LSU Health NEW ORLEANS
School of Medicine

Approach to the Urinalysis for Primary Care

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Live Activity

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Learning Objectives

- By the end of this lecture, participants should be able to:
  - Interpret findings on urinalysis dipstick
  - Correlate findings on urine microscopy to specific clinical diseases
  - Contrast features that separate glomerular hematuria from non-glomerular hematuria
  - Recite causes of proteinuria
  - Illustrate examples of urinalysis findings that warrant referral to Nephrology or Urology
  - Apply information on urinalysis findings to clinical cases

General Principles

- The Urinalysis (UA) consists of 3 primary parts:
  - Gross analysis
  - Urine dipstick
  - Urine microscopy

Indications for Urinalysis

- Vary widely, but may include:
  - Urinary complaints
    - Change in color/hematuria
    - Dysuria
    - Change in frequency
  - Assessment of Acute Kidney Injury
  - Evaluation of Chronic Kidney Disease
  - In asymptomatic patients as part of disease screening/monitoring (e.g. monitoring for proteinuria in patient with Diabetes mellitus or pregnancy)

Urine Collection

Clean, dry container

Patients asked to clean external genitalia prior to collection

Mid-stream specimen

- Generally, if greater than 10 epithelial cells/hpf noted, considered a contaminated or improperly collected specimen, making microscopy interpretation prone to false positive error

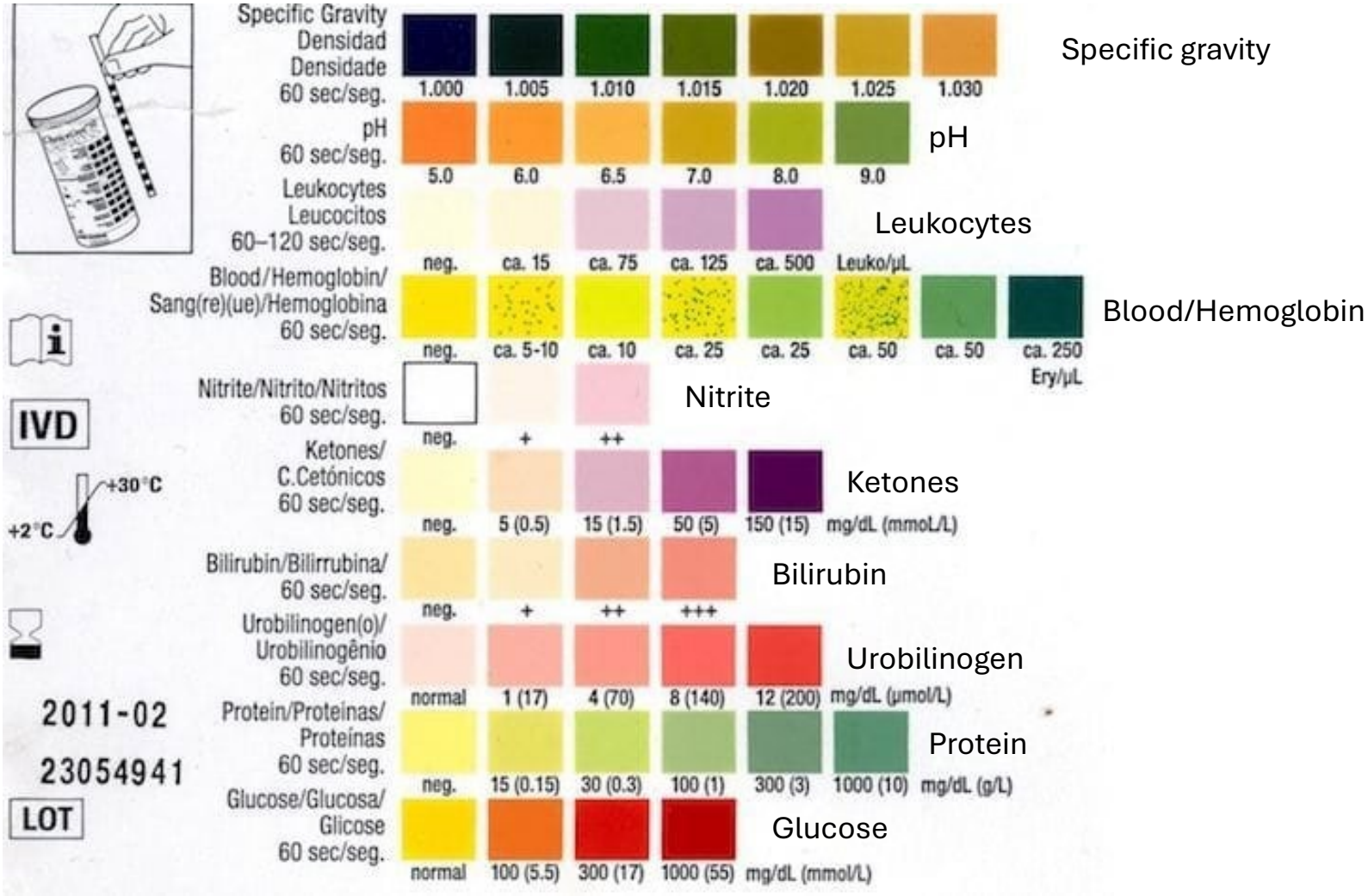
Examined within two hours of collection, or stored in refrigerator then rewarmed if immediate assessment not feasible

Urine: Gross Examination

- Rarely done in outpatient setting
- Predominantly looking for color change:
  - Red or Brown
    - May signify hemoglobin or myoglobin pigments
    - Acute Intermittent Porphyria
    - Ingestion of foods/medications:
      - Rifampin/phenytoin
      - Beets, rhubarb, or food dyes
  - Purple
  - Green

Hitzeman N, Greer D MD, MPH, Carpio E. Office-Based Urinalysis: A Comprehensive Review. Am Fam Physician. 2022 Jul;106(1):27-35B. PMID: 35839369.

Objective: Interpret findings on urinalysis dipstick



Objective: Interpret findings on urinalysis dipstick Specific Gravity and pH

Specific gravity

- Weight of the solution
- Correlates with urine osmolality, and thus urine concentration
  - Isosthenuria- specific gravity of 1.010- correlates to a urine osm of ~300 mosmol/kg
  - Specific gravity of $\leq$ 1.003 is generally dilute urine
  - Specific gravity of $\geq$ 1.020 is generally concentrated urine
  - Large molecules like glucose and radiocontrast can increase specific gravity without being associated with change to urine osmolality

pH

- Urine hydrogen ion concentration
- Physiologic range is 4.5 to 8.0
  - Should interpret urine pH in clinical context
- Very high urine pH ($\geq$ 8.0) can be seen in urinary tract infections with urease producing organisms

Objective: Interpret findings on urinalysis dipstick Ketones and glucose

Ketones

- Utilize nitroprusside test and reacts with acetoacetate and acetone. Does not react with beta-hydoxybutyrate
- Can be seen with conditions like starvation ketosis and DKA, less helpful in alcoholic ketosis

Glucose

- Triggers production of peroxide in urine, which catalyzes reaction on dipstick
- Glycosuria can occur with:
  - Elevated serum glucose over 200 mg/dL- exceeds the Tm of the proximal tubule to reabsorb glucose
  - Proximal tubular dysfunction- occurs in the setting of a normal serum glucose
  - SGLT2 inhibitor

Objective: Interpret findings on urinalysis dipstick Bilirubin and Urobilinogen

Bilirubin

- If present, can signify hepatic or biliary disease

Urobilinogen

- Breakdown product of bilirubin in intestines
- Small amount is normal
- In conditions like hemolysis or hepatic disease, can be elevated
- If completely absent, but serum bilirubin is elevated, suggests complete biliary obstruction

Objective: Interpret findings on urinalysis dipstick Leukocytes and Nitrites

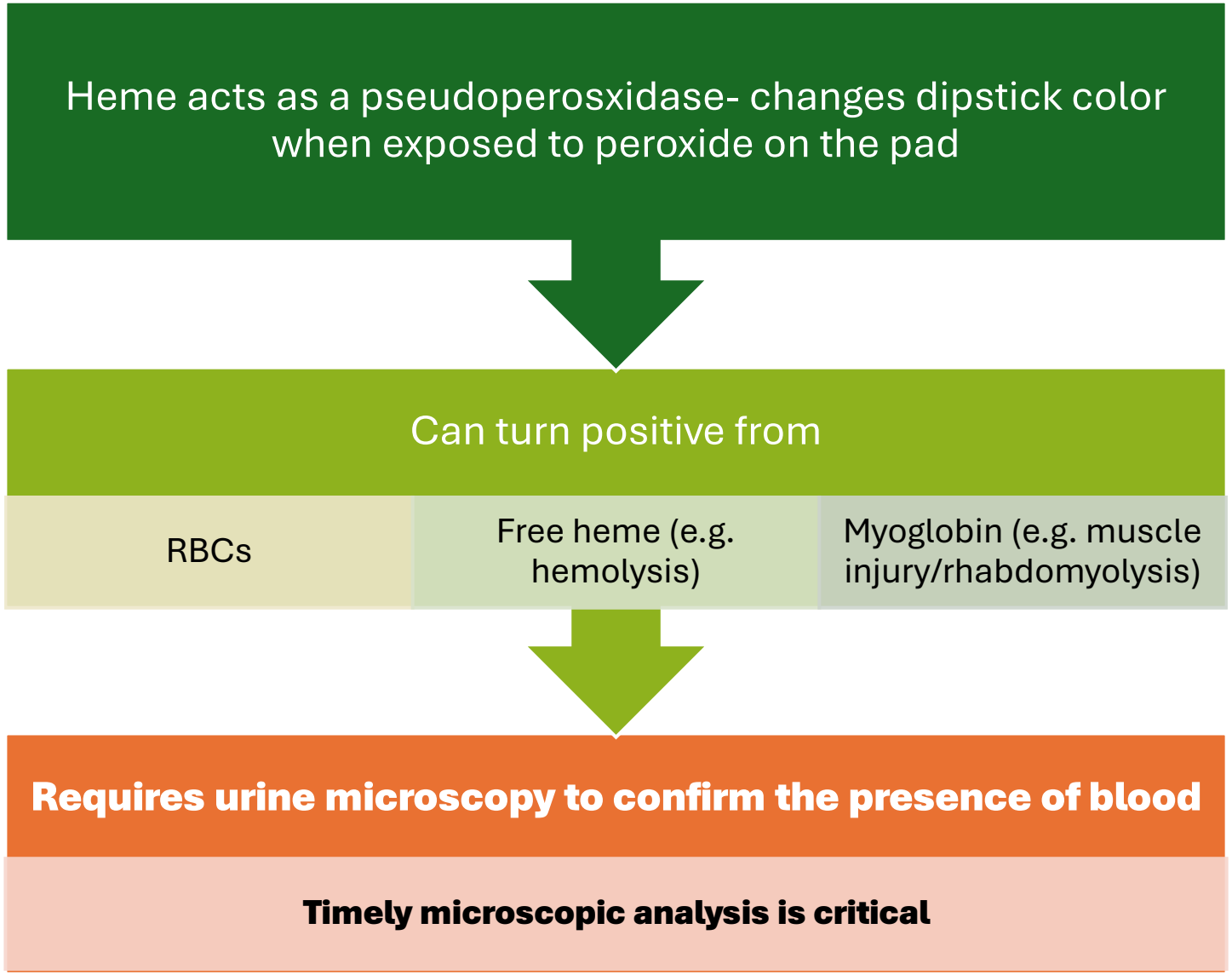
Leukocytes

- Checks for leukocyte esterase that is released by neutrophils and macrophages
- Proteinuria and glucosuria can lead to false-negative tests

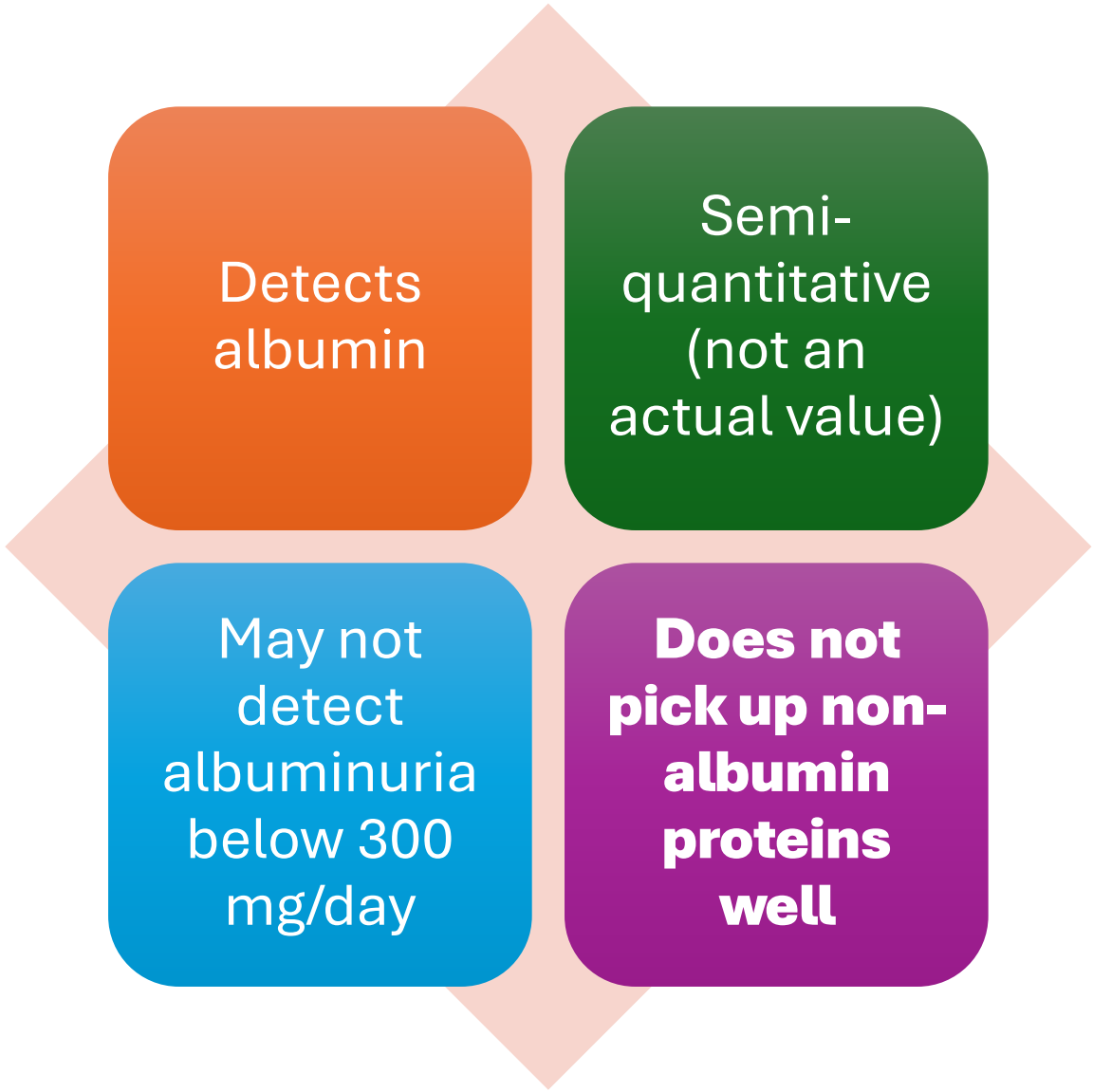
Nitrites

- Enterobacteriaceae species produce nitrate reductase with produces nitrite

Objective: Interpret findings on urinalysis dipstick Blood/Hemoglobin



Objective: Interpret findings on urinalysis dipstick Proteinuria



Correlate findings on urine microscopy to specific clinical diseases
Pyuria

Greater than 5 WBC/hpf considered abnormal

Can be any type of WBC, though most commonly neutrophils

Seen in a variety of clinical conditions:

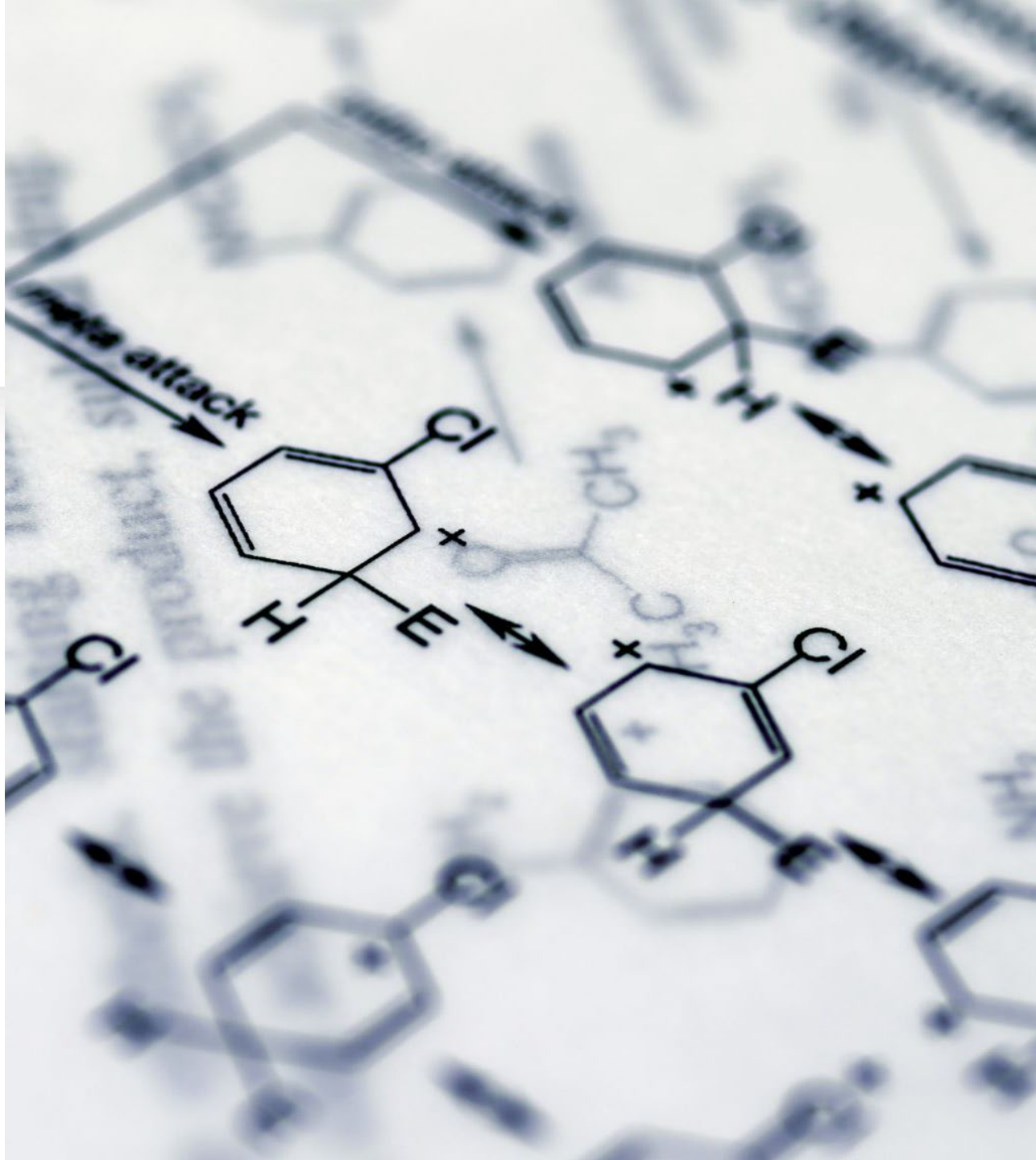
- Urinary tract infection
- Malignancy of the GU tract
- Nephrolithiasis
- Glomerulonephritis
- Acute Interstitial Nephritis
  - Generally advise **against** checking for urine eosinophils
- Improperly collected specimen

Acute Interstitial Nephritis (AIN)

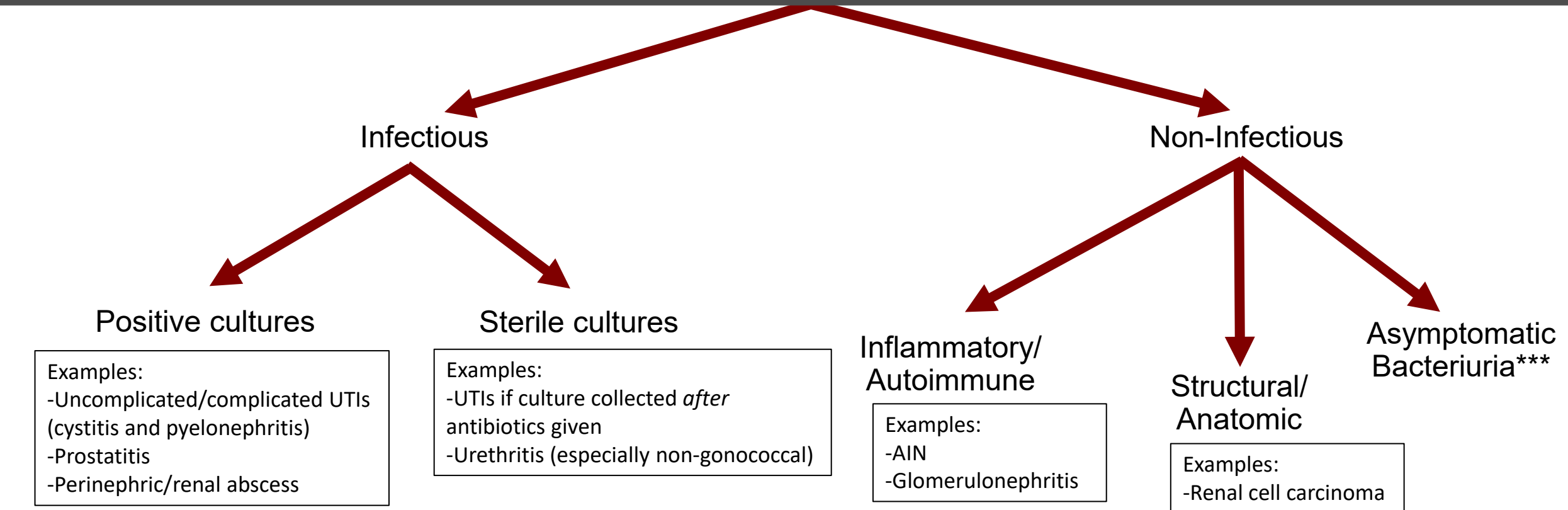
- Decline in renal function due to inflammation of the renal insterstitium, ultimately leading to permanent fibrosis
- Typically an allergic response to medications
- Also can be autoimmune or infectious in nature
- Generally see slower reductions in GFR compared with ATN or glomerulonephritis

Acute Interstitial Nephritis- Drug causes

- Common Drugs Causing AIN:
  - **Penicillins and Cephalosporins**
  - **Flouroquinolones**
  - Sulfas
  - Rifampin
  - **Proton pump inhibitors**
  - Cimetidine
  - **NSAIDs**
  - Allopurinol
  - Loop and Thiazide diuretics
  - Indinavir



A Conceptual Approach to UTIs and Mimickers of UTIs (i.e., things that cause pyuria and/or dysuria & frequency)



***Keep in mind that some patients with asymptomatic bacteriuria still require antibiotic therapy:

1. Pregnant patients
2. Patient's undergoing urologic procedure with anticipated disruption of mucosal barrier
3. Recent renal transplant (< 3 months since transplant)

Correlate findings on urine microscopy to specific clinical diseases
Hematuria

Greater than 3 RBC/hpf considered abnormal

Seen in a variety of clinical conditions:

- Urinary tract infection
- Malignancy of the GU tract
- Nephrolithiasis
- Glomerulonephritis
- Acute Interstitial Nephritis
- Menses
- Improperly collected specimen

Correlate findings on urine microscopy to specific clinical diseases
Casts

Casts are formed when material collects within the tubule

Hyaline cast

- Generally formed with low urine flow- can be seen with volume depletion

WBC cast

- Non-specific
- Can be seen with pyelonephritis, glomerulonephritis, and AIN

RBC cast

- Highly suggestive of glomerulonephritis

Granular/Muddy Brown cast

- Suggests tubular injury

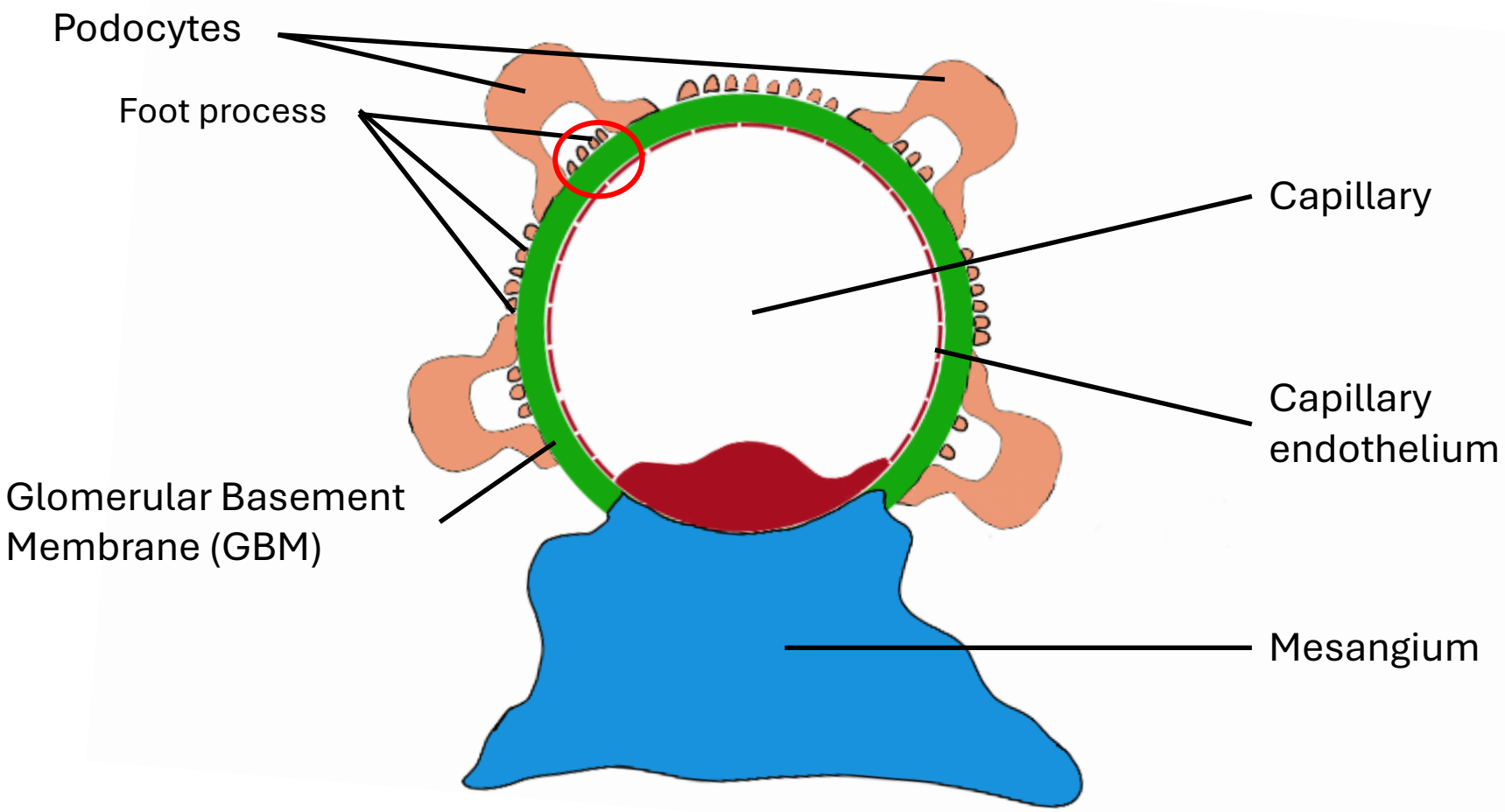
Epithelial cell cast

Objectives:

- Contrast features that separate glomerular hematuria from non-glomerular hematuria
- Recite causes of proteinuria

Proteinuria and Nephrotic Syndrome

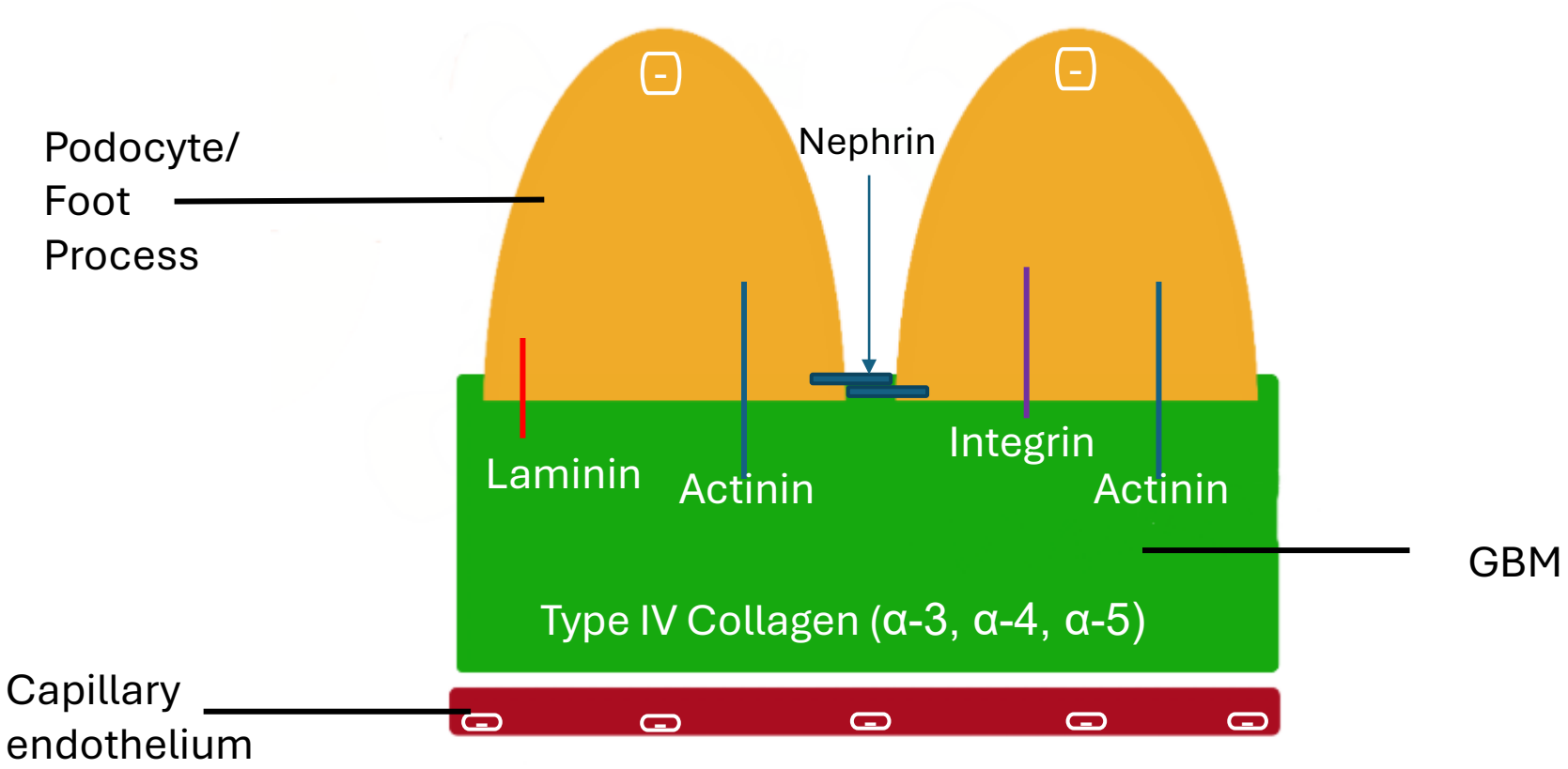
Objective 1: Diagram glomerular microanatomy



Modified from Figure 1.1. Brenner & Rector's The Kidney, 11th Ed. By Yu, A. S. L., Chertow, G. M., Luyckx, V. A., Marsden, P. A., Skorecki, K., & Taal, M. W. (2020)

Proteinuria and Nephrotic Syndrome

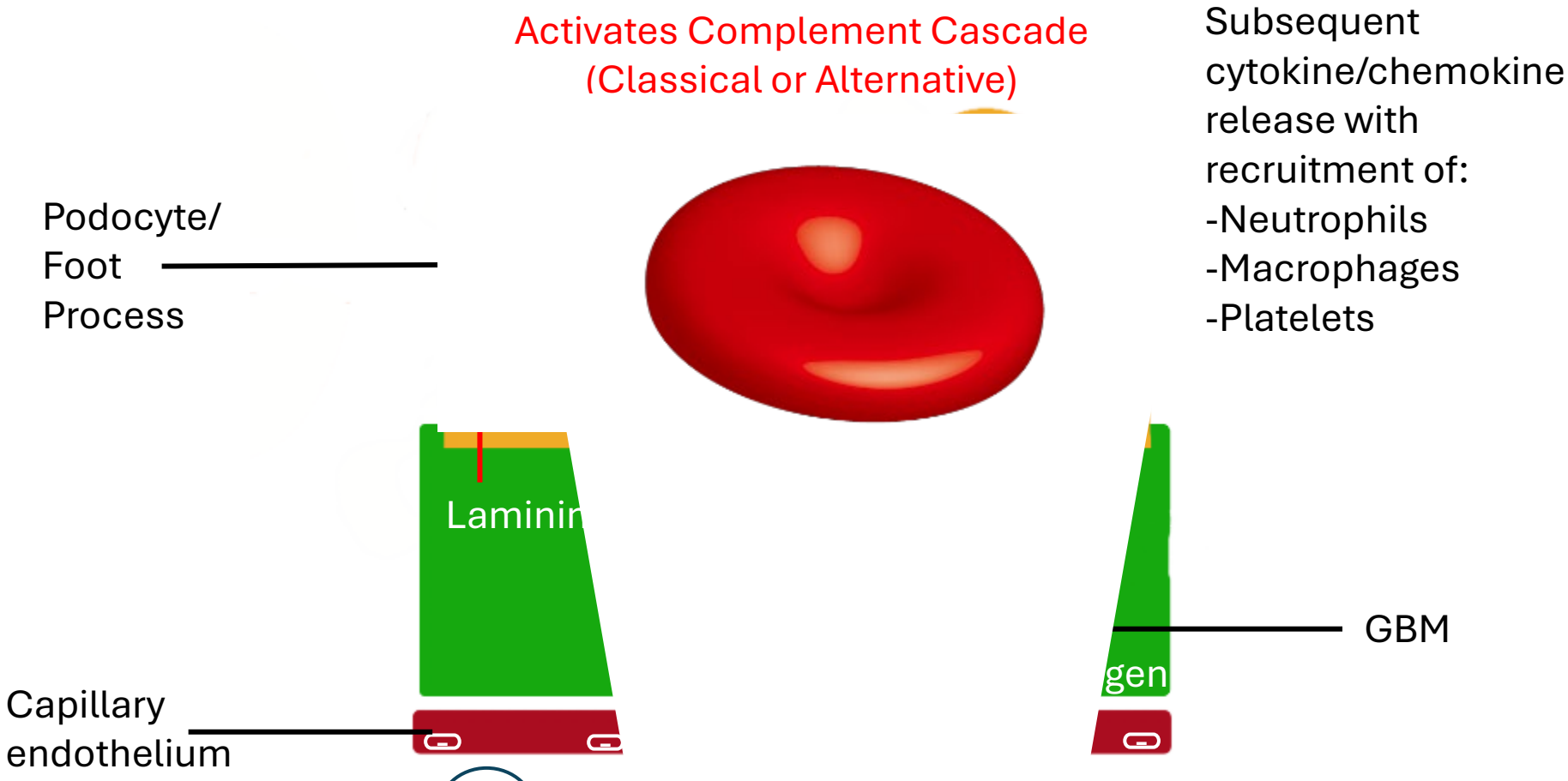
Objective 1: Diagram glomerular microanatomy



Proteinuria and Nephrotic Syndrome

- Pathogenesis
  - Immune complexes
    - Circulating antigen-antibody complexes
    - Circulating antigens that are “trapped” in GBM leading to antigen-Ab formation (in-situ formation)
  - Antibodies directly against the glomerular basement membrane
  - Complement activation
    - Classical through antigen/Ab complexes
    - Alternative pathway
    - Direct Complement deposition
  - Immunoglobulins with aberrant characteristics
  - Cellular activation
    - Neutrophils
    - Macrophages
    - Platelets
  - Cytokine and chemokine synthesis/release

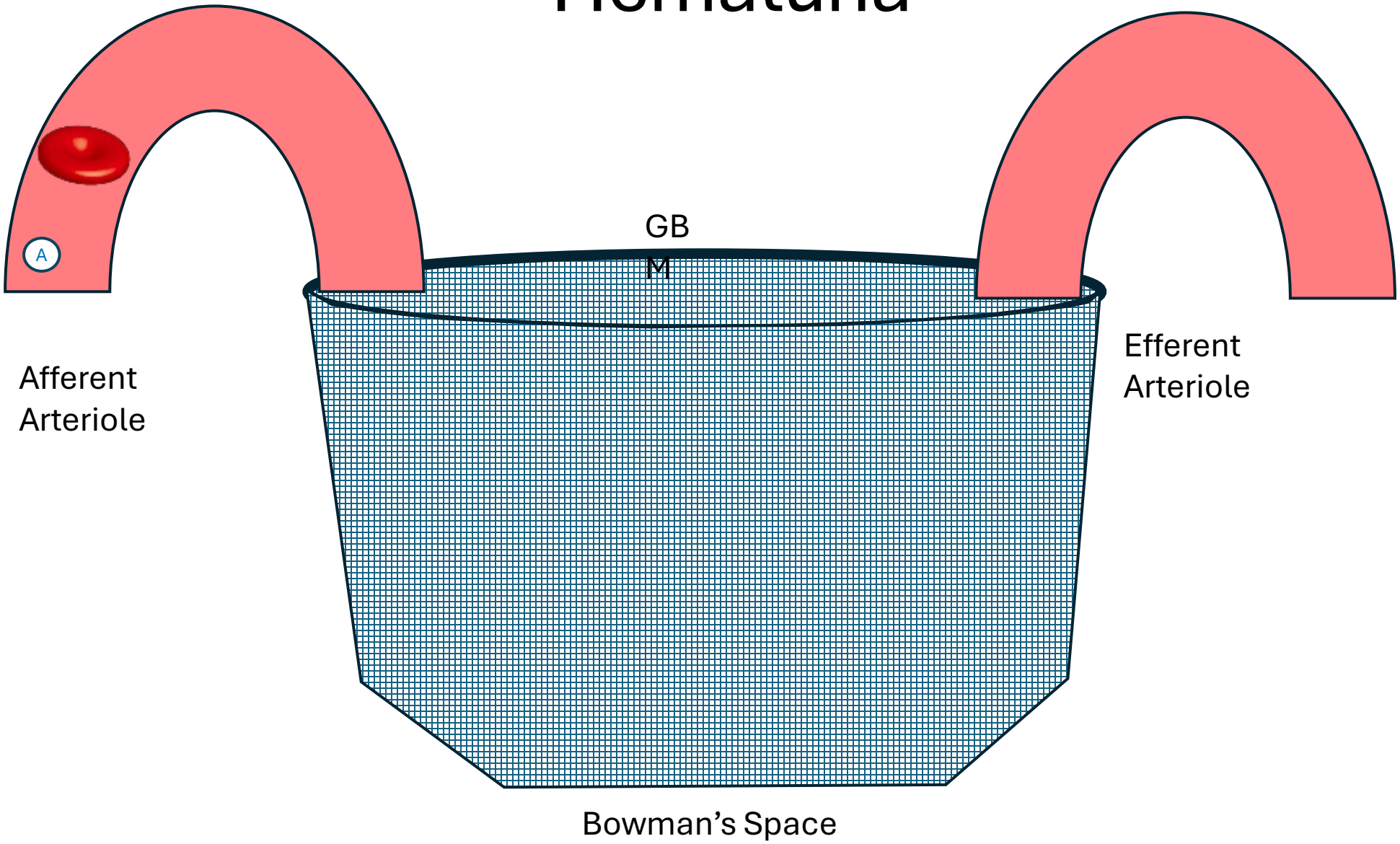
Objective 2: Explain the immune mechanisms of glomerular injury



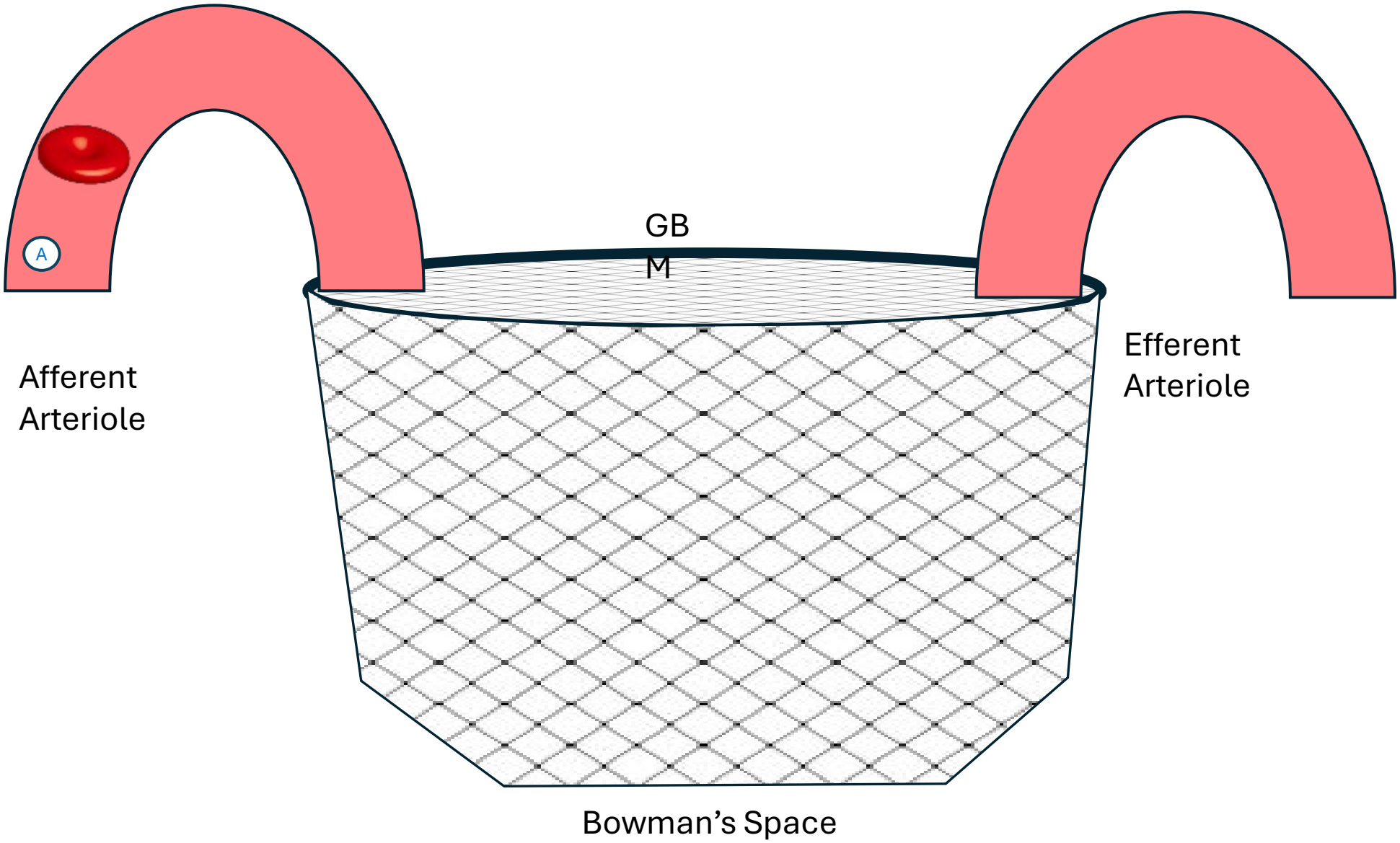
*Though the GBM and podocytes are highlighted here, similar immune reactions can occur in the mesangium (though generally with less severe clinical manifestations)

*Given role of immunity, many of these glomerular diseases are seen as complications of immunologically active disease- such as in autoimmune, infectious, or malignant conditions

Proteinuria vs Glomerular Hematuria



Proteinuria



Minimal Change Disease (MCD)

- Epidemiology:
  - Among children <10 years old, MCD is 90% of the causes for idiopathic nephrotic syndrome
  - Among children >10 years old, MCD accounts for 50%
  - MCD higher cause of nephrotic syndrome in Asian and Caucasian patient populations

- Clinical Presentation:
  - Often describe a rapid onset of signs/symptoms (days to weeks)
  - Nephrotic syndrome
  - AKI may be present, particularly in adults

- Diagnosis/Treatment:
  - To establish the diagnosis, need **Kidney Biopsy** (in children, this isn't necessary unless there other confounding elements)
  - Treatment: immunosuppression (very responsive to glucocorticoids- i.e. prednisone)

Minimal Change Disease (MCD)

- “Podocytopathy”
- Glomeruli appear normal on light and IF (hence, the minimal change…)
- EM shows diffuse podocyte effacement

Idiopathic (or primary)	Secondary MCD
• Etiology unclear • Possible T cell or B cell dysregulation • Possible glomerular “permeability factor” • Anti-nephrin Ab	Drugs (NSAIDs, antibiotics, pamidronate, lithium, immunizations)
	Neoplasms (hematologic- particularly Hodgkin lymphoma)
	Infections (mycoplasma, TB)

Membranous Nephropathy

(AKA Membranous glomerulonephritis or Membranous nephritis)

- Globally, most common cause of nephrotic syndrome in **nondiabetic adults**
  - Idiopathic more common in Caucasian men

Primary or Idiopathic (75% of all cases)	**Secondary**

• Known associated antibodies
  • Phospholipase A2 Receptor Ab (70% of idiopathic cases)
  • Thrombospondin type-1 domain-containing 7A Ab (3% of idiopathic cases)
  • Other antigen targets
  • Neural epidermal growth factor-like 1
  • Semaphorin 3B
  • Protocadherin 7
  • Serine protease HTRA1
  • Neutral endopeptidase
	• Infections: Hepatitis B, Syphilis
	• Autoimmune diseases
	  • Particularly Systemic Lupus Erythematosis
	• Drugs (NSAIDs, antibiotics, pamidronate, immunizations)
	• Malignancies
	  • Adenocarcinoma of the lung, GI tract, or breast

Focal Segmental Glomerulosclerosis (FSGS)

- Histologic diagnosis
  - The focal nature of FSGS may lead to the misclassification as minimal change disease due to kidney biopsy sampling error
- In the US, now the most common cause of idiopathic nephrotic syndrome (35% of all nephrotic syndrome cases)

Idiopathic (or primary)	Secondary FSGS
• "Podocytopathy" • Association with Apolipoprotein L1 gene variant (chromosome 22) in patients of African ancestry • Soluble form of urokinase plasminogen activator receptor (suPAR)? • Cardiotrophin-like cytokine factor 1 (CLCF1)?	• Adaptive response to hypertrophy or hyperfiltration • Association with Obesity

	• HIV- associated with "collapsing" variant
	  • Also known as HIV Associated Nephropathy (HIVAN)
	  • Seen more in uncontrolled HIV

	• Drugs/toxins (heroin, cyclosporine, pamidronate)
	• Scarring from other diseases (IgA, vasculitis, lupus nephritis)

HIV Associated Nephropathy (HIVAN)

- HIV infection has been associated with both acute kidney injury (AKI) and chronic kidney disease (CKD).
- HIV-associated nephropathy (HIVAN), characteristically is:
  - a collapsing form of focal sclerosing glomerulosclerosis (FSGS)
  - microcystic tubular dilatation
  - significant interstitial inflammation
- In patients with HIV-associated nephropathy (HIVAN), the following features are usually present:
  - Advanced HIV disease
  - Heavy proteinuria
  - Can lead to a rapid decline in renal function

Multiple Myeloma (MM)

- Monoclonal plasma cell proliferation with overproduction of immunoglobulins
- Diagnosis can be made on kidney biopsy, but can also be made if monoclonal serum light chains present with bone marrow biopsy consistent with MM and lytic bone lesions
- **Typically dipstick negative/trace protein (no albumin) but quantitative collection with significant protein**
- Tests that can differentiate types of immunoglobulin light chains and detect a clonal proliferation
  - Serum free light chain assay- quantitates circulating kappa and lambda free light chains
  - Serum protein electrophoresis (SPEP) and immunofixation- looking for M-protein
  - Urine protein electrophoresis (UPEP) and immunofixation- looking for M-protein

Multiple Myeloma (MM)

- AKI or CKD can occur
  - Tubular:
    - Light chain cast nephropathy
    - ATN from volume depletion and/or hypercalcemia
  - Glomerular:
    - Light chain amyloidosis
- MM can present with different electrolyte abnormalities
- Associated with Fanconi syndrome
  - Hypokalemia, metabolic acidosis, glucosuria, and/or hypophosphatemia

Amyloidosis

- A deposition disease
  - AL (primary)- a plasma cell dyscrasia
  - AA (secondary)- associated with chronic inflammatory conditions
- Clinical Presentation:
  - Nephrotic range proteinuria (especially AL – glomerular deposition)
  - Typically benign urinary sediment
  - CKD due to vascular deposition
  - AKI due to cast nephropathy
- Diagnosis: can check SPEP/UPEP, kappa/lambda ratio, fat pad biopsy, **kidney biopsy** (or affected primary organ)
- Therapy: depends on primary vs secondary amyloidosis
  - Primary: Bortezomib, melphalan, dexamethasone
  - Secondary: Treat the underlying condition

Diabetic Nephropathy

- DN can occur in both type 1 and type 2 DM
- Clinical Presentation:
  - Albuminuria or nephrotic range proteinuria
    - Natural progression is for progressively worsening degrees of proteinuria (i.e. the patient does not go from no proteinuria to 3.5 grams proteinuria over a few months)
  - Can see intermittent microscopic hematuria
    - Develop microaneurysms in glomeruli that may rupture
  - CKD
  - Other clinical characteristics of suggestive of small vessel disease in DM (retinopathy, neuropathy, etc)
- Pathologic findings include:
  - Mesangial expansion, GBM thickening, foot process effacement, glomerular sclerosis, Kimmelstiel-Wilson nodules

Diabetic Nephropathy

- Diagnosis: typically clinical diagnosis based on duration of DM (usually 10+ years), glycemic control (HbA1c), association of retinopathy and/or neuropathy, and if unsure- **Kidney Biopsy**
- Treatment:
  - Glycemic control (HbA1c target 6.5-8.0%)
  - Blood pressure control (under 130/80 in most cases)
  - *ACE/ARB* (Aldosterone receptor blocker)
  - *SGLT2 inhibitors* for type 2 diabetics
  - Finerenone for type 2 diabetics
  - GLP1 agonist for type 2 diabetics

Nephritic Syndrome/Glomerular Hematuria

Glomerulonephritis

Glomerular Hematuria

Direct Antibody Mediated

- Anti-GBM Disease
- If lung involvement, GoodPasture Syndrome

Immune Complex Mediated

Low C'

- IRGN/PIGN
- Lupus nephritis (Class III/IV)
- MPGN
- Cryoglobulinemia

Normal C'

- IgA Nephropathy

Pauci-Immune

ANCA-Associated

- Granulomatosis with polyangiitis (GPA)
  - c-ANCA
  - Anti-PR3 Ab
- Microscopic polyangiitis (MPA)
  - p-ANCA
  - Anti-MPO Ab
- Eosinophilic granulomatosis with polyangiitis

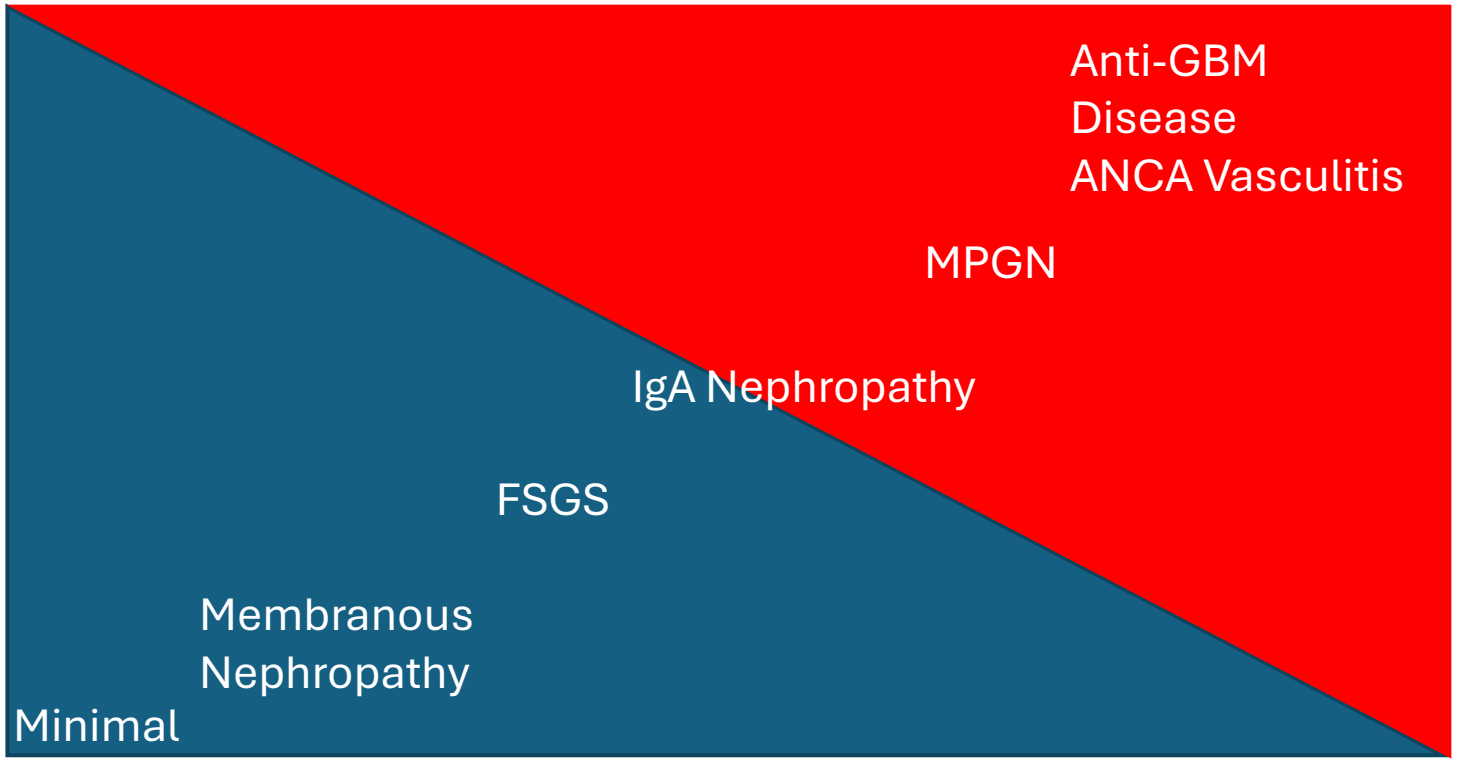
Non-ANCA

- HUS/TTP
- DIC
- HTN Emergency
- Scleroderma Renal Crisis
- Pre-E/Eclampsia

Genetic

- Thin Basement Membrane Ds
- Alport

Nephrosis or Nephritis- Overlap




= Nephrotic Urine


= Nephritic Urine

Obejective

Illustrate examples of urinalysis findings that warrant referral to Nephrology or Urology

Nephrology Referral

- KDIGO:
  - Albuminuria (≥300 mg/g) in combination with hematuria, or a twofold or greater increase in albuminuria in patients being monitored for significant albuminuria, or an albumin-creatinine ratio that is consistently >700 mg/g
  - Erythrocyte casts
  - >20 Erythrocytes/hpf that is sustained and not readily explained*
    - *with concomitant proteinuria

Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2024 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. Kidney Int. 2024 Apr;105(4S):S117-S314. doi: 10.1016/j.kint.2023.10.018. PMID: 38490803.

Nephrology Referral

Sidebar 8: Potential Indications for Nephrology Consultation
• eGFR <30 mL/min/1.73 m^2
• Rapid decline of eGFR (>5 mL/min/1.73 m^2 per year)
• 5-year risk of kidney failure >3-5% (see Risk Equations Table)
• Non-diabetics with confirmed heavy albuminuria (UACR >300 mg/g, 24-hr urine protein >500 mg, UPCR >0.5 g/g)
• Diabetes with persistent (>1000 mg/g) albuminuria despite RAASi/SGLT2i, or inability to use RAASi/SGLT2i
• Hematuria with albuminuria, glomerular hematuria (e.g., dysmorphic RBC, RBC casts), or hematuria after negative urologic work-up
• Polycystic kidney disease (PKD)
• Kidney transplant recipient
• CKD in a patient <45 years
• Suspected genetic cause of CKD
• Unclear origin of kidney dysfunction or albuminuria
• Metabolic management (prevention) of kidney stone disease
• Electrolyte abnormalities (e.g., hyperkalemia, hyponatremia)
• Complications of CKD (e.g., anemia, metabolic acidosis, hyperphosphatemia, hyperparathyroidism)
• Patient's level of disease exceeds the comfort level of the primary care provider

U.S. Department of Veterans Affairs & U.S. Department of Defense. (2025). The primary care management of chronic kidney disease: VA/DoD Clinical Practice Guideline (Version 4.0). VA/DoD Evidence-Based Practice Work Group. https://www.healthquality.va.gov/guidelines/CD/ckd

Urology Referral

Sidebar 7: Indications for Urology Consultation
• Gross hematuria
• Microhematuria in the absence of albuminuria
• Kidney masses or complex kidney cysts
• Symptomatic or obstructing nephrolithiasis
• Hydronephrosis or bladder abnormalities
• Persistent urinary symptoms despite treatment (e.g., nocturia, hesitancy, urgency, incontinence)
• Urinary retention

U.S. Department of Veterans Affairs & U.S. Department of Defense. (2025). The primary care management of chronic kidney disease: VA/DoD Clinical Practice Guideline (Version 4.0). VA/DoD Evidence-Based Practice Work Group. https://www.healthquality.va.gov/guidelines/CD/ckd

Case 1

- A 58 yo woman presents to your clinic to establish care as a new patient. She has diabetes mellitus type 2 treated with metformin and hypertension treated with Lisinopril. She has had diabetes for 18 years and has been treated for hypertension for 12 years. The patient's most recent HbA1c one month shows good control of her blood glucose with a value of 7.2%. Review of records indicates that 5 years ago (and prior), her diabetes was less well controlled- with HbA1c values consistently in the 9-9.5% range. She takes no other medications.
- On exam her blood pressure is 146/80. Her BMI is 33. She has mild ankle edema, but her exam is otherwise unrevealing.
- Labs reveal Na 138, K 4.8, Cl 100, HCO3 24, BUN 26, Cr 1.3 (1.1 6 months ago), calcium 9.8, albumin 3.5 g/dL, glucose of 120.
- UA dipstick with 2+ proteinuria, mild glucosuria, but normal microscopy. A spot urine protein to creatinine ratio reveals 3000 mg/g Cr (~3 grams protein/24 hours). Review of urine protein measurements from 1 year ago reveal ~1.5 gram/24 hours and 500 mg/24 hours 3 years ago.
- What is the most likely diagnosis?

A. Minimal Change Disease
B. Amyloidosis
C. Diabetic Nephropathy
D. Membranous Nephropathy

Case 2

- A 62 yo man comes to clinic for routine follow up. He has a history of hypertension controlled on stable doses of hydrochlorothiazide and losartan for several years, GERD on pantoprazole, and hyperlipidemia on atorvastatin. He comes to clinic for routine follow up. He takes no over the counter medications and is without complaints.
- On exam his blood pressure is 136/80. He has trace pretibial edema, but exam and vital signs are otherwise unremarkable.
- Labs reveal Na 140, K 4.6, Cl 98, HCO3 20, BUN 26, Cr 1.7 mg/dL (1.3 mg/dL 3 months ago, 1.0 mg/dL 6 months ago). Remainder of his chemistry panel and CBC are normal. UA dipstick with trace proteinuria, otherwise unremarkable. Urine microscopy shows 10-20 white blood cells/hpf, 0-5 RBC/hpf, no casts.
- Which of the following is the next best step in management?

A. Begin trimethoprim-sulfamethoxazole
B. Discontinue losartan
C. Discontinue pantoprazole
D. Obtain a urine culture
E. Refer to Nephrology

Case 3

- A 52 yo man comes to clinic to establish care. He has not routinely sought healthcare. History is significant for a 40-pack year tobacco use habit. In general, he has been feeling more run down recently and notes intermittent fevers over the past couple of weeks. He has chronic joint aches for which he takes occasional ibuprofen. He does not take any other over the counter medications. The patient notes his urine is intermittently darker, but otherwise has no complaints.
- On exam his blood pressure is 152/90. He has 1+ pretibial edema, and mild coarse breath sounds to his right lung base. but exam and vital signs are otherwise unremarkable.
- Labs reveal Na 136, K 5.0, Cl 102, HCO3 20, BUN 38, Cr 2.0 mg/dL with no known baseline. Remainder of his chemistry panel and CBC are normal. UA dipstick with + proteinuria, +heme, + leukocyte esterase. Urine microscopy shows 10-20 white blood cells/hpf, >50 RBC/hpf, no casts. Spot urine protein to creatinine ratio is 1000 mg/g creatinine.
- Which of the following is the next best step in management?

A. Repeat testing in one week
B. Refer to Urology
C. Refer to Nephrology
D. Begin antibiotic therapy

Case 4

- A 52 yo man comes to clinic to establish care. He has not routinely sought healthcare. History is significant for a 40-pack year tobacco use habit. In general, he has been feeling more run down recently and notes intermittent fevers over the past couple of weeks. He has chronic joint aches for which he takes occasional ibuprofen. He does not take any other over the counter medications. He had an episode of frank hematuria once two weeks ago that is now resolved.
- On exam his blood pressure is 152/90. He has 1+ pretibial edema, and mild coarse breath sounds to his right lung base. but exam and vital signs are otherwise unremarkable.
- Labs reveal Na 136, K 5.0, Cl 102, HCO3 20, BUN 18, Cr 1.0 mg/dL. Remainder of his chemistry panel and CBC are normal. UA dipstick with +heme, + leukocyte esterase. Urine microscopy shows 10-20 white blood cells/hpf, >50 RBC/hpf, no casts. Spot urine protein to creatinine ratio is < 100 mg/g creatinine.
- Which of the following is the next best step in management?

A. Repeat testing in one week

B. Refer to Urology

C. Refer to Nephrology

D. Begin antibiotic therapy