Glomerular disease

Nephrotic Vs. Nephritic

Presented by: Sarah Al Qubaiban

Objectives

- Anatomy of glomerulus.
- Proteinuria and its types.
- Glomerulonephritis.
- Nephrotic syndrome (briefly).
- Nephritic syndrome (briefly).

Glomerular Filtration Barrier (GFB)

- GFB is composed of three layers:
  - **The endothelial layer** of the glomerulus capillaries
  - **The basement membrane**
  - **The epithelial layer** of bowman capsule
    - The visceral part which contains podocytes

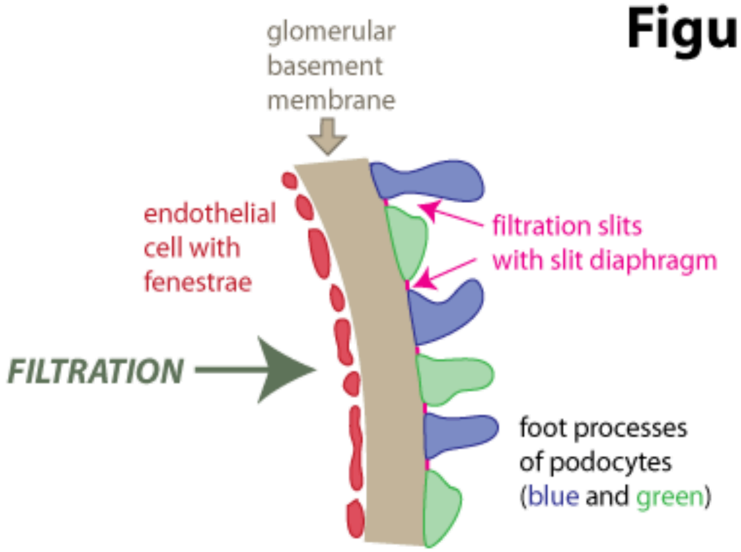
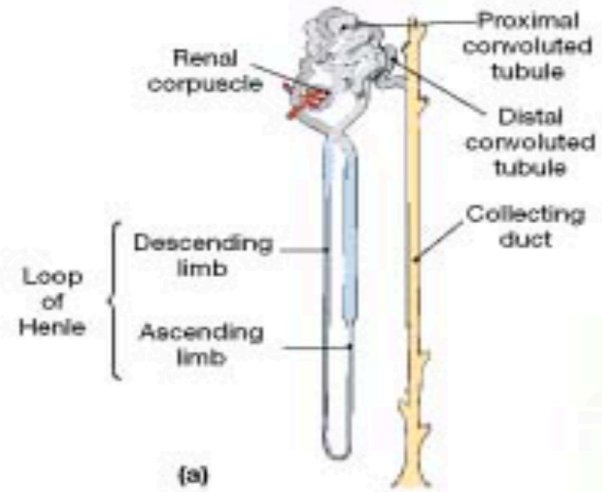
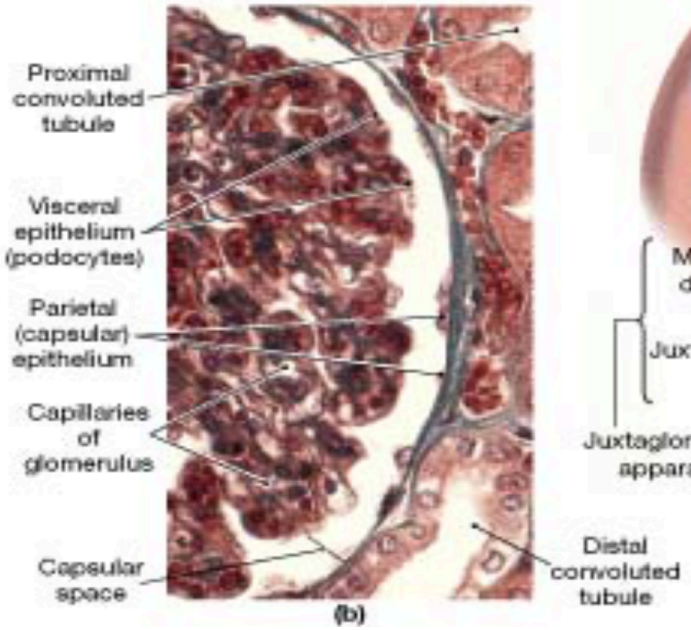


Figure 2





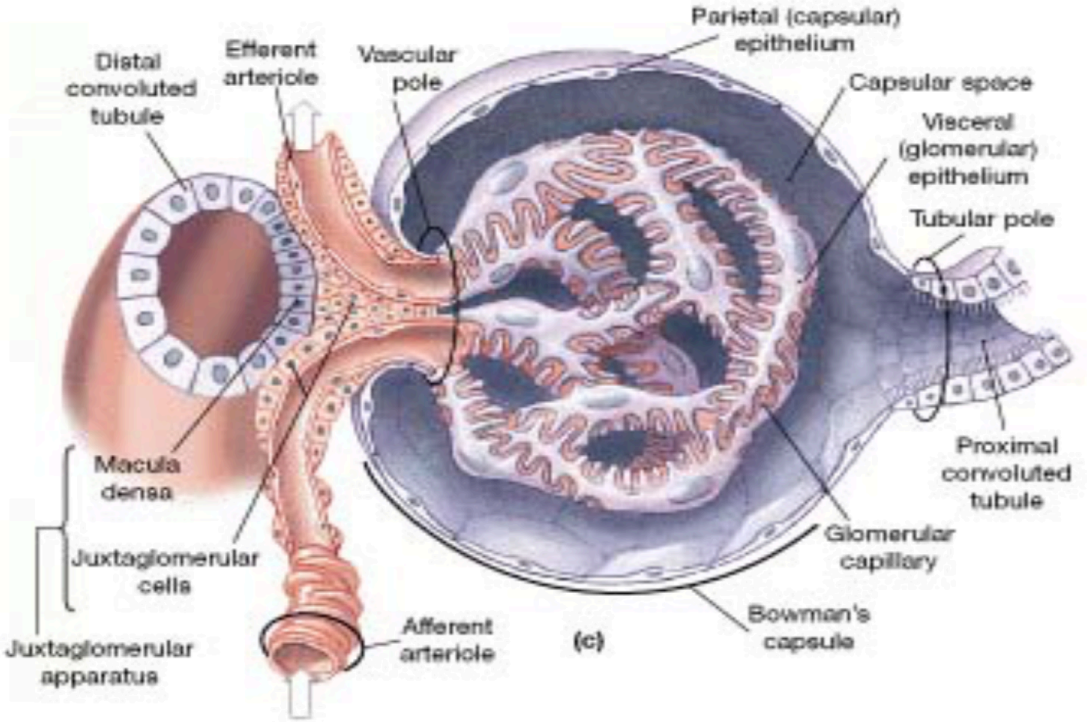
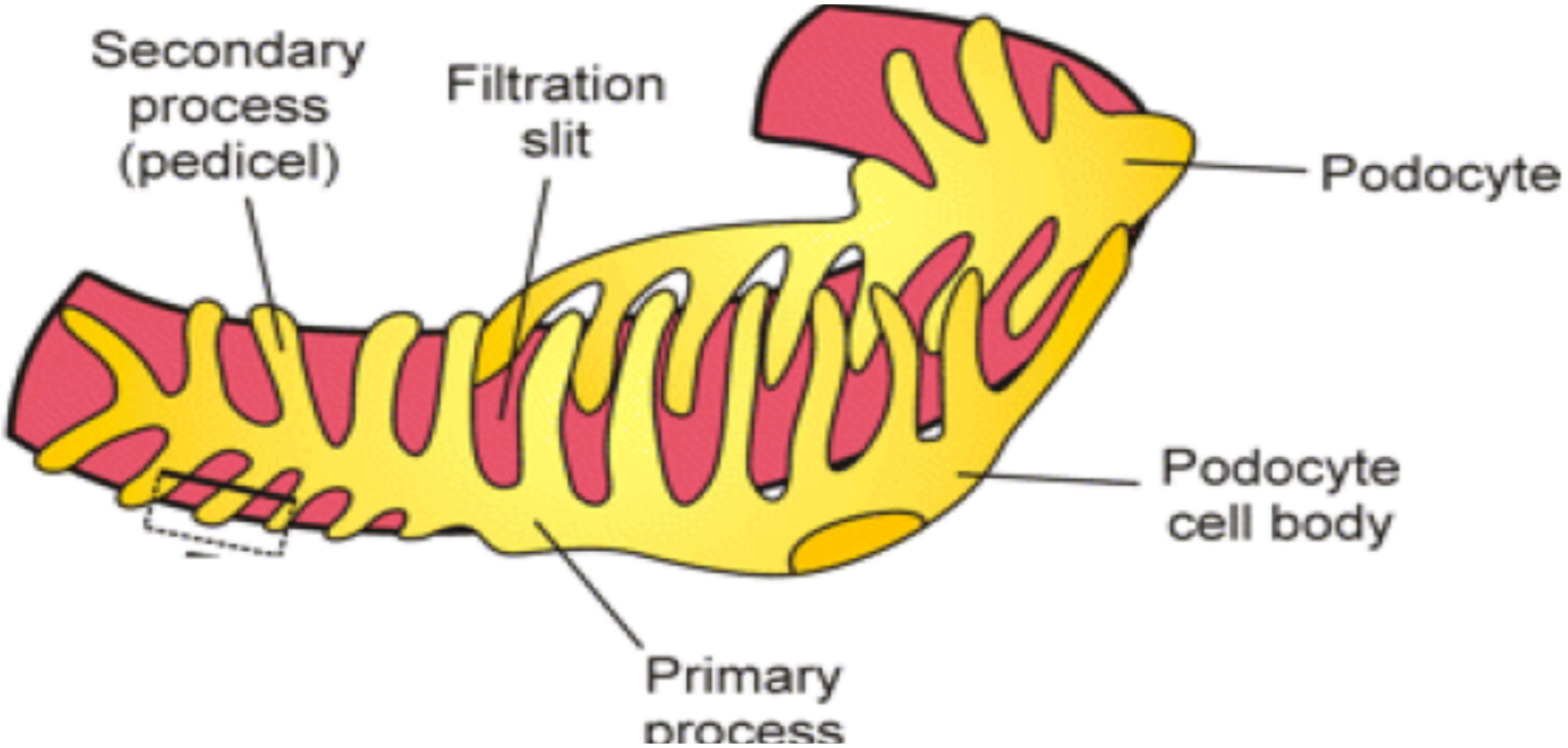


FIGURE 26-5 The Renal Corpuscle. **(a)** A more realistic view of a juxtamedullary nephron, showing the coiling of the renal tubule. **(b)** Micrograph of a renal corpuscle, showing a portion of the glomerular capillary network. (LM × 1120) **(c)** The renal corpuscle, showing important structural features.

Properties of these layers

- **Endothelial layer**
  - Fenestrated cells
  - Contain pores 60 – 100 nm
- **Glomerular basement membrane**
  - Nega7vely charged because of Heparan-sulfate proteoglycans
  - Thickness 321 nm*
- **Epithelial layer**
  - Contains slits which are the gaps between the inter-digita7on of the podocytes, size 20-30 nm
  - Niphrin and podocin are major component of the slits

– *hRp://www.ncbi.nlm.nih.gov/pubmed/16366093

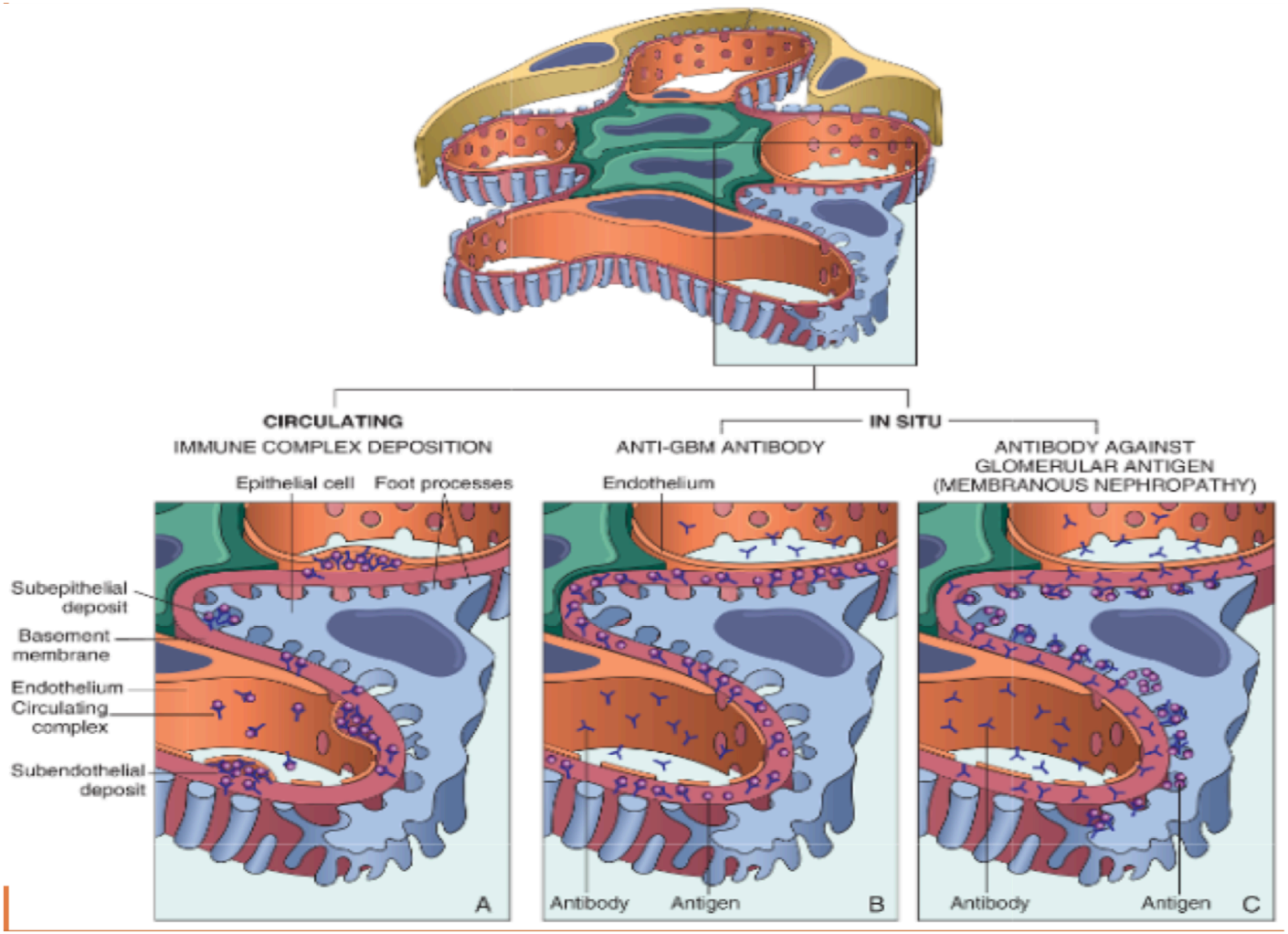

Secondary process (pedicel)
Filtration slit
Podocyte
Podocyte cell body
Primary process

- Any molecule that has to inter the tubules, it needs to pass through the
  - Charge barrier
  - Physical (size) barrier
    - o <4nm: all charged molecules pass.
    - 4-8: only + charge pass.
    - >8 : no filtration.

Glomerulonephritis

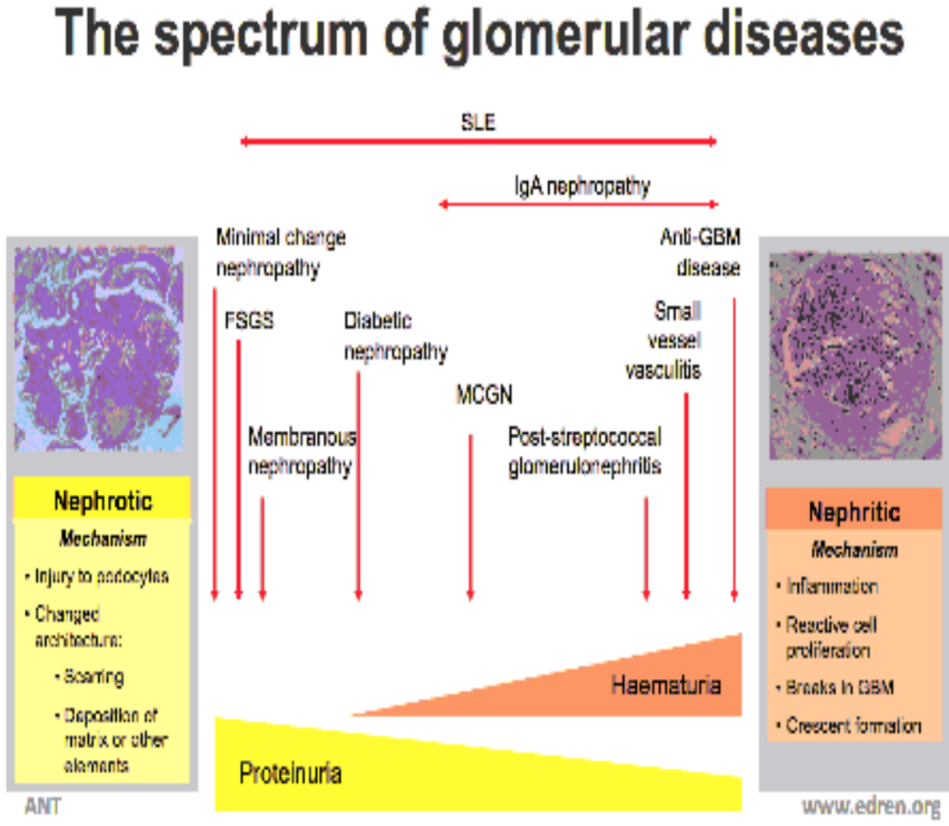
- Classified as
  - **Hereditary** (e.g. Alport's and Fabry's syndromes)
  - **Primary** (most common): disease process originates from the glomerulus
  - **Secondary** to systemic diseases: e.g. systemic lupus erythematosus (SLE), diabetes mellitus, bacterial endocarditis.

Primary GN

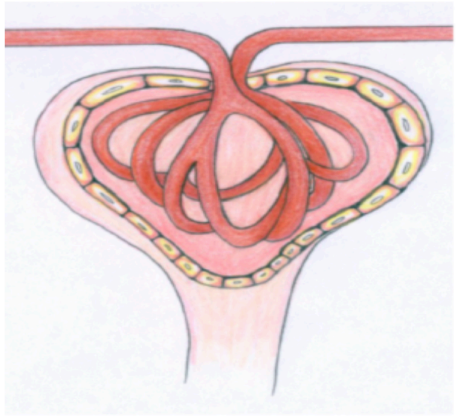

CIRCULATING
IMMUNE COMPLEX DEPOSITION
IN SITU
ANTI-GBM ANTIBODY
ANTIBODY AGAINST
GLOMERULAR ANTIGEN
(MEMBRANOUS NEPHROPATHY)
Epithelial cell
Foot processes
Endothelium
Subepithelial deposit
Basement membrane
Endothelium
Circulating complex
Subendothelial deposit
Antibody
Antigen
Antibody
Antigen
A
B
C

Presentation of GN

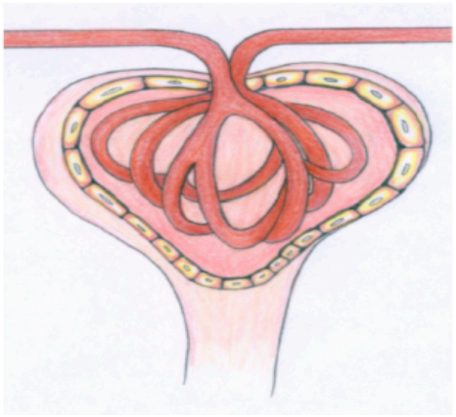
- Asymptomatic proteinuria
- Asymptomatic heamatoureia
- Nephrotic syndrome
- Nephritic syndrome
- Rapidly progressive GN
- Chronic kidney disease



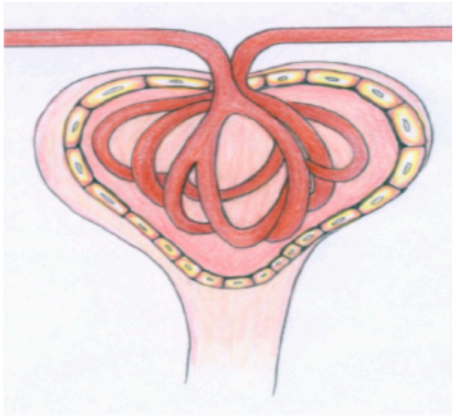
Proteinuria



Selective proteinuria



Non-selective proteinuria
albumen urea Less than 3.5
Sub-nephrotic range



Non-selective proteinuria
more than 3.5
Nephrotic range

Proteinuria cnt.

- Types
  - Selective: only albumin
  - Non-selective: albumin + globulin
    - Sub-nephrotic range: ↓3.5\day
    - Nephrotic range: ↑3.5\day
- pt. complains of frothy urine because of high protein level.
- Other symptoms appear.

Proteinuria

Hypoproteinemia

- Liver compensates hypoprotenuria by synthesizing new proteins including : LDL, IDL, VLDL, Triglycerides

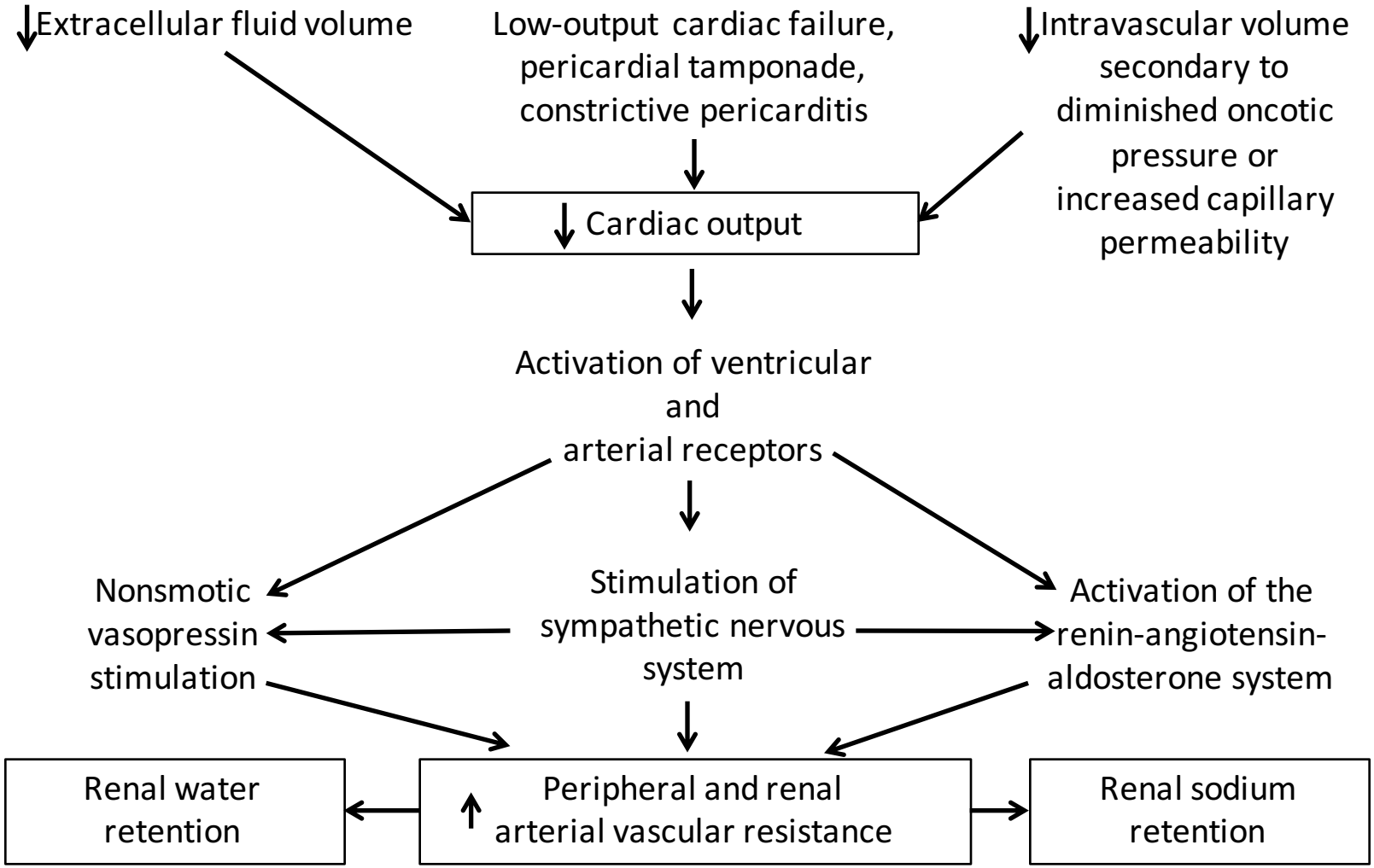
Dyslipidemia

- Other causes of HL:
  - ↓ level of lipoprotein lipase which aids the breakdown of lipids.

Lipiduria

- If HL is chronic.
- PCT cell will uptake the fat and form lipoid nephrosis , later these cells become dysfunc7onal and shed with urine.

- Despite the production of protein, it is still leaking into the urine.
- Hydrostatic & oncotic pressure disturbed
- Fluid leaks out to the interstitiam
- Hypovolemia develops
- Renin-Angiotensin-System will be activated & ADH will be produced in large amount because of ↑ in the osmolality which will be sensed by the hypothalamus as will as aldosterone
- Protein concentration is still low so more edema will develop.


↓Extracellular fluid volume
Low-output cardiac failure, pericardial tamponade, constrictive pericarditis
↓Intravascular volume secondary to diminished oncotic pressure or increased capillary permeability
↓ Cardiac output
Activation of ventricular and arterial receptors
Nonsmotic vasopressin stimulation
Stimulation of sympathetic nervous system
Activation of the renin-angiotensin-aldosterone system
Renal water retention
↑ Peripheral and renal arterial vascular resistance
Renal sodium retention

- NEPHROTIC SYNDROME triad:
  - Proteinuria
  - Edema
  - Hyperlipidemia

NEPHROTIC SYNDROME: is clinico-pathological condition which develops when there is significant damage to the glomeruli leading to proteinuria >3.5g\day.

Causes of Nephrotic syndrome

Fig. 2.11 Summary of types of glomerular disease and their clinical presentation.

Clinical presentation	Primary glomerular cause	Secondary cause
Nephrotic syndrome	Minimal change disease	HSP SLE
	Membranous glomerulonephropathy	Tumour amyloid
	membranoproliferative GN	Diabetes mellitus drugs (e.g. penicillamine, gold)
	focal segmental glomerulosclerosis	Bacterial endocarditis congenital nephrotic syndrome

- **Complications**
  - Hypercoagulable state
    – Loss of an7-thrombin 3
    – Increase in blood concentra7on and thus decrease the flow
    – Increase in plasma lipid will irritate platelets and the vessels walls
  - Immunosuppression • Hyperlipidemia
  - Hypertension
  - Edema
    – Generalized edema(anasarca) which start peri-orbital then in the dependent areas then allover the body.
  - Iron deficiency Anemia
    – Leak down of transferrin into urine

Investigation

- Urinalysis
- Urine sediment examination
- Urinary protein measurement
- Serum albumin
- Serologic studies for infection and immune abnormalities
- Renal ultrasonography
- Renal biopsy

How to manage NS

- Usually management is ***symptomatic + treating the underlying cause if possible***.
- Symptomatic management will include:
  - Blood pressure control
  - Reduction of proteinuria, (ACE) inhibitors
  - Control of hyperlipidemia
  - Anticoagulation if hypercoagulable
  - Diuretics if the ptx complaining of edema

Nephritic syndrome

- Due to severe glomerular injury;
- **Hematuria**
  - RBC cast
  - Dysmorphic RBS
- Oliguria ↓400ml due to decrease in the GFR
- Increase in blood pressure → RAS because decrease in kidney perfusion
- azotemia
- Kidney enlargement
- Proteinuria but less than nephro7c syndrome because the total filtra7on is reduced.

Causes of nephritic syndrome

Fig. 2.11 Summary of types of glomerular disease and their clinical presentation.

Clinical presentation	Primary glomerular cause	Secondary cause
Acute nephritic syndrome	Post-streptococcal GN non-streptococcal GN rapidly progressive GN focal proliferative GN mesangial IgA GN	SLE Microscopic polyangiitis Wegener's granulomatosis

Nephrotic vs Nephritic

eodema	heamatouria
Nephrotic range protienuria	Non-nephrotic range protienuria
dyslipidemia	oligouria
No cellular inflamatory reaction	Cellular inflamatory reaction
Immune complex deposition	Immune complex deposition

Summary

- **The filtration barrier, its components and properties.**
  - ✓ Charge barrier
  - ✓ Size barrier
- **Proteinuria and its types**
  - ✓ Selective
  - ✓ Non- selective
- **Glomerular diseases**
  - ✓ Primary
  - ✓ Secondary
  - ✓ Hereditary
- **Nephrotic and nephritic syndromes**
  - ✓ Clinical presentation
  - ✓ Pathogenesis
  - ✓ Common causes
  - ✓ Investigations and management

References

- Dr. Najeeb lectures
  - Nephtotirc vs. nephritic
- Crash course renal and urinary system

For any questions or comments please contact us at:

info@letstalkmed.com