If your patient is doing well,
don't just do something
—
Stand there.*

* During my talk there will be little sayings and such as printed on our house. They are from various sources.

HEMATURIA

Is It Benign or Cause for Concern?

WILLIAM O. JONES, PA-C

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Hematuria

HemaTuria HemaCHuria

Hematuria is defined as the presence of **5 or more red blood cells (RBCs) per high-power field in 3 of 3 consecutive centrifuged specimens obtained at least 1 week apart.**

Hematuria can be either gross (ie, overtly bloody, smoky, or tea-colored urine) or microscopic.

It may also be either symptomatic or asymptomatic, either transient or persistent, and either isolated or associated with proteinuria and other urinary abnormalities.

Homer Smith's Law: The function of heart is to pump blood to the kidneys.
*~Robert Matz, MD, "PRINCIPLES OF MEDICINE", Published 24 April 1937**

The presence of Red Blood Cells must be confirmed by microscopic evaluation.

Dipstick test for blood detects the peroxidase activity of erythrocytes which is **also present in myoglobin**. Betadine may cause False Positive.

Character of RBCs (~50,000,000 Da) must be defined:

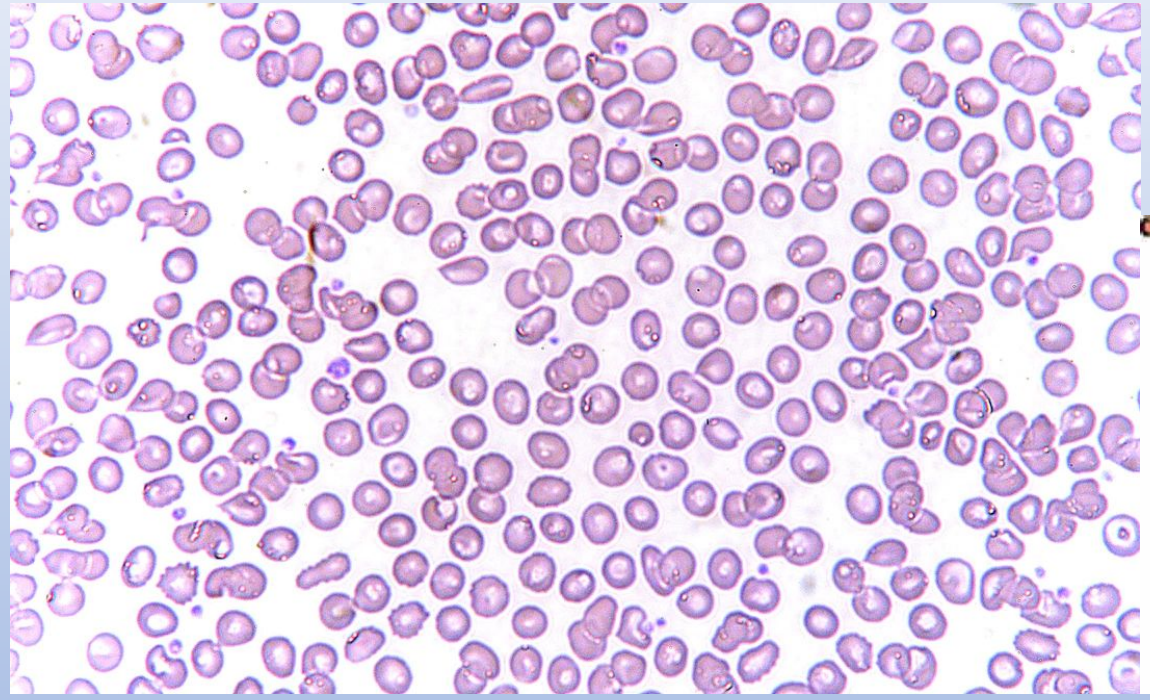
Normal appearing cells can originate in any part of the urinary system

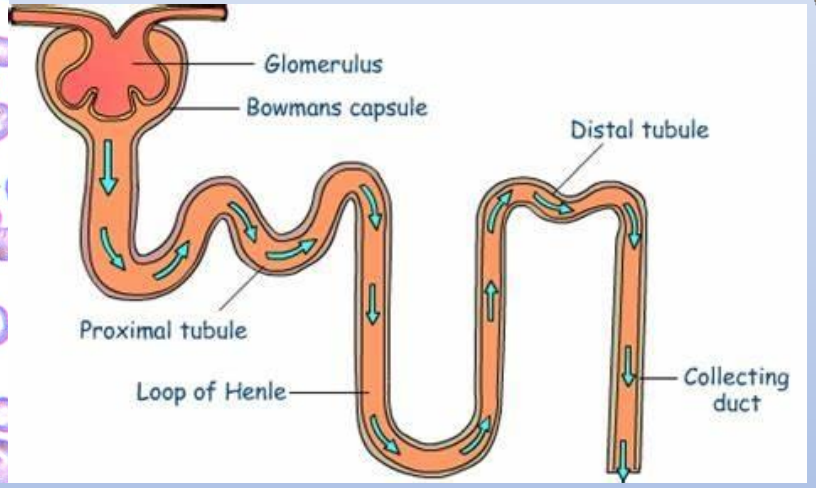
Dysmorphic / Crenated cells indicate a **renal parenchymal source**. Cells become disrupted when transiting the Glomerular Filtration Barrier (~65,000 Da)

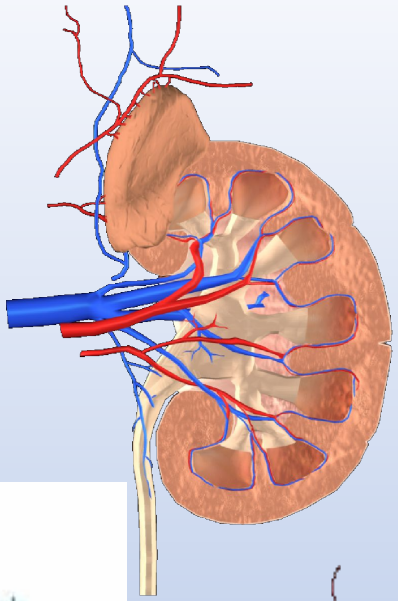
Hematuria <u>without</u> RBC casts or proteinuria may originate in any part of the GU system

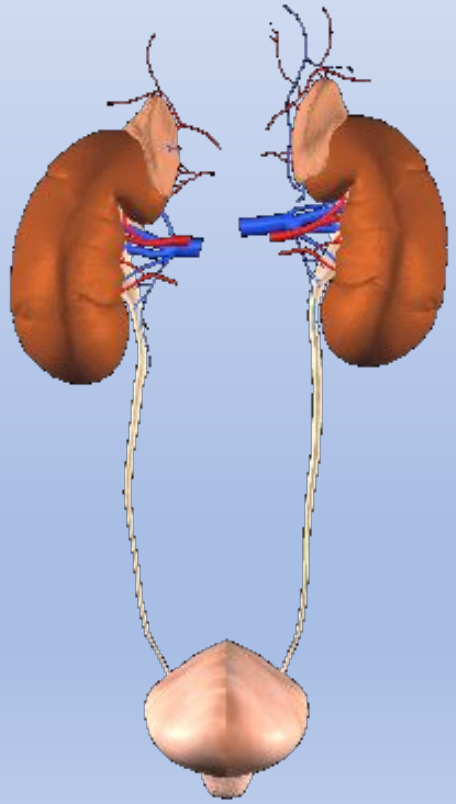
Hematuria <u>with</u> RBC casts, dysmorphic cells, and/or proteinuria is usually of Glomerular origin.

Normal RBCs in Urine







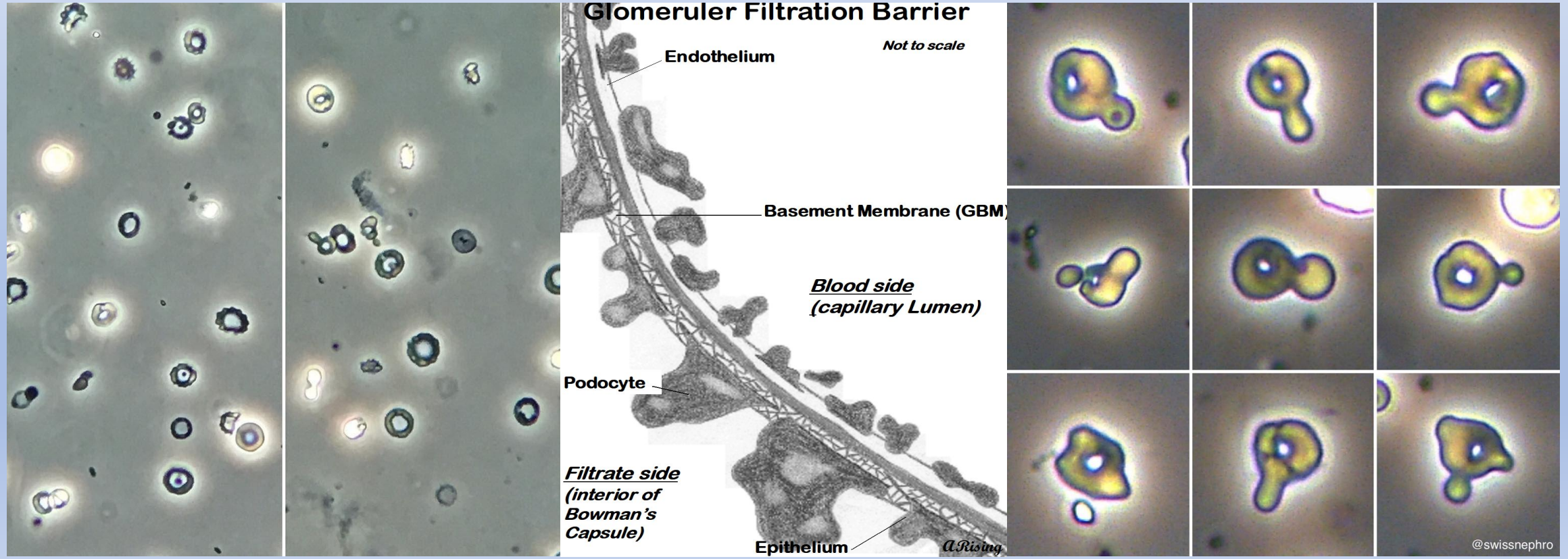


Normal appearing cells indicate a <u>post-glomerular</u> origin of the blood

The Art of Medicine consists of amusing the patient while nature cures the disease. *Voltaire**

Dysmorphic or Crenated Red Blood Cell

Dysmorphic / Crenated cells indicate a renal parenchymal source. Cells become disrupted when transiting the glomerular Filtration Barrier. May appear to have spicules instead of a smooth cellular membrane.



Red Blood Cell Casts

The presence of red blood cell casts is usually accompanied by the presence of free red blood cell in the sediment. When red blood cells casts are observed in urine, the glomerular basement or the lining of the renal tubule may be injured. Thus, red blood cell cast are frequently found in glomerulonephritis.

If you order a lab test to reassure a patient, the results will always be abnormal. ~ *Howard Bennett, MD**

Hematuria

Most Common Causes of Hematuria in the Newborn to 20 Years old

Acute Glomerulonephritis

Acute Urinary Tract Infection (UTI)

Congenital Urinary Tract Anomalies with Obstruction

Acute Glomerulonephritis

Post Streptococcal GN

Most common form of GN in children. Develops ~ 7 – 14 days after pharyngeal patient, about 14 – 28 days in the post pyodermal patient. ASO titer will give indirect evidence of recent exposure.

Usually self-limiting when the strep is treated. Children may continue to have proteinuria for up to a year.

Worse prognosis for adults. A number will develop Focal And Segmental Glomerulonephritis and ESRD after about 10 years.

People with POSITIVE strep throat cultures never have telephones.*

Urinary Tract Infection

Hemorrhagic Cystitis caused by E. Coli. Frequency have dysuria, frequency pressure, urgency, and gross hematuria.

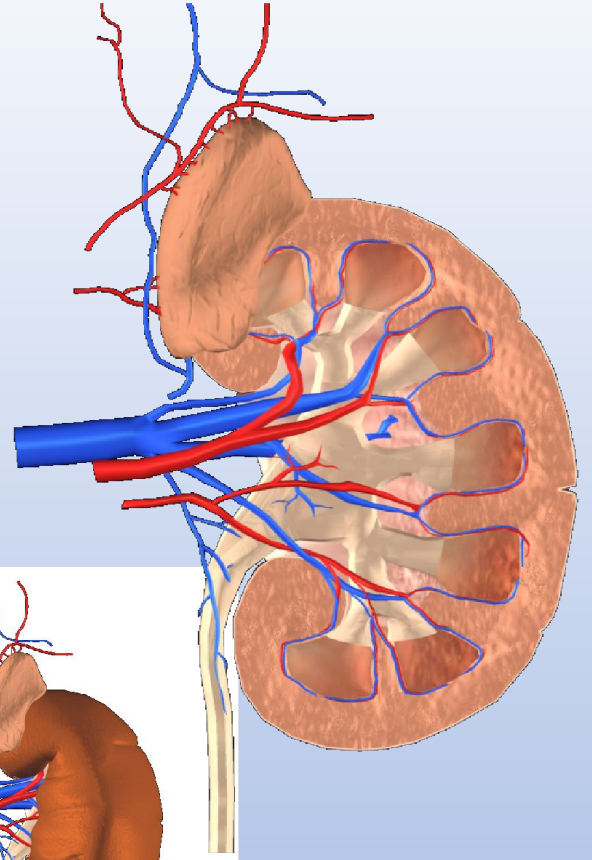
Probably will see White Blood Cells and Bacteria on microscopic examination.

Culture ALL.

Refer to Urologist is infections become chronic or persistent.

It is better to have turfed and lost than to never have turfed at all.*

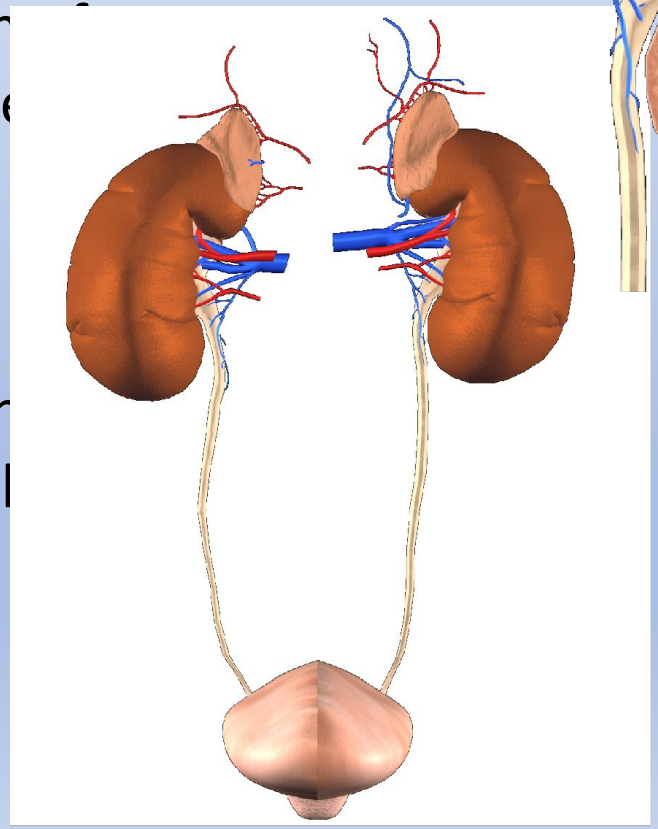
Congenital Urinary Tract Anomaly



Uretero-pelvic Junction. Hydronephrosis forms at the junction of the Renal Pelvis and Ureter

Uretero-vesical Junction. Blockage at the junction [illegible] the ureter and urinary bladder can cause mega-ure[illegible]

Vesico-ureteral Reflux. Trigonal weakness, other abnormality complications: pyelonephritis, hydroureteronephrosis. Can lead to Hypertension Proteinuria, Glomerulosclerosis; Chronic Renal Fail[illegible] can lead to ESRD.



Male, a few months old, with Hematuria and UTIs.

Steven. **Vesico-ureteral Reflux**

Renal Failure, Growth Retardation

Surgeries, Infections, HGH, Transplant, Pitched a no-hitter in Little League baseball

2 years old female with Hematuria, Hypertension, and Abdominal Mass

Wilm's Tumor. Nephroblastoma – 95% of all urinary tract malignancies occurring in childhood. 90% of these occur under the age of seven, mean is 3 years old.

Solitary and Unilateral. Embryonic – primitive tubules and glomerular structures in blastemal tissue. Horrible in adults.

6 years old female with Hematuria and Edema after SORE THROAT.

Post Strep Glomerulonephritis.

9 year old female with microscopic Hematuria and vague loin pain.

Biopsy showed: **“Thin Basement Membrane Syndrome but Loin – Pain Hematuria Syndrome cannot be ruled out”.**

18 year old male with Sickle Cell Disease and Hematuria

Sickle SS disease Sickle Nephropathy >> Membranous Glomerulonephritis >> Infarction

The difference between a pediatrician and an internist is how they feel when their patient pees on them. *Andy Biles**

Hematuria

Most Common Causes of Hematuria in the 20 to 40 year olds

UTI

Calculi

Bladder Tumor

Three vampires walk into a bar.
The first one orders blood.
The second one orders blood.
The third one orders plasma.
The waitress calls out “Two bloods and a blood lite”.*

Renal Calculi

Various philosophies of stone formation.

75% are Calcium Oxalate

More frequent in 30 – 50 year olds; male : female – 1:4

Blacks less than whites

Caliceal stones – Asymptomatic except gross hematuria

Renal Pelvis Stones – Asymptomatic unless they obstruct

Ureteral stones – Renal colic, severe pain; Hematuria

Calcium Oxalate (75%) – can occur with normal serum calcium levels

Struvite stones (15%) - harbor bacteria usually Proteus, Pseudomonas, Klebsiella.

Difficult to image

Bladder Tumor

Usually begin to see in the 40's., more common in later life

90% are Transitional Cell Carcinoma

Men : woman, 3:1
Smokers : Nonsmokers, 4:1;

Occupational Exposure

Arise mainly in the bladder neck and lateral walls

Prognosis demands on staging

22 year old long distance runner with episodic hematuria

Occasionally red blood casts can be seen in an individual who has been playing contacts sports. The urines of these individuals will return to normal within 24 to 48 hours

"I believe that every human has a finite number of heartbeats. I don't intend to waste any of mine".
*Neil Armstrong**

23 and 50 year old females with hematuria and rising creatinine; history of Ephedrine and NSAID use

Analgesic Nephropathy, Medication Induced Interstitial Nephritis

NSAIDs work by blocking cyclooxygenase (COX-1, COX-2) which prevents synthesis of various prostaglandins. Renal prostaglandins have a supportive role in maintaining renal perfusion. Prostaglandin inhibition results in decreased renal perfusion >> papillary necrosis >> CKD >> Dialysis.

Papillary Necrosis – Beethoven, 1827. Uncontrolled way of taking medication. SaliCin, a commonly used analgesic substance of that time (dried and powdered willow bark), is able to cause papillary necrosis. The autopsy report of Beethoven is the first case of papillary necrosis recorded in the literature.

24 year old RN on Renal Metabolic Unit with microscopic hematuria on UA done while bored.

Biopsy proven **IgA Nephropathy**

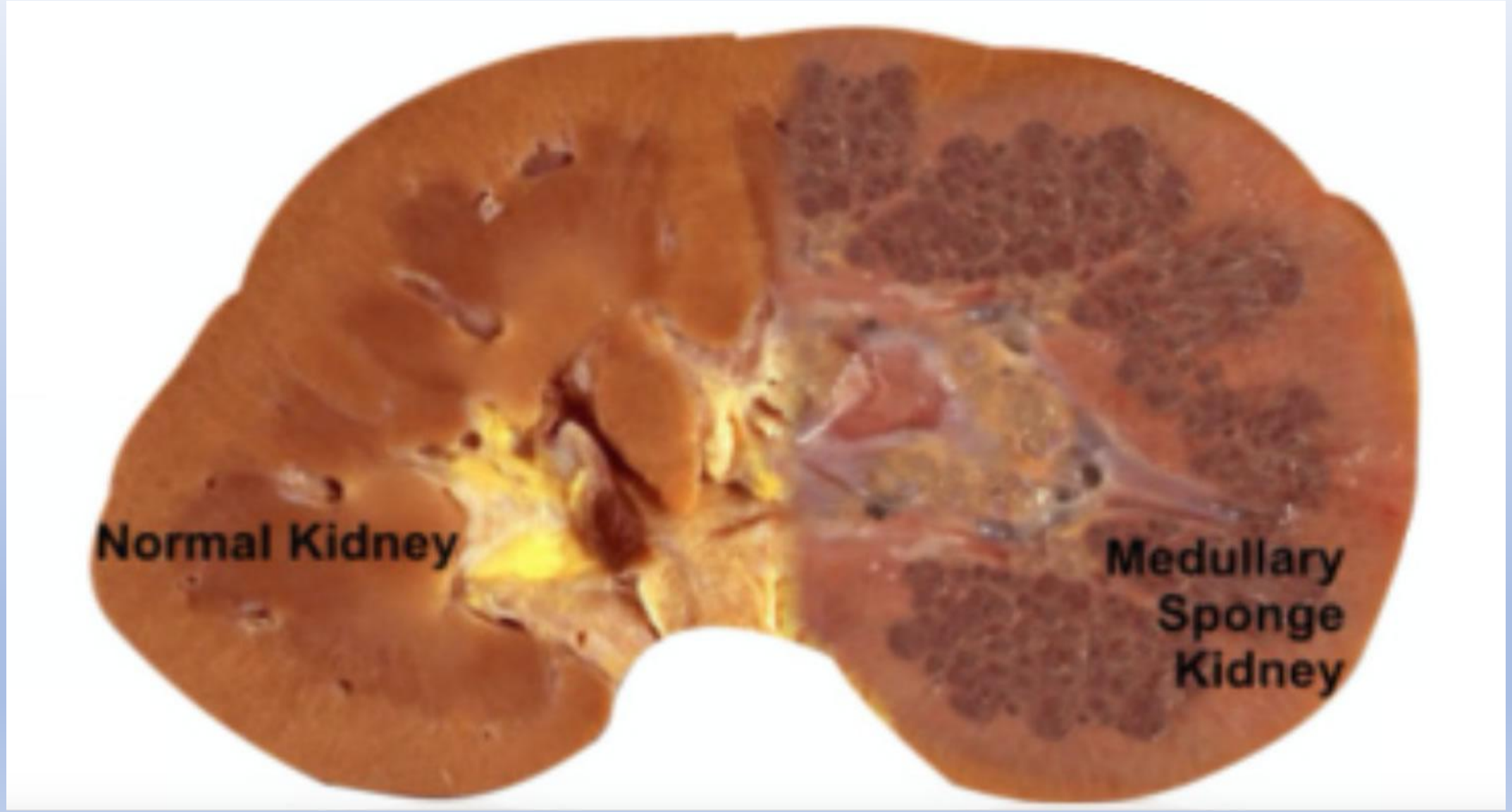
32 year old male with Episodic Gross Hematuria especially after URI

Biopsy showed **IgA Nephropathy**
Most common type of GN

Whole bunch of male cousins with hematuria, ESRD, and hearing loss;
Family history -> Alport's Syndrome

34 year old female with "Blush" seen on IVP
Medullary Sponge Kidney

Medullary Sponge Kidney



40 year old female with acute onset of hematuria …
Progresses to ESRD in less than 6 months.
RAPIDLY PROGRESSIVE GLOMERULONEPHRITIS

Classification of Rapidly Progressive Glomerulonephritis Based on Immunofluorescence Microscopy

Type 1 PRGN – Anti-glomerular basement membrane antibody disease

Anti-glomerular basement membrane (GBM) antibody disease (type 1 RPGN) is autoimmune GN and accounts for **up to 10% of RPGN cases.** It may arise when respiratory exposures (eg, cigarette smoke, viral URI) or some other stimulus exposes alveolar capillary collagen, triggering formation of anti-collagen antibodies. The anti-collagen antibodies cross-react with GBM, fixing complement and triggering a cell-mediated inflammatory response in the kidneys and usually the lungs.

The term **Goodpasture syndrome** refers to a combination of GN and alveolar hemorrhage in the presence of anti-GBM antibodies. GN without alveolar hemorrhage in the presence of anti-GBM antibodies is called **anti-GBM glomerulonephritis**. Immunofluorescent staining of renal biopsy tissue demonstrates linear IgG deposits.

*** Type 2 RPGN - Immune complex RPGN**

Immune complex RPGN (type 2 RPGN) complicates numerous infectious and connective tissue disorders and also occurs with other primary glomerulopathies. Immunofluorescent staining demonstrates nonspecific granular immune deposits. **The condition accounts for up to 40% of RPGN cases. Pathogenesis is usually unknown.**

Type 3 -RPGN - Pauci-immune RPGN

Pauci-immune RPGN (type 3 RPGN) is distinguished by the absence of immune complex or complement deposition on immunofluorescent staining. It constitutes up to **50% of all RPGN cases**. **Almost all patients have** elevated **antineutrophil cytoplasmic antibodies (ANCA**s, usually antiproteinase 3-ANCA or myeloperoxidase-ANCA) and **systemic vasculitis.**

Type 4 RPGN - Double-antibody disease

Double-antibody disease (type 4 RPGN) has features of types 1 and 3, with the presence of anti-GBM and ANCA antibodies. It is **rare**.

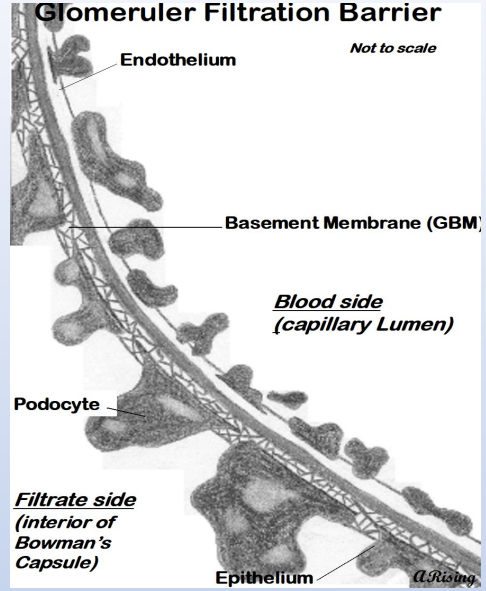
Type V RPGN - IMMUNE COMPLEXES

SIMILAR TO TYPE 2 BUT NO OBVIOUS CAUSE SUCH AS INFECTION, CONNECTIVE TISSUE DISORDER, OR GLOMERULAR DISORDER.
PAUCI-IMMUNE FEATURES (Similar to Type 3) But absence of ANCA antibodies.

Idiopathic RPGN

Idiopathic cases are rare.

"The discovery of anti-nephrin antibodies thoroughly changes our understanding of **idiopathic nephrotic syndrome, minimal change disease (MCD), and primary focal segmental glomerulosclerosis (FSGS),** which classify as **anti-nephrin-associated podocytopathies** in many cases," co-author Nicola Martin Tomas, MD, University Medical Center Hamburg-Eppendorf, Hamburg, Germany, told *Medscape Medical News.*



The study was presented on May 25 at the 61st European Renal Association (ERA) Congress 2024 and simultaneously published in the *New England Journal of Medicine.*

Hematuria

Most Common Causes of Hematuria in the 40 to 60 year old females

UTI
Calculi
Bladder Tumor

Youth is a disease from which we all recover. *Dorothy Parker**

45 year old female with painless hematuria and a history of stones

Spiculed Bladder Stone causing local trauma and hemorrhage

Urinary Tract Infections

Hematuria can be caused by acute, chronic, or persistent urinary tract infections and trigonitis. Can lead to papillary necrosis. Hemorrhagic Cystitis.

A friend asked her doctor if a woman should have children after thirty-five. She was told, "no, thirty-five is enough for any woman."*

Hematuria

Most Common Causes of Hematuria in the 40 to 60 year old males

Bladder Tumor

Calculi

UTI

At my age, I need all the preservatives I can get. *George Burns**

46 year old male with hematuria which worsens with URI UA done because wife worked in our office. SCr – Normal, Total Protein = 140 mg/24 hours

Biopsy Proven IgA Nephropathy

52 year old retired Gunnery Sergeant, USMC

59 year old male with abdominal "fullness" on exam, flank pain, hematuria

PKD and **Primary Renal Cell Carcinoma**

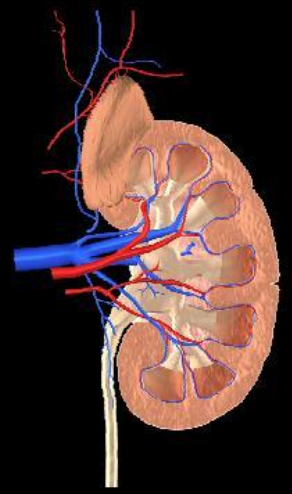
72 and 40 year old males with asymptomatic hematuria and associated flank pain

(Don / Chris)

Polycystic Kidney Disease – Hereditary, Associated with cerebral aneurysms.

Tx - Rabies

The human body is a beautiful thing, man, but beauty's only skin deep. Beneath the surface lurks a disgusting and frightening world of guts, gore, and glandular disorders. *Bart Simpson**



Normal is a Relative Term *(Me)*

Hematuria

Most Common Causes of Hematuria in the 60+ year old

(BPH)

Bladder Tumor

UTI

A man spends the first 65 years of his life trying to make money; he spends the rest of it trying to make water.
Robert Matz, MD*.

Benign Prostatic Hypertrohy (BPH)

Hematuria can be a sign of progressive BPH, but bladder cancer MUST be ruled out

65 year old cigarette smoker with intermittent and increasing hematuria

Bladder Tumor. Usually occurs in inferior & lateral walls, Much **more common in smokers**. There has been evidence that hairdressers who work with **dark colored hair dyes** have a higher incidence of Bladder Cancer.

65 year old male found to have a SCR of 8.4 after undergoing bronchoscopy for hemoptysis. Positive ANCA. Renal-Pulmonary Syndrome.

Polyarteritis with Renal Involvement (Wegener's Granulomatosis)

***Scary for Pulmonologists*.**

An old man from Denver named Lee
Had a prostate as big as a tree
Because of his plight
His sphincter was tight
*And it took him two hours to pee**

79 year old male with frank painless hematuria "*that always went away*". PKD.

ANYONE ON ANTI-COAGULANT THERAPY

Confidence is the feeling you have before you understand the situation.*

Past Medical History

Family History

Review of Systems

Physical Examination

Laboratory Determinations

Imaging Studies

Refer to Nephrologist

Referral to UROLOGIST – Evaluation and Possible Renal Biopsy

When all else fails, do an H & P.*

Physical Examination

Physical examination with evaluation of fluid volume status(I&O, weight, edema, neck veins) cardio-pulmonary status, gross abnormalities

Laboratory determinations to include: CBC, CMP (SCr, BUN, K+, CO2, Ca++, Albumin, Total Protein, Pro/Cr Ratio, 24 hour urine for TPCC, Urine Cytology, Phos, MG, ASO, WESR, ANA, C3, C4 ANCA, SPEP, anti-GBM, anti-nephrin antibodies, Others

Imaging: Ultrasound, KUB, IVP, CT, MRI, MRA

The most important part of the stethoscope is the part between your ears. *

Physical Examination

UROLOGICAL EVALUATION

IV Urography, IVP

Cystoscopy +/- Retrograde Urogram

Voiding Cystourethrogram VCUG

Angiography, Selective Renal arteriography

Renal Biopsy

The only indication for kidney biopsy is having two kidneys. *

On urinalysis:

Normal appearing red blood cells indicate a collecting system origin of the urinary blood.

Dysmorphic RBCs indicate a renal parenchymal source.

Hematuria without RBC casts or proteinuria can originate in any part of the GU tract

Hematuria with RBC casts and/or proteinuria is usually of glomerular origin.

NSAIDS

Act to reduce inflammation by inhibiting the effects of COX-2.

They also **blocks COX- 1** which is responsible for **producing heavy mucus as a protection of the gastric mucosa** and **interferes with the maintenance of small vessel integrity.**

Hgb = 6.1

ACE-I, ARB'S

ACE-I's - **block the production of ANGIOTENSIN – 2 (A-2)** by interfering with the conversion of A-1 to A-2 by blocking the release of ANGIOTESIN CONVERTING ENZYME (ACE). This can lead to the typical ACE cough due to a build- up of ACE in the pulmonary vasculature.

ARB's – block the active A-2 at the end-organ site.

The effects are to reduce the systemic blood pressure as well as the effective eGFR.

Interfere with kidney's intrinsic ability of "Auto Regulation". Can lead to renal failure in setting of hypotension.

RENIN INHIBITORS - Not very effective.

AVOID IN PREGNANCY – Fetal Neural damage and fetal death occur before pregnancy is detected.

Other patients:

“The Big Man”

Jamaica Honeymoon

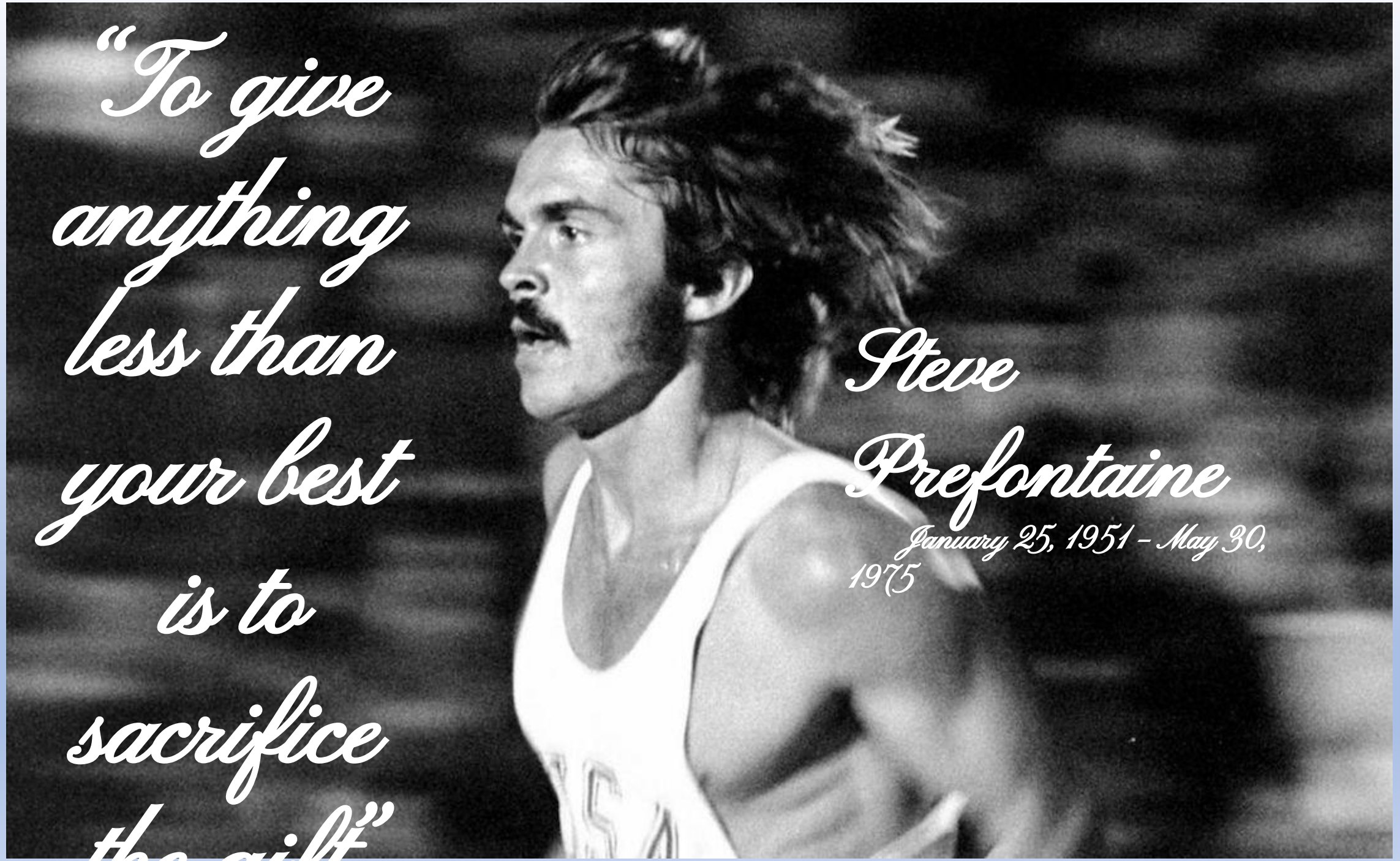
Mr. METH – BUN – 264, SCr – 41.8, K+ - 9.2

ARF after C - Section (JW) – HGB = 1.5, HCT = 5%

ARF after medication – K+ = 10.2

“The Roady”

On practicing the art of medicine: **"Look wise, say nothing, and grunt". *William Osler, MD****


"To give anything less than your best is to sacrifice the gift"
Steve Prefontaine
January 25, 1951 – May 30, 1975

DOOR PRIZE questions and answers will be revealed at conference.

William O. Jones, II, M.A., PA-C, DF-AAPA

- Lieutenant, U.S. Navy Retired
- Distinguished Fellow – American Academy of Physician Assistants
- Physician Assistant – George Washington University, 1982
- Master of Arts – Webster University, 1987
- Life Member, Veteran's Caucus
- Founding Vice President, American Academy of Nephrology Physician Assistants
- Past President, South Carolina Academy of Physician Assistants
- Who's Who In The World
- Who's Who In America
- Who's Who In Medicine and Health Care
- Member, American MENSA
- Vietnam Veteran; FMF SAR Corpsman, USMC
- https://pahx.org/bios/william-osborne-jones/

U.S. Navy Mustang (HMC, CWO4, LT)

HEMATURIA 101 Objectives:

During this period of instruction, the student will be exposed to an oral presentation from a lecturer as well as the presentation of various multi-media sources in the following topics:

- **Signs, symptoms, and evaluation of hematuria,**
- **Identification of various medical conditions presenting with hematuria,**
- **Treatment options of various hematuria causing conditions and describing when the treatment option is referral,**
- **Provide the audience an opportunity to ask questions of, and enter discussions with, the presenter.**

I have no financial interests or relationships to disclose.