Chronic Kidney Diseases

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ETIOLOGY AND EPIDEMIOLOGY

- True estimate of CKD in population is difficult because CKD is asymptomatic.
- least 6% of the adult population in the United States has chronic kidney disease at stages 1 and 2.
- 4.5% of the U.S. population is estimated to have stages 3 and 4 CKD

Risk for CKD with normal GFR.

- Gestation birth weight
- Childhood obesity
- Hypertension
- diabetes mellitus,
- autoimmune disease
- advanced age
- African ancestry
- a family history of kidney disease
- a previous episode of acute kidney injury,
- presence of proteinuria
- abnormal urinary sediment
- Structural abnormalities of the urinary tract.

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			

Source: J.L. Jameson, A.S. Fauci, D.L. Kasper, S.L. Hauser, D.L. Longo, J. Loscalzo: Harrison's Principles of Internal Medicine, 20th Edition

PATHOPHYSIOLOGY AND BIOCHEMISTRY OF UREMIA

- These include water soluble, hydrophobic, protein-bound with or without charged, and nitrogen containing metabolism
- The uremic syndrome involves more than renal excretory failure
- (1) Accumulation of toxins that normally undergo renal excretion
- (2)loss of other kidney functions, such as fluid and electrolyte homeostasis and hormone regulation
- (3) progressive systemic inflammation

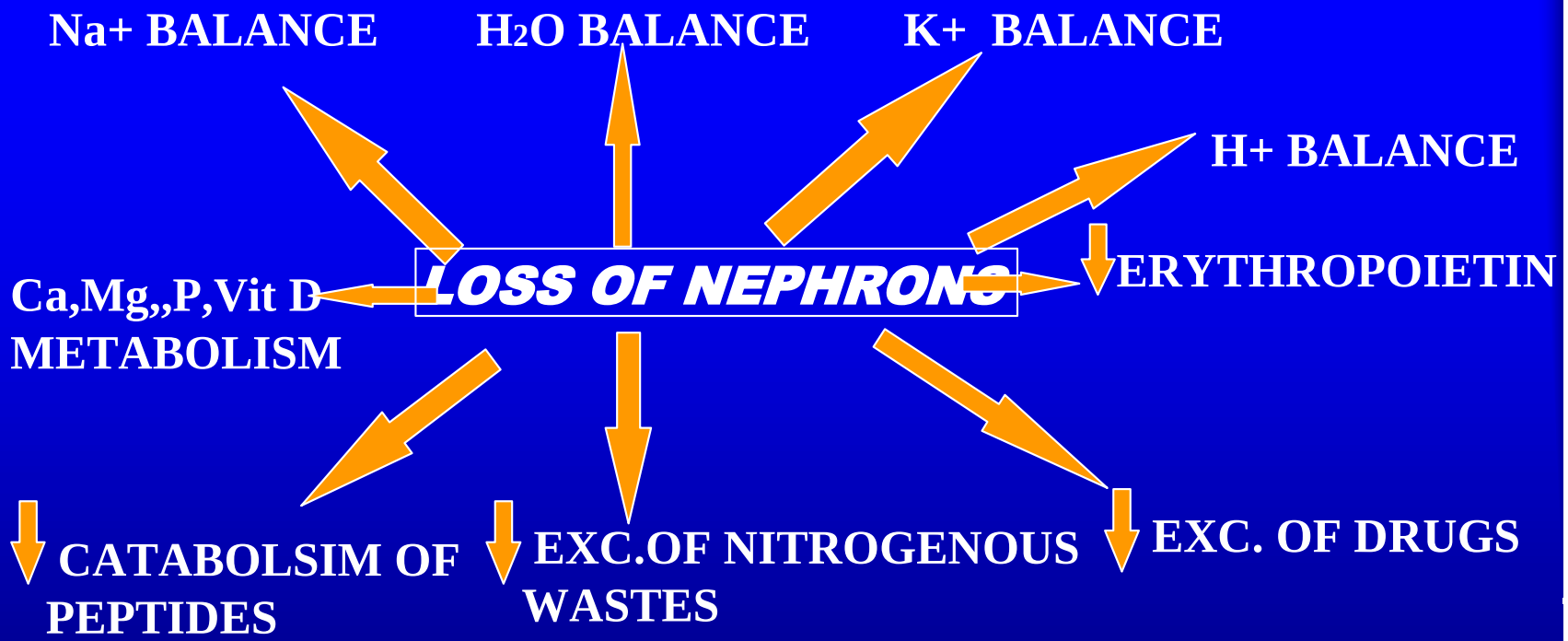
uremic syndrome

- Metabolic and endocrine functions normally performed by the kidneys is also impaired, and this results in anemia, malnutrition, and abnormal metabolism of carbohydrates, fats, and proteins
- plasma levels of many hormones, including PTH, FGF-23, insulin, glucagon, steroid hormones including vitamin D and sex hormones, and prolactin change with CKD as a result of reduced excretion, decreased degradation, or abnormal regulation.

CKD is associated with increased systemic inflammation.

- Elevated levels of C-reactive protein are detected along with other acute- phase reactants
- levels of so-called negative acute-phase reactants, such as albumin, fetoin
- *Inflammation CKD syndrome malnutrition-inflamemation-atherosclerosis/ calcification*, which contributes in turn to the acceleration of vascular disease and comorbidity associated with advanced kidney disease.

UREMIA PATHOPHYSIOLOGY



DR.V.KANNAN

Sodium and Water Homeostasis

- Sodium retention and extracellular fluid volume(ECFV) expansion This expansion may contribute to hypertension
- Hyponatremia is not commonly seen in CKD patients
- The patient with ECFV expansion (peripheral edema, sometimes hypertension) poorly responsive to therapy
- Thiazide diuretics have limited utility in stages 3–5 CKD
- The combination of loop diuretics with metolazone maybe helpful
- Diuretic resistance with intractable edema and hypertension in advanced CKD may serve as an indication to initiate dialysis

Potassium Homeostasis

- aldosterone-dependent secretion in the distal nephron is impaired excretion in the GI tract.
- These include increased dietary potassium intake, hemolysis, hemorrhage, transfusion of stored red blood cells, and metabolic acidosis.
- important medications include the RAS inhibitors and spironolactone and other potassium-sparing diuretics such as amiloride, eplerenone, and triamterene.
- The benefits of the RAS inhibitors: very close monitoring of plasma potassium concentration.

Potassium Homeostasis

- Hyperkalemia is not compatible GFR associated with hyporeninemic hypoaldosteronism, such as diabetes renal diseases that preferentially affect the distal nephron,such as obstructive uropathy and sickle cell nephropathy.
- Hypokalemia is not common in CKD

reduced dietary potassium intake, excessive diuretic therapy or concurrent GI losses.

The use of potassium supplements and potassium-sparing diuretics may be risky in patients with impaired renal function, and needs to be monitored closely.

Management Hyperkalemia

- Kaliuretic diuretics promote urinary potassium excretion,
- potassium-binding resins, such as calcium resonium, sodium polystyrene or patiromer can promote potassium loss through the GI tract and may reduce the incidence of hyperkalemia
- Intractable hyperkalemia is an indication (although uncommon) to consider institution of dialysis in a CKD patient

Metabolic Acidosis

- The combination of hyperkalemia and hyperchloremic metabolic acidosis is often present, even at earlier stages of CKD (stages 1–3)
- In most patients, the metabolic acidosis is mild; the pH is rarely <7.32
- Modest degrees of metabolic acidosis may be associated with

the development of protein catabolism

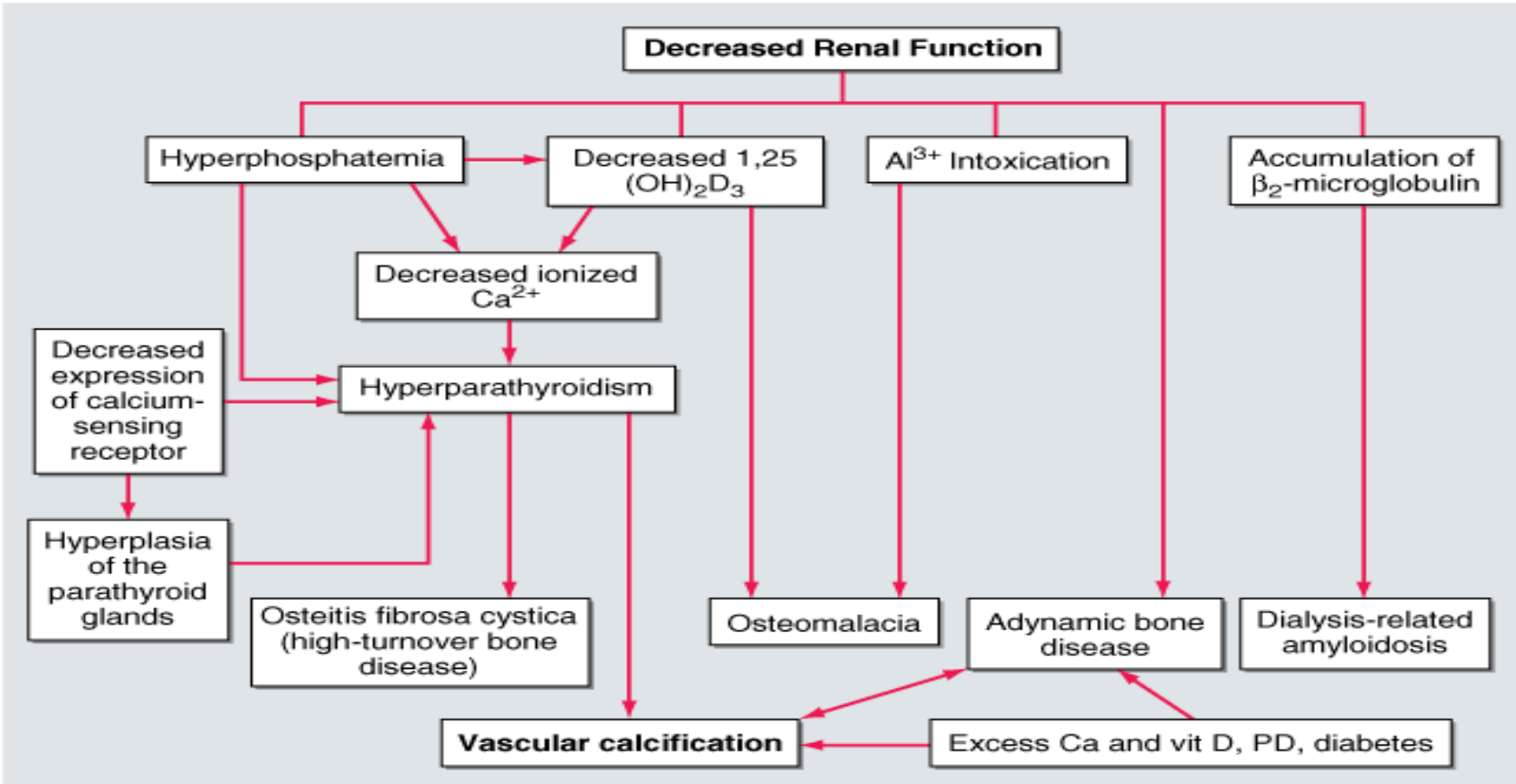
- Alkali supplementation recommended when the serum bicarbonate concentration falls below 20–23 mmol/L

Fluid, Electrolyte, and Acid-Base Disorders treatment

Euvolemia

- Dietary salt restriction and the use of loop diuretics, occasionally in combination with metolazone
- Water restriction is indicated only if there is a problem with hyponatremia.
- Hyperkalemia often responds to dietary restriction of potassium,
  - kaliuretic diuretics, and avoidance of both potassium supplements
  - avoidance of potassium-retaining medications

ROD



Source: Fauci AS, Kasper DL, Braunwald E, Hauser SL, Longo DL, Jameson JL, Loscalzo J: *Harrison's Principles of Internal Medicine*, 17th Edition: http://www.accessmedicine.com

FGF-23 is part of a family of phosphatonins that promotes renal phosphate excretion

- This hormone, secreted by osteocytes, increase early in the course of CKD, even before phosphate retention and hyperphosphatemia.
- FGF-23 may defend normal serum phosphorus in at least three ways:
- (1) increased renal phosphate excretion;
- (2) stimulation of PTH, which also increases renal phosphate excretion;
- (3) suppression of the formation of 1,25(OH)2D3, leading to diminished phosphorus absorption from the GI tract.
- Interestingly, high levels of FGF-23 are also an independent risk factor for left ventricular hypertrophy and mortality in CKD, dialysis, and kidney transplant patients.
- Moreover, elevated levels of FGF-23 may indicate the need for therapeutic intervention (e.g., phosphate restriction), even when serum phosphate levels are within the normal

CARDIOVASCULAR ABNORMALITIES

- The incremental risk of cardiovascular disease in those with CKD compared to the age- and sex-matched general population ranges from 10- to 200-fold, depending on the stage of CKD.
- Traditional risk factors include hypertension, hypervolemia, dyslipidemia, sympathetic overactivity, and hyperhomocysteinemia.
- The CKD-related risk factors comprise anemia, hyperphosphatemia, hyperparathyroidism, increased FGF-23, sleep apnea, and generalized inflammation
- low levels of fetuin may permit more rapid vascular calcification,

especially in the face of hyperphosphatemia

CARDIOVASCULAR ABNORMALITIES

- **Heart Failure**
  - Myocardial ischemia, left ventricular hypertrophy, diastolic dysfunction, and frank cardiomyopathy
- **Hypertension and Left Ventricular Hypertrophy**

Anemia

- A normocytic, normochromic anemia is observed as early as stage 3 CKD and is almost universal by stage 4. The primary cause is insufficient production of EPO by the diseased kidneys

additional

- Diminished red blood cell survival
- Bleeding diathesis
- Iron deficiency due to poor dietary absorption and gastrointestinal blood loss
- Hyperparathyroidism/bone marrow fibrosis
- Chronic inflammation
- Folate or vitamin B12 deficiency
- Hemoglobinopathy
- Current practice is to target a hemoglobin concentration of 100–115 g/L.

NEUROMUSCULAR ABNORMALITIES

- Central nervous system (CNS), peripheral, and autonomic neuropathy

as well as abnormalities in muscle structure and function are all well-recognized complications of CKD

- Early manifestations of CNS complications include mild disturbances

in memory and concentration and sleep disturbance

- Neuromuscular irritability, including hiccups, cramps, and twitching, becomes evidentat later stages.
- In advanced untreated kidney failure, asterixis, myoclonus,seizures, and coma can be seen.

GI

- **GASTROINTESTINAL AND NUTRITIONAL**
- **ABNORMALITIES**
  - Gastritis, peptic disease, and mucosal ulcerations at any level of the GI tract occur in uremic patients and can lead to abdominal pain, nausea, vomiting, and GI bleeding.

- **DERMATOLOGIC ABNORMALITIES**

ENDOCRINE-METABOLIC DISTURBANCES

- Glucose metabolism is impaired in CKD
- kidney contributes to insulin removal from the circulation, plasma levels of insulin are slightly to moderately elevated in most uremic patients,
- In women with CKD, estrogen levels are low,
- Men with CKD have reduced plasma testosterone levels
- Many of these abnormalities improve or reverse with intensive

dialysis or successful renal transplantation.

10 A's of CKD

- **Anemia**
- **Atherosclerosis**
- **Anti-angiotensin therapy**
- **Albumin**
- **Anions and Cations**
- **Arterial Blood Pressure**
- **Arterial Calcification**
- **Access**
- **Avoidacne of Nephrotoxic Drugs**
- **Allograft**

INDICATIONS FOR DIALYSIS / TRANSPLANATATION

- ***INTRACTABLE UREMIC SYMPTOMS***
- ***PERICARDITIS / PULMONARY OEDEMA***
- ***OSTEO DYSTROPHY***
- ***BLEEDING DIATHESIS***
- ***ENCEPHALOPATHY / NEUROPATHY***
- ***METABOLIC COMPLICATIONS (ESP. HYPERKALEMIA)***