Pediatrics TeamWork

437

Proteinuria & Hematuria

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Notes Previous Notes Book Important!

Hematuria

Prevalence:

Hematuria is a common finding on urinalysis with a prevalence rate between 1% and 2%. It's the presence of blood in the urine. NOT discoloration because discoloration could be caused by drugs or dyes. It is the first presentation of renal disease in pediatrics, and is secondary to inflammation.

Presentation:

1- Gross hematuria.
2- Microscopic hematuria with clinical symptoms. Such as: Arthritis, Skin rashes, b/c we are dealing with autoimmune diseases like SLE, HSP.
3- Asymptomatic microscopic **(isolated) hematuria.** Ex: benign familial hematuria.
4- Asymptomatic microscopic **hematuria with proteinuria**. Most dangerous means there is severe progressive irreversible inflammation of the kidney.

Once you find proteinuria with hematuria you have to send and investigate the patient immediately because there is severe inflammation

Diagnosis:

- **Urine Strip Test (urine dipstick):**
  The **most sensitive** test for detecting the presence of blood in the urine is abnormal urine strip test. The reagent utilizes the pseudoperoxidase activity of hemoglobin (or myoglobin) to catalyze a reaction between hydrogen peroxide and the chromogen tetramethylbenzidine to produce an oxidized chromogen, which has a **green blue color**.
  Strips can detect concentration of 2-5 RBC/HPF. (Very sensitive)
  - False negative urine dipstick:
    High specific gravity urine.
    High ascorbic acid concentration in the urine.
  - False positive urine dipstick:
    Delayed reading.
    Cross contamination of urine from other chemicals such as oxidized agent, (household bleach)

- **Urine Microscopy: Confirmation of hematuria**
  Centrifuge 10 ml of urine for 5 minute, Decant the supernatant, Re-suspend the sediment in 0.5 ml of urine, Place on a slide with a cover slip, Count the number of RBC. In 20 fields and report the average.
  Positive Test: > 5 RBC/HPF.

Definition:

≥ 5 RBC's /HPF in three of **three consecutive**, fresh, centrifuged urine specimens obtained at least **1 week apart.**

Hematuria

Classification:

We should localize the Hematuria to limit diagnostic possibilities for patients and prevent unnecessary testing.
It could be:

- Upper (kidney)
- Lower (ureter, bladder, urethra)

Hematuria + Proteinuria -> Glomerular in origin which is more serious
Hematuria w/o Proteinuria or HTN -> Non-Glomerular, most likely cystitis

Hematuria

Glomerular

1- Post-infectious glomerulonephritis Most common in Saudi Arabia
2- IgA nephropathy Most common worldwide, 2nd in Saudi Arabia
3- Henoch-Schönlein purpura Same pathology as IgA but with system involvement
4- Hereditary nephritis Alport Disease
5- Benign familial hematuria
6- Membranoproliferative glomerulonephritis
7- Lupus nephritis

Non-Glomerular

Caused by irritation to the tract.
1- Hypercalciuria similar presentation to renal stones
2- Infections (bacterial or viral) UTI mainly pyelonephritis in pediatric. It's serious condition lead to scarring of the kidney if not treated.
3- Papillary necrosis (HbS) Ischemia to the kidney in sickler lead to gross hematuria
4- Urolithiasis rare in pediatric
5- Trauma Do not forget to examine the genitalia to exclude child abuse!
6- Foreign body
7- Exercise-induced hematuria

The main causes are hypercalciuria or infections (UTI)

Glomerular Hematuria

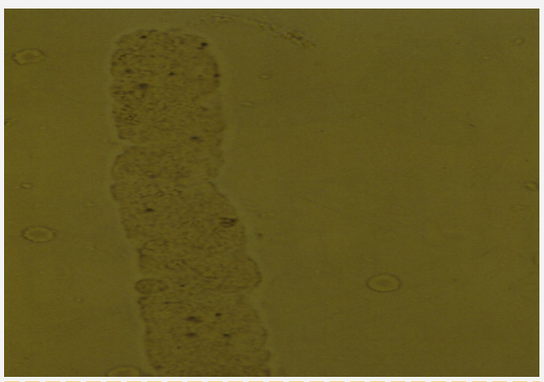
Clinical Presentation:

Usually it's very serious and present with systemic manifestations.
1- Oliguria. Alarming sign Normal UOP in pediatric is 2-5 ml/kg/hr, Oliguria <1 ml/kg/hr
2- Edema.
3- Hypertension due to intravascular edema.
4- Symptoms of systemic disease (e.g. arthritis, rash). Like in HSP present with mild fever, arthritis, purpura.

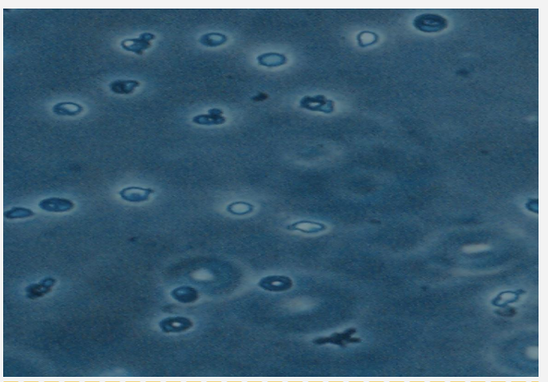
Features:

1- Brown tea, cola-colored urine. Oxidized blood due to long distance from the kidney, fresh blood is seen in cystitis
2- Concomitant proteinuria.
3- Cellular cast. Coming from tubules indicate inflamed both glomerulus and tubules.
4- Dysmorphic erythrocytes in phase-contrast microscopy. RBCs pass and squeezed through the gaps in glomerular basement membrane.
5- Low MCV of erythrocyte by automated analyzer.

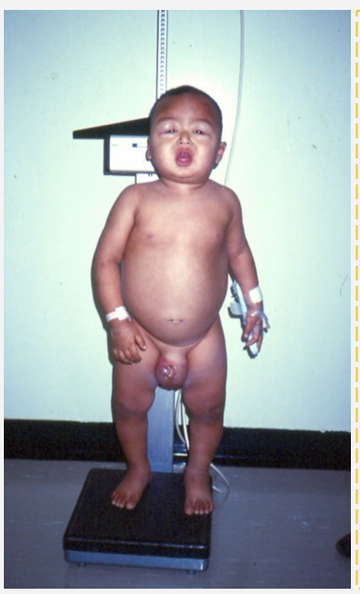
RBC casts: Are best visualized at the edges of the cover slip, and tend to dissolve in urine of high pH.



Cellular Cast
Usually take the shape of tubule
Characteristic for acute
post-infectious glomerulonephritis



Dysmorphic Erythrocytes
+ve if >13% of cells are distorted
(elongated)



Child presents with oliguria, generalized edema (Anasarca) including lower limbs, genitalia, ascites even the tongue is edematous
And the characteristic description of periorbital swelling

Glomerular diseases are either Nephrosis or Nephritis
Based on examination only you can't differentiate
you need to check the urine & blood test

Nephritis: Hematuria, Proteinuria, Oliguria, HTN, High serum CR Renal Failure
Nephrosis: Edema, Proteinuria, normal BP, normal renal

The difference between nephrotic and nephritis is IMPORTANT for the exam

Glomerular Hematuria

1- Postinfectious Glomerulonephritis:

- Known before as Post-streptococcal GN but since 50% are caused by non-strept (viruses), it now called as PIGN.
- Begins **7-21 days after** group A beta-hemolytic by streptococcal infection (throat infection).
- Antibiotic treatment for the infections will not prevent the nephritis. B/c the Antigen-Antibody Complex already formed.
- Present with **tea colored urine**, edema and hypertension.
- May present with only **microscopic hematuria**.
- ASO may be negative early in the course.
- **C3 low** in 90% of patients for 6 weeks **C4 normal**. B/c it's using the alternative pathway
- Microscopic hematuria my persist for 2 yrs.
- Self limiting diseases.

-In Classical pathway both C3 and C4 are low, one of the differential is SLE
-Alternative pathway only C3 is low -> PIGN
-**OSCE:** You found blood in urine by dipstick, what is the next step? BP measurement, it is mandatory in any patient with hematuria

2- IgA Nephropathy:

- The most common chronic GN in Europe and Asia.
- The most common cause of hematuria in children.
- 15% of children with Prolonged hematuria (> 1 year) will have IgA nephropathy.
- Present with **gross hematuria during viral illness.** Presents in same day of illness
- **Microscopic hematuria** present between episodes of gross hematuria.
- There is no laboratory test diagnostic of GN.
- Diagnosis by histopathologic demonstration of mesangial deposition of IgA. By Renal biopsy.
- 25% of children with IgA nephropathy will progress to chronic renal insufficiency. Even after transplant the diseases will recur.
- **Poor outcome**: crescentic GN, older age group, hypertension, nephrotic range proteinuria.
- HSP is the other face of IgA Nephropathy.

PIGN	IgA Nephropathy
- Hematuria after 2 weeks of throat infection - Hematuria once a life	- Hematuria concomitant with the viral infection (same day) - Recurrent hematuria (every 2 months)

Glomerular Hematuria

3- Alport's hereditary nephritis:

- Mainly X-linked affecting boys only.
- Episodes of recurrent or persistent **microscopic hematuria.** Similar to IgA nephropathy and will develop progressive proteinuria
- Family History: male individuals with nerve **deafness** and progression to ESRD. By the age of 20s.
- Type IV collagen is abnormal and the basement membrane is disrupted. (And in ear canal as well)
- The diagnosis is confirmed by renal biopsy & now we do genetic testing. No need to do biopsy for all siblings if they all have the same symptoms, one is enough.
- Hearing test should be done regularly to prevent speech or educational handicap. They can have ocular defects
- Good-posture diseases post transplant (small risk)
- Female may have a hearing deficit without any urinary abnormalities
- No treatment. Only transplant. If proteinuria give ACEi

4- Benign Familial Hematuria:

- Thin glomerular basement membrane nephropathy. So RBCs are passing otherwise they are healthy.
- Occurs in at least 1% of the population.
- Inherited as AD or AR manner. Usually the parents & half of the siblings have it.
- Absence of proteinuria, renal failure, hearing deficits, or ophthalmologic abnormalities.
- **Microscopic hematuria**, dysmorphic RBC's.

5- Rapidly Progressive GN:

- It is a complication of all previously mentioned diseases.
- Presents with symptoms and signs similar to APIGN.
- Require the urgent attention of a Pediatric Nephrologist.
- Laboratory Studies show ARF.
- Renal biopsy demonstrates glomerular crescent.
- Untreated RPGN can result in ESRD in a few weeks.
- Need to start high dose steroid, 30 mg / kg

Non-Glomerular Hematuria

Hypercalciuria:

- Increased urinary excretion of Ca despite normal serum Ca.
- Present in 5% of healthy children.
- Most frequent cause of isolated hematuria in non-glomerular hematuria patients.

Idiopathic Hypercalciuria:

- Renal hypercalciuria: result from a tubular leak of calcium.
- Absorptive hypercalciuria : results from increased gastrointestinal absorption of calcium.

- There is often a family history of renal stones.
- Symptoms include dysuria, suprapubic pain, renal colic.
- Present with microscopic hematuria and episodic gross hematuria.
- Urine RBC's are shaped normally with no cast.
- The mechanism of the hematuria involve irritations to the renal tubules by ca-containing crystals.
- High risk of development of renal stones.

- Screening for hypercalciuria:
  - spot urinary ca/creatinine ratio.
  - A ration of > 0.21 is indicative of hypercalciuria.

- Confirmation of hypercalciuria by collecting a timed (either 12 or 24 hours) urine for ca excretion.
  - An excretory rate of greater than 4 mg/kg/day is abnormal.

- Management:
  - Increase fluid intake to dilute the urine.
  - Severe ca restriction should be avoided.
  - Hydrochlorothiazide (HCT) decrease urinary ca excretion. Used in pediatric for severe cases.
  - HCT in a child with isolated hematuria with no previous nephrolithiasis is not recommended.

Hematuria

History clues:

- Duration and pattern of hematuria
- Family history (hematuria, renal failure, deafness (Alport syndrome) , urolithiasis)
- Pharyngitis, URTI (PIGN, IgA Nephropathy) before 2 weeks or now
- Dysuria or other symptoms of urinary infections
- Rash (HSP)
- Abdominal pain (infections, stone, HSP (intussusception)
- Drugs (anticoagulant)

Physical Examination clues:

- **Hypertension**, edema, pallor. You have to measure BP for any pt present with hematuria.
- Rash, impetigo. for Streptococcal
- Abdominal or flank tenderness (infection).
- Abdominal mass (tumors) Rare except Wilms tumor which present at first year of age.
- Ecchymoses, petechiae, hemangiomas.
- Evidence of abdominal trauma.
- External genitalia for trauma or bleeding.
- Growth pattern.
- Hearing test. (Alport syndrome)

Basic Laboratory Evaluation:

- Urine culture rule out pyelonephritis
- CBC (ITP)
- Serum creatinine
- ASO titre
- Urine ca: creatinine ratio (hypercalciuria)
- Urine protein: creatinine ratio. In pediatrics, do comparison of random samples, ratio > 0.2 is significant
- C3 and C4
- Renal ultrasonography For renal stones and kidney size Nephromegaly inflammation (acute nephritis), Small kidney (chronic renal failure)
- First degree relatives urine test For benign familial hematuria.

The initial referrals are to the Pediatric Nephrologist rather than to the Pediatric Urologist.

Other Evaluation Procedures:

- Renal biopsy
- Cystoscopy
- Renal angiography (rarely indicated)

Do we need biopsy for all suspected Nephritis?
Acute postinfectious no need for biopsy
But if progressive renal failure (creatinine doubled every 24h) we need biopsy to role out RPGN

The initial referrals are to the pediatric nephrologist rather than to the pediatric urologist

Proteinuria

- Associated with progressive renal disease Protein is toxic to the kidney
- Involved in the mechanism of renal injury The Protein is produced by disease which lead to more damage to the kidney.
In diabtic nephropathy we give ACEI to decrease protein toxic effect on the kidney. First thing to do is dipstick

Clinical testing for proteinuria:

- **Urinary dipstick**
- Screening test
- Color reaction between urinary albumin and tetrabromophenol blue
  Trace ≅ 15 mg/dl
  1 + ≅ 30 mg/dl
  2 + ≅ 100 mg/dl
  3 + ≅ 300 mg/dl
  4 + ≥ 2000 mg/dl

- **False-negative:** Diluted urine
- **False-positive:**
  Alkaline urine (PH>8.0)
  Concentrated urine (sp.gravity>1:025)
  Antiseptic contamination (Chlorhexidine, benzalkonium chloride)
  After intravenous radiography contrast

- **24-hour urine collections** Difficult to measure in a child
- **Urinary protein/creatinine (pr/cr) ratio** Used in pediatric
  - Spot urine specimen inpediatry
  - First morning specimen
  - Normal values:
    <0.2 mg protein/mg creatinine in children > 2 years
    <0.5 mg protein/1 mg creatinine in children 6-24 months old

Protein Handling by the Kidneys in Normal Children	Protein Handling in Renal Disorders
Normal rate of protein excretion <4 mg/m2/hr <100 mg/m2/day – 50% Tamm-Horsfall protein – 30% Albumin – 20% other protein Restricted filtration of large Proteins (albumin & Immunoglobulin) Proximal tubules reabsorb most of LMW protein (insulin, B2 microglobulin)	Excess urinary protein losses: 1. Increase permeability of the glomeruli (glomerular) 2. Decrease reabsorption of LMW proteins by the renal tubules (tubular)

Proteinuria

Types of Proteinuria:

1- Transient (Not heavy 0.2 - 0.6 mg)
- Fever
- Stress
- Dehydration
- Exercise

2- Orthostatic proteinuria
- Common in young people, teachers
- Excess urine protein in upright position but normal during recumbency.
- School age and teachers
- <1 gm/m2/day
- You ask the pt to empty his bladder before sleep and take the sample when he wake up it will be -ve and the pm sample will be positive

3- Persistent proteinuria:
- Proteinuria of ≥1 + by dipstick in multiple occasions
- Persistent proteinuria should be viewed as a marker of renal disease and also as a cause of progressive renal injury.

Evaluating a child with proteinuria:

1- First stage
- Complete history and physical examination (BP)
- Complete urinalysis
- Urine Dipstick before going to bed and after arise
- Blood level of Albumin, creatinine, cholesterol, electrolyte

2- Second stage
- Renal ultrasonography
- Measurement of serum C3, C4, complement
- Antinuclear antibody
- Serology for hepatitis B, C, ± HIV

From the book !

Box 19.3 Investigations performed at presentation of nephrotic syndrome

- *Urine protein – on test strips (dipstick)* to confirm heavy proteinuria (≥3+ protein)
- *Full blood count* to assess whether there is an infection. Also a high haemoglobin suggests intravascular fluid depletion
- *Urea, electrolytes, creatinine, albumin* Hyponatraemia is common in presentation of nephrotic syndrome. Intravascular fluid depletion is indicated by high urea and/or creatinine
- *Complement levels – C3, C4* to differentiate from other causes of proteinuria such as postinfectious glomerulonephritis, when C3 will be low, or SLE, when both C3 and C4 are low
- *Antistreptolysin O or anti-DNAse B titres and throat swab* to differentiate from poststreptococcal glomerulonephritis
- *Urinary sodium concentration* which can be helpful to indicate intravascular fluid depletion if low (<10 mmol/L) in a child who is oedematous
- *Hepatitis B and hepatitis C screen* to detect secondary causes of nephrotic syndrome caused by hepatitis B and C viruses. This will also alter the treatment
- *Malaria screen if recent travel abroad* as may cause nephrotic syndrome

Nephrotic Syndrome:

- Heavy proteinuria (very thick white urine), hypoalbuminemia, hypercholesterolemia and edema (due to changes in oncotic pressure because of low serum protein)
- Prevalence 2-3 cases per 100,000 children
- The majority will have steroid responsive MCNS (minimal change NS)(good response to treatment)
- In pediatrics who have MCNS, we don't do biopsy. Instead we start with steroid therapy. If it resistant after month of therapy, we do biopsy.

Pretreatment Renal Biopsy in NS
- Infantile NS
- Adolescence
- Persistent hematuria
- Hypertension
- Depressed serum complement
- Reduced renal function
- Note that the low complement in APIGN will rise after 3 months, if it persisted it's not APIGN and you have to think of other diseases

Proteinuria

Clinical Features of NS:

1- Edema

- Gravity dependent.
- Periorbital in the early morning (earliest sign) then generalized.
- Severe edema present as ascites, pleural effusions, scrotal or vulvar edema, skin breakdown.

2- Hyperlipidemia

- Transient and severe hypercholesterolemia during relapses.
- Persist in treatment-resistant NS.
- Atherosclerosis in young NS.
- Dietary modification : limited benefit.
- Cholestyramine is approved in NS.

3- Infection:

- Nephrotic syndrome patients are immunocompromised b/c they lose immunoglobulin & they're on steroids.

- Varicella (the cause of death in the past)
  - Varicella antibody should be obtained.
  - Varicella – zoster immunoglobulin within 72 hours of exposure.
  - Steroid should be tapered to 1 mg/kg/day.
  - Acyclovir or valacyclovir if varicella does develop.

- Other infection
  - Cellulitis
  - 1° peritonitis
  - Septic arthritis, sepsis
  - The organisms usually Pneumococcus & E-coli.

Immunization in NS:

- Live viral vaccines should not be given if patient on high dose of steroids.
- Pneumococcal vaccine is recommended to all NS (off steroids).
- Varicella vaccine (varivax) in 2 doses regimen is safe and efficacious.
- Antibodies to vaccines may fall during relapses (still controversial).

From the book

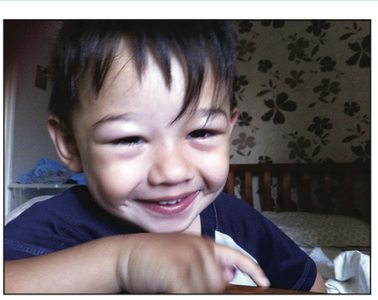


Figure 19.17 Facial oedema in nephrotic syndrome which improves during the day and is often misdiagnosed as an allergy.

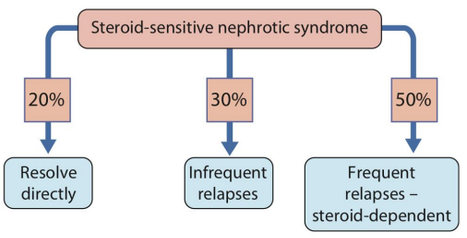


Figure 19.18 Clinical course in steroid-responsive nephrotic syndrome.

Proteinuria

Treatment of NS:

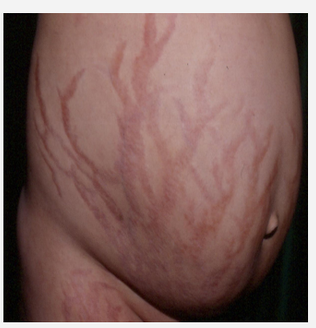
1- Prednisone/ prednisolone:

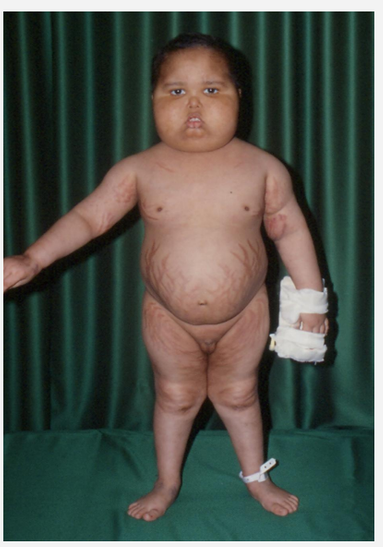
- Mainstay of treatment of NS
  - Typical protocol:
    - 2 mg/kg/day (60 mg/m2/day) for 3 month
    - (4+4 wks treatment)
    - 4 wks daily steroid
    - 4 wks every other day B/c it suppress the growth hormone
    - Recently: 6+6 weeks induce a higher rate of long remissions than the standard (4+4)(german guideline)

  - Treatment of Relapses of NS:
    - 60-80% of patients will relapse.
    - Prednisolone 2 mg/kg/day until the patient is free of proteinuria for 3 days then 4-6 wks of every other day treatment.

- Nephrotic syndrome divided into:
  - steroid sensitive dependent: if you lower the dose to .5 ml/kg/day he'll have relapse.
  - steroid frequent relapsing: they relapse 3 times a year.
  - steroid resistant: if persist more than 1 month, you need to do biopsy (mostly not MCNS).

- Side effects of Glucocorticoids: (Must be discussed with the family)
  - Cushingoid habitus
  - Ravenous appetite
  - Behavioral and psychological changes (mood lability)
  - Gastric irritation (including ulcer)
  - Fluid retention
  - Hypertension
  - Steroid-induced bone disease
  - (avascular necrosis, bone demineralization)
  - Decreased immune function
  - **Growth retardation**
  - Night sweats
  - Cataracts
  - Pseudotumor cerebri
  - **Steroid-related diabetes**





2- IV Pulse Steroids

- May give success in steroid-resistant NS
- High dose IV methylprednisolone 30 mg/kg (max lgm).
- To be given every other day for 6 doses.
- To continue in tapering regimen for period up to 18 months.
- Side Effects: Hypertension, Arrhythmias.

-If the patient is not responding to steroids (after 4-6 weeks) then do: renal biopsy, gene study, and refer to transplantation.
-If he is sensitive and dependant on steroids they will relapse once you stop it so they need second line immunosuppressive

Proteinuria

Treatment of NS:

3- Cytotoxic Drugs: used in steroid resistant

- Cyclophosphamide
  - Over 12 weeks
  - Total cumulative dose 170 mg/kg
  - Side Effects:
    - Bone marrow suppressions
    - Oligospermia, azoospermia and ovarium fibrosis (If given close to puberty
    - Hemorrhagic cystitis
    - Risk of malignancy
- Chlorambucil
  - May cause seizure

4- Cyclosporin A

- Steroid dependent or resistant NS
- To be given after renal biopsy
- Relapses high after withdrawal
- Side Effects:
  - Hypertension
  - Nephrotoxicity
  - Hyperkalemia
  - Hypomagnesemia
  - Hypertrichosis
  - Gingival hyperplasia

5- Levamisole

- Weak steroid sparing drug
- Long term use
- Side Effects:
  - Neutropenia
  - Rash
  - Gastrointestinal disturbances
  - Seizures

Other Practical Aspects of the Management of NS:

- Fluid intake should be limited to double of insensible water loss in severely edematous NS.
- Combined diuretics and IV albumin can be given in severe edema.
- Diuretics should not be given in mild edema.
- ACE: should not be given in the initial course of prednisolone because of the risk of hypotension and thrombosis in the diuretic phase.
- ACE: can be given to steroid-resistant NS.
- Schooling, activities, diet should be individualized

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Nephrotic Syndrome

- **Steroid sensitive nephrotic syndrome (minimal change disease):** these children do NOT progress to chronic kidney disease, features suggesting this type:

- Age between 1-10 years
- No macroscopic hematuria
- Normal blood pressure
- Normal complement levels
- Normal renal function

- **Complications:**

Hypovolemia	Thrombosis	Infections	Hypercholesterolemia
The child characteristically complains of abdominal pain and may feel faint. Low urinary sodium < 10 mmol/L, high Hgb concentration or packed cell volume of RBCs are all indications of hypovolemia. **Treatment:** IV fluids normal saline or 4.5% albumin solution, those kids at risk of thrombosis and shock	Urinary losses of antithrombin III, thrombocytosis exacerbated by steroids therapy, increased synthesis of clotting factors, and increased blood viscosity from raised Htc	Higher risk in patients with relapse Encapsulated bacteria especially pneumococcus Pneumococcal and influenza vaccination are recommended Penicillin prophylaxis is used whilst the child in relapse	Not fully understood but it correlates inversely with the serum albumin

Table 19.3 Steroid-resistant nephrotic syndrome

Cause	Specific features	Prognosis
Focal segmental glomerulosclerosis	Most common Familial or idiopathic	30% progress to stage 5 chronic kidney disease; 20% respond to tacrolimus, or rituximab Recurrence post-transplant is common
Mesangiocapillary glomerulonephritis (membranoproliferative glomerulonephritis)	More common in older children Haematuria and low complement level present	Decline in renal function over many years Treated with ACE inhibitors and/or immunosuppression with mycophenolate mofetil
Membranous nephropathy	Associated with hepatitis B May precede SLE (systemic lupus erythematosus)	Most remit spontaneously within 5 years

Treatment of edema, is by diuretics, salt restriction, ACEis and NSAIDs.

Genetic testing is recommended.

- **Congenital nephrotic syndrome:** It presents in the first 3 months of life. The most common type is autosomal recessive. Albuminuria can be so severe that unilateral nephrectomy can be necessary, and followed by dialysis for severe CKD until the child is no longer nephrotic and old enough to do transplantation.

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Glomerulonephritis

- **Acute glomerulonephritis:** there may be a rapid deterioration in renal function (**rapidly progressive glomerulonephritis**). This may occur with any cause of acute glomerulonephritis, but is uncommon when the cause is poststreptococcal. If left untreated, irreversible chronic kidney disease may occur over weeks or months, so renal biopsy and subsequent treatment with immunosuppression and plasma exchange may be necessary.

- **Henoch Schonlein purpura:** If proteinuria is more severe, nephrotic syndrome may result. Risk factors for progressive chronic kidney disease are heavy proteinuria, oedema, hypertension, and deteriorating renal function, when a renal biopsy will determine if treatment is necessary. All children with Henoch–Schönlein purpura should be followed for a year to detect those with persisting haematuria or proteinuria (5%–10%). Children who have persistent renal involvement or required treatment for Henoch–Schönlein purpura nephritis require long-term follow-up. This is necessary as hypertension and progres- sive chronic kidney disease may develop after an interval of several years

Vasculitis

The most common vasculitis to involve the kidney is Henoch–Schönlein purpura. However, renal involvement may occur in rarer vasculitides such as polyarteritis nodosa, microscopic polyarteritis, and granulomatosis with polyangiitis (formerly known as Wegener granulomatosis). Characteristic symptoms are fever, malaise, weight loss, skin rash, and arthropathy with prominent involvement of the respiratory tract in granulomatosis with polyangiitis. ANCA (antineutrophil cytoplasm antibodies) are present and diagnostic in these diseases. Renal angiogram may demonstrate the presence of aneurysms in polyarteritis nodosa. Renal involvement may be severe and rapidly progressive. Treatment is with corticosteroids, plasma exchange, and intravenous cyclophosphamide, and increasingly biological monoclonal antibody therapy.

Systemic lupus erythematosus (SLE)

SLE predominantly affects female teenagers and young adults although it can occur at any age and also in males. It is much more common in certain ethnic groups (Asian and Afro-Caribbean). It is characterized by the presence of multiple autoantibodies, including antibodies to double-stranded DNA. The C3 and C4 components of complement may be low, particularly during active phases of the disease. Haematuria and proteinuria are indications for renal biopsy, as immunosuppression is always necessary and its intensity will depend on the severity of renal involvement.

Box 19.5 Investigation of haematuria

All patients

- Urine microscopy (with phase contrast) and culture
- Urinary protein:creatinine and calcium:creatinine ratios
- Kidney and urinary tract ultrasound
- Plasma urea, electrolytes, creatinine, calcium, phosphate, albumin
- Full blood count, coagulation screen, sickle cell screen

If suggestive of glomerular haematuria

- ESR, complement levels, and anti-double stranded DNA antibodies
- Throat swab and antistreptolysin O/anti-DNAse B titres
- Hepatitis B and C screen
- Renal biopsy if indicated (see text)
- Test family for blood in urine
- Hearing test (if Alport syndrome suspected)