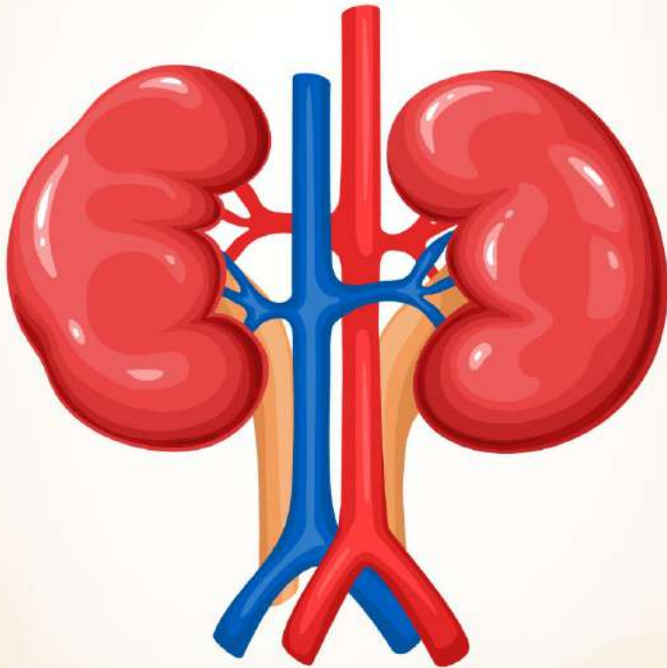




Internal Medicine



Topic : CKD Notes
Done by : Johainah Taha

Chronic Kidney Disease (CKD) Lecture

Kidney Anatomy & Functions

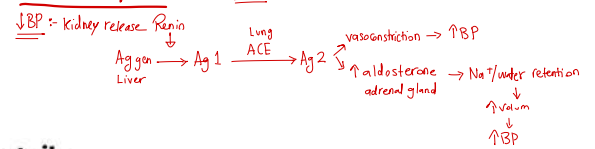
Kidney Overview

Feature	Details
Weight	~150 g (heart ~300 g)
Size	~12 cm (left kidney larger than right)
Nephrons <i>عدم بقل في kidney injury</i>	~1.3 million per kidney (<u>fixed</u> number, formed early in life)
Nephron Types	- Cortical (85%): Short loop of Henle - Juxtamedullary (15%): Long loop of Henle, associated with vasa recta, contributes to urine concentration

Kidney Functions

Function Type	Details
Regulation	Fluid balance, pH, blood pressure (<u>Short-term: RAAS; Long-term: blood volume</u>)
Homeostasis	Electrolyte balance $\rightarrow Ca^{+2}, K^+, Na^+$
Endocrine <i>* it acts as a gland.</i>	- RAAS activation (Blood pressure control) - Erythropoietin (85%) (Red blood cell production) - Vitamin D activation (Calcium homeostasis)
Paracrine	Prostaglandin E2 (PGE2), Nitric oxide (NO)
Clearance	Excretion of endogenous (e.g., urea, creatinine) and exogenous (e.g., drugs, toxins) waste products
Metabolism	Gluconeogenesis (~10%) (during fasting)

* RAAS system :



* what is Filtration fraction?

how much of plasma flowing is getting filtered = $\frac{GFR}{RPF} \approx 20\%$

glomerular filtration rate
renal plasma flow

Glomerular Filtration Rate (GFR).

- Estimated vs. Measured GFR
- Estimated: eGFR (using creatinine or cystatin C-based formulas) $\rightarrow$
- Measured: Requires exogenous filtration markers (e.g., inulin, iothexol)

$\oplus$ works as buffer system in Acid-Base - Balance.

- **Constant production** ✓
- **Freely filtered at the glomerulus** ✓
- No tubular secretion or resorption
– Some tubular secretion X
- No extra-renal metabolism ✓
- No extra-renal loss
– Some GIT loss X
- **Loss of creatinine** through avenues other than **glomerular filtration** means **Creatinine Clearance is slightly higher than the GFR**

* high protein diet $\rightarrow$ $\uparrow$ creatinine in urine.

* high protein in urine $\rightarrow$ Focal segmental glomerulosclerosis.

BOX 1

Examples of Common Glomerular Filtration Markers

Radionuclides

✓ Inulin labeled with carbon 14 (¹⁴C-inulin)

- Technetium Tc 99m diethylenetriaminepentaacetic acid (^{99m}Tc-DTPA)
- Chromium Cr 51 ethylenediaminetetraacetic acid (⁵¹Cr-EDTA)

Nonradionuclides

- Iodinated
 - Ionic: Iothalamate
 - Nonionic: Iohexol, iopamidol
- Noniodinated
 - Inulin
 - Creatinine (endogenous or exogenously administered)

Factors Related:

* NSAIDs $\rightarrow$ $\downarrow$ GFR

* ARBs + ACEi $\rightarrow$ $\downarrow$ GFR : But they decrease the progression of CKD.

* Trimethoprim + Sulfamethoxazole $\rightarrow$ $\uparrow$ creatinine clearance.

* Lower creatinine production
or
high creatinine secretion $\rightarrow$ over eGFR (False $\uparrow$ GFR)

Chronic Kidney Disease (CKD) Definition

- Progressive, irreversible loss of kidney function

Diagnostic Criteria:

- Pre-2002 (KDOQI): Termed "chronic renal failure"
- 2002 (KDOQI): Kidney abnormalities (structural or functional) for ≥ 3 months, with or without $\text{GFR} < 60 \text{ mL/min/1.73m}^2$
- NICE – UK (2008): Stage 3 subdivided into 3a and 3b
- KDIGO (2012): Albuminuria classification (A1-A3) added

← أنماط في مدى التضرر من GFR
وعدم اختلال في الكلى
A1 A2 A3

Pathophysiology of CKD

- Initiating Injury: (e.g., diabetes, hypertension, glomerulonephritis)
- Inflammatory Cell Recruitment
- Release of Growth Factors: Balance between fibrosis and repair
- Matrix Remodeling: (Collagen damage)
- RAAS Activation: Angiotensin II promotes fibrosis
↳ We can give ACEi to prevent fibrosis.

Stages of CKD

Stage	GFR (mL/min/1.73m ²)	Description
1	≥ 90	Kidney damage with normal or high GFR
2	60-89	Mildly decreased GFR
3a	45-59	Mild-moderate decrease
3b	30-44	Moderate-severe decrease
4	15-29	Severe decrease
5	< 15	Kidney failure (End-stage renal disease - ESRD)

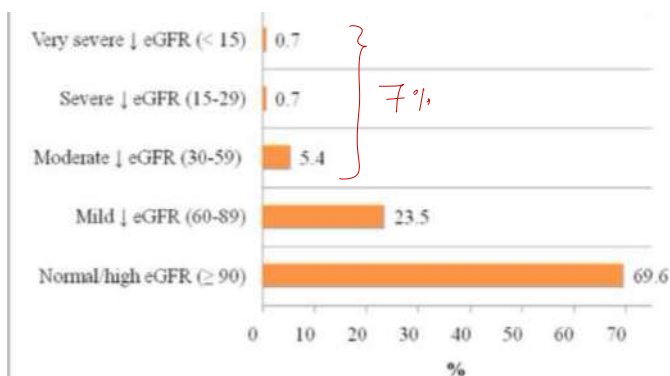
		Albuminuria categories (mg/g creatinine)		
		A1	A2	A3
		< 30	30-300	> 300
GFR categories (mL/min $\times$ 1.73 m ²)	G1	≥ 90		
	G2	60-89		
	G3a	45-59		
	G3b	30-44		
	G4	15-29		
	G5	< 15		
G5 D/T		Kidney failure	Usually defined by KRT	

* Patients with kidney diseases are at high risk to have Cardiovascular diseases.

* it's useful for DM patients to start dialysis $\rightarrow$ help them to $\downarrow$ risk of having Cardiovascular progression.

Epidemiology of CKD

- Global Prevalence: $\sim 10\%$ of adults (Stages 1-5)
- Diagnosis & Registration: Varies between countries
- High-Risk Population:**
 - $\sim 31\%$ of individuals at high risk had undiagnosed CKD (eGFR < 90)
 - 7% had significantly reduced eGFR
- Higher Mortality Risk: CKD patients have increased mortality vs. non-CKD individuals

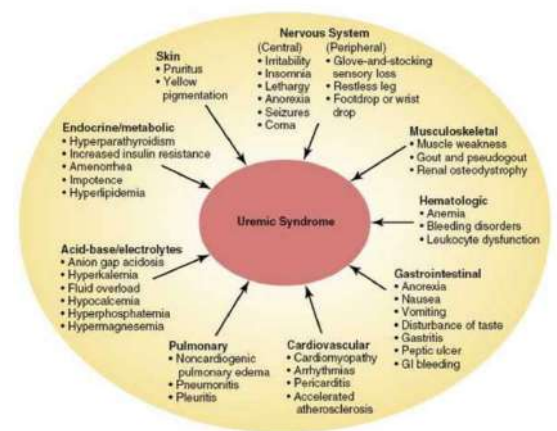


Risk Factors for CKD

Risk Factor	Description
Age	>60 years
Diabetes Mellitus (DM)	Leading cause of CKD
Hypertension (HTN)	Major contributor to CKD progression
Family History	Genetic predisposition

Leading Causes of CKD

1. Diabetes Mellitus (Diabetic nephropathy) → *أشهر سبب في الأورام*
2. Hypertension
3. Obstructive Nephropathy (e.g., kidney stones, BPH) → *↑ hydrostatic pressure → ↓ Filtration*
4. Primary Kidney Diseases (TIN, GN, ADPKD, recurrent UTI/pyelonephritis)
5. Renovascular Diseases
6. Nephrotoxic Medications (e.g., NSAIDs, heavy metals) → *Nephrotoxins → GFR related nephropathy*
لأنه يخفض معدل الترشيح وامتصاصه
7. Fetal Developmental Abnormalities
8. Infections (e.g., Hep C, HIV, malaria, yellow fever)
9. Substance Abuse (e.g., heroin, cocaine)
10. Acute Kidney Injury (AKI) leading to chronic damage



Clinical Manifestations

Urinary Symptoms

- Polyuria, oliguria, anuria → *affecting urine output*
- Frothy urine (proteinuria), hematuria

Metabolic Disturbances

System	Manifestations
Uremia	Accumulation of nitrogenous waste
Volume	Hypervolemia
Electrolytes & Acid-Base	- Sodium imbalance - Hyperkalemia - Acidosis - Hypocalcemia, hyperphosphatemia

* What is the difference between =

1) Uremia → Azotemia + Symptoms (nausea, vomiting, fatigue, pericarditis...)

2) Azotemia → ↑ BUN + ↑ creatinine without symptoms

* Due to Ca^{2+} loss =

1. ↑ turn over in bone leading to Osteod Cystic Fibroma
2. Ca^{2+} + P_i deposition in tissues.

Uremic Forest

→ Crystalline white deposit of urea on skin
→ appear as white, powdery
→ Pruritus



Systemic Involvement

System	Manifestations
Hematological	Anemia (↓ EPO), platelet dysfunction (bleeding, infection risk)
Cardiovascular (CVS)	CAD, LVH, HF, arrhythmias, * The most common cause of death is CV complications. pericarditis (called Uremic Pericarditis)
Respiratory	Pulmonary edema
Gastrointestinal	Nausea, vomiting, ulcers, uremic fetor
Neurological	Encephalopathy, peripheral neuropathy, restless leg syndrome
Skin	Earthy skin color, pruritus , petechiae , nail changes <i>→ due to ↑ in Phosphorus + Urea</i> <i>→ Leukonychia</i>

* ار Urea نقيج مر toxic ولكن ارشاعها دليل على تراكم toxin آخرن .

* نفع الانبياح CKD ← normocytic, normochromic .

نفع الانبياح في AKI ← macrocytic .

Investigations for CKD

Test	Purpose
Serum Urea/Creatinine	Kidney function assessment
Urinalysis	Proteinuria quantification
Electrolytes	K ⁺ , acidosis, Ca ²⁺ , phosphate, PTH, Albumin level.
Blood Tests → Anemia	CBC, iron, ferritin, folate, B12, HbA1c, lipids
Imaging	Renal ultrasound (size, asymmetry, cysts) → Atrophic, echogenicity ← ردى الى Fibrosis
Serology	Hepatitis, HIV
ECG	Cardiac complications
SPEP/Serological Tests	Autoimmune or plasma cell disorders

*SPEP:-

Serum protein electrophoresis to detect abnormal protein levels to identify Multiple Myeloma or Amyloidosis → these can cause kidney damage.

* Serological Tests:-

① ANA, anti-dsDNA → Lupus nephritis.

② ANCA → Vasculitis

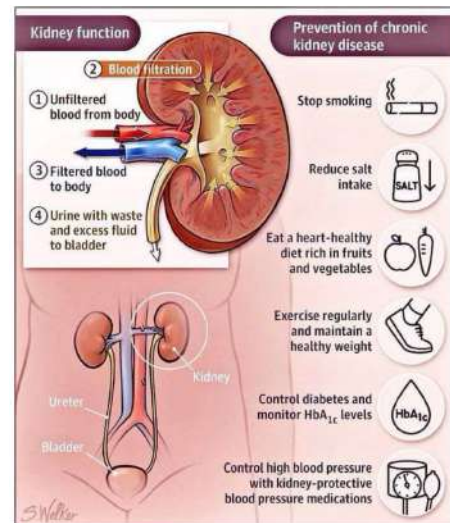
③ Anti-GBM → Goodpasture Syndrome

Management of CKD

General Approach

- Differentiate Acute vs. Chronic CKD
- Identify Reversible Causes
- Slow Progression & Treat Complications
 ← مبطون تقدم المرافقة لاشي
- Prepare for Renal Replacement Therapy (RRT) if GFR < 20 or do dialysis.

	Acute Kidney Injury	Chronic Kidney Disease
History	Short duration History of acute illness	Long duration History of kidney disease and/or causative co-morbidity
Examination	Acutely ill May have hypotension, fluid overload, metabolic acidosis,	Better toleration of biochemical abnormalities Anaemia, cachexia, grey discoloration of skin
Creatinine	Rapidly increasing values	History indicating derangement Stable serial measurements
Calcium	Usually normal	Low in untreated chronic disease
Haemoglobin	May be normal or low	Due to erythropoietin deficiency- chronic normocytic anaemia
Renal ultrasound	Often normal When the cause is acute obstruction- hydronephrosis	Scars from reflux nephropathy Renovascular disease- asymmetry Large kidneys in • Diabetes, • Amyloidosis, • Chronic Hydronephrosis • Polycystic Kidney disease



Treating Underlying Causes

Cause	Treatment
Glomerulonephritis	Immunosuppressants
Pyelonephritis	Antibiotics
Acute Interstitial Nephritis (AIN)	Discontinue offending drug, steroids
Obstruction	Surgical intervention
Renovascular Disease	BP control, revascularization

Slowing Progression

- BP control: RAAS blockers (ACEi/ARBs)
- Glycemic control (DM)
- SGLT2 inhibitors
- Lifestyle: Smoking cessation, diet (low protein, salt, phosphate, K⁺), exercise
- Correct acidosis ($\text{HCO}_3^- < 22$) → give them Na⁺ Bicarbonate
- Manage dyslipidemia → to ↓ cardiovascular complication

* Uric Acid ?

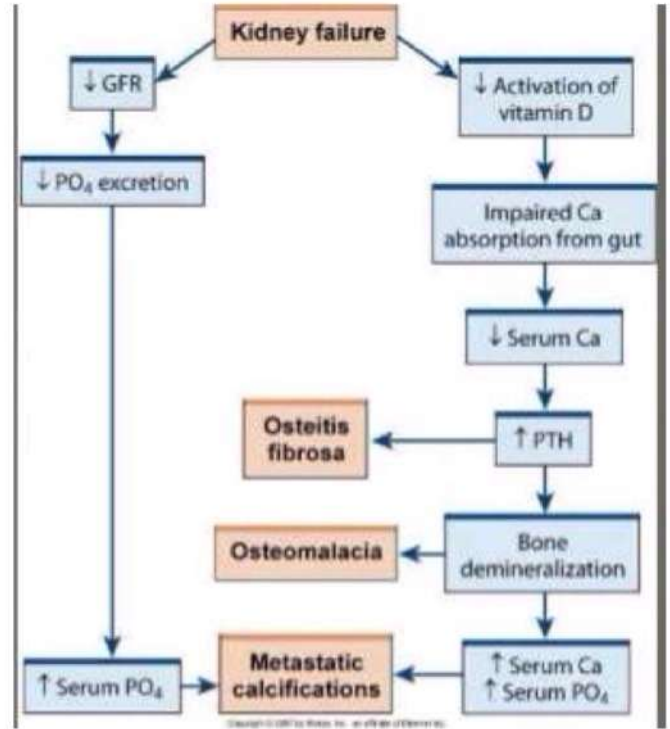
* ACEi → ↓ proteinuria, ↓ Fibrosis, ↓ Filtration

* تأخير توتيت القديس على CV أسرع من RS

⊕ don't forget to treat complications :

1. Anemia target = 10-11
2. 2ry hyperparathyroidism.
3. CV disease.

Major Dosage Reduction	Minor or No Reduction	Avoid Usage
Antibiotics		
Aminoglycosides	Erythromycin	Nitrofurantoin
Penicillin	Nafcillin	Nalidixic acid
Cephalosporins	Clindamycin	Tetracycline
Sulfonamides	Chloramphenicol	
Vancomycin	Isoniazid, rifampin	
Quinolones	Amphotericin B	
Fluconazole	Aztreonam, tazobactam	
Acyclovir, ganciclovir	Doxycycline	
Foscarnet		
Imipenem		
Others		
Digoxin	Antihypertensives	Aspirin
Procainamide	Benzodiazepines	Sulfonylureas
H ₂ antagonists	Quinidine	Lithium carbonate
Meperidine	Lidocaine	Acetazolamide
Codeine	Spirolactone	NSAIDs
Propoxyphene	Triamterene	Phosphate-containing bowel-preps



Renal Replacement Therapy (RRT)

Option	Description
Transplant	Preferred long-term solution
Hemodialysis	Requires vascular access
Peritoneal Dialysis	Home-based option
Future Options?	Artificial/animal kidney research