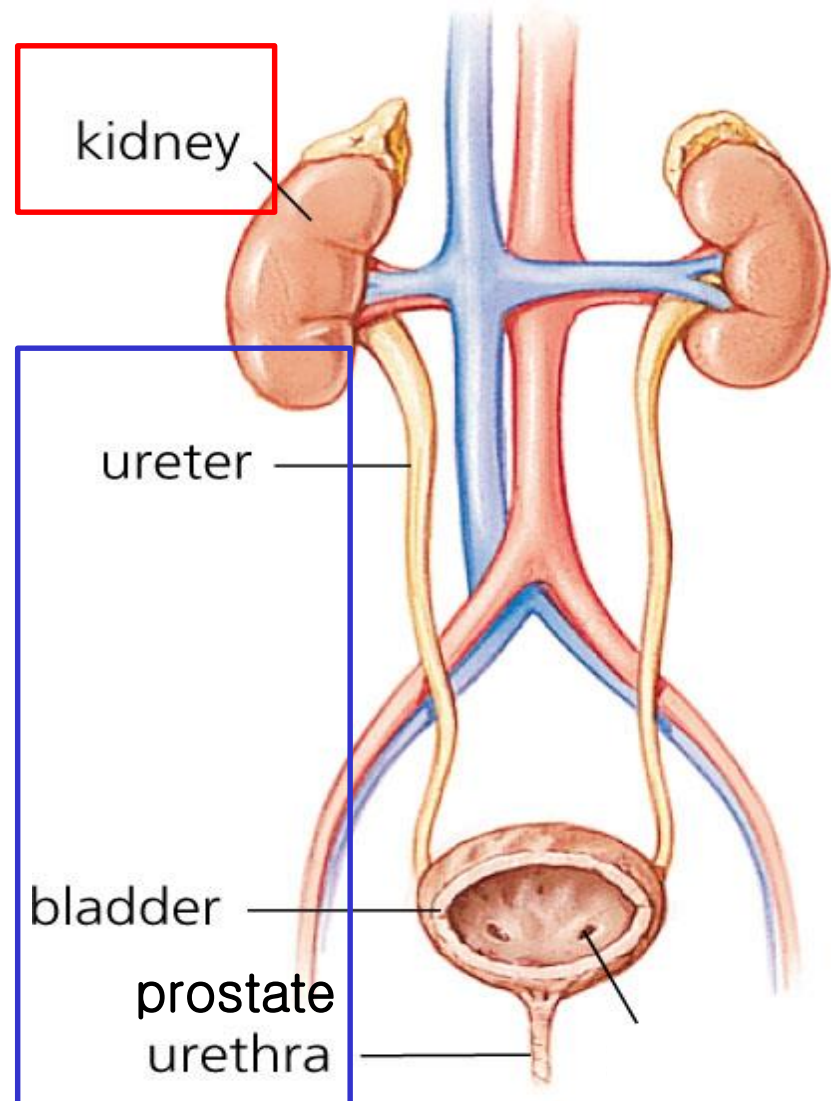


APPROACH TO THE PATIENT with RENAL DISEASES

Structure of Kidney and Urinary tract system

→ 신, 요로계



CLINICAL MANIFESTATION

Clinical symptoms due to impaired renal function

1. Reduction in GFR (**azotemia**)
2. Abnormalities of urine sediment (**RBC,WBC,cast**)
3. Abnormal excretion of serum protein (**proteinuria**)
4. Disturbance in urine volume (**oliguria, anuria, polyuria**)
5. Presence of **hypertension** or
expanded total body weight (**edema**)
6. Electrolyte abnormalities(**hyperkalemia,hyponatremia**)
7. Inflammation and infection (**fever / pain**)

I. Cardinal Manifestations of Renal Disease

- Hematuria and proteinuria**
- Azotemia**
- Dysuria, frequency, polyuria and nocturia**
- Oliguria and anuria**
- Renal colic and flank pain**
- Renal mass**
- Edema**
- Hypertension and uremia**

Hematuria

- excretion of erythrocyte in urine
: defined as 2 – 5 (3) RBC / HPF
- **Isolated hematuria**
: common cause
→ stone, neoplasm, tuberculosis ,trauma, prostatitis
glomerular Ds
- Gross hematuria with **blood clot**
→ is postrenal cause
is almost **never** indicative of glomerular bleeding



Hematuria

Glomerular hematuria

- hematuria with
dysmorphic RBC(especially acanthocyte),
RBC cast,
proteinuria > 500mg/day
→ *diagnostic of GN*
- most common causes of isolated glomerular hematuria
: IgAN, TBMD, hereditary nephritis

Hematuria

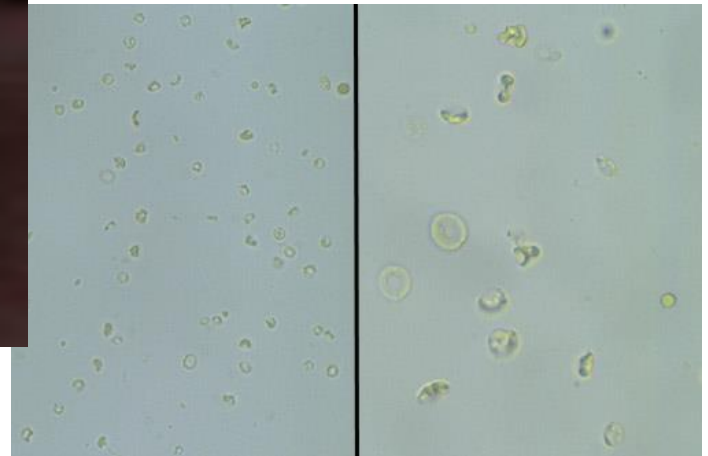
Glomerular hematuria



RBC cast



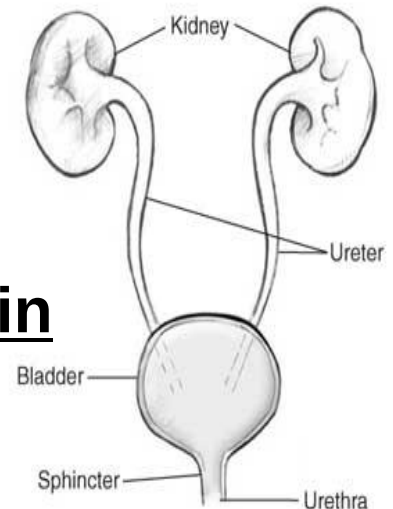
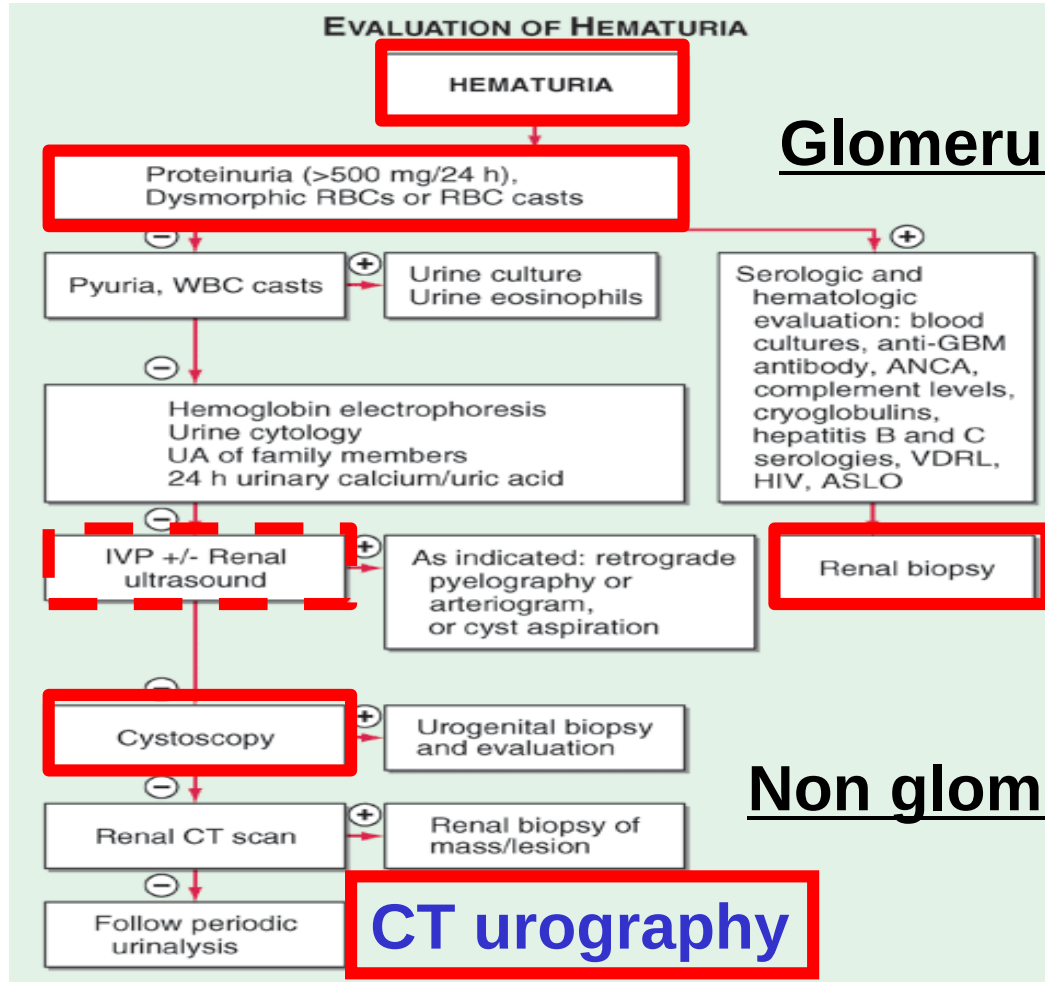
Proteinuria
> 500mg/day



Dysmorphic RBC

Hematuria

Approach to the patient with hematuria



Proteinuria

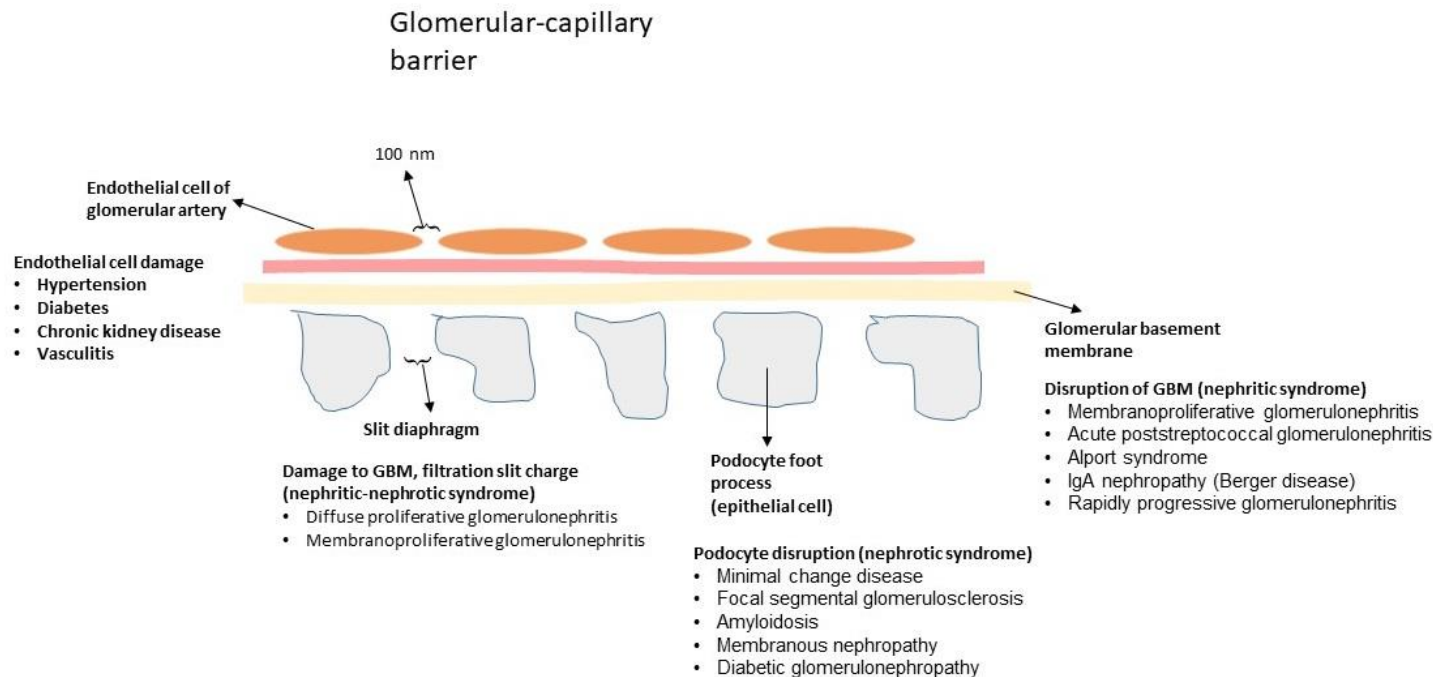
Pathophysiology

Two major mechanism of proteinuria in GDs

1.abnormal transglomerular passage of protein

due to **increased permeability of glomerular capillary wall**

2.Impaired **tubular reabsorption** of protein in Proximal tubule



Proteinuria

Type of proteinuria

TABLE 73-3. TYPES OF PROTEINURIA*

Type	Mechanism	Quantity†	Molecular Weight	Examples
<u>Overflow</u>	Increased filtration of abnormal plasma proteins across normal glomeruli	Variable (0.2 to >10 grams)	Low (<40,000)	Bence Jones proteinuria, myoglobinuria
<u>Glomerular‡</u>	Defective glomerular retention of normal plasma proteins	>3 grams	60,000	Minimal-change nephrotic syndrome
Selective				
Nonselective		>3-5 grams	High (>68,000)	Glomerulonephritis, diabetes
<u>Tubular</u>	Defective reabsorption of normally filtered plasma proteins	<2 grams	Low (<40,000)	Interstitial nephritis, antibiotic injury, heavy metals
<u>Hemodynamic</u>	Increased filtration and possibly decreased reabsorption	<2 grams	Variable (20,000-68,000)	Transient proteinuria, congestive heart failure, fever, seizures, exercise

Functional proteinuria

Obesity, sleep apnea, emotional stress

Proteinuria

Normal excretion rate

: protein <150 mg/24 hrs, albumin <30 mg/day

Proteinuria

> 150 mg/day : pathologic proteinuria

> 3.5 g/day : massive proteinuria (→ glomerular damage)

Detection method

: dipstick for microalbuminuria

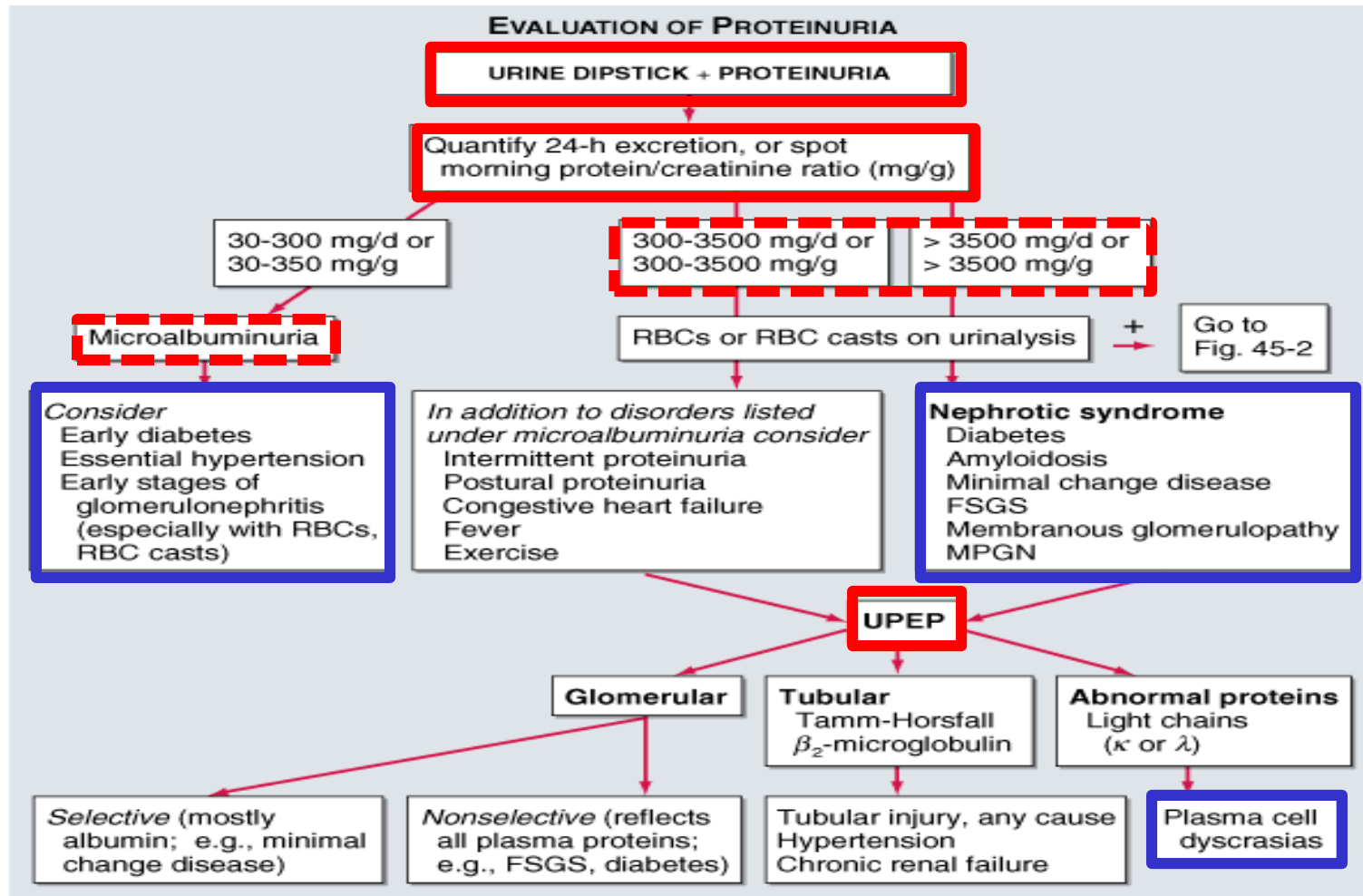
: spot urine PCR

: 24 hr urine protein with UEP



Proteinuria

Approach to the patient with proteinuria



Proteinuria

Approach to the patient with proteinuria

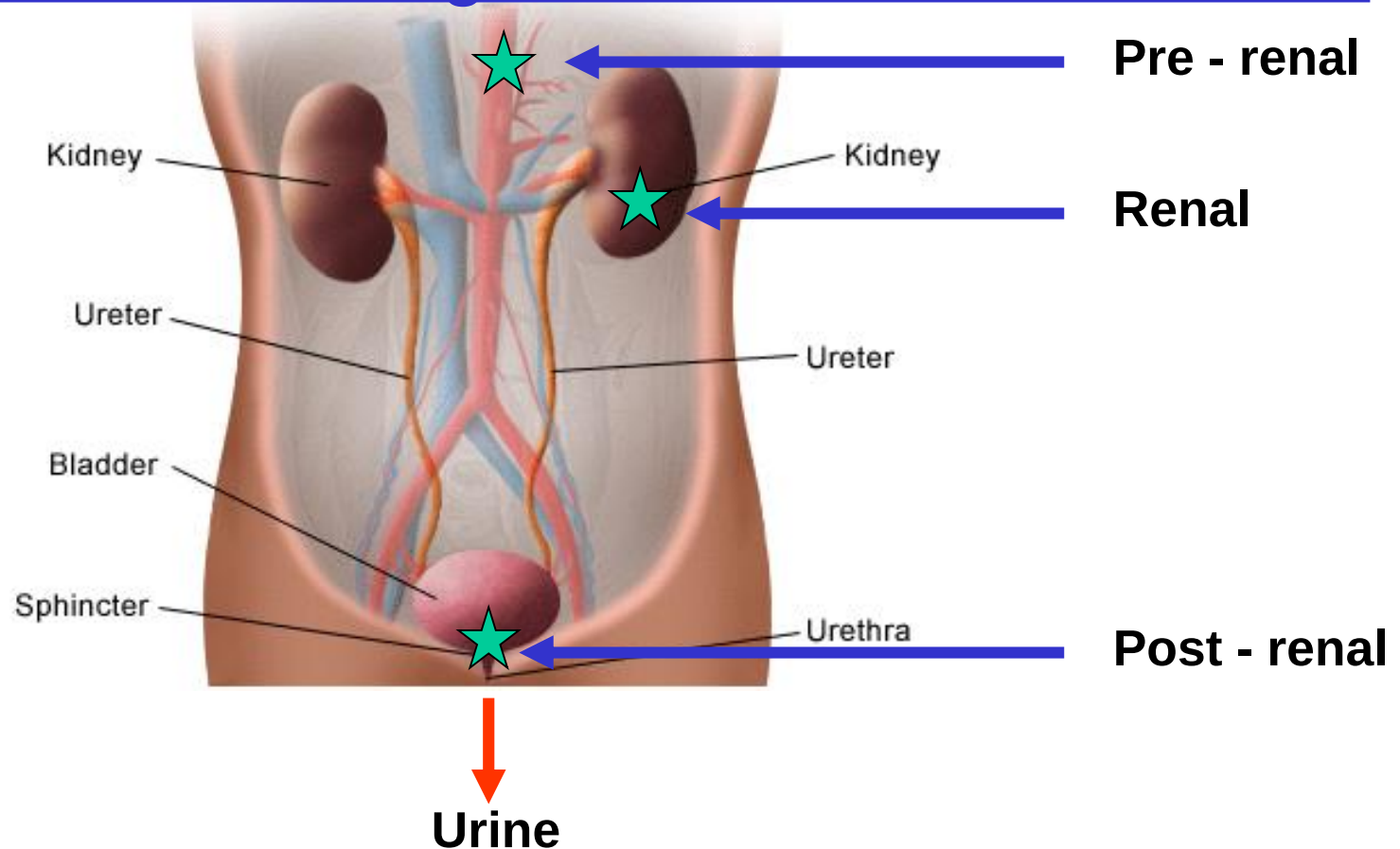
Kidney biopsy

- indicated in U pr > 2 g / day,
in U pr 1 – 2g/day
with systemic disease
(ex, lupus, amyloidosis)
- usually not indicated in U pr < 1 g/day

Azotemia

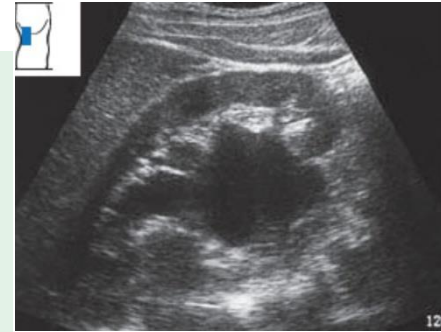
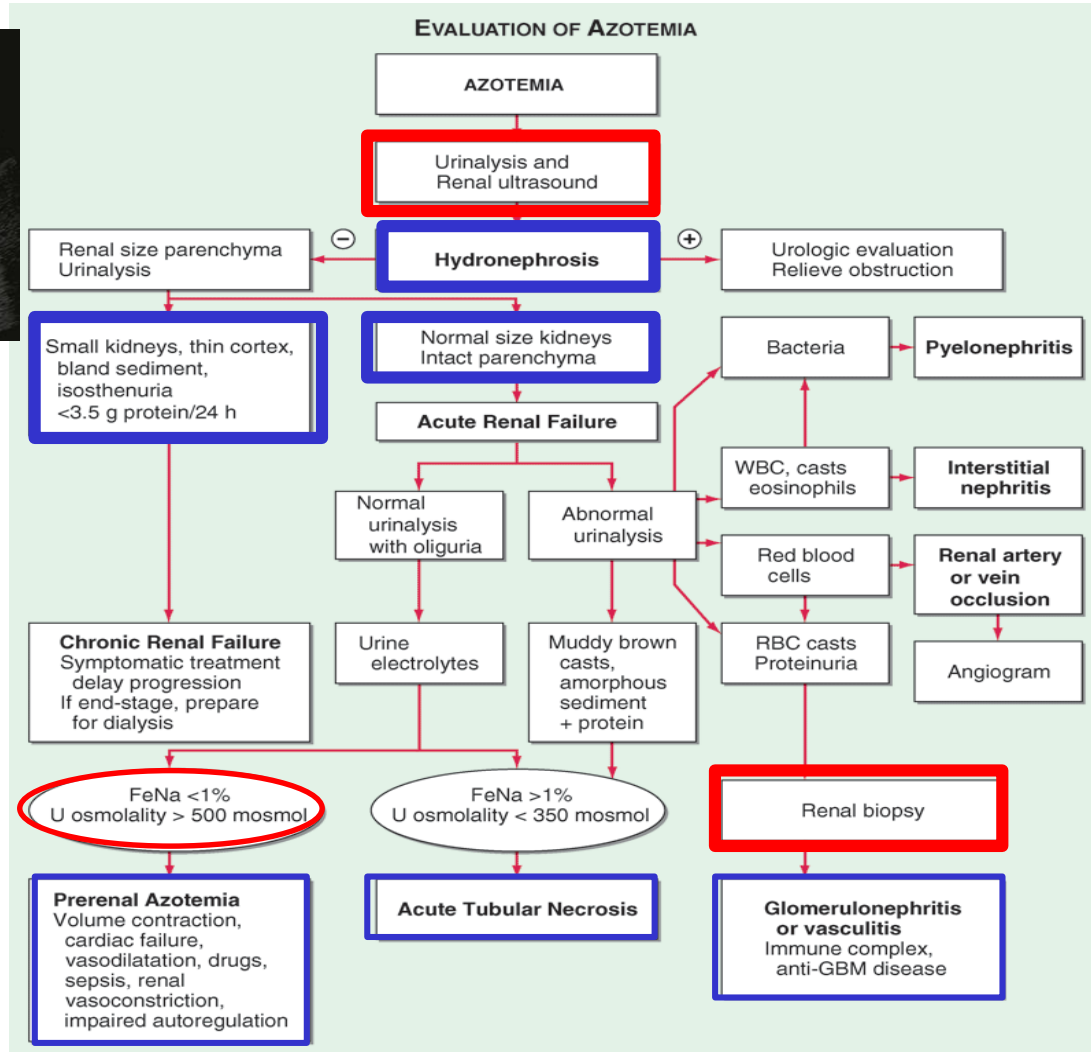
Azotemia(retention of nitrogenous waste product)
→ suggest reduced GFR

Three anatomic categories of cause of azotemia

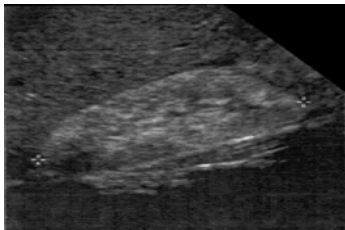


Azotemia

Approach to the patient with azotemia



Postrenal AKI



CKD

AKI

Dysuria and Frequency

Definition

: dysuria → painful passage of urine

: frequency → frequent urination

Etiology

: inflammation of UT

Polyuria and Nocturia

Definition

: Polyuria

→ urine volume **> 3L/24hrs**
(normal urine volume, about 1.6-2 L/day)

: Nocturia

→ wake at night **one or more times** for voiding

Oliguria and Anuria

Oliguria

- oliguria → urine volume < **400**- 500 ml/24hrs(< 20ml/hr)
- Etiology
 - three major cause (similar to azotemia cause)
 - 1) prerenal disease
 - 2) renal disease
 - 3) postrenal disease

Oliguria and Anuria

Anuria

- urine volume <50-**100** ml/24hrs
- Etiology
 - usually
 - obstruction of UT,
 - total renal artery or vein occlusion,
 - shock(by severe hypotension and
 - intense renal vasoconstriction

Renal colic and Flank pain

Renal colic

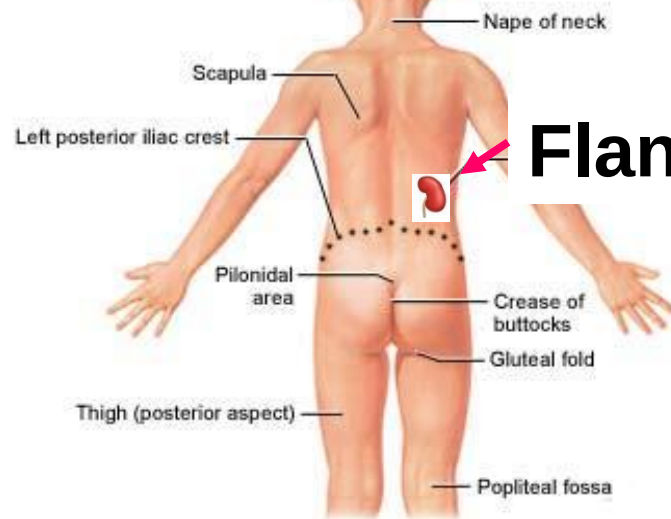
- : pain syndrome when urinary tract is acutely dilated because of obstruction
- : causes are **stone**, blood clot, sloughed renal papilla

Flank pain

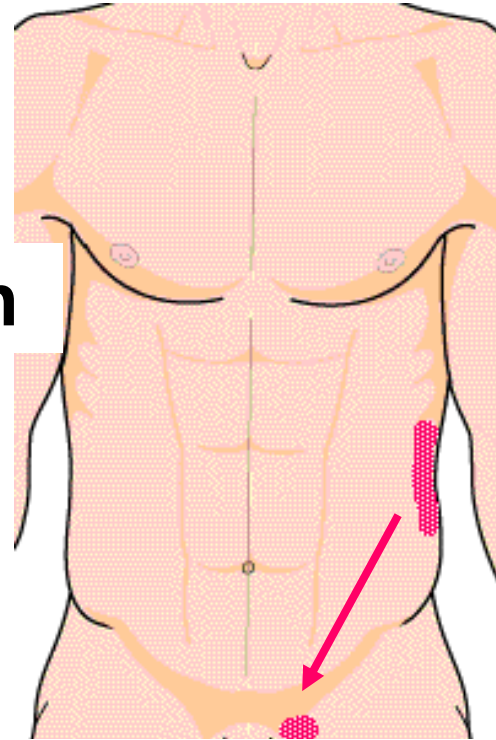
- : by renal origin
(renal swelling, perinephric **inflammation**),
extrarenal origin

Renal colic and Flank pain

Anatomical landmarks
(back view)



Flank pain

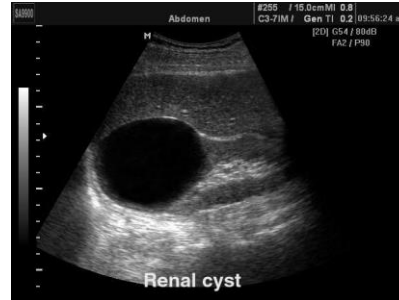


Renal colic

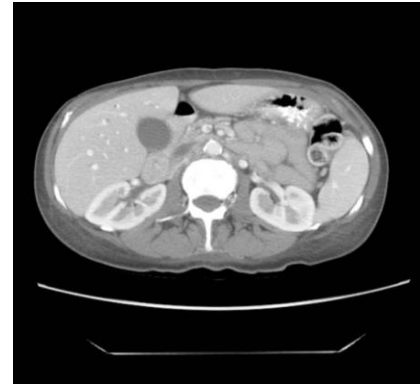
Renal mass

Evaluation

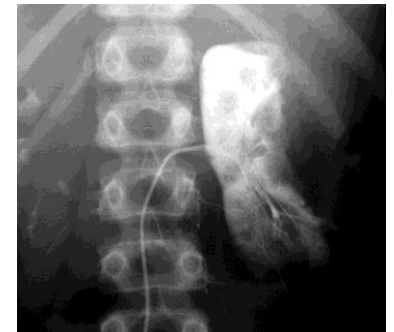
1. Ultrasonography



2. CT



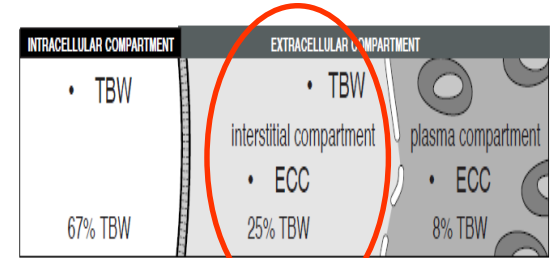
3. MRI, Angiography



Edema

Definition and causes

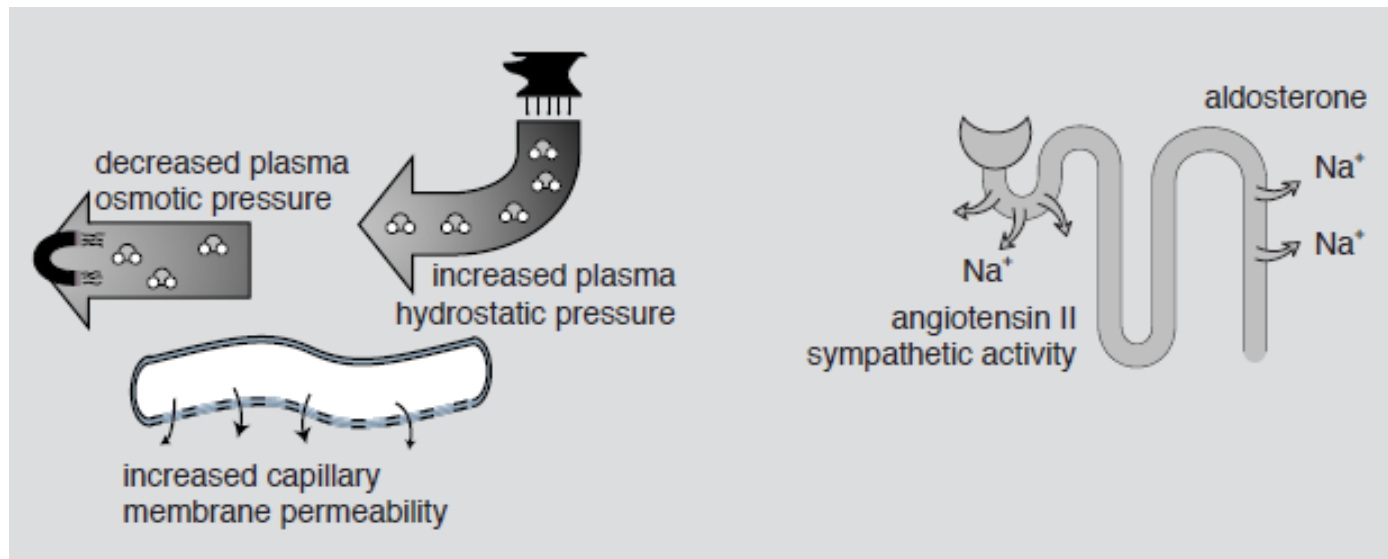
- is defined as a palpable swelling by expansion of the IS volume. (2 – 3 L)
- by cause and mechanism
 1. generalized edema
ex, heart failure, cirrhosis, and NS
 2. localized edema
ex, venous obstruction
(ex, CVI,DVT),
allergic reactions
(laryngeal edema)



Edema

Pathophysiology of edema formation

- There are two basic steps involved in edema formation
 - 1) an alteration in **capillary hemodynamics** that favors the movement of fluid from IV space into ISS
 - 2) the retention of dietary or intravenously administered sodium and water by the **kidneys**.



Hypertension

Hypertension

- BP > 140 / 90 mmHg

- renal hypertension

 - by renal parenchymal disease (AGN, CKD)

 - by renovascular disease (RAS)

Uremia

Symptoms due to decreased GFR

(usually begin GFR < 15ml/min)

- : neurological manifestation(**behavioral change,convulsion,coma**)
- : gastrointestinal manifestation(**anorexia,nausea,vomiting,GI bleeding**)
- : cardiovascular manifestation(**hypertension,pericarditis**)

- : pulmonary manifestation(**pleuritis,dyspnea**)
- : dermatologic manifestation(**pruritus**)
- : hematologic manifestation(**anemia**)

- : musculoskeletal manifestation(**arthralgia**)
- : fluid and electrolyte disorder(**hyperkalemia**)
- : endocrine disorder(**insulin resistance**)

II. Medical History

1. previous evidence of renal disease

: elevated BUN/Cr, proteinuria, HT

2. history of systemic disease

: DM, collagen disease, HT

3. history of drug exposure

: NSAIDs, aminoglycoside

4. history of factors contributing to prerenal or postrenal azotemia

: CHF, LC

5. uremic symptoms

: nausea, anorexia, vomiting, weight loss, pruritus, weakness, fatigability, lethargy, drowsiness

III. Physical Examination

Vital sign

Volume status

- volume depleted : orthostatic change in BP and pulse, skin tenting
- volume overload : jugular venous distension, rales, ascites, edema

Cardiovascular

- JVP_r → crucial role in bedside evaluation of volume status
- pericardial friction rub → serositis in SLE or uremic pericarditis

III. Physical examination

Abdomen

- abdominal bruit → renovascular disease
- hepatomegaly → passive congestion and amyloidosis
- splenomegaly → amyloidosis, endocarditis, lymphoma
- kidney and liver enlargement → ADPKD

Neurologic examination

- peripheral neuropathy
→ vasculitis with nerve involvement(mononeuritis multiplex)
- cerebrovascular accident
→ SLE and antiphospholipid antibody syndrome

Others

- edema of lower extremities → LC, CHF, NS

INVESTIGATION OF RENAL DISEASE

Methods available to assess renal function

1. functional integrity of glomerular ultrafiltration barrier
2. presence of urogenital inflammation
3. overall rate of glomerular filtration
4. the ability to dilute, concentrate, acidify urine
5. ability to conserve or to excrete specific solutes
6. visualization of kidney and urogenital system
7. morphologic examination of renal tissue

Kidney biopsy

Renal biopsy in evaluation of renal disease
: mostly percutaneous approach

Indication of renal biopsy

1. RPGN without serologic diagnosis
2. Nephrotic syndrome without obvious cause
: especially in adult
3. SLE with renal involvement
4. Unexplained renal failure of any cause
with immunosuppressive therapy
5. Unexplained proteinuria below the nephrotic range
to exclude nephrosis in evolution
: proteinuria > 1g/24 hrs or reduced GFR
6. Renal transplant with acute and chronic renal failure

*** rarely indicated in CKD with small kidney,
classic diabetic nephropathy**

Kidney biopsy

Contraindication of percutaneous renal biopsy

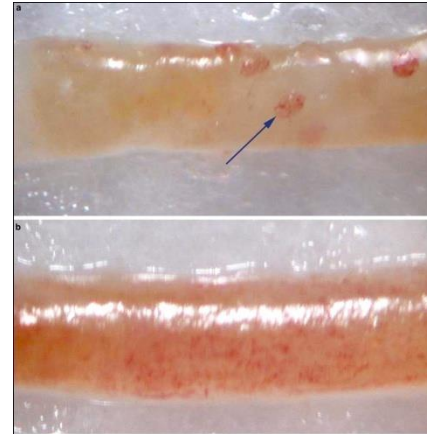
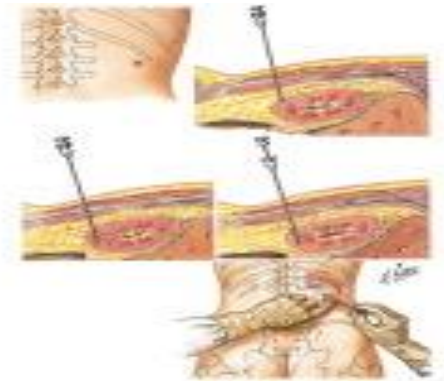
- : uncooperative**
- : presence of single kidney (if percutaneous biopsy)**
- : bleeding disorder(platelet < 60,000, PT > 3 sec, prolonged BT)**
- : uncontrolled hypertension(diastolic Pr > 90 mmHg)**

Complication

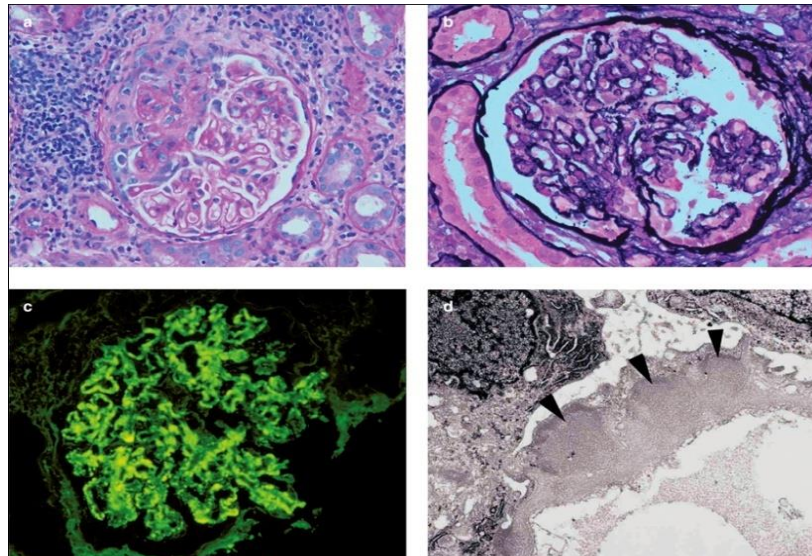
- : occur in 5-10 %**
- : microscopic hematuria → common, not complication**
gross hematuria → resolve within 24-48 hrs
perirenal hematoma → may be require surgical evacuation

Kidney biopsy

Information : by EM,IF,LM



specimen



LM, IF, EM

TREATMENT OF RENAL DISEASE

Conservative treatment

- hypertension control by antihypertensive agent(ACEI, ARB)
- proteinuria, hyperlipidemia control
(low protein diet, ACEI, cholesterol lowering agent)
- edema control by diuretics (furosemide)
- diet therapy
 - : protein restriction is important role in prevention of renal disease
 - : salt restriction in edema, hypertension

Specific treatment

- immunosuppressive agent
 - : steroid, azathioprine, cyc -A, tacrolimus, cyclophosphamide, MMF

Renal replacement therapy

- dialysis (hemodialysis, peritoneal dialysis , CRRT)
- transplantation

THE MAJOR RENAL SYNDROME

Renal disorder

are often nonspecific in manifestation,
appeared as **syndrome**

Interpretation of a group of finding
obtained by **Hx, P/E, Lab finding**

By structure

: glomerulus, tubule, interstitium, vessel

By duration of renal failure

: acute, chronic

Types of Syndromes

1. Nephritic syndrome(AGN)
2. Nephrotic syndrome(NS)
3. Tubulointerstitial disease(TID)
4. Vascular disease

5. Acute kidney injury (AKI, ARF), AKD
Rapidly progressive renal failure(RPRF)
(mostly due to RPGN)
6. Chronic kidney disease(CKD, CRF)

7. Others

- Asymptomatic urinary abnormality(AUA)
- Urinary tract infection(UTI)
- Renal tubule defect(functional or structural defect)
- Hypertension, Nephrolithiasis, Urinary tract obstruction

Nephritic syndrome

- is a **Glomerulonephritis** (AGN, ANS)
- manifested clinically by
acute reduction in GFR, salt and water retention
- damage to glomerular wall (**inflammation**)
 - : gross or microscopic hematuria, RBC cast,
dysmorphic RBC, proteinuria
 - : **hallmark of ANS is the presence of RBC cast**
- prototype of AGN
 - : **PSGN** (poststreptococcal glomerulonephritis)
- when AGN is associated with necrotizing **crescentic GN**,
rapid and irreversible renal dysfunction
→ is a **RPGN**

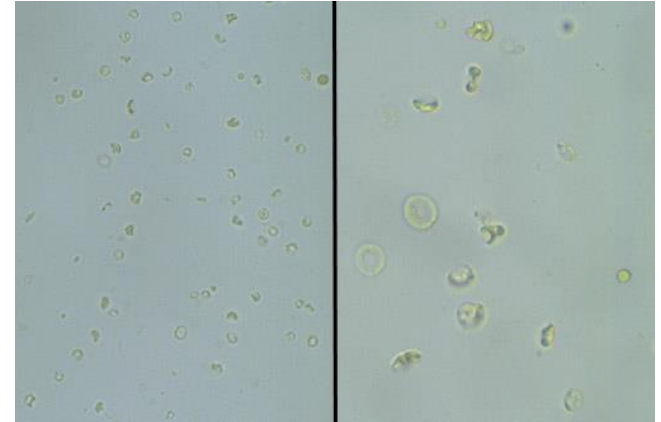
Nephritic syndrome



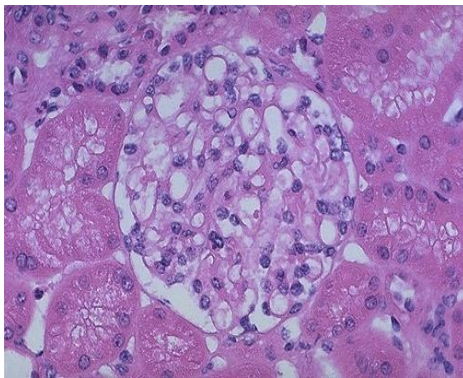
Tonsillitis



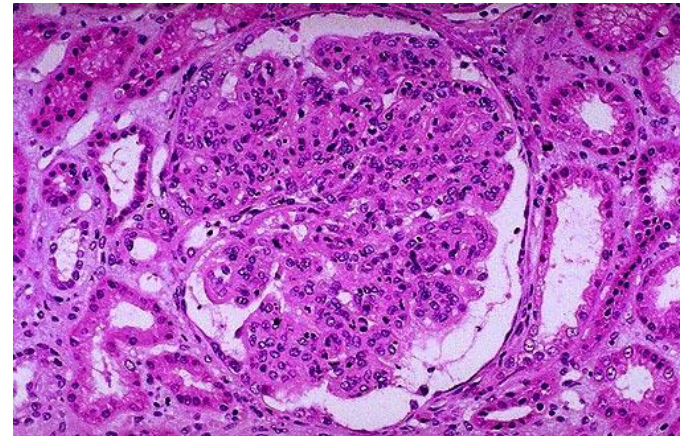
RBC cast



Dysmorphic RBC



Normal glomerulus



proliferative GN

Nephrotic syndrome

4 major manifestation

: heavy **proteinuria**($> 3.5 \text{ g} / 1.73\text{m}^2 \text{ /day}$, mostly albumin), hypoalbuminemia, edema, hyperlipidemia

Common causes

: primary and secondary cause

1) idiopathic or primary cause

→ **FSGS, MGN, MCNS, MPGN** (in adult incidence)

2) secondary cause

→ diabetic nephropathy, amyloidosis, SLE

Nephritic and Nephrotic syndrome



Nephrotic vs Nephritic Syndrome

 Nephrotic Syndrome		 Nephritic Syndrome
• Low serum albumin (<30g/L) • Proteinuria (>3.5g/day) • Oedema • Dyslipidaemia • Hypercoagulability (loss of antithrombin III) • Reduced immunity (loss of immunoglobulins)	Characteristics	• Haematuria • Hypertension • Mild proteinuria (<3.5g/day) • Mild oedema • Temporary oliguria and uraemia
Peripheral oedema (adults), facial oedema (children), frothy urine, fatigue, recurrent infections	Symptoms	Haematuria (frank/microscopic), mild oedema, oliguria, signs of uraemia (fatigue, pruritus, nausea)
++++	Proteinuria	++
May or may not be present	Haematuria	+++
Absent	Red blood cell casts	Present
• Minimal change disease (most common in children) • Membranous nephropathy (most common in adults) • Focal segmental glomerulosclerosis	Causes	• IgA nephropathy • Post-streptococcal glomerulonephritis • Rapid progressive glomerulonephritis (RPGN): • Anti-GBM glomerulonephritis • ANCA Vasculitis

Tubulointerstitial disease

Major cause

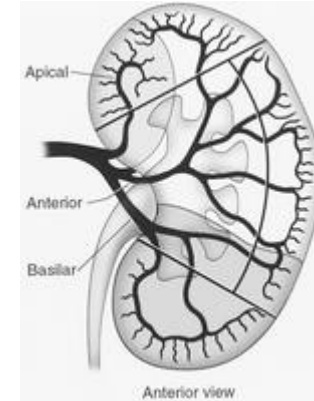
- : **ischemic and toxic ATN**
- : **allergic interstitial nephritis**
- : interstitial nephritis secondary to immune complex related collagen vascular disease(SLE)
- : granulomatous disease(sarcoidosis)
- : pigmented related tubular injury(myoglobinuria,hamaglobulinuria)
- : hypercalcemia with nephrocalcinosis
- : myeloma kidney or cast nephropathy
- : infection related interstitial nephritis
- : infiltrative disease(lymphoma)

Vascular disease

- divided into large vessel obstruction and medium to small vessel disease

1. Renal artery stenosis

- : atherosclerotic renal artery stenosis
→ M/C cause
- : fibromuscular dysplasia
→ common in 20-50 yrs women

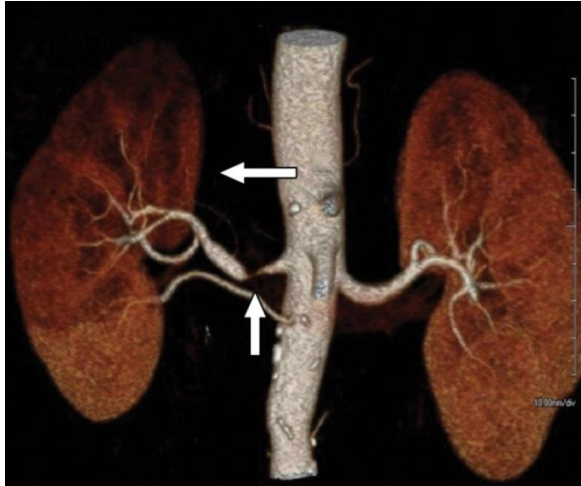


2. Medium to small vessel disease

- 1) classic polyarteritis nodosa
: with HBV, HIV
- 2) atheroembolic disease
- 3) thrombotic microangiopathy(TTP, HUS),
antiphospholipid antibody syndrome,
scleroderma renal crisis

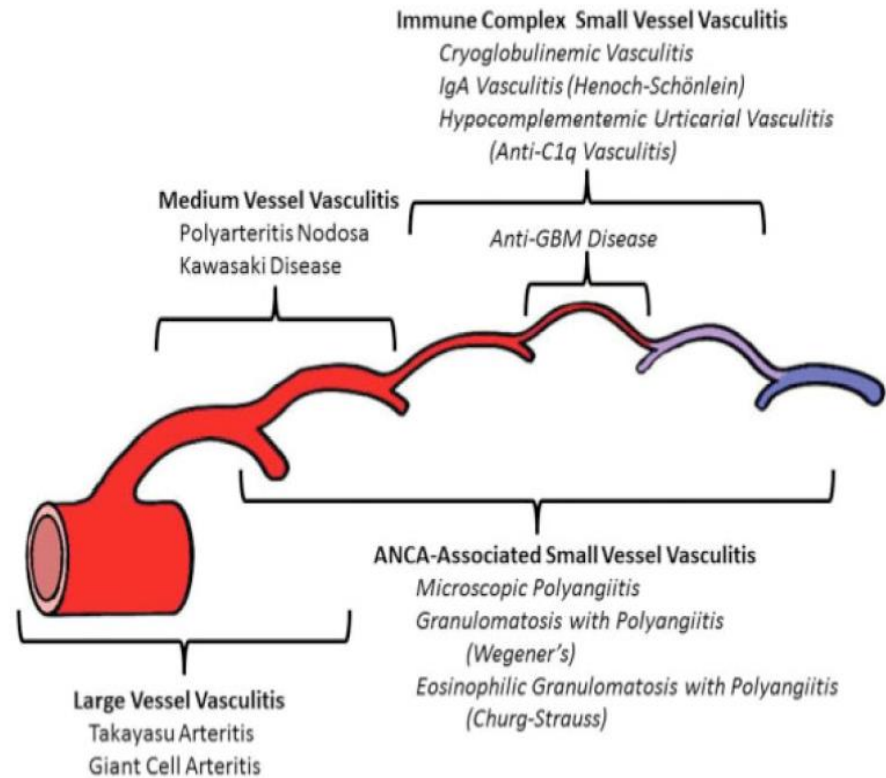


Vascular disease



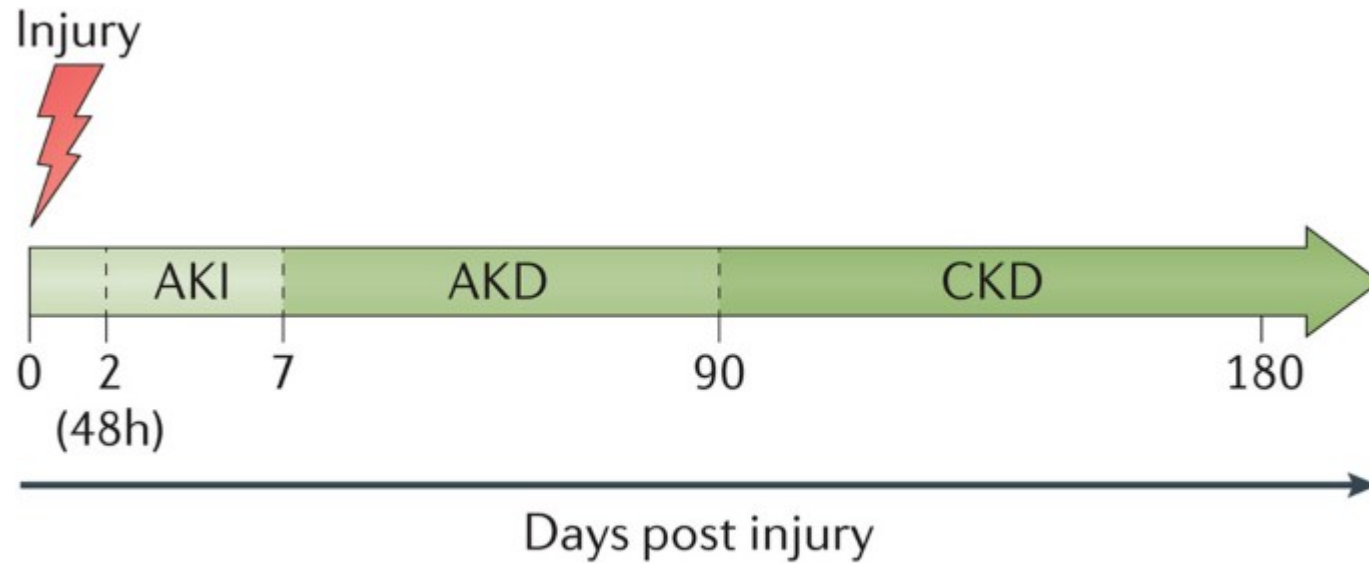
RAS

vasculitis



Renal failure

- AKI, AKD, CKD -

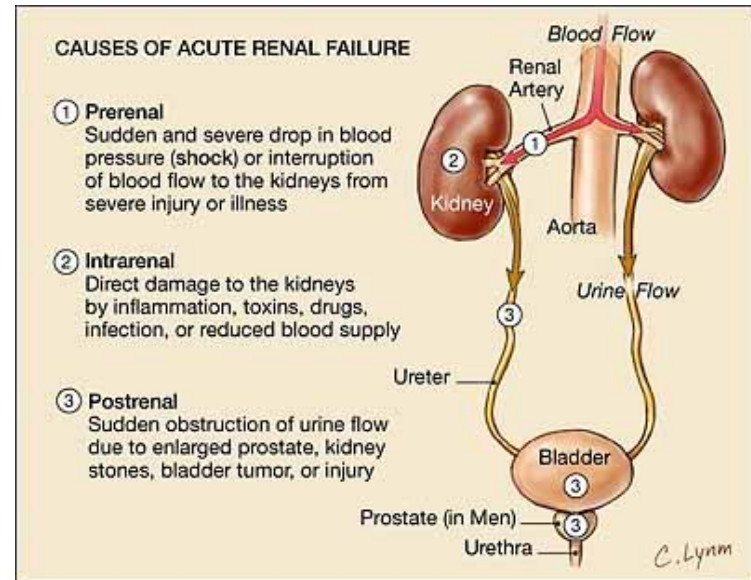


Acute Kidney Injury(AKI,ARF)

- acute decreased Glomerular filtration rate(GFR)
: GFR fall over a period of days(within 48 hrs)
- proof for the existence of ARF
: require serial determination of GFR,BUN and Cr level

Cause

1. prerenal →
volume depletion
2. renal →
ATN due to sepsis,
nephrotoxin
3. postrenal → BPH



Chronic kidney disease(CKD)

CKD definition and causes

- either kidney damage or
GFR less than 60 mL/min/1.73m² for **more 3 months**
kidney damage is defined as
pathologic abnormalities or
marker of kidney damage (in blood,urine or in imaging tests)
- major cause are **DM, GN, HT**

Stage of chronic kidney disease(by NKF)

stage	description	GFR
1	kidney damage with normal or increased GFR	> 90
2	kidney damage with mild or decreased GFR	60 – 89
3	moderate decreased GFR	30 – 59(CKD)
4	severe decreased GFR	15 – 29(CKD)
5	kidney failure	< 15 (ESRD)

AKI and CKD

	ACUTE KIDNEY INJURY	CHRONIC KIDNEY DISEASE
Onset	Sudden	Gradual, often over many years
Most common cause	Acute tubular necrosis	Diabetic nephropathy
Diagnostic criteria	Acute reduction in urine output and/or Elevation in serum creatinine	GFR <60 mL/min/1.73m ² for >3 mo and/or Kidney damage >3 mo
Reversibility	Potentially	Progressive and irreversible
Mortality	High (about 60%)	19%-24% (patients on dialysis)
Primary cause of death	Infection	Cardiovascular disease

Rapidly progressive renal failure (RPRF/RPGN)

- acute decreased Glomerular filtration rate(GFR)
: GFR fall over a period of weeks

Cause

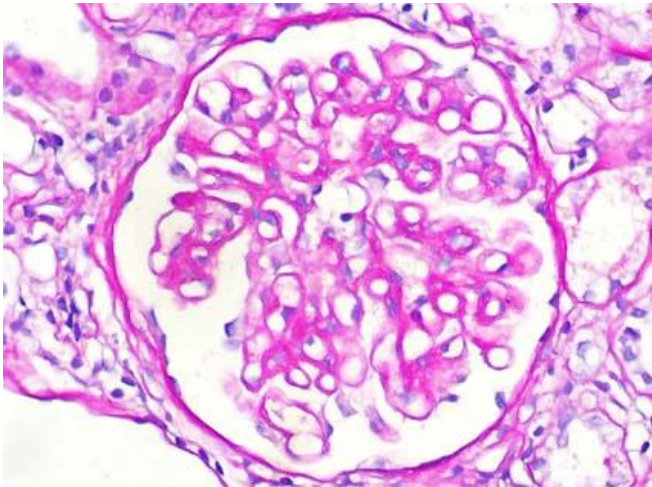
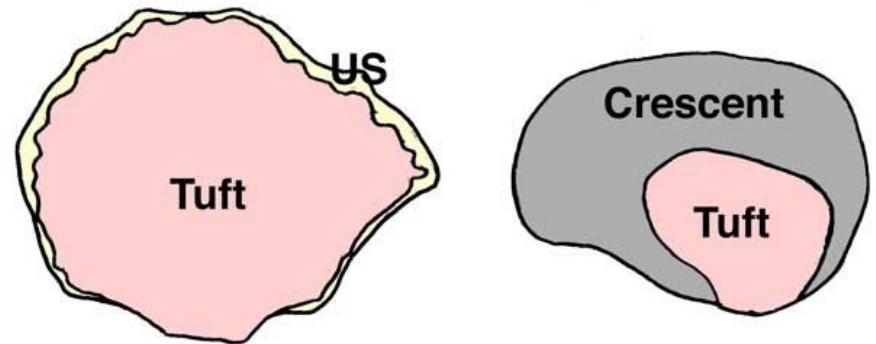
- extracapillary proliferative (**crescentic**) GN
due to immunologic injury or vasculitis

Manifestation

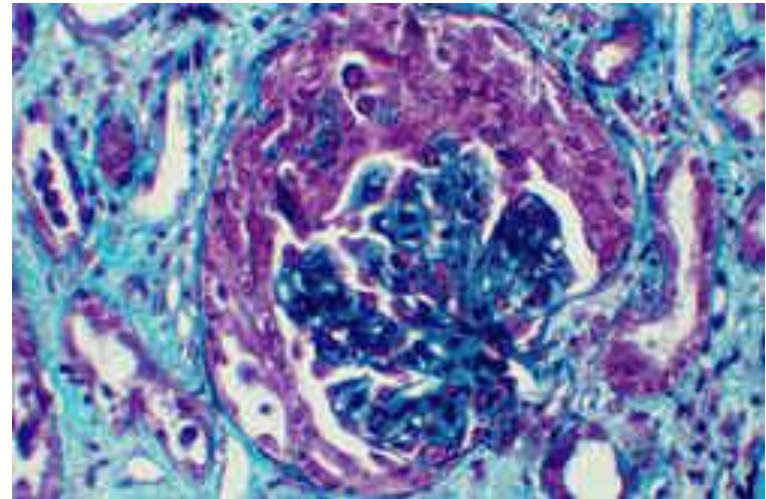
- : usually manifest with dramatic ARF
- : associated with systemic feature of vasculitis,
nephritic sediment,
rapid decrement of GFR

Rapidly progressive renal failure

Crescentic GN



normal



Crescentic GN

Rapidly progressive renal failure

4 major group

1) **Anti-GBM disease**

- : present with or without pulmonary hemorrhage
- : is the most dramatic of cause of RPGN

2) **ANCA-associated** vasculitis

- : GPA(granulomatosis with polyangiitis),
eGPA(eosinophilic GPA), MPA(microscopic polyangiitis)

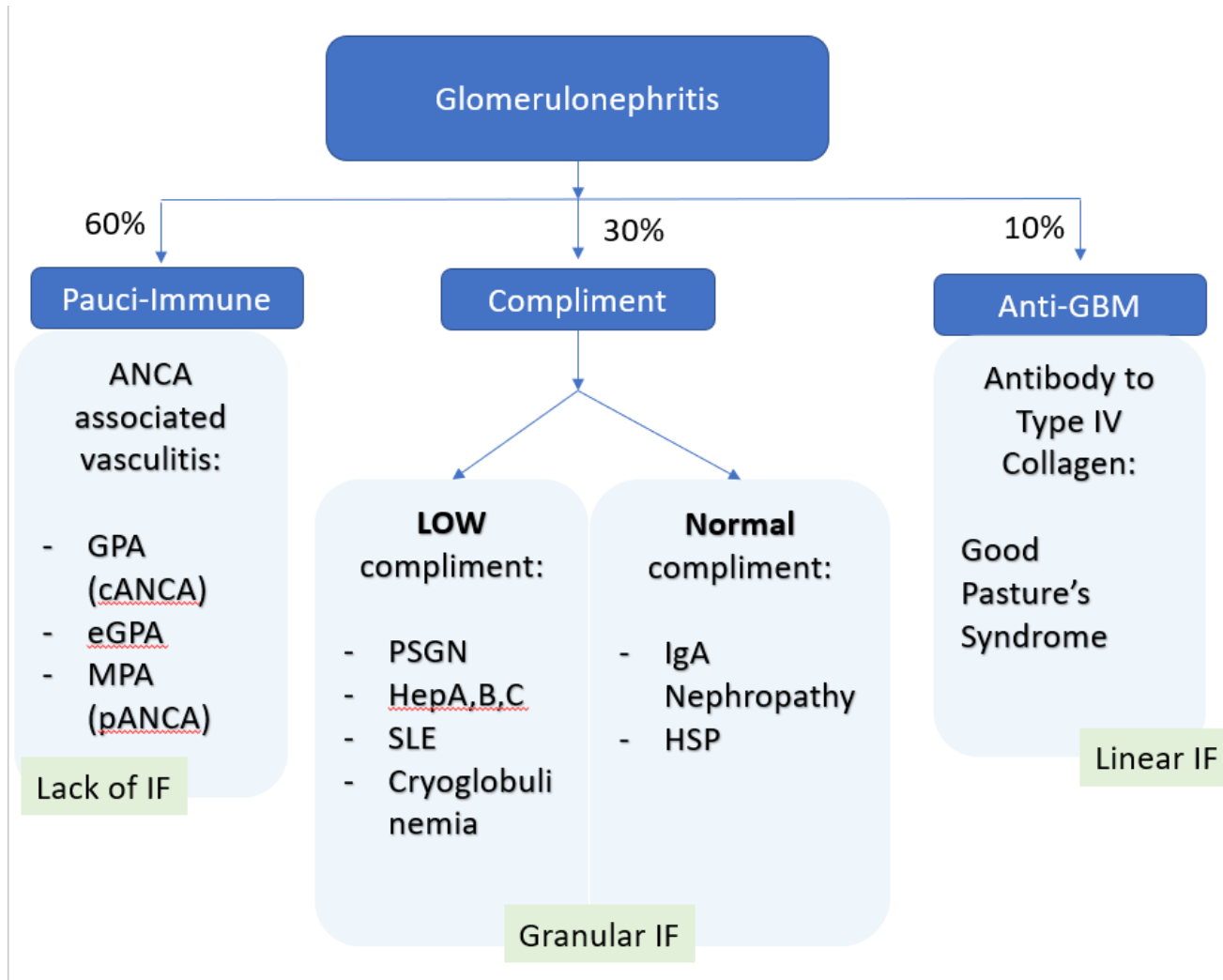
3) **Hypocomplementemic immune complex GN**

- : associated with low complement, immune complex GN
- : SLE, PSGN, infective endocarditis,shunt nephritis,
MPGN, cryoglobulinemia, GN associated with visceral abscess

4) **Immune complex** GN associated with **normal complement**

- : IgA nephropathy, HSP

Rapidly progressive renal failure



Asymptomatic urinary abnormalities

- mild degree of microscopic hematuria, pyuria, cast, less than 3.5 g protein/day
 - : may be present in urine of patient with no evidence of other nephrologic syndrome
 - considered to syndrome of **AUA**

Isolated hematuria

- : without proteinuria or cast
 - may be the sole clue to the presence of **neoplasm, stone, infection** in UT
- : hematuria with cast
 - in benign recurrent hematuria and IgAN

Isolated proteinuria

- : without RBC or other formed element in urinary sediment
 - characteristic of renal disease which manifest little or no inflammatory reaction within the glomeruli (ex, DM, amyloidosis)

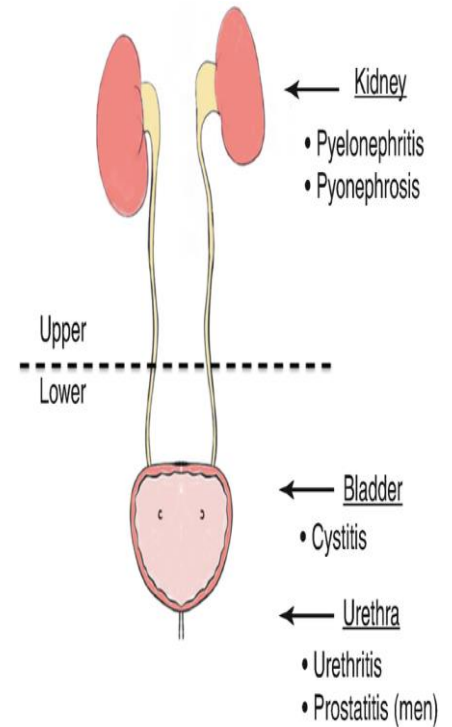
Urinary tract infection(UTI)

Causative organism

- : in anatomically normal UT
→ **E-coli** is common
- : in prolonged antibiotic treatment,
especially in impaired urinary drainage or stone
→ Klebsiella, Enterobacter, Proteus

Infection site

- : dysuria, frequency, urgency, suprapubic tenderness
→ suggest bladder and urethral inflammation (**lower UTI**)
- : flank pain, chill, fever, nausea, vomiting, hypotension
from sepsis, leukocyte cast
→ suggest renal parenchymal infection (**upper UTI**)



Renal tubule defect

- large number of acquired and **hereditary disorder**
tend to affect tubule more than glomeruli

Hereditary anatomic defect

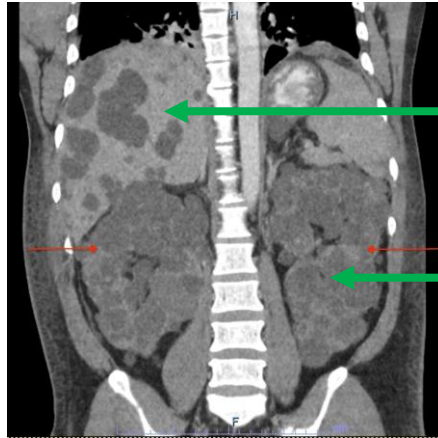
: **PKD**, medullary cystic disease, medullary sponge kidney

Defect in tubule transport function

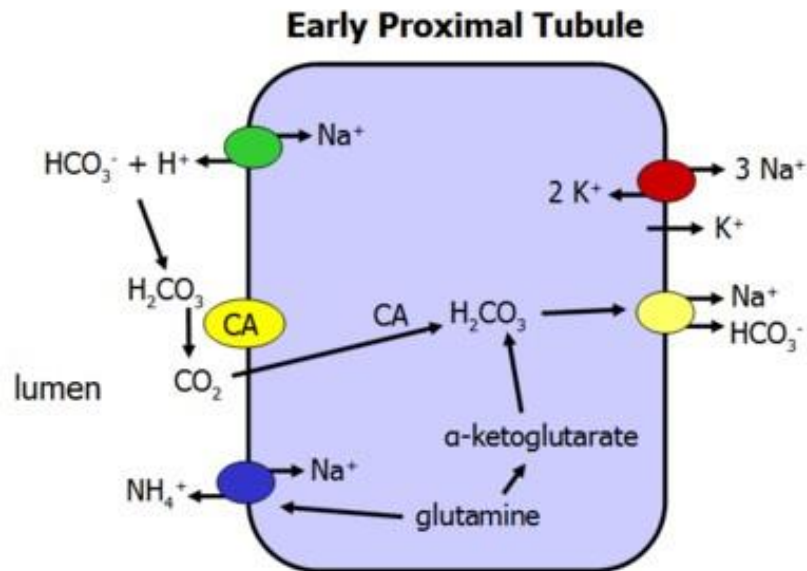
: impair secretion and reabsorption of electrolyte, organic solute
or
limit urinary concentration and diluting ability
→ cause polyuria, nocturia, metabolic acidosis,
disorder of fluid and electrolyte balance

Renal tubule defect

PKD



Multiple cyst in kidney,liver



Transport defect

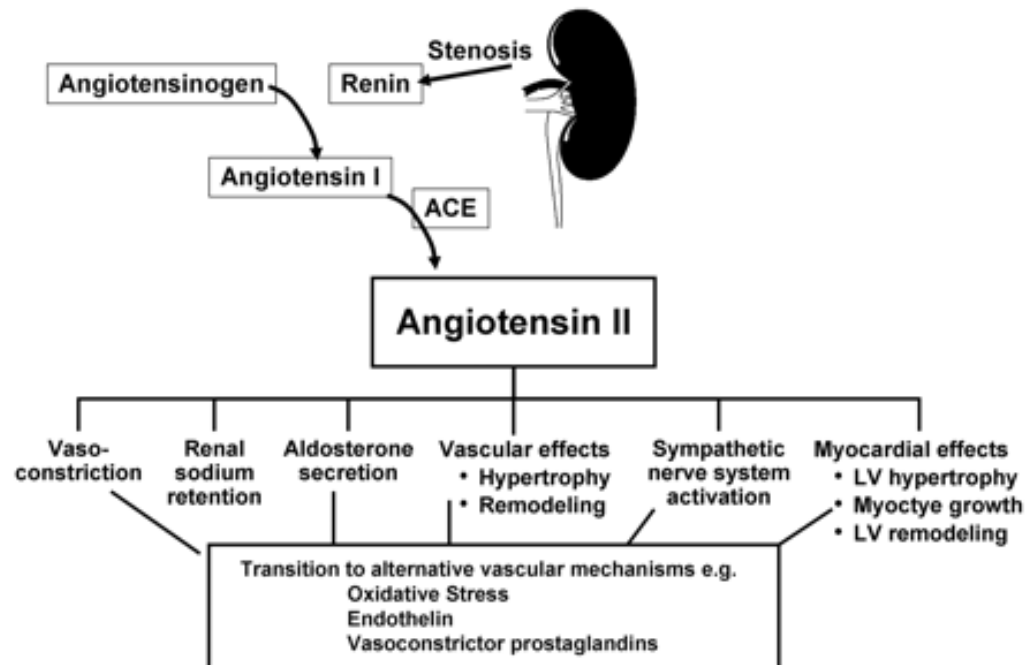
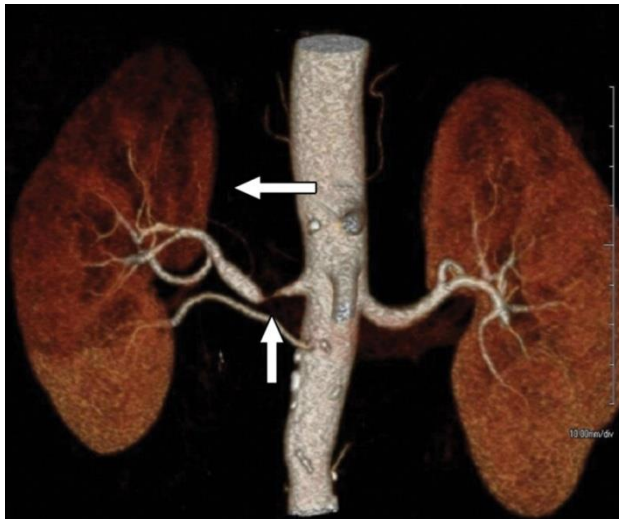
Hypertension

- blood pressure > 140 / 90 mmHg

Renal cause of Hypertension

1. renal parenchymal disease
(ex, AGN, CGN)

2. renovascular hypertension



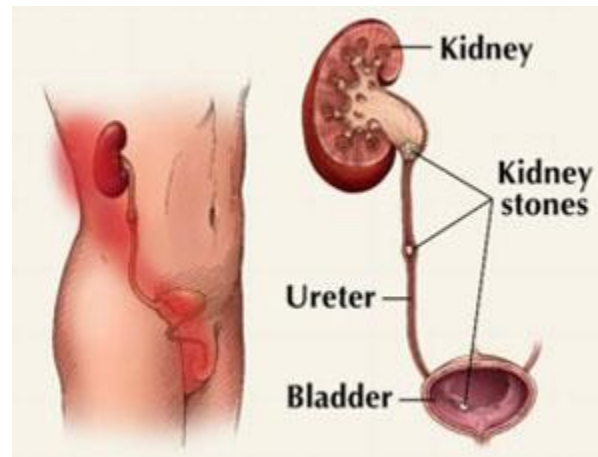
Nephrolithiasis

Stone composition

- calcium
- uric acid(radiolucent)
- cystine, struvite(magnesium ammonium phosphate)

Manifestation

→ renal colic, painful hematuria, unexplained pyuria, dysuria, urinary frequency



Urinary tract obstruction(UTO)

- anuria in adult
→ is almost due to obstruction of bladder outflow
- outflow obstruction
: nocturia, frequency,
overflow incontinence,
slowing or hesitancy of micturition
- obstruction (**obstructive uropathy**)
→ stasis
→ infection
→ progressive loss of renal function
(**obstructive nephropathy**)

