Approach to Hematuria

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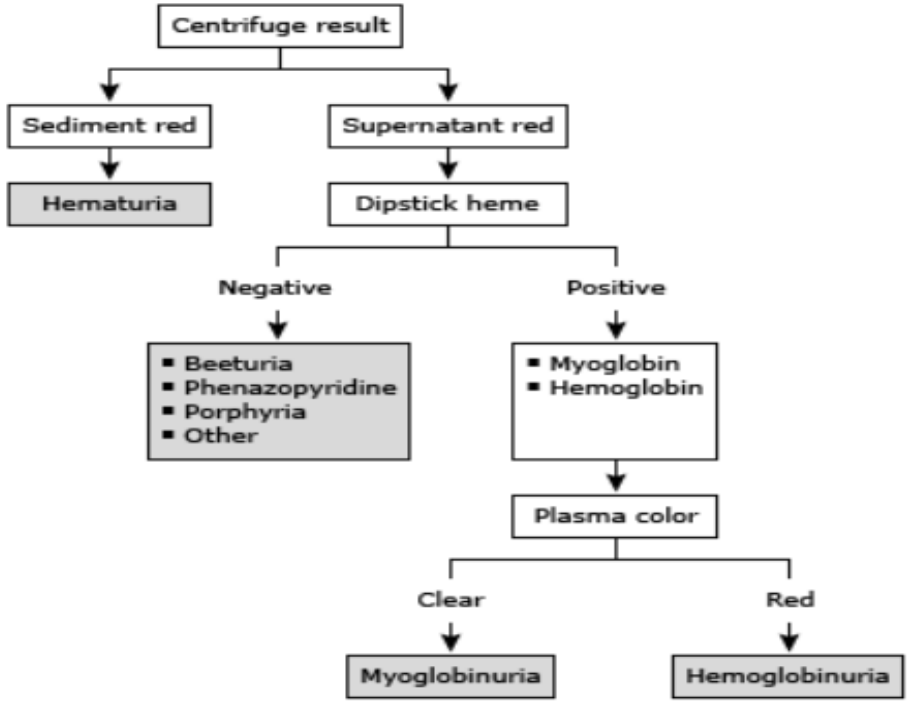
* Hematuria is one of the most important signs of renal or bladder disease, but, proteinuria is a more important diagnostic and prognostic finding, except in the case of calculi or malignancies.

* Hematuria is almost never a cause of anemia.

* 49% ; either confirmed or suspected UTI,
* only 4% ; renal parenchymal disease.

Hematuria

* Approach to the evaluation of hematuria in a child ……. No consensus
* The initial step in the evaluation of patients with red urine is to establish whether or not the urine discoloration is due to blood or another substance.


Centrifuge result
Sediment red
Supernatant red
Hematuria
Dipstick heme
Negative
Positive
Beeturia
Phenazopyridine
Porphyria
Other
Myoglobin
Hemoglobin
Plasma color
Clear
Red
Myoglobinuria
Hemoglobinuria

* Gross (Macroscopic) hematuria
  → blood that can be seen with the naked eye
  urinary tract ; bright-red, visible clots, or crystals with normal-looking RBCs
  glomerular; Cola-colored, RBC casts, and dysmorphic RBCs

* Microscopic hematuria
  → detected by a dipstick test during a routine exam.
  ; should be confirmed by microscopic examination

  (10 ml of urine, spun at 2000 rpm for 5 min → 9 ml, decanted
  → sediment, resuspended and examined by microscopy by Hpf (x 400)

Definition

* Microscopic hematuria ≥ 5-10 RBCs/hpf is considered significant.

  asymptomatic child → at least 2 postive UA of 3 over 2- to 3-week period

  symptomatic child → in a single urine sample

* AAP recommends a screening urinalysis

  at school entry (4–5 years of age) &

  once during adolescence (11–21 years of age)

  as a component of well child–care.

Causes of red urine

- Dark brown, black

Disease states

* Alkaptouria
* Homogentisic acid
* Melanin
* Methemoglobinuria
* Tyrosinosis
* Ingestions
* Alanine
* Cascara
* Resorcinol
* Thymol

- Pink, red, tea-colored

Disease states

- Hemoglobinuria
- Myoglobinuria
- Porphyrinuria
- Serratia marcescens
- Bile pigments
- Urates
- Ingestions
- Aminopyrine
- Beets
- Benzene
- Blackberries
- Ibuprofen
- Lead
- Rifampin …

Causes of hematuria in children

* Glomerular diseases
  - Recurrent gross hematuria
    (IgA nephropathy, Benign familial hematuria, Alport's syndrome)
  - Acute PSGN
  - MPGN
  - SLE
  - Membranous nephropathy
  - RPGN
  - Henoch-Schonlein purpura
  - Goodpasture's disease
* Interstitial and tubular
  - Acute pyelonephritis
  - Acute interstitial nephritis
  - Tuberculosis
  - Hematologic (sickle cell disease, von Willebrand's coagulopathies renal vein thrombosis, thrombocytopenia)
* Urinary tract
  - Bacterial or viral (adenovirus) infection-related
  - Nephrolithiasis and hypercalciuria
  - Structural anomalies, congenital anomalies, polycystic kidney disease
  - Trauma
  - Tumors
  - Exercise
* Medications (aminoglycosides, amitryptiline, anticonvulsants, aspirin, chlorpromazine, coumadin, penicilline cyclophosphamide, diuretics, thorazine)

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.

Hematuria evaluation

* Based on documentation of
  history
  family history
  physical findings
  laboratory findings (RBC morphology, ± proteinuria)

* Initial evaluation should be directed toward important and potentially life-threatening causes

  hypertension, edema, oliguria,

  Significant proteinuria (≥ 500mg/24hrs), or RBC casts

* Next step → CBC, streptozyme panel, serum C3/C4, serum Cr/K …

* BP & Urine output must be monitored frequently

Hematuria evaluation

* Dysuria, frequency, urgency or flank or abdominal pain
  → Urinary tract infection or nephrolithiasis

* Recent trauma, strenuous exercise, menstruation, catheterization
  → transient hematuria

* Sore throat or skin infection within past 2 to 4 wks
  → postinfections glomerulonephritis Drugs and toxin ingestion

* Family history
  : hematuria, hearing loss, hypertension, nephrolithiasis, renal disease, renal cystic disease, hemophilia, dialysis or transplant …

Hematuria evaluation

* Presence of absence of hypertension or proteinuria

* Fever or CVA tenderness → UTI
* Abdominal mass → Tumor, hydronephrosis, MCK or PCK disease
* Gross hematuria with proteinuria → Glomerulonephritis.
* Rashes & arthritis → Henoch-Schonlein purpura and SLE.
* Edema → Nephrotic syndrome

Hematuria evaluation

* Presence of absence of hypertension or proteinuria

* Fever or CVA tenderness → UTI
* Abdominal mass → Tumor, hydronephrosis, MCK or PCK disease
* Gross hematuria with proteinuria → Glomerulonephritis.
* Rashes & arthritis → Henoch-Schonlein purpura and SLE.
* Edema → Nephrotic syndrome

Lab studies

* Proteinuria
  may be present regardless of the cause of bleeding
  blood origin ; usually not >2+(100 mg/dL) (especially, microscopic)
  1- 2+ proteinuria ; R/O orthostatic(postural) proteinuria.

a condition in which protein appears in the urine
in otherwise healthy people who have been standing for a period of time
in approximately 3 -15% of healthy young adults
Dx ; 2 urine specimens - one right after waking
the second about 2 hours after being upright

> 2+ proteinuria ; glomerulonephritis & nephritic syndrome

* RBC casts → a highly specific marker for GN, not confirmative
* Dysmorphic RBC → Glomerular origin

* Additional test (by suspected source of bleeding & Sx and Hx)
  → Serum Cr, CBC, C3/C4, ANA, ASO, urine culture, Ca/Cr ratio

Diagnostic approach to hematuria

* By history, physical examination and simple laboratory tests
* Diagnostic algorithms for hematuria

- Gross hematuria
- Microscopic hematuria without abnormal findings
-Microscopic hematuria with abnormal findings

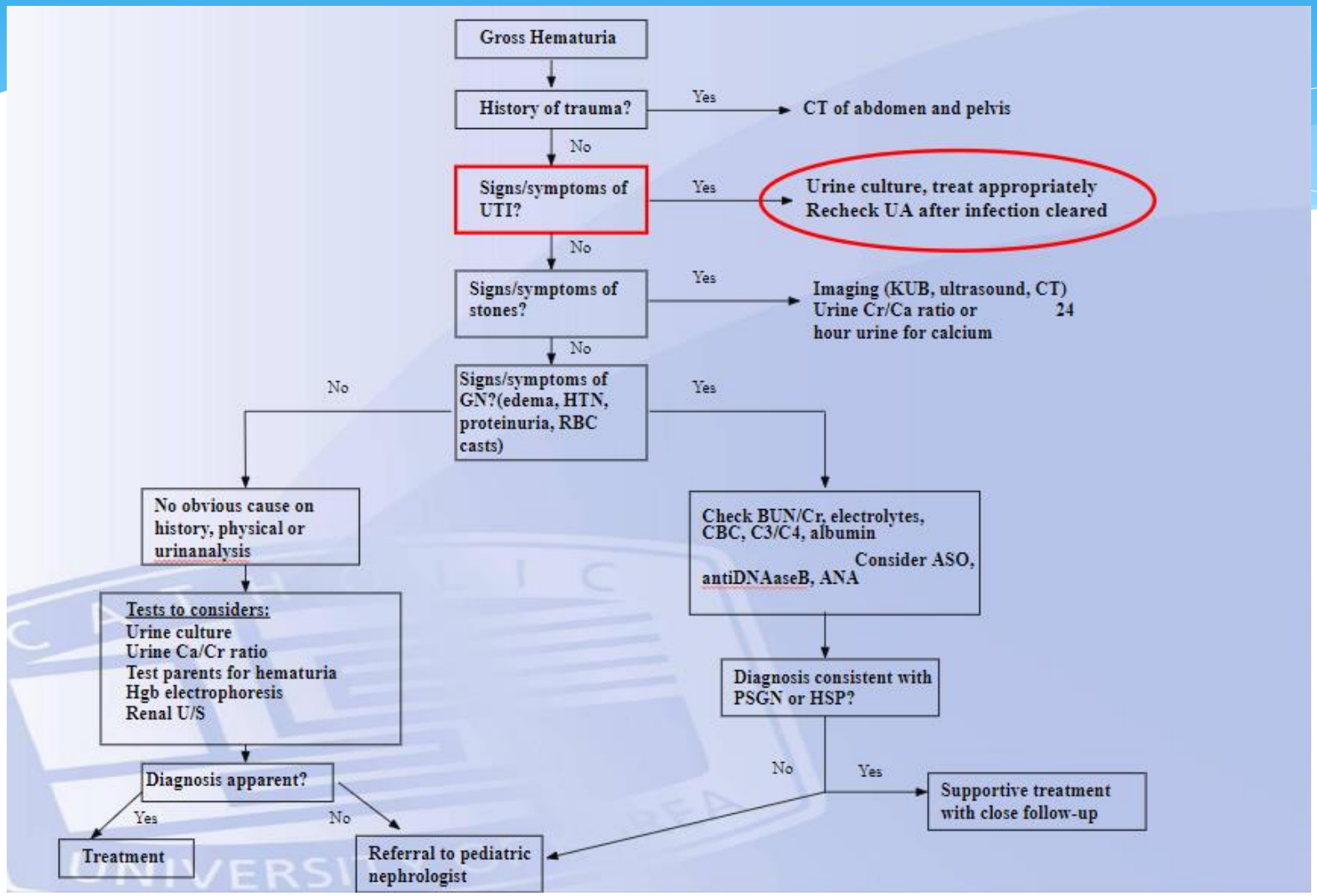
* Painful ; usually urologic conditions. (Glomerular ; painless)

* Cystoscopy → rarely reveals a cause for hematuria

Indications ; suspicious bladder pathology
to lateralize the source of bleeding (esp. during active bleeding)

* Young girls with recurrent gross hematuria
→ a history of child abuse or insertion of a vaginal FB
→ P/Ex for the genital area

* The most commonly identified etiologies for gross hematuria in children include urinary tract infection (UTI), irritation of the meatus or perineum, and trauma.
* Other less common causes include nephrolithiasis, sickle cell disease/trait, coagulopathy, glomerular disease.


Gross Hematuria
History of trauma?
Yes
CT of abdomen and pelvis
No
Signs/symptoms of UTI?
Yes
Urine culture, treat appropriately
Recheck UA after infection cleared
No
Signs/symptoms of stones?
Yes
Imaging (KUB, ultrasound, CT)
Urine Cr/Ca ratio or 24 hour urine for calcium
No
Signs/symptoms of GN?(edema, HTN, proteinuria, RBC casts)
No
Yes
No obvious cause on history, physical or urinanalysis
Tests to considers:
Urine culture
Urine Ca/Cr ratio
Test parents for hematuria
Hgb electrophoresis
Renal U/S
Diagnosis apparent?
Yes
No
Treatment
Referral to pediatric nephrologist
Check BUN/Cr, electrolytes, CBC, C3/C4, albumin
Consider ASO, antiDNAaseB, ANA
Diagnosis consistent with PSGN or HSP?
No
Yes
Supportive treatment with close follow-up

CAUSES

* Most children with isolated microscopic hematuria

-Do not have a treatable or serious cause

-Do not require an extensive evaluation

Transient Hematuria

Causes of transient microscopic hematuria in children

Exercise
Fever
Trauma to kidney and/or urinary tract
Urinary tract infection
Urethritis

Cause of asymptomatic isolated M/H

Common

* Undetermined
* Benign familial
* Idiopathic hypercalciuria
* IgA nephropathy
* Sickle cell trait or anemia
* Transplant

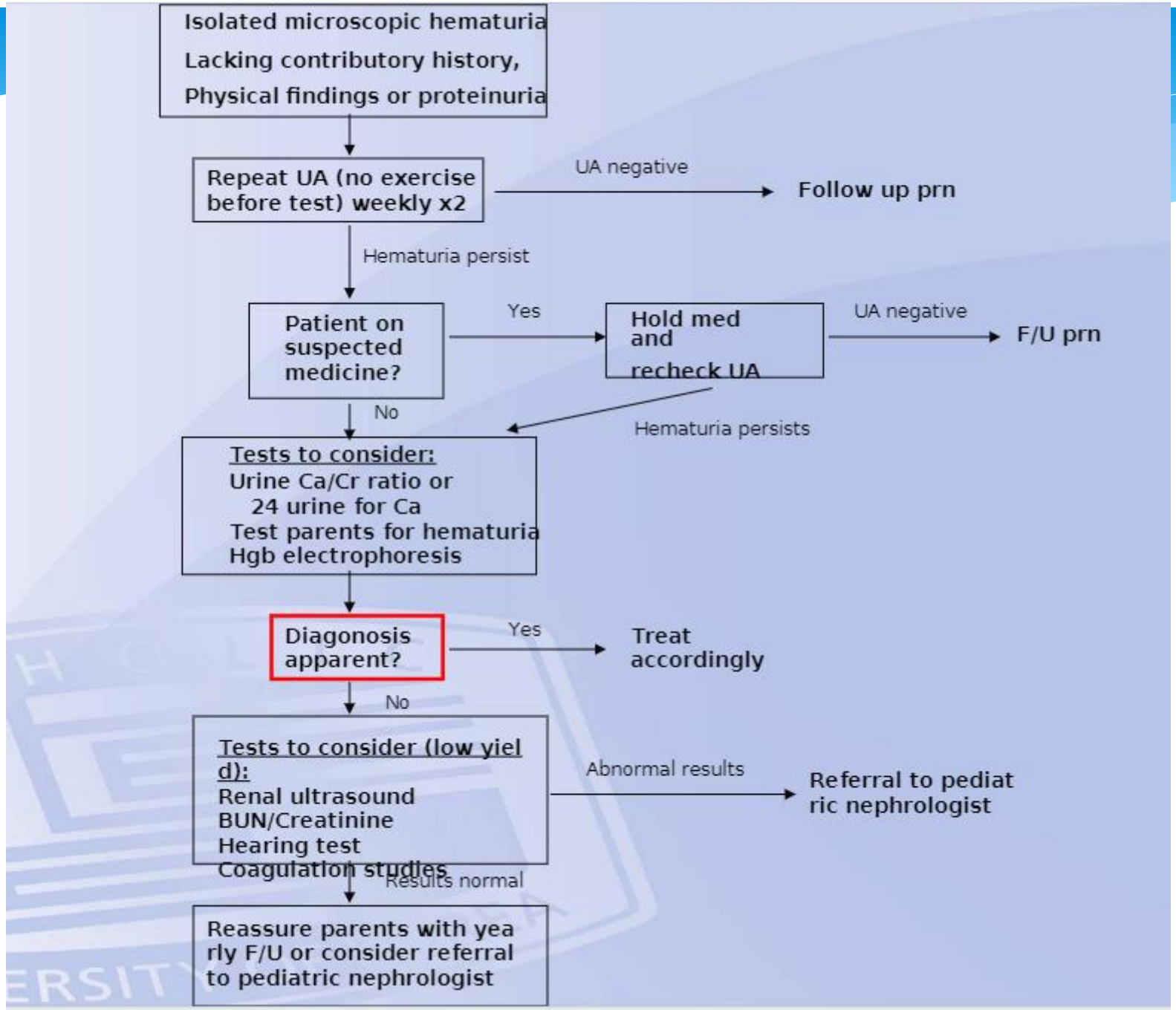
Less common

* Alport nephritis
* Postinfectious GN
* Trauma
* Exercise
* Nephrolithiasis
* Henoch-Schonlein purpura

Cause of asymptomatic isolated M/H

Uncommon

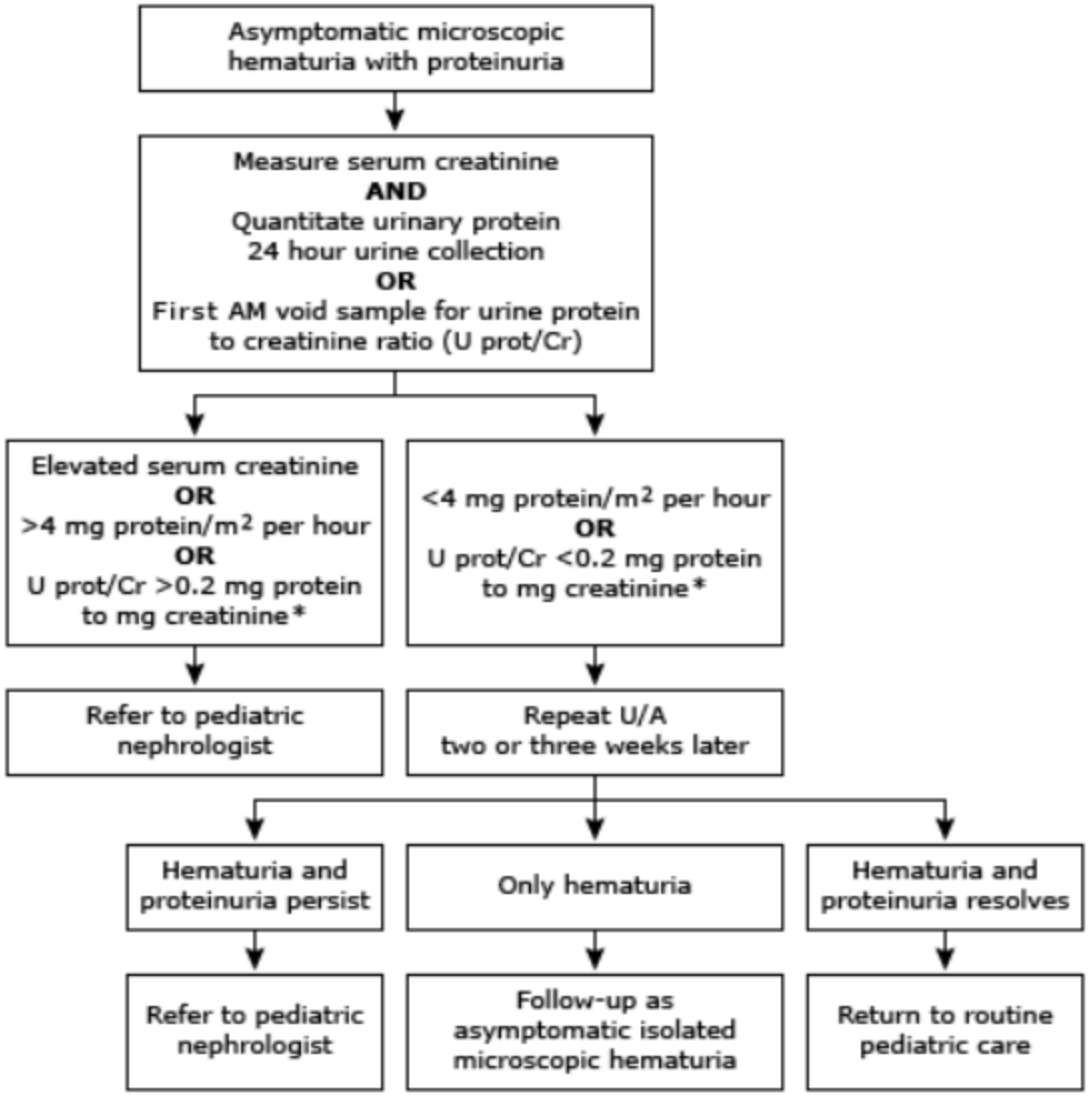
Drugs and toxins
Coagulopathy
Ureteropelvic junction obstruction
Focal segmental glomerulosclerosis
Membranous glomerulonephritis
Membranoproliferative glomerulonephritis
Lupus nephritis
Hydronephrosis
Pyelonephritis
Vascular malformation
Tuberculosis
Tumor

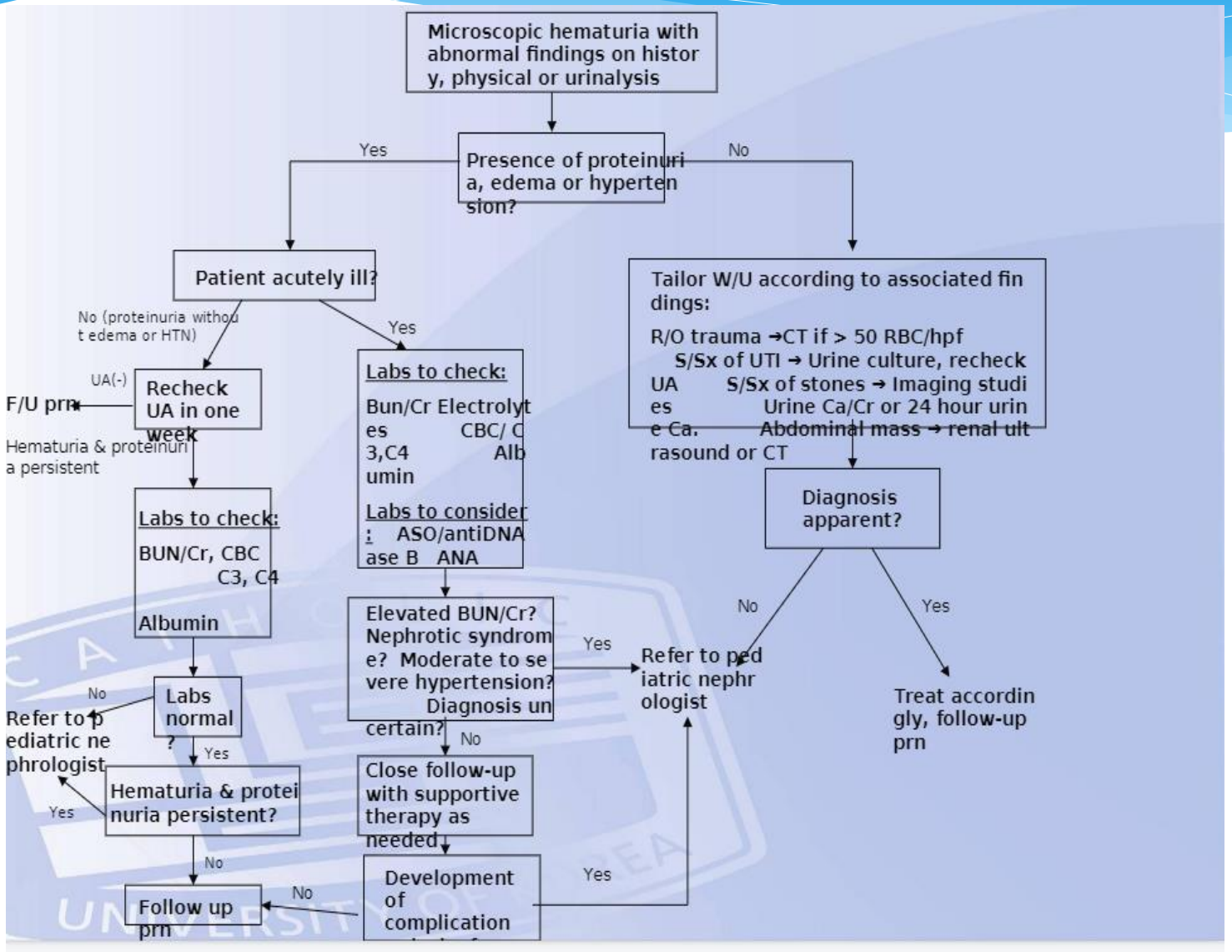

Isolated microscopic hematuria
Lacking contributory history,
Physical findings or proteinuria
Repeat UA (no exercise before test) weekly x2
UA negative
Follow up prn
Hematuria persist
Patient on suspected medicine?
Yes
Hold med and recheck UA
UA negative
F/U prn
No
Hematuria persists
Tests to consider:
Urine Ca/Cr ratio or
24 urine for Ca
Test parents for hematuria
Hgb electrophoresis
Diagonosis apparent?
Yes
Treat accordingly
No
Tests to consider (low yiel d):
Renal ultrasound
BUN/Creatinine
Hearing test
Coagulation studies
Abnormal results
Referral to pediat ric nephrologist
Results normal
Reassure parents with yea rly F/U or consider referral to pediatric nephrologist

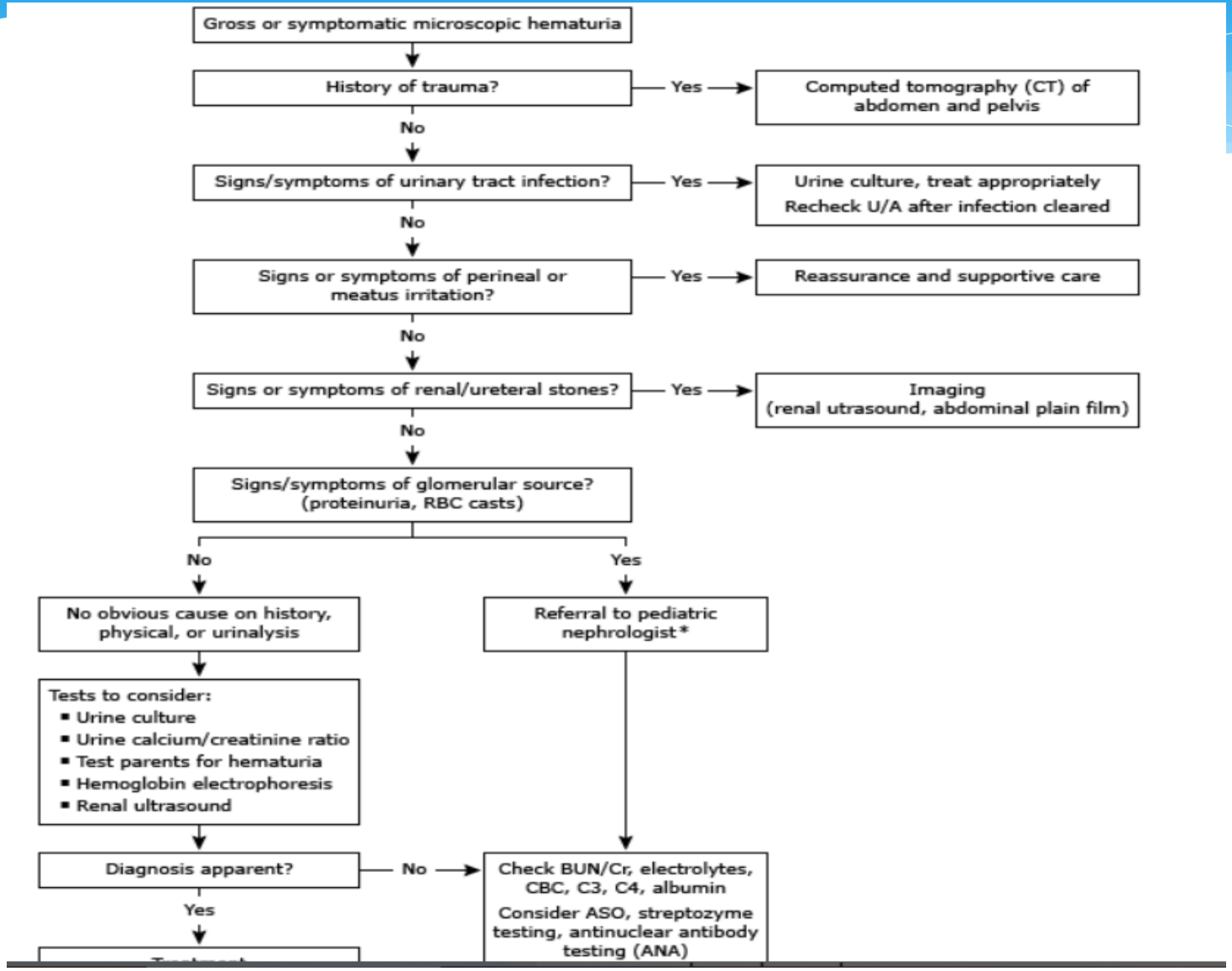
Diagnostic approach to M/H With abnormal findings

* Varied clinical presentation and wide range of diagnositic possibilities .
* Patients with hematuria from glomerular causes have the high risk for morbidity.
* Microscopic hematuria with substantial proteinuria

- Minimal change nephrotic syndrome
-IgA nephropathy
-Alport's syndrome
- MPGN
- Membranous nephropathy
-FSGN


Asymptomatic microscopic hematuria with proteinuria
Measure serum creatinine
AND
Quantitate urinary protein
24 hour urine collection
OR
First AM void sample for urine protein to creatinine ratio (U prot/Cr)
Elevated serum creatinine
OR
>4 mg protein/m2 per hour
OR
U prot/Cr >0.2 mg protein to mg creatinine*
<4 mg protein/m2 per hour
OR
U prot/Cr <0.2 mg protein to mg creatinine*
Refer to pediatric nephrologist
Repeat U/A two or three weeks later
Hematuria and proteinuria persist
Only hematuria
Hematuria and proteinuria resolves
Refer to pediatric nephrologist
Follow-up as asymptomatic isolated microscopic hematuria
Return to routine pediatric care


Microscopic hematuria with abnormal findings on history, physical or urinalysis
Presence of proteinuria, edema or hypertension?
Yes
No
Patient acutely ill?
Yes
No (proteinuria without edema or HTN)
Tailor W/U according to associated findings:
R/O trauma →CT if > 50 RBC/hpf
S/Sx of UTI → Urine culture, recheck UA
S/Sx of stones → Imaging studies Urine Ca/Cr or 24 hour urine Ca. Abdominal mass → renal ultrasound or CT
Recheck UA in one week
UA(-)
F/U prn
Hematuria & proteinuria persistent
Labs to check:
Bun/Cr Electrolytes CBC/ C3,C4 Albumin
Labs to consider: ASO/antiDNAase B ANA
Diagnosis apparent?
No
Yes
Labs to check:
BUN/Cr, CBC
C3, C4
Albumin
Elevated BUN/Cr? Nephrotic syndrome? Moderate to severe hypertension? Diagnosis uncertain?
Yes
Refer to pediatric nephrologist
Treat accordingly, follow-up prn
Labs normal?
No
Refer to pediatric nephrologist
Yes
Hematuria & proteinuria persistent?
Yes
No
Close follow-up with supportive therapy as needed
Development of complication
Yes
No
Follow up prn


Gross or symptomatic microscopic hematuria
History of trauma?
Yes
Computed tomography (CT) of abdomen and pelvis
No
Signs/symptoms of urinary tract infection?
Yes
Urine culture, treat appropriately
Recheck U/A after infection cleared
No
Signs or symptoms of perineal or meatus irritation?
Yes
Reassurance and supportive care
No
Signs or symptoms of renal/ureteral stones?
Yes
Imaging (renal utrasound, abdominal plain film)
No
Signs/symptoms of glomerular source? (proteinuria, RBC casts)
No
Yes
No obvious cause on history, physical, or urinalysis
Referral to pediatric nephrologist*
Tests to consider:
Urine culture
Urine calcium/creatinine ratio
Test parents for hematuria
Hemoglobin electrophoresis
Renal ultrasound
Diagnosis apparent?
No
Check BUN/Cr, electrolytes, CBC, C3, C4, albumin
Consider ASO, streptozyme testing, antinuclear antibody testing (ANA)
Yes

Persistent microscopic hematuria

* 33 children with persistent microscopic hematuria, 27 proteinuria(-)

→ Renal biopsies (in 21/25) except 2 cases ofUPJO

- 2 IgA nephropathy

-1 hereditary nephritis

-8 normal renal biopsies

-10 nonspecific abnormalities

* 325 children with isolated persistent microhematuria (1985–1994) → Hypercalciuria in 11%
* Renal U/S in 87% & VCUG in 24% → no clinically significant findings.

* The most common diagnoses in persistent micro-hematuria without proteinuria :

-Benign persistent or benign familial hematuria,

-Idiopathic hypercalciuria,

-IgA nephropathy,

-Alport's syndrome ,

→ a more extensive evaluation is indicated only when **proteinuria** or other indicators are present.

Conclusion

* Require a through history and physical examination !
* Only lab. test uniformly required for chidren with various presentat ion of hematuria is a complete UA with a microscopic examination !
* The rest of evaluation is tailored according to the pertinent history , PEx, and other abnormalities on the urinalysis .