
From:
God

NEPHROTIC SYNDROME

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Protein Excretion

- **Normal** range protenuria in children is :
(≤۴ mg/m۲/hr) or (<۱۰۰ mg/m²/day) or totaly۱۵۰ mg/d

- **Abnormal**(۴-۴۰mg/m۲/hr) or (۱۰۰< &<۱۰۰۰mg/m²/d)

- **Nephrotic**(>۴۰ mg/m۲/h) or (>۱gr/m²/day)

Abnormal Protein Excretion

- **Urinary protein excretion >١٠٠ mg/m²/day is abnormal in children.**

- **In neonates, is higher, up to ٣٠٠ mg/m²/day,**

  (reduced reabsorption of filtered proteins.)

- **Nephrotic range proteinuria *(heavy proteinuria)* is Urinary protein ١ g/m²/day or > ٥٠ mg/kg/day**

low urinary protein excretion

١. ***Restriction*** of the filtration of proteins across the **glomerular capillary wall**.

٢. ***Reabsorption*** of freely filtered low molecular weight (LMW) proteins (< ٢٥٬٠٠٠ Daltons) by the **proximal tubule**.

Mechanisms

١. *Glomerular*

٢. *Tubular*

٣. *Overflow proteinuria*

Proteinuria in children presents in three ways

- ١. *Transient or intermittent*
- ٢. *Orthostatic*
- ٣. *Persistent*

Transient proteinuria

- *Most common* cause

- **Fever**, **Exercise**, **Stress**, **Seizures**, and **Hypovolemia**, or **Exposure to extreme cold**, act by altering *renal hemodynamics*.

Transient proteinuria

- Follow-up routinely
- Repeat U/A on a first morning void in one year

Orthostatic Proteinuria

- Increased protein excretion in the *upright position* (to ١٠-fold) which returns to normal in the supine position.
- Common cause of proteinuria, in adolescent boys.
- Generally *<١ g/day*.

Orthostatic Proteinuria

- The disorder is uncommon over the age of ٣٠ years.
- The diagnosis by a negative dipstick ***on the first morning*** voided specimen.

Orthostatic Proteinuria

- A short period (١٥ to ٢٠ minutes) of maximal **exercise** increased ***Pr/Cr*** ratios.

- It is wise to **delay measurement**, for a period of ٢٤ ***hours*** after exercise.

Orthostatic Proteinuria

- ***Pathogenesis***
  - **Exaggeration normal response of transient increase protein in upright posture.**
  - **Subtle glomerular abnormalities.**
  - **Renal vein compression by aorta or superior mesenteric artery.**

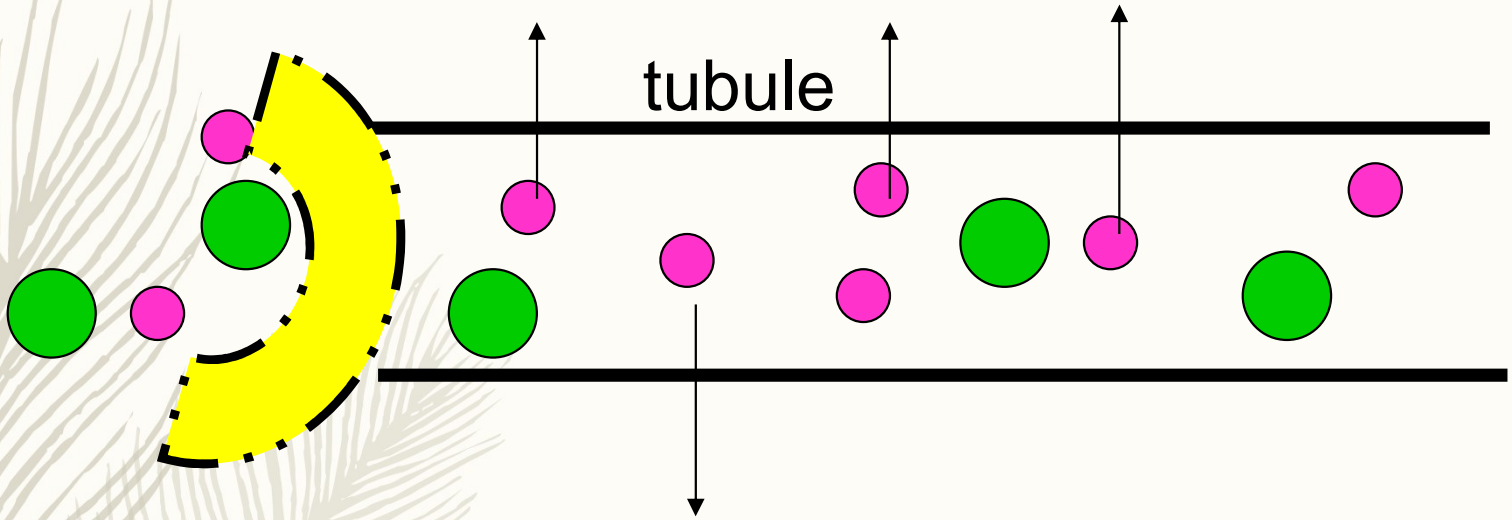
Prognosis

- ***Benign condition***, **normal renal function after as long as ٥٠ y of follow-up.**

- The ***proteinuria*** resolves ***spontaneously***, being present ٥٠ percent at ١٠ years and only ١٧ percent at ٢٠ years.

Glomerular proteinuria

- Minimal change disease
- Focal segmental glomerular sclerosis
- Membranoproliferative glomerulonephritis
- Membranous nephropathy
- Congenital nephrotic syndrome
- IgA nephropathy (Berger's disease)
- Alport syndrome

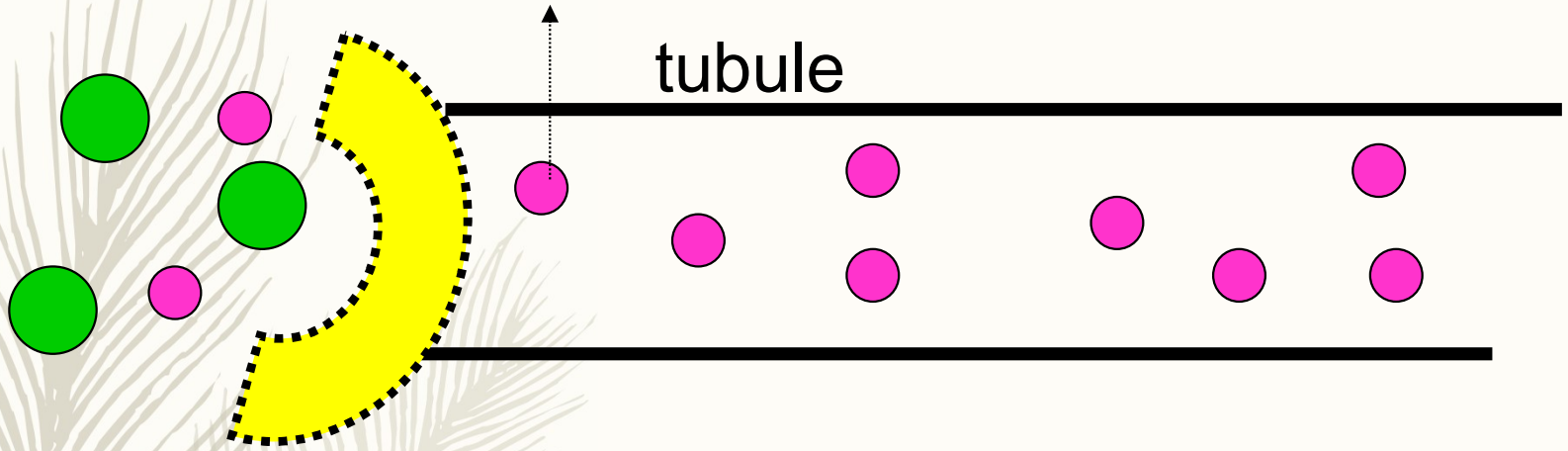


- Large proteins are able to pass by the abnormal **glomerular** barrier.

Tubular Proteinuria

- ***low molecular weight proteins*** such as β۲-microglobulin, α۱-microglobulin, and retinol-binding protein.

- Filtered across the glomerulus and reabsorbed in the proximal tubule.
  - Associated with other defects in proximal.tubular .. function(glycosuria,RTA ۲ , and ...phosphaturia).



Malfunctioning **tubules** unable to reabsorb the smaller proteins filtered at the glomerulus.

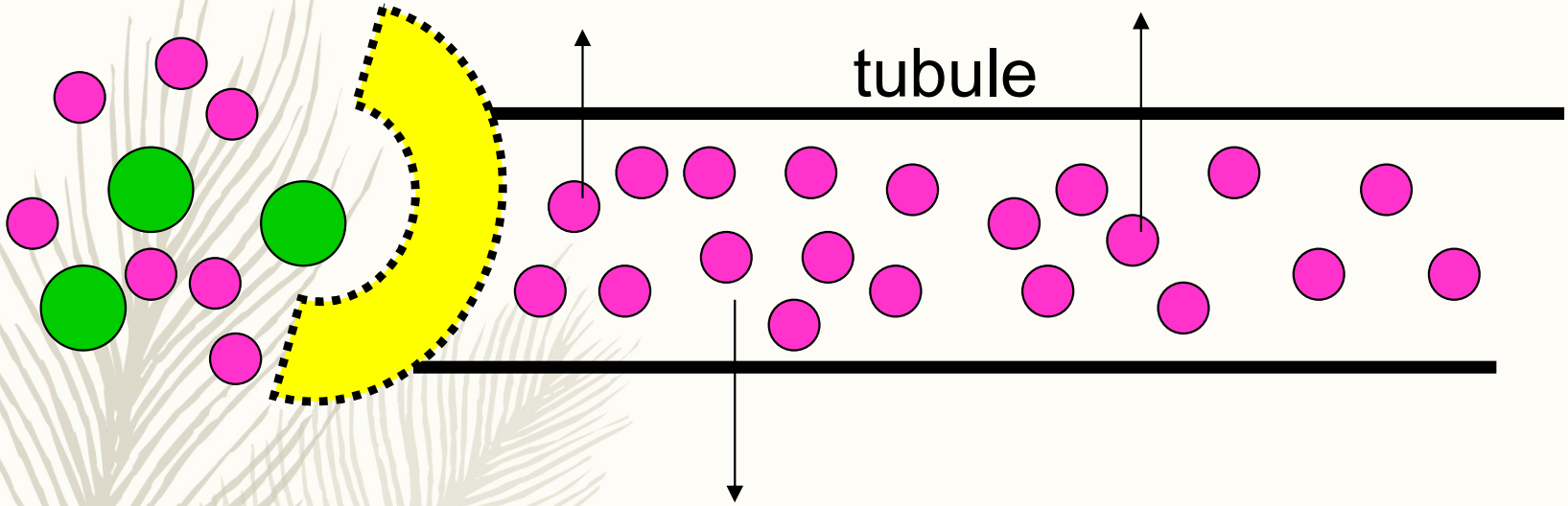
Tubular proteinuria

- Fanconi syndrome
- Heavy metal poisoning
- Acute tubular necrosis
- Tubulointerstitial nephritis
- Secondary to obstructive uropathy

Overflow Proteinuria

- ***Overproduction*** of a particular protein **>**tubular reabsorptive capacity.

- Primarily in adults with a plasma cell dyscrasia (multiple myeloma) Hemolysis,Rhabdomyolysis.



- Filtered **load** of proteins **exceeds** the tubular reabsorption rate (glucosuria in hyperglycemia)

MEASUREMENT OF URINARY PROTEIN

Qualitative

- Urine dipstick
- Sulfosalicylic acid test

Quantitative

- timed 24-hour urine collection
- measurement of the urinary protein/creatinine ratio

Urinalysis Strips

Results

- **Negative**
- **Trace** : between ١٥ and ٣٠ mg/dL
- **١+** : between ٣٠ and ١٠٠ mg/dL
- **٢+** : between ١٠٠ and ٣٠٠ mg/dL
- **٣+** : between ٣٠٠ and ١٠٠٠ mg/dL
- **٤+** : >١٠٠٠ mg/dL

False-Negative

- Dilute urine (specific gravity <١٠٠٥)
- Urinary protein is **not albumin**

False-Positive

- Highly concentrated urine (SG >١٠٢٥)
- Gross hematuria
- Urinary pH >٧/٠
- Contaminated by antiseptic agents (*chlorhexidine, benzalkonium chloride, hydrogen peroxide*)
- Phenazopyridine
- Iodinated radiocontrast

Nephrotic syndrome

- ١٥ times more common in children than adults
- Incidence ⇨
  ٢-٢/١٠٠٠٠٠ children /year

- ***Heary proteinuria***
- ***Hypoaluminemia (<٢/٥g/dl)***
- ***Edema***
- ***Hyperlipidemia***

Etiology

–٩٠% idiopathic NS

MCD (٨٥%)

MP (٥%)

FSGS (١٠%)

١٠% secondary NS: MN, MPGN

Pathophysiology

- ↑ed In permeability of the GCW
- Loss of negatively charged glycoproteins within the GCW
- In FSGS ⇨ Plasma factor

Mechanism of Edema Formation

- Urinary protein loss
- Activating the RAAS
- Release of ADH

Edema Mechanism

Massive proteinuria leads to decreased

- serum proteins, especially albumin.
- Plasma oncotic pressureis diminished.
- leading to fluid shifts from vascular to interstitial compartments and plasma volume contraction.

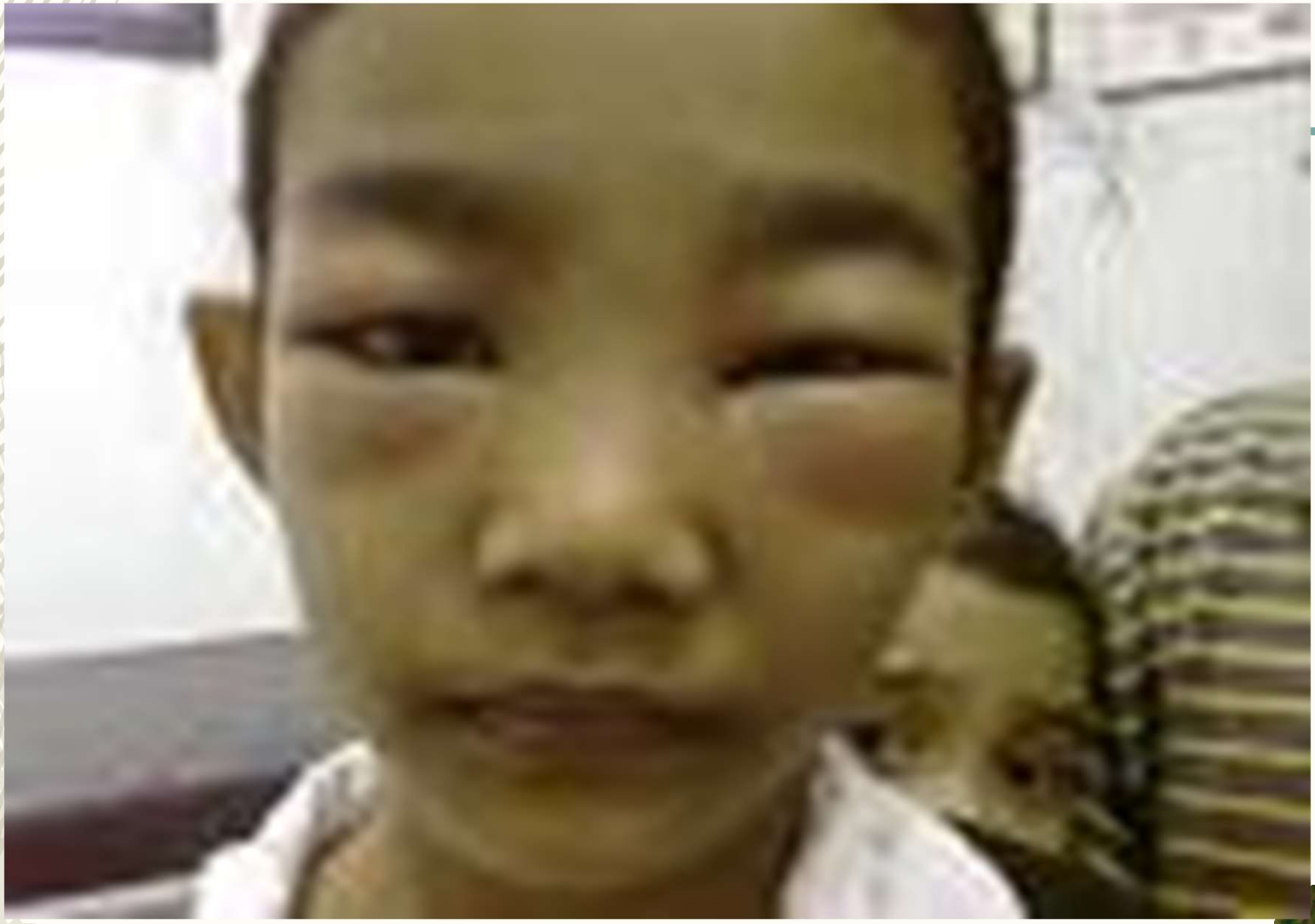
Edema

Reduction in effective circulating blood volume

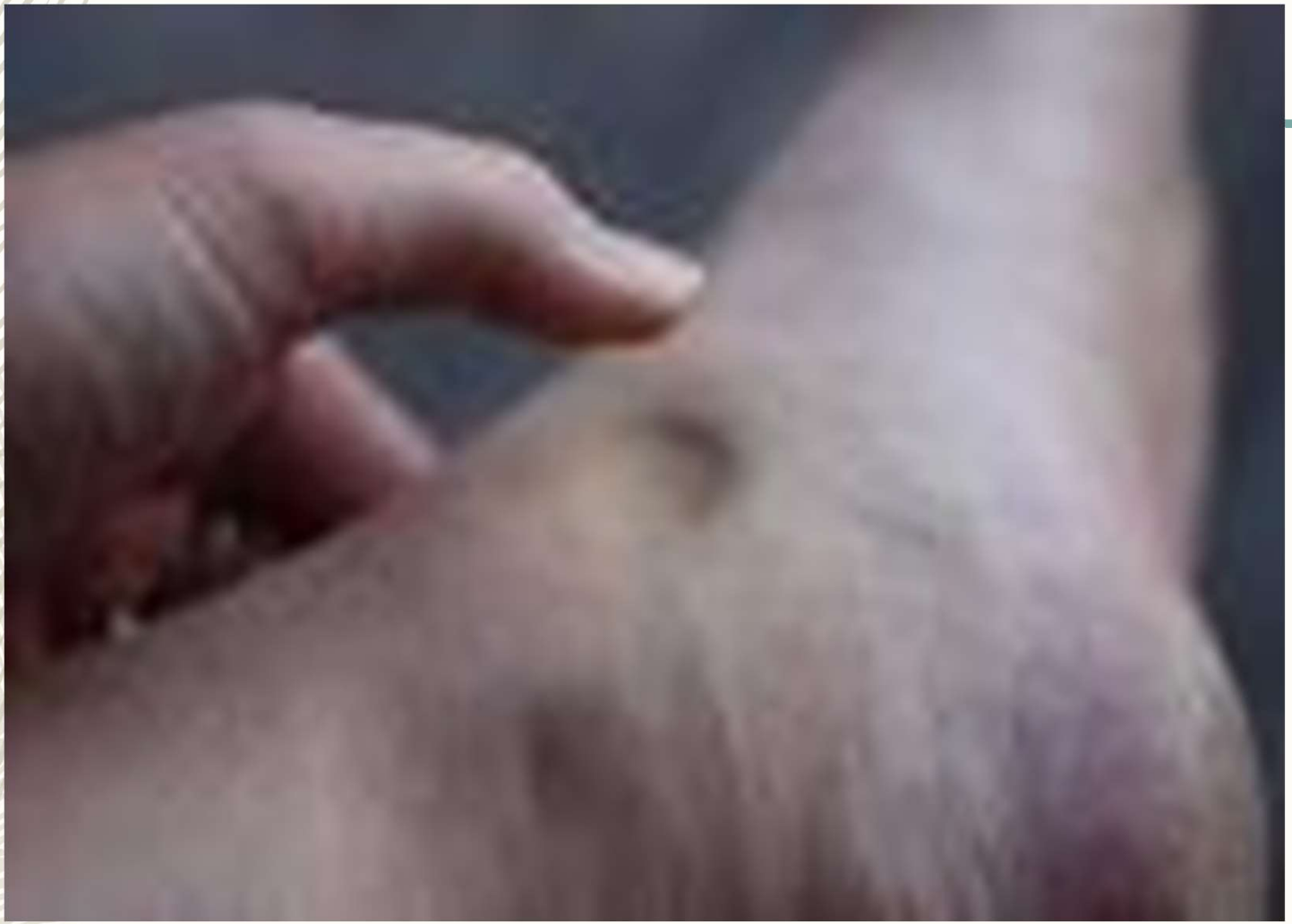
&

Increase in tubular Nacl reabsorption secondary to activation of RAAS system.

Nephrotic syndrome



Pitting Edema



Mechanism of Hyperlipidemia

- Hypoalbuminemia
- ↓ Lipoprotein lipase

Hyperlipidemia

- Hypoproteinemia stimulates hepatic lipoprotein synthesis & diminishes lipoprotein metabolism(LPL)

- Elevated serum lipids (cholesterol, triglycerides) and lipoproteins.

Idiopathic Nephrotic Syndrome

Pathology

–In minimal change disease

–Glomeruli ⇨ Nl or minimal increase in mesangial cell & matrix

In mesangial proliferation

- Diffuse increase in mesangial cells & matrix on LM.
- Trace to \+mesangial IgM and/or IgA staining on IF.
- ↑ed numbers of mesangial cells & matrix & effacement of the epithelial cell foot processes on EM.

In FSGS

Mesangial proliferation & segmental scarring on LM.

IgM &C٣ staining in the areas of segmental sclerosis on IF.

Segmental scarring of the glomerular tuft with obliteration of the glomerular capillary lumen

HIV infection, VUR, IV heroin abuse.

Clinical Manifestations:

M : F ⇨ ٢: ١ (ages of ٢ & ٦yr)
Infection, insect bites, bee stings , poison IVY

- Edma
- Anorexia
- Irritability
- Abdominal pain
- Diarrhea
- HTN & Gross hematuria (Uncommon)

Differential diagnosis

- –Protein- losing enteropathy
- –Hepatic failure
- –CHF
- –Acute or chronic GN
- –Protein malnutrition

Diagnosis:

- U/A⇨ ٣+or ٤+ Proteinuria microscopic hematuria (٢٠%)
- ٢٤h urine for protein ⇨ ٤٠ mg/m٢/hr
- Spot urine protein to creatinine ratio ⇨٢/٠
- Serum albumin ⇨ <٢/٥g/dl
- TG& cholesterol levels are elevated
- C٣ & C٤ level are NL

Treatment

–Low salt diet

–Fluid restriction (hyponatremia)

–Albumin

–Prednisolone ⇨

۶۰mg/m۲/day (۴WK)

۴۰mg/m۲/day (QOD)

- Relapse
- Steroid dependent
- Frequent relapsers
- Steroid resistant
  - **Cyclophosphamide (٢-٣mg/kg/day)**
  - **Cyclosparine (٣-٦mg /kg/day)**
  - **ACE- I & Angiotensin II blockers**

Indications of Hospitalization:

- Severe symptomatic edema
- Large pleural effusions
- Ascites
- Severe genital edema

Indications of Renal Biopsy:

- –Hematuria
- –HTN
- –Renal insufficiency
- –Hypocomplementemia
- –Age < \yr or > Λyr

Complications :

- ***Infection***
  - Urinary lasses of Igs & properdin factor B
  - Defective cell- mediated immunity
  - Immunosuppressive therapy
  - Malnutrition
  - Edema/ascites
- ***Thromboembolic events***

Prognosis:

- Age > ٨yr
- HTN
- Hematuria
- Renal dysfunction
- Extra renal symptomatology (rash, arthralgia , etc)
- Depressed serum complement

Secondary Nephrotic syndrome

- MNP
- MPGN
- PIGN
- Lupus nephritis
- HSPN

Secondary Nephrotic syndrome

–Malaria

–Schistosomiasis

–Hepatitis B virus

–Hepatitis C virus

–Filaria

–Leposy

–HIV

- Carcinomas of the lung & GI tract ⇨ ***MNP***
- Hodgkin lymphoma ⇨ ***MCD***

– Penicillamine , Captopril, Gold , NSAIDs, Mercury Compounds ⇨ ***MNP***

– Probenecid, Ethosuximide, Methimazole, Lithium ⇨ ***MCD***

– Procainamide, Chlorpropamide, Phenytion, Trimethadione, Paramethadione ⇨ ***MPGN***