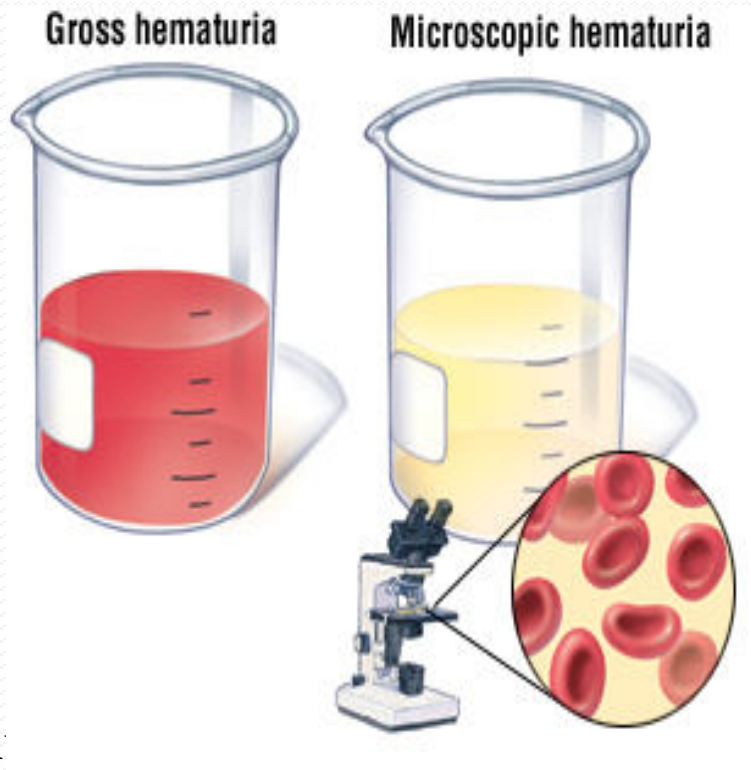
HEMATURIA

UROLOGY

- Hematuria is the presence of blood in the urine.

CLASSIFICATION



A) Based on Intensity:

MICROSCOPIC HEMATURIA

- > 3 RBCs/HPF is significant.

GROSS HEMATURIA

- It is visible hematuria that can resul
  from as little as one ml of blood

Gross versus Microscopic Hematuria.

- The significance of gross versus microscopic hematuria is simply that the chances of identifying significant pathology increase with the degree of hematuria.
- The patients with gross hematuria usually have identifiable underlying pathology
- It is common for patients with minimal degrees of microscopic hematuria to have a negative urologic evaluation.

CLASSIFICATION

B) Based on Origin:

1- Glomerular

2- Non-glomerular

C) Based on Relation to micturition:

1- **Total hematuria(MC)** is present all over the voided urine. Underlying pathology may be in kidney, ureter, bladder or prostate or systemic.

Bleeding from kidney is associated with cylindrical worm-like clots.

Hematuria from bladder and prostate is associated with big irregular or discoid clots.

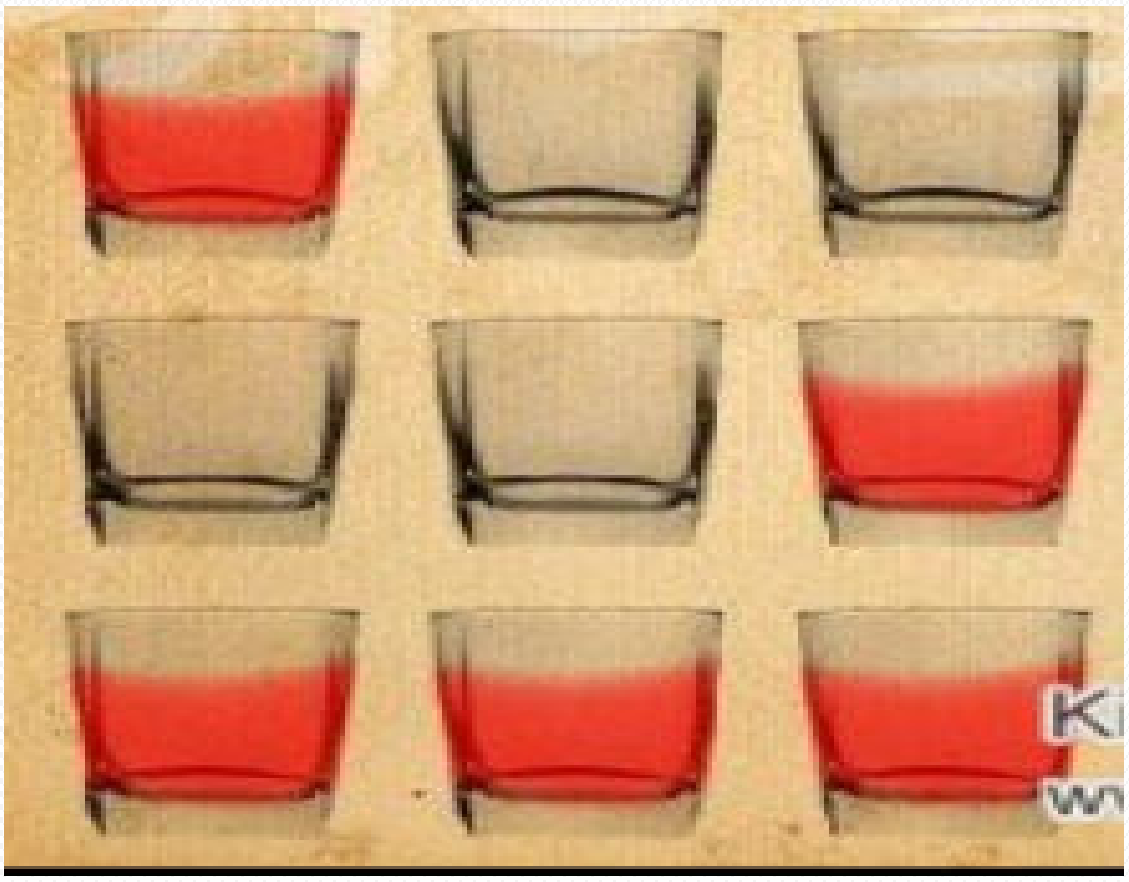
2- **Terminal hematuria** at the end of micturition is of vesical origin e.g. active bilharzial cystitis.

It is usually due to bladder neck or prostatic inflammation.

It occurs at the end of micturition as the bladder neck contracts, squeezing out the last amount of urine.

3- **Initial hematuria** at the beginning of micturition indicates urethral pathology.

Timing during micturition



Urethra

Trigone
Bladder neck
Posterior urethra

Bladder
Upper urinary tract

D) Based on Associated symptoms:

Painless hematuria: No other urinary symptoms: All cases should be investigated for urologic malignancy.

Bladder cancer is the most common and should be excluded.

Hematuria associated with other symptoms:

- Simple cystitis: frequency, burning, urgency and terminal hematuria.
- Malignant cystitis: severe frequency, pain, urge incontinence, total hematuria with clots or necroturia
- Ureteral obstruction due to blood clots is the most common cause of pain associated with gross hematuria.
- Stones: Renal pain.
- BPH, prostate cancer: associated LUTS (prostatism).
- Surgical trauma to kidney and bladder e.g. PCNL & TURBT.

E) Based on Etiology:

General or systemic:

- Bleeding disorder: thrombocytopenic purpura, leukemia, hemophilia.
- Liver cirrhosis.
- Anticoagulants.
- Hypertension.

Renal causes:

A) Nephrologic: dysmorphic RBCs

Acute glomerulonephritis is the most common cause in children and young adults. It is associated with proteinuria.

B) Urologic: Eumorphic RBCs - oval

- Congenital: Polycystic kidney.
- Inflammation: Pyelonephritis, TB.
- Trauma: Accidents, Iatrogenic.
- Stones
- Kidney cancer
- Vascular: Hemangiomas, AV fistula.

- Nephrologic origin

- **Casts**
- **Almost always significant proteinuria(often 100 to 300 mg/dL /2+ to 3+ range on dipstick).**

- Urologic origin

- **Even significant hematuria of urologic origin will not elevate the protein concentration in the urine in above range.**

Glomerular

- Presence of Dysmorphic RBC, RBC casts, and proteinuria.

- IgA nephropathy (Berger disease) 30%
- Mesangioproliferative GN
- Focal segmental proliferative GN
- Familial nephritis (e.g., Alport syndrome)
- Membranous GN
- Focal segmental sclerosis
- Systemic lupus erythematosus
- Postinfectious GN
- Subacute bacterial endocarditis

NONGLOMERULAR

- Medical or Surgical

❑ Medical-

1. Tubulointerstitial
2. Renovascular, or systemic disorders.

Medical

- Blood dyscrasia
- Familial urolithiasis
- MSK & ADPKD
- Papillay necrosis
- Uncorrected coagulopathy
- Medication (G/NG)
- Exercise-induced haematuria (G/NG)
- Vascular disease (RAE,RVT, AV ,CVD, INFRACT)

Vascular disease may also result in nonglomerular hematuria like

1. Renal artery embolism and thrombosis
2. Arteriovenous fistulae, and
3. Renal vein thrombosis.

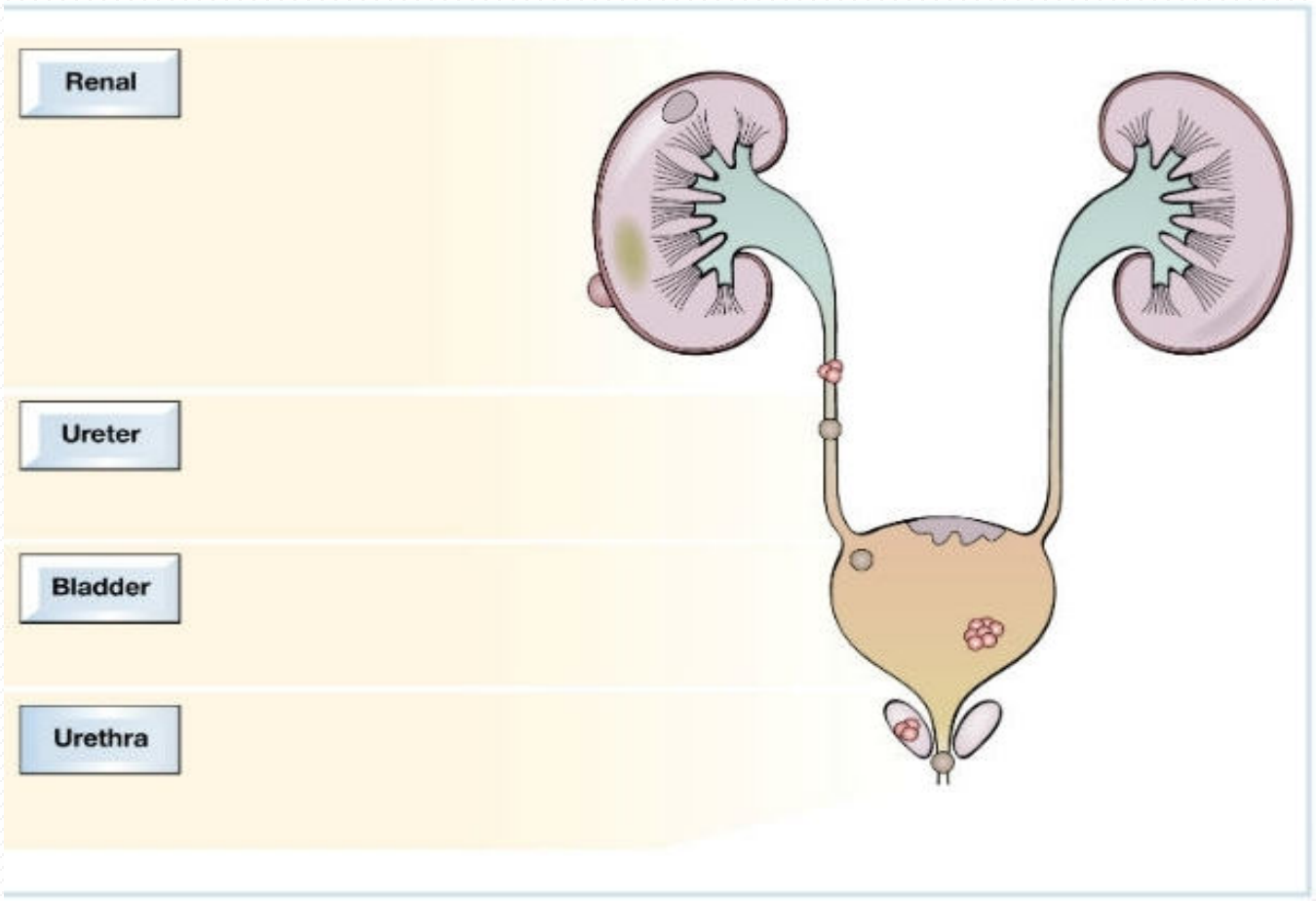
- Physical examination may reveal

1. severe hypertension
2. flank or abdominal bruit, or
3. atrial fibrillation.

- In such patients, further evaluation for renal vascular disease should be undertaken.

Surgical / Essential

- TUMOR, STONE , UTI & TRAUMA.



Ureteral:

- Stones.
- Iatrogenic trauma e.g. ureteroscopy.
- Tumors: TCC of pelvis and ureter.

Bladder:

- Bladder cancer is the most common cause of gross hematuria in a patient above 60 years.
- Cystitis: Bacterial, bilharzial, T.B.
- Stones
- Trauma e.g. post TURBT

Prostate

- BPH
- Prostate cancer
- Prostatitis
- Surgical: after prostatectomy

Posterior urethra:

- Inflammation
- Trauma
- Tumor

EVALUATION

- Hematuria of any degree should never be ignored

- In adults, should be regarded as a symptom of urologic malignancy until proved otherwise.

History -

- Questions should always be asked

1) Is the hematuria gross or microscopic?

2) At what time during urination does the hematuria occur (beginning or end of stream or during entire stream)?

3) Is the hematuria associated with pain?

4) Is the patient passing clots?

5) If the patient is passing clots, do the clots have a specific shape?

- The answers will enable the urologist to target the subsequent diagnostic evaluation efficiently

Discoloration of urine

COLOR	CAUSE
Colorless	Very dilute urine Overhydration
Cloudy/milky	Phosphaturia Pyuria Chyluria
Red	Hematuria Hemoglobinuria/myoglobinuria Anthocyanin in beets and blackberries Chronic lead and mercury poisoning Phenolphthalein (in bowel evacuants) Phenothiazines (e.g., Compazine) Rifampin
Orange	Dehydration Phenazopyridine (Pyridium) Sulfasalazine (Azulfidine)
Yellow	Normal Phenacetin Riboflavin
Green-blue	Biliverdin Indicanuria (tryptophan indole metabolites) Amitriptyline (Elavil) Indigo carmine Methylene blue Phenols (e.g., IV cimetidine [Tagamet], IV promethazine [Phenergan]) Resorcinol Triamterene (Dyrenium)
Brown	Urobilinogen Porphyria Aloe, fava beans, and rhubarb Chloroquine and primaquine Furazolidone (Furoxone) Metronidazole (Flagyl) Nitrofurantoin (Furadantin)
Brown-black	Alcaptonuria (homogentisic acid) Hemorrhage Melanin Tyrosinosis (hydroxyphenylpyruvic acid) Cascara, senna (laxatives) Methocarbamol (Robaxin) Methyldopa (Aldomet) Sorbitol

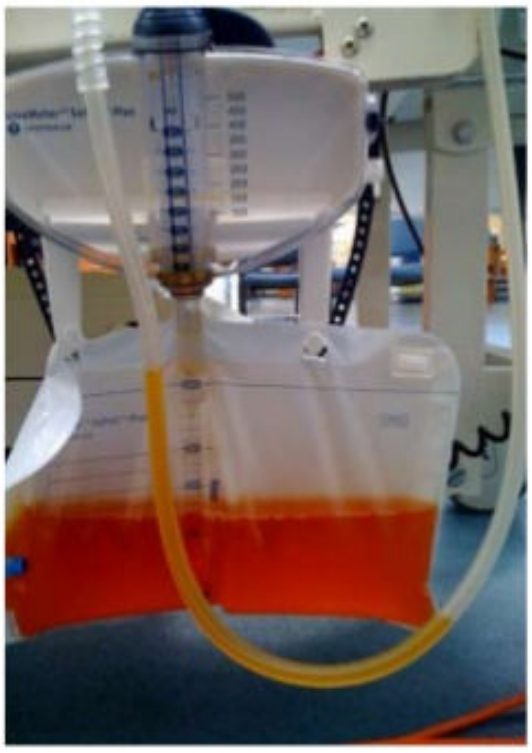
- **Drug History :** should be taken with special attention to :

–**Antibiotic :** Rifampin (orange urine)
–**analgesics** (papillary necrosis)
–**cyclophosphamide** (hemorrhagic cystitis)
– **anticoagulants,**
–drugs known to cause acute interstitial nephritis

Antibiotics
Penicillins (esp. methicillin, ampicillin)
Cephalosporins
Sulfonamides
Rifampin
Isoniazid
NSIDs
Indomethacin
Phenylbutazone
Fenoprofen
Naproxen
Tolmetin
Mefenamic acid
Diuretics
Thiazides
Furosemide
Triamterene
Miscellaneous
Phenytoin
Cimetidine
Allopurinol
Azathioprine

Drugs Associated with Acute Interstitial Nephritis.

rifampicin



beetroot

Association with Pain:

- Hematuria, although frightening, is usually not painful unless it is associated with inflammation or obstruction.
- Thus patients with cystitis and secondary hematuria may experience painful urinary irritative symptoms
- The pain is usually not worsened with passage of clots.
- Pain in association with hematuria usually results from upper urinary tract hematuria with obstruction of the ureters with clots.
- Passage of these clots may be associated with severe, colicky flank pain similar to that produced by a ureteral calculus
- This helps identify the source of the hematuria.

Association with Clots:

- The presence of clots usually indicates a more significant degree of hematuria

- Accordingly, the probability of identifying significant urologic pathology increases.

Shape of Clots:

Amorphous : bladder origin or Prostatic urethral origin

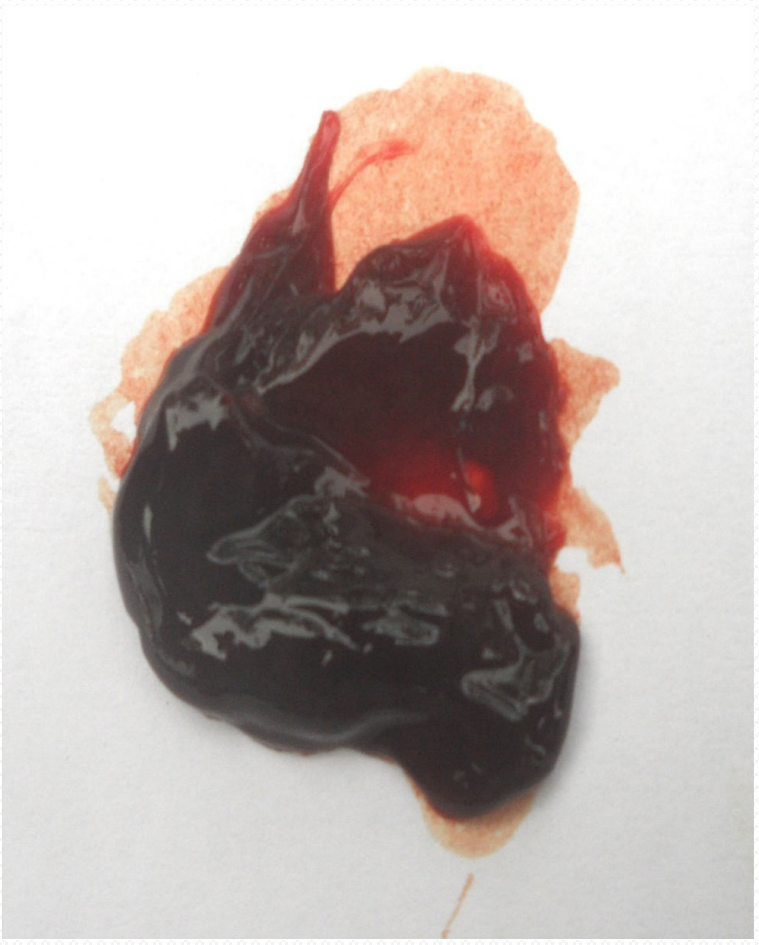
Vermiform (wormlike) clots, particularly

- If associated with flank pain,

- Hematuria coming from the upper urinary tract,

- Suggests from within the ureter.

Shape of clots



Examinations

General examination- Vitals

Pallor ,

Diffuse bruise

Per abdomen – Suprapubic fullness or mass

Fullness or mass in lumber area

External genitalia- Blood at meatus, haematoma, tumor

DRE- Hard /nodular prostate

Investigations

- Routine and microscopic examination
- Urine cytology
- Cystoscopy
- Urinary tract imaging (CT/IVU)

Haematuria detection in urine

- Dipstick detection of hematuria →sensitivity of over 90%
- Detection of blood is due to peroxidase-like activity of hemoglobin.
  - Hb catalyzes the oxidation of a chromogen indicator

↓

color change in direct proportion to the amount of blood in urine

- The results of urine dipstick tests must be confirmed on urinalysis with microscopy.

Hematuria v/s hemoglobinuria and myoglobinuria

Hematuria, hemoglobinuria, and myoglobinuria will all result in positive dipstick for blood

Differentiation is done by microscopic examination of the centrifuged urine

- Erythrocytes present = Hematuria.
- Erythrocytes are absent = Hemoglobinuria
  Myoglobinuria

Haemoglobinuria vs Myoglobinuria

- A sample of blood is centrifuged.
- In hemoglobinuria, the supernatant will be pink.
  This is because free hemoglobin in the serum binds to haptoglobin
  ↓
  water insoluble and has a high molecular weight
  ↓
  complex remains in the serum & gives a pink color

- In myoglobinuria, the myoglobin released from muscle is of low molecular weight and water soluble.

↓

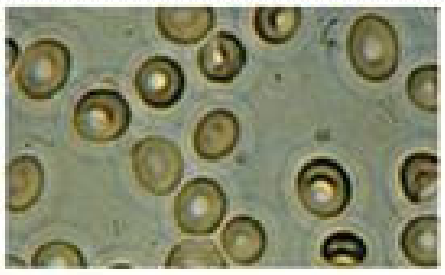
- It does not bind to haptoglobin and is therefore excreted immediately into the urine.

↓

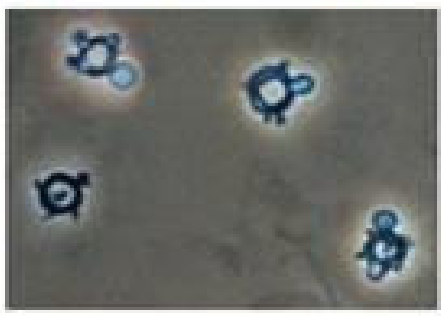
- Therefore in myoglobinuria the serum remains clear

- There is also a higher false-positive rate & causes include
  (i) Urine contamination with menstrual blood
  (ii) Dehydration
  (iii) Exercise
  (iv) Oxidizing agents
  (v) Bacterial peroxidase

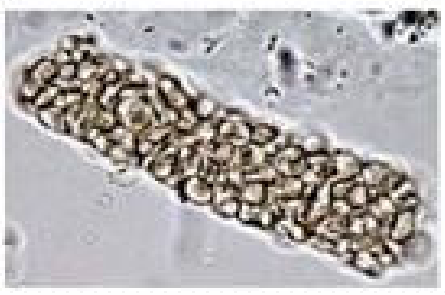
MICROSCOPY



Isomorphic RBC



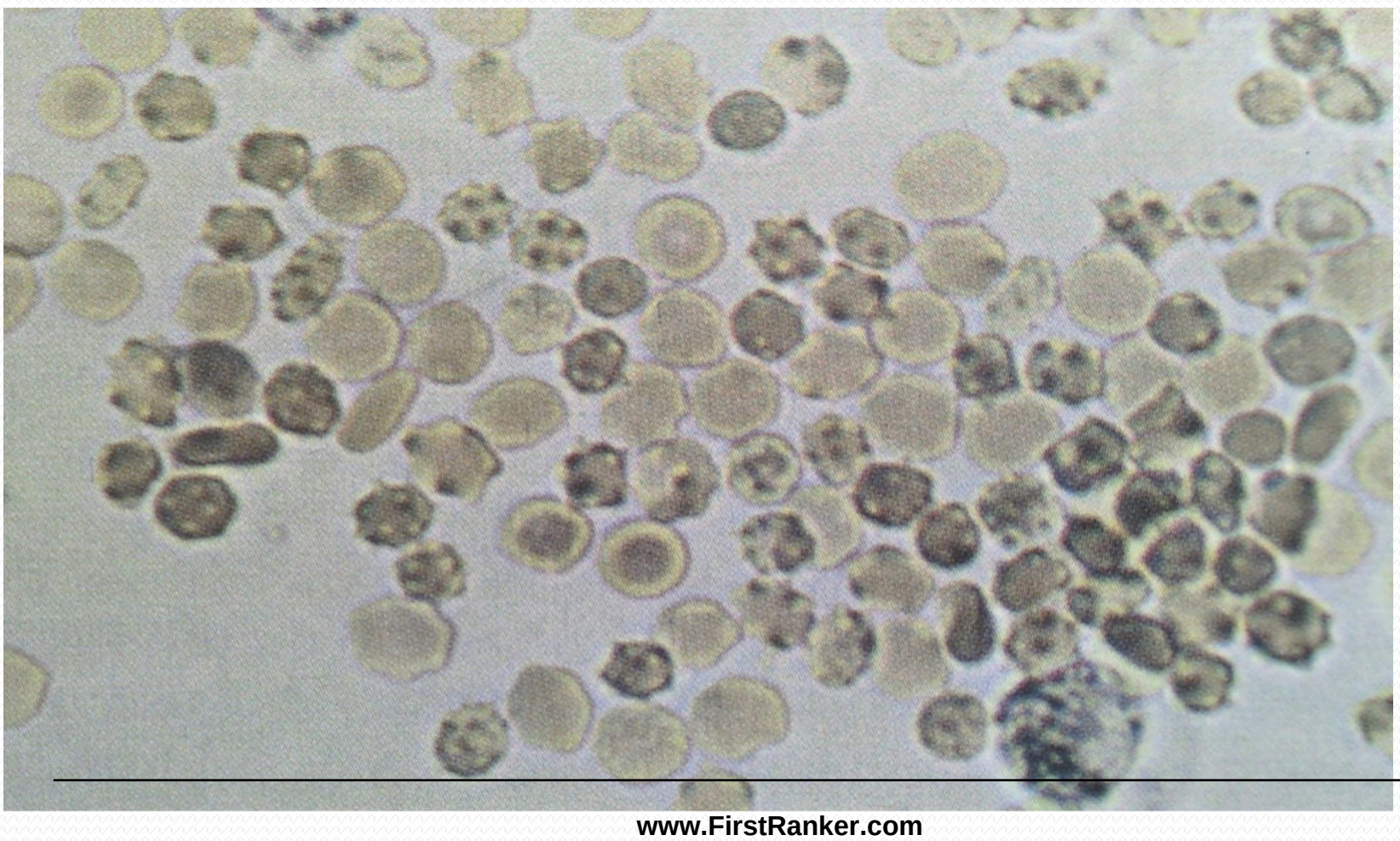
Dysmorphic RBC



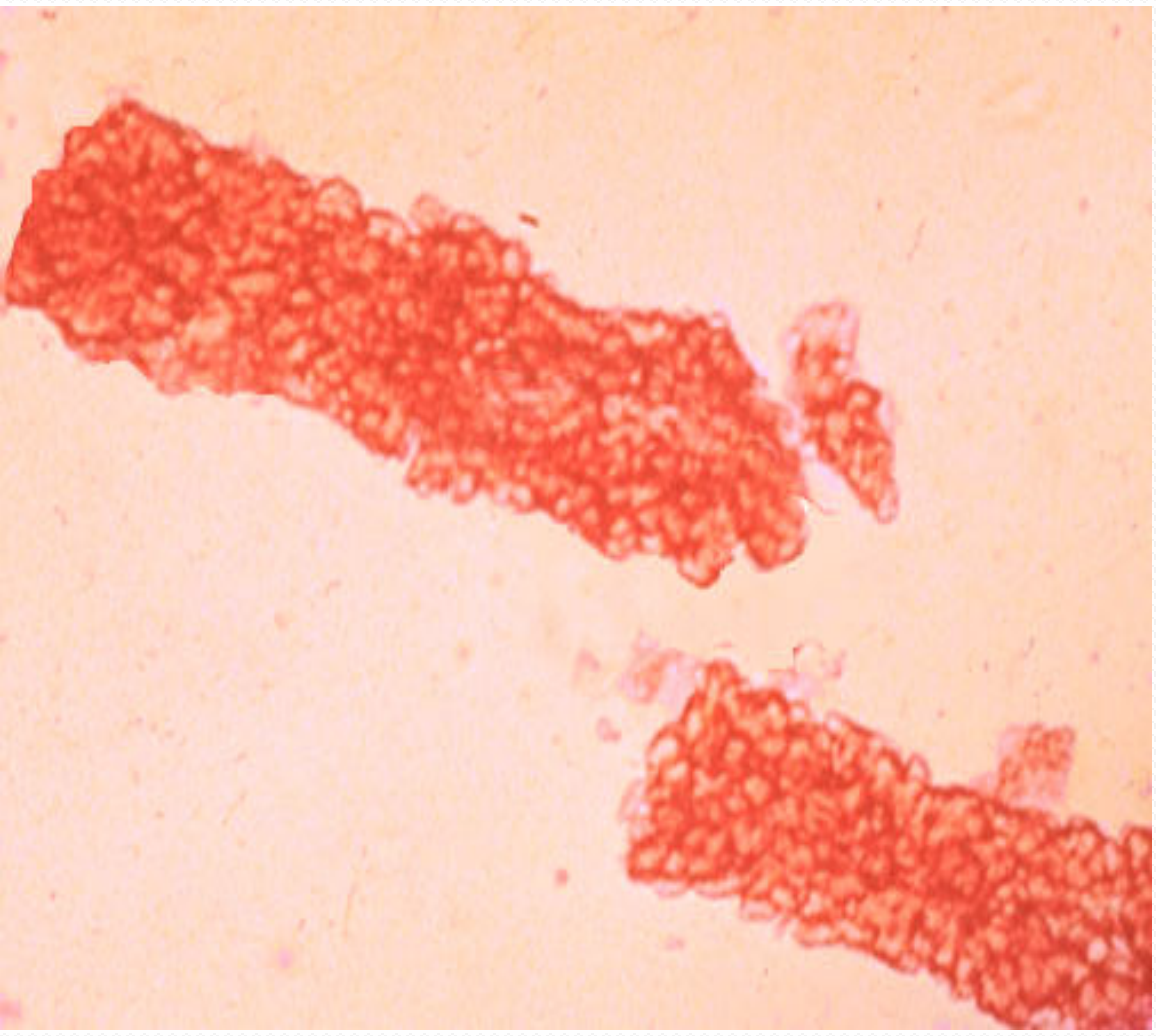
RBC cast

These erythrocytes may or may not retain their hemoglobin (“ghost cells”)

RBC in Ca Bladder



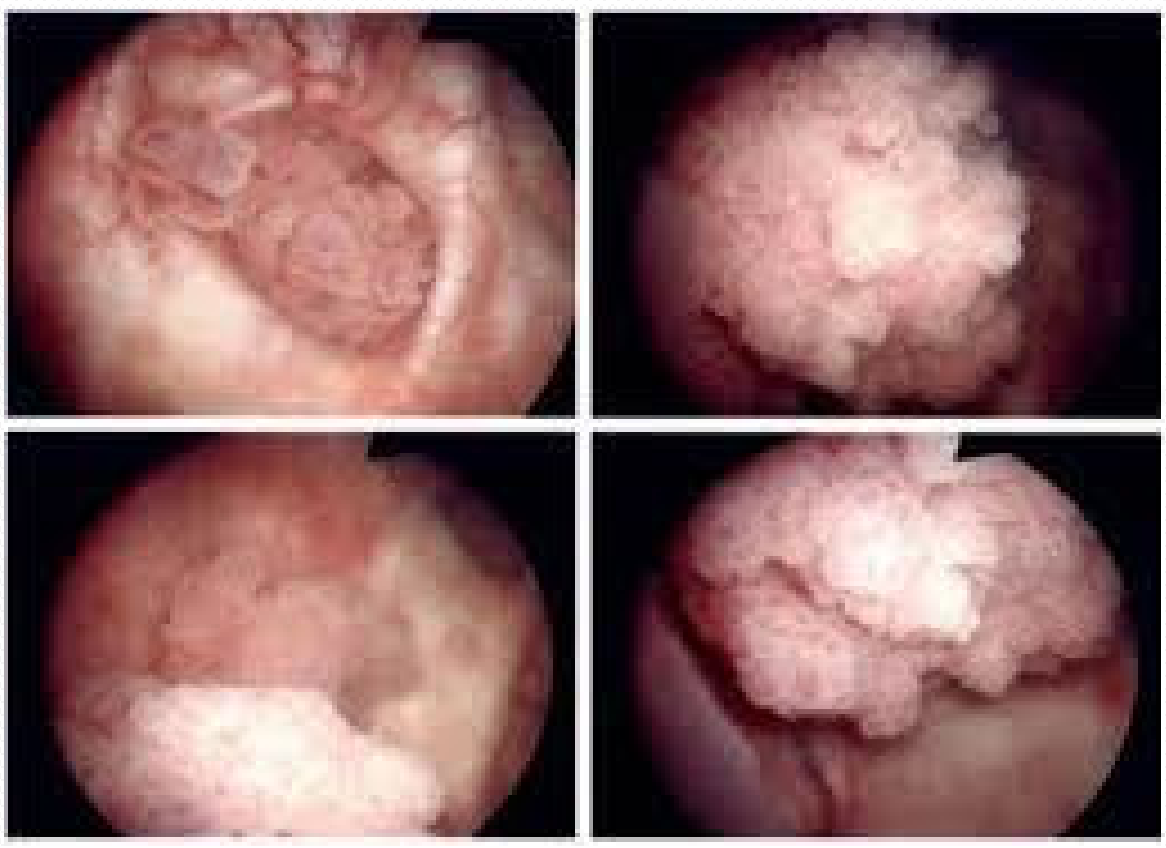
Red cell Casts in Urine



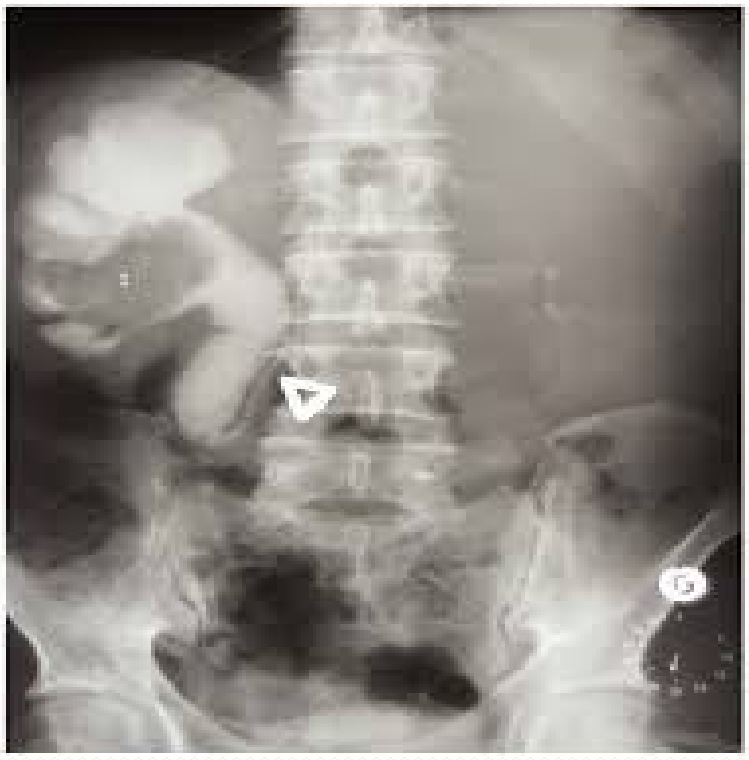
Red cell casts indicate renal hematuria

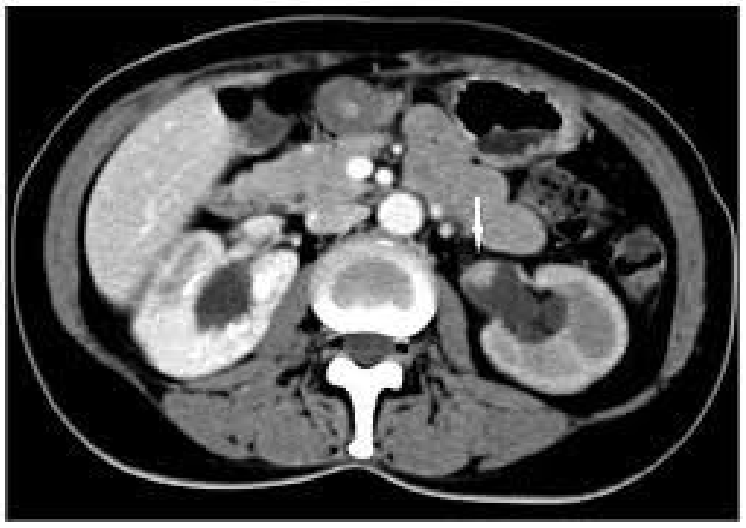
Red cell casts may appear brown to almost colorless and are usually diagnostic of glomerular disease

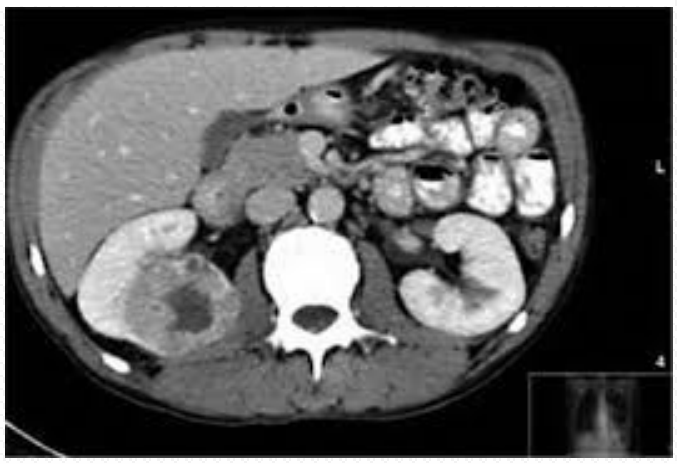
Cystoscopy

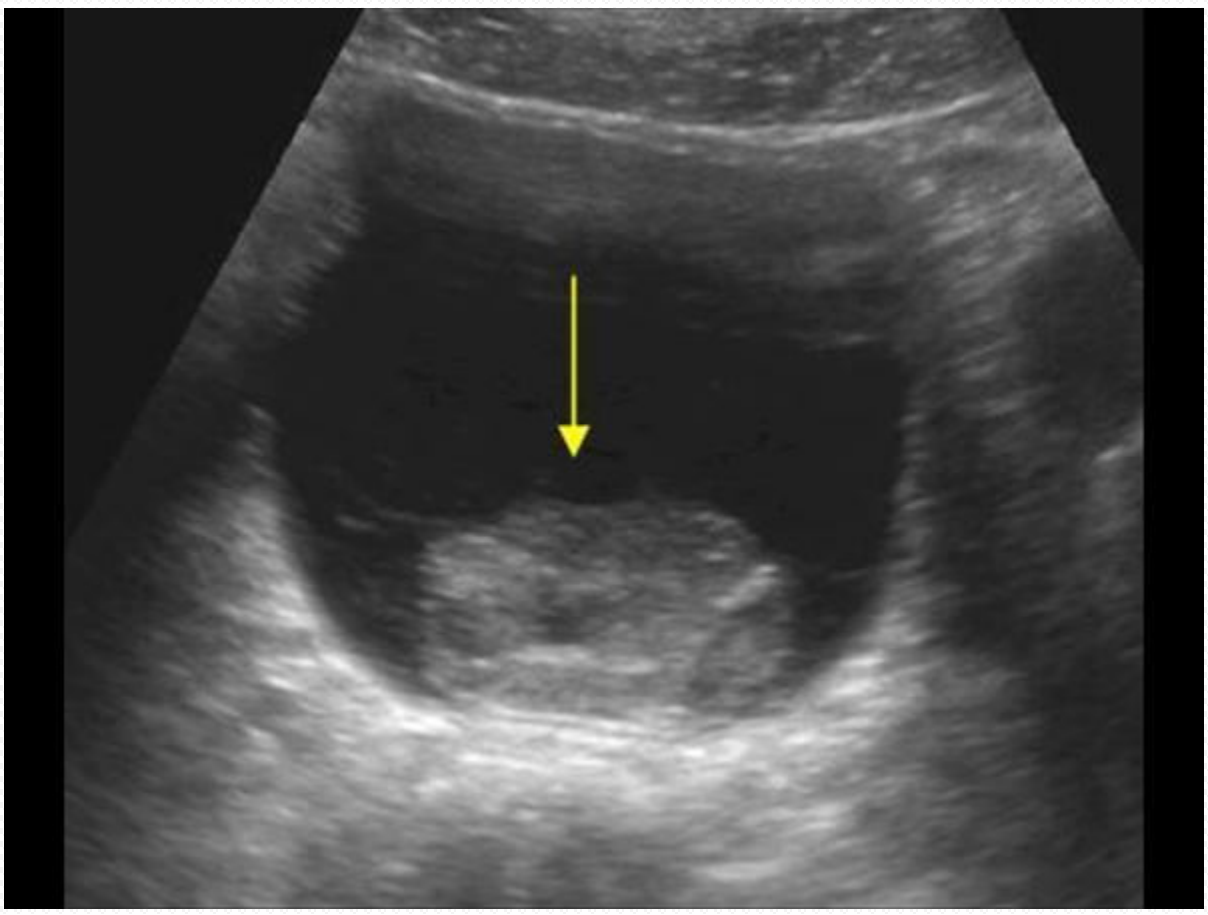


IVP/CT scan

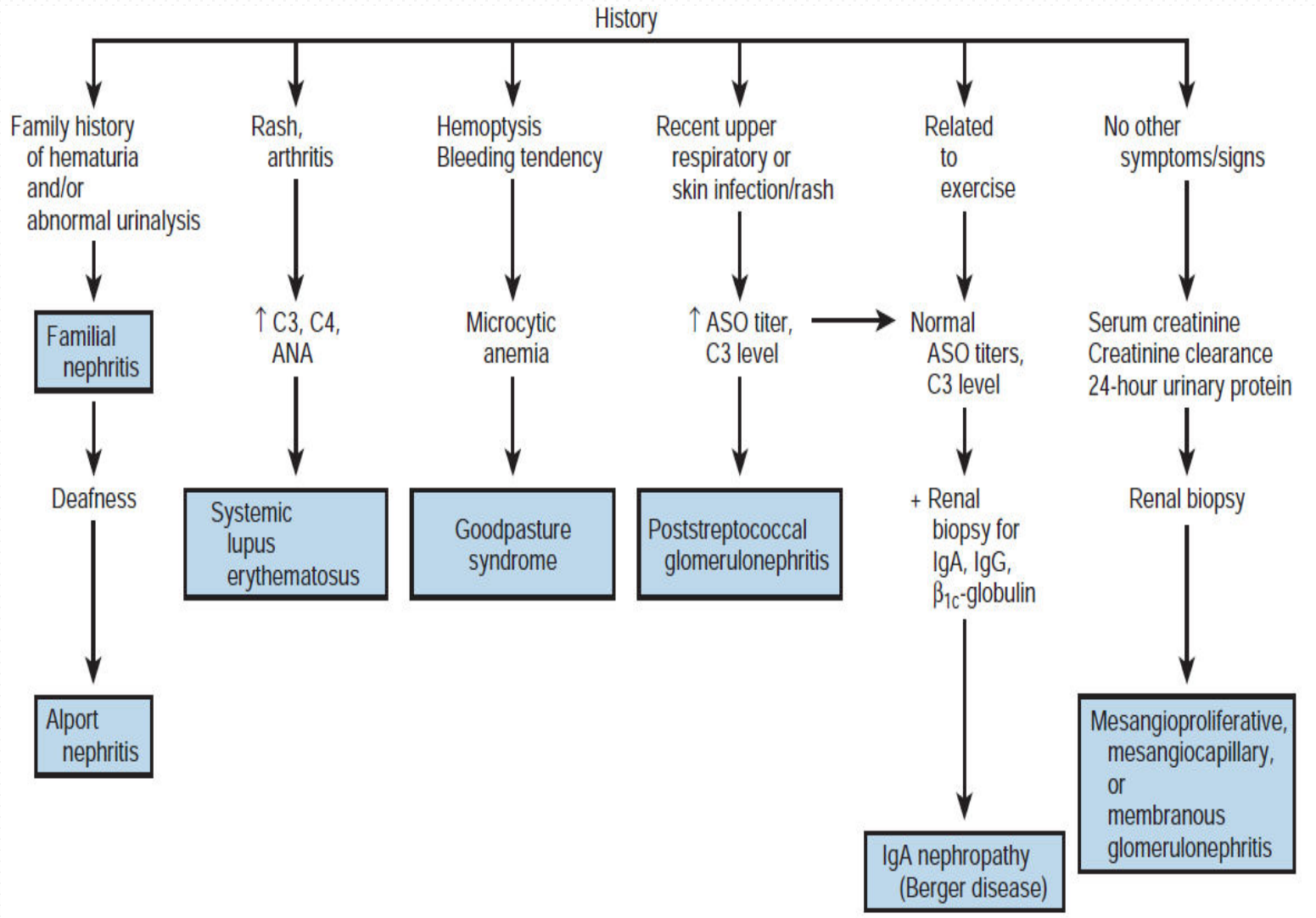




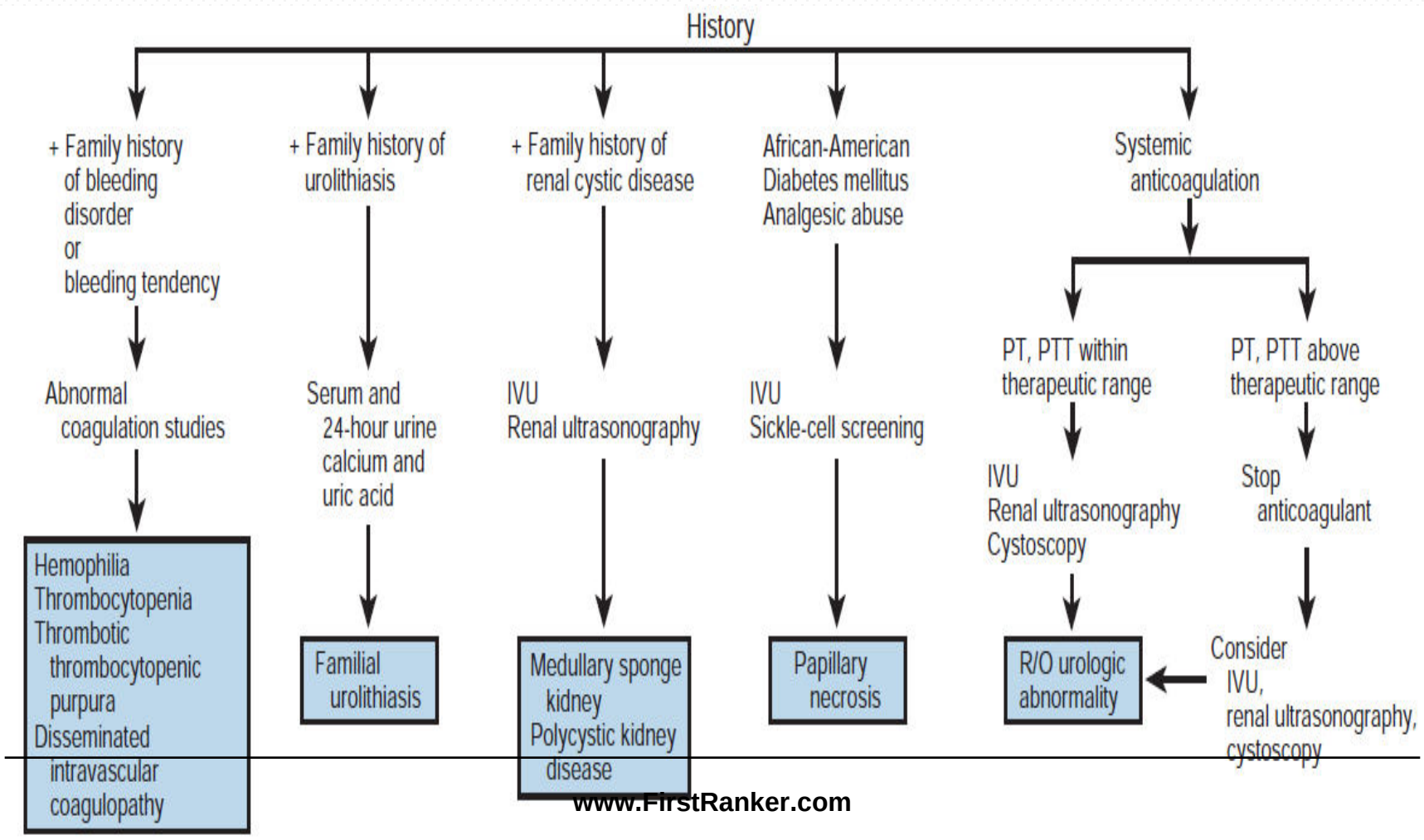




Algorithm for diferential diagnosis of glomerular hematuria



Algorithm for diferential diagnosis of nonglomerular renal hematuria



IgA Nephropathy (Berger Disease):

- IgA nephropathy, or Berger disease, is the most common cause of glomerular hematuria.
- Accounts for about 30% of cases
- Nephropathy occurs most commonly in children and young adults, with a male predominance.
- Patients typically present with hematuria after an upper respiratory tract infection or exercise

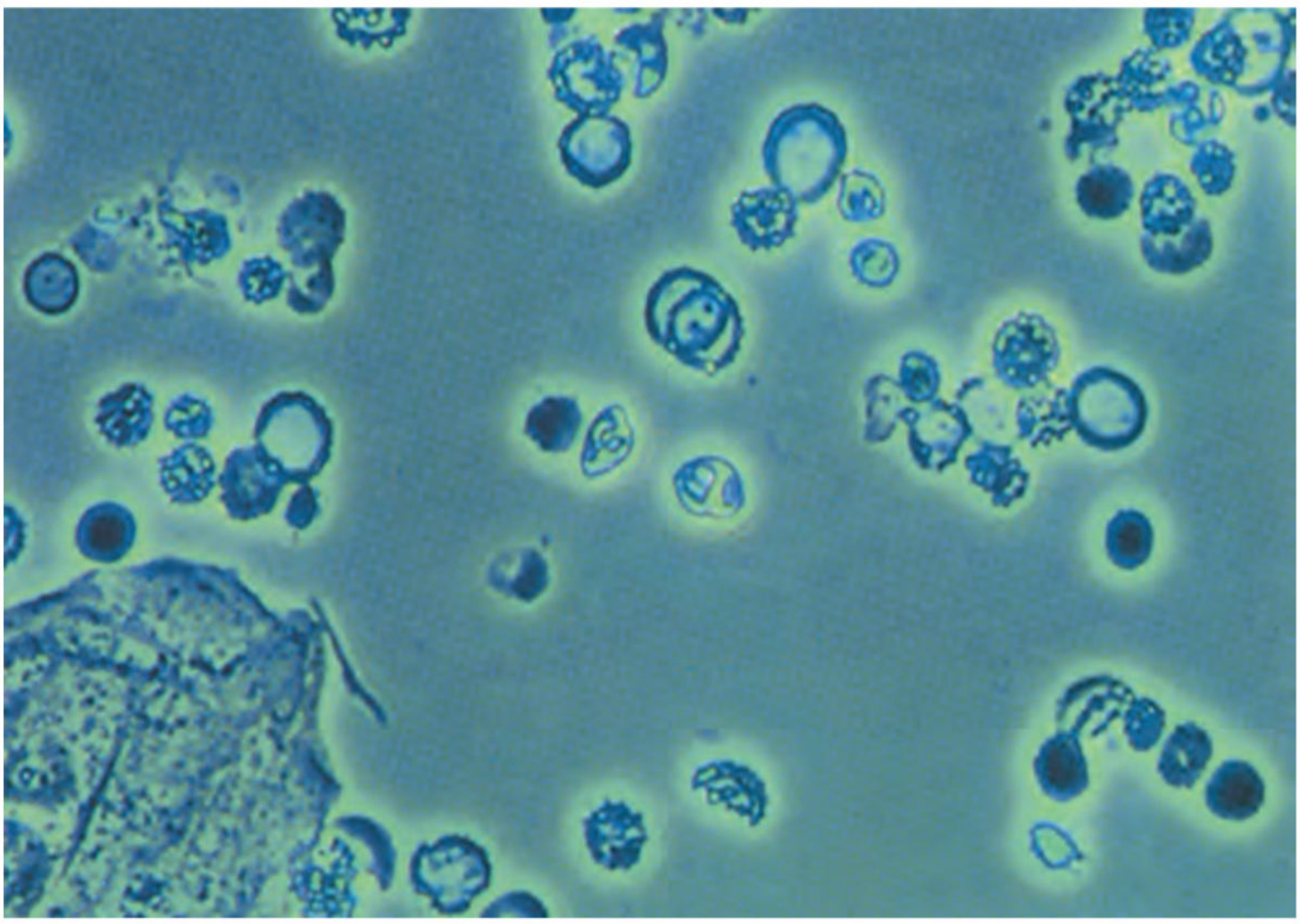


Figure 1-14. Red blood cells from a patient with Berger disease. Note variations in membranes characteristic of dysmorphic red blood cells.

- Hematuria may be associated with a low-grade fever or rash.
- Most patients have no associated systemic symptoms.
- Gross hematuria occurs intermittently, but microscopic hematuria is a constant finding in some patients.
- The disease is chronic.
- Prognosis in most patients is excellent.

- Pathologic findings in Berger disease are limited to either focal glomeruli or lobular segments of a glomerulus.
- The changes are proliferative and usually confined to mesangial cells.
- The presence of RBC casts establishes the glomerular origin of the hematuria.
- Renal biopsy reveals deposits of immunoglobulins in mesangial cells.

1. IgA
2. IgG, and
3. β1c-globulin.

Management

Goals for treatment of macroscopic haematuria

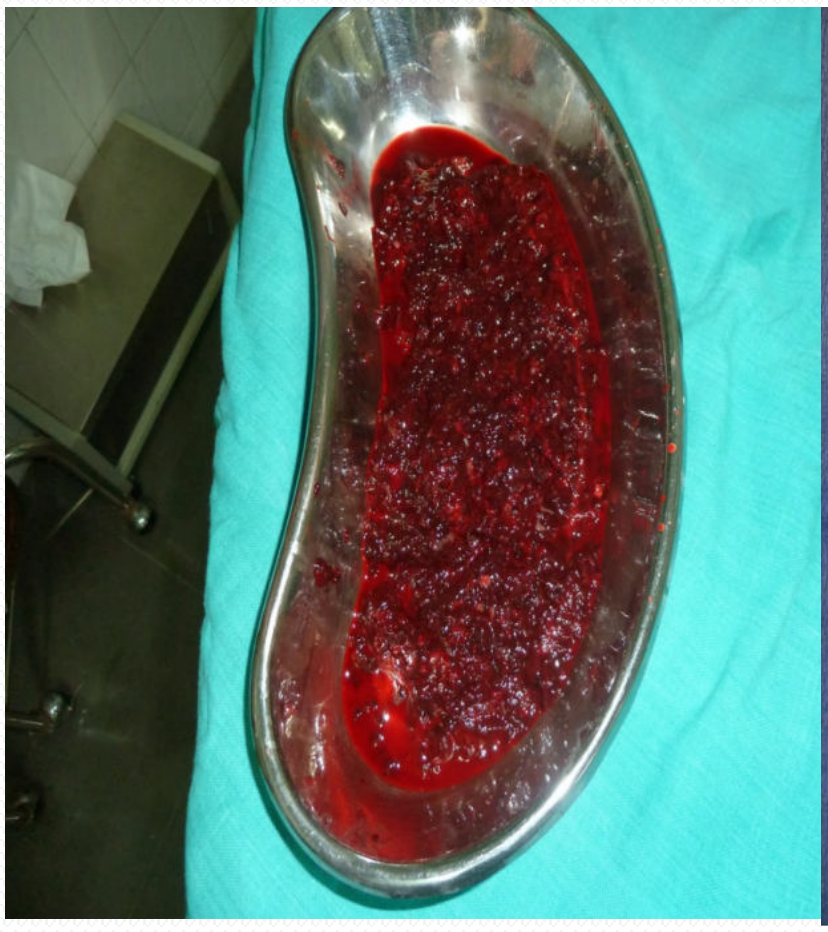
- R–resuscitate as appropriate
- E–ensure that urine can drain freely with or without catheter insertion
- S–safe discharge from the ED where appropriate
- P–prompt follow-up and further investigation

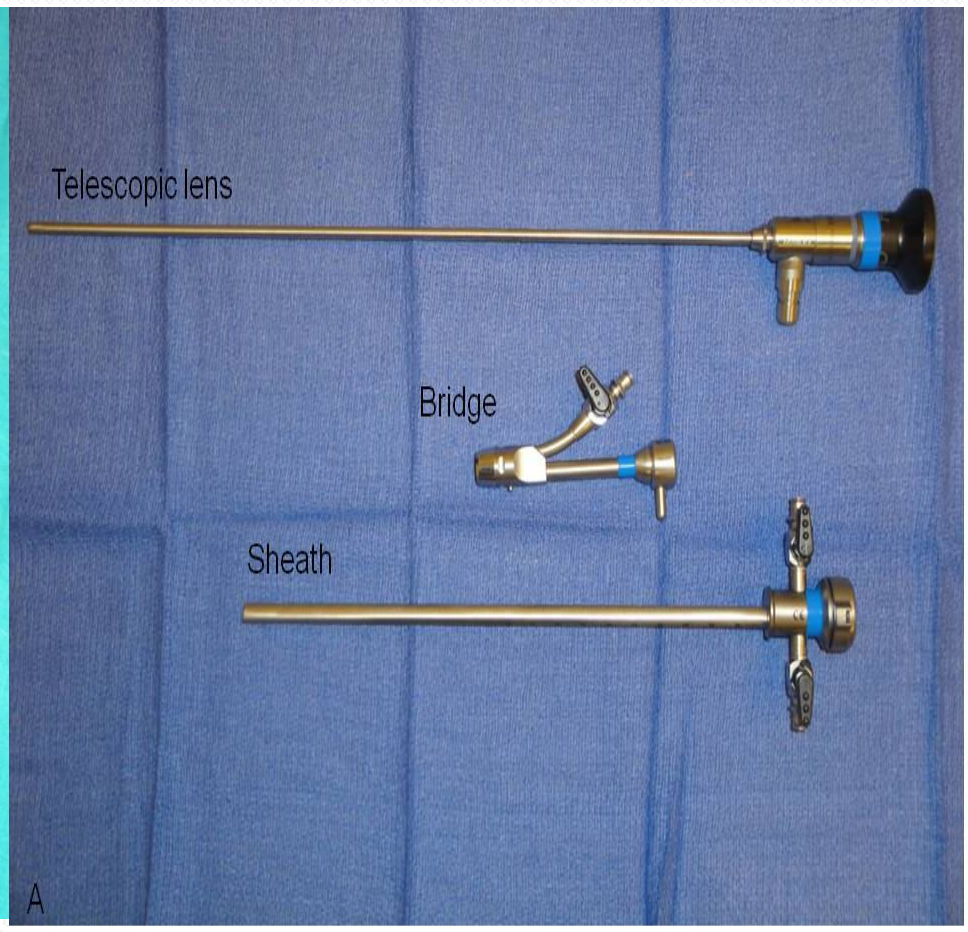
Management

- Initial management
  - Catheterisation and irrigation with saline/glycine
  - Clot evacuation
  - Fulgaration

Toomy's syringe Clot evacuation

Ellick's evacuator





Haemorrhagic cystitis:

- Intractable hematuria localized in the bladder

- Hemorrhagic cystitis is characterized by diffuse inflammation and bleeding from the bladder mucosa

Causes of haemorrhagic cystitis:

Infectious
- Bacterial
- Viral (especially BK virus, adenovirus)
- Fungal
- Parasitic

Trauma
- External
- Postsurgical (e.g., transurethral resection of the bladder)

Malignancy
- Bladder primary
- Bladder invasion from local/distant primary

Vascular malformation

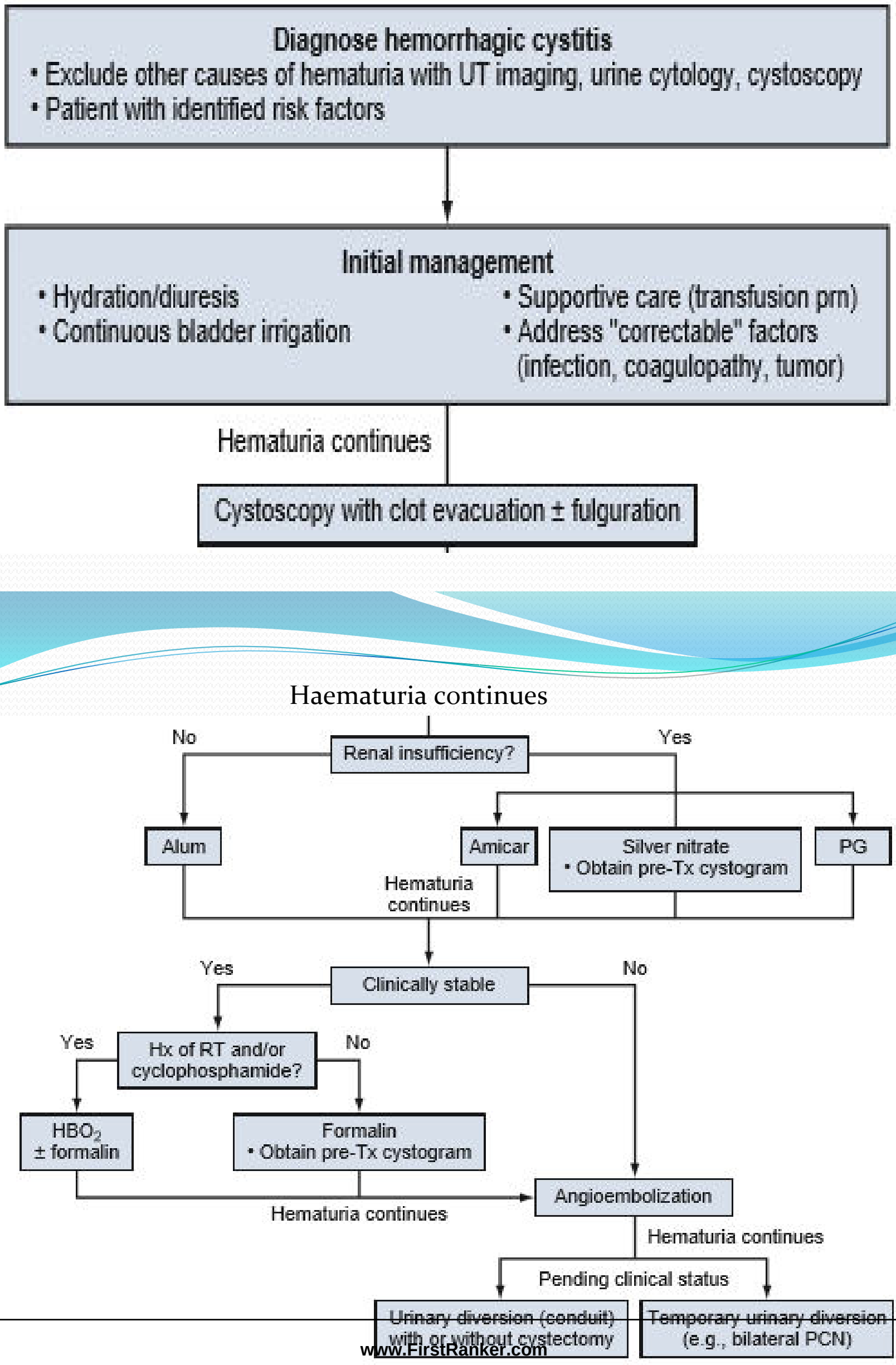
Chemical exposure
- Cyclophosphamide
- Ifosfamide
- Busulfan
- Thiotepa
- Temozolomide
- Aniline dye
- Ether
- Nonoxynol-9 (accidental urethral insertion of vaginal contraceptive)

Radiation therapy history (e.g., prostate cancer, cervical cancer)

Medication induced
- Penicillin and derivatives (via immune reaction)
- Bleomycin
- Danazol
- Tiaprofenic
- Allopurinol
- Phensuximide
- Methenamine mandelate
- Acetic acid

Manifestation of systemic disease
- Amyloidosis
- Rheumatoid arthritis
- Crohn disease

Management of haemorrhagic cystitis:



- Renal cell carcinoma

1. Localised
2. Locally advanced
3. Metastatic

- Upper tract TCC

1. Localised
2. Locally advanced
3. Metastatic

carcinoma bladder

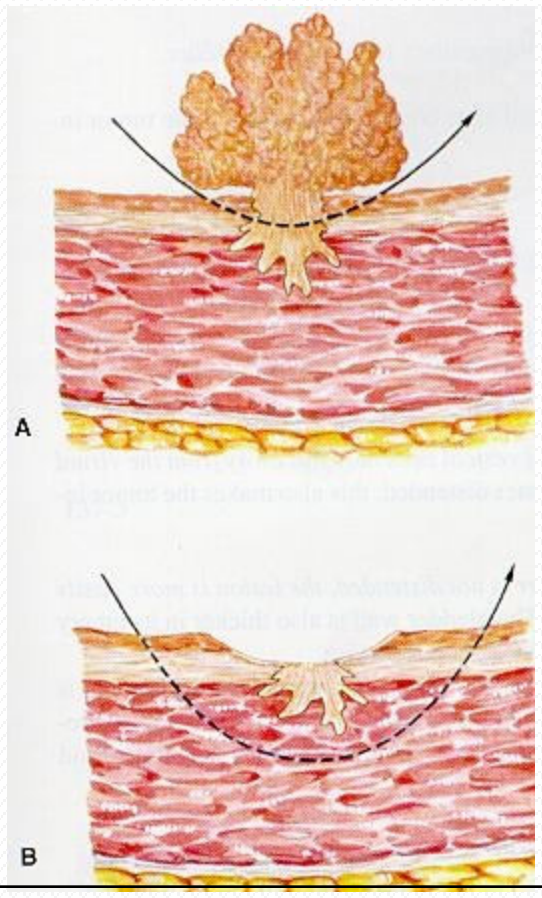
Histology

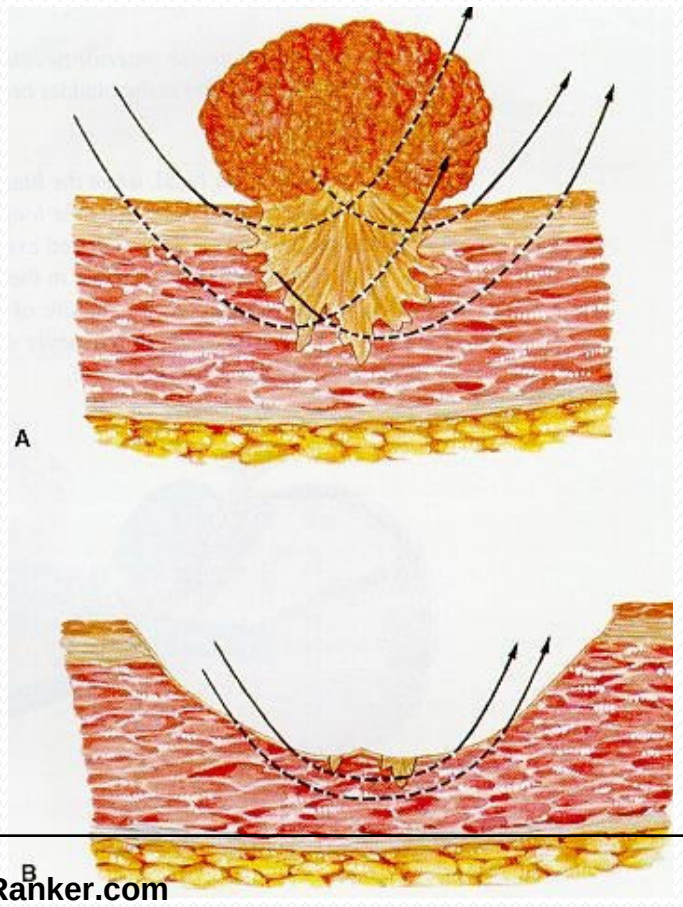
- **90-95%** **transitional-cell carcinoma**
- **3%** **squamos-cell carcinoma**
- **2%** **adenocarcinoma**
- **<1%** **small-cell carcinoma**
- **99%** **primary tumors**

Entities

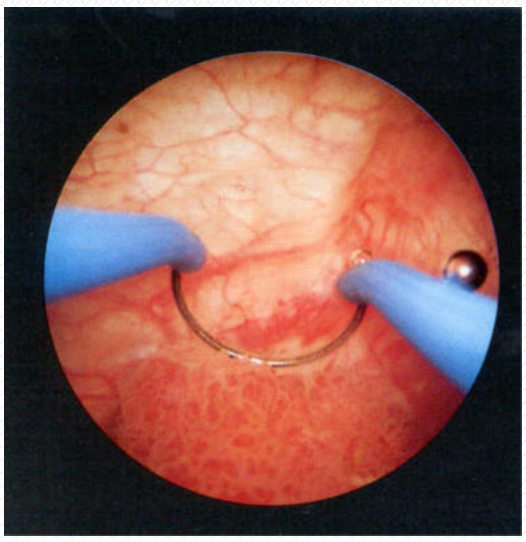
- 75-85% superficial bladder cancer
  pTa, pTis, pT1
- 10-15% muscle-invasive bladder cancer
  pT2, pT3, pT4
- 5% metastatic bladder cancer
  N+, M+

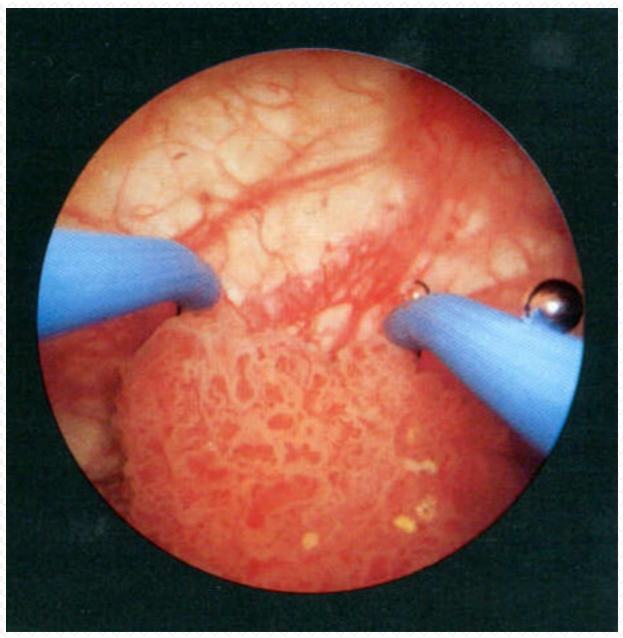
Superficial Bladder Cancer - TURBT

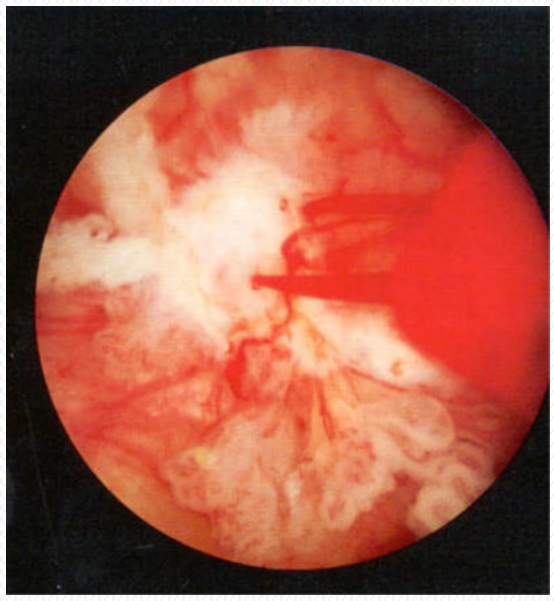




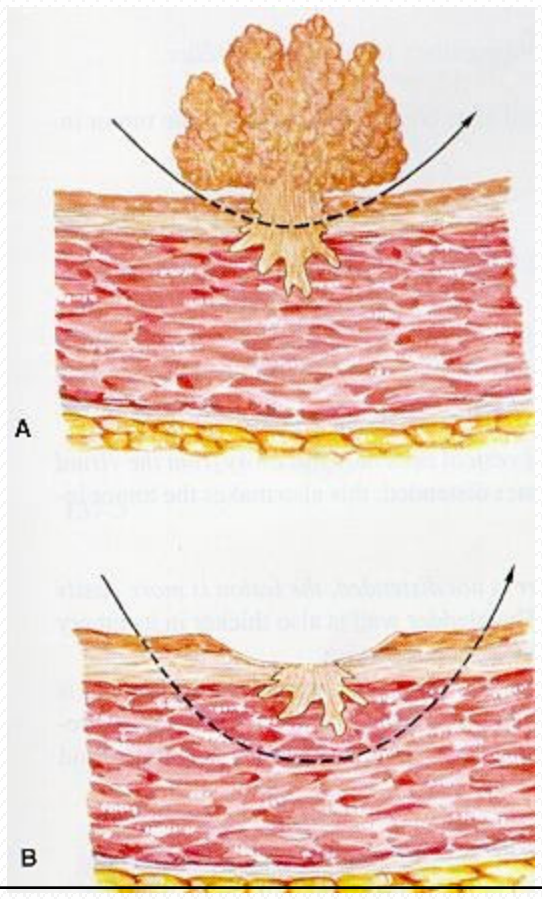
TURBT

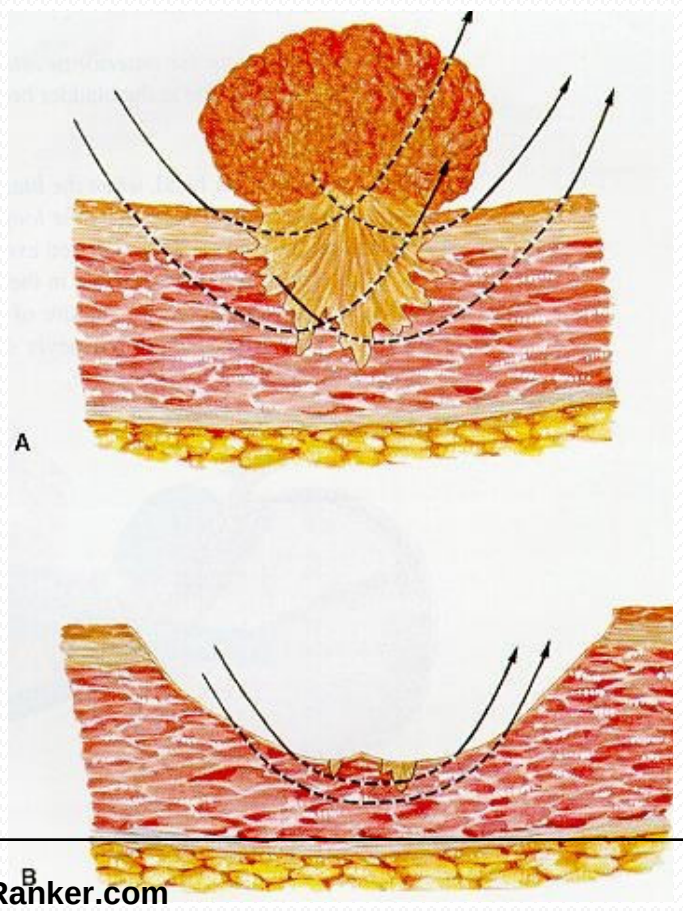






Superficial Bladder Cancer - TURBT

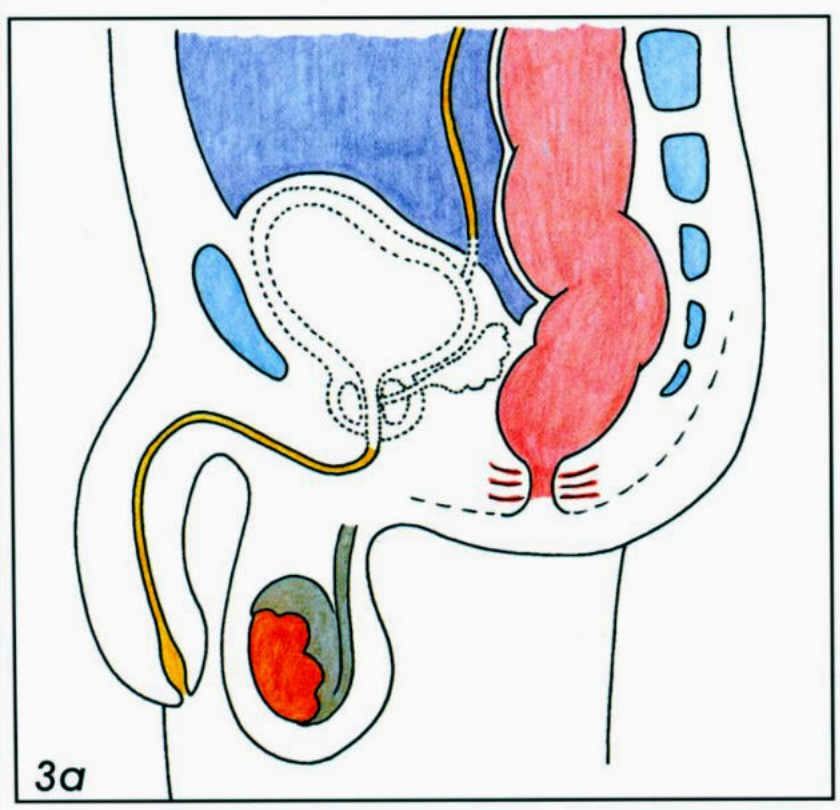


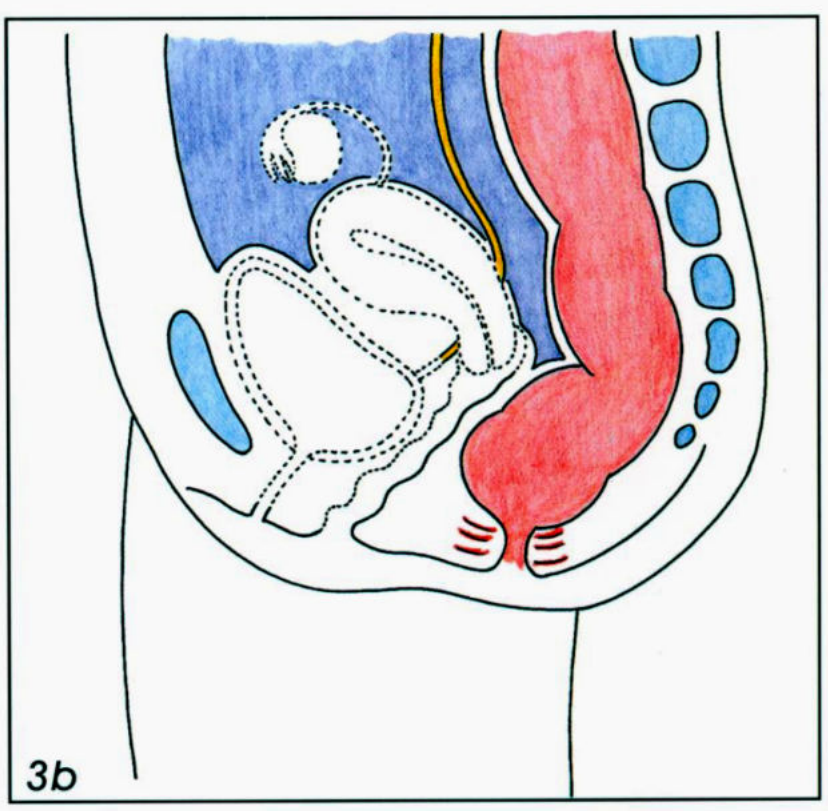


Invasive bladder cancer

- **Standard of care = Radical cystectomy with urinary diversion with pelvic lymphadenectomy**
- Only about 50% of patients with high-grade invasive disease are cured

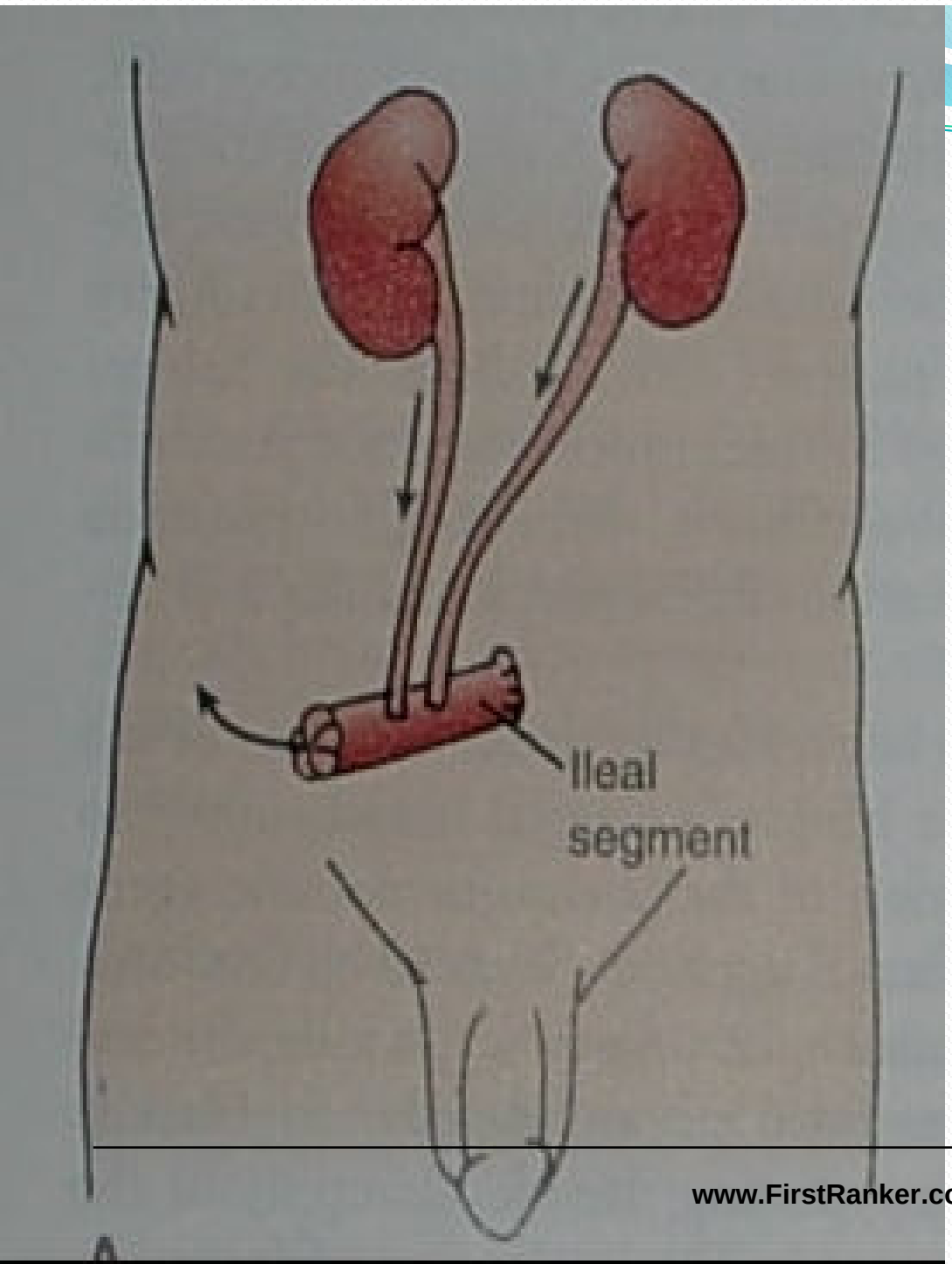
Radical cystectomy





Urinary diversion

- Uretero – sigmoidostomy
- Ileal conduit
- Colon conduit
- Ileocaecal segment
- Orthotopic neobladder



Cutaneous urinary diversions

Ileal conduit (ileal loop)
A 15 cm loop of ileum led out through abdominal wall
Stents used
The space at cystectomy site drained by a drainage system
After surgery a skin barrier and a transparent disposable urinary drainage bag
Constantly drains

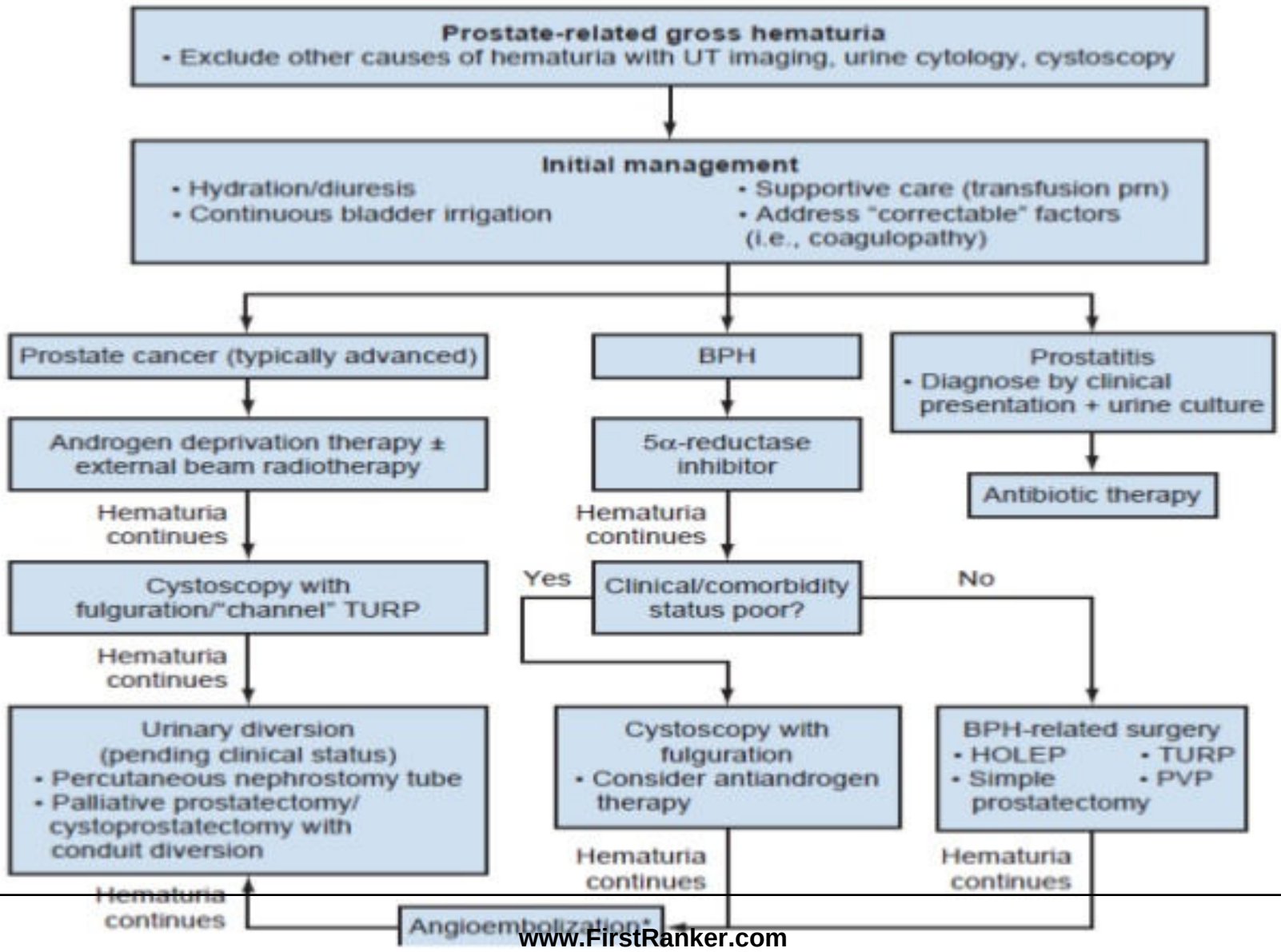
Haematuria from prostatic origin:

- Hematuria from prostatic origin is a diagnosis made after a complete evaluation (including cytology, upper tract imaging, and cystoscopy) to confirm that no other source of hematuria exists.

- Most common causes are:

  - BPH
  - Prostate carcinoma
  - Prostatits

- BPH -> m/c cause of prostate-related bleeding



Haematuria of urethral origin:

- Urethral bleeding (urethrorrhagia) is defined as bleeding distal to the bladder neck, occurring separate from micturition

- Blood at the urethral meatus in the absence of volitional micturition, initial hematuria, or blood at the start of urination frequently implies pathologic processes distal to the external urinary sphincter.

Causes of urethral bleeding:

MALE

Trauma
- Blunt (straddle injury, kick to perineum)
- Penetrating (foreign body insertion, failed urethral catheterization)
- Intercourse related (penile fracture, masturbation)

Urethritis
- Bacterial (gonococcal, nongonococcal)
- Viral
- Chemical
- Autoimmune (Reiter syndrome)

Malignancy
- Urothelial carcinoma
- Squamous cell carcinoma (meatus/glans)

Condyloma

Calculus disease

FEMALE

Trauma
- Blunt (pelvic fracture)
- Penetrating (foreign body)

Urethral diverticulum

Urethral caruncle

Urethritis

Malignancy

Calculus disease

- RGU and cystourethroscopy remain the mainstays for diagnosis in patients with suspected urethral bleeding

- Perineal or penile bruising, accompanied by a hematoma, often is a clear indication of injury related to trauma.

- RGU is essential in instances of trauma when a urethral injury is suspected

ASYMTOMATIC MICROHAEMATURIA:

- The American Urological Association (AUA) has published guidelines regarding patients with asymptomatic microhematuria (AMH)

- It is defined as three or more RBCs per HPF in the absence of an obvious benign cause.

- A determination of AMH should be based on microscopic, not dipstick, examination of the urine.

To rule out benign causes of AMH, such as

1. Infection
2. Medical renal disease, and others.

- Careful history
- Physical examination
- Laboratory examination should be done

- Once these causes are ruled out, urologic evaluation that includes a measurement of renal function is recommended.
- If factors such as dysmorphic RBCs, proteinuria, casts, or renal insufficiency are present, nephrologic workup should be considered in addition to the urologic evaluation.
- AMH that occurs in patients who are anticoagulated still warrants urologic evaluation.

- The evaluation of patients over 35 years of age with AMH should include cystoscopy

- It is optional in younger patients.

- All patients should have cystoscopy if risk factors such as

1. Irritative voiding symptoms
2. Tobacco use, or
3. Chemical exposures are present.

- Radiologic evaluation should be performed in the initial evaluation

- The procedure of choice is multiphasic CT urography with and without IV contrast.

- Magnetic resonance urography, with or without IV contrast, is an acceptable alternative in patients who cannot undergo multiphasic CT scan.

- In cases where collecting system detail is needed and there is a contraindication to the use of IV contrast , options are:

1. Noncontrast CT
2. MRI or
3. Renal ultrasonography with retrograde pyelograms is an acceptable alternative.

Cytology may be useful in those patients with persistent AMH

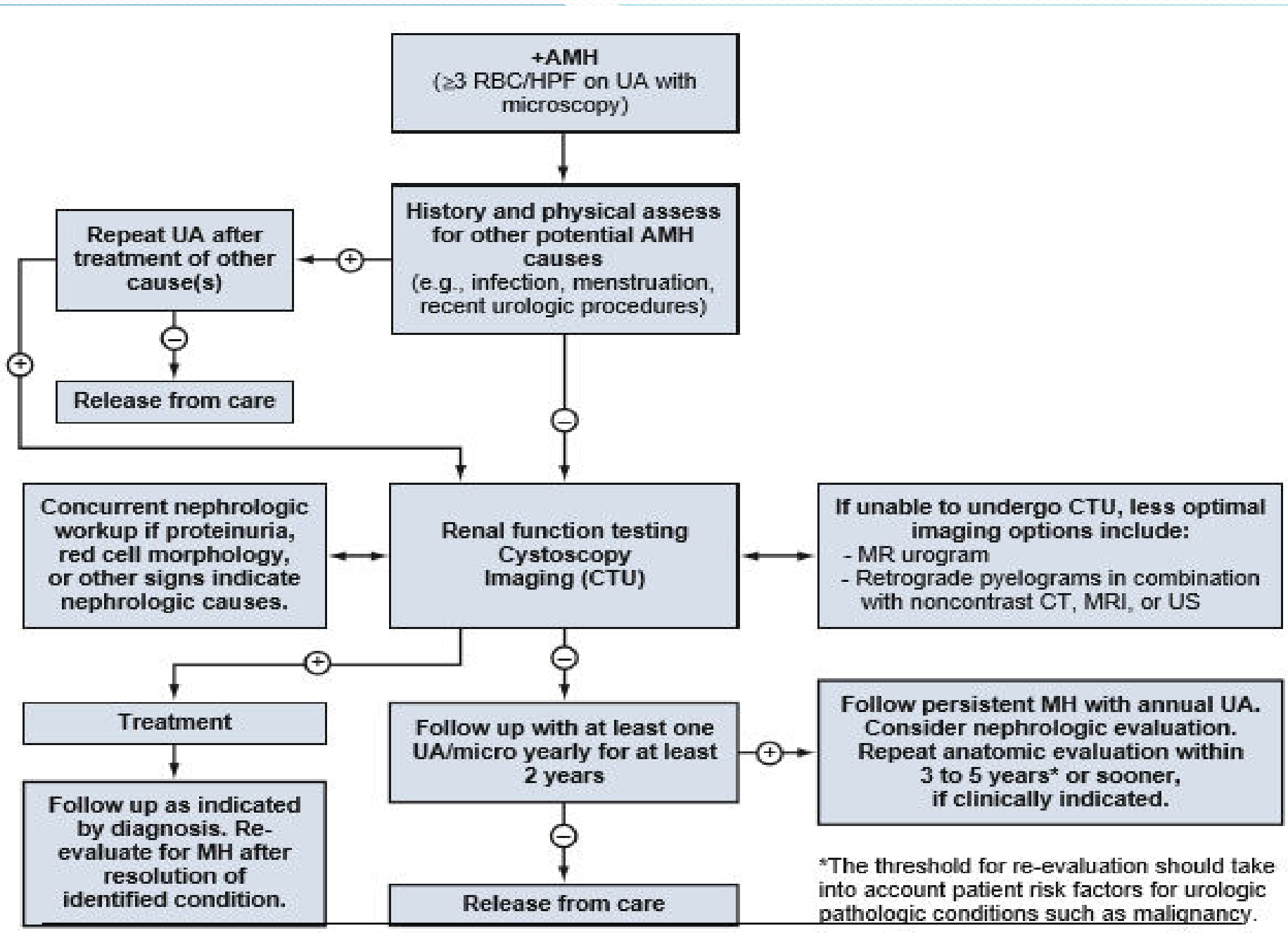
- Following a negative workup

- Those with other risk factors for carcinoma in situ, such as

1. Irritative voiding symptoms
2. Use of tobacco, or
3. Chemical exposures.

Patients with persistent AMH:

- Yearly urinalysis should be performed.
- The presence of two consecutive annual negative urinalyses indicates that no further urinalyses are needed for this purpose.
- For patients with persistent or recurrent AMH, repeat evaluation within 3 to 5 years should be considered.



Management algorithm of asymptomatic microhaematuria: