Chronic Kidney Disease and Laboratory Challenges

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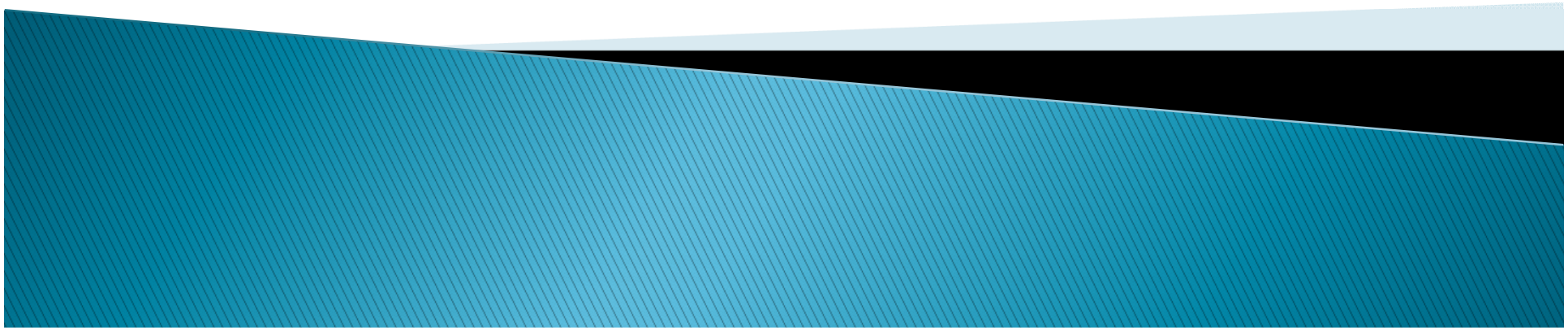
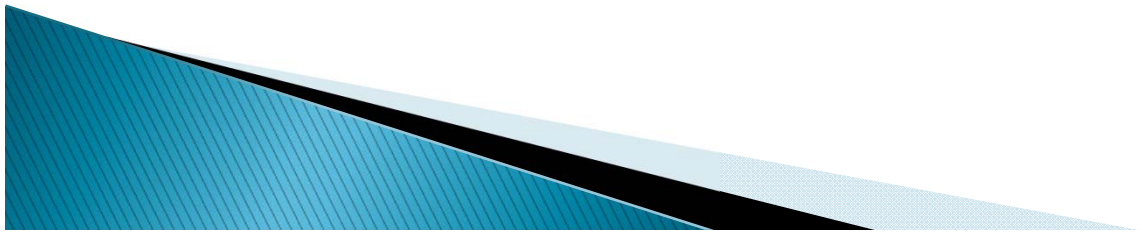


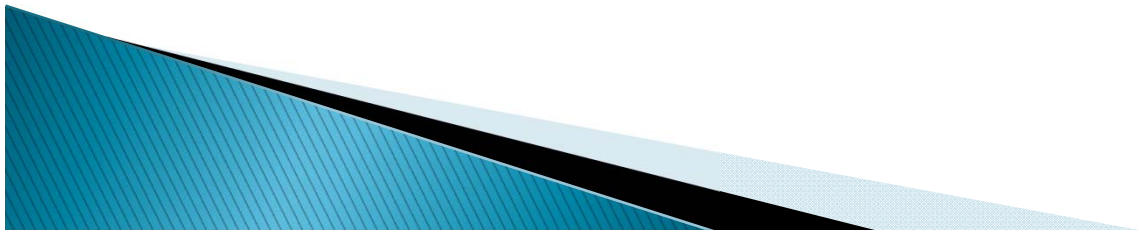
Background

- chronic kidney disease (CKD) as either kidney damage or a decreased kidney glomerular filtration rate (GFR) for 3 or more months.



History:

- Patients with CKD stage 3 or lower (GFR >30 mL/min) generally are asymptomatic.
- Generally, these disturbances clinically manifest with CKD stages 4 and 5 (GFR <30 mL/min).

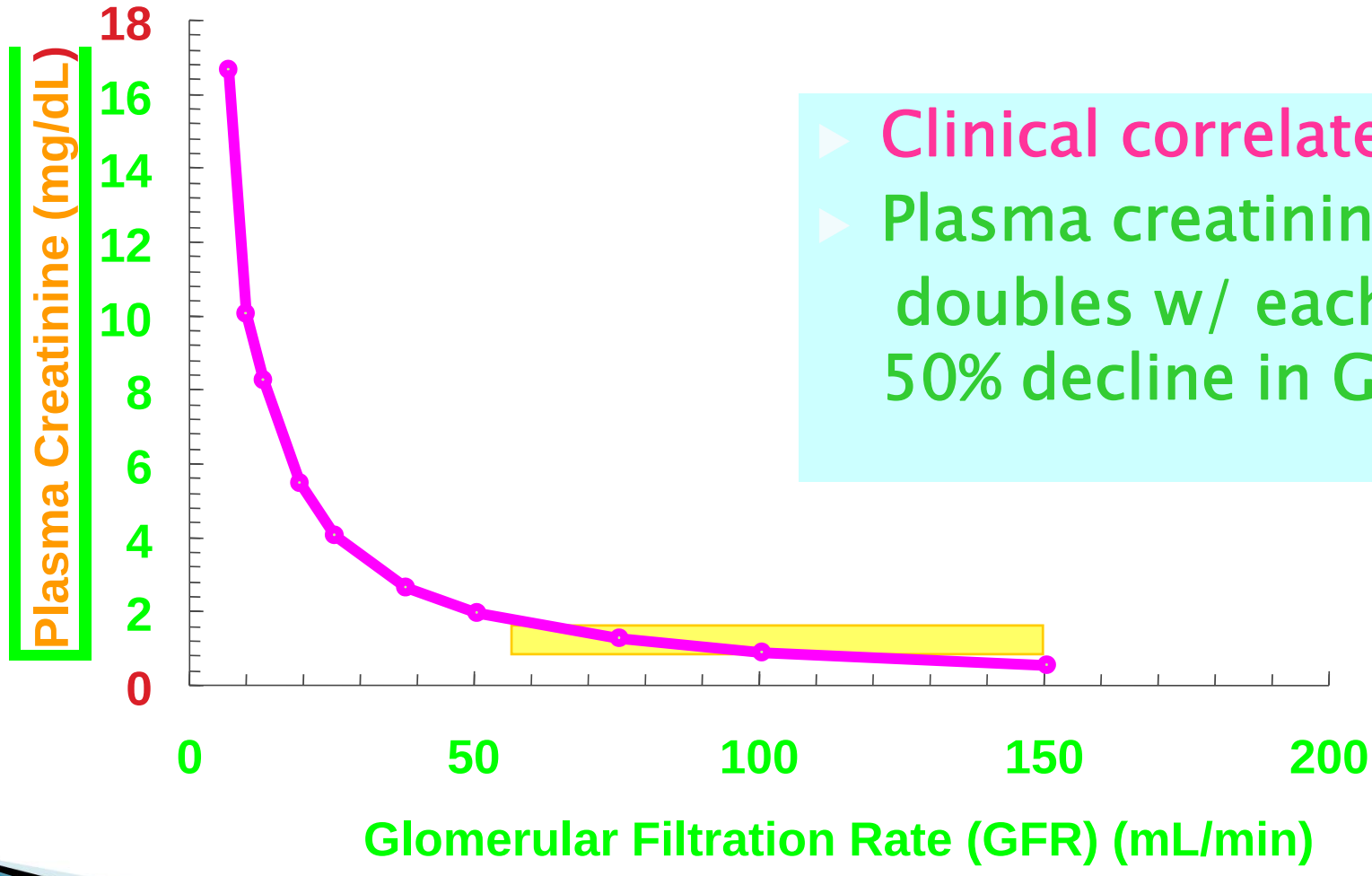


Measurement of Glomerular Filtration Rate (GFR)

- GFR is essential to renal function
- Most frequently performed test of renal function.
- Measurement is based on concept of clearance: –

"The determination of the volume of plasma from which a substance is removed by glomerular filtration during it's passage through the kidney"

Relationship between Cr and GFR



- Clinical correlate:
- Plasma creatinine doubles w/ each 50% decline in GFR

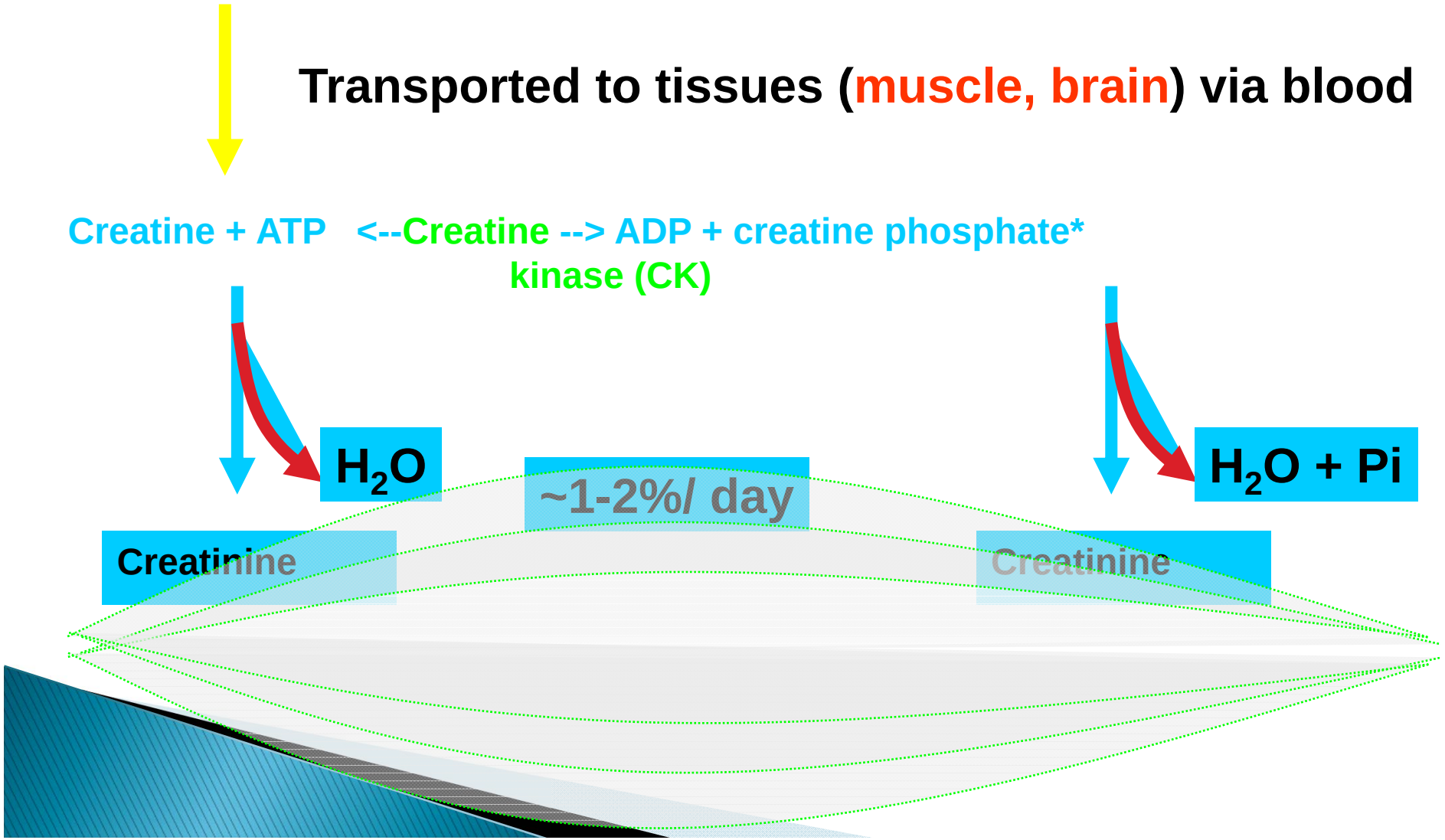
Determination of Clearance

- Clearance = (U xV)/P

  Where U is the urinary concentration of substance x
  V is the rate of urine formation (mL/min)
  P is the plasma concentration of substance x

- Units = volume/unit time (mL/min)
- If clearance = GFR then substance x properties: -
  - freely filtered by glomerulus
  - glomerulus = sole route of excretion from the body (no tubular secretion or reabsorbtion)
  - Non-toxic and easily measurable

CREATINE: synthesized in: muscle, pancreas, kidney



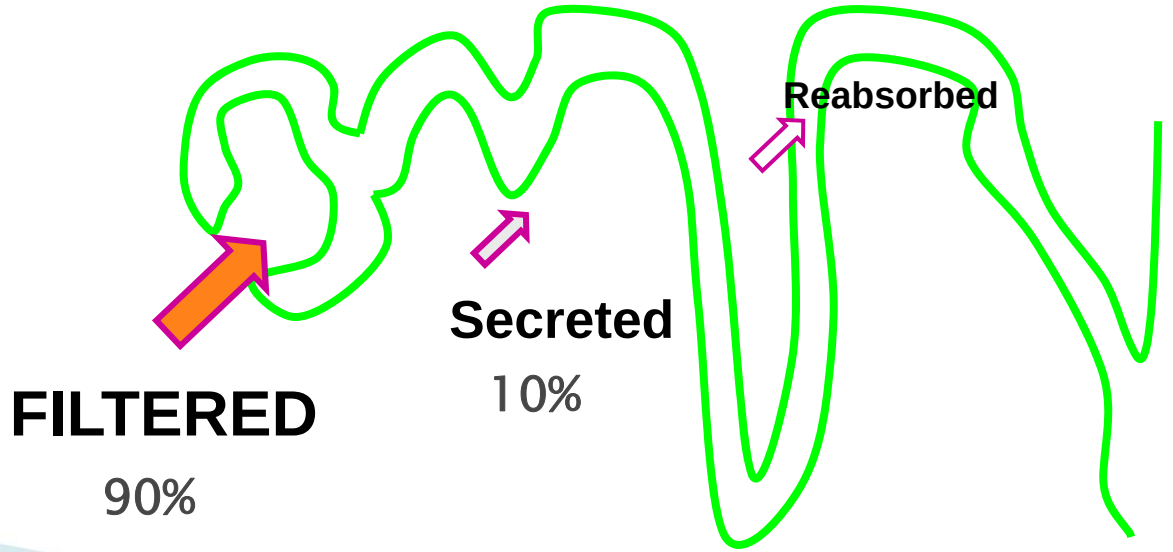
CREATININE: breakdown product of: creatine

- concentration in blood is related to:
  - muscle mass
  - creatine intake (body builders)
  - excretion by the kidney

- concentration in blood is *inversely* proportional to:
  - clearance via the kidney (GFR)

CrEATININE: renal excretion

- – Cr: freely filtered through GBM
- – Cr: secreted via tubules
- – Cr: negligible amount: reabsorbed



USEDTO ESTIMATE GFR --->CREATININE CLEARANCE (CrCl)

$$CrCl = \frac{\text{Urine Volume} \times UCr}{PCr}$$

UCr = [urine creatinine]

PCr = [plasma or serum creatinine]

Express CrCl: mL/min (or) mL/min/1.73 M2

Serum creatinine vs creatinine clearance

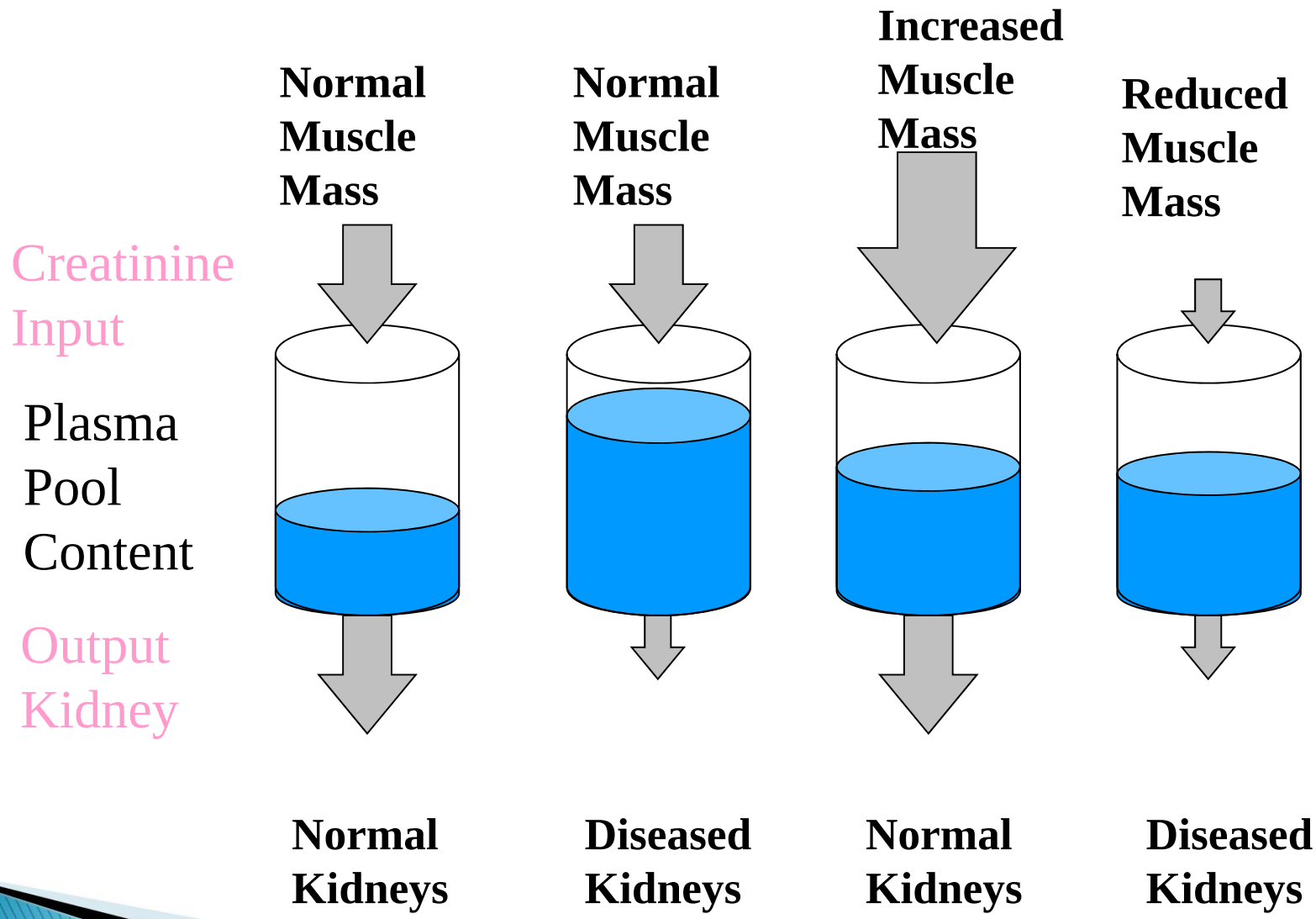
- Cockroft-Gault Equation:

Creatinine clearance =

$$\frac{(140 - \text{age}) \times \text{wt(kg)}}{72 \times \text{S cr(mg/dl)}}$$

X %85 for female

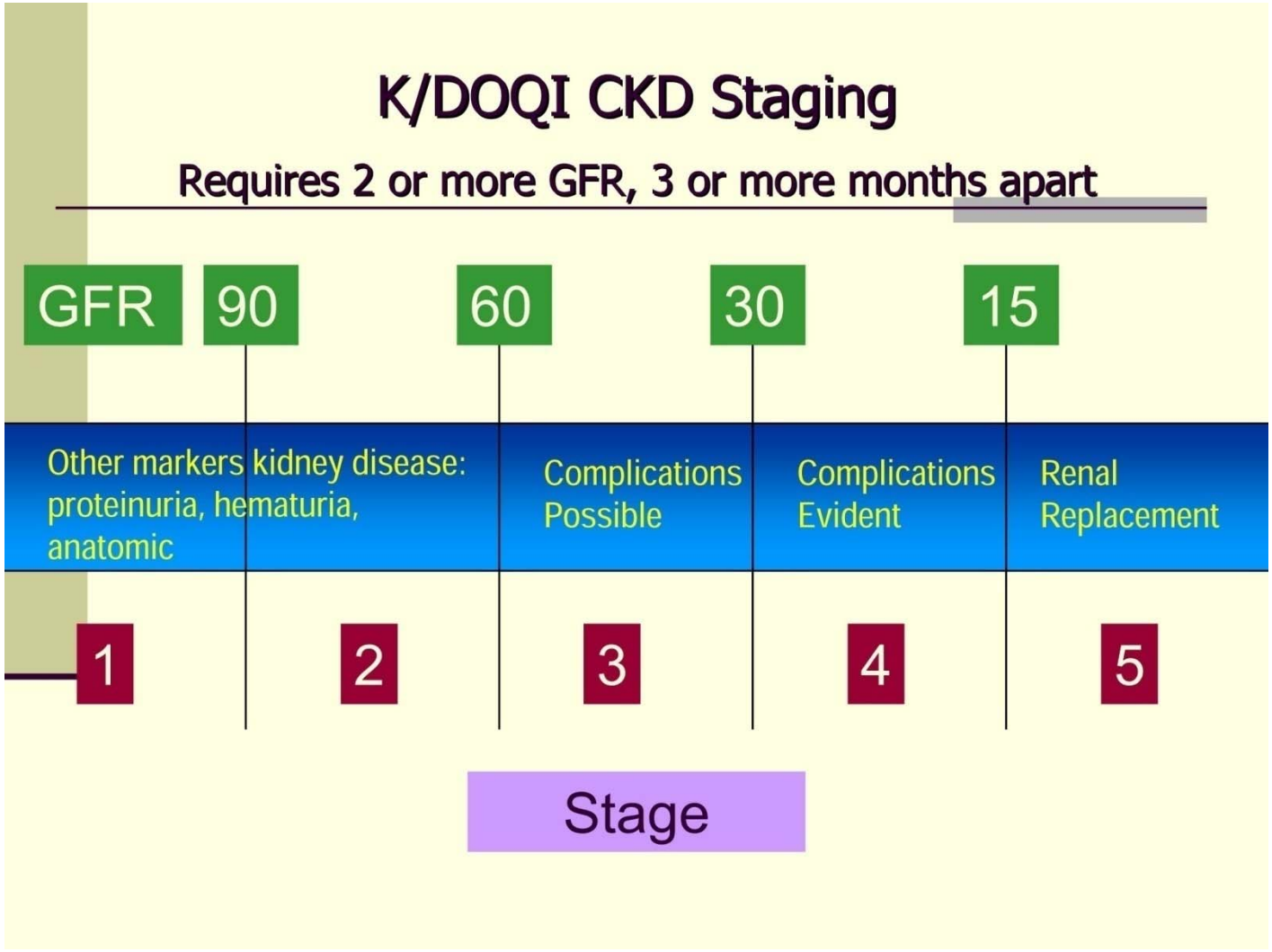
Effect of Muscle Mass on Serum Creatinine

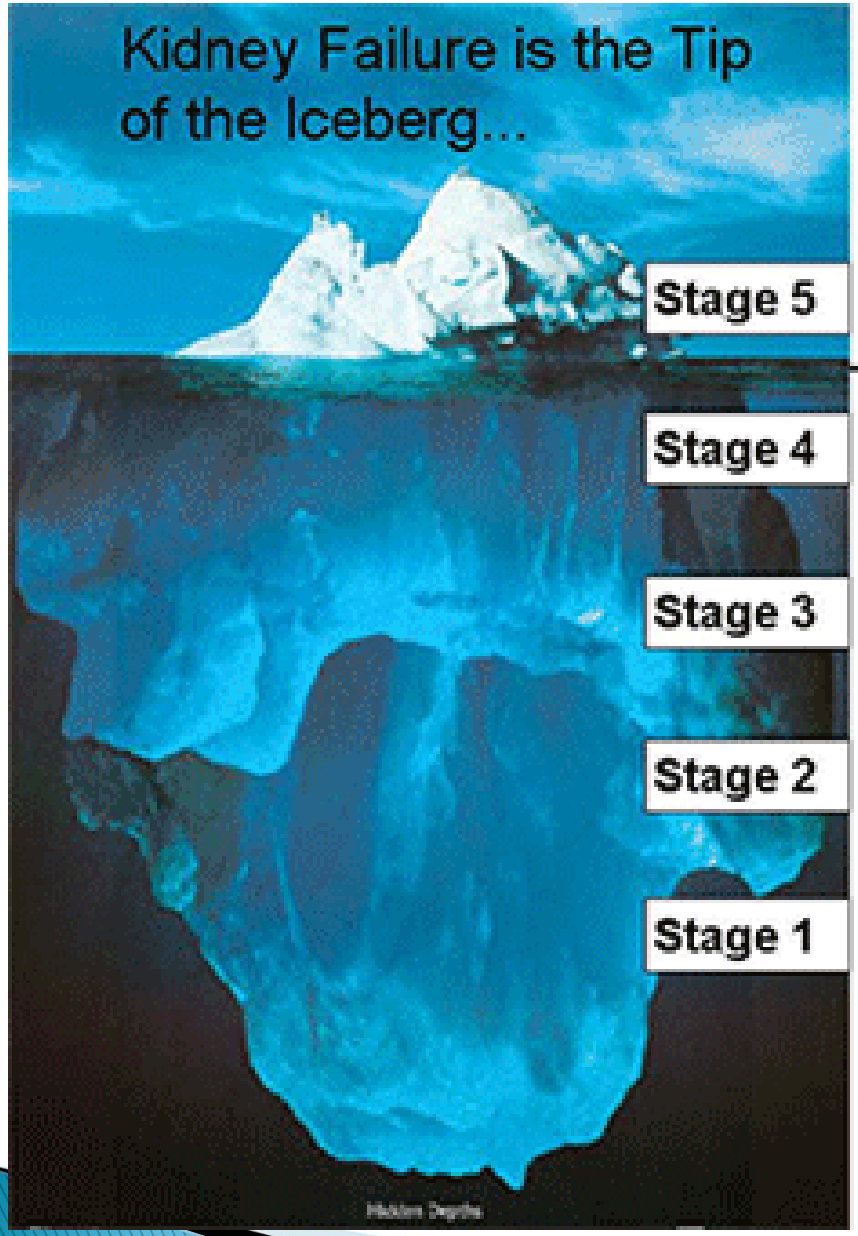


BUN

- Almost all urea is filtered out of blood by glomerular function. Some urea reabsorbed with water but most is removed in urine.
- Many non-renal conditions can increase BUN, i.e. hypovalemia, shock, burns, dehydration, congestive heart failure, excess protein catabolism.
- Thus, BUN needs to be compared to creatinine to determine true renal dysfunction

Property	Urea	Creatinine	Inulin	^{99m}TcDTPA
Not Protein Bound	*Yes*	*Yes*	*Yes*	*Yes*
Freely Filtered	*Yes*	*Yes*	*Yes*	*Yes*
No secretion or absorbtion	*Flow related reabsorption*	*Some secretion*	*Yes*	*Yes*
Constant endogenous production rate	*No*	*Yes*	*No*	*No*
Easily Assayed	*Yes*	*Yes*	*No*	*No*


K/DOQI CKD Staging
Requires 2 or more GFR, 3 or more months apart
GFR
90
60
30
15
Other markers kidney disease: proteinuria, hematuria, anatomic
Complications Possible
Complications Evident
Renal Replacement
1
2
3
4
5
Stage



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/ind

Prognosis of CKD by GFR and albuminuria categories: KDIGO 2012

GFR categories (ml/min/1.73 m²) description and range				Persistent albuminuria categories description and range		
				A1	A2	A3
				Normal to mildly increased	Moderately increased	Severely increased
				<30 mg/g <3 mg/mmol	30–300 mg/g 3–30 mg/mmol	>300 mg/g >30 mg/mmol
	G1	Normal or high	≥90			
	G2	Mildly decreased	60–89			
	G3a	Mildly to moderately decreased	45–59			
	G3b	Moderately to severely decreased	30–44			
	G4	Severely decreased	15–29			
	G5	Kidney failure	<15			

MDRD STUDY EQUATION
(MODIFICATION OF DIET IN RENAL DISEASE)

- $eGFR = 175 \times (S_{Cr})^{-1.154} \times (age)^{-0.203} \times 0.742$ [if female] x1.212 [if Black]

The CKD-EPI creatinine equation
(chronic kidney disease epidemiology collaboration)

- The CKD-EPI creatinine equation is based on the same four variables as the MDRD Study equation, but uses a different relationship for age, sex and race. The equation was reported to perform better and with less bias than the MDRD Study equation, especially in patients with higher GFR.

The CKD-EPI Creatinine Equation (2009)

$GFR = 141 \times \min(Scr/\kappa, 1)^{\alpha} \times \max(Scr/\kappa, 1)^{-1.209} \times 0.993^{Age} \times 1.018[\text{if female}] \times 1.159[\text{if black}]$

$\kappa = 0.7$ if female
$\kappa = 0.9$ if male

$\alpha = -0.329$ if female
$\alpha = -0.411$ if male

min = The minimum of Scr/κ or 1
max = The maximum of Scr/κ or 1

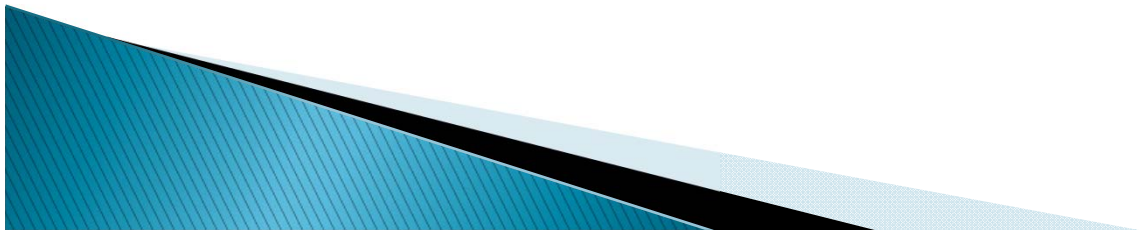
Scr = serum creatinine (mg/dL)

CKD-EPI CYSTATIN C EQUATION (2012)

- $eGFR = 133 \times \min(S_{cys}/0.8, 1)^{-0.499} \times \max(S_{cys}/0.8, 1)^{-1.328} \times 0.996^{Age} \times 0.932$ [if female]

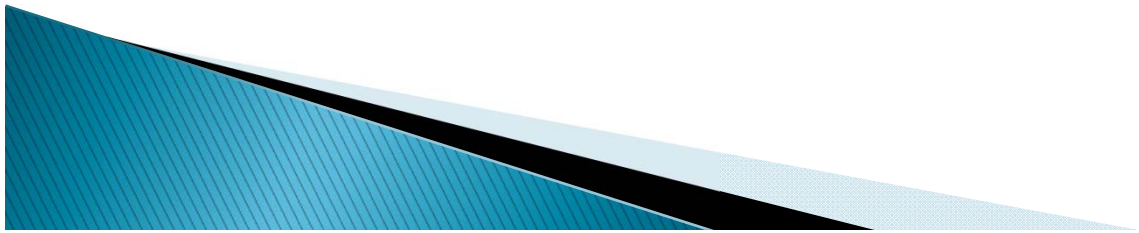
CKD-EPI CYSTATIN C :Clinical Use

- Can be used as a confirmatory test for the diagnosis of CKD in patients with a decreased GFR as estimated from creatinine.
- Considering some patients as not having CKD and not being at high risk.
- to obtain a more accurate estimation of GFR in patients with muscle wasting or chronic illness.

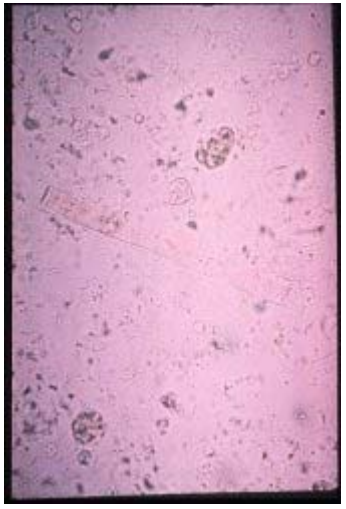


Other lab tests in CKD

- U/A
- Sodium
- Potassium
- Calcium
- Phosphate
- PTH
- Acidosis
- Hb



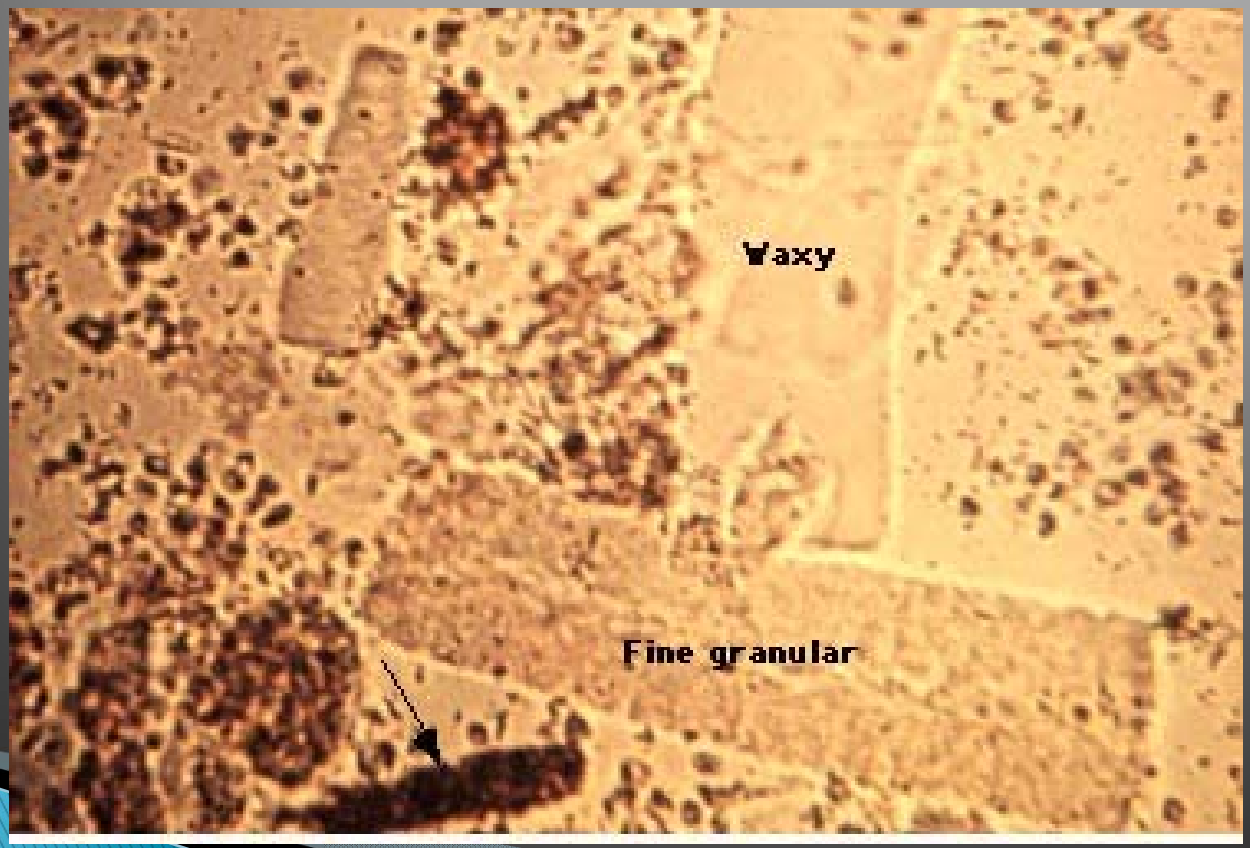
6.Waxy Cast in CRF



8.Broad casts

(form in dilated, damaged tubules)

CRF



Sodium and Water Homeostasis

- volume expansion may contribute to hypertension, which itself can accelerate the nephron injury.
- As long as water intake does not exceed the capacity for water clearance, the ECFV expansion will be isotonic and the patient will have a normal plasma sodium concentration

Sodium and Water Homeostasis

- In addition to problems with salt and water excretion, some patients with CKD may instead have impaired renal conservation of sodium and water.
- When an extrarenal cause for fluid loss, such as gastrointestinal (GI) loss, is present, these patients may be prone to ECFV depletion because of the inability of the failing kidney to reclaim filtered sodium adequately.

Potassium Homeostasis

- In CKD, the decline in GFR is not necessarily accompanied by a parallel decline in urinary potassium excretion, which is predominantly mediated by aldosterone-dependent secretion in the distal nephron.
- Another defense against potassium retention in these patients is augmented potassium excretion in the GI tract.

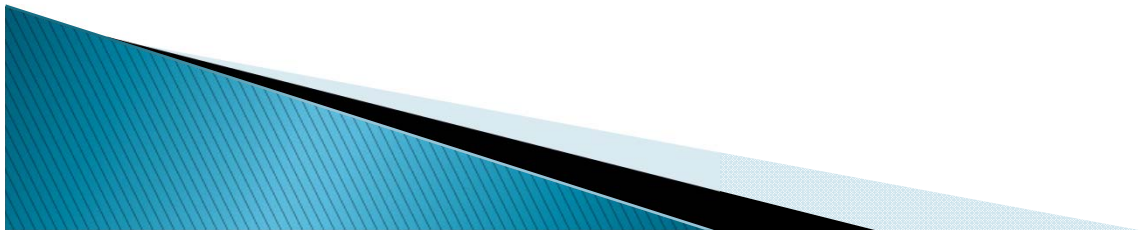
Hyperkalemia

- 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

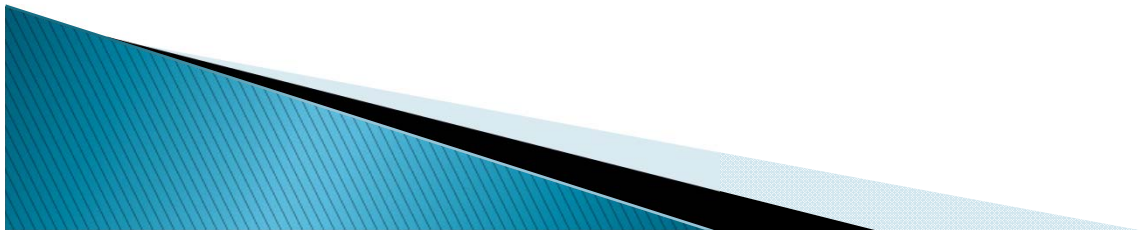
- CKD stage 5
- Non-anion gap and anion gap

- 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.



Ca & P

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



Anemia

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