Chronic Kidney Disease

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Chronic kidney disease (CKD)

- Chronic kidney disease (CKD) is defined as an abnormality of kidney structure or function that persists for > 3 months.

@Kidney Failure
↳ Part of chronic

Risk factors for CKD

- Diabetes
- Hypertension
- Obesity
- Advanced age (> 60 years of age) [2]
- Substance use (smoking, alcohol and drugs)
- Acute kidney injury
- Family history of CKD
- African American or Hispanic descent [3]

Pathophysiology

- Pathophysiology depends on the underlying condition, any of which will eventually lead to progressive nephron loss, structural damage, and impaired kidney function.

Un controlled

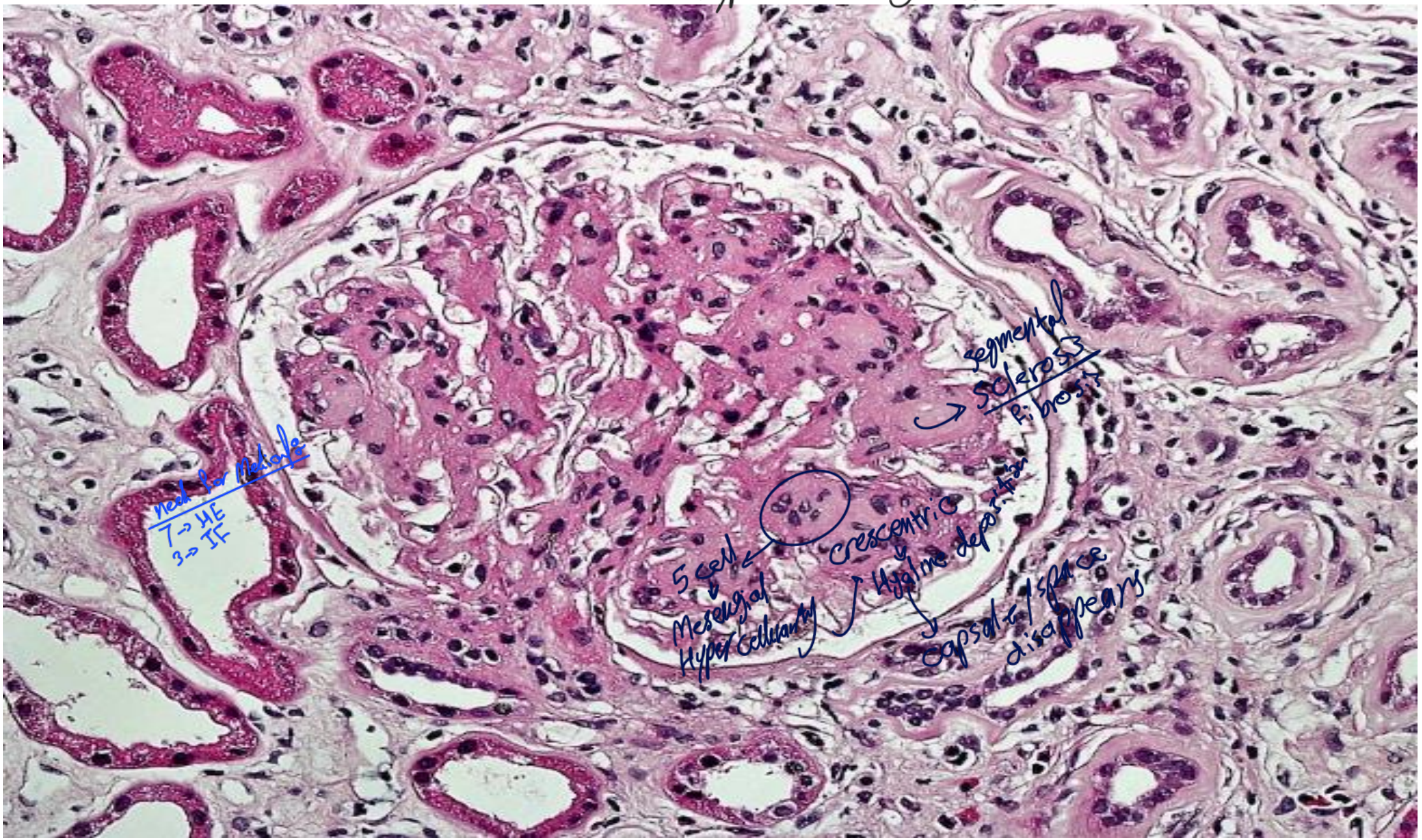
Diabetic nephropathy

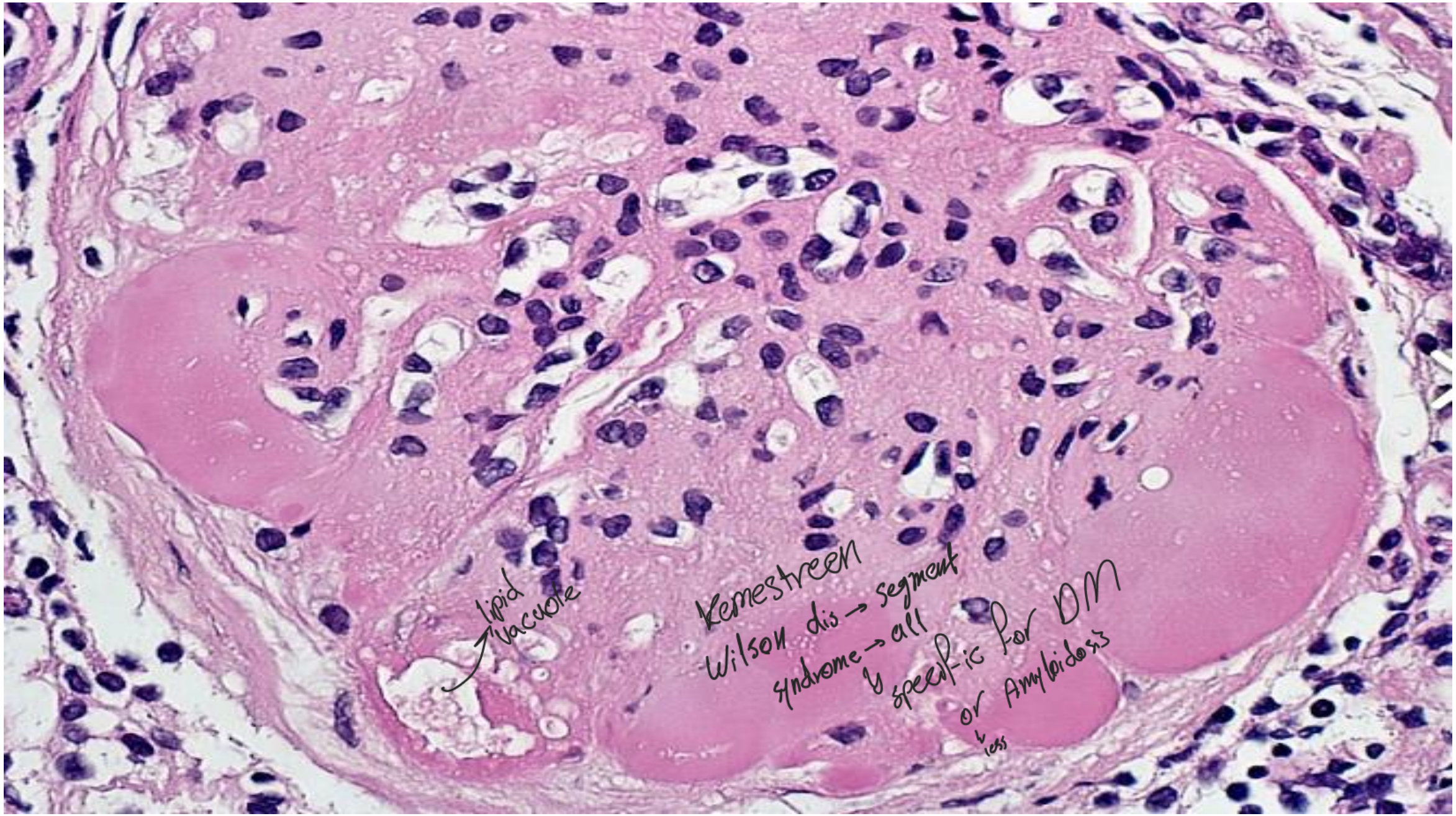
- Hyperglycemia → nonenzymatic glycation of proteins → varying degrees of damage to all types of kidney cell.
- Pathological changes include:
  - Hypertrophy and proliferation of mesangial cells, GBM thickening, and ECM proteins accumulation → eosinophilic nodular glomerulosclerosis
  - Thickening and diffuse hyalinization of afferent and efferent arterioles/interlobular arteries
- Interstitial fibrosis, TBM thickening, and tubular hypertrophy.

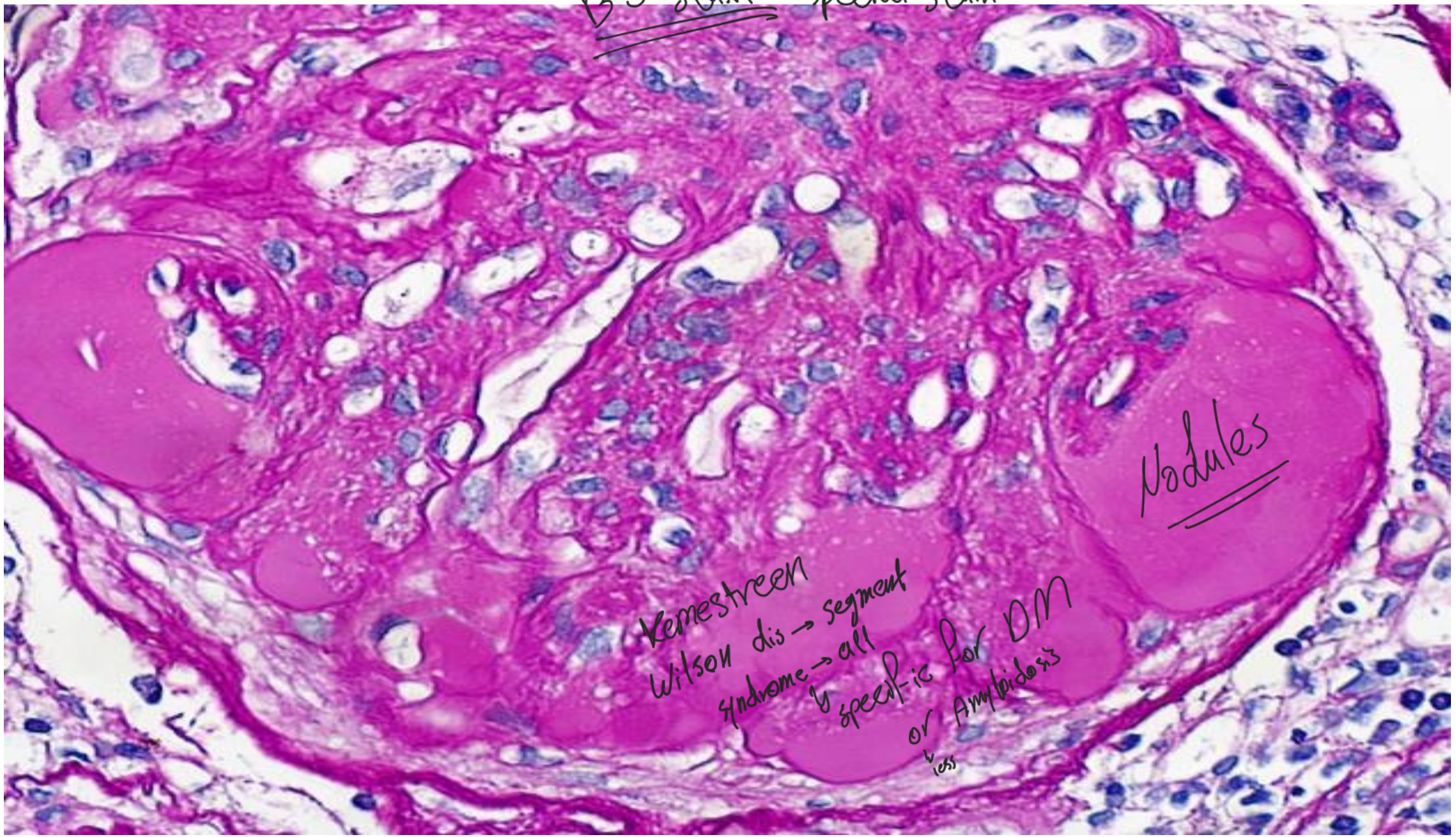
deposition

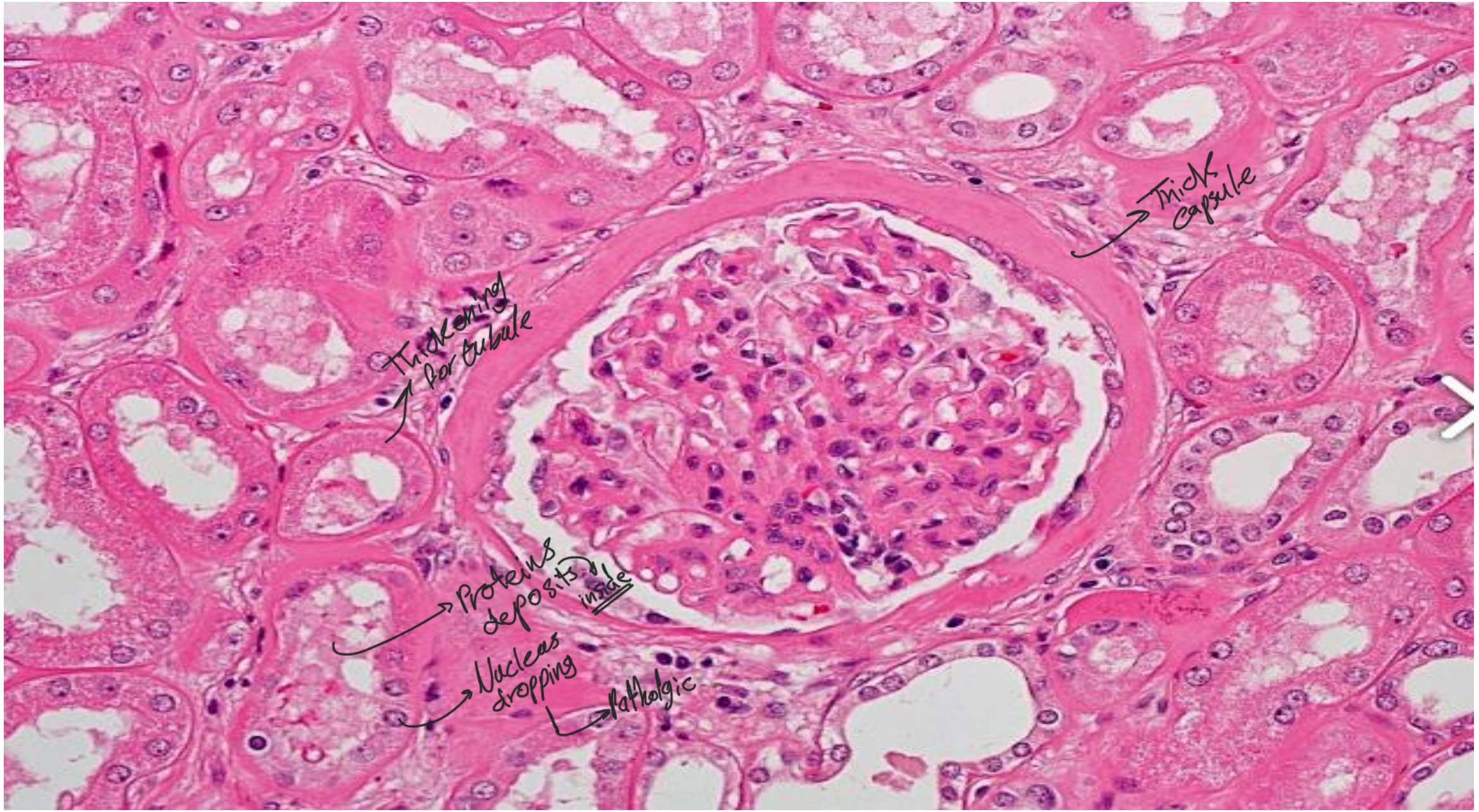
1st to be affected → glomeruli

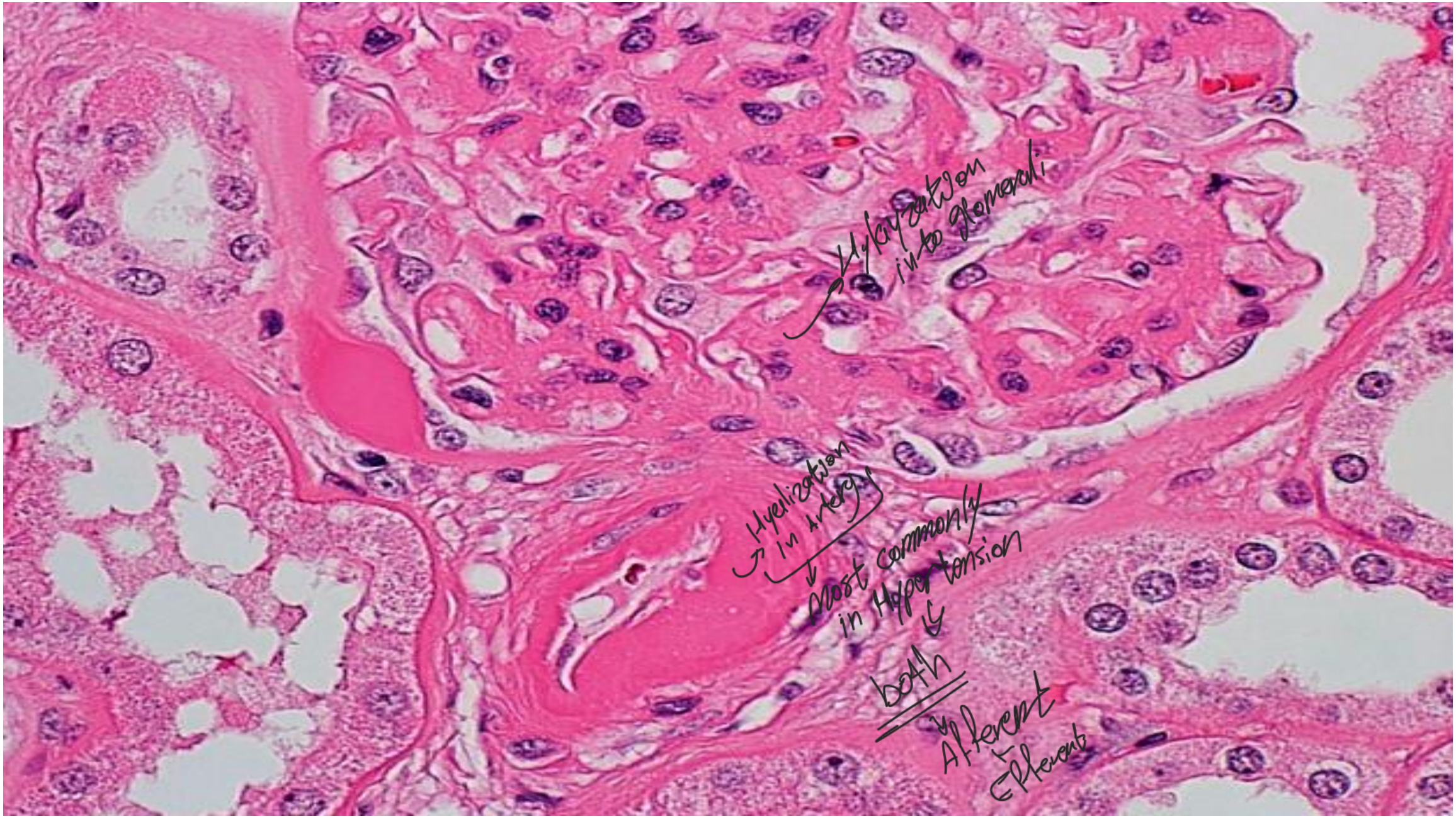
Hypercellularity (before Nodules)

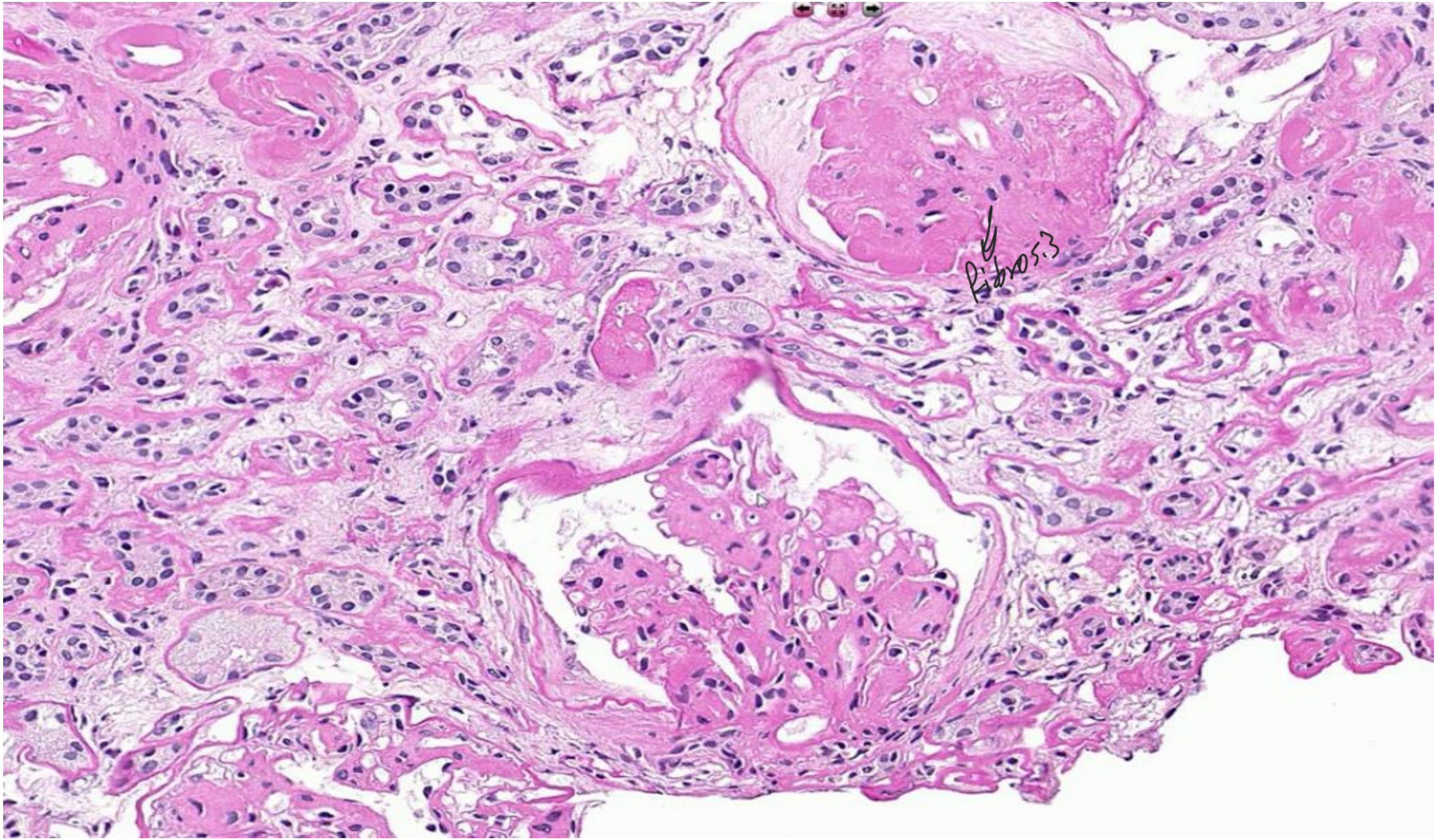


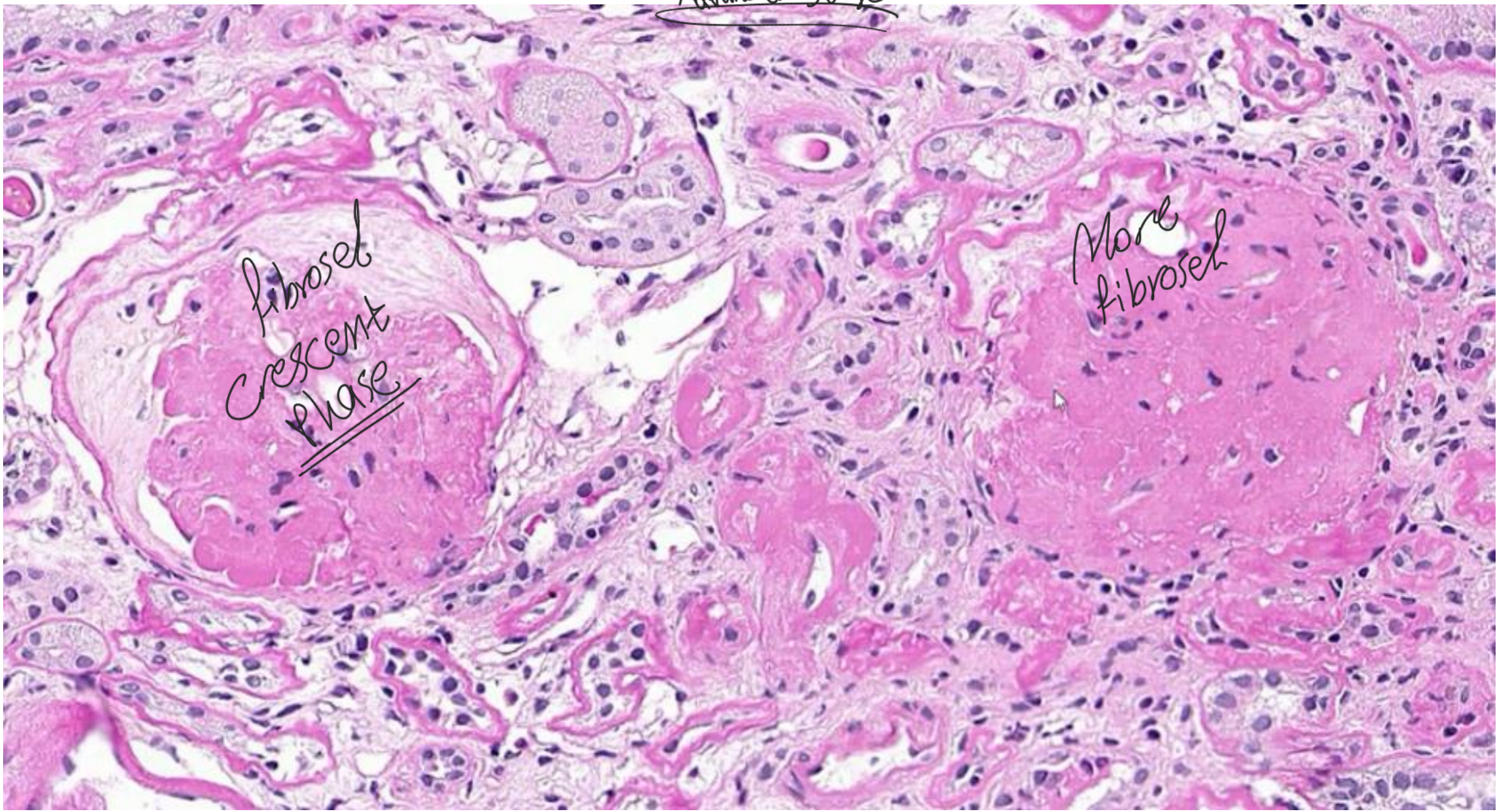

lipid vacuole
Kemestreen
Wilson dis → segment
syndrome → all
& specific for DM
or Amyloidosis
↳ less

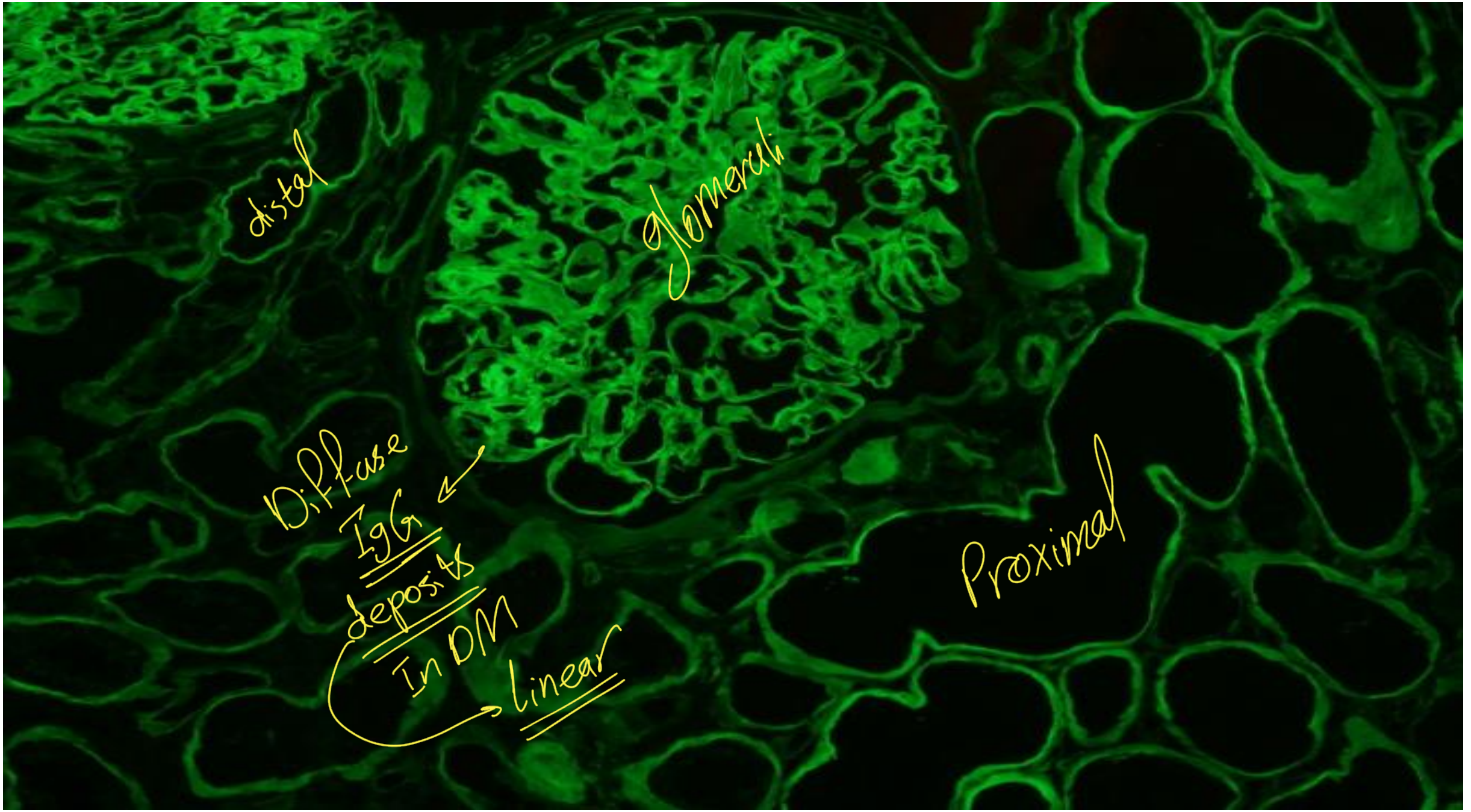

BS stain special stain
Nodules
Kemestreen
Wilson dis → segment
syndrome → all
y specific for DM
or Amyloidosis
less

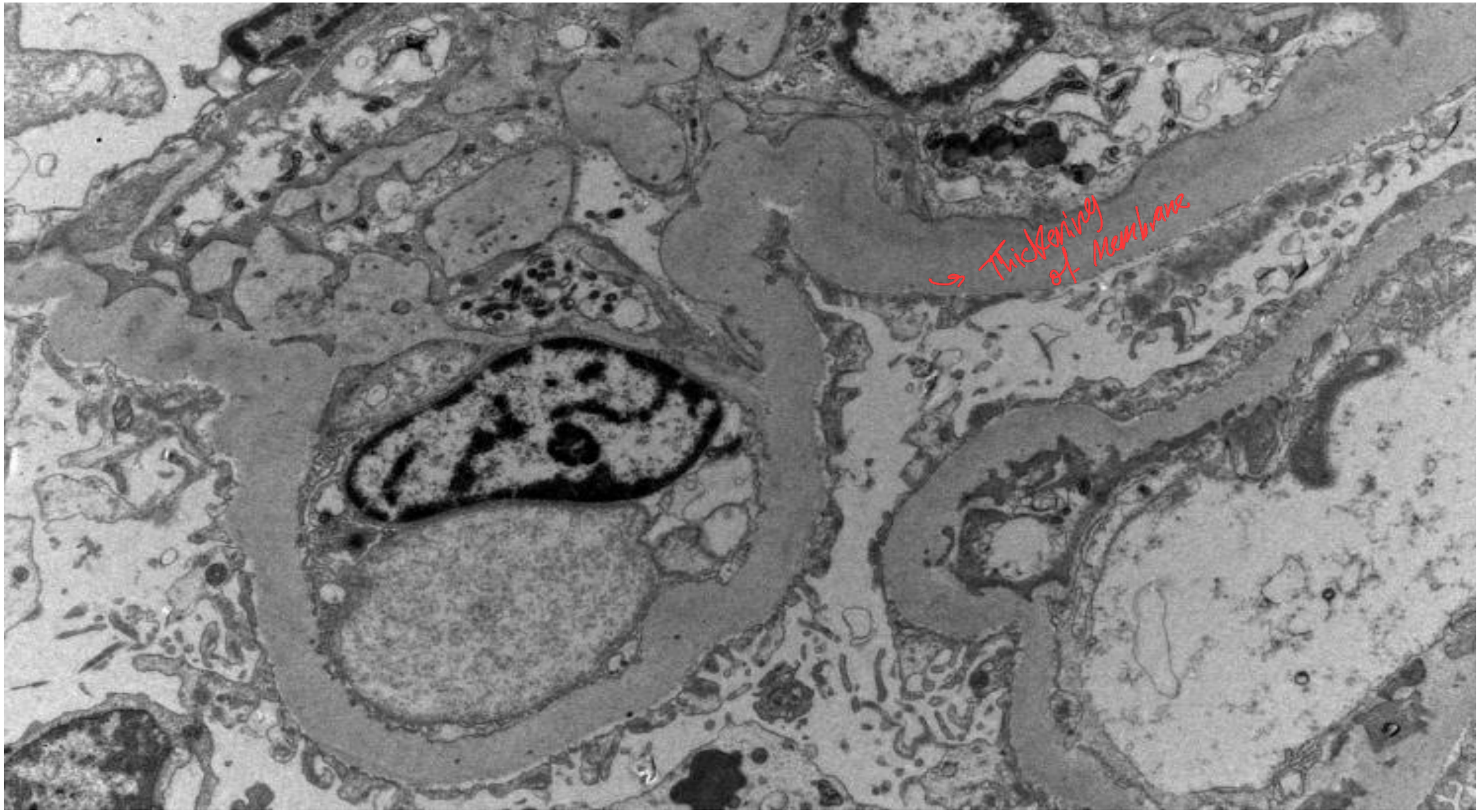

Thickening of Bowman capsule
Thick capsule
Proteins deposits inside
Nucleus dropping
Pathologic


Hyalinization in glomeruli
Hyelinization in artery
most commonly in Hypertension
both
Afferent
Efferent


Fibrosis


Advanced Stage
Fibrosed crescent Phase
More fibrosed

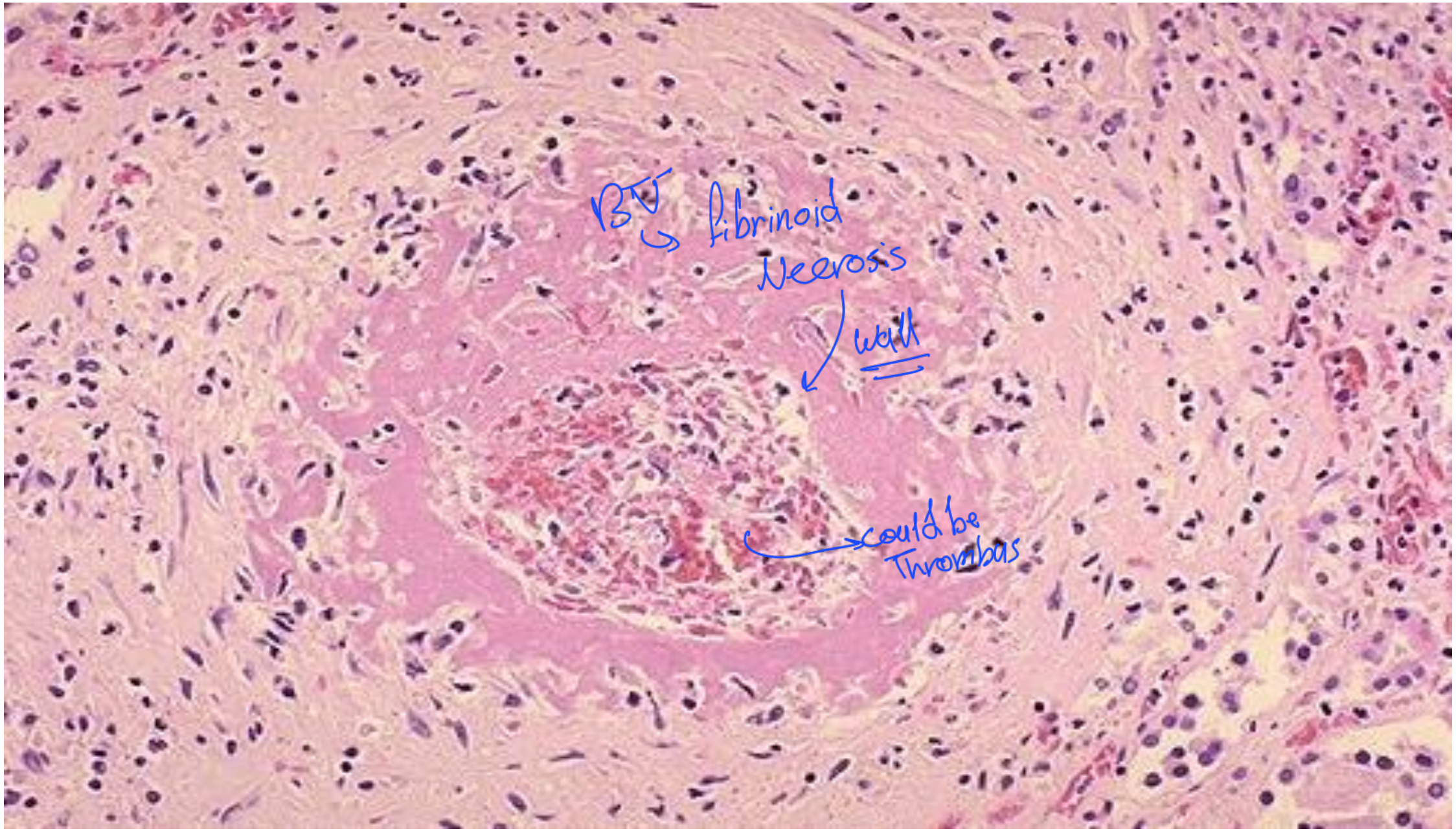

distal
glomeruli
Diffuse
IgG
deposits
In DM
linear
Proximal


Thickening
of Membrane

Uncontrolled

Hypertensive nephropathy

- Increased systemic blood pressure (e.g., due to chronic hypertension) below the protective autoregulatory threshold → benign nephrosclerosis (sclerosis of afferent arterioles and small arteries) → ↓ perfusion → ischemic damage → Not specific
- In case BP exceeds threshold → acute injury → malignant nephrosclerosis (petechial subcapsular hemorrhages, visible infarction with necrosis of mesangial and endothelial cells, thrombosis of glomeruli capillaries, luminal thrombosis of arterioles, and red blood cell extravasation and fragmentation) → failure of autoregulatory mechanisms → ↑ damage


BV → fibrinoid Necrosis
wall
could be Thrombus

Consequences

- **Reduced GFR:**
  - ↓ Production of urine → ↑ extracellular fluid volume → total-body volume overload
  - ↓ Excretion of waste products (e.g., urea, drugs)
  - ↓ Excretion of phosphate → hyperphosphatemia → Ca ↓ → Vit. D ↓ → Hypocalcemia → Parathyroid hormone ↑
- During the early stages of CKD, plasma phosphate levels will typically be normal due to the increased secretion of fibroblast growth factor 23 (FGF23).
  - ↓ synthesized by osteoclast

    - FGF23 is produced by osteoblasts in response to initial hyperphosphatemia and increased calcitriol.
    - Increased secretion of FGF23 leads to increased phosphate secretion and suppressed conversion of 25-hydroxyvitamin D to 1,25-dihydroxyvitamin D.
    - In advanced CKD, the effects of FGF23 subside (most likely due to development of resistance in target tissues). [8]
- ↓ Maintenance of acid-base balance → metabolic acidosis
- ↓ Maintenance of electrolyte concentrations → electrolyte imbalances (e.g., Na^+ retention)

- **<u>Reduced endocrine activity:</u>**
  - ↓ Hydroxylation of calcifediol → ↓ production of calcitriol → (in combination with ↓ excretion of phosphate) → ↓ serum Ca → ↑ PTH
  - ↓ Erythropoietin → ↓ stimulation of erythropoiesis

Inactive form of Vit.D

Clinical features

- Patients are often asymptomatic until later stages due to the exceptional compensatory mechanisms of the kidneys.
- **Manifestations of Na^+/H_2O retention**

Hypertension and heart failure → Right → Pulmonary Edema → Left → Peripheral Edema

Pulmonary and peripheral edema

- **Manifestations of uremia**

Definition: Uremia is defined as the accumulation of toxic substances due to decreased renal excretion. These toxic substances are mostly metabolites of proteins such as urea, creatinine, β_2 microglobulin, and parathyroid hormone.

- **Constitutional symptoms**
  - Fatigue
  - Weakness
  - Headaches
- **Gastrointestinal symptoms**
  - Nausea and vomiting
  - Loss of appetite
  - Uremic fetor: characteristic ammonia- or urine-like breath odor
- **Dermatological manifestations**
  - **Pruritus**
  - Skin color changes (e.g., hyperpigmentation, pallor due to anemia)
- Uremic frost: uremia leads to high levels of urea secreted in the sweat, the evaporation of which may result in tiny crystallized yellow-white urea deposits on the skin.

Diagnostic criteria

- **Criteria for chronic kidney disease** (CKD) include the persistence of eGFR < 60 mL/min/1.73 m^2 (≥ G3a) **and/or** of any of the following markers of kidney damage for > 3 months:
  - Albuminuria: e.g., urine albumin-to-creatinine ratio (UACR) > 30 mg/g (≥ A2)
  - Urine sediment abnormalities: e.g., hematuria
  - Abnormalities due to tubulointerstitial dysfunction, e.g.:
    - Electrolyte and acid-base imbalances
    - Retention of nitrogenous wastes
    - Reduced production of erythropoietin, 1,25-dihydroxyvitamin D, and/or renin
  - Histological abnormalities on biopsy
  - Imaging showing structural abnormalities: e.g., polycystic kidney disease
- History of renal transplant

familial

- **Stages of chronic renal failure:**
  - Diminished renal reserve (GFR 50% normal) with normal BUN/creatinine
  - Renal insufficiency: azotemia, anemia, hypertension, polyuria and nocturia
  - Renal failure: GFR < 20% normal, kidneys cannot regulate volume of solutes and patient develops edema, metabolic acidosis and hypocalcemia
  - End stage renal disease: GFR < 5% normal, represents the end stage of various renal diseases

CGA classification of chronic kidney disease

- CKD is classified according to the cause, eGFR category, and albuminuria category; this is referred to as the CGA classification.
- **Clinical uses**
  - Standardized documentation of CKD stages
  - Identification of CKD progression
  - Determination of the frequency of patient monitoring
- **Interpretation**: Higher stages correlate with a poorer prognosis. [11]
  - Increased risk of CKD progression and mortality (e.g., all-cause mortality, cardiovascular mortality)
- Increased risk of developing complications (e.g., AKI, CKD-mineral and bone disorder)

End-stage renal disease (ESRD)

- Irreversible kidney dysfunction with eGFR < 15 mL/min/1.73 m^2
- Manifestations of uremia requiring chronic renal replacement therapy with either dialysis or renal transplantation

Stage of CKD	eGFR result	What it means
Stage 1	90 or higher	- Mild kidney damage - Kidneys work as well as normal
Stage 2	60-89	- Mild kidney damage - Kidneys still work well
Stage 3a	45-59	- Mild to moderate kidney damage - Kidneys don't work as well as they should
Stage 3b	30-44	- Moderate to severe damage - Kidneys don't work as well as they should
Stage 4	15-29	- Severe kidney damage - Kidneys are close to not working at all
Stage 5	less than 15	- Most severe kidney damage - Kidneys are very close to not working or have stopped working (failed)

Cause

- **Systemic vs. primary cause**: Determine if kidney disease is associated with a systemic disease (e.g., diabetes) or if it is primary kidney disease (e.g., polycystic kidney disease).
- **Location**: Determine the location (presumed or confirmed) of the damage within the kidney.
  - Glomerular
  - Tubulointerstitial
  - Vascular
  - Cystic and congenital

Diagnostics

- The goals of the diagnostic evaluation include confirming the chronicity of kidney dysfunction and identifying the cause of kidney disease.
- **Parameters of renal function:**

Serum markers:

↑ creatinine and BUN (alternatively, ↑ cystatin C)

could be dehydration but not that high.

first stages of kidney failure

Glomerular filtration rate: ↓ eGFR

Ultrasound of the kidneys and urinary tract

- First-line imaging technique for the assessment of kidney structure
- Consider obtaining for all patients to further support the diagnosis and help determine the etiology.
- Findings that suggest chronic kidney damage include: [12]
  - ↓ Kidney length (< 10 cm)
  - ↓ Parenchymal and/or cortical thickness
  - ↑ Cortical echogenicity
  - Cysts
  - Calcifications → specially → artery
- Findings that suggest specific etiologies
  - Ureteral or renal pelvic dilation suggests obstructive nephropathy.
  - Bilaterally enlarged kidneys with multiple cysts suggest polycystic kidney disease.

Renal biopsy

- Not routinely indicated
- Consider in either of the following situations:
  - Rapid and unexplained decline in eGFR
  - Need for diagnostic confirmation of the underlying etiology (e.g., glomerulonephritis) prior to initiating disease-specific therapy
- Renal biopsy is only indicated in patients in whom the underlying cause of CKD is still unclear after noninvasive testing, the results are likely to influence management, and the potential benefits are thought to outweigh the risks.

Management

2nd cause → treat the cause

- **Nutritional management:**

Fluid intake: Ensure appropriate fluid intake and avoid dehydration.

Protein and energy consumption

  - Mediterranean diet, ↑ fruit and vegetable intake
  - Protein restriction (e.g., 0.55–0.60 g/kg/day)

- **Electrolytes**
  - Sodium restriction (< 2.3 g/day)
  - Potassium intake adjustment ↳ عالية → dialysis
  - Phosphorus intake adjustment
- **Micronutrients**: Consider multivitamin supplementation for patients with inadequate dietary vitamin (e.g., vitamin D) intake.

Medication management

✳Don't give NSAID's or overload fluid for Renal failure patients.

- **Renally cleared medications**: Adjust dosing based on the patient's eGFR.
- **Potentially nephrotoxic substances**
  - Avoid use (except when the benefits outweigh the risks).
  - Contrast imaging
  - The risk of contrast-induced nephropathy is highest in patients with eGFR < 30 mL/min/1.73 m^2.