KIDNEY DISEASES

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Kidney Diseases

- Renal failure (acute & chronic)
- Glomerular Syndromes
- Interestitial Diseases
- Vascular Disease
- Nephrolithiasis
- Urinary obstructions
- Asymptomatic urinary abnormalities

Acute Renal Failure

- Sudden interruption of kidney function resulting from obstruction, reduced circulation, or disease of the renal tissue
- Results in retention of toxins, fluids, and end products of metabolism
- Usually reversible with medical treatment
- May progress to end stage renal disease, uremic syndrome, and death without treatment

Acute Renal Failure

- Causes
  - Prerenal
    - Hypovolemia, shock, blood loss, embolism, pooling of fluid d/t ascites or burns, cardiovascular disorders, sepsis
  - Intrarenal
    - Nephrotoxic agents, infections, ischemia and blockages,
  - Postrenal
    - Stones, blood clots, BPH, urethral edema from invasive procedures

Acute Renal Failure

- Stages
  - Onset – 1-3 days with ^ BUN and creatinine and possible decreased UOP
  - Oliguric – UOP < 400/d, ^BUN,Crest, Phos, K, may last up to 14 d
  - Diuretic – UOP ^ to as much as 4000 mL/d but no waste products, at end of this stage may begin to see improvement
  - Recovery – things go back to normal or may remain insufficient and become chronic

Acute Renal Failure

- Subjective symptoms
  - Nausea
  - Loss of appetite
  - Headache
  - Lethargy
  - Tingling in extremities

Acute Renal Failure

- Objective symptoms
  - Oliguric phase –
    - vomiting
    - disorientation,
    - edema,
    - ^K+
    - decrease Na
    - ^ BUN and creatinine
    - Acidosis
    - uremic breath
    - CHF and pulmonary edema
    - hypertension caused by hypovolemia, anorexia
    - sudden drop in UOP
    - convulsions, coma

Acute Renal Failure

- Objective systoms
  - Diuretic phase
    - Increased UOP
    - Gradual decline in BUN and creatinine
    - Hypokalemia
    - Hyponaturmia
    - Tachycardia
    - Improved LOC

Acute Renal Failure

- Diagnostic tests
  - H&P
  - BUN, creatinine, sodium, potassium. pH, bicarb. Hgb and Hct
  - Urine studies
  - US of kidneys

Background---CKD

- chronic kidney disease (CKD) as either kidney damage or a decreased kidney glomerular filtration rate (GFR) of <60 mL/min/1.73 m2 for 3 or more months.

Chronic Renal Failure

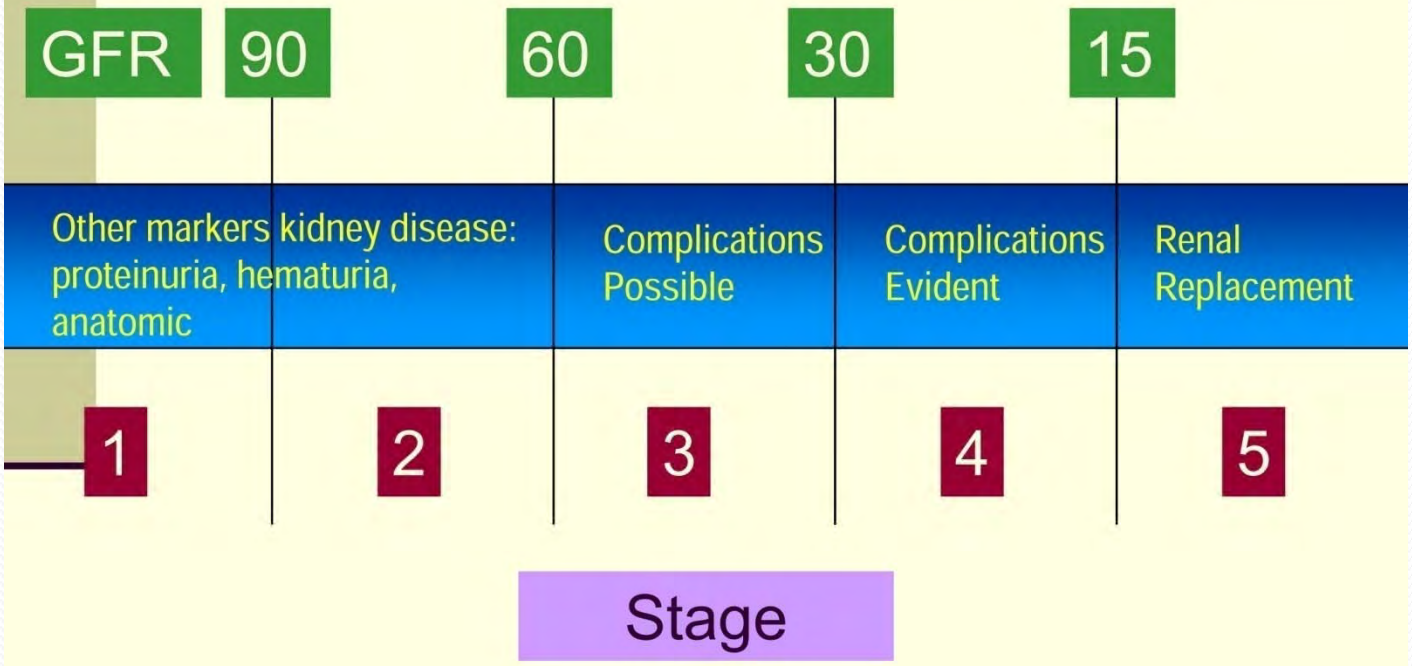
- Objective symptoms
  - Skeletal
    - Muscle and bone pain
    - Bone demineralization
    - Pathological fractures
    - Blood vessel calcifications in myocardium, joints, eyes, and brain
  - Skin
    - Yellow-bronze skin with pallor
    - Puritus
    - Purpura
    - Uremic frost
    - Thin, brittle nails
    - Dry, brittle hair, and may have color changes and alopecia

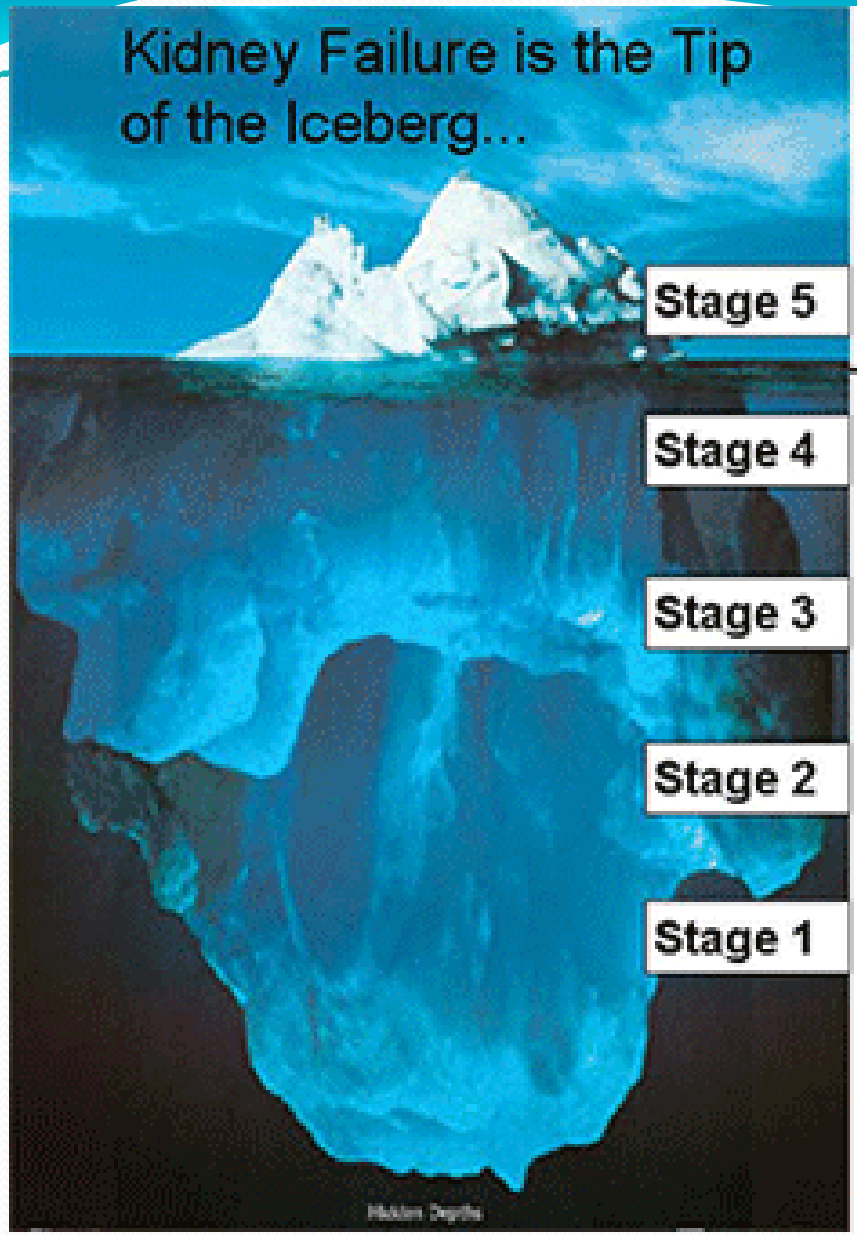
Chronic Renal Failure

- Other abnormal findings
  - Metabolic acidosis
  - Fluid imbalance
  - Insulin resistance
  - Anemia
  - Immunoligical problems

K/DOQI CKD Staging

Requires 2 or more GFR, 3 or more months apart





Prevalence of Chronic Kidney Disease (CKD):

Kidney Failure/End-stage kidney disease (GFR <15): 400,000

GFR 15–29: 300,000

GFR 30–59: 7,400,000

Kidney damage & GFR 60–89: 5,700,000

Kidney damage & GFR >90: 5,600,000

19 million Americans with CKD

8 million Americans with GFR<60

Coresh et al. J Am Soc Nephrol 2005;16(1):180-8

http://www.unckidneycenter.org/kcpp/i

Pathophysiology

- Regardless of the etiology of renal injury, with progressive destruction of nephrons, the kidney has an innate ability to maintain GFR by hyperfiltration and compensatory hypertrophy of the remaining healthy nephrons.

- The residual nephron hyperfiltration and hypertrophy, although beneficial for the reasons noted, has been hypothesized to represent a major cause of progressive renal dysfunction. This is believed to occur because of increased glomerular capillary pressure, which damages the capillaries and leads initially to focal and segmental glomerulosclerosis and eventually to global glomerulosclerosis.,

Pathophysiology

- Factors other than the underlying disease process and glomerular hypertension that may cause progressive renal injury include the following:
- Systemic hypertension
- Acute insults from nephrotoxins or decreased perfusion
- Proteinuria
- Hyperlipidemia
- Hyperphosphatemia with calcium phosphate deposition

Hyperkalemia

- when GFR falls to less than 20-25 mL/min .
- It can be observed sooner
  - ingest a potassium-rich diet
  - if serum aldosterone levels are low, such as in type IV renal tubular acidosis
    - Diabetes
    - ACE inhibitors & ARB
    - NSAIDs
  - extracellular shift of potassium
    - acidemia
    - lack of insulin

Metabolic acidosis

- CKD stage 5

- Unable to produce enough ammonia in the proximal tubules to excrete the endogenous acid into the urine in the form of ammonium.
- In CKD stage 5, accumulation of phosphates, sulphates, and other organic anions are the cause of the small anion gap.

Fluid overload

- Extracellular volume expansion and total-body volume overload
- GFR falls to less than 10-15 mL/min,
  - Peripheral edema
  - Pulmonary edema
  - Hypertension

Ca & P

- Secondary hyperparathyroidism
- Hypocalcemia
- Decreased renal synthesis of 1,25-Dihydroxycholecalciferol
- Hyperphosphatemia

Osteodystrophy

- severe CKD

  Osteitis fibrosa (high–bone turnover PTH↑)
- Osteomalacia (aluminum accumulation)
- Adynamic bone disease
- Dialysis-related amyloidosis
  - Beta2-microglobulin accumulation
  - Chronic dialysis for at least 8-10 years .

Anemia

- Normochromic normocytic anemia
  - Decreased renal synthesis of erythropoietinIt
  - RBC survival is decreased
  - Tendency of bleeding
    - platelet dysfunction

Diagnostic Workup in HTN

- Assess risk factors and comorbidities
- Reveal identifiable causes of HT
- Assess presence of target organ damage
- Thorough history and physical
- Labs: UA, glucose, Hct, lipids, K^+, Cr, Ca, uric acid,
- Optional: TSH
- EKG

Acute nephritic syndrome

- 1–2 g/24 h of proteinuria,
- hematuria with red blood cell casts,
- pyuria,
- hypertension,
- fluid retention,
- rise in serum creatinine associated with a reduction in glomerular filtration.

IMMUNE COMPLEX MARKERS

- ANA..... LUPUS GN
- ASO TITER..... POSTSTREPT. GN
- OTHER INFECTIVE MARKERS ...AntiHCVAb, HBsAg

ANCA + GN

pauci-immune glomerulonephritis

- No Extra Renal disease..... ANCA associated crescentic GN
- Extra renal disease....

1. Systemic vasculitis...
   Microscopic polyangitis
2. Respiratory granulomas...
   Wegener's Granulomatosis
3. Asthma+ Eosinophilia...
   Churg strauss syndrome

- Low serum C3:
  - cryoglobulinemia,
  - systemic lupus erythematosus,
  - bacterial endocarditis,
  - shunt nephritis,
  - membranoproliferative
  - poststreptococcal glomerulonephritis
- Normal serum C3:
  - polyarteritis nodosa, ANCA Asociated GN
  - visceral abscess,
  - Goodpasture syndrome,Anti GBM Dis
  - Henoch-Schönlein purpura, and IgA nephropathy.

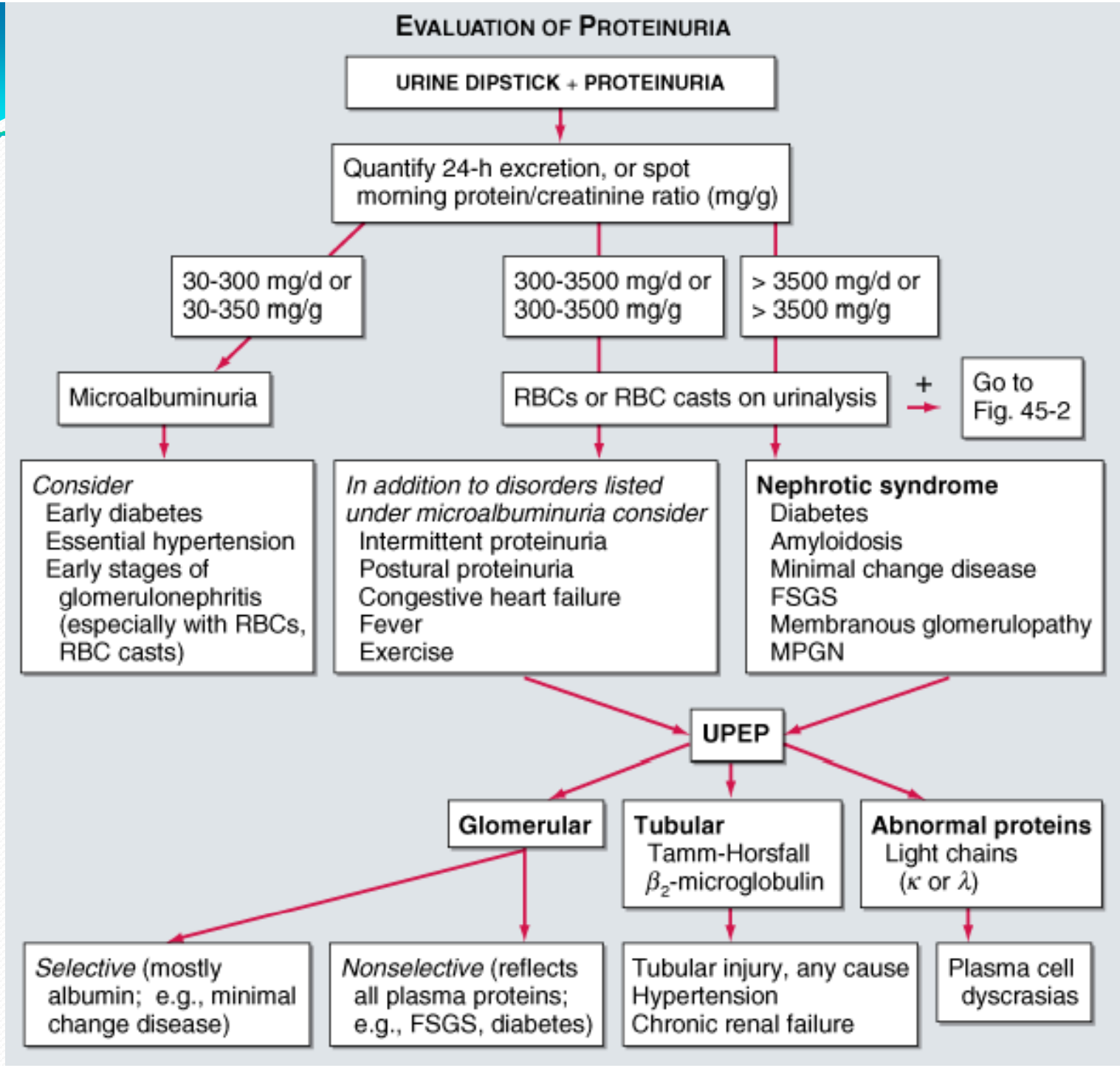
Albominuria-Proteinuria

Table 277-1 Urine Assays for Albuminuria/Proteinuria

	24-Hour Albumin[a] (mg/24 h)	Albumin[a]/Creatinine Ratio (mg/G)	Dipstick Proteinuria	24-Hour Urine Protein[b] (mg/24 h)
Normal	8–10	<30	–	<150
Microalbuminuria	30-300	30–300	–/Trace/1+	–
Proteinuria	>300	>300	Trace–3+	>150

Major causes of and approach to nonnephrotic proteinuria

Type	Frequency in office practice	Pathophysiology
Exclude first		
Transient proteinuria secondary to stress such as fever or heavy exercise	4 percent of men 7 percent of women	Possibly transient angiostensin II or norepinephrine-mediated alterations in glomerular permeability
Orthostatic proteinuria	2 to 5 percent of adolescents Uncommon over age 30	Not clear; ? neurohumoral or altered glomerular hemodynamics
Hemodynamic causes		
Heart failure; renovascular hypertension		Possibly angiotensin II and, in heart failure, norepinephrine-mediated increase in glomerular permeability
Glomerular proteinuria	Major cause when above disorders excluded; responsible for all causes of nephrotic syndrome	Abnormalities in glomerular capillary wall
Glomerular diseases Diabetic nephropathy	Increasing frequency with prolonged duration of diabetes	
Reflux nephropathy and other tubulointerstitial diseases		Secondary glomerular injury due to hemodynamic and structural changes resulting from nephron loss
Overflow proteinuria		
Multiple myeloma with cast nephropathy	Uncommon	Overproduction of light-chains, leading to tubular obstruction; suspect if acute renal failure, bland urine sediment, negative dipstick for protein, and positive sulfosalicylic acid test, indicating nonalbumin proteinuria


EVALUATION OF PROTEINURIA
URINE DIPSTICK + PROTEINURIA
Quantify 24-h excretion, or spot morning protein/creatinine ratio (mg/g)
30-300 mg/d or 30-350 mg/g
300-3500 mg/d or 300-3500 mg/g
> 3500 mg/d or > 3500 mg/g
Microalbuminuria
RBCs or RBC casts on urinalysis
+
Go to Fig. 45-2
Consider
Early diabetes
Essential hypertension
Early stages of glomerulonephritis (especially with RBCs, RBC casts)
In addition to disorders listed under microalbuminuria consider
Intermittent proteinuria
Postural proteinuria
Congestive heart failure
Fever
Exercise
Nephrotic syndrome
Diabetes
Amyloidosis
Minimal change disease
FSGS
Membranous glomerulopathy
MPGN
UPEP
Glomerular
Tubular
Tamm-Horsfall
β_2-microglobulin
Abnormal proteins
Light chains
(κ or λ)
Selective (mostly albumin; e.g., minimal change disease)
Nonselective (reflects all plasma proteins; e.g., FSGS, diabetes)
Tubular injury, any cause
Hypertension
Chronic renal failure
Plasma cell dyscrasias

Hematuria

- Hematuria is defined as two to five RBCs per high-power field (HPF)
- It can be detected by dipstick.
- Common causes of isolated hematuria stones, neoplasms, tuberculosis, trauma, and prostatitis.
- Gross hematuria with blood clots is almost never indicative of glomerular bleeding

Historical clues — hematuria

- • Concurrent pyuria and dysuria, : urinary tract infection, may also bladder malignancy.
- • A recent upper respiratory infection: postinfectious glomerulonephritis or IgA nephropathy.
- • A positive family history of renal disease: hereditary nephritis, polycystic kidney disease, or sickle cell disease.
- • Unilateral flank pain, which may radiate to the groin, : ureteral obstruction due to a calculus or blood clot,occasionally malignancy

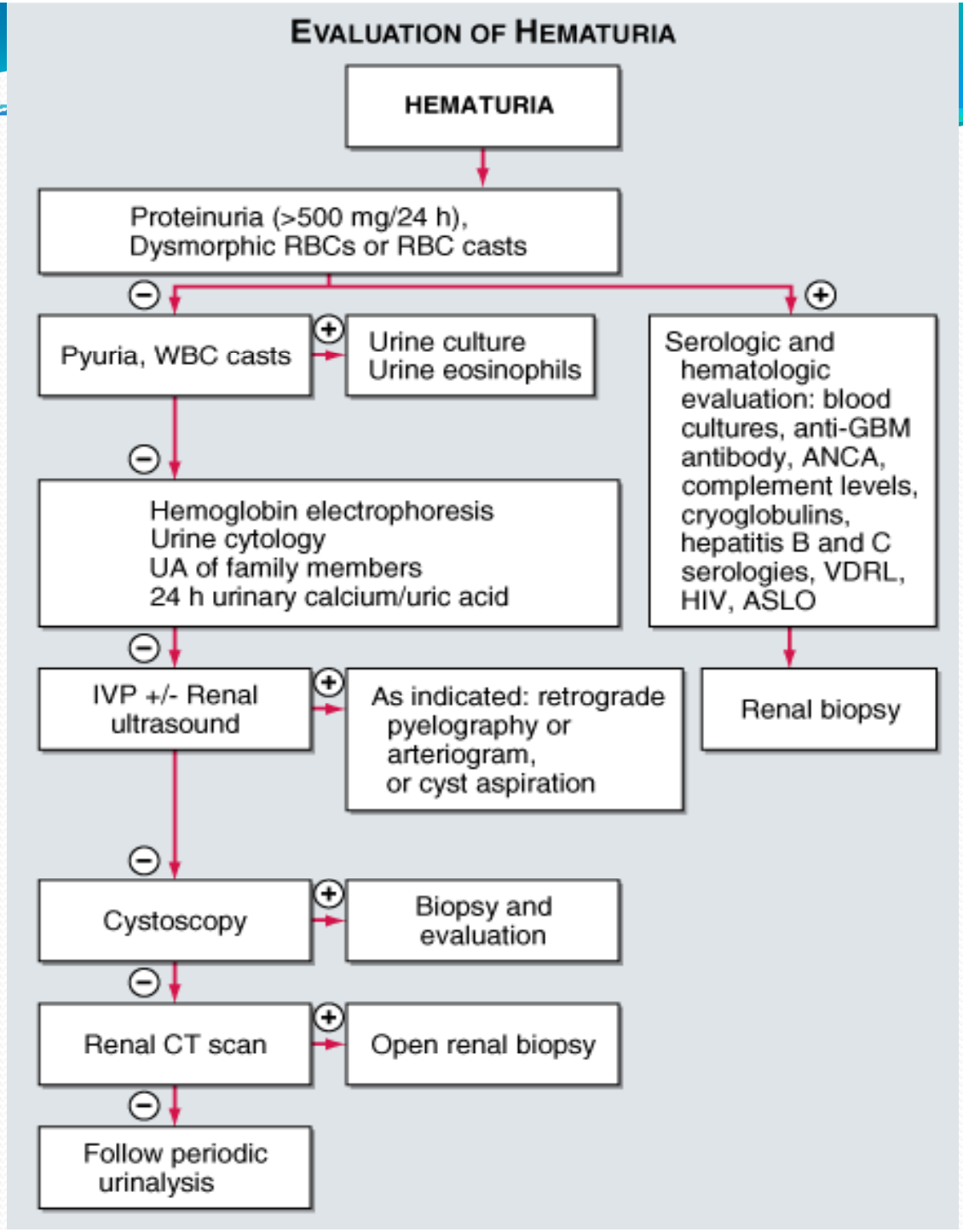
Historical clues — hematuria.cONT

- • Symptoms of prostatic obstruction in older men such as hesitancy and dribbling: (BPH)
- • Recent vigorous exercise or trauma.
- • History of a bleeding disorder or bleeding from multiple sites due to excessive anticoagulant therapy

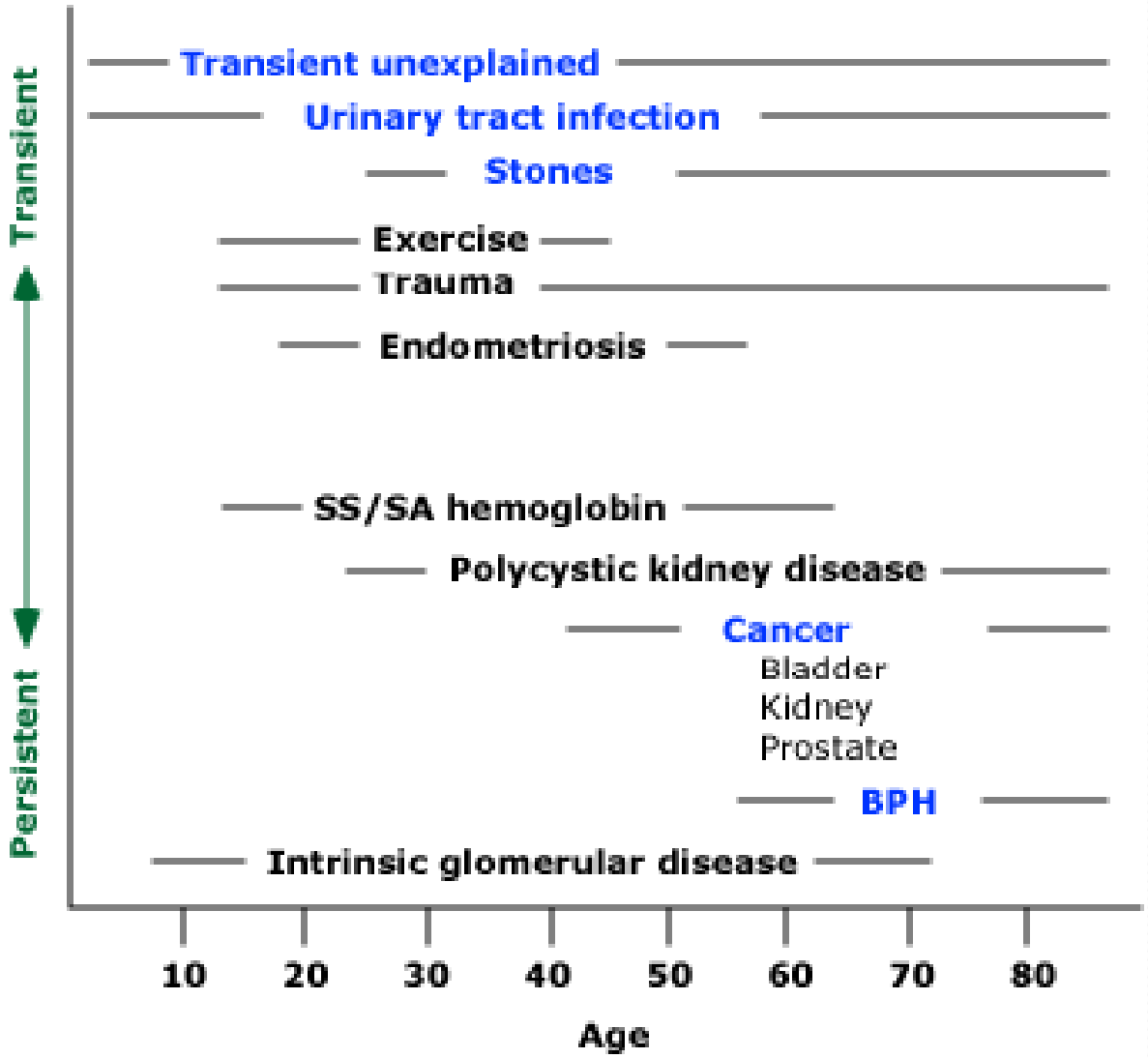
GLUMERUL & EXTRAGLUMERUL

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	<500 mg/day	May be >500 mg/day
RBC morphology	Normal	Dysmorphic
RBC casts	Absent	May be present


EVALUATION OF HEMATURIA
HEMATURIA
Proteinuria (>500 mg/24 h), Dysmorphic RBCs or RBC casts
Pyuria, WBC casts
Urine culture
Urine eosinophils
Serologic and hematologic evaluation: blood cultures, anti-GBM antibody, ANCA, complement levels, cryoglobulins, hepatitis B and C serologies, VDRL, HIV, ASLO
Hemoglobin electrophoresis
Urine cytology
UA of family members
24 h urinary calcium/uric acid
IVP +/- Renal ultrasound
As indicated: retrograde pyelography or arteriogram, or cyst aspiration
Renal biopsy
Cystoscopy
Biopsy and evaluation
Renal CT scan
Open renal biopsy
Follow periodic urinalysis

HEMATURIA & AGE



Pyuria

- *Isolated pyuria* is unusual
- inflammatory reactions in the kidney or collecting system are also associated with hematuria.
- The presence of bacteria suggests infection, and white blood cell casts with bacteria are indicative of pyelonephritis.
- White blood cells and/or white blood cell casts may also be seen in tubulointerstitial processes such as interstitial nephritis, systemic lupus erythematosus, and transplant rejection

Nephrotic Syndrome

- Massive proteinuria (> 3.5 gms,for 1.73 m2 body surface/24 hours in urine)-glomerular permeability problem
- Pathogenesis: varies with disease; most are immune complex deposition
- Laboratory and Clinical:
  - Hypoalbuminemia, generalized edema, Hyperlipidemia, lipiduria, fatty casts and oval fat bodies in urine.

Nephrotic Syndrome

- **Complications**
  - **Generalized edema (anasarca)-massive amounts of albumin in urine, hypoalbominemia**
  - **Susceptibility to hypercoagulation due to loss of antithrombin III in urine and increases in fibrinogen, increased platelet aggregation ; bilateral renal vein thrombosis can occur**
  - **susceptibility to infections due to Loss of immunoglobulins and complement in urine (infections-Staphylococcus aureus and Streptococcus pneumoniae; spontaneous bacterial peritonitis due to Strep. pneumoniae)**
  - **Protein malnutrition**

Nephrotic Syndrome

- **Complications**
  - **Iron resistant microcytic hypochromic anemia due to loss of transferrin**
  - **Hypocalcemia and secondary hyperparathyroidism due to vitamin D deficiency with enhanced urinary excretion of cholecalciferol-binding protein**
  - **Depressed thyroxine levels due to loss of thyroxine-binding globulin**

Primary Causes of Nephrotic Syndrome

- Minimal change disease (nil disease; lipoid nephrosis)
- Focal segmental glomerulosclerosis
- Idiopathic membranous glomerulonephritis
- Membranoproliferative glomerulonephritis

Diabetic Nephropathy-clinical course

- After the onset of proteinuria >500 mg/24 h, renal function declines, with 50% of patients reaching renal failure in 5–10 years;

- thus, from the earliest stages of microalbuminuria, it usually takes 10–20 years to reach end-stage renal disease.

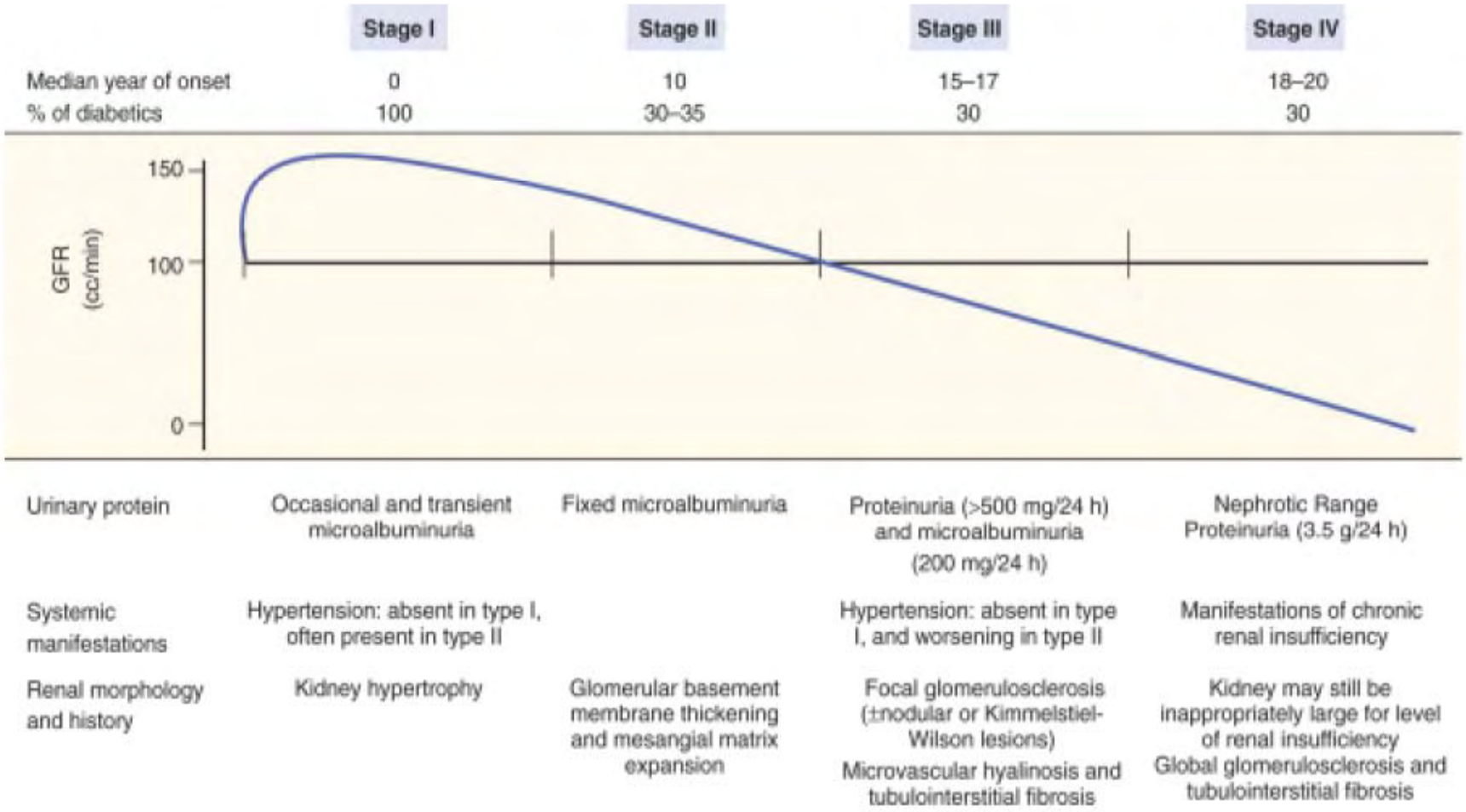


FIGURE 125-1 Stages of diabetic nephropathy. GFR = glomerular filtration rate.

Clinical Case1

- S.E. is a 10 year-old with acute lymphocytic leukemia receiving chemotherapy
- Has fever, neutropenia and thrombocytopenia
- UOP is 1.2 cc/kg/hour
- On clinical exam she has very moist mucus membranes
- BUN and creatinine are 110 and 0.7. Albumin is 3.5

Assessment of case #1

- Is she in renal failure?
  - Creatinine is normal, so NO!
- Why is BUN so high?

Use of plasma BUN: Cr ratio

- In pre-renal BUN:Cr > 20 usually
- However, BUN may be increased disproportionately with blood products, excess amino acids in TPN, GI or other bleed; increased catabolism (treatment with steroids, fever).

Clinical Case #2

- CE is a 15 yo male who presented with URI symptoms, then headache, vomiting, abdominal pain, knee pain, edema, and a purpuric rash on his legs. He had not voided for 24 hours.
- What is diagnosis?
  - HSP

Physical exam and labs

- BP was 152/94. He had anasarca. Heart and lung exams were normal.
- A urinalysis revealed hematuria and proteinuria. BUN and Creatinine were 76 and 8.0. Albumin was 3.1
- He has aggressive HSP nephritis