primed

Pediatrics

NEPHROLOGY

FIRST EDITION
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eyadprimed
FIRST EDITION
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VERSION 2.6

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“Two men looked out from prison bars, one saw the mud, the other saw stars.”

Which one will you be?

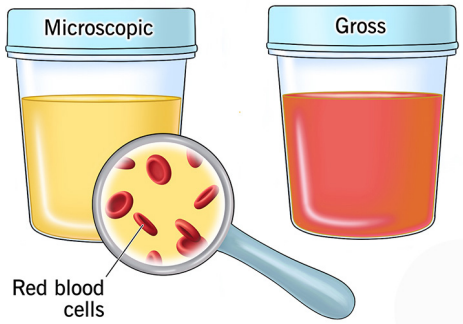
HEMATURIA

The presence of blood in urine in significant amount; > 5 RBCs/ HPF in sediment from 10 ml centrifuged freshly voided urine.

It may be microscopic or macroscopic (gross) hematuria:

Microscopic hematuria: detected by dipstick or microscopic examination.

Gross hematuria: Visible by the naked eye; pink, red, brown or smoky urine.



Causes of hematuria

Heme +ve vs. Heme -ve

Heme positive: Hemoglobin - Myoglobin

Heme negative: Dyes - Drugs - Pigments

Upper vs. Lower urinary tract

1. Upper urinary tract:

Glomerular:
- ***Immunologic injury:*** GN
- ***Structural disorder:*** thin basement membrane disease
- ***Toxin-mediated injury:*** HUS

Tubulointerstitial:
- ***Inflammation:*** interstitial nephritis, pyelonephritis
- ***Vascular:*** sickle cell disease
- ***Structural:*** cyst rupture, Wilms' tumor, renal trauma

2. Lower urinary tract:

- ***Inflammation:*** cystitis
- ***Injury:*** trauma, stone

Glomerular vs. non-glomerular

	From kidney (Glomerular)	From lower urinary tract (non glomerular)
1- Colour of urine	Brown or cola-coloured	Red
2- Relation of Hematuria to Urine Stream	All through	May be terminal (bladder) or initial (urethra)
3- RBC Morphology	Dysmorphic, RBC casts	Eumorphic, may be clots
4- Proteinuria	≥ 40 mg/m²/hour	< 40 mg/m²/hour
5- Associated Manifestations	• Edema • Hypertension • Impaired Renal Functions	• Dysuria • Suprapubic pain • Disturbed urine stream

Causes of Glomerular hematuria

Acute post-infections GN

Recurrent gross hematuria syndrome:

- IgA nephropathy
- Alport syndrome
- Benign familial hematuria (Thin basement membrane disease)

Membranoproliferative glomerulonephritis (MPGN)

Membranous glomerulonephritis (MGN)

Secondary to other diseases and vasculitides e.g.

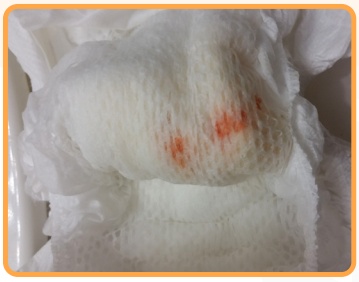
- Systemic Lupus Erythematosus nephritis
- Henoch Schoenlein Purpura nephritis
- Hemolytic uremic syndrome
- Good pasture syndrome
- Sickle cell Glomerulopathy

Causes of Non glomerular hematuria

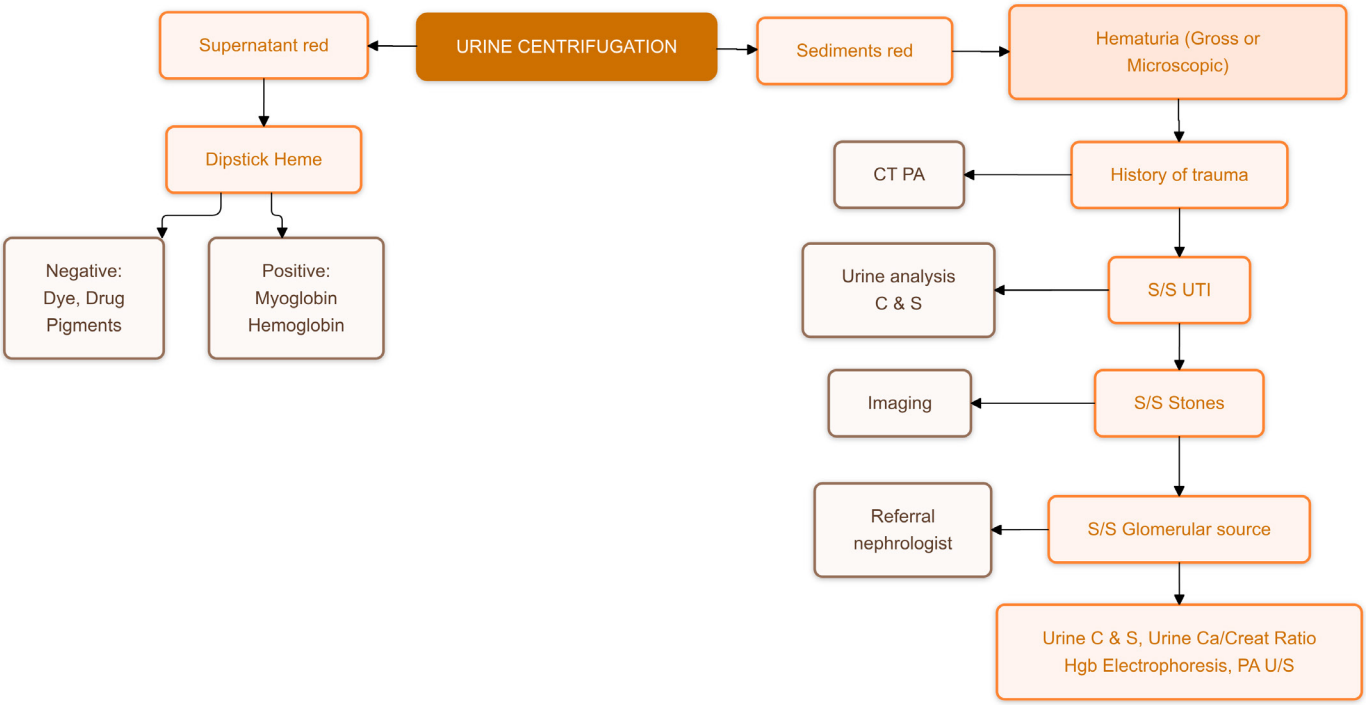
- Urinary tract infection (UTI)
- Urolithiasis
- Hypercalciuria
- Bilharziasis
- Renal vein thrombosis (RVT)
- Coagulopathy
- Sickle cell disease/trait
- Drugs (anticoagulants, cyclophosphamide)
- Tumors
- Factitious
- Foreign bodies
- Fever
- Trauma
- Exercise

Urate Crystalluria

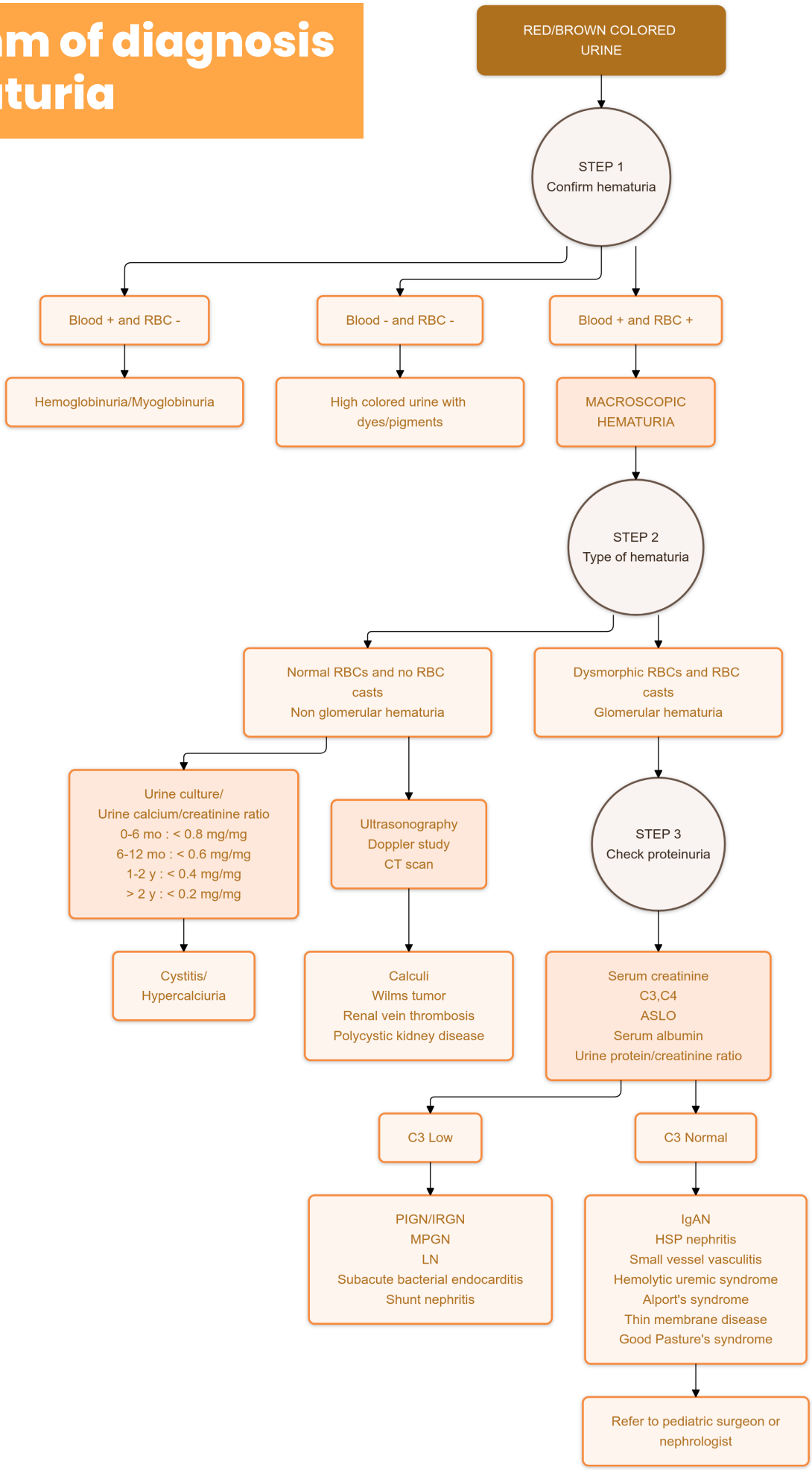
Causes pink or red-orange staining ***(Pink Diaper Syndrome)***



Approach



Algorithm of diagnosis of hematuria



GLOMERULAR DISORDERS

Pathogenesis of immune-mediated glomerulopathy

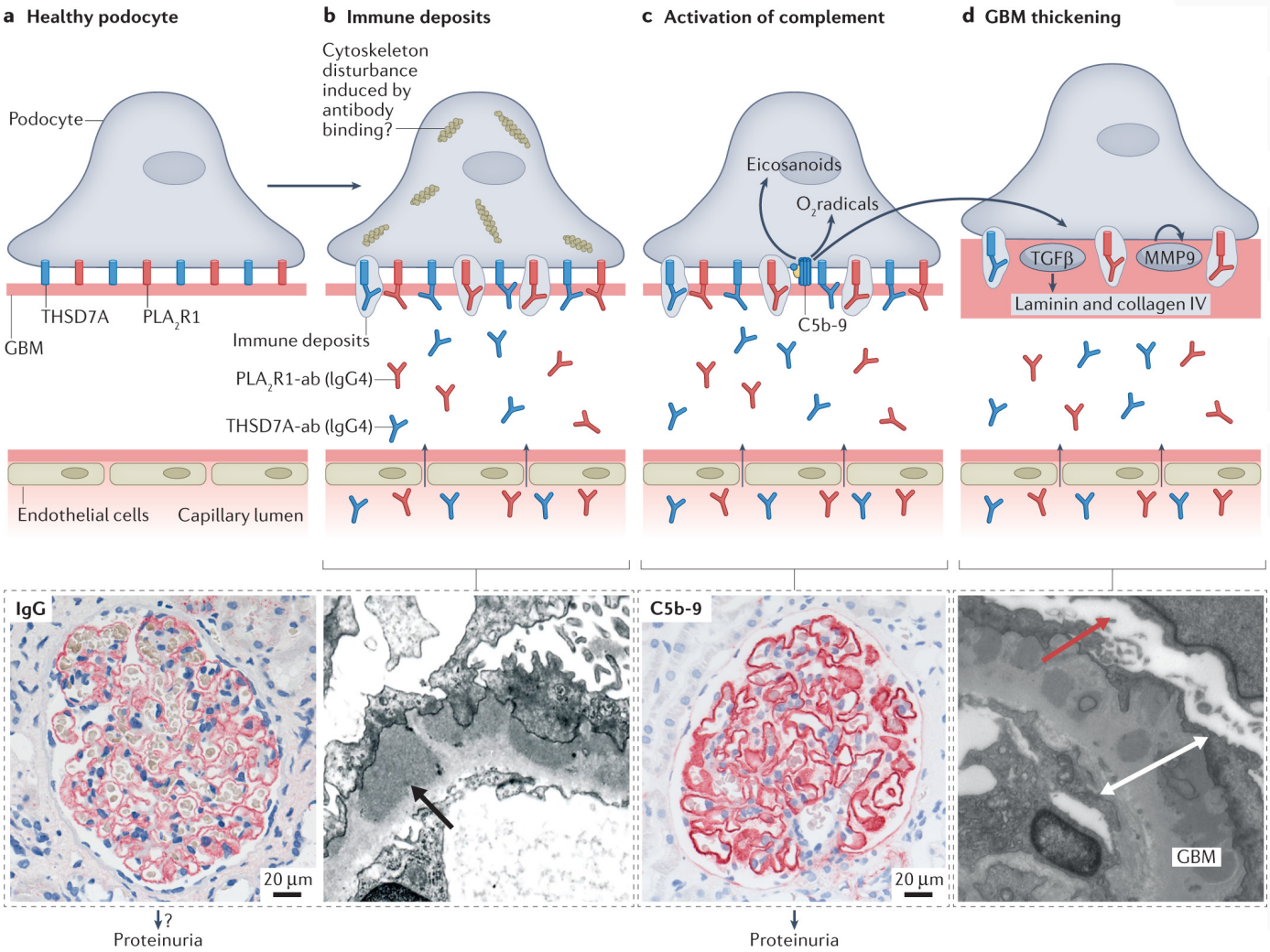
Hypersensitivity reactions occurring within the kidney (type II Cytotoxic).

- Circulating antibodies + Antigen at the glomerular basement membrane (GBM); e.g., Goodpasture's syndrome and rapidly progressive glomerulonephritis.

Immune complex disease (type III hypersensitivity)

- Antigen (exogenous or endogenous) + antibody + complement → kidney deposition and → initiate inflammatory process in the kidney (glomerulus is an innocent bystander) e.g., poststreptococcal glomerulonephritis.

Initiation of cellular immunity by GBM antigens e.g., chronic glomerulonephritis.



Clinical presentations

- Asymptomatic proteinuria.
- Nephrotic syndrome.
- Recurrent or persistent hematuria.
- Acute glomerulonephritis.
- Rapidly progressive glomerulonephritis (with crescent).
- Acute renal failure.
- Chronic renal failure.

Examples of Glomerulonephritis

1. Alport syndrome:

- **Nephritis + nerve deafness + various eye disorders** ***(lenticonus is pathognomonic)***
- Histologically; segmental proliferation or sclerosis or both. Increased mesangial matrix and sometimes presence of fetal glomeruli may be seen. Tubular epithelium shows foamy appearence with acummulutaion of neutral fats and mucopolysaccharides.
- **Presenting clinically** with recurrent gross hematuria or persistent microscopic hematuria.
- **Inherited** as Autosomal dominant, recessive or X linked inheritance.
- **Age of presentation** is usually 5-20 years, renal impairment is usually 20-50 years in men.

2. IgA Nephropathy:

- **Age:** Occurs in ***all ages*** most commonly second and third decades of life.
- **Sex:** Male: female = 2 :1
- Presentation might be ***asymptomatic persistent microscopic hematuria*** with or without proteinuria
- Another presentation is ***recurrent macroscopic hematuria associating infections*** (during the infection episode), most probably upper respiratory tract infection, clearing within 2-4 days

The interval between the precipitating infection and the appearance of hematuria ranges from 1 to 2 days compared with 1 or 2 weeks in acute postinfectious glomerulonephritis.

- **Diagnosis** depends on finding predominant IgA deposits in kidney biopsy using immunohistochemical staining NOT on serum IgA levels (low sensitivity and specificity)

3. Henoch Schoenlein purpura nephritis:

- Characteristic ***vasculitic rash with or without abdominal pain*** (mesenteric vasculitis) or ***nephritis***
- ***Urine analysis*** is mandatory in those cases to exclude nephritis
- Long term follow up and treatment are needed in documented nephritis
- **Follow up** with urine analysis monthly is mandatory in the cases, who are negative for nephritis, for six months

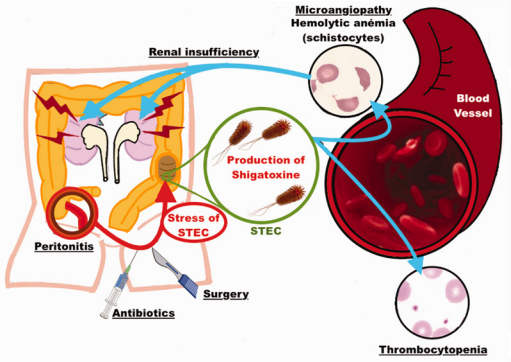
4. Rapidly progressive glomerulonephritis:

- Also called ***cresentic glomerulonephritis***, a clinicopathological condition that is characterized by ***rapid deterioration of renal functions and demonstration of crescents*** affecting at least 50% of the glomeruli in adequate biopsy specimen. Severely affected glomeruli may eventually progress to global sclerosis.
- Crescents are believed to be the result of ***severe nonspecific glomerular injury*** with numerous underlying causes, they may be cellular (most favorable prognosis), fibrocellular, or fibrous crescents (least favorable prognosis).
- Treatment is mainly by immunosuppressants.

5. Hemolytic Uremic Syndrome (HUS)

Definition:

One of thrombotic microangiopathic hemolytic anemias (TMA) & TRIAD of:



- Microangiopathic hemolytic anemia
- Thrombocytopenia
- Acute kidney injury (AKI)

It predominantly, but not exclusively, affects children.

Causes:

The most common form of HUS is associated with Shiga-Toxin producing Escherichia Coli (STEC) and is termed STEC-HUS.

Children with STEC-HUS experience a prodromal diarrheal illness due to hemorrhagic enterocolitis following exposure to a pathogenic agent (most commonly E. coli O157:H7).

STEC-HUS occurs in ~5–15% of children with STEC infection.

HUS may also occur unrelated to STEC infection (non- STEC-HUS) e.g., infection with Streptococcus pneumoniae.

Genetic and acquired defects in complement regulation, medications, malignancy, & systemic lupus erythematosus, may also be associated with non-STEC-HUS.

The clinical course of non-STEC-HUS is usually more severe than STEC-HUS and more likely to lead to chronic kidney disease (CKD).

Symptoms and signs:

- Bloody diarrhea, vomiting, abdominal pain & dehydration if severe diarrhea (STEC-HUS)
- Pallor, lethargy & tachycardia, hypertensions
- May present with bleeding under skin, & from orifices
- Manifestation of AKI.
- Manifestation of underlying causes.

Investigations:

1. Evidence of microangiopathic hemolytic anemia:

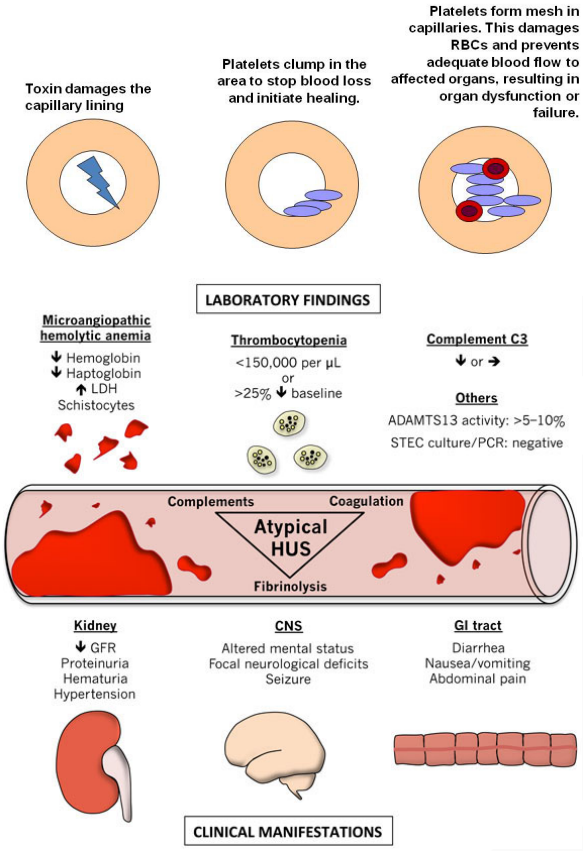
- Anemia, Elevated reticulocyte count
- Thrombocytopenia
- Presence of schistocytes, helmet cells, and burr cells on peripheral blood smear
- Increased LDH
- Decreased haptoglobin
- Increased indirect bilirubin
- Increased AST

2. Evidence of renal injury:

- Elevated serum creatinine
- Oliguria
- Presence of hematuria, proteinuria, pyuria, casts on urinalysis.

3. Other potential findings:

- Leukocytosis
- Positive stool culture for E. coli O157:H7
- Positive stool test for Shiga toxin
- Elevated amylase/lipase



Differential diagnosis of TMA:

HUS

Thrombotic thrombocytopenic purpura (TTP):

- Typically have predominantly central nervous system (CNS) symptoms but may also have significant kidney disease.
- Because CNS involvement is also seen in HUS, TTP can be difficult to distinguish from HUS.

Children with TTP have severe deficiency of ADAMTS13, a von Willebrand factor–cleaving protease.

Disseminated intravascular coagulopathy (DIC):

- Thrombocytopenia
- An elevated partial thromboplastin time and prothrombin time
- Increased levels of plasma D-dimers (or serum fibrin degradation products)
- A decreasing plasma fibrinogen level.

Immediate treatment of HUS:

- Hospital **admission**
- Correct **dehydration**
- Strict **fluid balance, electrolyte monitoring and management.**
- Treat **hypertension.**
- **For anemia:** follow up ***CBC*** & ***only transfuse if indicated.***
- **For thrombocytopenia:** follow up ***CBC*** & ***DO NOT TRANSFUSE PLATELETS unless there are life-threatening bleeds/operation required.***

AVOID antibiotics, anti-diarrheal treatment, NSAIDs, and other nephrotoxic medication.

- **Observe for non-renal complications** e.g., encephalopathy and seizures, cardiomyopathy.
- Start **renal replacement therapy** when indicated.

Follow-up of HUS after hospital discharge:

- Weekly until renal function normal
- Morning blood pressure & urinary proteins/RBCs
- Monitor growth & nutrition

6. Post streptococcal glomerulonephritis

Also known as acute proliferative glomerulonephritis

- It is an ***immune complex disease*** due to group A-Beta hemolytic streptococci - pharyngeal infective strain 12 or skin infection strain 49, leading to ***nephritis.***
- **Age:** Preschool & school age (4-12 years).
- **Sex:** Male: female = 2 :1
- **Course:** 2-3 weeks

Clinical picture of acute glomerulonephritis

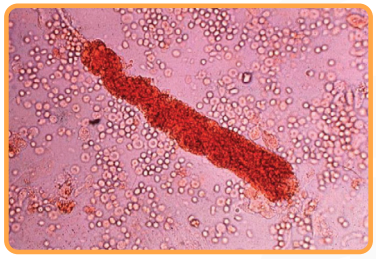
- ***Oliguria*** due to decreased renal blood flow.
- ***Edema*** (toxic capillaritis & salt, and water retention)
- ***↓ GFR***
- ***Hematuria*** smoky or frank hematuria, red urine.
- ***Hypertension +/- hypervolemia and ↑ peripheral resistance*** (proliferation of mesangial cells may result in a decrease in kidney blood flow, resulting in a decrease in the production of urine. The renin-angiotensin system may be subsequently activated, because of the decrease in perfusion of juxtaglomerular apparatus, which may result in HTN with ↑ renin).
- ***Metabolic acidosis.***
- ***Circulatory congestion*** (salt & water retention).

Abnormal Presentation:

- **Hypertensive Encephalopathy:** coma + vomiting & severe headache.
- **Anuria** = Acute renal failure.
- **Congestive heart failure** due to:
  1. Hypertensive heart failure.
  2. Toxic carditis.
  3. Over circulatory congestion.

Investigations

Urine:



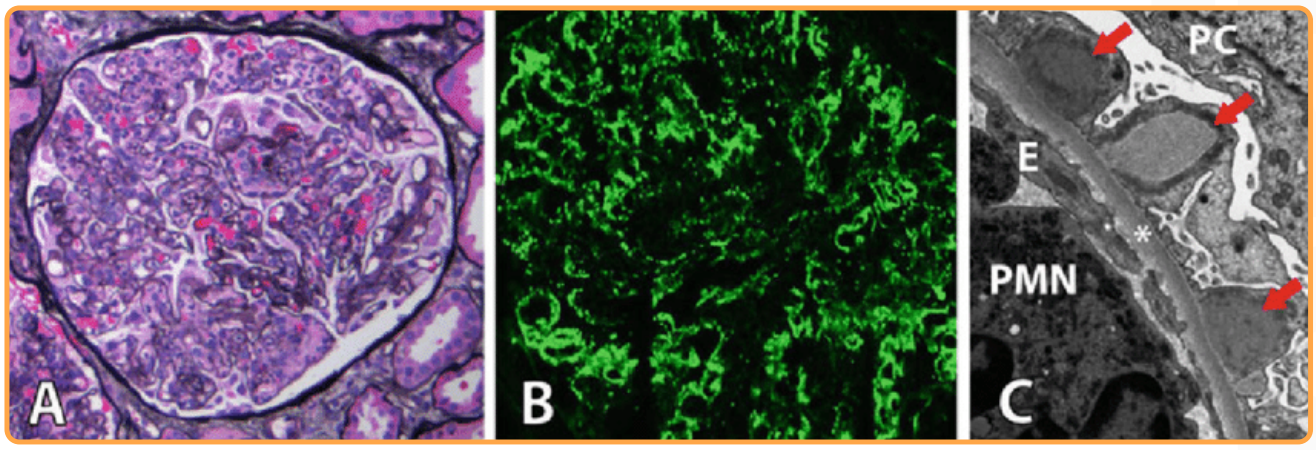
1. **Elevated specific gravity.**
2. **Urine Volume:**
   - **Oliguria:** urine output that is less than 1 mL/kg/h in infants, less than 0.5 mL/kg/h in children,
   - **Anuria:** urine output < 1 ml/kg/day (child)
3. **Hematuria** with dysmorphic RBCs and RBCs casts.
4. **Proteinuria**.

Blood:

1. **Azotemia:** Elevated BUN and serum Creatinine.
2. Increased serum **Na and K with metabolic acidosis.**
3. Elevated **Antistreptolysin O titre in pharyngitis**
4. Elevated **Antihyaluronidase in impetigo**.
5. **Diminshed C3** (consumed in immune complexes).

Renal Biopsy:

- **Light microscope:** diffuse proliferative glomerulonephritis.
- **Immunofluorescent microscope:** Lumpy deposits of C3 and IgG.
- **Electron microscope:** The presence of large sub-epithelial electron-dense deposits with a "hump-like" appearance.



Prevention & Treatment

Usually resolves spontaneously.

Treatment is focused on relief of symptoms.

Recovery > 90%.

Treatment is done by:

1. Early antibiotic therapy for streptococcal infection for ***10 days.***
2. Fluid restriction to urine volume/24 hr. +400 ml/m2/24 h.
3. Diet = mainly carbohydrate + protein 2 gm/kg + limitation of Na.
4. Treatment of hypertension
5. Treatment of hyperkalemia
6. Dialysis.

Indications for Renal Biopsy

1. **Persistently** low C3 beyond 8 weeks
2. **Persistent** heavy proteinuria after 6 months
3. **Atypical presentation:** nephrotic syndrome, severe acute renal failure with estimated GFR <30ml/min/1.73m2
4. **Atypical course:** failure of renal functions to improve after initial improvement during the acute phase which usually last no more than 2 weeks.

PROTEINURIA & NEPHROTIC SYNDROME

Physiology

The Nephron

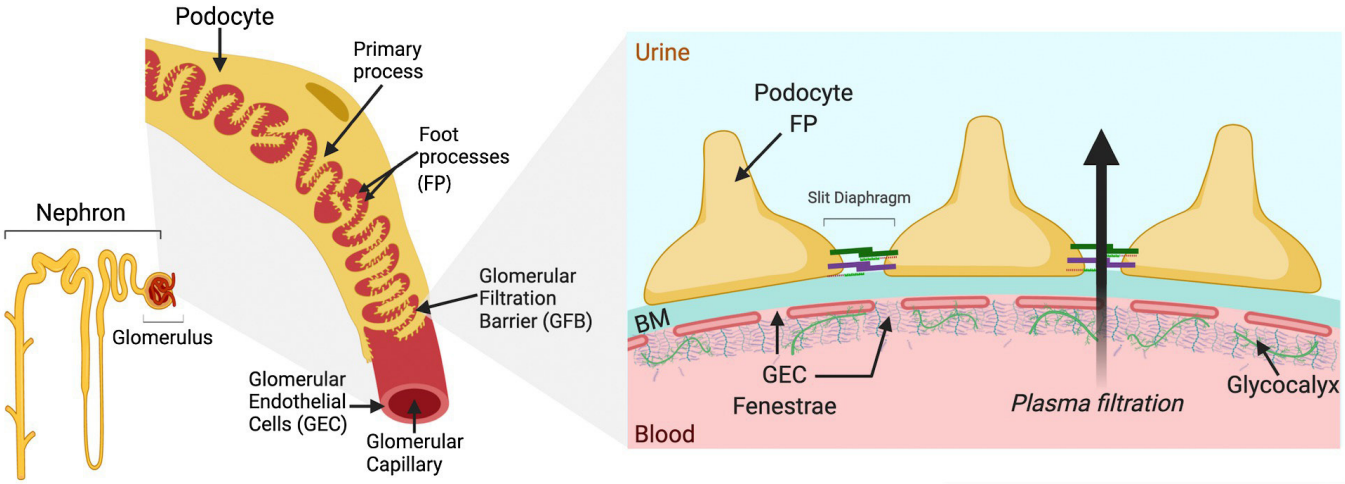
- The glomerular capillaries are lined on the inside with fenestrated endothelial cells, which are attached to the glomerular basement membrane (GBM).
- Podocytes cover the outer aspect of GBM with large cell bodies and interdigitating foot processes. Mesangial cells and their associated extracellular matrix (ECM) connect adjacent capillaries, and the capillary bundle is contained within Bowman's capsule.

The Glomerular Filtration Barrier

- The renal glomerulus controls the filtration of water and solutes while at the same time acting as a barrier retaining vital molecules such as plasma proteins.
- The glomerular filter functions as a semipermeable, macromolecular sieve capable of excluding molecules larger than serum albumin.
- **The components of the GFB include three layers:**
  a. The fenestrated endothelial cells lined by a glycocalyx,
  b. The glomerular basement membrane (GBM), and
  c. The slit diaphragm, which links the neighboring podocyte foot processes.

Proteinuria

- The charge and size selective properties of the glomerular capillary wall prevent significant amounts of albumin, globulin, and other large plasma proteins from entering the urinary space.
- Smaller proteins (low-molecular-weight proteins) do cross the capillary wall but are reabsorbed by the proximal tubule. A very small amount of protein that normally appears in the urine is the result of normal tubular secretion.



Pathophysiology of Proteinuria

Abnormal amounts of protein may appear in the urine from 3 possible mechanisms:

1. ***Glomerular proteinuria:*** which occurs as a result of disruption of the glomerular capillary wall.
2. ***Tubular proteinuria:*** a tubular injury or dysfunction that leads to ineffective reabsorption of mostly low-molecular-weight proteins.
3. ***Increased production of plasma proteins:*** (multiple myeloma, rhabdomyolysis, or haemolysis) which may cause the production or release of very large amounts of protein that are filtered at the glomerulus and overwhelm the absorptive capacity of the proximal tubule.

Methods for assessment of Proteinuria

	Indications	Normal Range
Dipstick testing	Routine screening for proteinuria performed in the office	Negative trace
24-hour urine for protein excretion	Quantitation of proteinuria	***< 4 mg/m²/h*** in a documented 24-hour collection
Spot urine for protein/ creatinine ratio	Semiquantitative assessment of proteins	***< 0.2 mg/mg*** in children > 2 years old ***< 0.5 mg/mg*** in those 6-24 months old

Causes of Proteinuria

Transient (functional) proteinuria

- Idiopathic.
- Related to medical condition (e.g., fever, seizure).
- Unrelated to medical condition (e.g., exercise, stress, dehydration, cold exposure).

Orthostatic Proteinuria:

- The most common cause of persistent proteinuria in school-age children and adolescents.
- Occurring in up to 60% of children with persistent proteinuria.

- Children with this condition are usually asymptomatic.
- Patients with orthostatic proteinuria excrete normal or minimally increased amounts of protein in the supine position.
- In the upright position, urinary protein excretion may be increased 10-fold, up to 1,000 mg/24 hr (1 g/24 hr).

Hematuria, hypertension, hypoalbuminemia, edema and renal dysfunction are absent

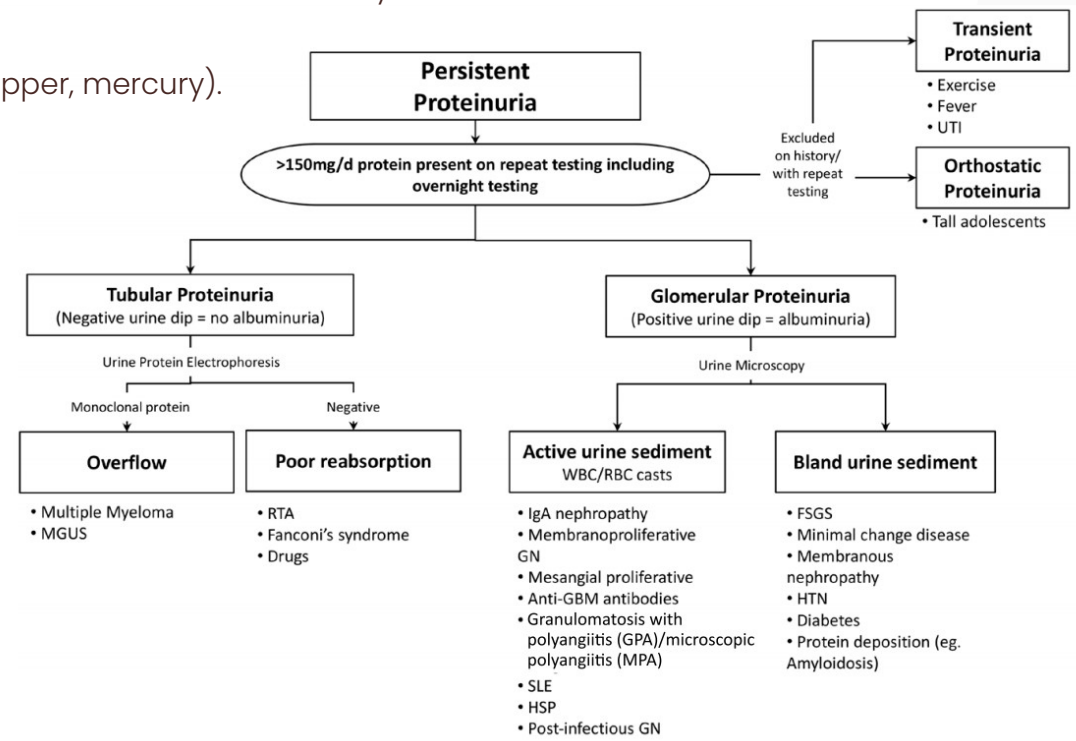
Persistent Proteinuria:

A. Glomerular:

- Alport syndrome.
- Collagen vascular disease or vasculitis: Henoch-Schönlein purpura, systemic lupus erythematosus.
- Diabetes mellitus.
- Glomerulopathy (Nephrotic Syndrome).
- Infection: group A beta-hemolytic streptococcus infection, viral infection (hepatitis B, hepatitis C, human immunodeficiency virus, infectious mononucleosis), other infection (malaria, syphilis).
- Malignancies (lymphoma, solid tumors).
- Toxin (mercury).

B. Tubulointerstitial:

- Acute tubular necrosis: aminoglycosides, NSAIDs, radiocontrast media.
- Acute tubulointerstitial nephritis: NSAIDs, penicillin, cephalosporins.
- Polycystic kidney disease.
- Proximal renal tubular acidosis: Fanconi syndrome.
- Pyelonephritis.
- Toxins (lead, copper, mercury).

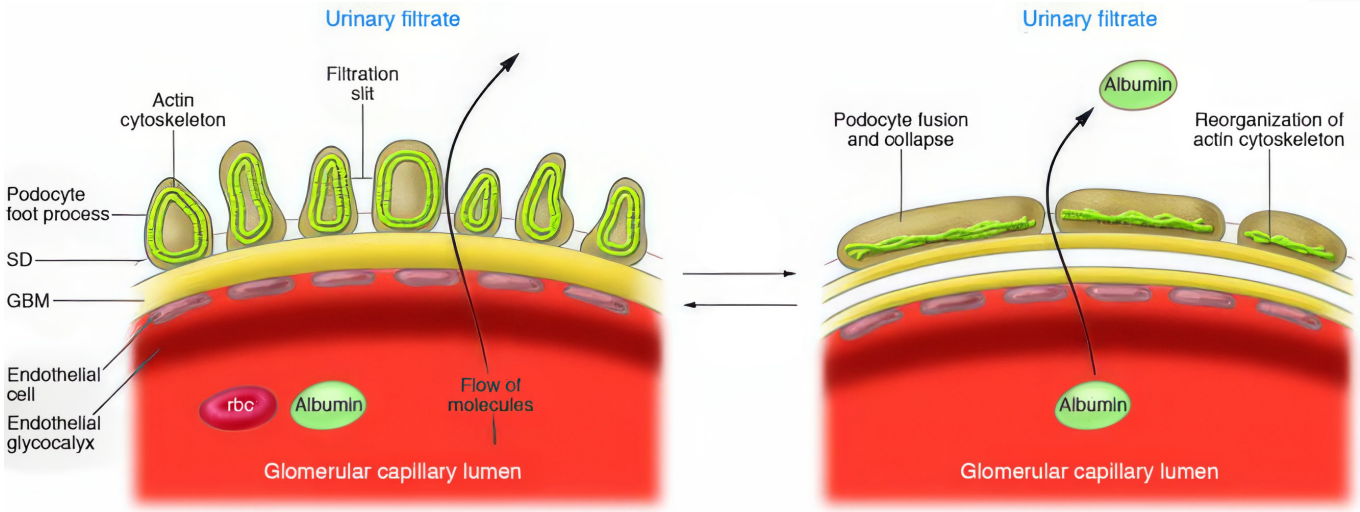


Nephrotic Syndrome

Nephrotic syndrome is defined by

1. ***Heavy selective proteinuria*** (> 40 mg/m2 hour)
2. ***Hypoalbuminemia***
3. ***Generalized edema***
4. ***+/- Hyperlipidemia.***

Proteinuria is secondary to a defect of the glomerular filtration barrier. The main complications of nephrotic syndrome are infections and thromboembolic events. Although nephrotic syndrome may be secondary to many renal diseases, idiopathic nephrotic syndrome is the most frequent cause in childhood with a complete remission following corticosteroid therapy in 90% of cases. Less frequently, nephrotic syndrome is due to a primary or secondary glomerulonephritis or to a genetic defect of podocyte or glomerular basement membrane proteins.



Genetic testing is proposed in children with steroid-resistant idiopathic nephrotic syndrome, children less than 1 year, children with familial history of proteinuria, or those with extrarenal symptoms. Kidney biopsy is performed in children older than 12 years and children who do not respond to steroid therapy.

Classification

According to the age at presentation

1. ***Congenital:*** before 6 months
2. ***Infantile:*** 6 m-2 years
3. ***Childhood (idiopathic):*** 2-8 years
4. ***Older:*** above 8 years

Etiology

I. Primary renal disease

1. Minimal change nephrotic syndrome (MCNS)
2. Congenital nephrosis.
3. Focal glomerulosclerosis.
4. Membranous GN.
5. Membranoproliferative GN.
6. Rapidly progressive GN.

II. Secondary to systemic disease.

1. Toxins and Drugs e.g., Gold & Penicillamine.
2. Infection e.g., Malaria, Toxoplasmosis, S. mansoni and syphilis.
3. Malignancies e.g., Hodgkin lymphoma.
4. Collagen diseases e.g., SLE.
5. Blood disease e.g., sickle cell anemia, Henoch-Schönlein purpura (HSP).

Pathogenesis

Proteinuria:

- ↑ glomerular basement membrane permeability for proteins; low molecular weight proteins (Selective proteinuria) → ***Loss*** of Albumin, IgG, and Transferrin, and ***retention*** of lipoproteins and macroglobulins.

Edema:

- ↓ osmotic pressure (hypoproteinemia)
- Salt and water retention (↑ aldosterone)
- Inappropriate release of ADH.

Hyperlipidemia:

- ↑ in serum lipoproteins to correct osmotic pressure 2ry to hypoalbuminemia → 2ry hypercholesterolemia.
- ↓ in Lipoprotein lipase activity.
- ↓ Low molecular weight proteins in blood stimulate ↑ production of large molecular weight lipoproteins.

Hypoproteinemia:

- Excess loss of proteins in urine
- Loss of proteins in the GIT

Minimal Change Nephrotic Syndrome (MCNS)

Most common cause of nephrotic syndrome in children> 70%

Age: 2-7yrs. M: F = 2:1

Pathogenesis:

- Idiopathic - unknown - allergic disorder
- **Immunologic disorders** (T. cell dysfunction), loss of negative charges on the fenestra of glomerular basement membrane leads to loss of repelling power of albumin.

Clinical Evaluation at Onset

1. The child should be examined to detect ***peripheral edema, ascites, or pleural or pericardial effusion.***
2. ***Blood pressure*** should be measured as hypotension may be related to hypovolemia, whereas hypertension may be related to glomerulonephritis.
3. ***Physical examination*** is important to detect ***infection or thrombosis as a complication*** of the nephrotic syndrome.

Diagnostic Labs

- Nephrotic range ***proteinuria*** is defined as urine protein excretion ***greater than 50 mg/kg per day or 40 mg/m2 per hour.***
- ***Total protein/creatinine ratio*** in a spot urine sample ***greater than 2 mg protein/mg creatinine.***
- ***Plasma protein levels*** are reduced, ***less than 5 g/dl***, due to hypoalbuminemia.
  - ***Albumin*** level is ***lower than 3g/dl and may be less than 1 g/dl.***
- ***Total cholesterol and LDL cholesterol*** are ***elevated***, while ***HDL cholesterol*** is ***unchanged or low.***
- ***Serum sodium*** is often ***reduced***. ***Hypocalcemia*** is related to hypoalbuminemia, and the level of ionized ***calcium*** is usually ***normal.***
- ***Hemoglobin levels and hematocrit*** are ***increased in patients with plasma volume contraction.***
- ***Thrombocytosis*** is common.
  - Fibrinogen and factors V, VII, VIII, and X are increased, whereas antithrombin III, the heparin cofactor, protein C and protein S are decreased.

Clinical characteristics

1) Edema and weight gain:

- Generalized edema starts by affecting the eyelids then ankles.
- Progresses to affect both L.L., scrotum or vulva, sacrum, and anterior abdominal wall
- Maximum in the morning and decreases by evening.
- Bilateral Painless pitting edema.
- May lead to ascites, pleural effusion, and pericardial effusion (anasarca).

2) Anorexia and abdominal pain (Edema of the intestinal wall).

3) Lethargy.

4) Blood pressure:

- Normal (Mild transient increase is found in 5-10% of cases).

5) Relapse:

- The disease is liable for many relapses that may follow RTI or UTI.

Complications

1) Infections

- Children with nephrotic syndrome are immunocompromised due to hypoproteinemia, low levels of IgG and urinary losses of opsonins, and immunosuppressive therapy.

Increased susceptibility to infections is due to:

- Decreased immunoglobulins and complement components (loss in urine).
- Use of steroids (Immunosuppression).
- Local factors as edema and ascites.

Common organisms:

- Gram negative organisms e.g., E. coli.
- Encapsulated organisms e.g., pneumococci, meningococci.

Common infections are:

- Peritonitis (most common) ii) Skin infection & U.T.I.

2) Thromboembolism/ Hypercoagulability

Factors associated with this complication include:

- Prolonged bed rest
- Hypovolemia with hemoconcentration (due to edema and ascites).
- Increased platelet count and aggregation
- Urinary loss of anticoagulant factors (antithrombin-iii, protein C and S).
- Decreased fibrinolytic functions.
- increased biosynthesis of coagulation factors (fibrinogen).
- Precipitated cholesterol on vessel wall.

3) Hypovolemic shock and acute kidney injury

- Use of loop diuretics in patients with contracted blood volume, or GIT losses (vomiting, diarrhea with poor oral intake are suggested causes)

4) Complications of drugs used in treatment

- Osteoporosis, hypertension, hyperglycemia, cushingoid facies, hirsutism with ***steroid therapy.***
- Cosmetic side effects (gingival hyperplasia, hypertrichosis with cyclosporin therapy).

Investigations

1) Urine:

a) Heavy selective ***proteinuria.***
b) ***Hematuria***: in less than 10% of cases transient and microscopic.
c) An evidence of ***UTI*** may be present (inc. pus cells).
d) ***Lipoid, hyaline and granular casts.***

2) Blood:

a) Decreased total ***plasma proteins & serum albumin.***
b) ***Hyperlipidemia*** (mainly 2ry hypercholesterolemia).
c) Normal ***Kidney Function Tests.***
d) Normal ***C3.***
e) Elevated ***ESR***

3) Renal biopsy:

a) ***Light microscopy:*** minimal changes.
b) ***Electron microscopy:*** fusion of epithelial cell foot processes.
c) ***Immunofluorescent studies:*** negative.

Differential diagnosis

Differential diagnosis of edema:

1- Cardiac edema:

- ***History*** of cardiac diseases, congenital heart disease or rheumatic fever.
- ***O/E:*** Other manifestations of heart failure: enlarged tender liver, congested pulsating neck veins, orthopnea.
- ***Cardiac examination:*** manifestations of the cardiac disease (murmurs, abnormality in heart sounds, abnormal rhythm).
- ***Edema:*** generalized, pitting, painless, affecting mainly the dependant parts (Lower Limbs and sacrum in bed-ridden patients and infants).

2- Renal edema:

Nephrotic syndrome:

- There may be ***history*** of previous attacks with remissions & relapses.
- ***Edema:*** bilateral, pitting, painless starts as puffy eyelids & in the dorsa of the hands and feet.
- ***Progresses*** to affect the L.L. sacrum scrotum/vulva abdominal wall.
- In severe cases it causes ***ascites, pleural effusion & pericardial effusion (anasarca).***
- ***Maximum in the morning and decreases by the evening.***

Nephritic disease (glomerulonephritis):

- ***History:*** there may be history of preceding streptococcal infections.
- ***Associated manifestations:*** oliguria, hematuria, and hypertension.
- ***Edema:*** bilateral, pitting starts as puffy eyelids & in the dorsa of the hands and feet.
- ***It is maximum in the morning and decreases by the evening.***

3- Hepatic edema:

- ***History*** of liver disease.
- ***Associated manifestations*** of portal hypertension & jaundice.
- ***Edema:*** preceded by ascites "Ascites Precox".

4- Angioneurotic edema:

- ***History*** of allergic manifestations.
- ***Edema:*** Affects eyelids, dorsa of the hands & feet, lips, penis, scrotum, vulva...
- ***Associated manifestations*** severe itching, may be associated with urticarial rash, hoarseness of voice, stridor (laryngeal edema),
- It is of ***acute onset***.
- It shows ***good response to anti-allergic drugs*** e.g., S.C adrenaline.

5- Other causes of edema:

- **Lymphatic edema** (non-pitting).
- **Myxedema** (hypothyroidism). (non-pitting).

Treatment

The goal of therapy should be

a. A gradual reduction of edema
b. with judicious use of diuretics
c. Sodium restriction
d. Cautious use of intravenous albumin infusions, if indicated

Steroid therapy

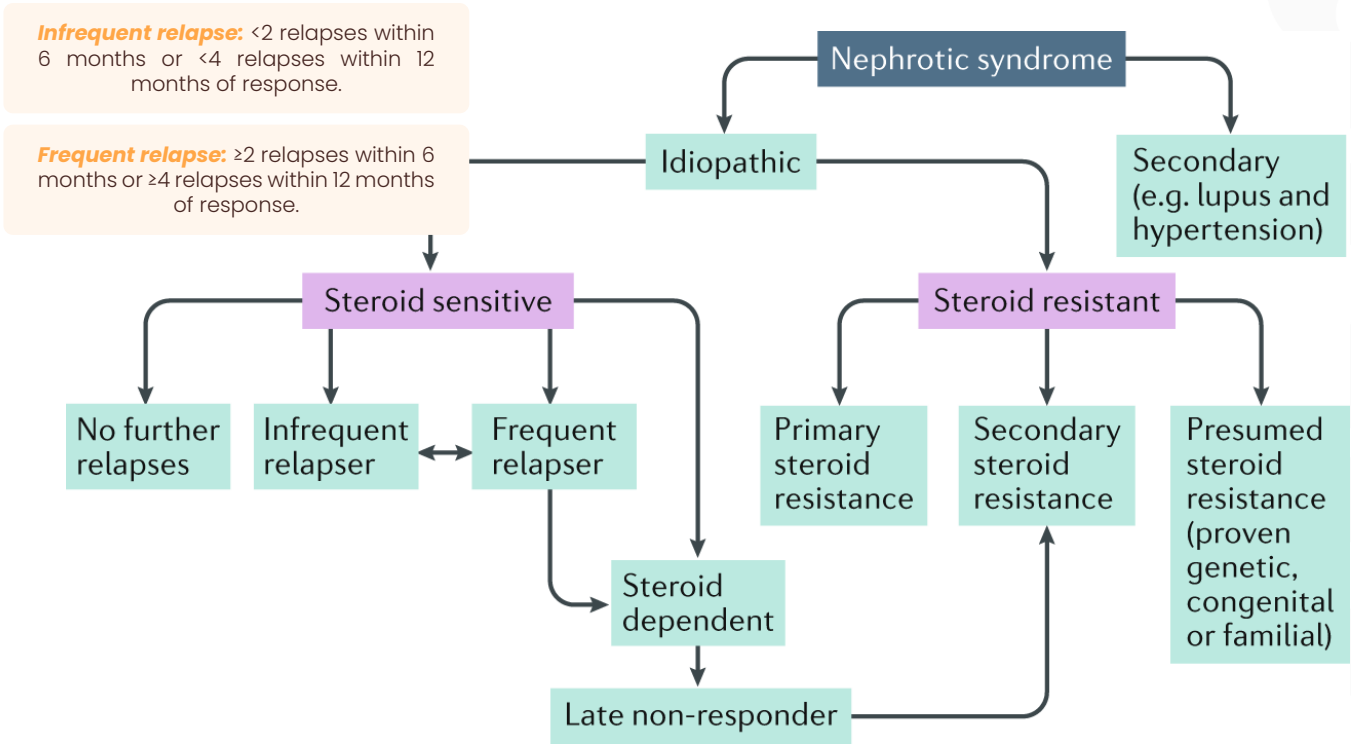
- Prednisone is best given following food; therapy with antacids, ranitidine, or proton pump inhibitors is not routinely required.
- While the disease course varies in patients with SSNS, more than 75% patients show one or more relapses on follow-up.
- Almost one-half of the relapses are precipitated by minor infections, usually of the upper respiratory tract.
- Approximately 80-90% of children respond to steroid therapy.
- Response is defined as attainment of remission within the initial 6 weeks of steroid therapy.
- If proteinuria persists after 6 weeks ***(steroid resistant)***, it is an indication for renal biopsy.

Initial episode

- **Prednisone** at a dose of ***60 mg/m²/day (2 mg/kg/day, maximum 60 mg*** in 1–2 divided doses) for ***4– 6 weeks***, followed by 40 mg/m² (1.5 mg/kg, maximum 40 mg as single morning dose) on alternate-days for a period ranging for the next ***4–6 weeks***, and then discontinued.
  (***ALTERNATIVELY:*** for a period ranging from 8 weeks to 5 months, with tapering of the dose).

Relapse

- A relapse is treated with prednisone at ***60 mg/m2 /day (2 mg/kg/day; maximum 60 mg)*** in single or divided doses until remission (protein trace/nil for 3 consecutive days), followed by 40 mg/m2 (1.5 mg/kg, maximum 40 mg) on alternate days for 4 weeks. Remission is achieved by 7–10 days and daily therapy is seldom necessary beyond 2 weeks.



Corticosteroid Alternatives

- ***Cyclophosphamide*** (Endoxan)
- ***Calcineurin inhibitors***

  a. Cyclosporine A (Sandimmune)

  b. Tacrolimus (Prograf)
- ***Mycophenolate mofetil*** (Cellcept)
- ***Levamisole***
- ***Rituximab*** (Anti CD 20)
- Angiotensin converting enzyme inhibitors ***(ACEI)*** & angiotensin II receptor blockers ***(ARBs)***

Supportive Care

1) Nutrition

- Normal protein intake: Children with steroid sensitive nephrotic syndrome (SSNS) and normal renal function are advised protein consumption and caloric intake, as appropriate for healthy children of that age.
- Sodium and cholesterol restriction.

2) Edema, Hypovolemia, and Fluid Overload

- Mild edema can be managed with dietary sodium restriction to <2 mEq/kg/day and fluid restriction to two-thirds of maintenance.
- The use of diuretic agents or human albumin in these cases is not recommended.
- For symptomatic edema, the combination of sodium restriction, and use of diuretic agents or human albumin, based on evaluation of fluid status, are recommended.

3) Immunizations

- Because acquired infection may lead to severe disease in patients with nephrotic syndrome, appropriate immunization is performed.
- Inactivated vaccines are preferred in patients receiving therapy with corticosteroids and immunosuppressive medications. There is no increased risk of relapses following these vaccines.
- Live attenuated vaccines should not be administered to patients receiving corticosteroids or other immunosuppressive agents.
- Vaccination of family members is recommended.
- In cases where a patient has been in contact with a patient with varicella, prophylaxis with acyclovir is advised.

4) Avoid complete bed rest to avoid Thromboembolism.

Indications of IV Albumin infusion:

1. Distressing ascites.
2. Oliguria.
3. Severe scrotal or labial swelling.

4 URINARY TRACT INFECTIONS

Prevalence and Etiology

The prevalence of urinary tract infections *varies markedly* with sex and age.

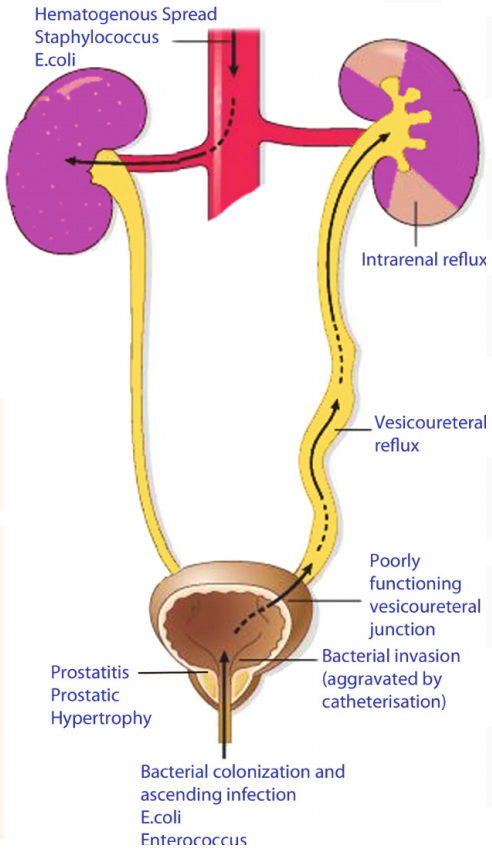
- ***Symptomatic urinary tract infections (UTI)*** occur in 1.4/1000 newborn infants. UTIs are more common in uncircumcised male infants compared to circumcised infants.
- Thereafter, infections are much more common in females. They occur in 1.2-1.9% of school-aged females and are most common in the 7-11-year-old age group (2.5%). Infections are quite rare in males of similar age.

Bacteriology:

- ***UTIs are caused mainly by colonic bacteria;*** 75-90% of all infections are caused by Escherichia coli followed by Klebsiella and Proteus.
- ***Other organisms*** include Staphylococcus saprophyticus and viral infections such as adenovirus.

Routes of infection:

1. ***Ascending route:***
   - Nearly all UTIs are ascending infections, the bacteria arise from the fecal flora, colonize the perineum and enter the bladder via the urethra.
   - This explains the higher incidence of UTIs among females owing to their short urethra.
   - In uncircumcised boys, the bacterial pathogens arise from the flora beneath the prepuce.
2. ***Hematogenous route*** occurs in rare cases (mainly in the neonatal period).



If bacteria ascend from the bladder to the kidney, acute pyelonephritis may occur.

Normally the simple and compound papillae in the kidney have an anti-reflux mechanism that prevents urine from flowing in a retrograde manner into the collecting tubules. Some compound papillae, typically located in the upper and lower poles of the kidney, allow intrarenal reflux. Infected urine then stimulates an immunologic and inflammatory response. The result may cause renal injury and scarring.

Risk factors for UTIs

- Females
- Uncircumcised boys
- Vesico-ureteral reflux (Risk increased for clinical pyelonephritis, not cystitis)
- Obstructive uropathy
- Urethral instrumentation
- Wiping from back to front
- Pinworm infestation
- Constipation, neuropathic bladder
- P-fimbriated bacteria (Risk increased for clinical pyelonephritis, not cystitis)

Classification of UTI

There are three basic forms of UTI: pyelonephritis, cystitis and asymptomatic bacteriuria.

Pyelonephritis

Is characterized by any or all of the following:

- High-grade fever, rigors, and malaise
- Abdominal or flank pain
- Nausea, vomiting, jaundice in neonates and occasionally diarrhea.
- Newborns may show poor feeding, irritability, and weight loss

Involvement of the renal parenchyma is termed acute pyelonephritis. It may result in renal injury, which is termed pyelonephritic scarring, which is an important risk factor for development of end-stage renal failure.

Cystitis

Indicates that there is bladder involvement and includes:

- Dysuria, urgency, frequency
- Suprapubic pain
- Incontinence
- Malodorous urine

Cystitis does not cause fever and does not result in renal injury.

Diagnosis

1- Urine analysis:

- ***Pyuria:*** pus cells >5 cells/HPF (high power field)
- ***hematuria***
- ***Proteus*** infections consistently produce ***alkaline urine.***
- ***Bacteriuria***, by microscopic examination of urine
- ***Positive Nitrites*** in urine by a dipstick (in a freshly voided sample < 4 hours)

2- Urine culture:

> The diagnosis of UTI depends on the culture and sensitivity of bacteria from the urine, according to the Egyptian guidelines the main 3 methods suggested for urine culture are: mid-stream sample, suprapubic aspiration, and urinary catheter.

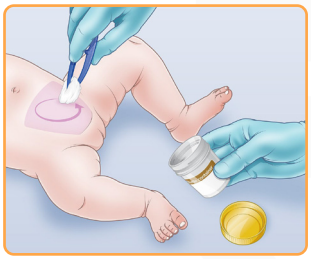
- ***In toilet-trained children***, a midstream urine sample is usually satisfactory. If the culture shows >100,000 colonies of a single pathogen per milliliter, or if there are 10,000 colonies and the child is symptomatic, it is considered a UTI.
- ***In infants less than 1 year,*** urine culture will be taken by suprapubic aspiration.
- ***In infants after the 1st year,*** urine culture can be taken by urinary catheter.

According to the AAP, diagnosis should be based on presence of pyuria and at least 50,000 colonies/ml of a single uropathogenic organism in an appropriately collected specimen of urine.

In a catheterized specimen or suprapubic aspiration, the finding of any colonies grown from the bladder urine should be considered as indicative of infection.

There is a practice point (or opinion) of obtaining urine sample for culture in children less than 2 years by (***Quick-Wee voiding stimulation*** method of gentle cutaneous suprapubic stimulation using gauze soaked in cold fluid and waiting for the baby to void and collect urine aseptically).

In situations where parents refused invasive maneuvers or due to lack of experience performing suprapubic aspiration or urinary catheterization.



3- CBC, CRP, ESR:

- In acute renal infection, leukocytosis, neutrophilia and elevated ESR and C-reactive protein are common.

4- Blood culture if sepsis is suspected particularly in neonates.

5- Imaging studies (U/S, VCUG, RNC)

Treatment

1- Cystitis

- ***Start antibiotic*** after obtaining urine for culture.

> ***If treatment is initiated before the results of a culture and sensitivity are available, a 3 to 5-day-course of therapy with an oral antibiotic like:***

- ***Trimethoprime-sulfamethoxazole:*** 20 mg/Kg/24 hours for sulfamethoxazole and 4 mg/Kg/24 hours for trimethoprime.
- ***OR Nitrofurantoin:*** 5-7 mg/Kg/day in 3-4 divided doses.
- ***OR Amoxicillin:*** 50 mg/Kg/day.

2- Acute pyelonephritis

A 10-14-day course of broad-spectrum antibiotics capable of reaching significant tissue levels is preferable.

- ***Ceftriaxone*** (50-75 mg/Kg/day not to exceed 2 gm/day)
- ***OR Ampicillin*** (100 mg/Kg/day) with an aminoglycoside as gentamicin (3-5 mg/Kg/day in 3 divided doses).

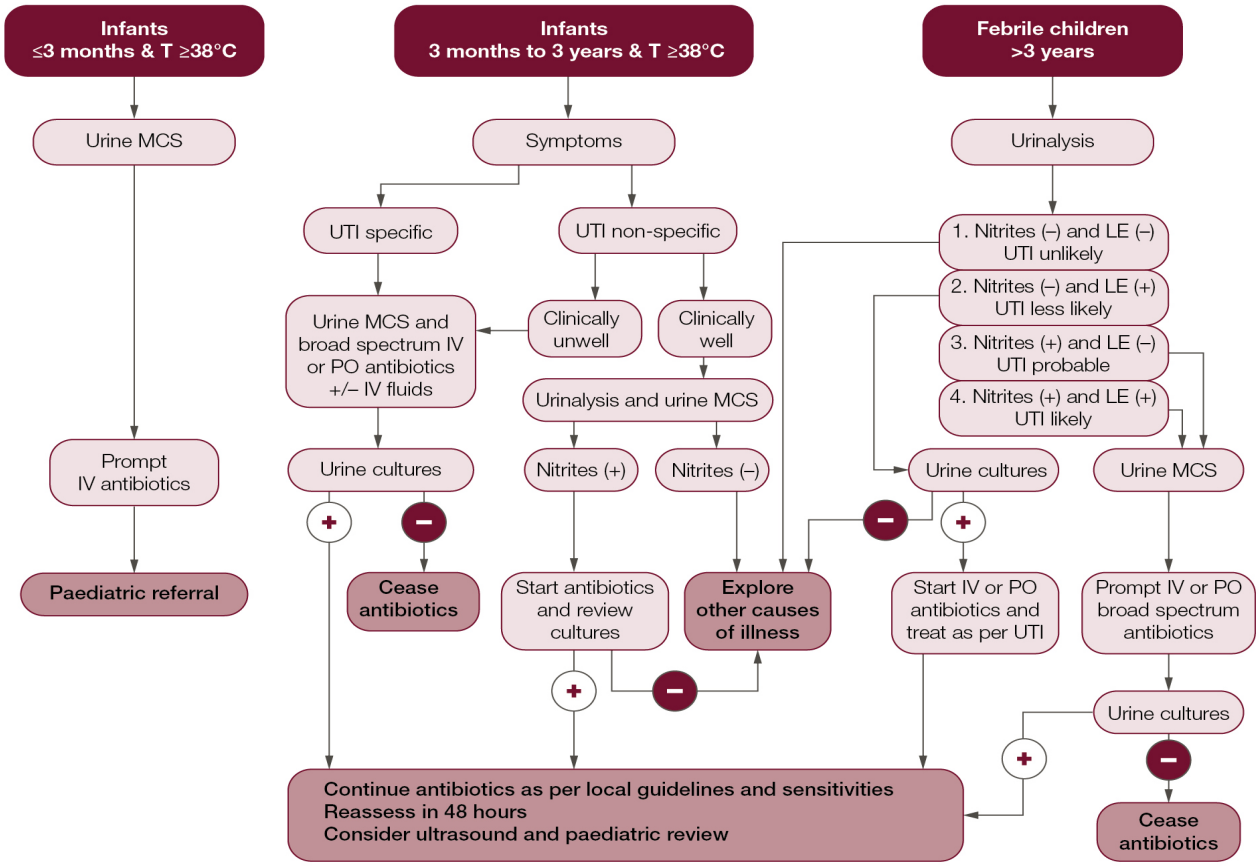
The potential ototoxicity and nephrotoxicity of aminoglycosides should be considered, and serum creatinine levels must be obtained prior to initiating treatment as well as daily thereafter as long as treatment continues. Drug level may be also monitored to avoid toxicity.

3- Renal/perirenal abscess or infection in obstructed urinary tracts

Require surgical or percutaneous drainage in addition to antibiotic therapy and other supportive measures.

Follow up

- Given the tendency of UTI to recur even in the absence of predisposing anatomic factors, ***follow-up urine cultures should be obtained with any symptoms suggestive of recurrence ad fever or abdominal pain.***



Imaging studies

The goal of imaging studies in children with a UTI is to identify anatomic abnormalities that predispose to infection.

1. **Renal ultrasonogram** to rule out hydronephrosis and renal or perirenal abscess.
2. **Voiding cystourethrography (VCUG):** indicated in recurrent febrile UTI or if the ultrasound shows any abnormality as hydronephrosis.
3. **Renal scanning with technetium labelled DMSA (DMSA scan):** If VUR is present, a DMSA scan is performed to assess whether renal scarring is present or not, to be performed after 4-6 month of UTI. If it is done during the acute phase of UTI, it is the most diagnostic test for pyelonephritis, however it is usually not needed during the acute phase.

Relative indications for surgical correction

- High grade reflux
- Breakthrough febrile UTI while on continuous antibiotic prophylaxis
- Renal scarring
- Recurrent pyelonephritis
- Parental preference
- Low probability of spontaneous resolution

5 ACUTE KIDNEY INJURY

Acute kidney injury (AKI) is defined as an abrupt decrease in kidney function, which in its most severe form, acute renal failure, is manifested by changes in blood chemistry and decreased urine output.

Acute renal failure (ARF) is the abrupt loss of kidney function that results in the retention of urea and other nitrogenous waste products and in the dysregulation of extracellular volume and electrolytes

Etiology of ARF

1. Pre-renal (60-70%)

Sudden and severe drop in blood flow to the kidneys.

This may be due to:

1. ***Hypovolemia:*** Loss of ***blood*** (hemorrhage), ***fluids*** (GE with dehydration, excessive use of diuretics, salt loosing renal or suprarenal diseases), or ***plasma proteins*** (NS, extensive burns).
2. ***Hypotension:*** decrease in ***cardiac output*** (heart failure), decrease in ***peripheral resistance*** (shock), ***septicemia*** and ***DIC.***

2. Renal (25-40%)

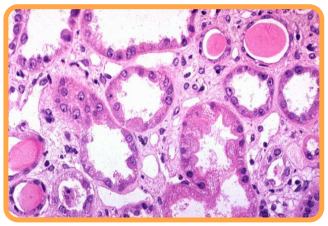
Direct damage to kidneys by inflammation, toxins, drugs, infection or ↓ blood supply.

This might lead to:

1. ***Glomerular:*** Post streptococcal glomerulonephritis, membranoproliferative, rapidly progressive, SLE, Henoch Schönlein purpura.
2. ***Acute tubular necrosis:*** Heavy metals, chemicals, drugs (aminoglycosides), shock, ischemia.
3. ***Acute interstitial nephritis:*** Infection, drugs.
4. ***Localized intravascular coagulation:*** Renal vein thrombosis, cortical necrosis, hemolytic uremic syndrome.
5. ***Tumors:*** Renal parenchymal infiltration, uric acid nephropathy.

Acute tubular necrosis

- Dilated tubules, Interstitial edema with wider than normal separation of tubules, Many tubules contain hyaline casts, Tubular cells are shed into the lumen and not replaced.

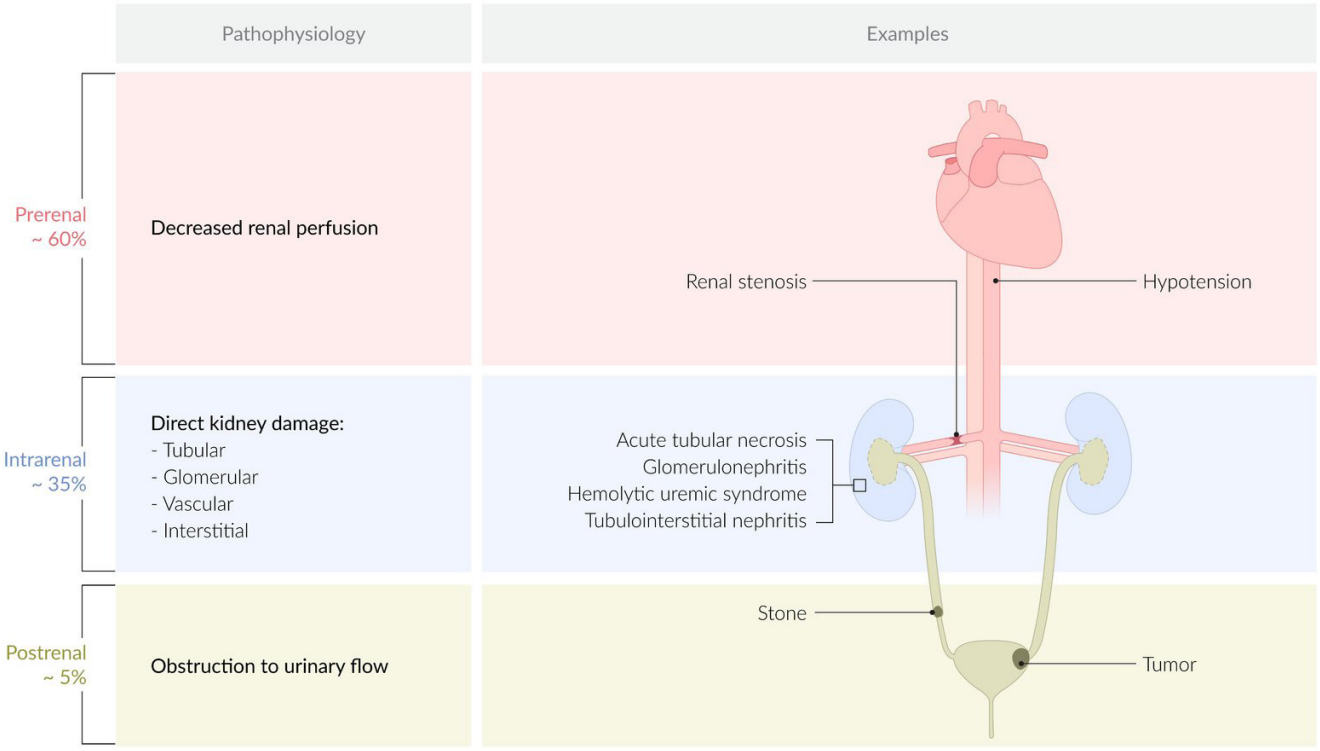


3. Post renal (5-10%)

Sudden obstruction of urine flow due to kidney/bladder stone, tumor or injury.

This might be lead to:

1. ***Obstructive uropathy:*** stones, blood clot, tumor, ureteropelvic junction, ureterocele, urethral valve.
2. ***Vesico-ureteral reflex***



Causes of ARF in the newborn

Renal agenesis / dysgenesis: Obstructive uropathy, Reno vascular accident, Congenital heart disease, Dehydration, Hemorrhage, Sepsis,

NEC

RDS: Shock, DIC, Renal vein thrombosis.

Clinical manifestations

The presenting symptoms & signs may be dominated or modified by the precipitating disease (RDS, NEC, sepsis, GE with dehydration) and renal failure

Clinical findings related to renal failure:

- Diminished urine output.
- Edema (salt &water overload).
- Hypertension.
- Vomiting.
- Lethargy (uremic encephalopathy).
- Dyspnea (overload).
- Rapid breathing (acidosis).
- Uremic breath odor.
- Bleeding (platelet dysfunction).

Clinical findings related to complications of AKI:

- Volume overload: Heart failure, Pulmonary edema.
- Arrhythmia due to hyperkalemia.
- GIT bleeding (stress ulcers, gastritis).
- Seizures, coma or behavioral changes (uremia).

Diagnosis

1: History

- Vomiting, diarrhea, dehydration
- Dark red urine, oliguria (PSG)
- Skin rash (SLE, HSP)
- Exposure to chemicals or drugs
- Abdominal colic, painful micturition & passing stones

2: Examination

- Signs of dehydration.
- Edema & dyspnea (volume overload).
- Rapid breathing (acidosis), uremic breath, arrhythmia (hyperkalemia).
- Level of consciousness.
- Skin rash distribution (HSP).
- ***BP:*** high in pre-renal & low in acute tubular necrosis.
- Flank mass (renal vein thrombosis, tumor, cystic disease, obstructive uropathy).
- Pulmonary rales, pleural or pericardial rub.

Investigations

1- Urine analysis

- ***Amount***/24 hour
- ***Microscopic*** (RBCs, WBCs, Cast)
- Urine ***proteins***
- Urine ***Na:***
  - < 30mEq/L ***pre renal***
  - > 30mEq/L ***renal***
  - > 70mEq/L ***tubular dysfunction***

2- Laboratory tests

- ***Blood picture:***
  - Anemia: dilutional, hemolytic (HUS, SLE, RVT)
  - Hematocrit value
  - WBC: decreased in SLE
  - Platelet count: decreased SLE, RVT, HUS
- ***Renal function tests:*** high blood urea nitrogen, S. creatinine
- ***Electrolytes:*** Na (high/low), K (hyperkalemia)
- High S. ***Phosphate***, S. ***uric acid***
- ***Metabolic acidosis*** (pH, PCO2,HCO3)
- Decreased C 3 level

Treatment

Treatment of AKI It is directed at:

- Treating the underlying cause
- Correcting fluid, electrolyte and uremic abnormalities
- Preventing complications
- Considering nutritional deficiencies.

How to proceed:

- Bladder catheterization to exclude obstruction & monitor urine volume and perform urine analysis.
- Test dose of IV. mannitol (0.2gm/kg within 20 min)+ IV. furosemide (1mg/kg), diuresis occurs in reversible case but if no diuresis within 2 hours suspect irreversible RF.
- Correction of dehydration.
- Treatment of acidosis (pH<7.2)
- Treatment of hypertension

- Fluid balance
- Electrolyte balance: K, Na, Ca, P
- Acid base balance
- Drug dosing
- Nutrition
- Therapeutics

Treatment of hyperkalemia (s. potassium >7mEq/L)

- ***IV Ca gluconate*** (0.5 ml/kg over 10 minutes) to counteract the K induced myocardial irritability.
- ***$NaHCO_3$*** (correct metabolic acidosis)
- ***K exchange resin*** (Sorbisterit)
- ***In severe cases:*** Regular insulin (1 U/kg, IV) + Glucose 50% (1 ml/kg, IV) over one hour, then 0.1 U/kg of insulin is given SC every 6 hr + glucose 5% (10 ml/kg/d)
- ***Dialysis***

Treatment of hyponatremia

- ***Fluid restriction*** during oliguria or anuria

Treatment of hypertension

- ***Oral antihypertensives.***
- Treatment of ***hypertensive encephalopathy.***

Indications of dialysis

- ***Anuria/oliguria***
- ***Volume overload*** with evidence of hypertension and/or pulmonary edema refractory to diuretic therapy
- ***Persistent hyperkalemia***
- ***Severe metabolic acidosis*** unresponsive to medical management
- ***Uremia*** (encephalopathy, pericarditis, neuropathy)
- ***Blood urea nitrogen*** 100-150 mg/dL (or lower if rapidly rising)
- ***Calcium:*** phosphorus imbalance, with hypocalcemic tetany that cannot be controlled by other measures
- ***The inability to provide adequate nutritional intake*** because of the need for severe fluid restriction

6 CHRONIC KIDNEY DISEASE

Definition

A patient has Chronic Kidney Disease (CKD) if either of the following criteria are present:

1. ***Kidney damage for ≥3 months***, as defined by structural or functional abnormalities of the kidney, with or without decreased GFR, manifested by 1 or more of the following features:
   - Abnormalities in the ***composition of the blood or urine***
   - Abnormalities in ***imaging tests***
   - Abnormalities on ***kidney biopsy***
2. ***GFR <60 mL/min/1.73 m² for ≥3 months***, with or without the other signs of kidney damage described above.

Etiology

The etiology of CRF in childhood correlates closely with the age of the patient at the time when renal failure is first detected.

Children <5 years

- Renal hypoplasia/dysplasia
- Congenital malformation of urinary tract (obstructive uropathy)

Children >5 years

- Acquired glomerular disease (glomerulonephritis, HUS)
- Hereditary disorders (Alport syndrome, cystic renal disease)

Other causes of CRF

- Hypertension.
- Diabetes.
- Chronic pyelonephritis.
- Medications taken regularly over long periods: ibuprofen, acetaminophen, indomethacin, gentamycin & sulpha
- Other medical conditions: SLE.

Kidney

Structure

1. Renal agenesis
2. Renal hypoplasia/dysplasia
3. Cystic kidney disease

Position

1. Pelvic kidney
2. Horseshoes kidney
3. Crossed fused ectopia

Renal pelvis

1. Duplicated renal collecting system
2. Hydronephrosis
3. Ureteropelvic junction obstruction

Ureter

1. Duplicated renal collecting system
2. Megaureter
3. Ectopic ureter
4. Ureterocele

Bladder

1. Vesicoureteral reflux
2. Bladder diverticulum
3. Bladder/cloacal exstrophy

Urethra

1. Posterior urethral valves
2. Urethral stricture
3. Hypospadias

Pathogenesis

Regardless of the cause of kidney damage, once a critical level of renal functional deterioration is reached, progression to end stage renal failure is inevitable.

Table 529-6 STANDARDIZED TERMINOLOGY FOR STAGES OF CHRONIC KIDNEY DISEASE

STAGE	DESCRIPTION	GFR (mL/min/1.73 m^2)
1	Kidney damage with normal or increased GFR	>90
2	Kidney damage with mild decrease in GFR	60-89
3	Moderate decrease in GFR	30-59
4	Severe decrease in GFR	5-29
5	Kidney failure	<15 or on dialysis

Risk factors for progression to ESRD:

- Ongoing immunologic injury.
- Hemodynamically mediated hyperfiltration in
- surviving glomeruli.
- Dietary protein & phosphorus intake.
- Persistent proteinuria.
- Systemic hypertension.

Table 529-5 PATHOPHYSIOLOGY OF CHRONIC KIDNEY DISEASE	
MANIFESTATION	**MECHANISMS**
Accumulation of nitrogenous waste products	Decrease in glomerular filtration rate
Acidosis	Decreased ammonia synthesis Impaired bicarbonate reabsorption Decreased net acid excretion
Sodium retention	Excessive renin production Oliguria
Sodium wasting	Solute diuresis Tubular damage
Urinary concentrating defect	Solute diuresis Tubular damage
Hyperkalemia	Decrease in glomerular filtration rate Metabolic acidosis Excessive potassium intake Hyporeninemic hypoaldosteronism
Renal osteodystrophy	Impaired renal production of 1,25-dihydroxycholecalciferol Hyperphosphatemia Hypocalcemia Secondary hyperparathyroidism
Growth retardation	Inadequate caloric intake Renal osteodystrophy Metabolic acidosis Anemia Growth hormone resistance

Table 529-5 PATHOPHYSIOLOGY OF CHRONIC KIDNEY DISEASE	
MANIFESTATION	**MECHANISMS**
Anemia	Decreased erythropoietin production Iron deficiency Folate deficiency Vitamin B_{12} deficiency Decreased erythrocyte survival
Bleeding tendency	Defective platelet function
Infection	Defective granulocyte function Impaired cellular immune functions Indwelling dialysis catheters
Neurologic symptoms (fatigue, poor concentration, headache, drowsiness, memory loss, seizures, peripheral neuropathy)	Uremic factor(s) Aluminum toxicity Hypertension
Gastrointestinal symptoms (feeding intolerance, abdominal pain)	Gastroesophageal reflux Decreased gastrointestinal motility
Hypertension	Volume overload Excessive renin production
Hyperlipidemia	Decreased plasma lipoprotein lipase activity
Pericarditis, cardiomyopathy	Uremic factor(s) Hypertension Fluid overload
Glucose intolerance	Tissue insulin resistance

Clinical picture

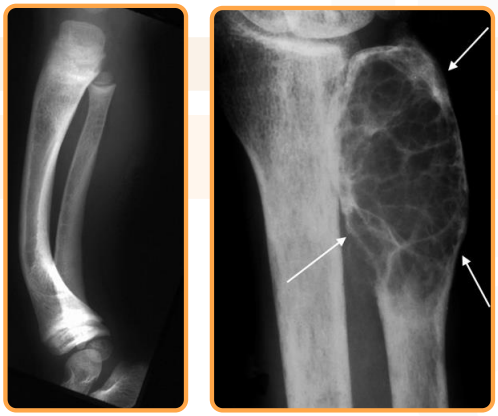
- Fatigue.
- Headache (hypertension).
- Puffiness of eyelids & edema of feet.
- Nausea, vomiting & anorexia.
- Polyuria (early) / oliguria (late).
- Bloody or foamy urine.
- Frequent hiccups.
- Anemia & easy bleeding or bruising.
- Skin discoloration & itching.
- Difficult breathing.
- Retarded growth.

Complications of CKD

Renal osteodystrophy

Bone deformities & short limbs

- Hypocalcemia & hyperphosphatemia will lead to 2ry hyperparathyroidism.
- Metabolic acidosis will lead to bone resorption.
- Deficient activation of vitamin D.



Retarded growth

Due to:

- Renal osteodystrophy.
- Protein-calorie deficiency.
- End-organ resistance to growth hormone.

Cardiovascular complications

- Hypertension (↑ renin, volume overload, hyperlipidemia).
- Pericarditis.
- Myocarditis.
- Heart failure.

Respiratory complications

- Air hunger (metabolic acidosis)
- Pneumonia

Bleeding tendency

- Defective platelet function
- Thrombocytopenia
- Coagulopathies

Recurrent infection (2ry immunodeficiency)

- Cellular immunity.
- Granulocyte function.

Neuropsychiatric changes

- Seizures, behavioral changes.
- Myopathy.
- Peripheral neuropathy.

Investigations

- ***CBC***
- ***Blood chemistry*** (urea, creatinine, Na, K, Ca, P, alk. phosphatase, PTH)
- ***Blood gases*** (pH, HCO3)
- ***Iron status*** (iron, transferrin, ferritin)
- ***ECG & echo***
- ***Radiological studies*** (CXR, extremities)
- ***Nutritional status*** (albumin, lipid profile)

Treatment (refer to nephrologists)

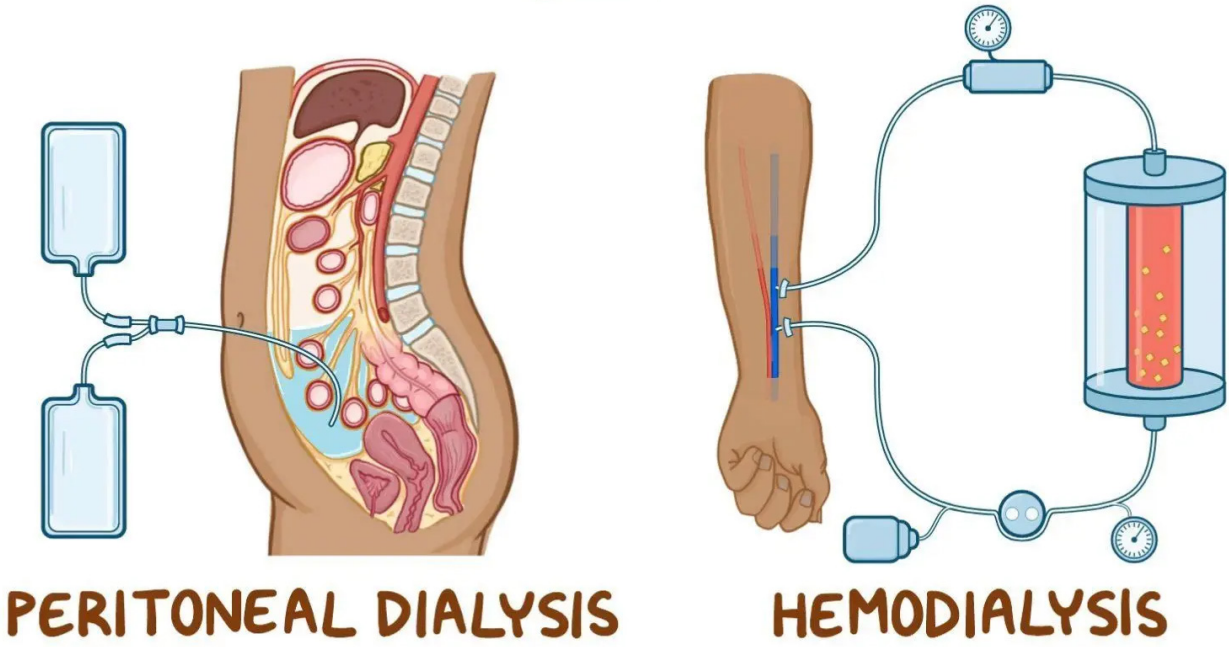
- Diet (calories, protein intake, vitamins, trace elements).
- Water electrolyte (water, Na, K, pH).
- Calcium-phosphorus homeostasis.
- Anemia (erythropoietin, Fe, vitamins).
- Cardiovascular complication.
- Adjustment of drug dosage.
- Dialysis.
- Renal transplantation.

  - This procedure requires the following: Team Donor Recipient Preparation Procedure Protocol Follow up and treatment of complications and possible rejection.

Modes of Dialysis

1: Peritoneal dialysis

2: Hemodialysis



Questions

1. A 3-year- old girl was admitted for failure to thrive. The parents said that she is drinking & passing urine excessively. Her BP 90/50

Investigations: Na 130 mg/dl - K 2.5 mg/dl - Creatinine 0.4 mg/dl - PH 7.5 - HCO3 38

MOST likely diagnosis:

A. Diuretic abuse
B. Renal artery stenosis
C. Ry hyperaldosteronism
D. Adrenal carcinoma
E. Barter's syndrome

2. A 5 year old boy has been treated with prednisolone for nephrotic syndrome for 28 days with no response. The best management is:

A. Renal biopsy
B. Stop steroids
C. Shift to acei
D. Start steroids withdrawal
E. Continue therapy for 14 more days

3. The most common causes of idiopathic nephrotic syndromes is:

A. Minimal change nephrotic syndrome
B. Membranous nephropathy
C. Focal segmental glomerulosclerosis
D. MPGN
E. Diffuse mesangial sclerosis

4. Side effects of cyclosporin A include all of the following EXCEPT:

A. Hypertrichosis
B. Tremors
C. Gingival Hypertrophy
D. Peripheral Neuropathy
E. Blindness

5. A 6 year-old girl had a history of Gastroenteritis 1 wk ago, presented to ER with disturbed conscious level, fever, on examination, Bp was 180/100, petechial rash allover her body and she was looking pale.

Investigations: S. creat 8 mg/dl, urea 150 mg/dl, INR 1.2, TLC 12, Hgb 7, MCV 98, plat 80.

What is your provisional diagnosis?

A. TMA/TTP
B. DIC
C. Sepsis
D. Homocystinuria
E. Renal vein thrombosis

A

6. A 5- year- old boy presented to ER with history of UTI & an acute onset of severe scrotal pain of few hours duration. Urine analysis was free and he was a febrile. On examination, Rt testis is swollen and tender. The most probable diagnosis is:

A. Epididymo-orchitis
B. Testicular torsion
C. Henoch-schonlein purpura
D. Idiopathic scrotal oedema
E. Torsion of appendix of testis

B

7. Which of the following child needs to be investigated for an underlying pathology:

A. A 4- year- old girl who wets the bed at night
B. A 6- year- old boy who was potty trained at age of 4 who has an accident at school.
C. A 7- year- old girl with Down syndrome who is still nappy.
D. A 5-year- old girl who started to wet the bed after her baby sister is born.
E. A 3-year- old boy who is wet by night.

B

8. which of the following is associated with renal osteodystrophy:

A. Hyperphosphatemia
B. Acidosis
C. High PTH
D. All of the following
E. None of the above

D

Ahmed, 5 y old child born & living in Suez, presented to ER as his mother is complaining that her child passed little urine during the last 24 hours. She describes that his urine is dark yellow and he does not complain of pain during urination or suprapubic pain. No similar attacks have occurred before and no similar conditions are known in the family. Mother reports that she had noticed occasional swelling of his eyelids more in the early morning over the last 3 weeks, which started shortly (within one week) after an attack of acute tonsillitis treated by an oral antibiotic. O/E: pulse was 95, temp.: 37.3, RR: 38, weight was 22.0 kg, the child had swollen upper eyelids and bilateral pitting lower limb edema reaching above knees. Abdominal examination showed positive bilateral shifting dullness. We asked to inspect a urine sample which was a very little amount (about 5 cc), clear and slightly dark yellow in color, with no sediment. The child was admitted at our hospital to be monitored and investigated. His metabolic profile showed the following results: s.Na: 136 mg/dl, s.K: 4.2 mg/dl, s.creat: 0.9 mg/dl, BUN: 33 mg/dl, s.albumin: 2.1 g/dl, CRP: -ve. Urine analysis revealed the following: specific gravity: 1015, PH: acidic, casts: Nil, glucose: -ve, protein: +++, RBCs: 8-10/HPF, Pus cells: 2/HPF.

1) What is your provisional diagnosis?

A case of generalized edema for investigation, mostly idiopathic nephrotic syndrome as he has puffy eyelids and bilateral lower limb edema + proteinuria and hypoalbuminemia and he is in the usual age (2-8y).

2) How to confirm your diagnosis and what other investigations would you like to order ?

Quantitation of proteinuria should be done by collection of 24h urine & measurement of 24h urinary proteins (above 40 mg/m2/h means there is nephrotic range or massive proteinuria)

Alternatively, if accurate collection of 24h urine is difficult you can send a single 2nd morning urine sample to measure albumin/creatinine ratio in urine (normally < 0.2, if > 2.0 it is nephrotic range proteinuria).

His 24h urinary proteins was 3250 mg/day.

Other investigations:

- lipid profile: s.total cholesterol & s.triglycerides.
- CBC: for checking hematocrit and WBC count.
- P/A ultrasound as a baseline (not essential for diagnosis).
- C3 : normal.

3) How can you interpret mentioned points of history and examination? And is there any missing data ?

Oliguria and dark yellow urine reported by the mother are mostly because of severe hypoalbuminemia and intravascular volume contraction leading to compromised renal blood flow and decreased UOP.

Edema started to appear shortly (1wk) after an attack of acute tonsillitis which is going with natural course of nephrotic syndrome, where initial presentation and subsequent relapses are triggered by infections (URTIs, UTI).

The child is tachypneic while being afebrile and this is most probably because of mechanical causes e.g. ascites or pleural effusion, or may be he has pneumonia.

No family history of nephrotic syndrome or other renal disease and this is a very important point in history to think of familial etiologies.

blood pressure measurement has been missed during the initial examination. (tell them it is a fatal mistake)

4) Interpret mentioned laboratory results.

Hypoalbuminemia.

Mild renal impairment with prerenal pattern of affection (BUN/creat ratio >20) without any further details.

Proteinuria +++ usually refers to (urinary proteins > 1000mg but not a confirmatory quantitative assessment).

Mild microscopic hematuria (RBCs> 3) which is an accepted finding in idiopathic nephrotic syndrome (in contrast to acute glomerulonephritis where hematuria is most commonly macroscopic).

After the child was admitted and confirmation of massive proteinuria was done, oral full dose corticosteroid therapy (2 mg/kg/day = 60 mg/m2/day) was started.

5) What are the advices and precautions you would like to tell his mother regarding the coming period?

Low salt diet, restriction of carbohydrates to avoid marked obesity, low fat in diet, and normal protein intake.

Corticosteroids are to be given following meals. Vitamin D supplement is also prescribed. Never to stop corticosteroid therapy suddenly. If any problems with taking the drug, return to your treating pediatrician or pediatric nephrologist urgently. Regular blood pressure monitoring is needed.

Corticosteroid therapy will be continued with full dose for 4 weeks while the patient has regular visits to our pediatric nephrology clinic.

After being admitted for 5 days at our hospital and while on D4 CS ttt, Ahmad was found to be feverish (38.6 ° C) and complaining of severe generalized abdominal pain.

6) What do you suspect and how to manage?

A common complication of childhood nephrotic syndrome is liability to infections and one of theses common infections in these patients is spontaneous bacterial peritonitis (SBP). The most common causative organism of this infection is streptococcus pneumoniae. Treatment is to give parenteral antibiotics with NPO (till improvement of severe pain and regain of normal intestinal sounds) together with pediatric surgery consultation.

Ahmad has finished his recommended 4 week course of full dose corticosteroid therapy and came to our pediatric nephrology clinic to be examined and to decide for further management. O/E: he has a moon-like face with cheek swelling and excess hair in the forehead. No eyelid swelling and no lower limb edema are observed. Chest, cardiac and abdominal examination is free. Urine analysis showed: (protein -ve).

7) What do you think about the response to treatment ? What about blood pressure ? And how to manage the case in the coming period?

This is a case of steroid responsive nephrotic syndrome. Complications of CS ttt started to occur in the form of cushinoid facies and steroid induced hypertension (to be confirmed by blotting readings on appropriate bl pr charts).

Blood pressure monitoring is mandatory and if still high readings are detected together with strict salt restriction, start oral antihypertensive (one of ACEIs or ARBs).

It is also time to start gradual tapering of CS by decreasing dose to 40 mg/m2/day EOD.

Total duration of tapering is 4 - 5 months, with regular visits and follow up of blood pressure and urine analysis.

Six months later, Ahmad has a regular visit to the pediatric nephrology clinic, he has stopped corticosteroid therapy one month before this visit, and now he presents by history of 4 days duration of low grade fever, dry cough and clear rhinitis, together with appearance of morning puffiness of upper eyelids. O/E: congested throat and postnasal discharge, with mild bilateral lower limb edema below knee. Urine analysis showed (protein +++).

8) What is your diagnosis of this situation ? How to manage ? And how to deal with parent's concerns?

This is a picture of nephrotic syndrome relapse. Clinical evidence of relapse is reappearance of edema (puffiness and L.L edema) and laboratory evidence is reappearance of proteinuria. Relapse is treated by restart of CS ttt 60 mg/m2/day till disappearance of proteinuria for 3 consecutive days, then gradual tapering over 4 - 6 weeks.

Parents usually get frustrated because of reappearance of symptoms again after stopping the initial course of ttt. U should reassure them and explain that this is the natural course of the disease and that 30% of cases of steroid responsive nephrotic syndrome develop subsequent relapses.

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Pediatrics