Glomerular membrane and its clinical importance

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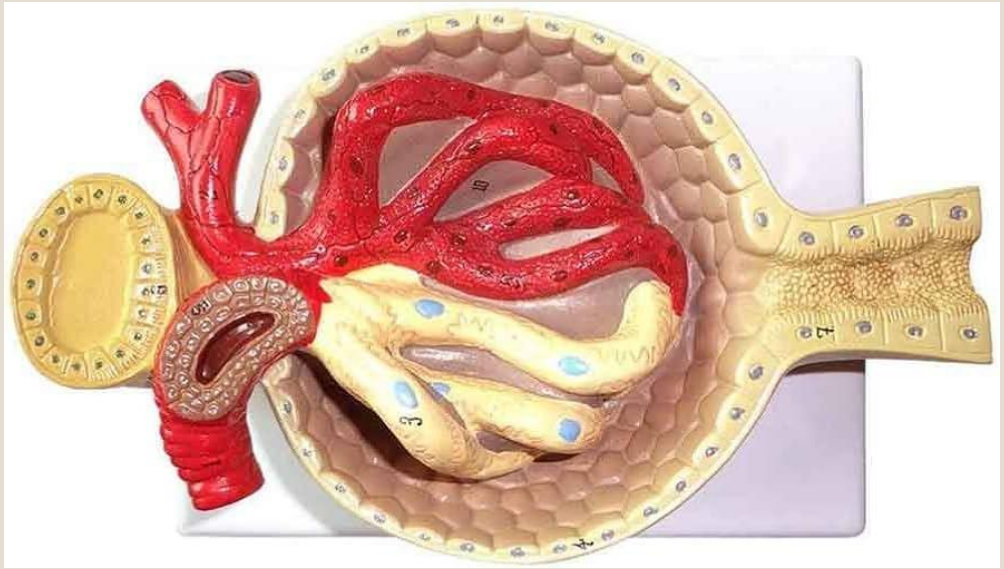
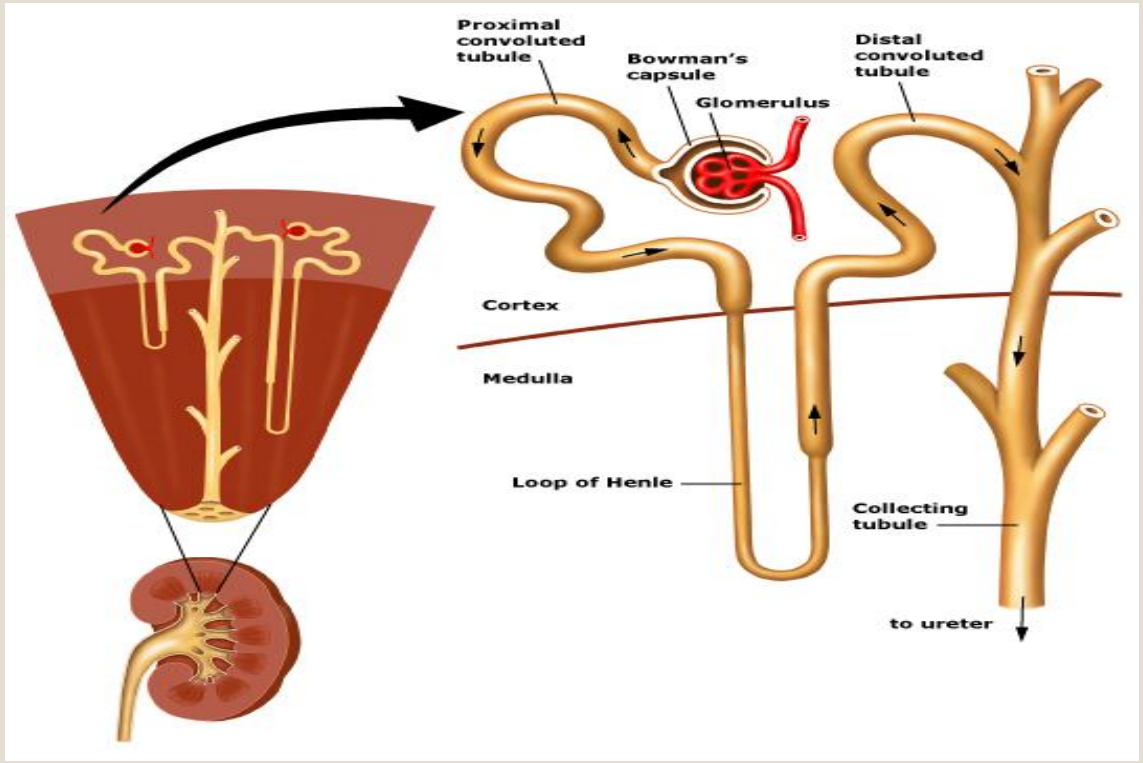


Learning Objective:

1. Basic structure of glomerular membrane
2. Function of glomerular membrane
3. Clinical aspects of glomerular membrane
4. Investigation regarding this

Nephron:

It is the basic structural & functional unit of kidney.



- Each human kidney contains about 1.5 million nephrons.

- After age 40 years, the number of functioning nephrons usually decreases about 10 percent every 10 years.

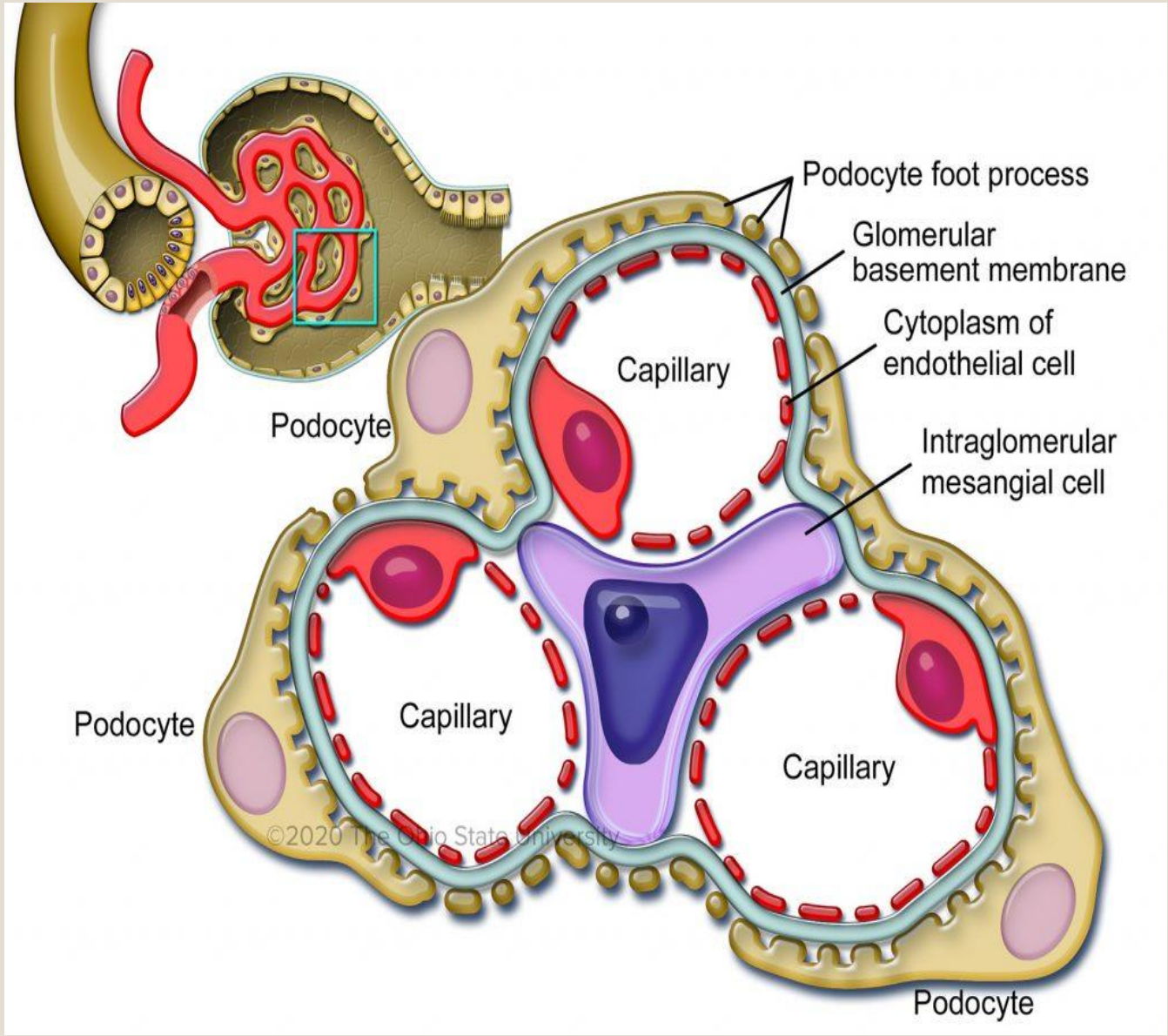
Glomerular membrane:

The glomerular membrane (or glomerular filtration barrier) is a critical structure in the kidneys that plays a key role in filtering plasma to form urine.

Structure:

It has 3 major layers:

(1) The endothelium of the capillary
(2) A basement membrane
(3) A layer of epithelial cells (podocytes) surrounding the outer surface of the capillary basement membrane


Podocyte foot process
Glomerular basement membrane
Cytoplasm of endothelial cell
Intraglomerular mesangial cell
Capillary
Podocyte
Capillary
Capillary
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Podocyte
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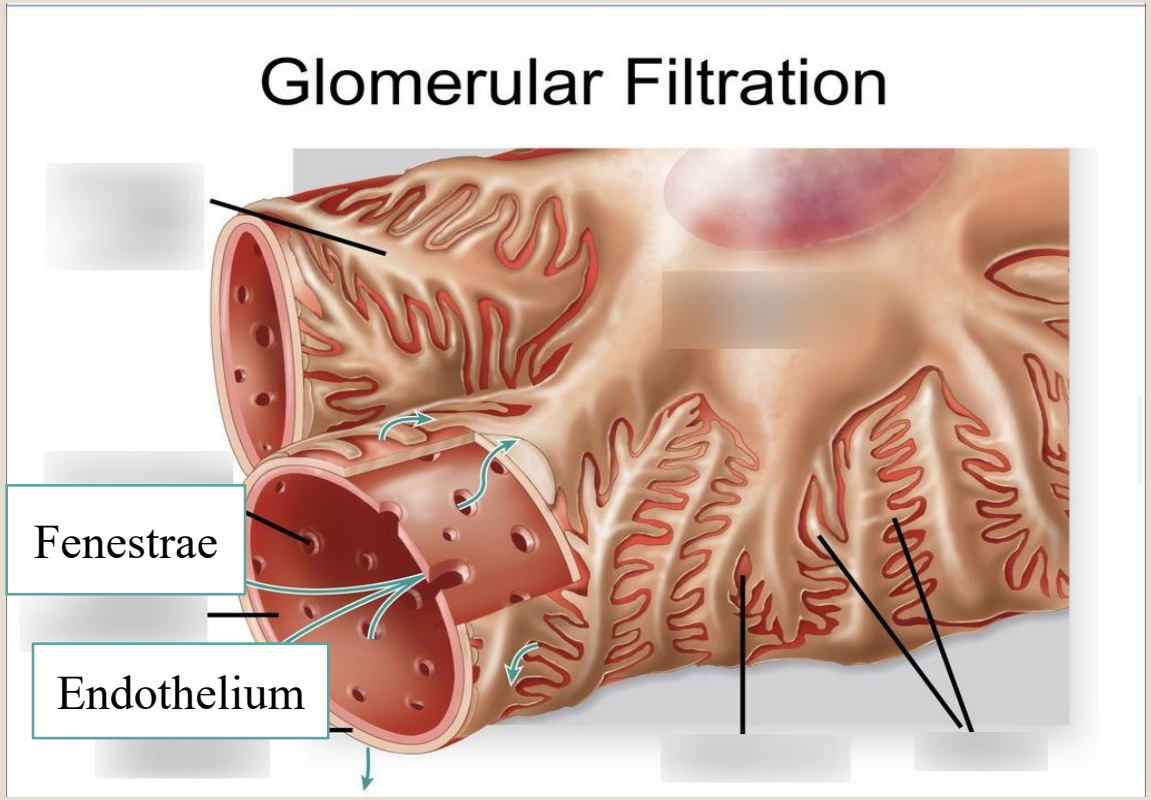
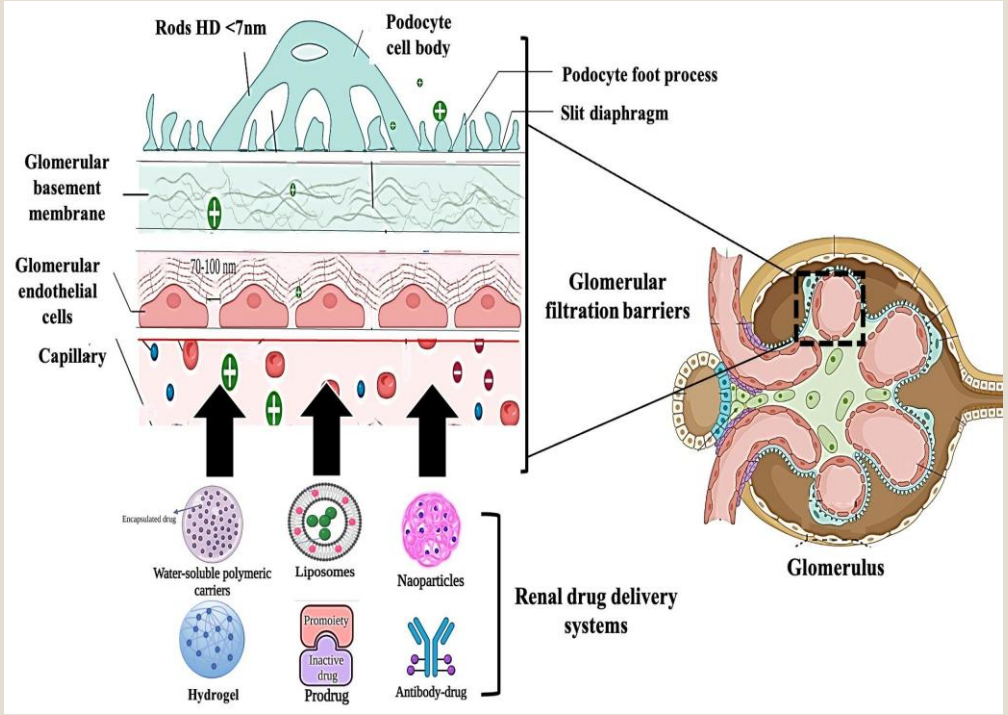
How does glomerular membrane work?

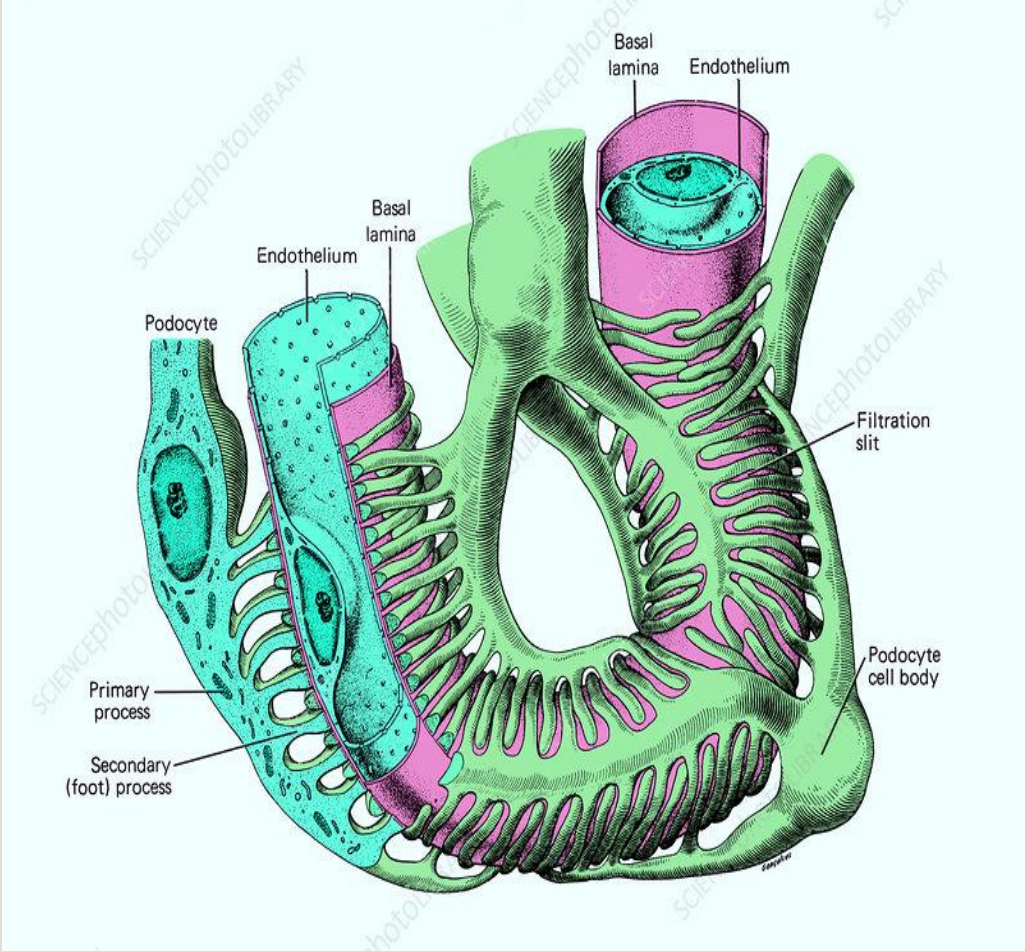
1. The endothelium has thousands of fenestrae but endothelial cell proteins has fixed negative charges oppose passage of plasma proteins.



2. The basement membrane has collagen and proteoglycan, prevents filtration of plasma proteins because of strong negative electrical charges associated with the proteoglycans.



3. Epithelial cells have long footlike processes (podocytes) on the surface of capillaries. There are gaps called slit pores for filtration. They have negative charges, restrict plasma proteins.

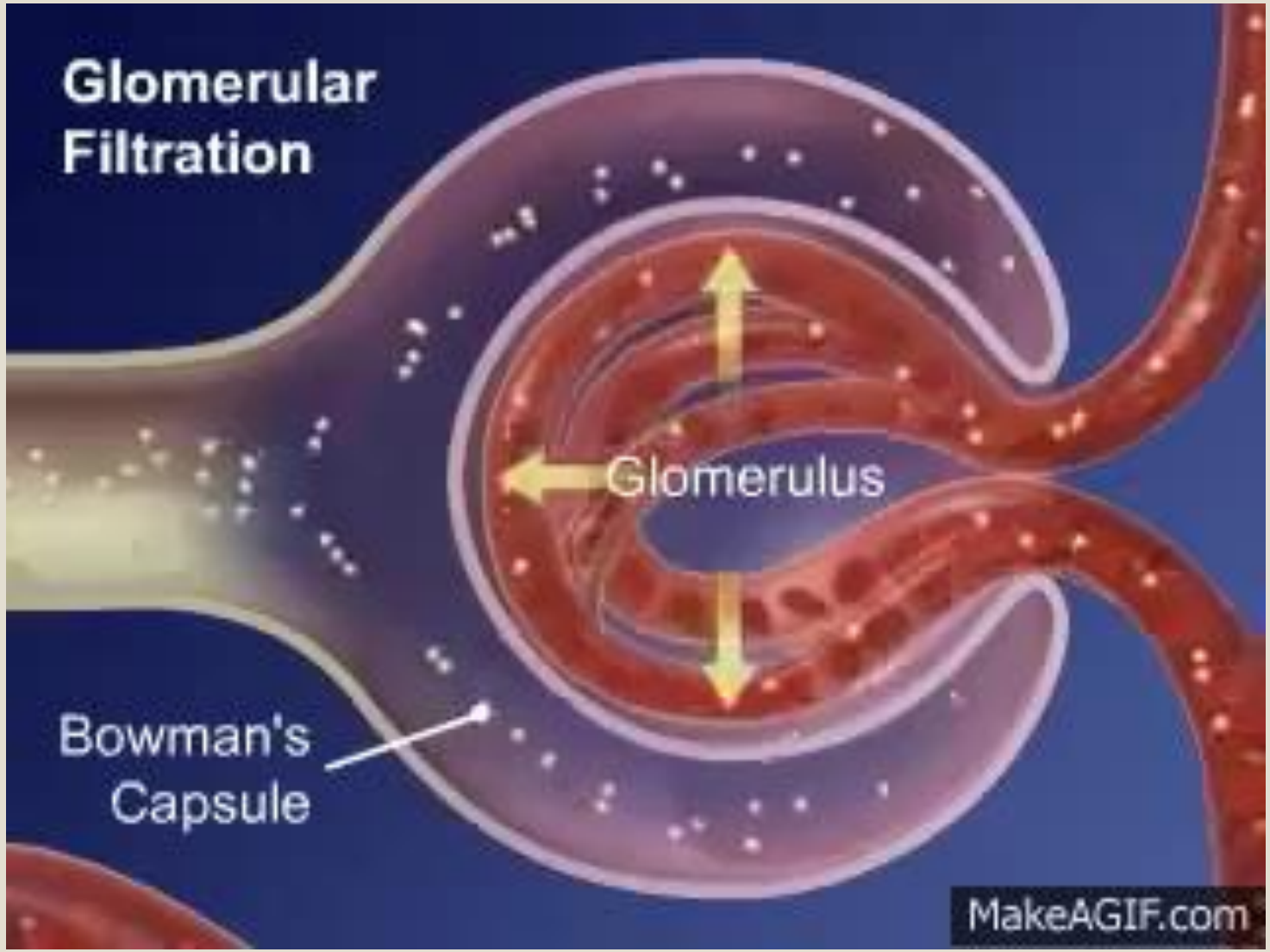


Function of glomerular membrane:

The glomerular membrane selectively filters-

1. It allows water, electrolytes, glucose, amino acid, urea, and other small molecules. Thus it forms glomerular filtrate.

2. It blocks proteins (especially large ones like albumin), cells (RBCs, WBCs).Thus it prevents proteinuria and hematuria.


Glomerular
Filtration
Glomerulus
Bowman's
Capsule
MakeAGIF.com

GFR:

It is the amount of glomerular filtrate that filtered in each minute by all the functioning nephrons of both kidney.

Normal value: 125 ml/min, 75 liter/hour, 180 liter/day

Clinical aspects of glomerular membrane

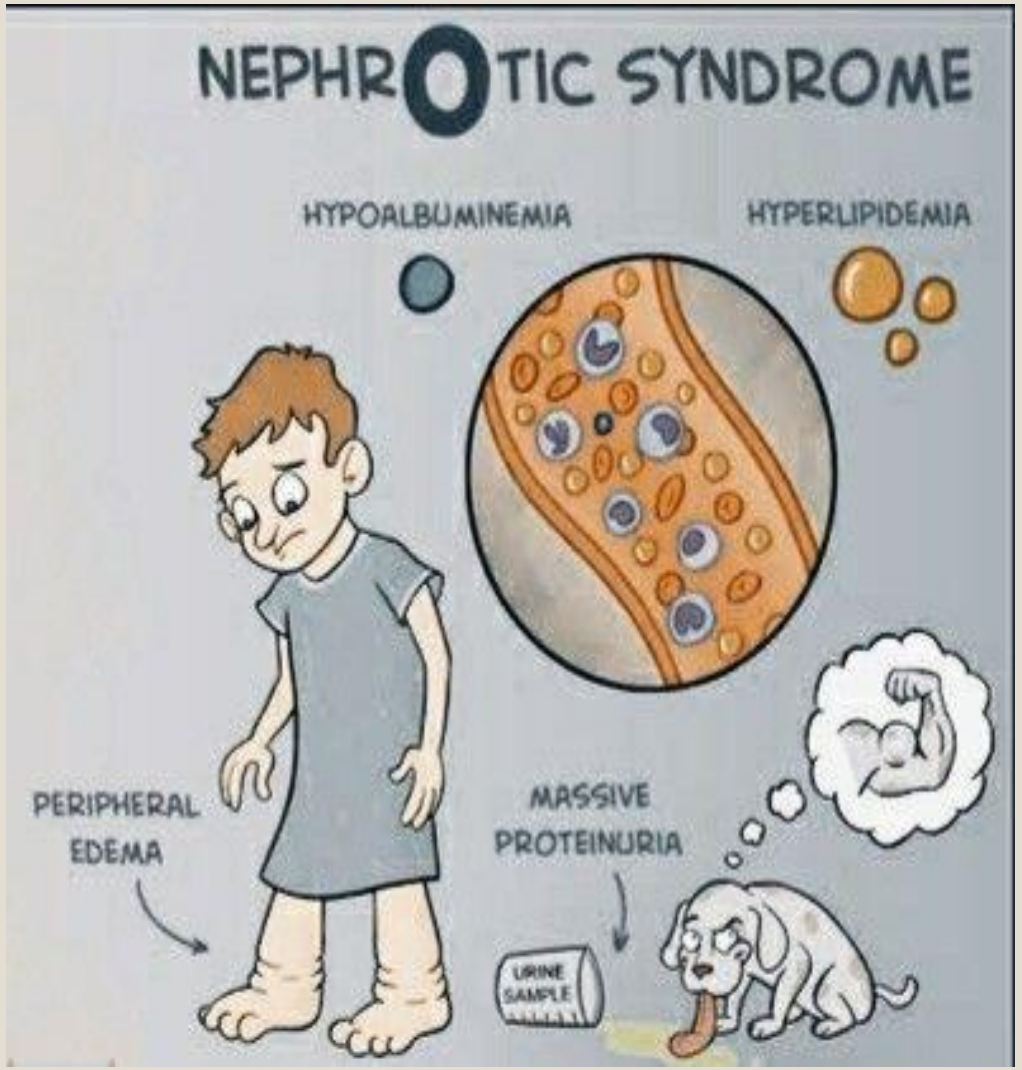
Any abnormality of glomerular membrane is collectively known as glomerulopathies.

This is divided into main two section-

1. Nephrotic syndrome
2. Nephritic syndrome or Acute Glomerulonephritis

Nephrotic Syndrome:

It is a kidney disorder where damaging of glomerular membrane occurs. It is the most common kidney problem in children .



Pathophysiology:

1. Injury to the podocytes
2. Changing in architecture
3. Scarring of tissue and matrix deposition in membrane

Cardinal features:

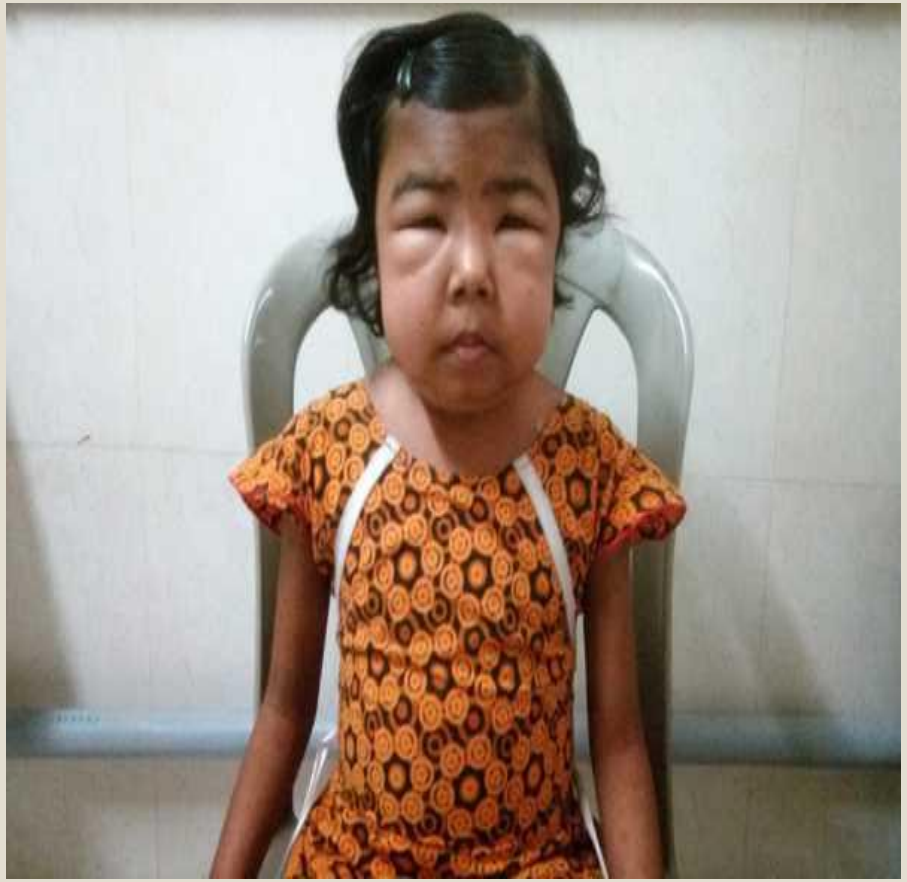
1. Overt proteinuria > 3.5gm/24hr
2. Hypo albuminemia <30gm/liter
3. Generalized Edema
4. Hyperlipidemia >200mg/dl

Symptoms:

1. Age: common between 2-8 years, peak 3 years

2. Puffiness of face up to chin & neck

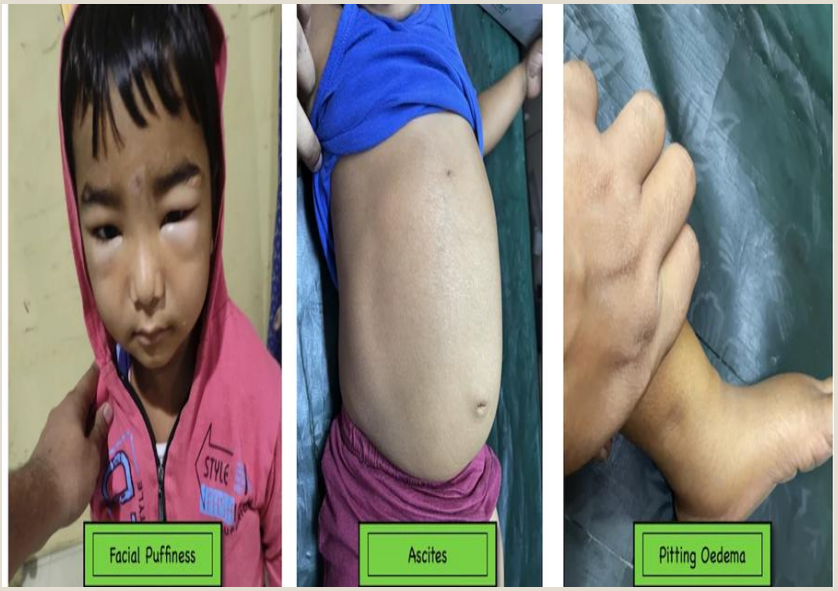
3. Periorbital swelling



4. Huge ascites, umbilical transverse slit present

5. Scrotum swelling, penis cracks, pitting edema of ankle and sacral region. Edematous chest wall, pleural effusion

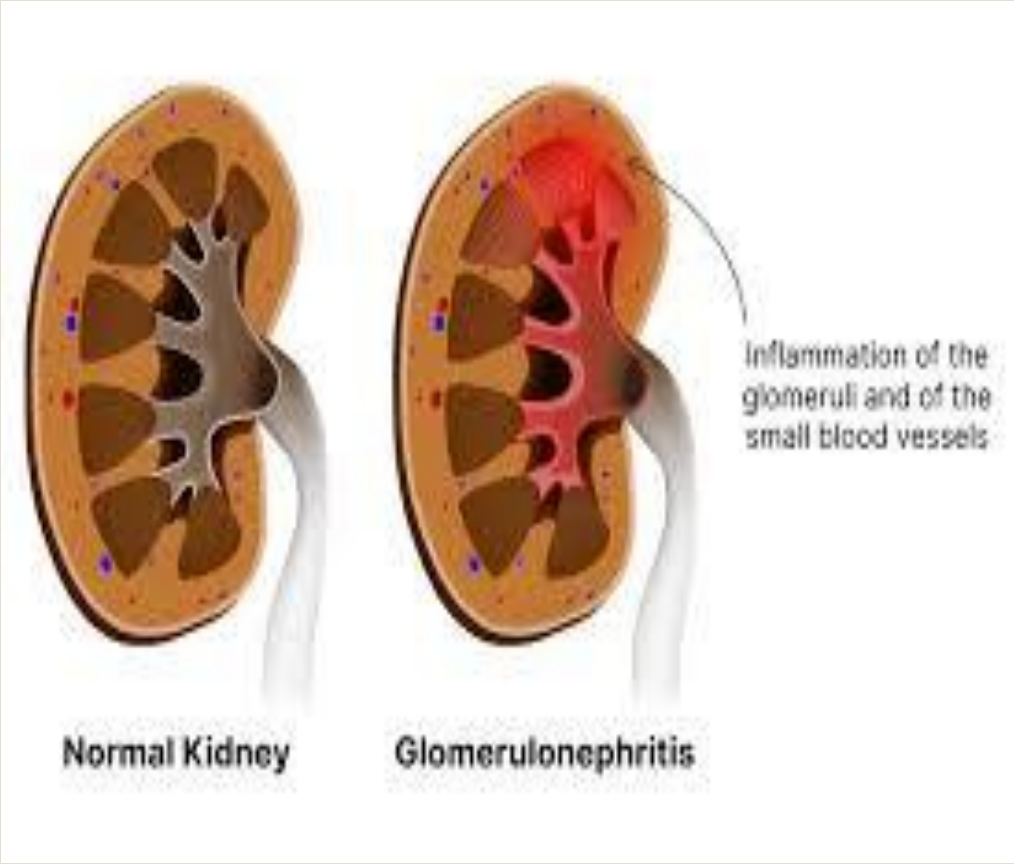
6. Anuria, low blood pressure



Acute Glomerulonephritis or Nephritic syndrome

Acute glomerulonephritis is a clinical condition where inflammation of glomerular membrane occurs.

This term used for describing all glomerular disease even without inflammation (like minimal change nephropathy)



Cause:

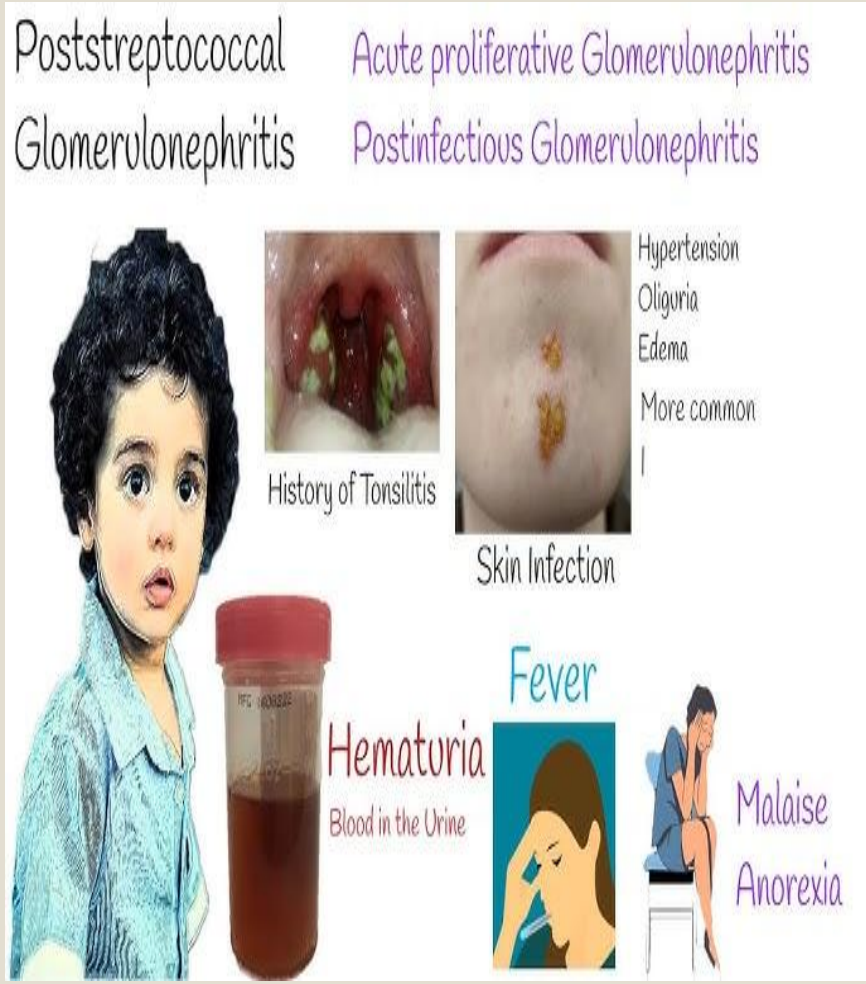
- Post-infections (eg: Streptococcal infection)
- Autoimmune disease (eg: Lupus)
- IgA Nephropathy
- Vasculitis
- Rapidly progressive glomerulonephrities

Pathophysiology:

- Immune complex deposit in glomeruli
- Inflammation & swelling of glomerular capillaries
- Reduced GFR
- Protein & RBCs leak into urine

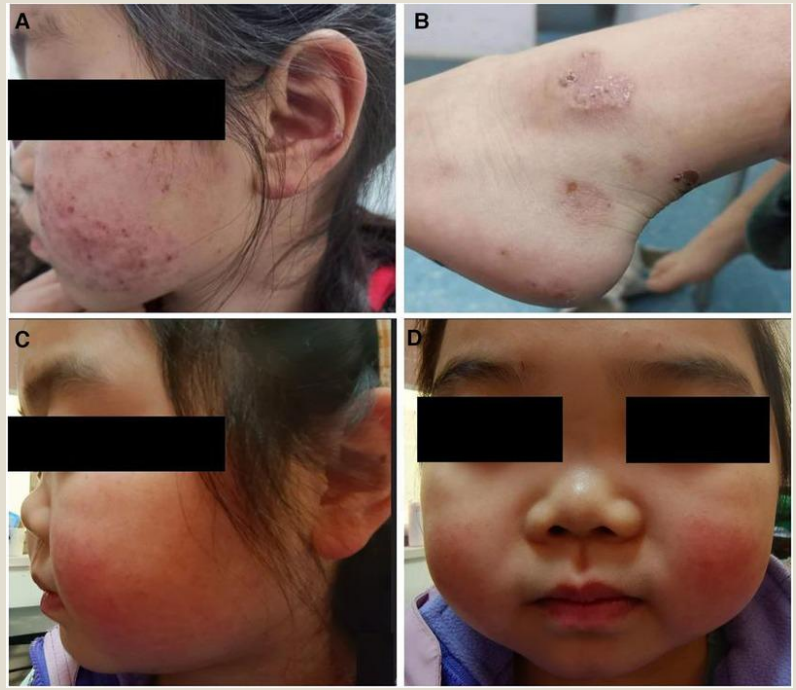
Cardinal features:

1. Hematuria (red or brown urine)
2. Oedema and generalized fluid retention
3. Hypertension
4. Oligouria
5. Reduced Renal function



Symptoms:

1. Puffy face with periorbital swelling
2. Mild Pallor
3. Previous scabies infection mark
4. High blood pressure
5. Generalized edema
6. Feature of LVF & RVF
7. Oliguria or anuria



Difference between AGN & Nephrotic syndrome

Characteristics	Acute Glomerulonephritis	Nephrotic Syndrome
Age of Onset	5-12 years	2-8 years
H/O sore throat or skin infection	More prominent	May Present
Extent of Swelling	Usually confined to face	Generalized
Ascites	Unlikely	Usually present
Urine Color	High/ reddish	Normal

Difference between AGN & Nephrotic Syndrome

Characteristics	Acute Glomerulonephritis	Nephrotic Syndrome
Hypertension	Present	Usually Absent
Proteinuria	Mild	Massive
Urine R/M/E	RBC,RBC Cast	Hyaline & Granular cast
Sereum Albumin	Normal	Decreased
Serum cholesterol	Normal	Increased
Serum C3	Decreased	Normal
Relapse & remission	Rare	Common

Glomerulopathies categorized by clinical and histological presentation

Present With Nephrotic presentation					
Disease	**Age**	**Cause**	**Pathogenesis**	**Electron microscopy**	**Immune Deposit**
Minimal Change	Child	Atopy, NSAID Hematological malignancy	Unknown, provable circulating factor causing podocyte injury	Fusion of podocyte foot process	None
Focal segmental glomerulo sclerosis	Adult	APOL1 gene , HIV patient, Heroine misuse , Obesity, Chronic Hypertension.	Unknown, provable circulating factor causing podocyte injury by increasing permeability	Segmental scars, no acute inflammation.	Non specific Trapping in scars
Membranous Nephropathy	Adult	Penicillamine, NSAID,Hepatistis B virus, Malignancy, Lupus	Antibody to podocyte surface antigen leads to podocyte injury by compliment.	Thickened GBM, matrix deoposition, Glomerulosclerosis.	Granular Subepithelial ig –G,C3

Present With Mild glomerulo nephritic presentation					
Disease	**Age**	**Cause**	**Pathogenesis**	**Electron microscopy**	**Immune Deposit**
Ig A nephropathy	Child	Idiopathic, triggered by upper RTI, Liver disease, coeliac disease.	Unknown, mucosal infection may be involved.	Increased mesangial matrix and cell , focal segmental nephritis	Mesangial Ig A & C3 deposit
Mesangiocapillary Glomerulonephritis					
Immunoglobulin type	Adult	Infection or autoimmunity.	Deposition of circulating immune complex or planted antigen.	deposit in mesangium cells and capillaries	Immunoglobulin
Complement type	Adult	Complement gene mutation, C3 nephritic factor.	Complement abnormality, Abnormal complement pathway activation.		Complement component

With Rapidly progressive glomerulo nephritic presentation					
Disease	**Age**	**Cause**	**Pathogenesis**	**Electron microscopy**	**Immune Deposit**
Focal necrotising glomerulonephritis	Adult	Primary or secondery small vessel vasculitis	Anti Neutrophil Cytoplasmic Antibody mediated vasculitis .	Segmental inflammation or necrosis in some glomeruli + cresent formation	Variable according to cause
Diffuse proliferative glomerulonephritis	Adult	Post streptococcus infection , Staphylococci infection, endocarditis.	Immune complex mediated reaction	Diffuse proliferation of endothelial or mesangial cell, neutrophil/macrophase infiltration	Subendothelial & subepithelial deposit
Anti glomerular basement membrane disease	Adult	HLA-DR15 complement	Auto antibodies to α3 chain of type IV collagen in GBM	Cresentic nephritis	Linear Ig G along GBM

Investigations to detect glomerulopathies:

Renal Function Test

1. **Urine R/M/E:**

- Albuminuria (done by Albutrix or heat coagulation test)
- Granular and hyaline casts.
- Pus cell if associated with UTI

2. Urinary total protein in 24 hours: >1gm/m^2/day

3. Spot urine protein : creatinine ration: >2
4. Serum albumin : <25gm/L
5. Serum cholesterol : >220 mg/dl
6. Blood urea, BUN.
7. Serum creatinine.
8. Serum electrolyte.
9. USG of KUB region.

To screen infection :

- Urine R/M/E and C/S : To rule out UTI
- CBC, PBF, ESR : Hematocrit and ESR may be raised.
- Blood for C/S : To identify organism & drug sensitivity.
- X ray Chest : To rule out pneumonia, TB, bilateral pleural effusion.

To find out Etiology:

- Blood for HBs Ag, Anti HCV.
- Blood C3,C4.
- ANA, Anti-dsDNA
- ASO titre

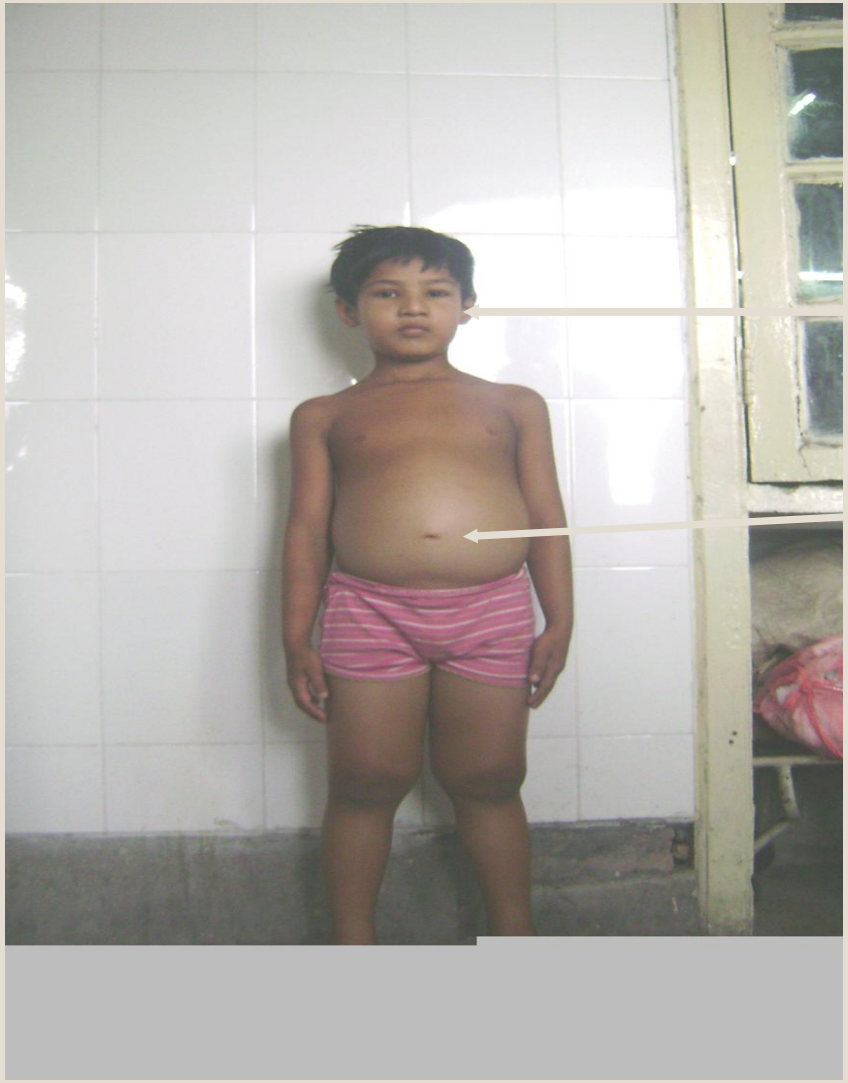
Renal Biopsy: To understand renal histology

Management:

- Symptomatic management
- According to the cause

Siam, a 4-years-old immunized boy was admitted with the complaints of swelling of whole body started from face for 10 days with scanty micturition for 5 days. His urine colour was normal. There was no H/O of sore throat or skin infection.

On examination patient had puffy face with generalised oedema, BCG mark was present. Bed side urine albumin was ++++. Signs of ascites was present , no organomegaly.



Puffy face

Transverse slit of
Umbilicus due to ascites

So, What is the probable diagnosis….. ?

Nephrotic syndrome

A 6-year-old boy is brought to emergency department with the complaints of facial swelling & dark coloured urine. His mother says his urine output is decreased. His skin shows healed scar mark. He has no history of fever.

On examination, his blood pressure is increased. His investigation shows low serum C3 level, In urine R/M/E RBC & RBC cast present.

So, What is the probable diagnosis….. ?

Acute Glomerulonephritis

Take home message

- Eat a healthy diet
- Stay hydrated
- Avoid extra salt intake, smoking
- Pay attention to any swelling in leg, face or body
- Pay attention about urine output & colour
- Annually asses kidney function

THANK YOU FOR YOUR ATTENTION!