Renal pathology

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Renal pathology seminar topics:

- Acute kidney injury & Chronic kidney injury, 1 seminar.
- Glomerulonephritis and nephrotic syndrome, 4 seminars.

Overview of todays seminar:

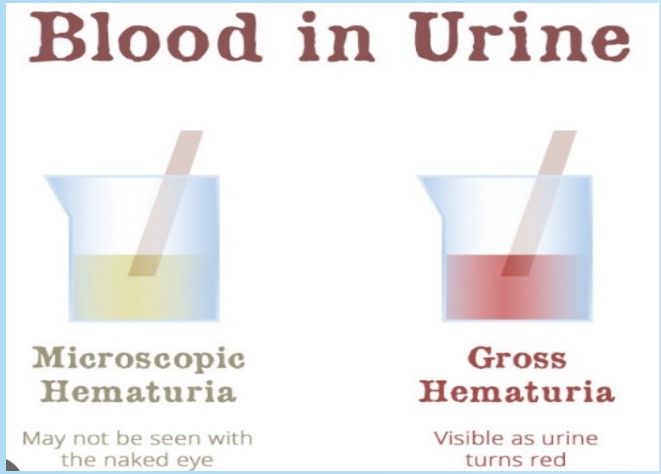
- Quick recap of properties and anatomy of the kidney.
- Acute & Chronic Kidney injury
- Nephritic and Nephrotic Syndrome

Properties of the kidney

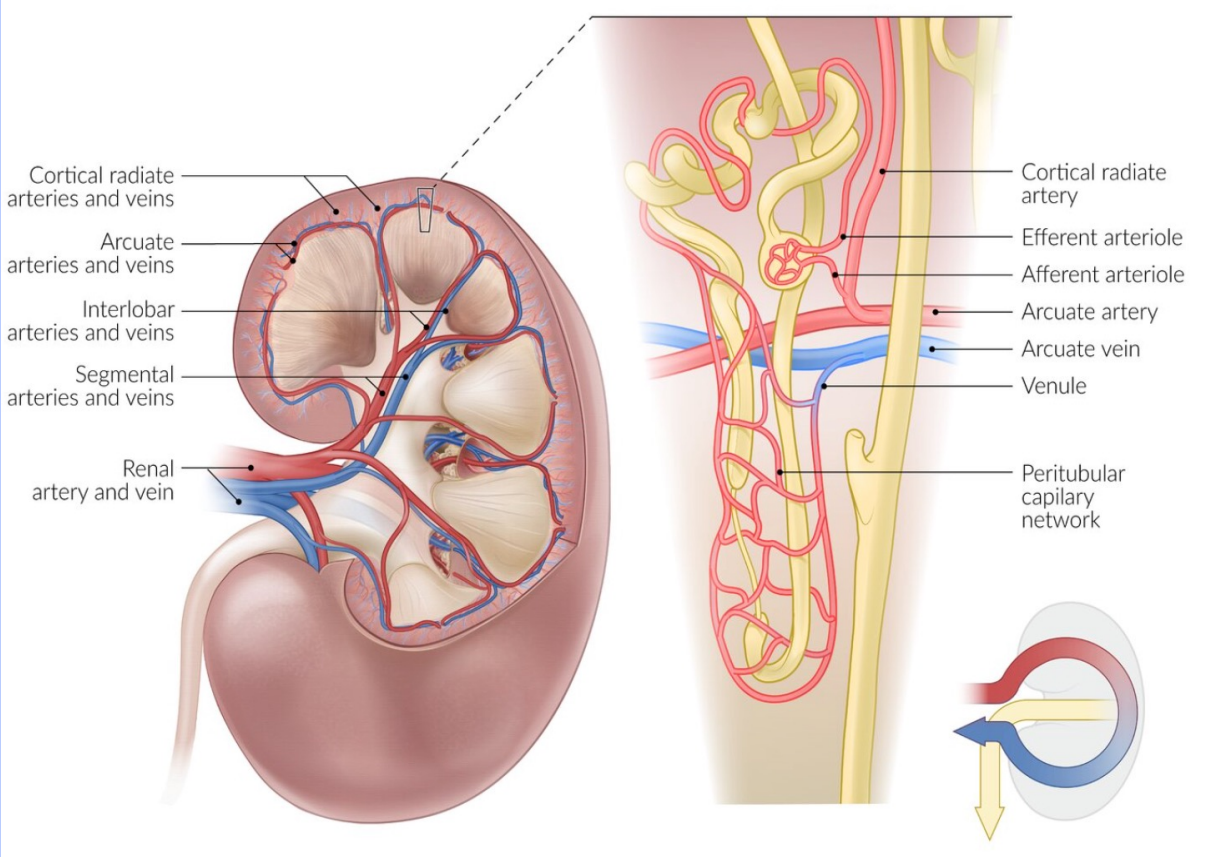
- **Filtration of blood:**
  - Excrete waste, excessive amounts of water and electrolytes
- **Regulation of blood**
  - pH, volume, pressure, osmolarity
- **Production:**
  - Hormones: Vitamin D and Erythropoietin.

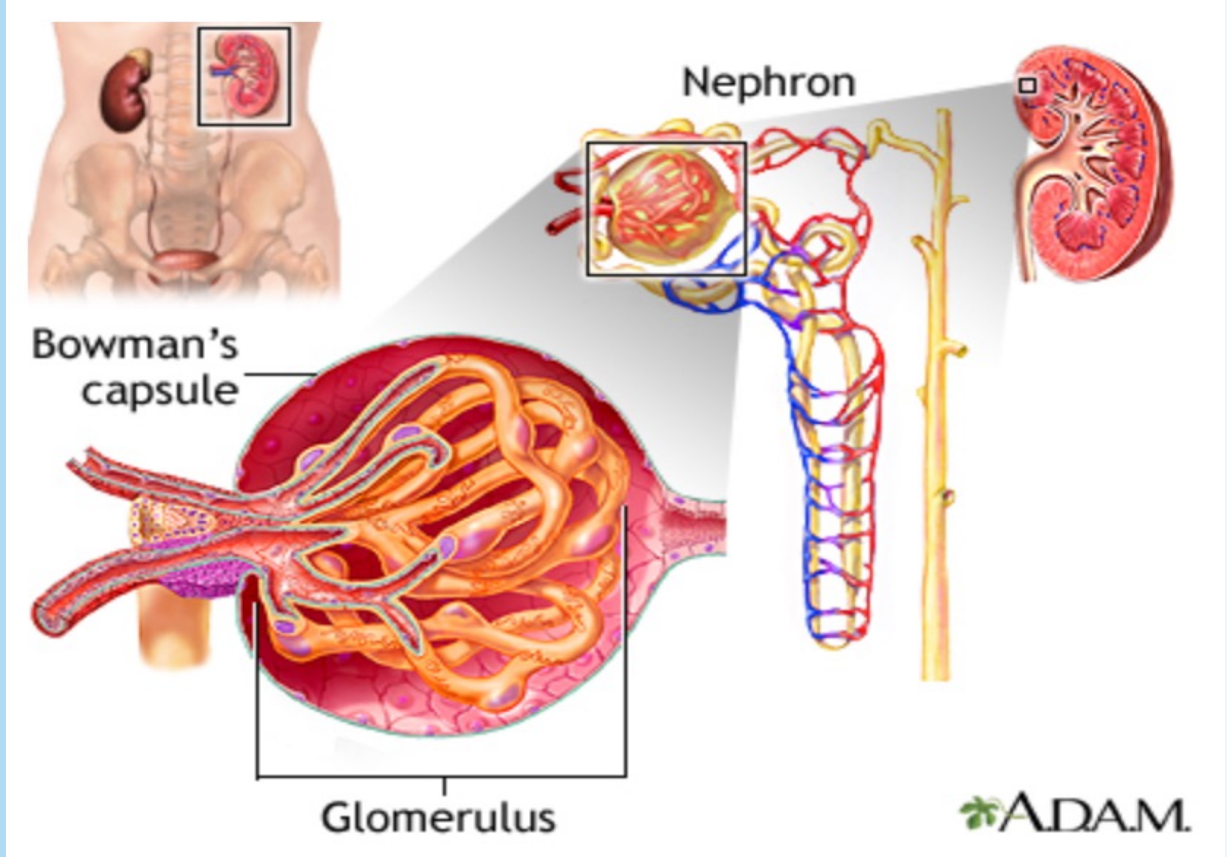
Typical signs of renal pathology:

- Hematuria
- Proteinuria
- Oliguria and Anuria
- Increased waste products in serum.



Anatomy recap

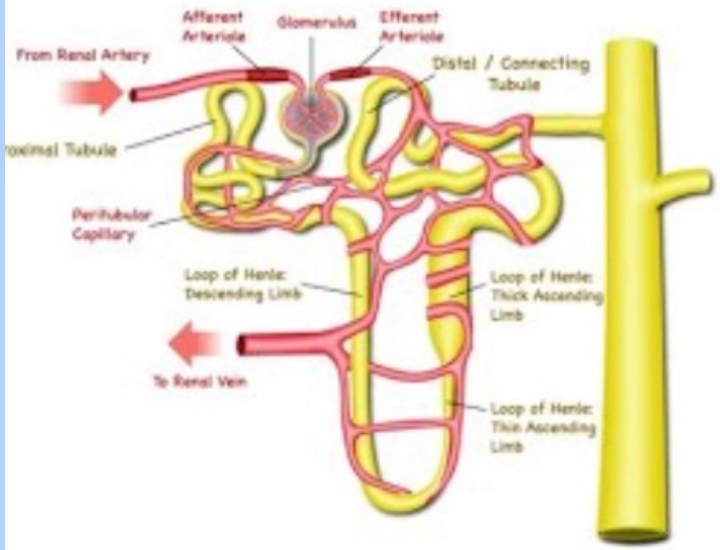


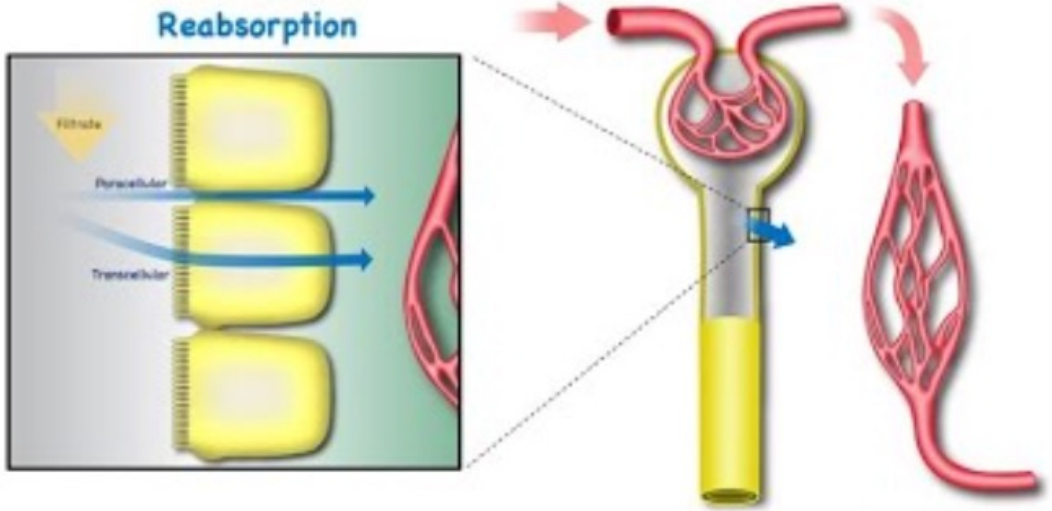


Each kidney consists of millions of nephrons, the functional filtration units, which produces urine.

Glomerulus is where the filtration process is initiated and is crucial for the functioning nephron.

The 4 Basic Renal Processes





Amount Excreted (4) = Amount Filtered (1) − Amount Reabsorbed (2) + Amount Secreted (3)

Acute Kidney Injury

Sudden and rapid decline of renal function. (*Within 48 hours acc. ppt*).
Leads to deterioration of filtrating & excretining properties of the kidney.

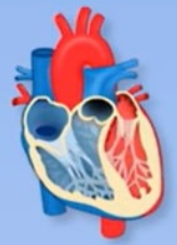
Diagnostic approach:
- Significant increase in *serum creatinine* (and blood urea nitrogen)
- Decrease in *urine output*

First clinical feature:
- Oliguria and Anuria

Creatinine is produced in the body at a constant rate and is freely filtered and not reabsorbed. Thus, it is a convenient marker for estimation of GFR.

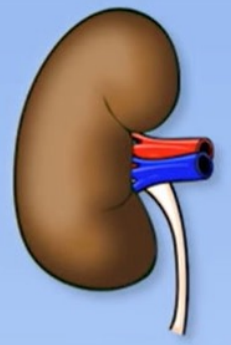
Further injury will lead to a decrease in endocrine functioning and regulatory functioning of the kidney.

Acute Kidney Injury (AKI)
Prerenal vs. Intrarenal vs. Postrenal Paradigm



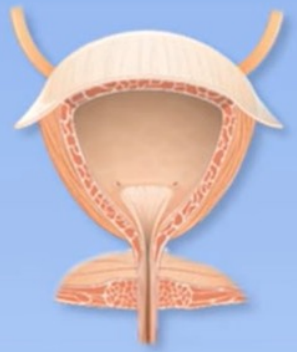
Prerenal

- Dehydration*
- Heart failure
  (a.k.a. cardiorenal syndrome)
- Liver failure
  (a.k.a. hepatorenal syndrome)



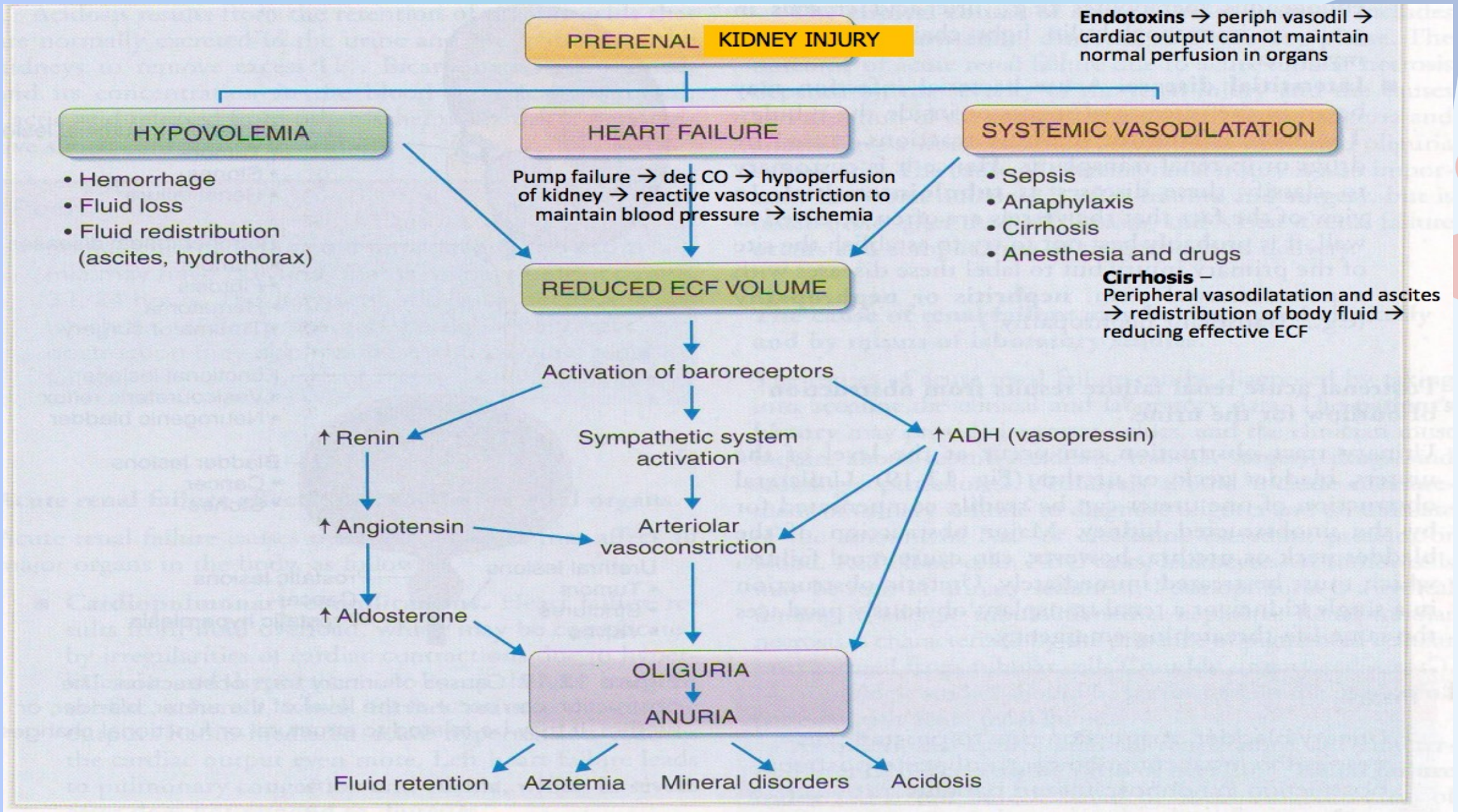
Intrarenal

- Intrinsic renovascular disease
  - Hypertensive emergency
  - Small vessel vasculitis
  - TTP / HUS
- Glomerular disease
  - Post-infectious glomerulonephritis
- Tubulointerstitial disease
  - Acute tubular necrosis (ATN)*
    (causes: sepsis, meds, contrast, rhabdo, prolonged prerenal AKI)
  - Acute interstitial nephritis (AIN)



Postrenal

- Ureteral obstruction
  (usually requires bilateral obstruction)
- Neurogenic bladder
- Urinary tract infection
- Medications
- Benign prostatic hypertrophy (BPH)


PRERENAL KIDNEY INJURY
Endotoxins → periph vasodil → cardiac output cannot maintain normal perfusion in organs
HYPOVOLEMIA
HEART FAILURE
SYSTEMIC VASODILATATION
• Hemorrhage
• Fluid loss
• Fluid redistribution (ascites, hydrothorax)
Pump failure → dec CO → hypoperfusion of kidney → reactive vasoconstriction to maintain blood pressure → ischemia
• Sepsis
• Anaphylaxis
• Cirrhosis
• Anesthesia and drugs
Cirrhosis – Peripheral vasodilatation and ascites → redistribution of body fluid → reducing effective ECF
REDUCED ECF VOLUME
Activation of baroreceptors
↑ Renin
Sympathetic system activation
↑ ADH (vasopressin)
↑ Angiotensin
Arteriolar vasoconstriction
↑ Aldosterone
OLIGURIA
ANURIA
Fluid retention
Azotemia
Mineral disorders
Acidosis

CKD – Chronic kidney disease

- Defined as an abnormality of kidney structure or function that persists for > 3 months.

Decreased excretory, endocrine and regulatory functioning of the kidney.

- Most common causes of CKD: Diabetes, hypertension and glomerulonephritis.
- CKD can lead to severe cardiovascular & pulmonoligical conditions, but also neurological & hematological conditions.

CKD - pathogenesis

Irreversible loss of nephrons

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Healthy nephrons compensate this loss by increase in their dimension via hyperperfusion

↓

Distension of afferent and efferent vessels of the nephrons

↓

Inc renal perfusion and hyperfiltration (a kind of „hypertension" at the level of the individual nephron)

↓

Hemodynamic overload of nephrons with their impairment

↓

Fibrosis, scarring → glomerulosclerosis

↓

Progression of nephron destruction and loss

↓

Uremia

(complex of symptoms and signs that occur when residual renal function is inadequate)

CKD – Clinical manifestations

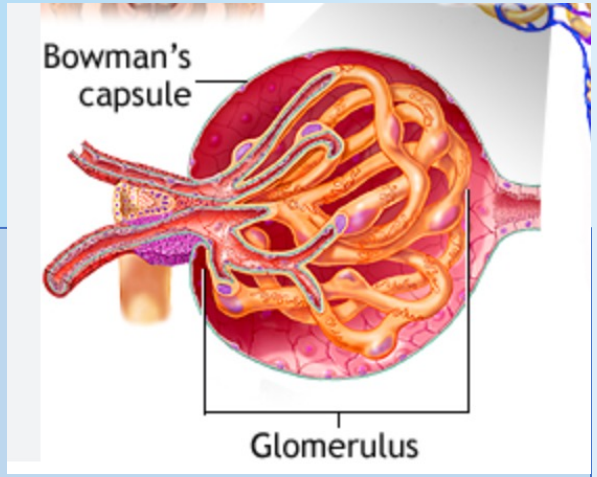
- **Na^+ balance and volume status**
  - Loss of kidney ability to Na^+ and water excretion → Na^+ and water excess
    - Congestive heart failure
    - Hypertension
    - Ascites
    - Peripheral edema
    - Weight gain
    - Hyponatremia

CKD – Clinical manifestations

- **Cardiovascular and pulmonary abnormalities**
  - Congestive heart failure
  - Pulmonary edema } a consequence of Na/water overload
  - Hypertension
    - a consequence of Na/water overload and hyper-reninemia
  - Pericarditis
    - irritation and inflammation of the pericardium by uremic toxins
  - Inc risk of
    - myocardial infarction
    - stroke
    - peripheral vascular disease

Nephrotic Syndrome:	Nephritic syndrome:
- is a collection of signs and symptoms indicating damage to the glomerular filtration barrier	- Is collection of signs and symptoms due to glomerular capillary damage due to Inflammation.

The problem is within the glomerulus!



Categories of disorders resulting in glomerular disease:

- Acute glomerulonephritis
- Rapidly progressive glomerulonephritis
- Chronic glomerulonephritis
- *Nephrotic syndrome :* Minimal change disease & Membranous nephropaty.
- Asymptomatic urinary abnormalities

Clinical syndrome:	Nephrotic	Nephritic
Basic patophysiology:	Structural damage of glomerular filtration barrier	Inflammatory response within Glomeruli.
Edema	Systemic and generalized	Mild
Blood pressure	Normal / Slightly elevated.	Markedly Raised
Proteinuria	Massive > 3.5g per day	Mild < 3.5g per day
Urine analysis findings:	Lipiduria,	Hematuria with RBC Casts, Oliguria
Serum findings	Hyperlipidemia	Azotemia
Conditions:	Minimal change disease, Membranous nephropathy	Acute Glomerulonephritis, Rapid progressive GN, IgA nephropathy/Bergers syndrome.

Nephrotic Syndrome		Nephritic Syndrome
• Low serum albumin (<30g/L) • Proteinuria (>3.5g/day) • Oedema • Dyslipidaemia • Hypercoagulability (loss of antithrombin III) • Reduced immunity (loss of immunoglobulins)	**Characteristics**	• Haematuria • Hypertension • Mild proteinuria (<3.5g/day) • Mild oedema • Temporary oliguria and uraemia
Peripheral oedema (adults), facial oedema (children), frothy urine, fatigue, recurrent infections	**Symptoms**	Haematuria (frank/microscopic), mild oedema, oliguria, signs of uraemia (fatigue, pruritus, nausea)
++++	**Proteinuria**	++
May or may not be present	**Haematuria**	+++
Absent	**Red blood cell casts**	Present

• Minimal change disease (most common in children)
• Membranous nephropathy (most common in adults)
• Focal segmental glomerulosclerosis
	Causes	• IgA nephropathy
		• Post-streptococcal glomerulonephritis
		• Rapid progressive glomerulonephritis (RPGN):
		  • Anti-GBM glomerulonephritis
		  • ANCA Vasculitis

Nephritic syndrome pathogenesis

Inflammation -> Cytokine release -> Glomerular capillary damage

Porous glomerular basement membrane -> leakage of RBC and some proteins

- Hematuria: RBC casts
- Proteinuria (<3.5g/24)
- Oliguria : inflammatory infiltrates reducie fluid movement across the membrane
- Azotemia : Inflammation prevents sufficient filtering and excretion of urea.
- Salt retention: -> Intravascular volume expansion -> Hypertension and edema.

Nephrotic Syndrome pathogenesis

Structural and physiochemical alteration in glomerular capillary wall

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Permeability to plasma proteins

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Massive proteinuria and hypoalbuminemia

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Decreased oncotic pressure

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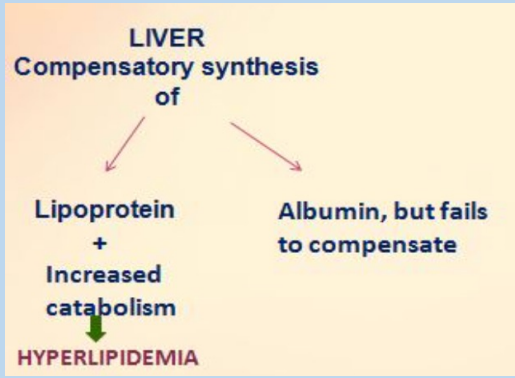
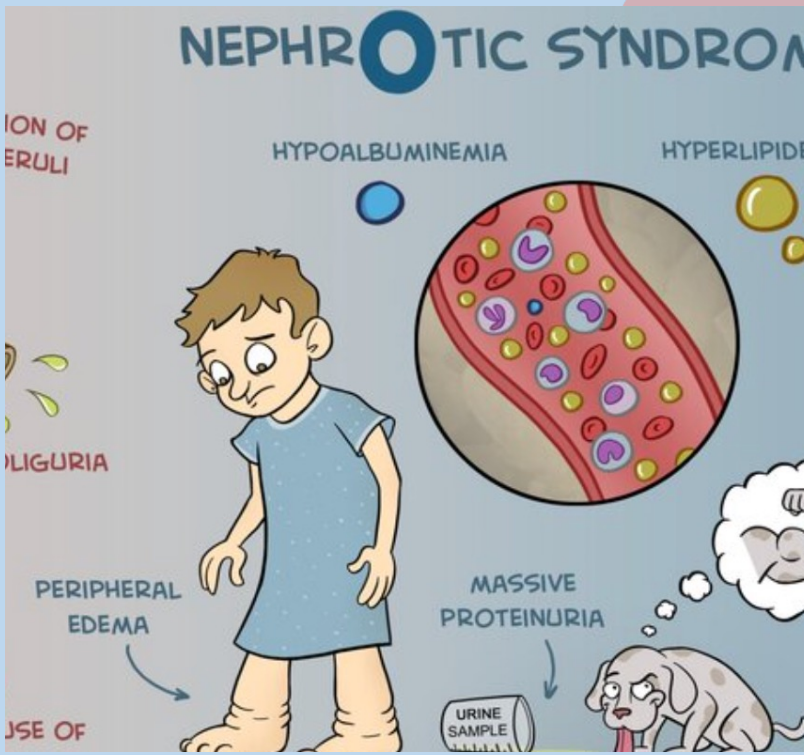
Fluid escapes the vessels : increased fluid in ISF → EDEMA





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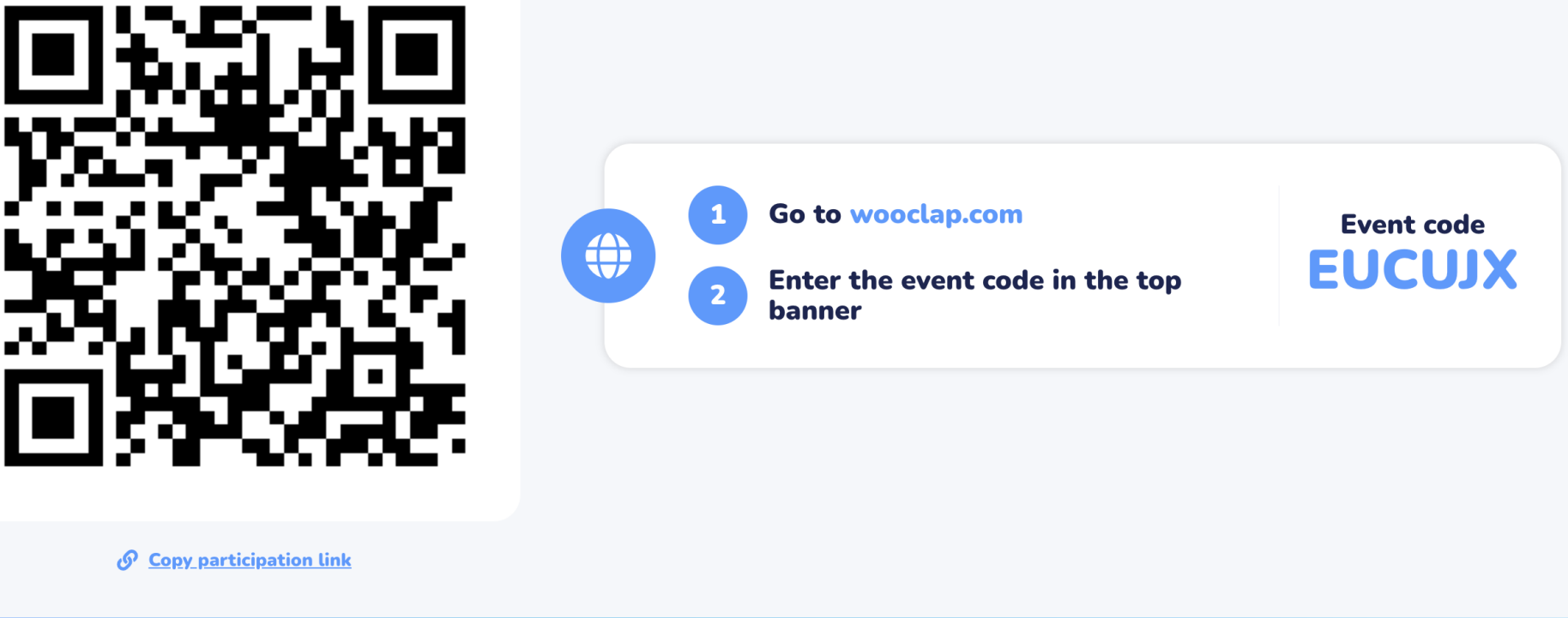
WHAT TIME IS IT?

ITS QUUUUUIZ TIME



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Thank you!