Hematuria in children

Dr. Jumana Albaramki
Professor of pediatrics/School of medicine/Jordan University
Consultant pediatric nephrology

Causes of red urine

- Hemoglobinuria : G6PD deficiency
- Myoglobinuria :trauma,seizures,rhabdomyolysis
- Drugs (rifampicin),food,dyes
- Inborn errors of metabolism(porphyria,bilirubin)
- Urate crystals
- Hematuria :macroscopic

Analysis of hematurea

- Onset
- Color :Red if fresh(bladder), or brown color as Hb converted to acid haematin by urinary acids in renal causes

- Timing :Early hematuria:urethral cause ,Terminal hematuria:bladder causes,continous
- Presense of clots : extrarenal causes

History and associated symptoms

- Fever, urinary symptoms ,dysuria, frequency, loin pain/ suprapubic pain .(looking for cystitis,pyelonephritris/stones
- Age/gender
- Periorbital edema,lower limb edema, decreased urine output
- Preceding URTI…..PSGN,IgA nephropathy

- History of previous attacks of red urine
- Rash,arthritis …HSP,SLE
- Coagulopathy,bleeding tendency,sickle cell
- Trauma
- drugs
- FH of hematuria,deafness,renal failure…Alport,FH of renal stones
- exercise

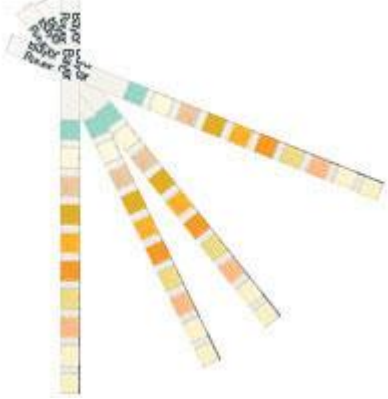
Hematuira

Gross	microsocpic
Painful	Painless
Transient	Persistent
Isolated	Hematuira with proteinurea
Glomerular	Extraglomerular

Examination

- Vital signs: fever for UTI, hypertension for glomerulonephritis
- Looking for edema :lower limbs,eyes
- Abdomen exam : masses ,(PCKD) ,tenderness
- Genitalia exam:
- Skin rashes

Investigation

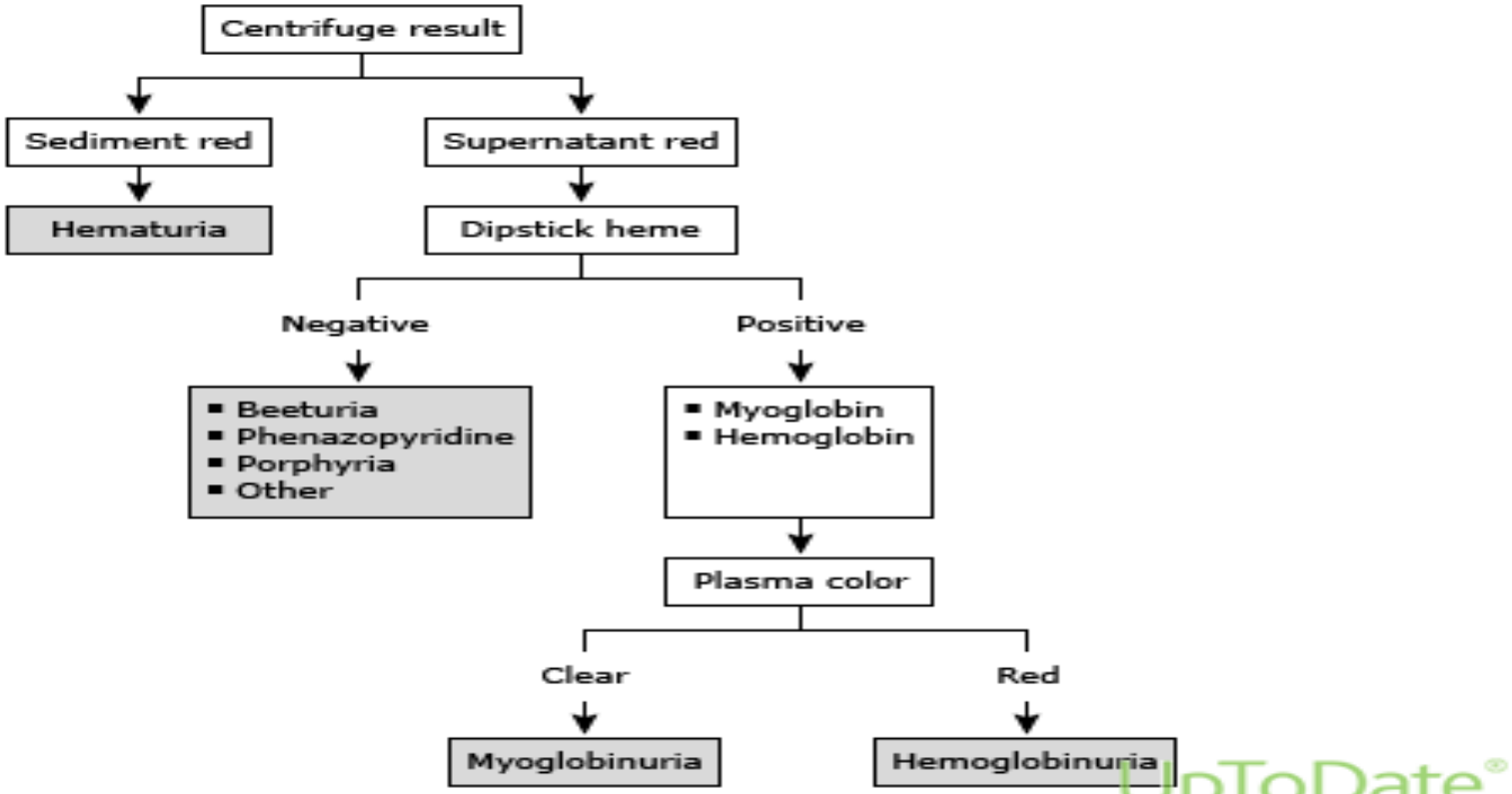


- Urine dipstick positive for heme,negative analysis (hemoglobinuria,myoglobin)
- Negative dipstick and UA (factitious)
- Positive dipstick and UA (hematuria)

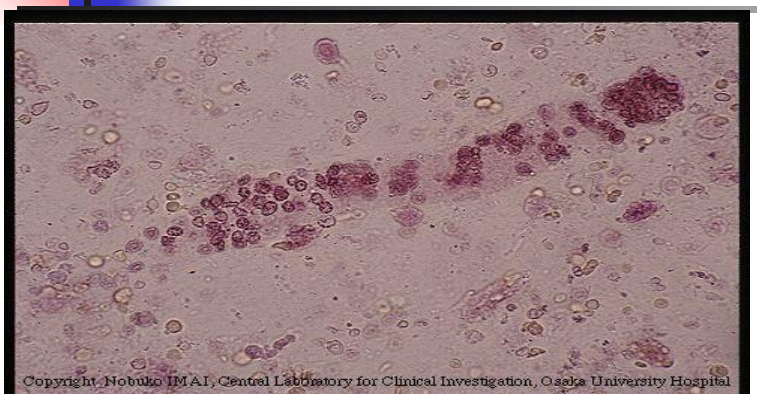
- Microscopy: look for RBC, wbc,bacteria (uti), high grade proteinurea (GN) ,crystals

- dysmprhic RBC by phase contrast microscopy ,RBC cast:glomerular bleeding

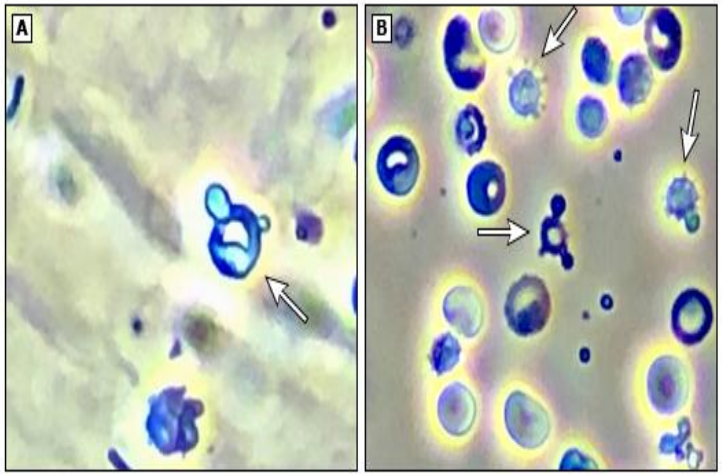
Approach to the patient with red or brown urine



Glomerular or extraglomerular



Phase-contrast micrograph showing dysmorphic RBCs in urine sediment



Distinguishing extraglomerular from glomerular hematuria

	Extraglomerular	Glomerular
Color (if macroscopic)	Red or pink	Red, smoky brown, or "Coca-Cola"
Clots	May be present	Absent
Proteinuria	Usually absent	May be present
RBC morphology	Normal	Dysmorphic
RBC casts	Absent	May be present

RBC: red blood cell.

UpToDate®

Prevalence

Definition of hematuria is the presense of more than 5 cells per high power field of centrifuged urine

Prevelance of isolated microscopic hematuria .5-2%which falls to 1 % for two or more positive samples

Transient hematuria seen with fever and exercise

Persistant asymptomatic hematuria weekly for three times needs to be investigated

Urethrorrhagia:urethral bleeding associated with blood spots after voiding,prepubertal

Pathophysiology

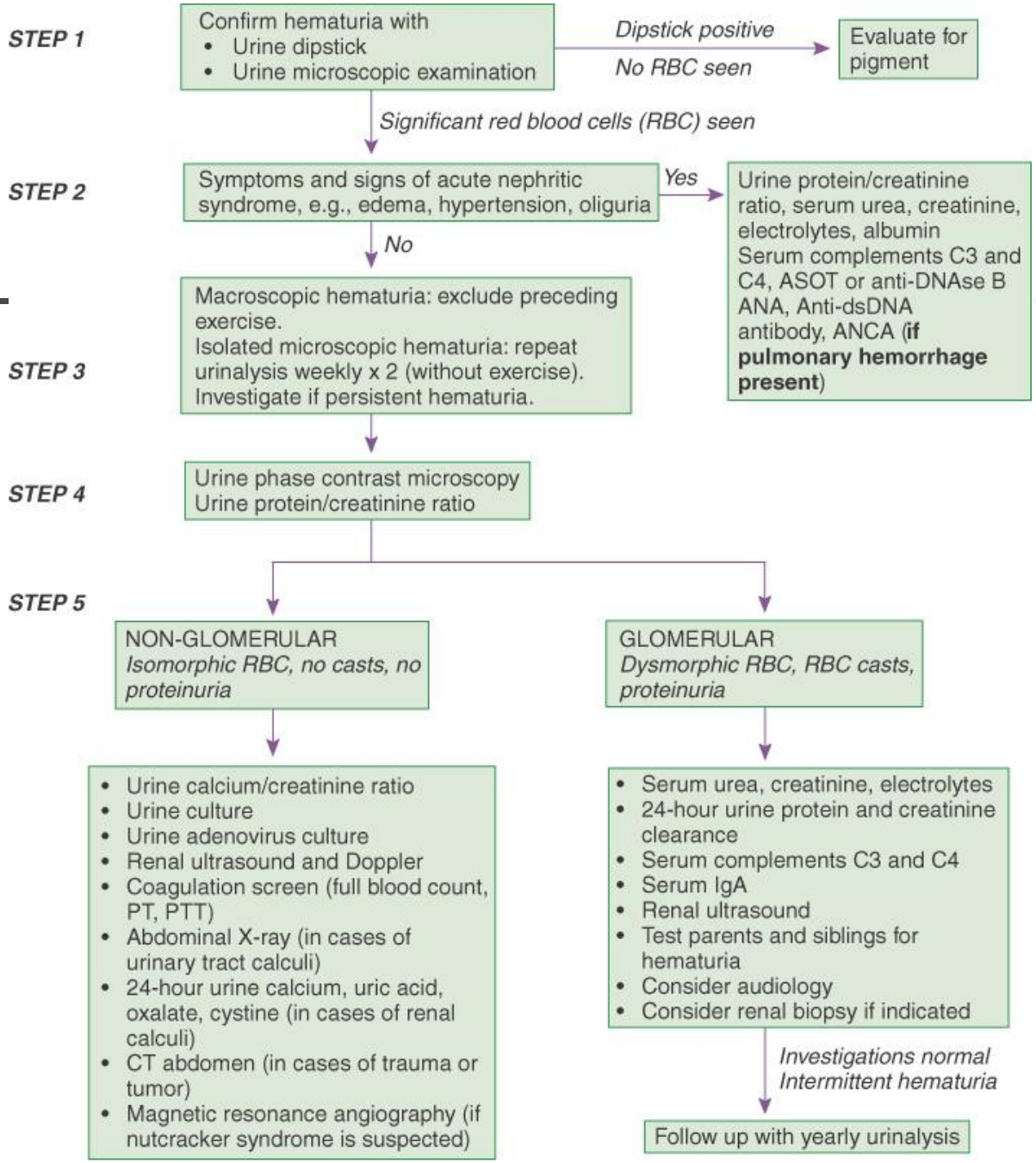
Structural disruption in the integrity of GBM caused by inflammatory or immunologic process

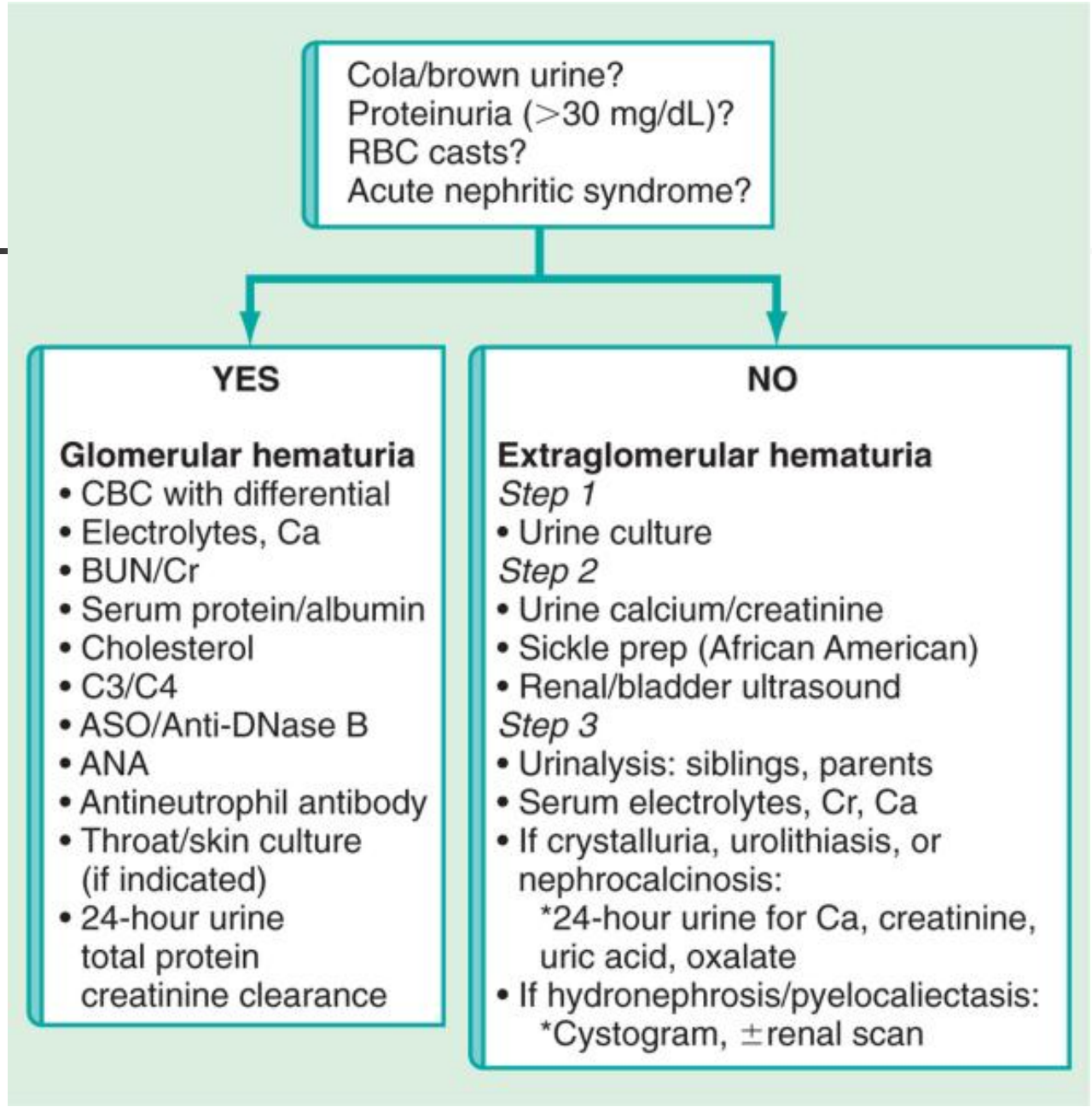
Toxic disruption of renal tubules

Mechanical erosion of mucosal surfaces in the genitourinary tract

Investigations

- Urine protein/creat ratio ,Electolytes,albumin,kft ,ASOT,C3,C4,ANA for GN causes
- Urine culture if UTI
- CBC if infection ,PT,PTT
- Urine calcium/creat ratio, 24 h urine collection
- U/S ,XRAY, spiral CT
- Later :Urine analysis on parents ,cystoscopy
- Renal biobsy




Cola/brown urine?
Proteinuria (>30 mg/dL)?
RBC casts?
Acute nephritic syndrome?
YES
Glomerular hematuria
• CBC with differential
• Electrolytes, Ca
• BUN/Cr
• Serum protein/albumin
• Cholesterol
• C3/C4
• ASO/Anti-DNase B
• ANA
• Antineutrophil antibody
• Throat/skin culture (if indicated)
• 24-hour urine total protein creatinine clearance
NO
Extraglomerular hematuria
Step 1
• Urine culture
Step 2
• Urine calcium/creatinine
• Sickle prep (African American)
• Renal/bladder ultrasound
Step 3
• Urinalysis: siblings, parents
• Serum electrolytes, Cr, Ca
• If crystalluria, urolithiasis, or nephrocalcinosis:
*24-hour urine for Ca, creatinine, uric acid, oxalate
• If hydronephrosis/pyelocaliectasis:
*Cystogram, ±renal scan

Gross hematuria

UTI

Irritation of meatus

Trauma

Stones /hypercalcuira

Glomerulonephritis

Recurrent

IgA nephropathy

Hypercalcuira

Alport syndrome

Nut cracker syndrome

Causes of hematuria

Upper urinary tract disease

Familial benign hematuria

GN: primary as postinfectious, MPGN, IgA nephropathy, Alport,

Multisystem disease

SLE,Hencoh scholein purpura
Hemolytic uremic syndrome

Tubulinterstitial disease

Acute tubular necrosis

Interstitial nephritis

Papillary necrosis

Pyelonephritis

Vascular :

Hemoglobinopathy as sickle cell

Vascular malformations (hemangioma)

Renal vein thrombosis

Nut cracker syndrome:seen in thin,compression of renal vein between SMA and aorta

anatomic :

Malignancy of the kidney (Wilms tumor) or bladder tumors

Cystic renal disease

Lower urinary tract disease

Cystitis

Urolithasis,hypercalcuira

Trauma

Exercise

A 7 year old child presents with dark cola colored urine of three days duration all through urination without clots.There was no history of fever ,urinary symptoms,abdominal pain,trauma.The child has decreased urine output and periorbital edema

FH: negative family history of renal disease

DH: mother gave him amoxcillin before one month because he had tonsillitis

examination

BP 140/90

There is mild lower limb edema

The child was admitted for observation and workup

His urine output was .7 ml/kg/hour

Urine analysis :+3 protein,numerous RBC,RBC casts

Kft : creat 1 mg/d

What is diagnosis ?

ASOT was positive

C3 was low

Diagnosis : Poststreptoccal glomerulonephritis

Management : Fluid restriction,diuretics ,anti hypertensive (vasodilators,Ca channel blockers)

Follow up

Gross hematuria resolved after one week and proteinuria decreased from +3 to +1

Acute kidney normalized with a week

Hypertension resolved

Upon discharge he was still having microscopic hematuria

6-8 weeks later complements were repeated and they rose to normal levels

Microscopic hematurea resolved in few month

There were no long term sequele

Epidemiology of PSGN

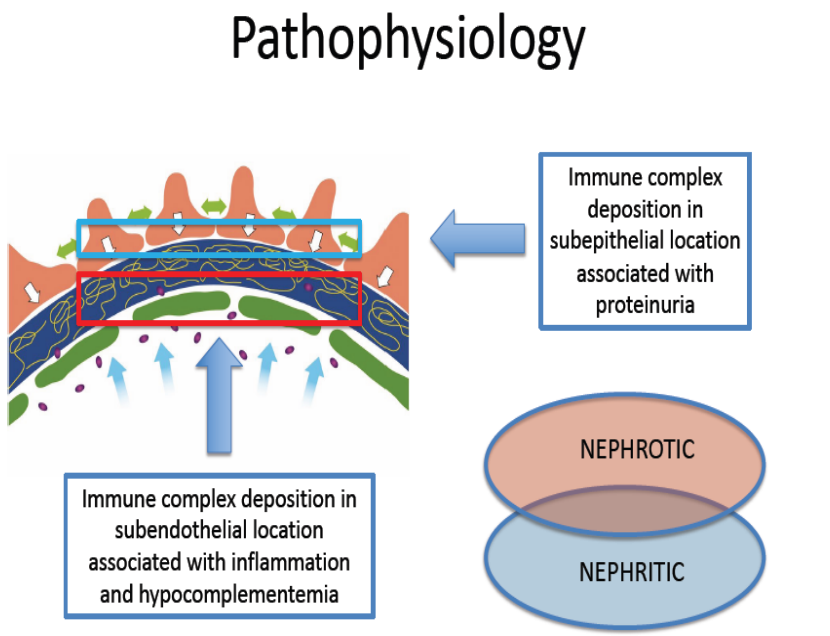
Follows GABHS pharyngitis in winter,pyodrema in summer

Certain nephritogenic M types,age 5-15 y,M:F 2:1

Risk of PSGN following GABHS is 15%

Antibiotic treatment doesn't prevent PSGN

Clinical features:latent period 10-14 days after pharyngitis, 3-6 wk pyoderma



Clinical Characteristics at Presentation

Hematuria

- Microscopic or gross
- Discolored urine reported in up to 80%

Hypertension

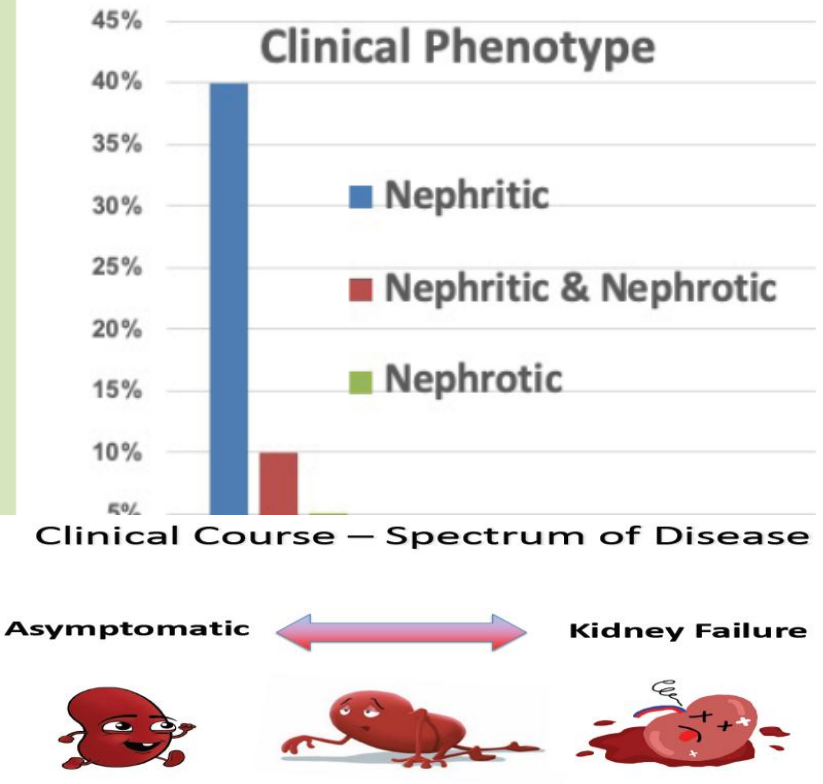
- Reported in 60-75%

Azotemia/Increased Cr

- Reported in 30-40%

Oliguria

- Reported in 25-35%



Laboratory investigations

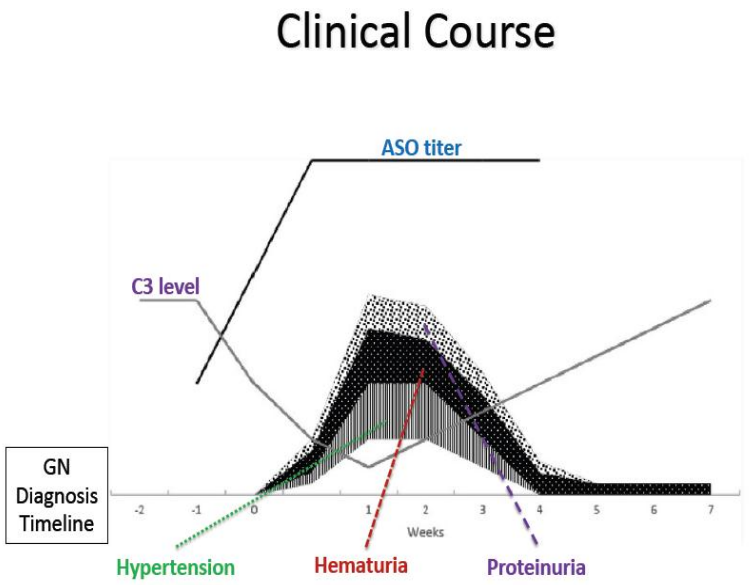
Urine : RBC casts

Low C3

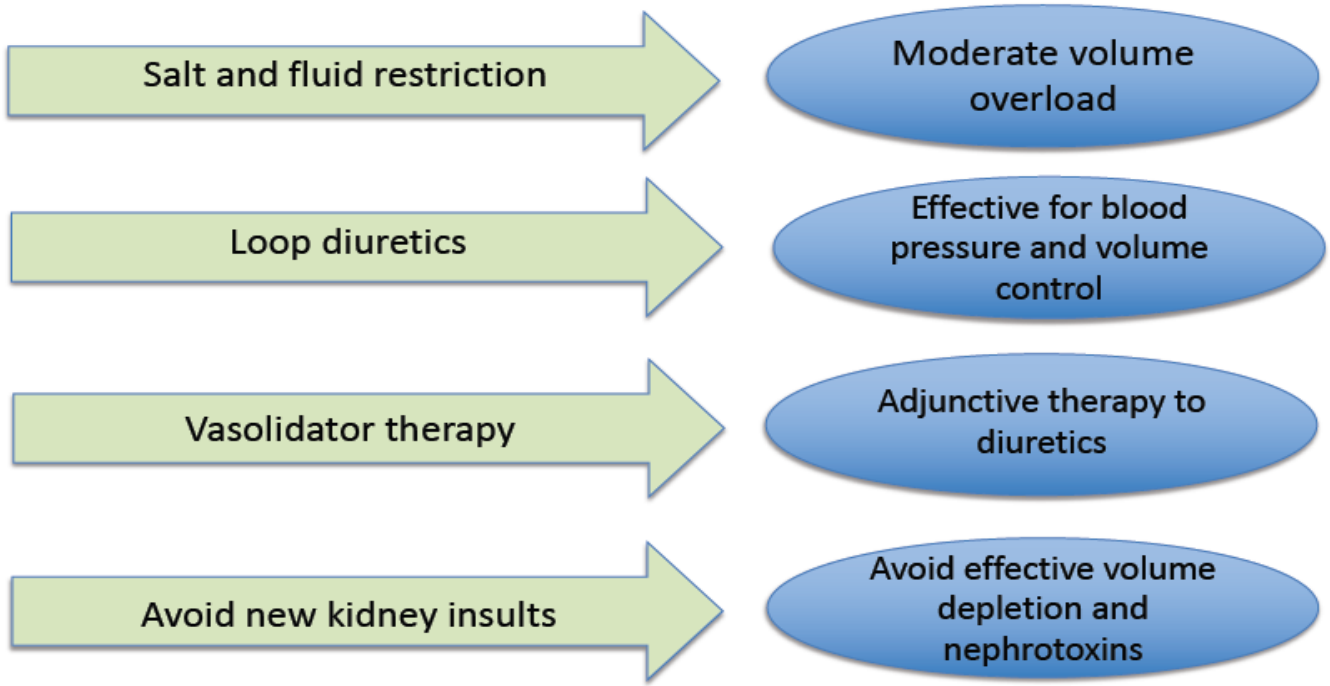
Positive ASOT

Renal azotemia

Hematuria and proteinurea stays for months



Management:
General Medical Care



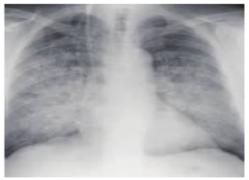
Clinical Course: Serious Sequelae

Encephalopathy/Seizures

- Around 5% of most large cohorts
- Generally related to hypertension

Symptomatic Pulmonary Edema/CHF

- 5-15% of most large cohorts
- Chest radiograph changes in up to 50%



Dialysis

- 1-2% of most large cohorts
- Most often related to RPGN

General Clinical Expectations

Most clinical signs and symptoms resolve spontaneously and within weeks

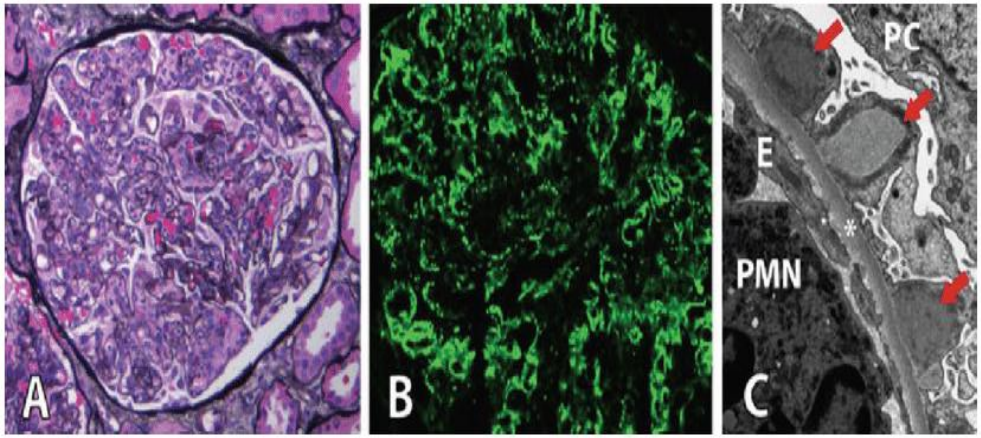
Hypocomplementemia >3 months should raise concern for a chronic hypocomplementemic GN

Recurrent gross hematuria is common with new acute illness early after diagnosis

Recurrent APSGN is quite rare

ESKD from APSGN is uncommon

APSGN: Immune Complex Nephritis



A. **Light microscopy:** proliferative and often exudative GN; findings vary within clinical spectrum; crescents less common

B. **Immunofluorescence:** diffuse C3 and IgG is typical; C3 deposition often described as "starry sky"

C. **Electron microscopy:** subepithelial electron-dense humps as well as subendothelial deposits

Pathology pictures from Rodriguez-Iturbe B et al, "Acute postinfectious glomerulonephritis in children," in Pediatric Nephrology, 7th ed. Berlin: Springer-Verlag, 2015

TABLE 20-2 Indications for Renal Biopsy

Early Stage	Recovery Phase
Short latent period	Depressed GFR >4 weeks
Severe anuria	Hypocomplementemia >12 weeks
Rapid progressive course	Persistent proteinuria >6 months
Hypertension >2 weeks	Persistent microhematuria >18 months
Depressed GFR >2 weeks	
Normal complement levels	
Nonsignificant titres of antistreptococcal antibodies	
Extrarenal manifestation	

Alport Syndrome

80% XL,20% AR

Deficiency of α5 of type 4 collagen

Renal failure, high frequency sensorineural deafness,ocular change as anterior lenticonus,retinal changes

Present as microscopic and rarely macroscopic hematauria with URTI

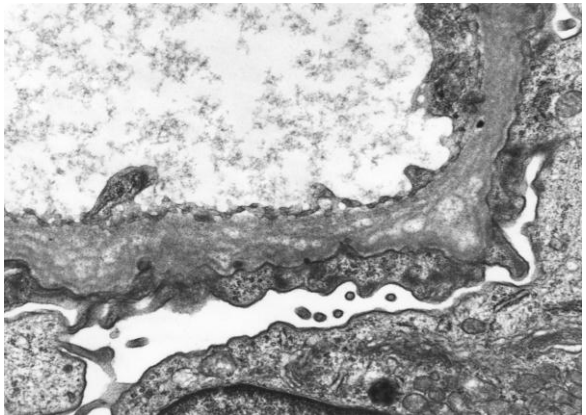
Proteinura,HTN later age

Diagnosis and course

Diagnosis by EM:Thinning of GBM,split and duplicated lamina densa,basket weave

Males progress to ESRD,deafness by 30y

ACEI may delay progression to ESRD



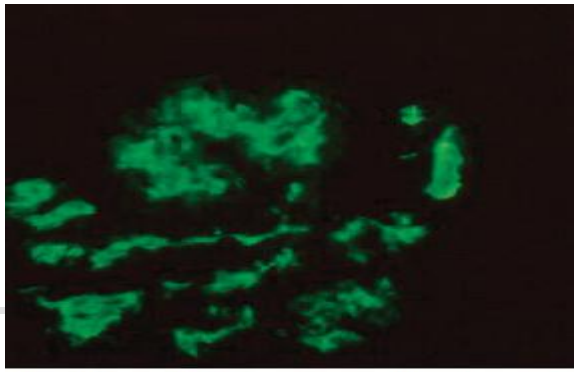
Benign Familial hematuira (TBMN)

- AD inheritance
- Present as microscopic hematuria,no proteinuria or renal failure
- EM:thinning of GBM
- Follow up for proteinuria,HTN

IgA nephropathy

- Recurrent macroscopic hematuria,loin pain 1-2 days following URTI,last < 3 days.
- Persistent microscopic hematuria ±proteinuria
- Nephritic,nephrotic syndrome rare
- Present second decade,more in males

Diagnosis and course



IgA high in 35-50%

Diagnosis: LM:focal or diffuse mesangial cell proliferation,expansion of mesangial matrix

IM:IgA,C3 deposits

Heavy proteinuria and hypertension are risk factors for progression to ESKD.

Progression to ESRD is slow

Prognosis for children better than adults

Young children without macroscopic hematuria have the best long term outcome

Treatment of IgA nephropathy

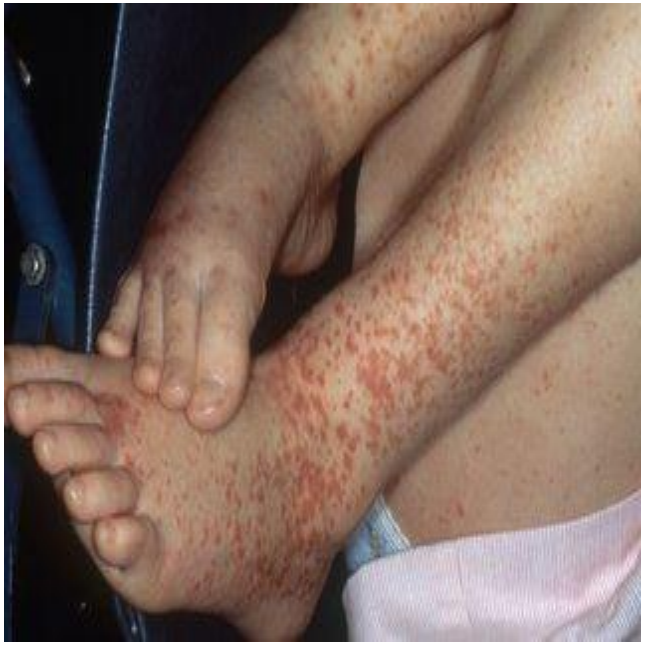
KDIGO 2021

Treatment

- There is strong evidence suggesting a benefit of RAS blockade in children.[132] All children with IgAN and proteinuria >200 mg/d or PCR >200 mg/g (>0.2 g/g [20 mg/mmol]) should receive ACEi or ARB blockade, advice on a low-sodium diet, and optimal lifestyle and blood pressure control (systolic blood pressure [SBP] <90th percentile for age, sex, and height).

In children with proteinuria >1 g/d or PCR >1 g/g (100 mg/mmol) and/or mesangial hypercellularity, most pediatric nephrologists will treat with glucocorticoids in addition to RAS blockade from time of diagnosis.

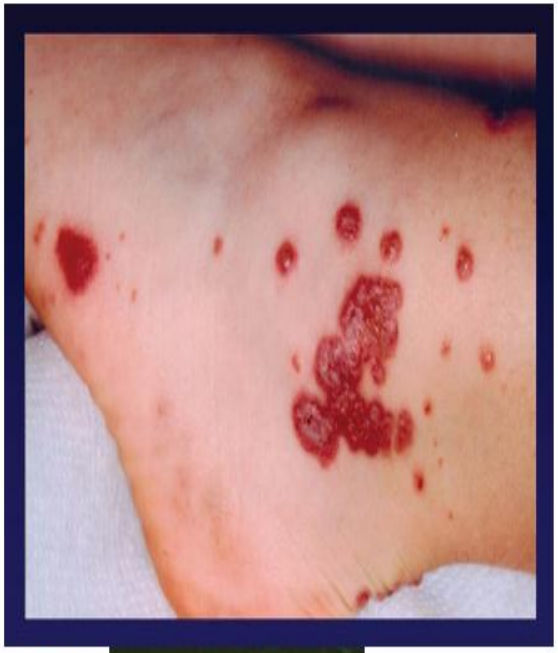
A 7 year old child presents with skin rash and hematuria



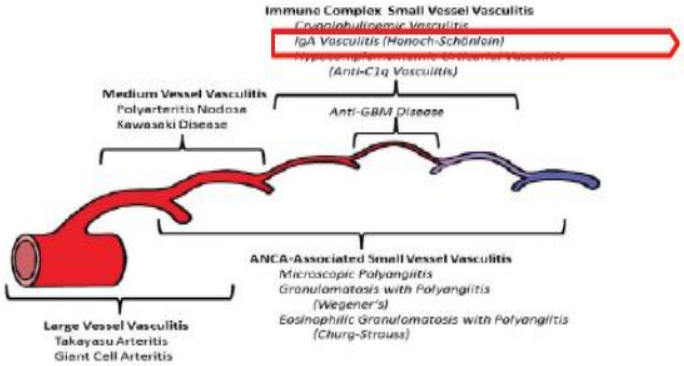
Criterion	Description
Mandatory criterion	Purpura or petechiae with lower limb predominance
Minimum 1 out of 4 criteria	1. Diffuse abdominal pain with acute onset 2. Histopathology showing leukocytoclastic vasculitis or proliferative glomerulonephritis, with predominant immunoglobulin A (IgA) deposits 3. Arthritis or arthralgia of acute onset 4. Renal involvement in the form of proteinuria or haematuria

EULAR/PRINTO/PRES: the European League Against Rheumatism, the Paediatric Rheumatology International Trials Organization and the Paediatric Rheumatology European Society (8, 9).

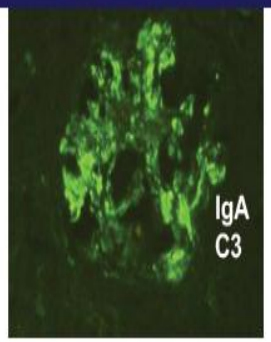
IgA Vasculitis (Henoch-Schoenlein purpura) is
a vasculitis whit IgA-dominant immune deposits
affecting small vessels (capillaries, venules, arterioles)
Involving skin, gut and glomeruli
and associated with arthralgia or arthritis



4 JENNETTE ET AL.



IgAVN



Onset:

- Palpable purpura and multiorgan signs with hematuria and proteinuria

Natural history.

- Most common in children
- In children most frequent remission, in rare cases rapid progression, possible progression over decades

HSP

Renal involvement seen in 20-55%

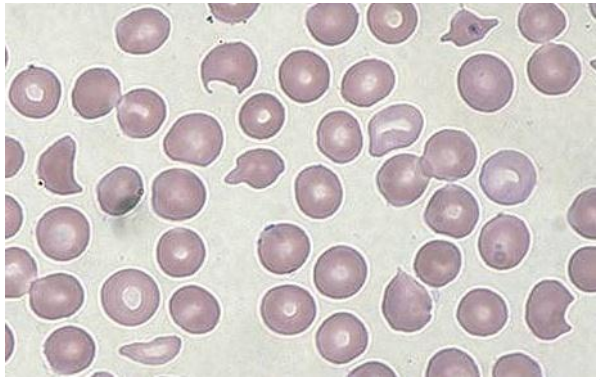
Most common is isolated microscopic hematuria with and without proteinurea

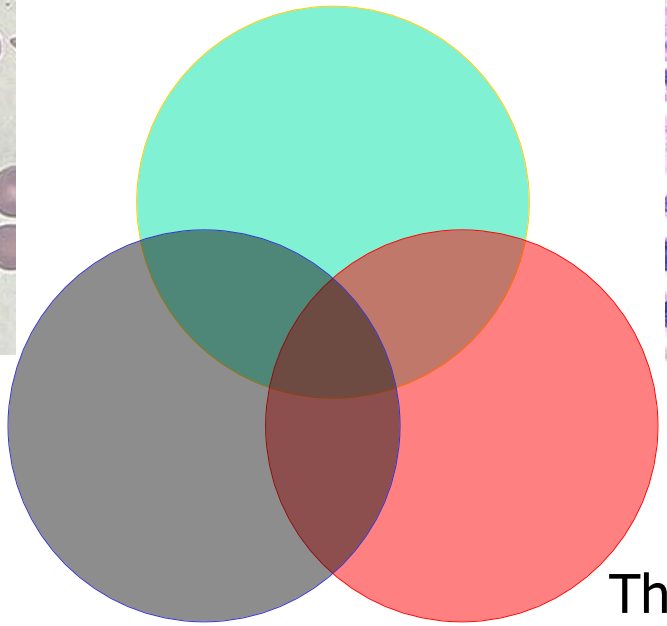
Nephrotic syndrome,hypertension,elevated creatinine are are manifestations

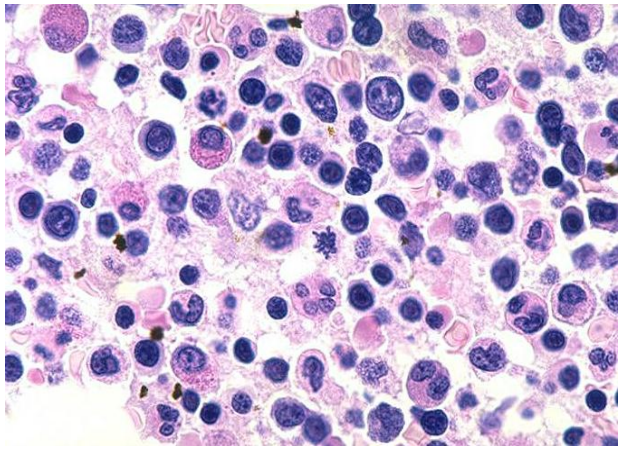
Monthly urine analysis is needed in the first 3-6 month

HUS

Acute haemolytic anaemia







Reduced GFR

Thrombocytopaenia

Diarrhae + HUS

- D+HUS:follows STEC, shigella
- O157:H7 E. coli most common serotype
- 5-15% of kids infected STEC develop HUS
- Risk of HUS increase with age <5y, WBC >13,000/mm^3,antimotiliy drugs (retention of toxin
- Antibiotic can increase risk?? Release toxin
- Can affect GIT,CNS

Nocturnal Enuresis

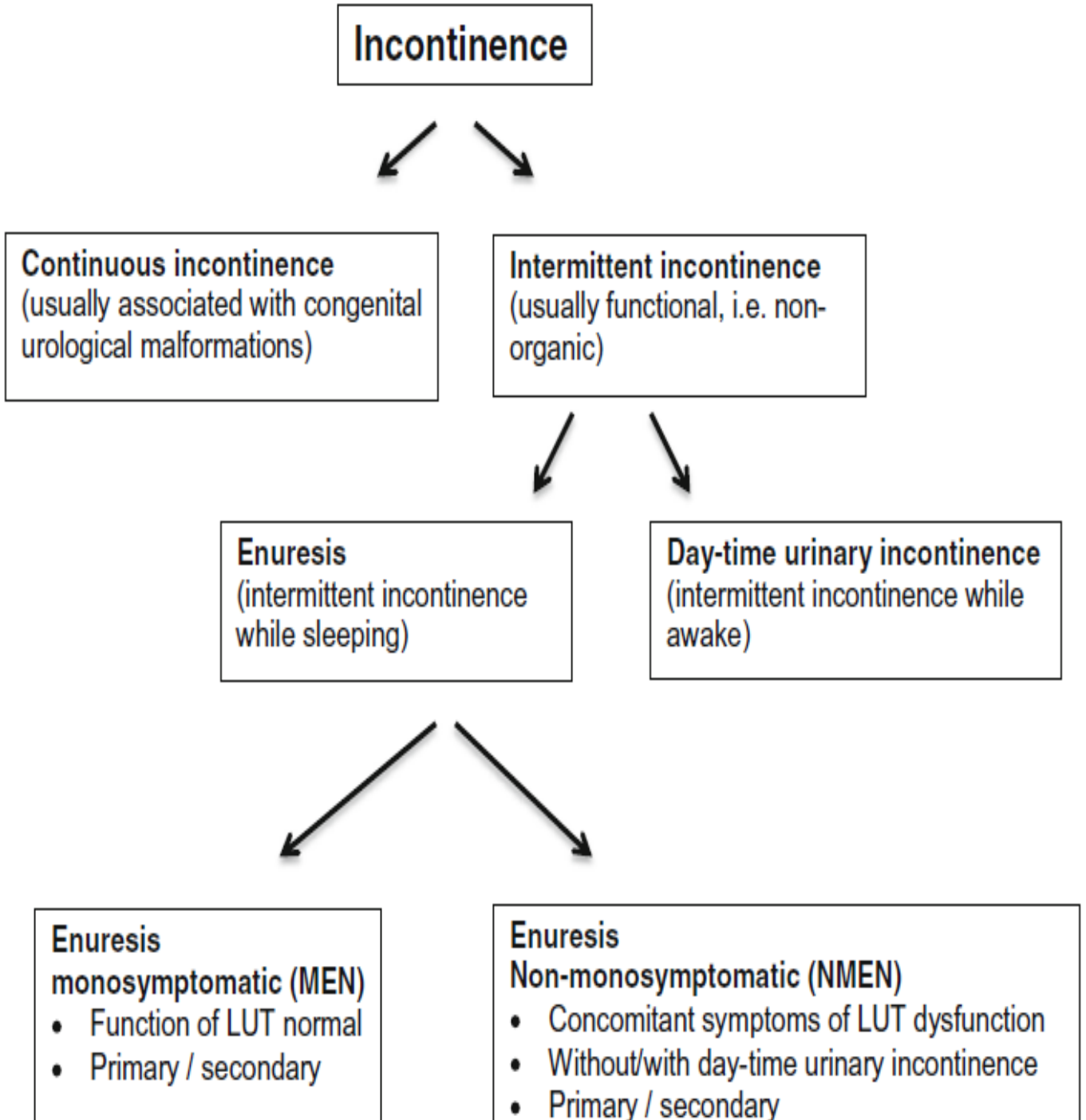
Nocturnal enuresis

- Definition :intermittent incontinence while at night after age of 5 year
- Prevalence :15-20 % in 5y, 5 % in 10 y, 1-2 % in 15 y

- Boys are affected more than girls
- 15 % become dry each year without treatment

- Primary , secondary if dry > 6 m
- Monosymptomatic NE (MNE)=absence of daytime voiding,LUT symptoms nonmonosymptomatic (NMNE)

Fig. 1 Subdivision and clinical management of urinary incontinence in children. *LUT* lower urinary tract



nonmonosymotomatic enuresis

- Daytime wetting
- Frequency; increased more than 8 times or decreased last than 3
- urgency
- Hesistancy
- Straining
- Weak stream
- Intermittent stream
- Holding maneuvers
- Feeling of incomplete emptying
- Genital or lower urinary tract pain

Table 1. Conditions That May Precipitate Secondary Enuresis.

Condition	Possible Mechanism
Cystitis	Reduced bladder capacity
Constipation	Reduced bladder capacity
Sleep-disordered breathing	Impaired arousal
Diabetes mellitus	Nocturnal polyuria
Diabetes insipidus	Nocturnal polyuria
Urethral obstruction	Reduced bladder capacity
Neurogenic bladder	Reduced bladder capacity
Seizure disorder	Neurogenic mechanism
Medications (selective serotonin-reuptake inhibitors, valproic acid, clozapine)	—
Psychological stress, sexual abuse	—

N Engl J Med 2009;360:1429-36.

Primary evaluation: case history

General
Health and development. Weight loss? Excessive thirst? UTIs?
Look for ckd

Timeframe
Primary/secondary enuresis? Frequent/sporadic accidents?

Bladder
Daytime bladder symptoms, now or previously? Voiding frequency.

Bowel
Constipation symptoms, fecal incontinence?

Behaviour
Problems at home or at school? Distressed by enuresis?

Table 2. Important Aspects of the History and Physical Examination in Enuresis.

Symptom, Sign, Condition	Possible Interpretation	Referral to Specialist
Urinary frequency	Reduced bladder capacity	Yes
Nocturia	Reduced bladder capacity	Yes
Urinary urgency		Yes
Daytime incontinence		Yes
Interrupted or otherwise abnormal stream		Yes
Absorbent underpants soaked (vs. damp or average wetness)	Nocturnal polyuria	No
Soaking through absorbent underpants into sheets	Nocturnal polyuria	No
Large volume of urine on first voiding in morning, despite enuresis	Nocturnal polyuria	No
Low daytime fluid intake, thirst at end of school day, majority of fluid intake in late afternoon and evening	Nocturnal polyuria	No
Thirst, polyuria	Nocturnal polyuria, possibly diabetes mellitus or diabetes insipidus	No
Cystitis	Reduced bladder capacity	Yes
Constipation or encopresis	Reduced bladder capacity	Yes
Snoring	Impaired arousal from sleep	Yes
Hard stool in abdomen	Constipation	Yes
Patulous anus, absence of anal wink	Neurogenic bladder	Yes
Dimple above cleft or other cutaneous abnormalities over lumbosacral spine	Neurogenic bladder	Yes
No improvement with therapy	—	Yes

Causes of primary NE

~~Delay in maturation of bladder control~~

- Genetic causes :75 % have affected relative
- Psychatric disorders,ADHD,social fatocrs ,stressful life events,

Causes of primary NE

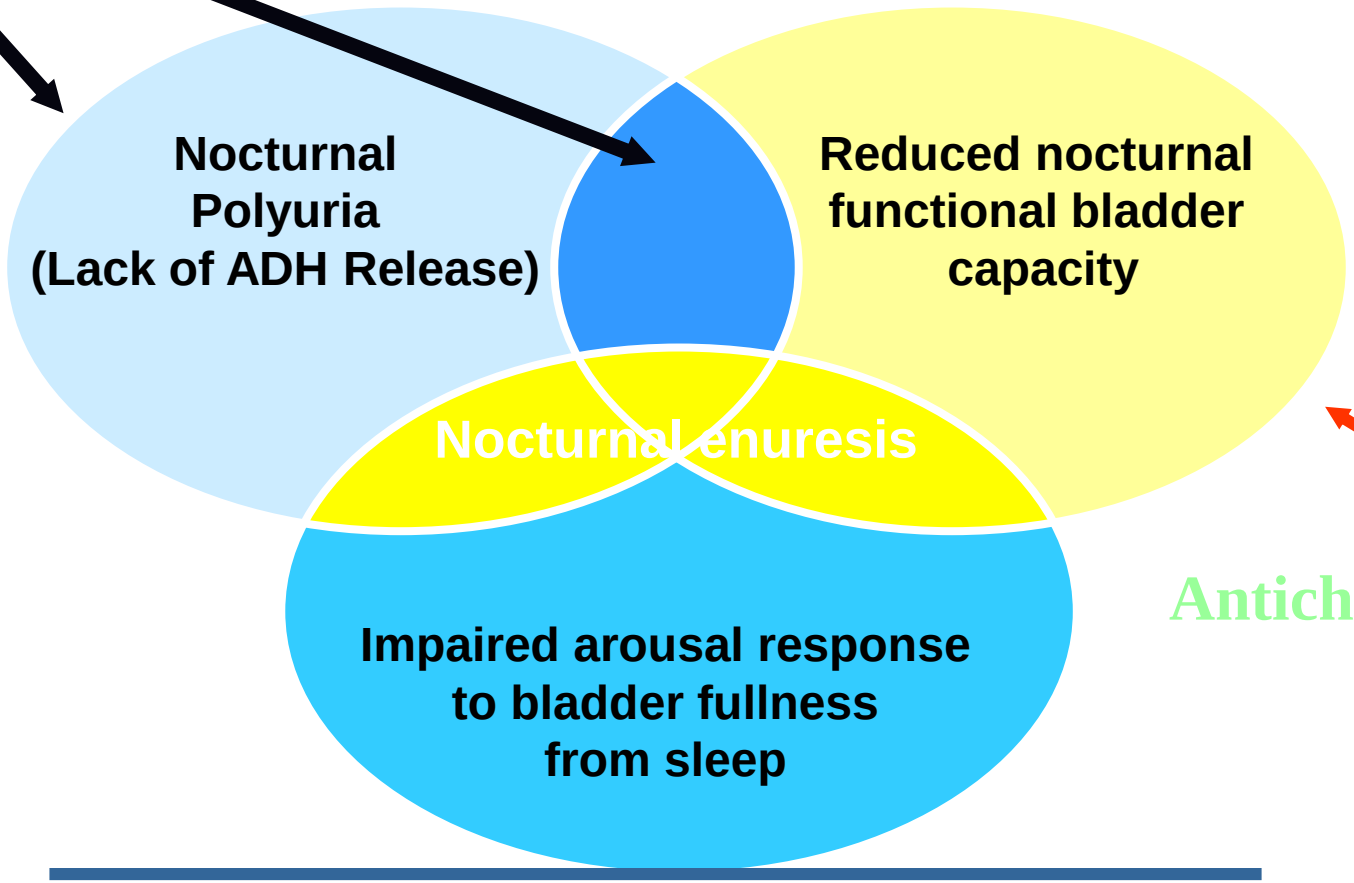
- nocturnal polyuria
- detrussor overactivity,reduced nocturnal bladder capacity
- poor arousability: have poor sleep quality,sleep fragmentation,enuresis related to OSA

Management strategies

- Behavioral thearpy :needs to achieve good bowel and bladder habits requires a supportive parent,a motivated child, patience and time
- Frequent regular voiding, decrease fluid intake at night
- Star charts
- Avoid caffeinated drink
- Treat constipation
- Decrease solute load (sugar,salt)

Treatment / Pathophysiology

Minirin (A heterogeneous disorder)



Anticholinergics

Genetics

Other thearpy

Overactive bladder

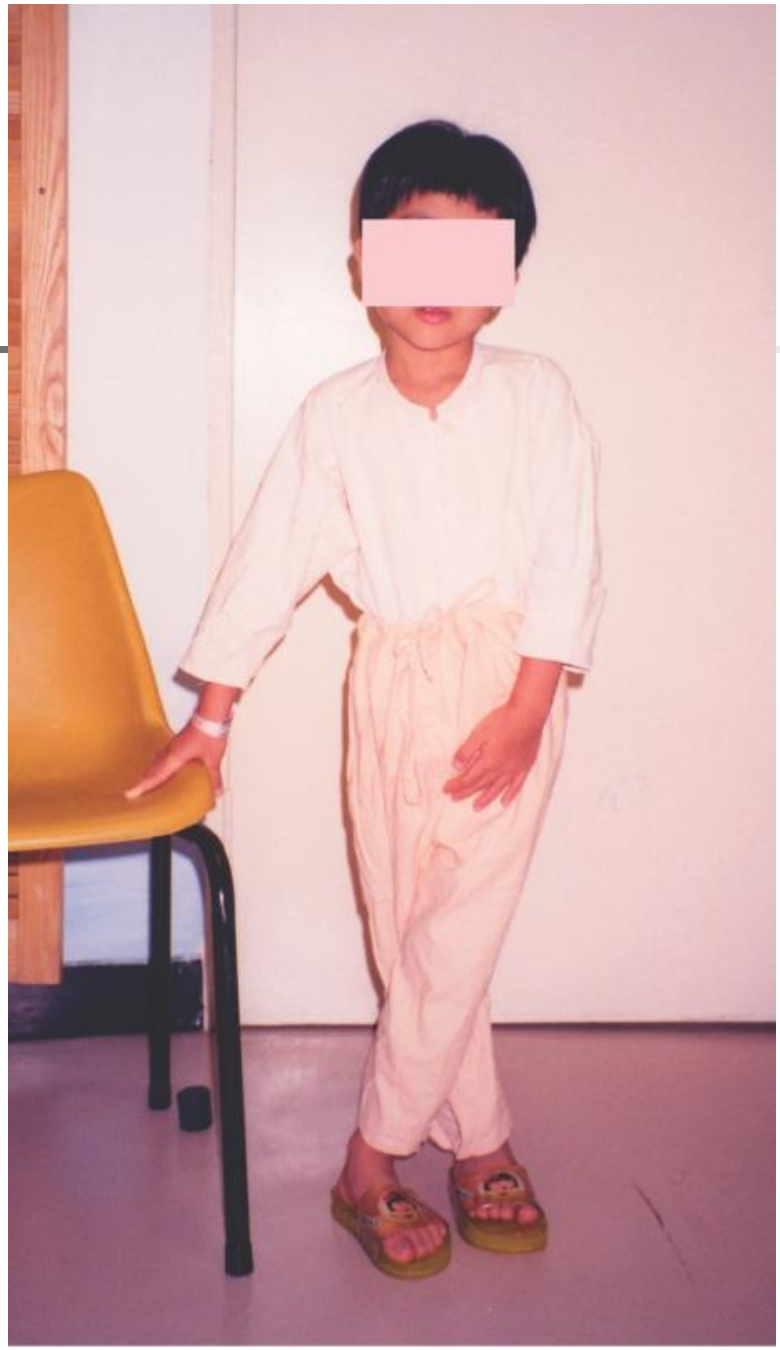
Reduced bladder capacity (MVV):

MVV < 65% of EBC

EBC = 30 x (age + 1) (ml)

NB: Is correct only if first morning voided volume is disregarded!!

- Urge incontinence,frequency
- Detrussor overactivity
- Holding manoeuvres,squatting,curtsey sign,daytime wetting
- Small bladder capacity,thickend bladder wall
- More in girls,onset around 4-5 y
- Result in recurrent UTI,reflux
- Associated with constipation



- Urodynamic findings : unstable detrussor contractions at low volume,high compliance
- management
- 1. bladder training , scheduled voiding
- 2.anticholingeric:increase FBC as oxybutynin , tolterodine,solfinacine
- Botox
- neuromodulation


THANK YOU