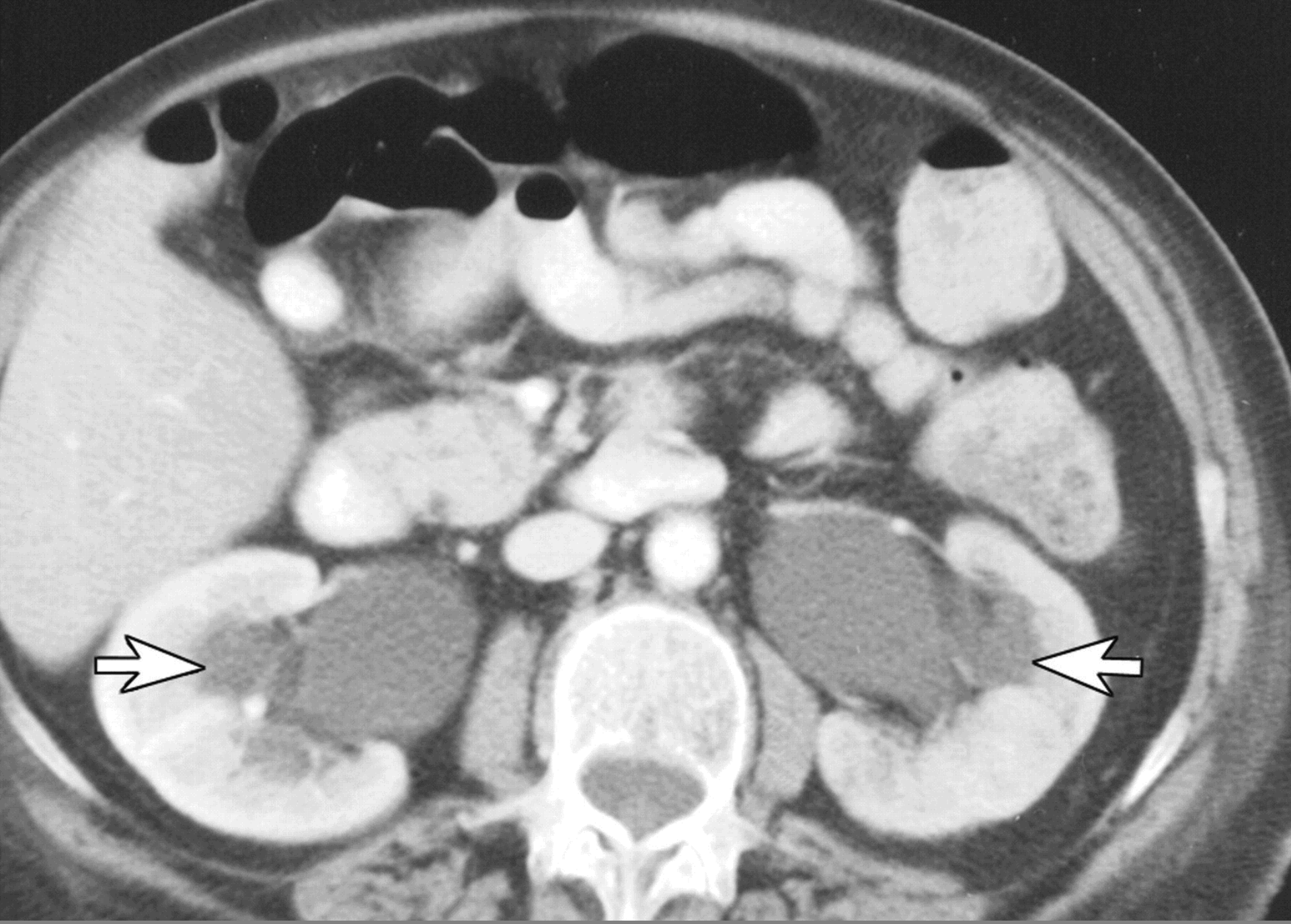
... Ten days later, after successful treatment, under general anesthesia...

Cystoscopy
revealed a bladder filled with a necrotic mass, which was a non-papillary infiltrating tumor.





Histology: Poorly differentiated squamous cell carcinoma of the bladder.

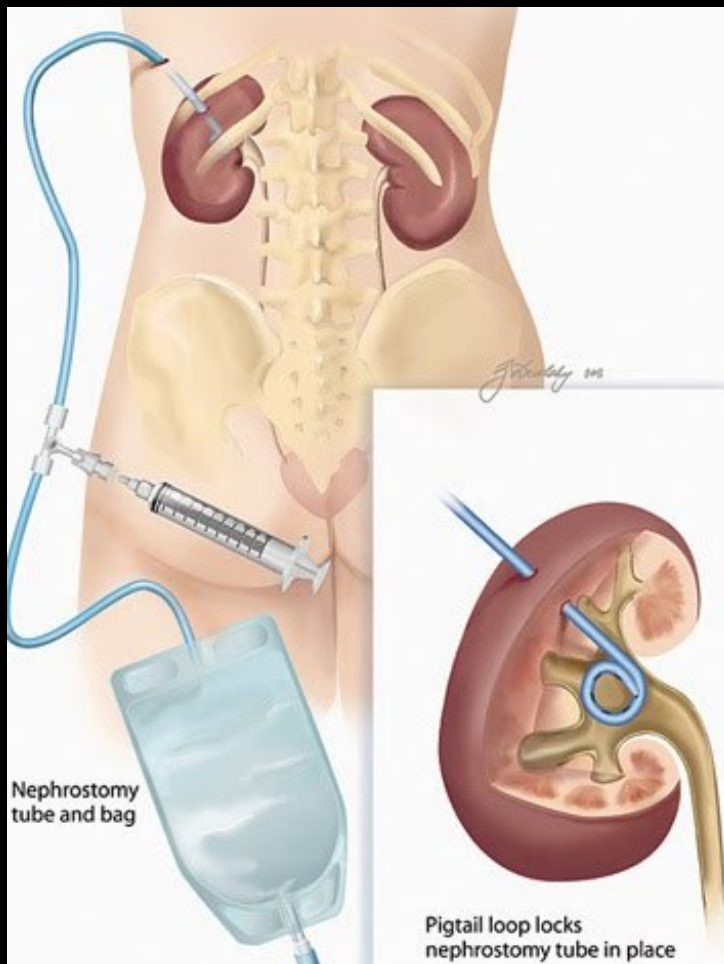


CT-scan of the abdomen and the pelvis confirmed bilateral hydronephrosis (left > right).

Case report (2)

Bone scan revealed no scintigraphic evidence of skeletal metastases.

Patient was discharged on day 32 with bilateral nephrostomic tubes,
serum creatinine of 170 umol/L.



Case report (3)

Male, 75 years old

Past history:

- diabetes mellitus type 2 on a diet
- onychomycosis, recovering eczema (low extremities and back), on a long-term corticoid therapy

The patient admitted to dermatology department to accurate a diagnosis of eczema and its treatment.

In day 6, diagnostic excision from eczematous foci was realized.

Case report (3)

The same day, febrile reaction, 42°C, tachypnoe.
The following day hypotension, altered consciousness.

The patients admitted to intensive care unit.

Case report (3)

4-day infusion treatment with catecholamines (dopamine), high-dose hydrocortisone, parental rehydration.

Anuria progression (in water intake 3000 ml per day, diuresis only 150 ml). The same water balance at following day.
Patient indicated to urgent hemodialysis.

Case report (3)

Concurrently quick progression of anemia.

Platelet decrease.

Changes of coagulation parameters.

	1.	1.	1.	2.	3.	4.	8.	10.	17.	32.
Ery	4,2	-	3,4	2,8	2,6	2,8	2,4	2,6	2,6	2,4
Leu	14,9	-	13,6	13,8	9,3	6,2	7,5	6,2	8,8	12,2
Tr	61	-	28	28	28	35	81	116	93	107
Quick INR	1,5	-	-	1,3	1,0	0,9	-	1,0		
APTT (s)	64	-	-	44	40	25	-	30		
fibrinogen (g/l)	1,9	-	-	3,2	2,9	1,9	-	6,8		
D-dimer (μg/l)	>2000	-	-	>2000	>2000	>2000	-	1000		
etanol. test	poz.	-	-	neg.	neg.	neg.	-	neg.		
ATIII (%)	44	-	-	31	44	37	-	83		
tromb.čas (s)	31	-	-	17	21	20	-	15		
Na (mmol/l)	142	146	145	143	140	142	140	138	137	134
K (mmol/l)	3,8	3,8	4,9	4,6	4,3	5,1	5,2	4,4	4,3	4,3
Cl (mmol/l)	110	110	109	107	106	108	108	106	104	99
urea (mmol/l)	16	15	15	20	26	33	33	29	25	49
kreatinin (μmol/l)	248	297	292	374	507	614	601	582	521	813
c.bílkovina (g/l)	75	72	56	55	56	54	56	54	50	49
bilirubin (mmol/l)	29	35	36	41	35	22	14	16	8	9
ALT (μkat/l)	38	87	88	80	44	20	6	2	0,9	0,8
AST (μkat/l)	65	115	199	114	24	3	1	0,6	0,5	0,5
ALP (μkat/l)	2,1	1,8	1,4	1,2	1,4	1,4	1,3	1,4	1,4	1,1
GMT (μkat/l)	4,6	4,2	3,1	1,1	1,1	1,0	1,5	1,3	1,1	1,1
LDH (:kat/l)	26,2	36,8	34,0	34,5	18,6	15,6	9,3	8,3	9,4	6,2
CK (μkat/l)	14,2	53,2	-	14,8	6,2	4,4	2,1	2,2	1,9	3,8
CK-MB (μkat/l)	3,3	6,5	-	2,1	0,9	0,5	-	-	-	-
AMS (μkat/l)	1,9	2,6	3,1	2,3	2,1	1,9	1,6	-	-	-
CRP (mg/l)	188	-	-	61	29	46	132	158	156	175
glykémie (mmol/l)	6,1	13,2	14,8	14,8	4,4	4,4	6,0	6,3	13,8	14,5

	1.	1.	1.	2.	3.	4.	8.	10.	17.	32.
Ery	4,2	-	3,4	2,8	2,6	2,8	2,4	2,6	2,6	2,4
Leu	14,9	-	13,6	13,8	9,3	6,2	7,5	6,2	8,8	12,2
Tr	61	-	28	28	28	35	81	116	93	107
Quick INR	1,5	-	-	1,3	1,0	0,9	-	1,0		
APTT (s)	64	-	-	44	40	25	-	30		
fibrinogen (g/l)	1,9	-	-	3,2	2,9	1,9	-	6,8		
D-dimer (μg/l)	>2000	-	-	>2000	>2000	>2000	-	1000		
etanol. test	poz.	-	-	neg.	neg.	neg.	-	neg.		
ATIII (%)	44	-	-	31	44	37	-	83		
tromb.čas (s)	31	-	-	17	21	20	-	15		
Na (mmol/l)	142	146	145	143	140	142	140	138	137	134
K (mmol/l)	3,8	3,8	4,9	4,6	4,3	5,1	5,2	4,4	4,3	4,3
Cl (mmol/l)	110	110	109	107	106	108	108	106	104	99
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ALP (μkat/l)	2,1	1,8	1,4	1,2	1,4	1,4	1,3	1,4	1,4	1,1
GMT (μkat/l)	4,6	4,2	3,1	1,1	1,1	1,0	1,5	1,3	1,1	1,1
LDH (:kat/l)	26,2	36,8	34,0	34,5	18,6	15,6	9,3	8,3	9,4	6,2
CK (μkat/l)	14,2	53,2	-	14,8	6,2	4,4	2,1	2,2	1,9	3,8
CK-MB (μkat/l)	3,3	6,5	-	2,1	0,9	0,5	-	-	-	-
AMS (μkat/l)	1,9	2,6	3,1	2,3	2,1	1,9	1,6	-	-	-
CRP (mg/l)	188	-	-	61	29	46	132	158	156	175
glykémie (mmol/l)	6,1	13,2	14,8	14,8	4,4	4,4	6,0	6,3	13,8	14,5

	1.	1.	1.	2.	3.	4.	8.	10.	17.	32.
Ery	4,2	-	3,4	2,8	2,6	2,8	2,4	2,6	2,6	2,4
Leu	14,9	-	13,6	13,8	9,3	6,2	7,5	6,2	8,8	12,2
Tr	61	-	28	28	28	35	81	116	93	107
Quick INR	1,5	-	-	1,3	1,0	0,9	-	1,0		
APTT (s)	64	-	-	44	40	25	-	30		
fibrinogen (g/l)	1,9	-	-	3,2	2,9	1,9	-	6,8		
D-dimer (μg/l)	>2000	-	-	>2000	>2000	>2000	-	1000		
etanol. test	poz.	-	-	neg.	neg.	neg.	-	neg.		
ATIII (%)	44	-	-	31	44	37	-	83		
tromb.čas (s)	31	-	-	17	21	20	-	15		
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K (mmol/l)	3,8	3,8	4,9	4,6	4,3	5,1	5,2	4,4	4,3	4,3
Cl (mmol/l)	110	110	109	107	106	108	108	106	104	99
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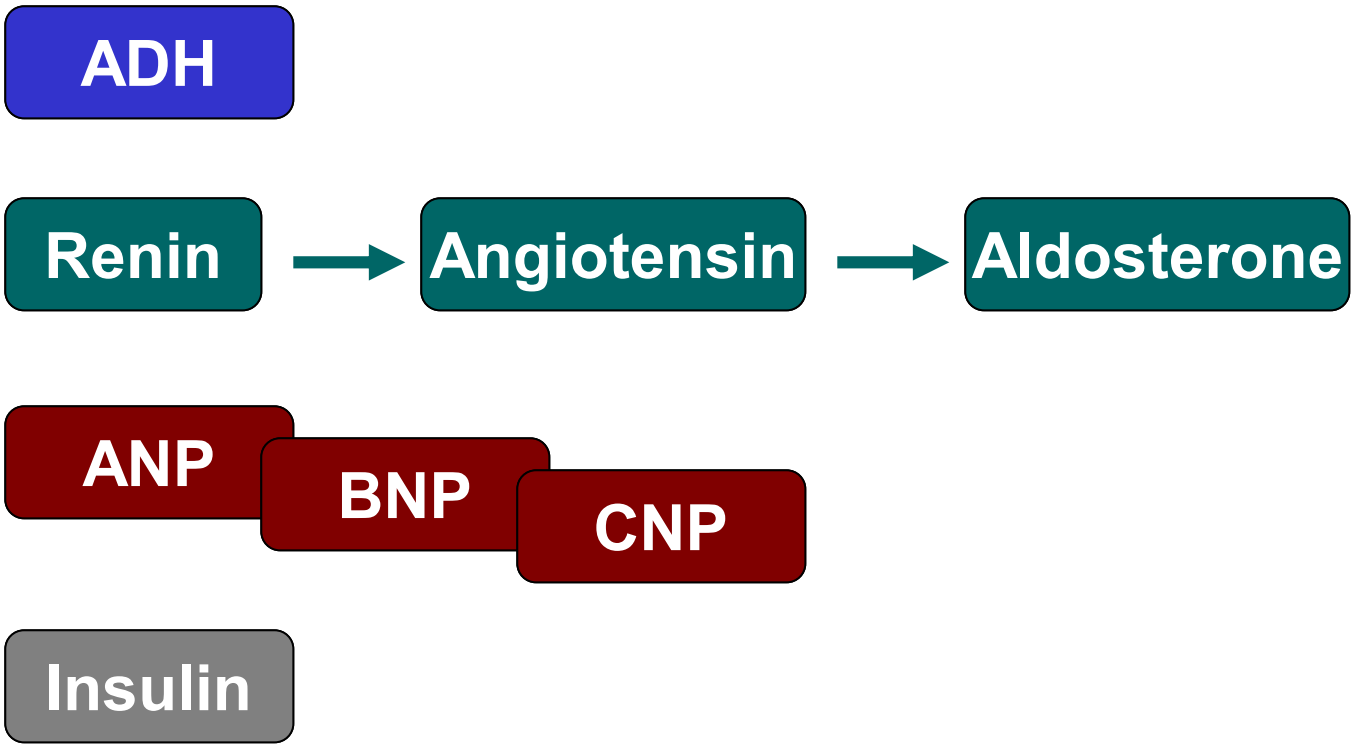
GMT (μkat/l)	4,6	4,2	3,1	1,1	1,1	1,0	1,5	1,3	1,1	1,1
LDH (:kat/l)	26,2	36,8	34,0	34,5	18,6	15,6	9,3	8,3	9,4	6,2
CK (μkat/l)	14,2	53,2	-	14,8	6,2	4,4	2,1	2,2	1,9	3,8
CK-MB (μkat/l)	3,3	6,5	-	2,1	0,9	0,5	-	-	-	-
AMS (μkat/l)	1,9	2,6	3,1	2,3	2,1	1,9	1,6	-	-	-
CRP (mg/l)	188	-	-	61	29	46	132	158	156	175
glykémie (mmol/l)	6,1	13,2	14,8	14,8	4,4	4,4	6,0	6,3	13,8	14,5

Case report (3)

From day 4, restitution of diuresis to 500 ml / day, fever decreased. Long-term alteration of consciousness with necessity of parental nutritional support.

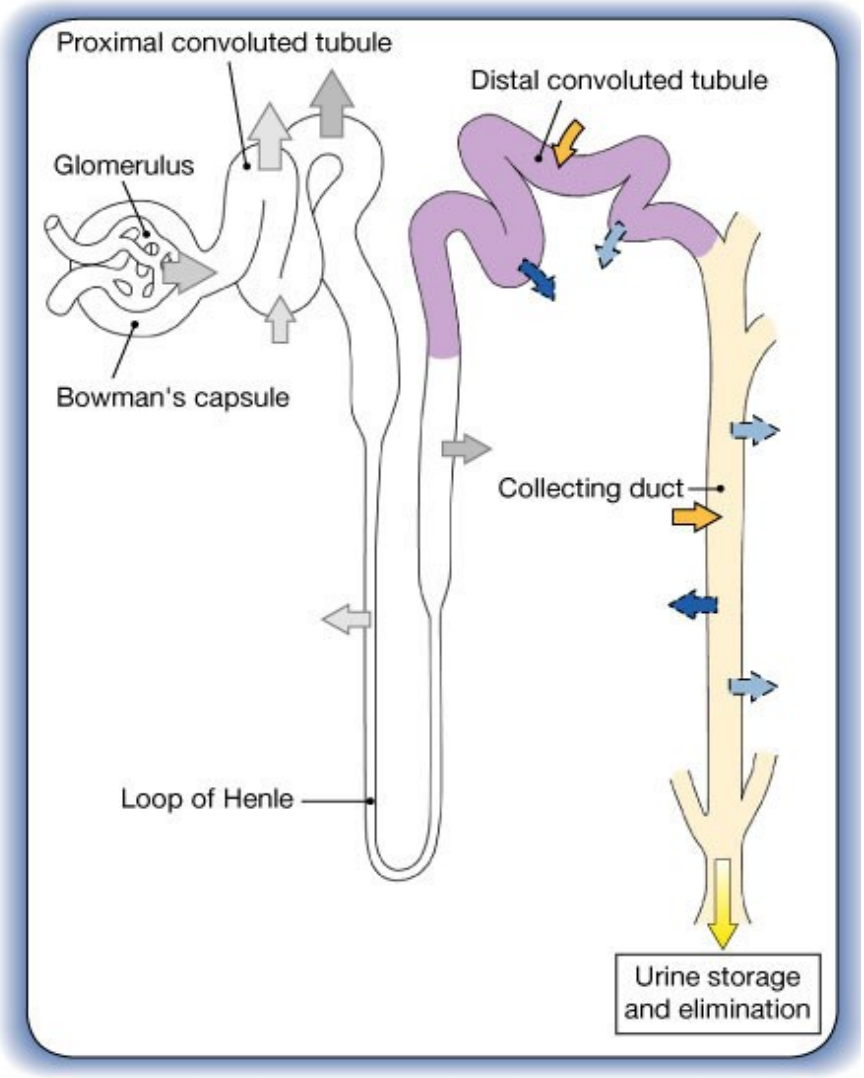
Hormonal regulation of diuresis



Hormonal regulation of diuresis

ADH

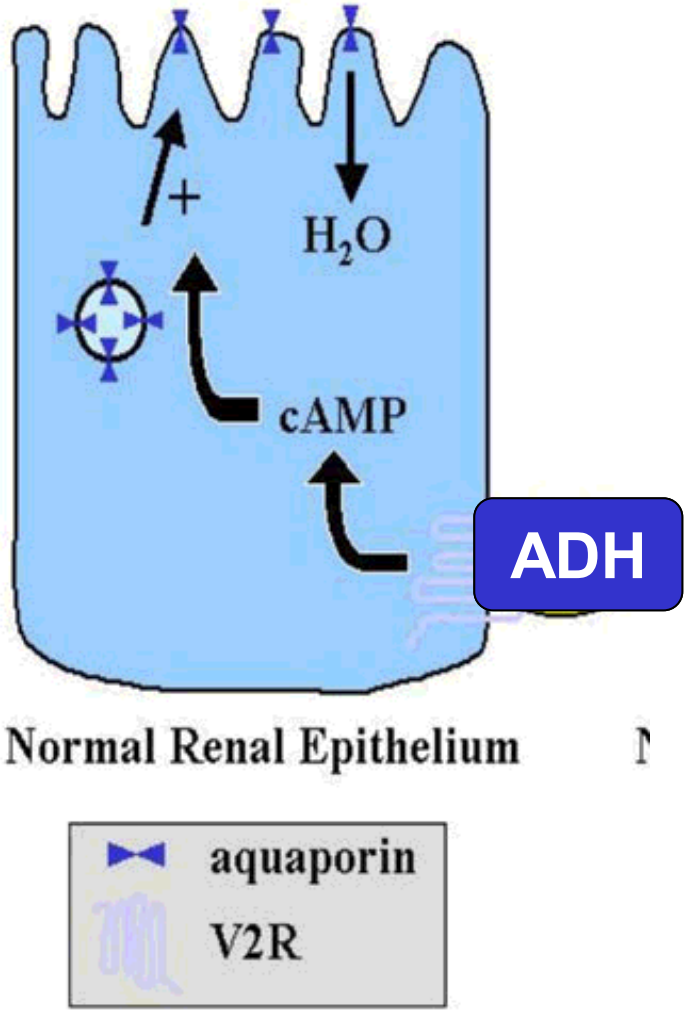
Regulating via V2 receptors selective water reabsorption in distal tubuli and collecting ducts



Hormonal regulation of diuresis

ADH

Regulating via V2 receptors selective water reabsorption in distal tubuli and collecting ducts

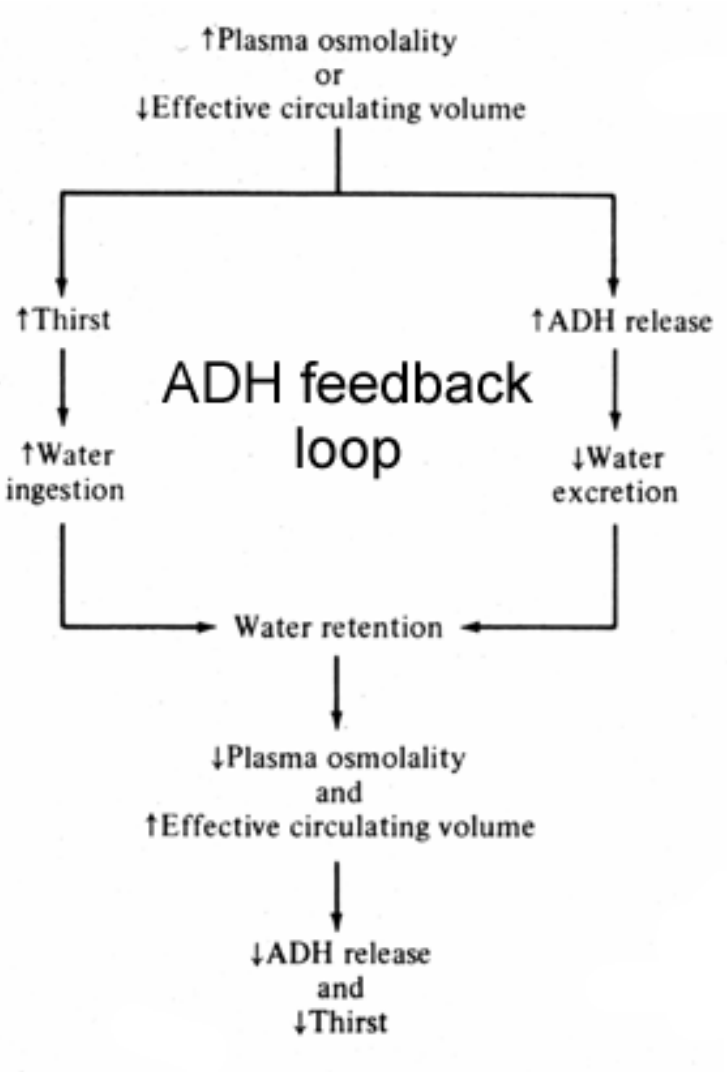


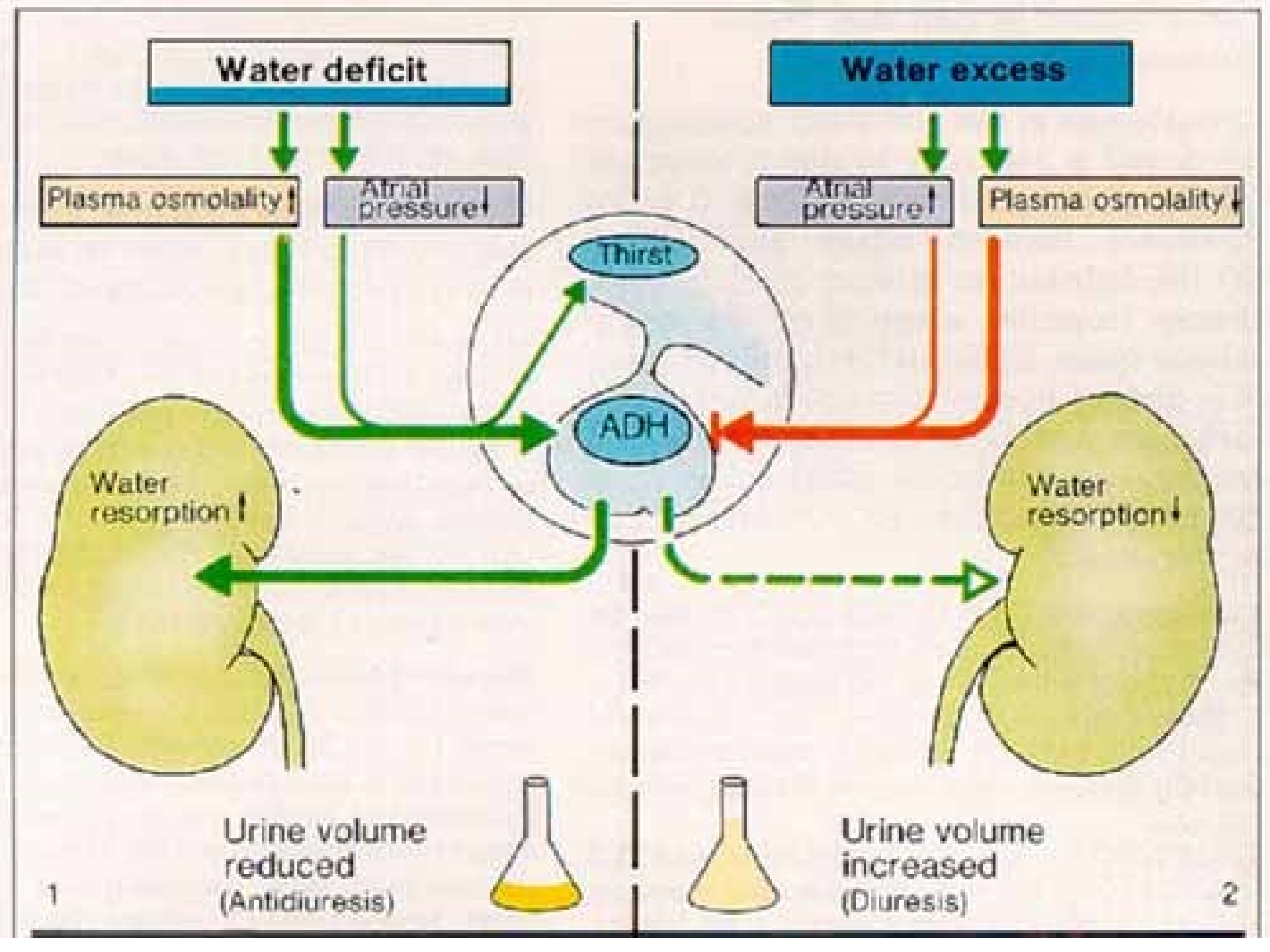
Hormonal regulation of diuresis

ADH

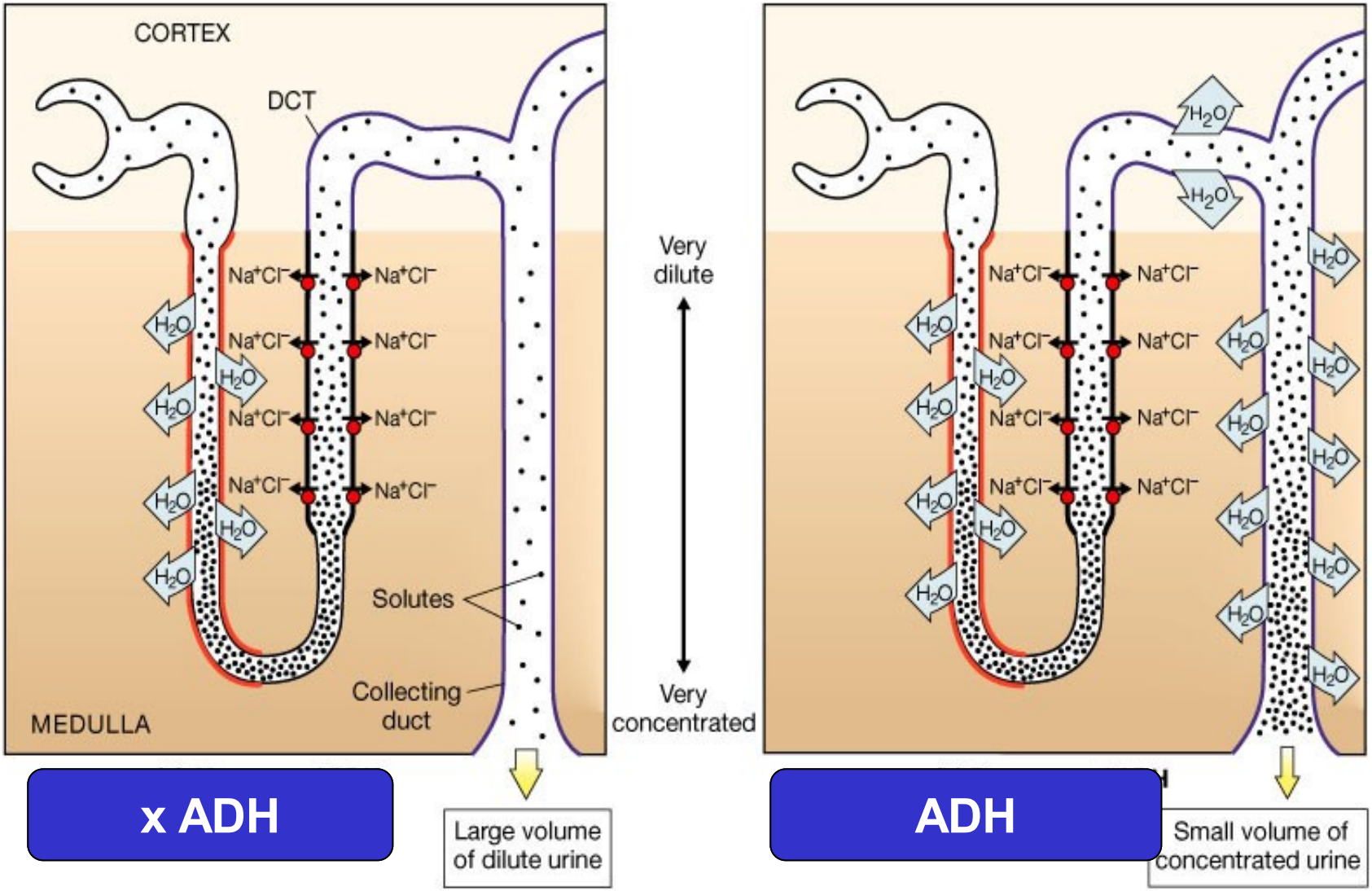
Regulating via V2 receptors selective water reabsorption in distal tubuli and collecting ducts

Negative feedback of ADH secretion




Water deficit
Water excess
Plasma osmolality ↑
Atrial pressure ↓
Atrial pressure ↑
Plasma osmolality ↓
Thirst
ADH
Water resorption ↑
Water resorption ↓
Urine volume reduced (Antidiuresis)
Urine volume increased (Diuresis)
1
2

Hormonal regulation of diuresis



Hormonal regulation of diuresis

ADH — **Diabetes insipidus**

= Syndrome of ADH deficiency

1. central (hypotalamic) DI

… ↓ ADH

(trauma and surgery 20 %, idiopatic 25 %, pituitary and hypothalamic tumors)

2. peripheral (nephrogenic) DI

… ↑ ADH

chronic renal failure

congenital abnormalities of ADH receptors...

Hormonal regulation of diuresis

ADH — **Diabetes insipidus**

Symptoms

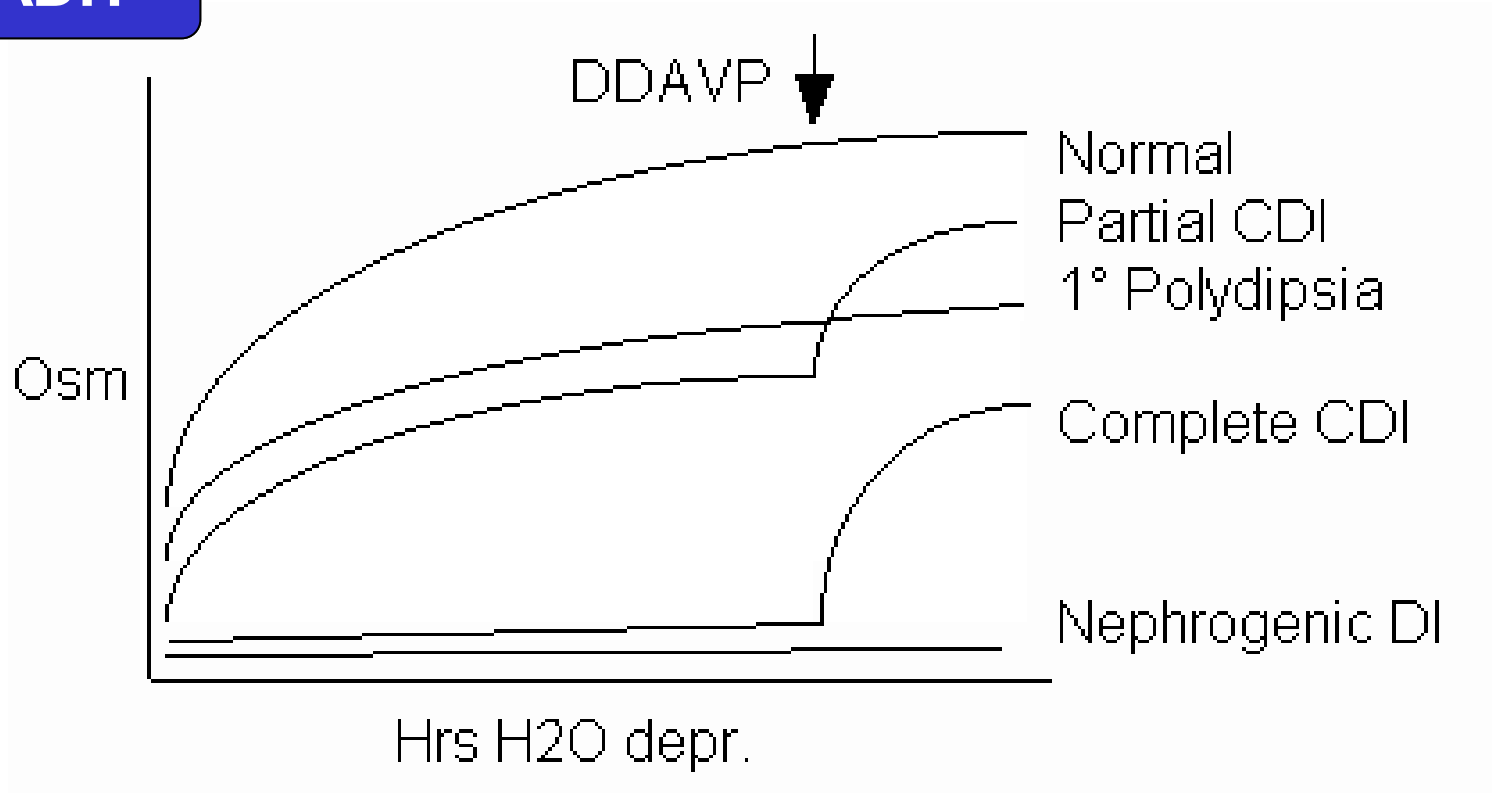
- polyuria – water diuresis (> 6 L / day)
- (secondary) polydipsia
- weight loss
- headache

Laboratory findings

- P-hyperosmolarity
- U-hypoosmolarity
- pathological results of concentration test (36 h; 12 + 4 h)

Hormonal regulation of diuresis

ADH



Concentration test + ADH

Hormonal regulation of diuresis

ADH

SIADH

= Syndrome of inadequate ADH secretion

Etiology

- **irritation of hypotalamic osmoreceptors (metastases)**
- **reflexive stimulation via n. vagus (bronchogenic ca)**
- **paraneoplastic production (small cell ca)**
- **carcinoid**

Symptoms

retention of water, solutes, edemas

Laboratory findings:

plasma hypoosmolarity
↓ Na, ↓ K, ↓ Cl

Hormonal regulation of diuresis

Maintenance of Na / K concentrations and extracellular volume

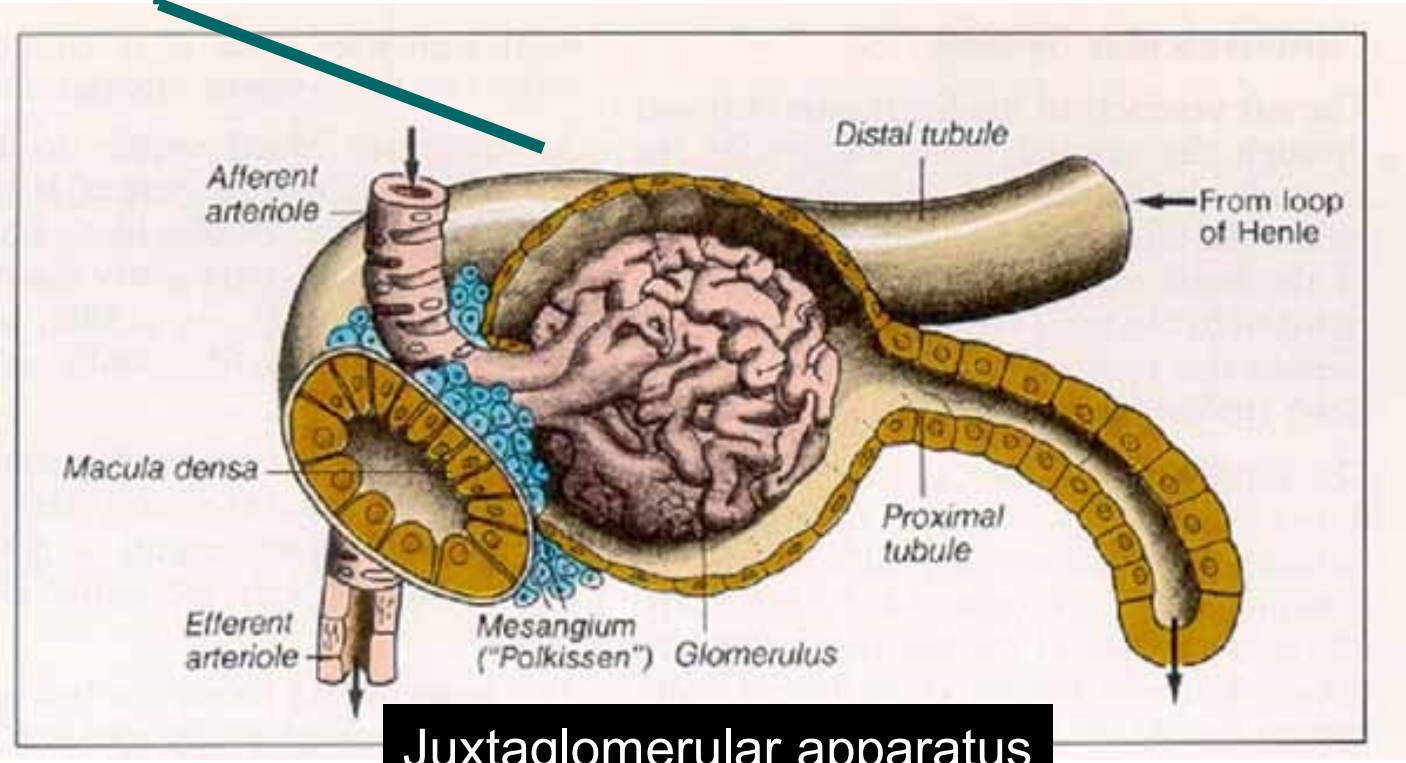
Stimulation of Na^+/K^+ATP-ase in proximal tubule

Reabsorption of Na^+

Secretion of K^+

Hormonal regulation of diuresis

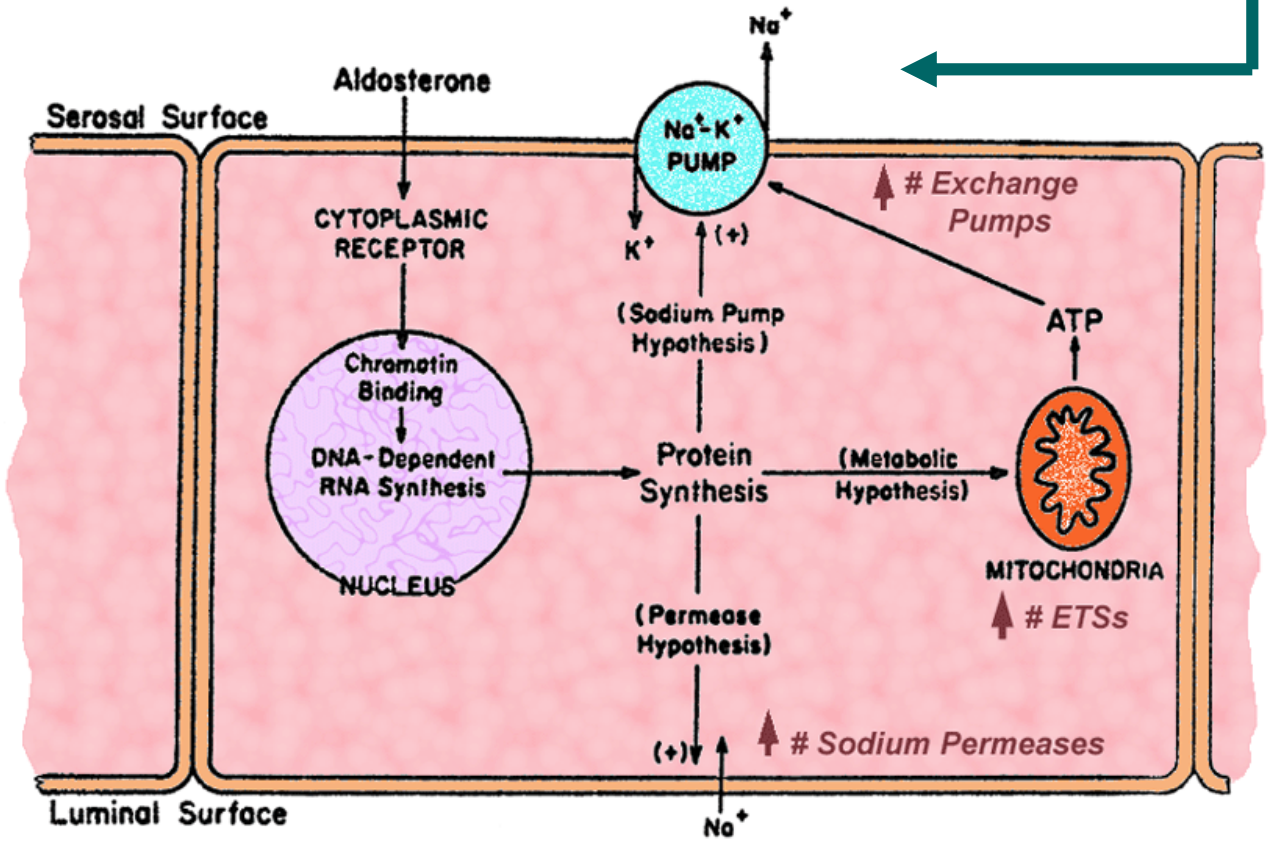
Renin → **Angiotensin** → **Aldosterone**



Juxtaglomerular apparatus

Hormonal regulation of diuresis

Renin → Angiotensin → Aldosterone



Hormonal regulation of diuresis

Addison´s syndrome, Addison´s disease

= syndrome of adrenocortical insufficiency

- **K^+ retention ... muscle weakness, myopathy, ECG, dyspepsy**
- **Na^+ loss ... osmotic diuresis ... dehydration ... hypotension, postural hypotension**
- **Hyperpigmentation (MSH from pituitary) x depigmentation (vitiligo)**
- **Hypoglycemia**

Hormonal regulation of diuresis

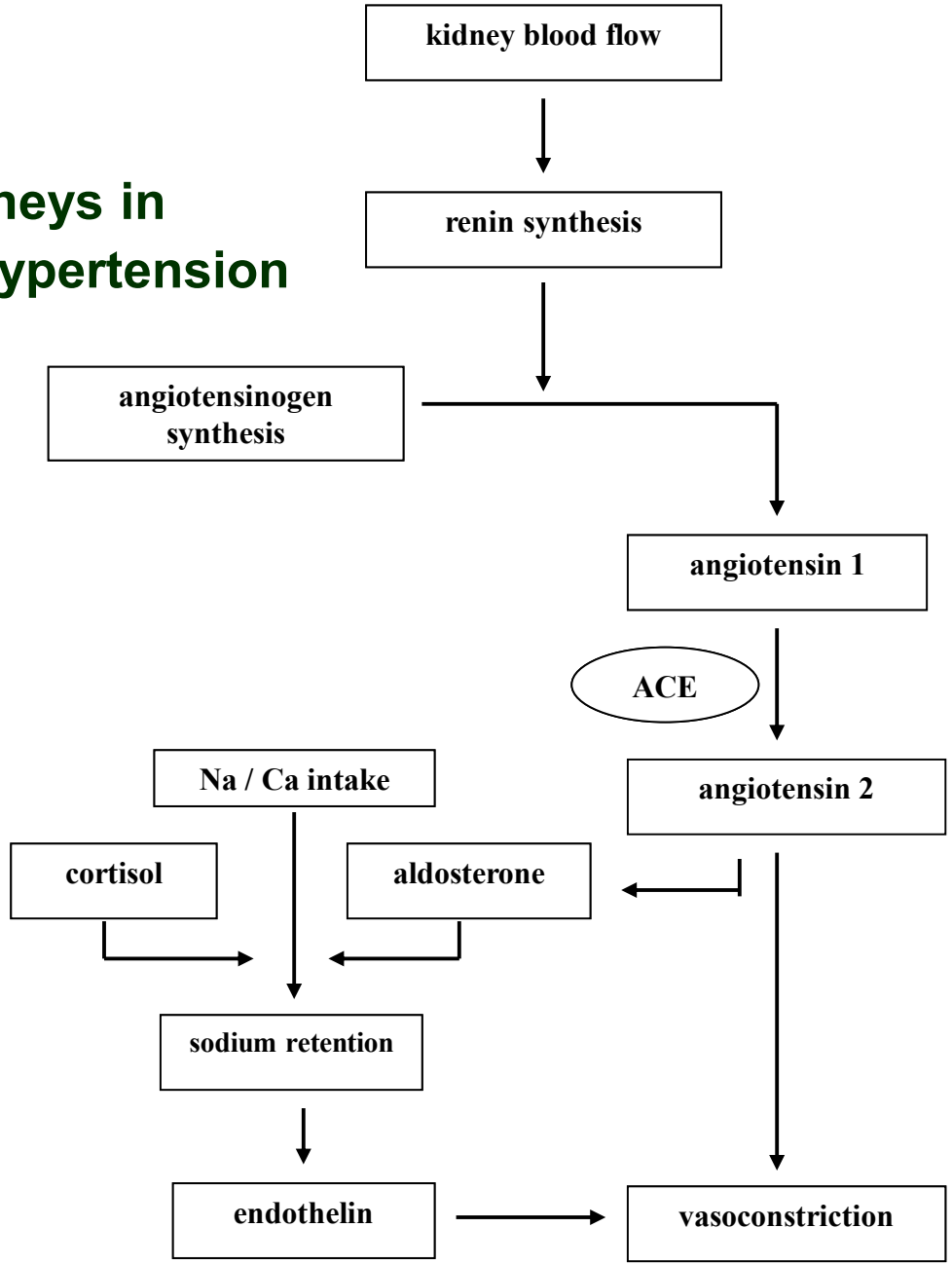
Primary / secondary hyperaldosteronism

Stimuli for renin synthesis:

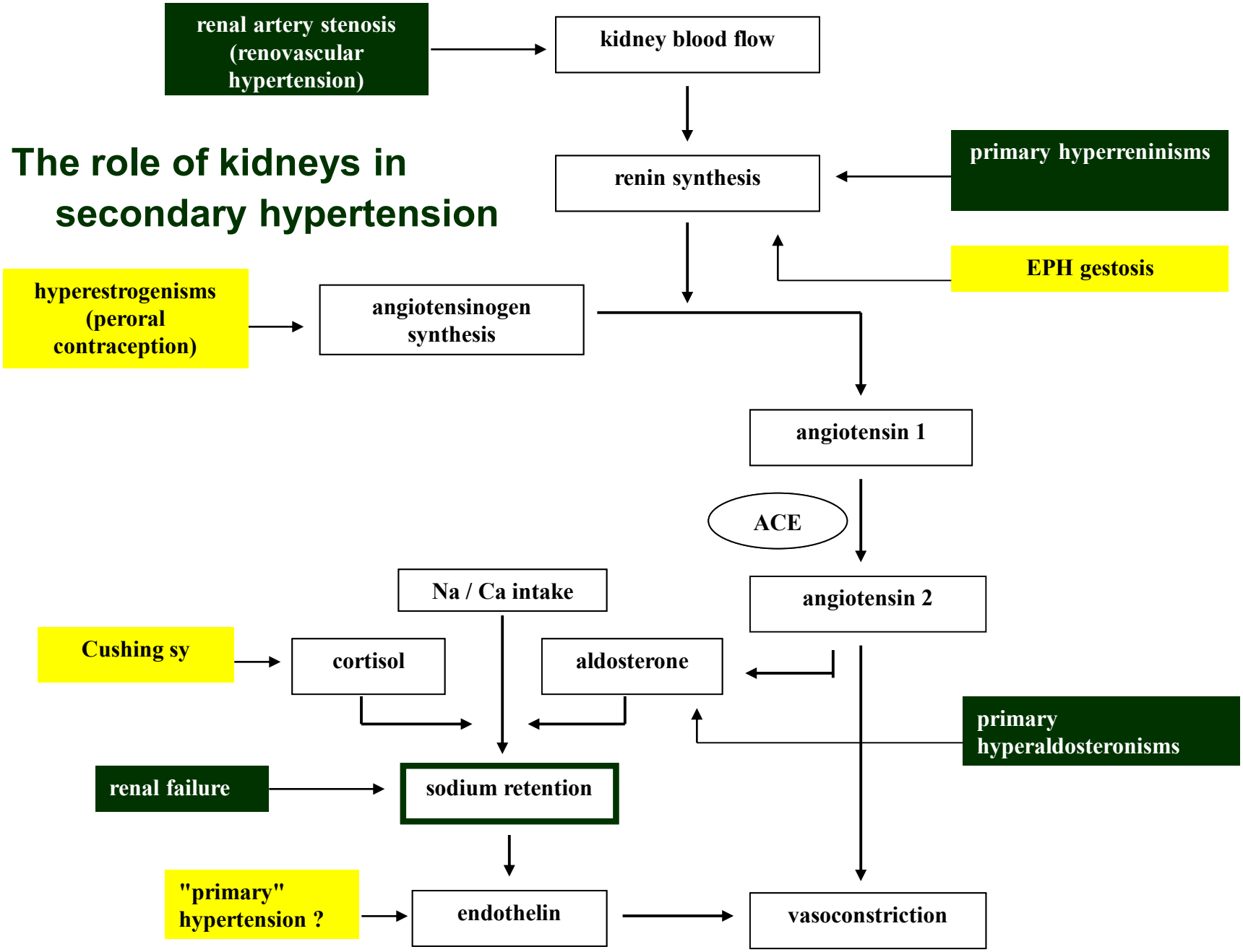
↓ kidney perfusion

↓ Na in proximal tubule

The role of kidneys in secondary hypertension



The role of kidneys in secondary hypertension



Hormonal regulation of diuresis

Natriuretic peptides

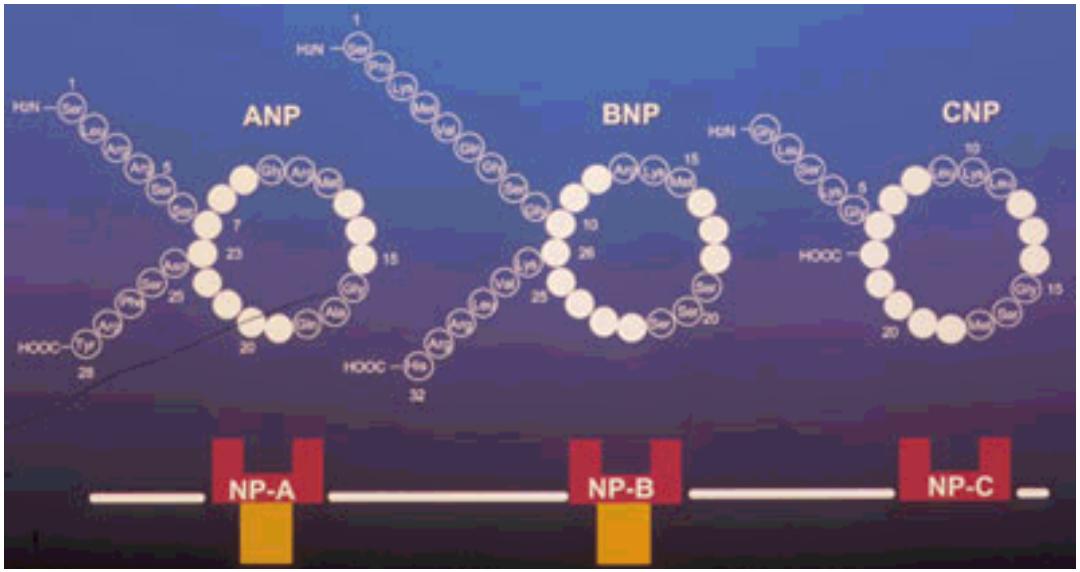
ANP

BNP

CNP

Natural antagonists of renin - angiotensin - aldosterone system.

Important role in water and mineral balance in patients in hemodynamic stress (e. g., cardiac failure).



Hormonal regulation of diuresis

Physiological effects:

- **vasodilation and hypotensive effect**
- **natriuresis and diuresis activation**
- **inhibition of sympathetic nervous system**
- **inhibition of pathol. actions responsible for hypertrophy and remodelation of heart ventricle and vessel wall**
- **positive effect on endothelial dysfunction in relation to atherosclerosis (including clothing cascade regulation and fibrinolysis and inhibition of platelet activities)**

Hormonal regulation of diuresis

ANP

BNP

CNP