CHRONIC KIDNEY DISEASE (CKD)

-OVERVIEW AND EPIDEMIOLOGY-

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WHAT IS CKD?

AKA:

- Chronic Renal Failure
- Chronic Renal Insufficiency ← **Archaic terms no longer used**
- Chronic Kidney Failure

Definition:

- Gradual impairment of kidney function
- Inability to properly excrete waste, water, electrolytes
- Usually, this functional loss is permanent

CKD SIDE EFFECTS

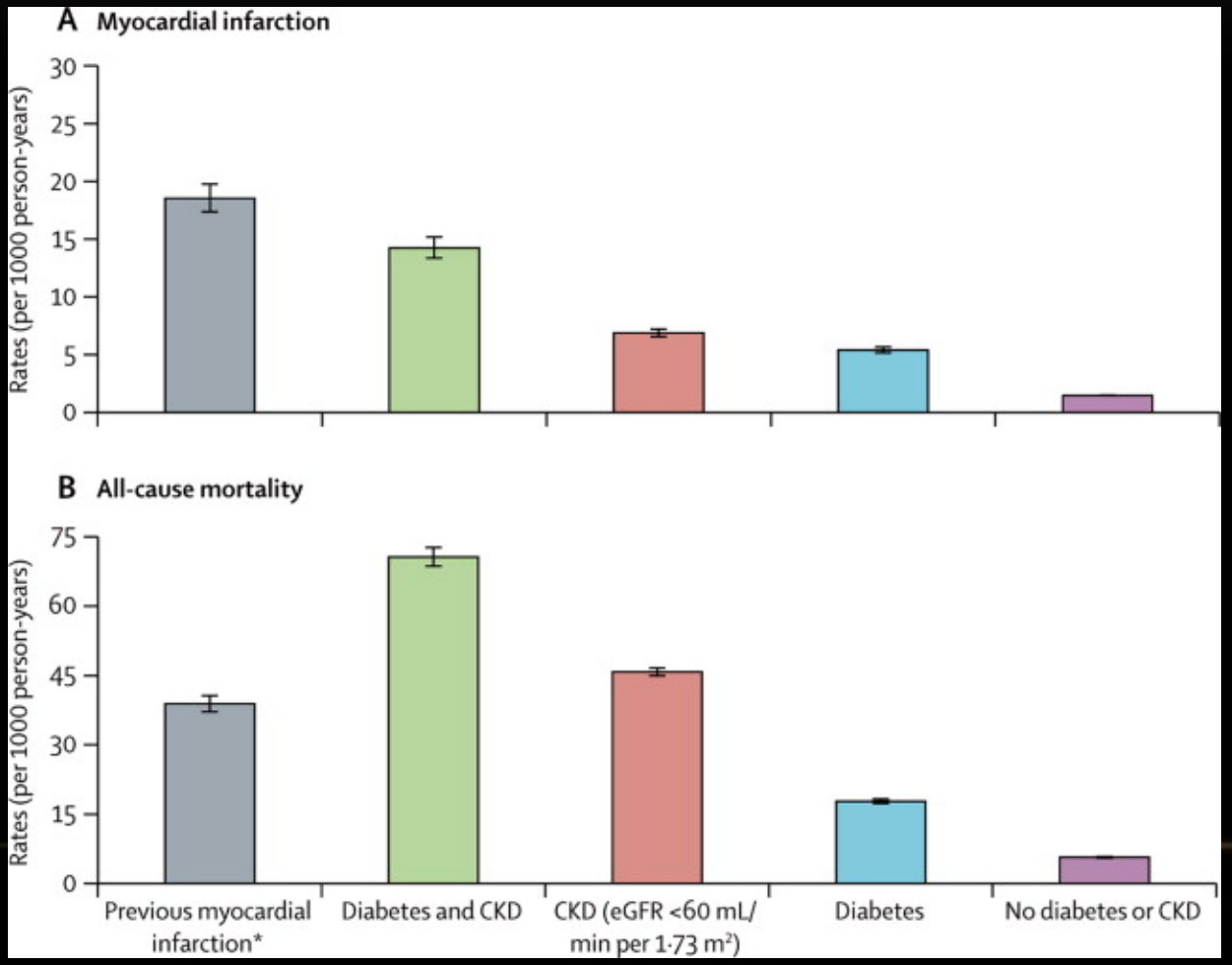
- Decreased kidney function can lead to:
  - Hypertension
  - Anemia
  - Acidosis
  - Bone disease
  - Heart disease and/or congestive heart failure
  - Hyperkalemia
  - And eventually, if untreated… Death

CKD PROGRESSION

- Some loss of kidney function is normal
  - Typically, we lose GFR 0.5 – 1.0 mL/min/year (due to aging and starting at age 35-40)
- CKD refers to an *abnormal* loss of kidney function
- 10-16% of adults are affected by CKD

CKD – SO WHAT?

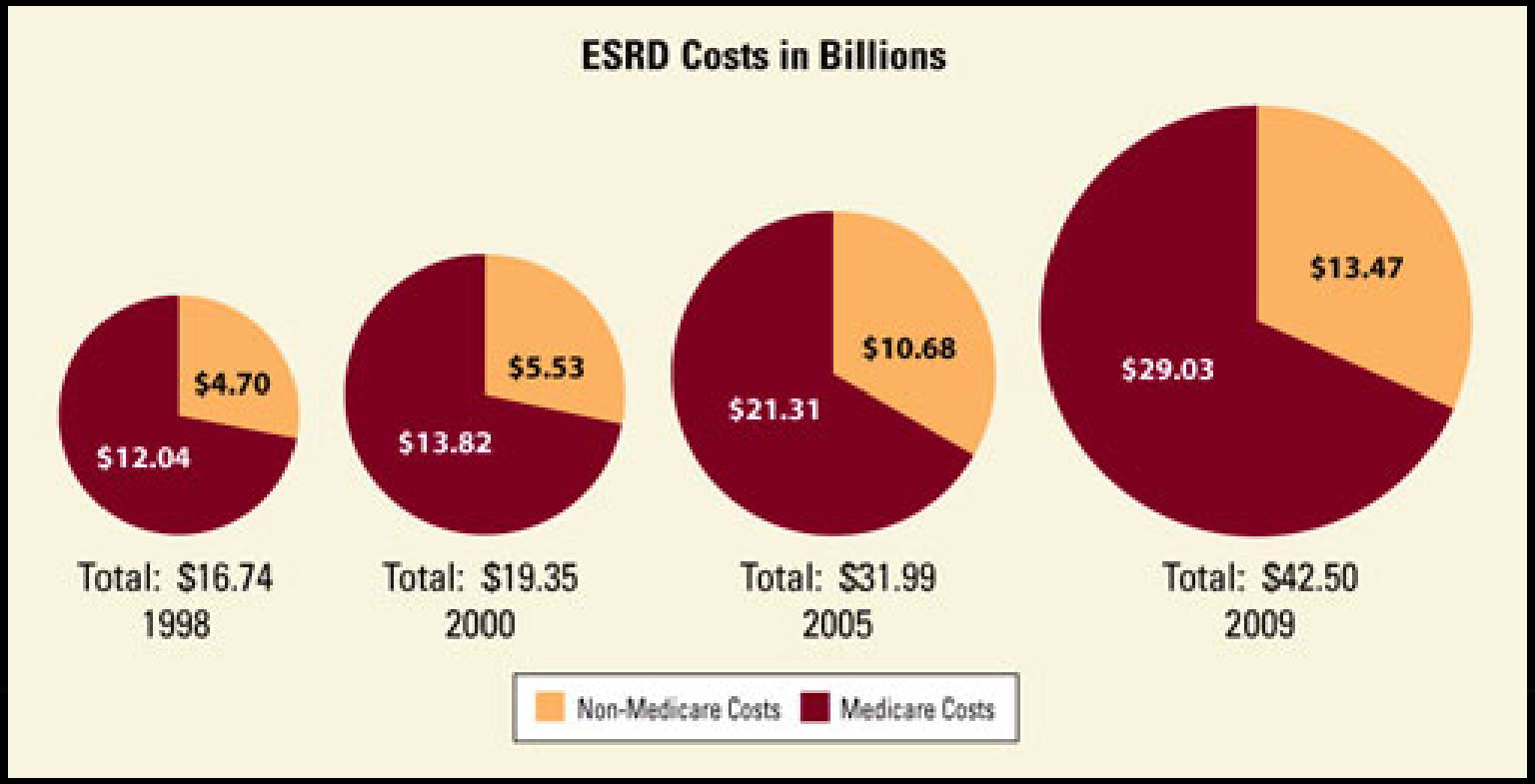
- It increases the risk of CAD, ESRD and death…



Adapted from The Lancet, Vol 380, 9844; 807-814, Sept 2012

CKD – SO WHAT?

- It's costly…
- Treating ESRD patients cost the U.S. > $40 billion in 2009



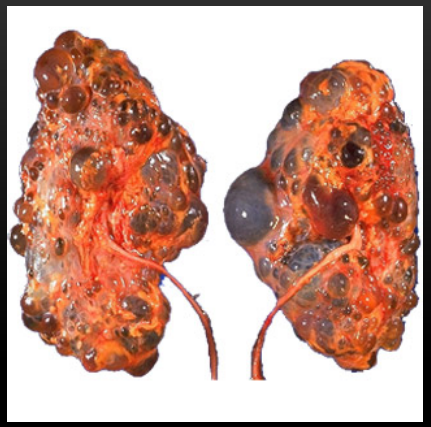
CKD – MOST COMMON CAUSES

- Diabetes

- Hypertension

CKD – OTHER CAUSES

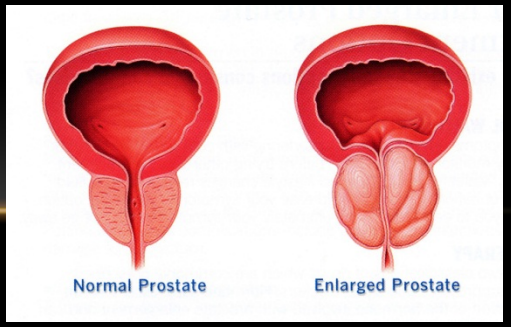
- Polycystic Kidney Disease



- Chronic NSAID usage

- Glomerulonephritis

- Obstructions of the urinary tract



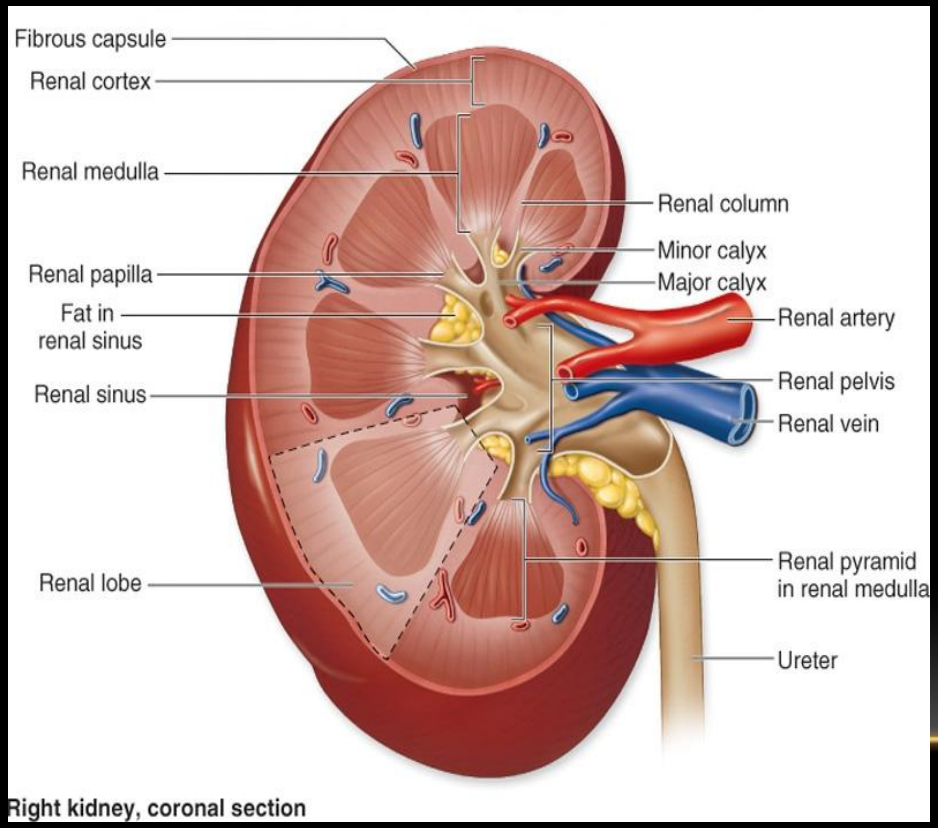
CKD STAGING

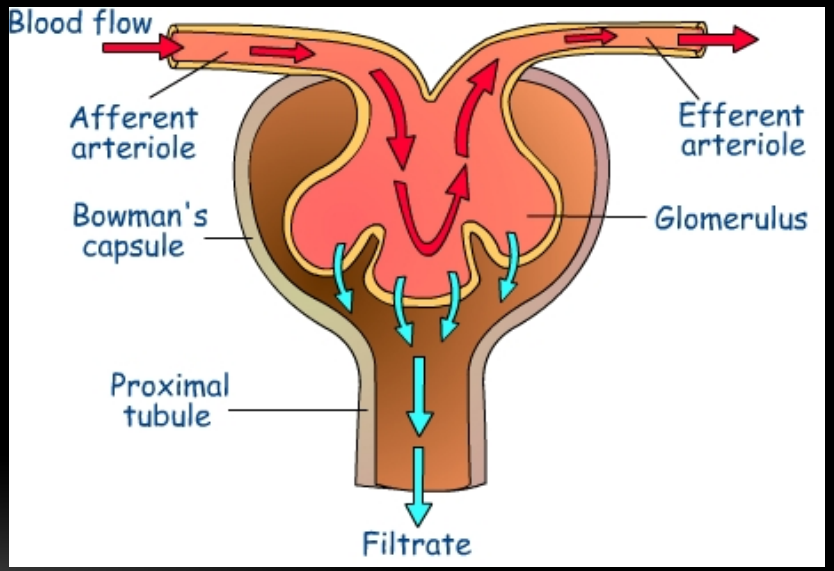
- GFR of > 90 mL/min is normal – usually…

- Stage I: GFR > 90 mL/min - but some other abnormality
- Stage II: GFR 60-89 mL/min – mild CKD
- Stage III: GFR 30-59 mL/min – moderate CKD
- Stage IV: GFR 15-29 mL/min – severe CKD
- Stage V: GFR < 15 mL/min – very severe CKD
- ESRD: GFR < 15 mL/min requiring RRT (dialysis or transplantation) to survive

STAGING – WHAT IS “GFR”?

- GFR: Glomerular Filtration Rate – how much filtrate is formed each minute in the nephrons





HOW DO WE ESTIMATE GFR?

- Use of serum creatinine
  - Produced by muscles at a constant rate
  - Problems associated with size, age, tubular secretion

- Formulas:
  - Cockcroft-Gault: (140 – age) x (Wt. kg) x 0.85 (♀)/(72 x Cr)
  - MDRD: $186 \times Cr^{-1.154} \times Age^{-0.203} \times 0.742$ (♀) x 1.21 (AA)
  - CKD-EPI: $141 \times \min Cr/0.7(♀)^{-0.329} \times \max Cr^{-1.209} \times 0.993^{Age} \times 1.018$ (♀) x 1.159 (AA)
  - Cystatin C: present in nucleated cells – not a superior marker

CKD STAGING – WHAT NOW?

- Stage I CKD: Identify the cause of the abnormality (if nephrotic syndrome is present – *why*? If hematuria – *why*?)
- Stage II CKD: Estimate progression – how fast is it decreasing?
- Stage III CKD: Identify sequelae and treat (anemia, bone dz, etc.)
- Stage IV CKD: Monitor and treat sequelae, prepare for RRT (i.e. dialysis or renal transplantation)
- Stage V CKD: Very close monitoring, RRT initiation or hospice

- Remember: more stage IV patients *die* than make it to ESRD!

IS CKD STAGING REASONABLE?

- “Overdiagnosis” of CKD?
- Isn’t “CKD” normal for the elderly?
- Stage III-a (GFR 45 – 59 mL/min)
  - Increased risk for adverse outcomes
- Stage III-b (GFR 30 – 44 mL/min)
  - Steep rise is risk for ESRD
- Proteinuria adds extra risk for progression

WHO SHOULD BE SCREENED FOR CKD?

- High-risk groups:
  - HTN
  - DM
  - Family History of CKD
  - Age > 60 years

COMPLICATIONS (SEQUELAE) OF CKD

- Anemia
- Renal Bone Disease
  - Hyperphosphatemia
  - Hyperparathyroidism
- Metabolic Acidosis
- Hyperkalemia

- Frequency of complications ↑ as GFR decreases

ANEMIA

ANEMIA

- Incidence increases with worsening CKD
  - 4.9% for eGFR ≥ 60
  - 39.7% for eGFR 15 – 29

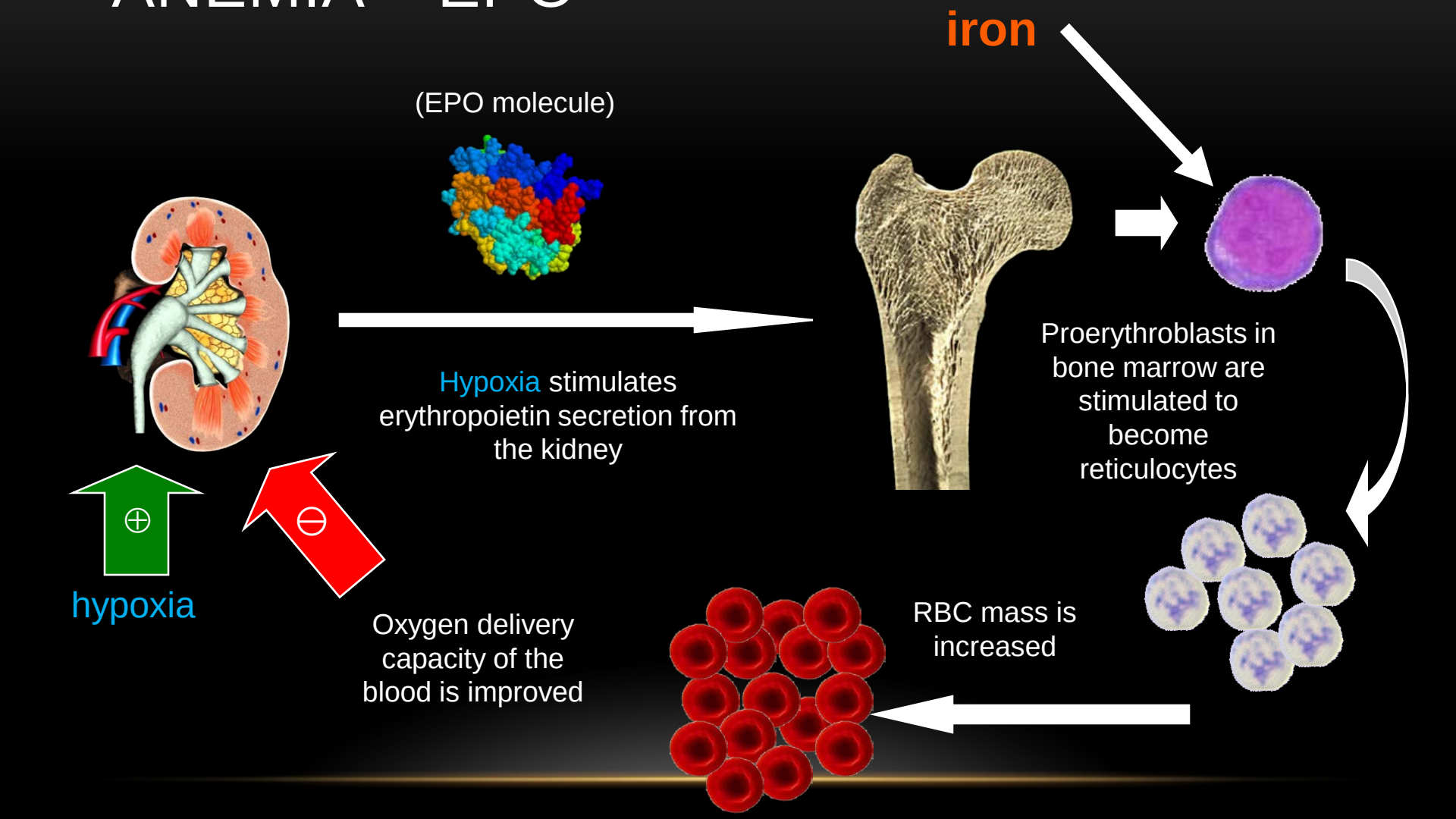
- Anemia = worse prognosis
  - ↑ hospitalization
  - ↑ progression to ESRD
  - ↑ mortality

ANEMIA – MECHANISMS IN CKD

- Not enough Erythropoietin (Epo)
  - Kidneys make Epo, needed for RBC manufacture
  - CKD decreases Epo production

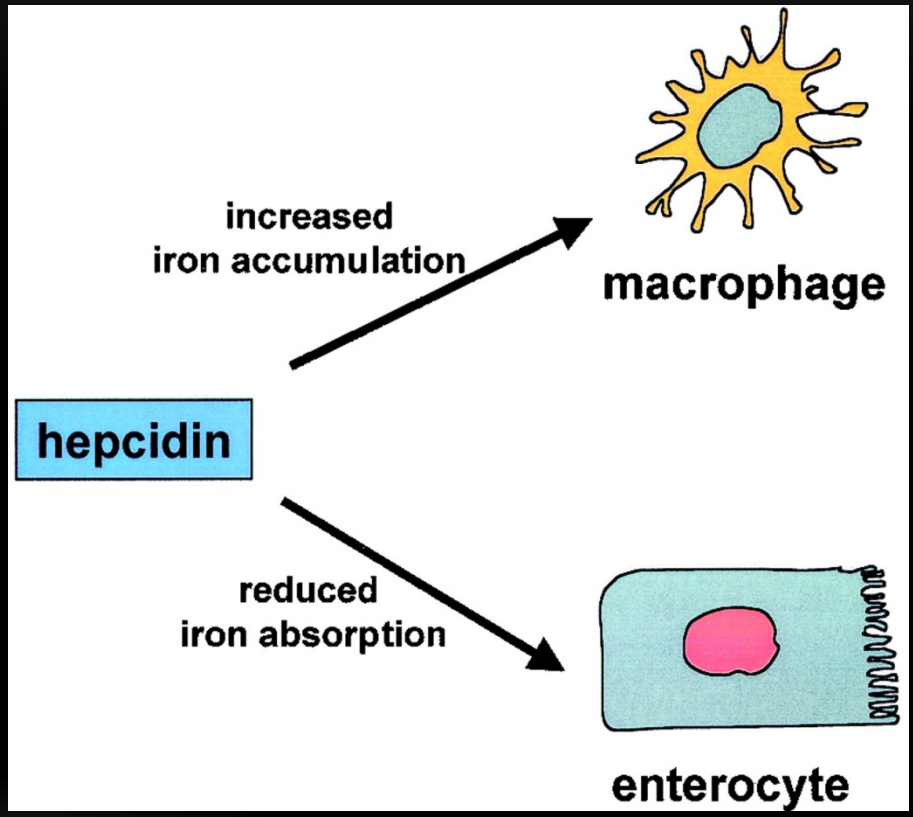
- Not enough Iron
  - Iron is the building block for RBC hemoglobin
  - CKD increases hepcidin
  - Too much hepcidin blocks iron absorption

ANEMIA – EPO


iron
(EPO molecule)
Hypoxia stimulates erythropoietin secretion from the kidney
Proerythroblasts in bone marrow are stimulated to become reticulocytes
RBC mass is increased
Oxygen delivery capacity of the blood is improved
hypoxia
⊕
⊖

ANEMIA - IRON

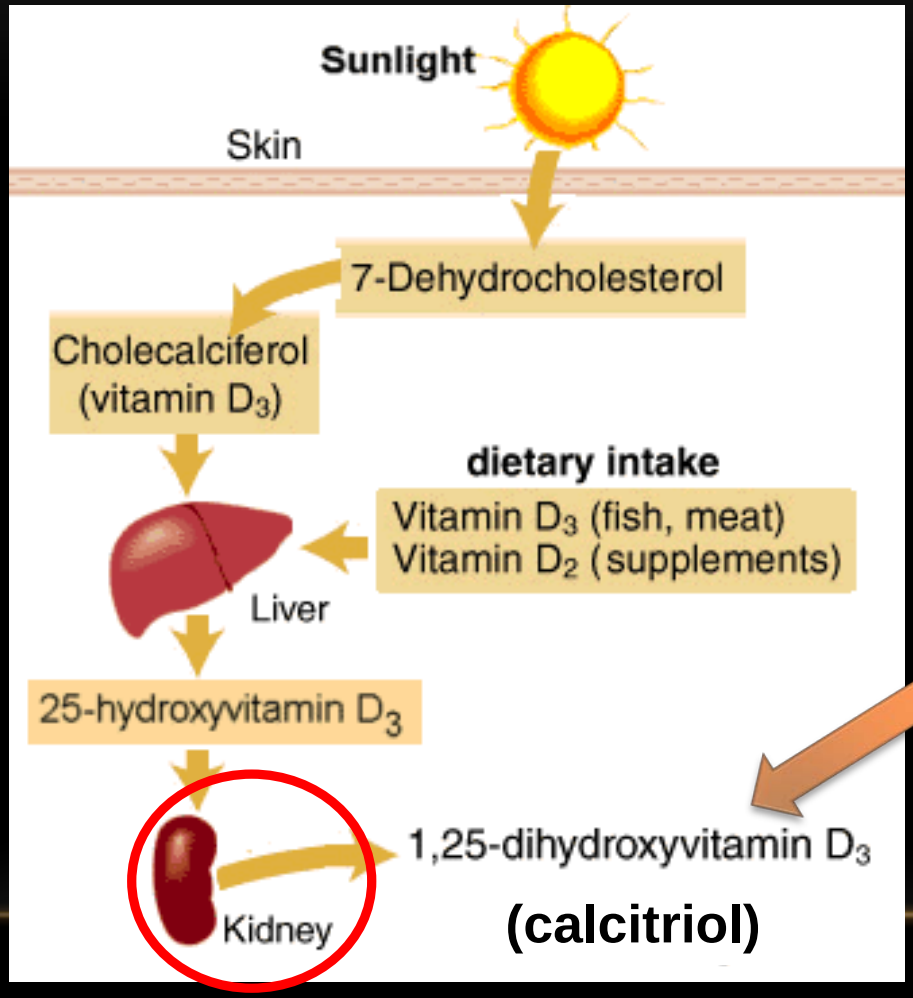
- CKD = ↑ Hepcidin
- Hepcidin blocks iron absorption from the gut
- Hepcidin increases unusable iron in cells



RENAL BONE DISEASE
(AKA: RENAL OSTEODYSTROPHY)

- Altered calcium, phosphorus, vitamin D, calcitriol and PTH levels lead to renal bone disease
- Bones become brittle and prone to fracture
- Vascular and metastatic calcifications can occur

VITAMIN D & CALCITRIOL



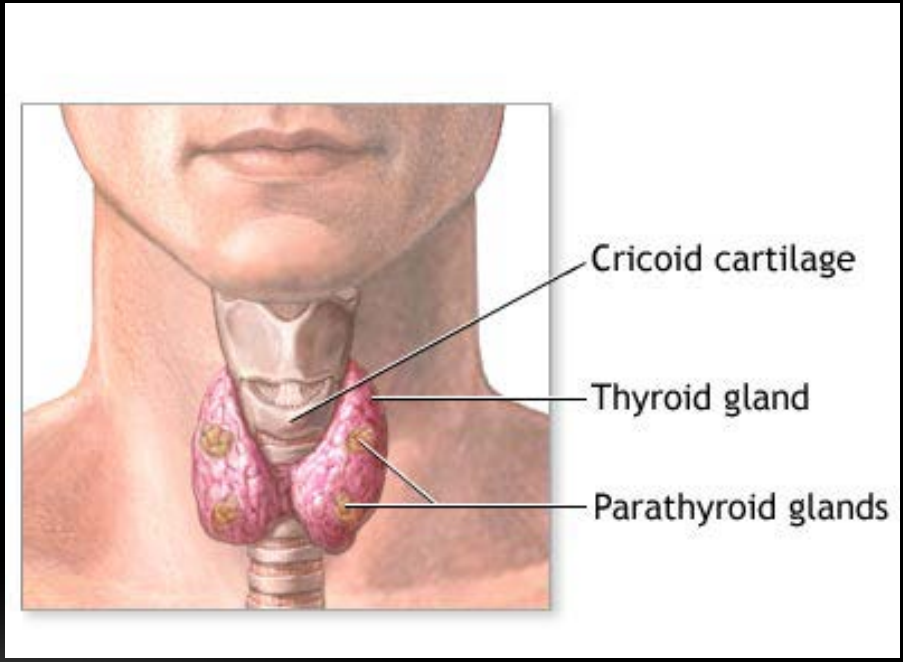
Misnomer!
NOT a vitamin!
It's a hormone!!

VITAMIN D & CALCITRIOL

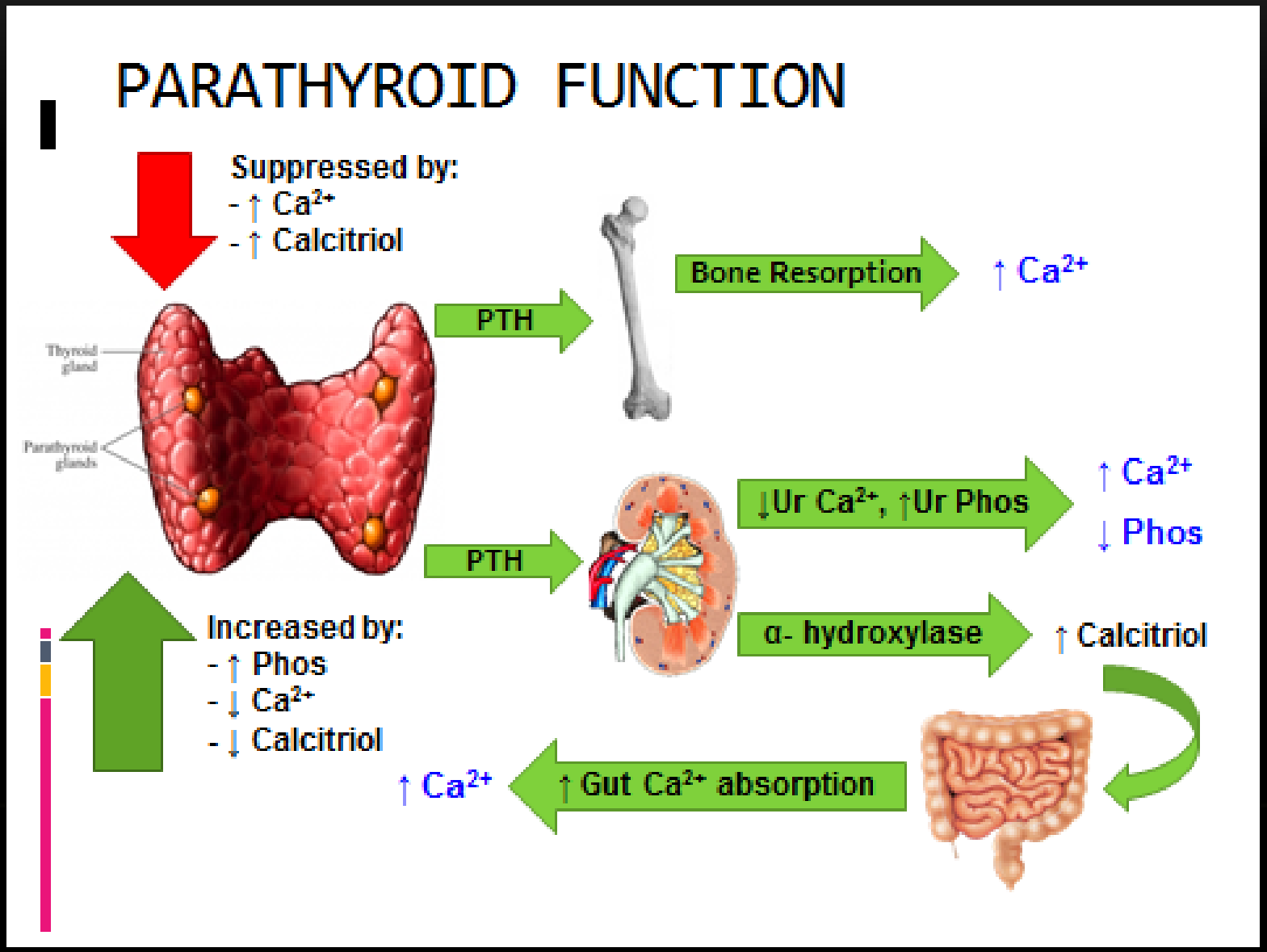
- Vitamin D2, D3:
  - Does not have significant biologic activity normally
  - Toxicity more likely to occur in hyperparathyroidism
- Calcitriol:
  - Made by the kidneys, primarily increases Ca^{++} levels
  - Promotes calcium absorption by the intestines
  - Releases calcium from bones
  - Decreases calcium excretion into the urine

PTH (PARATHYROID HORMONE)

- Produced by the parathyroid glands
- Functions are similar to calcitriol
- Stimulated by:
  - Low Ca^{++} levels
  - High phosphorus levels
  - Low calcitriol levels
- Suppressed by:
  - High Ca^{++} levels
  - High calcitriol levels

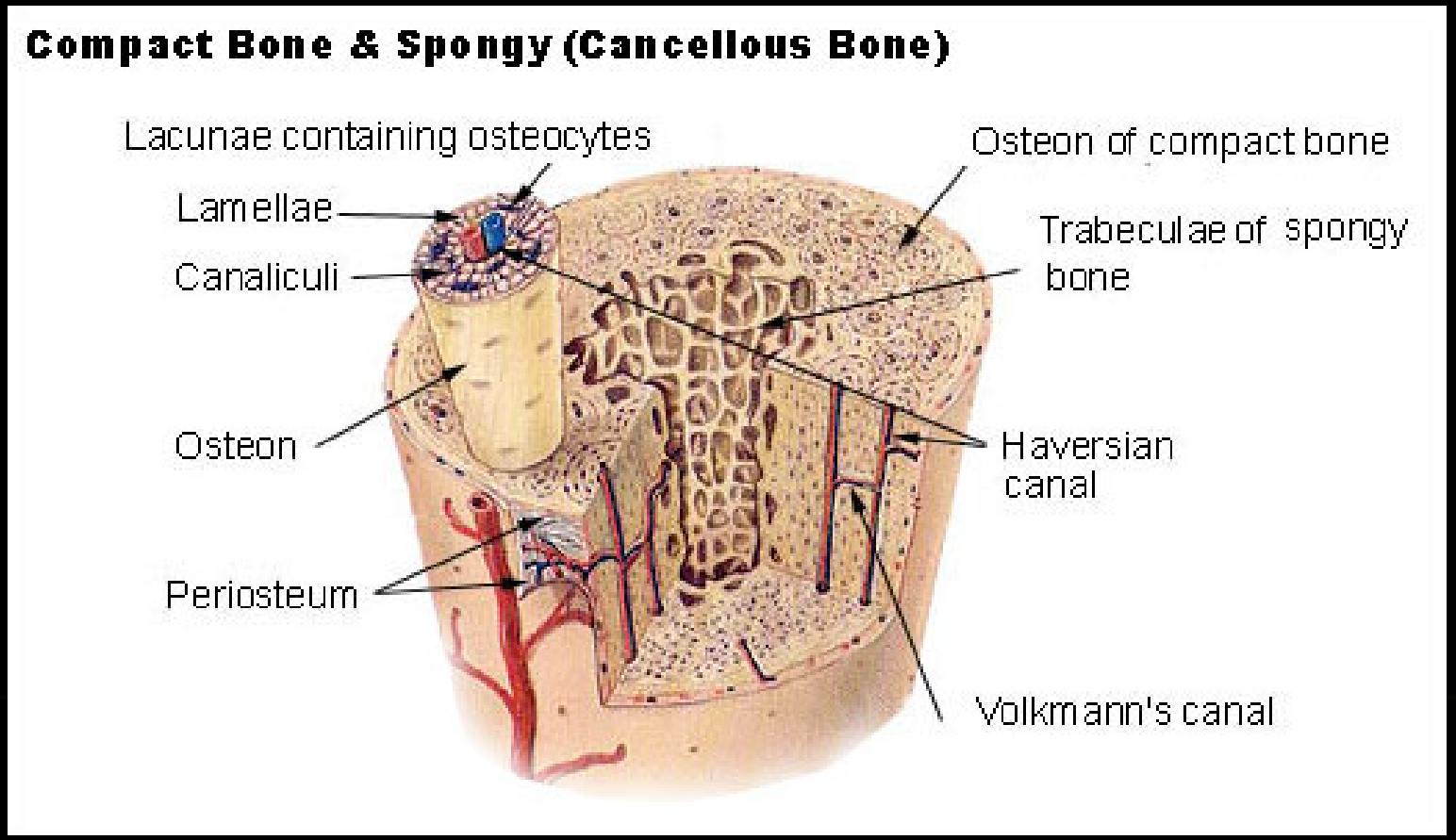


PTH (PARATHYROID HORMONE)



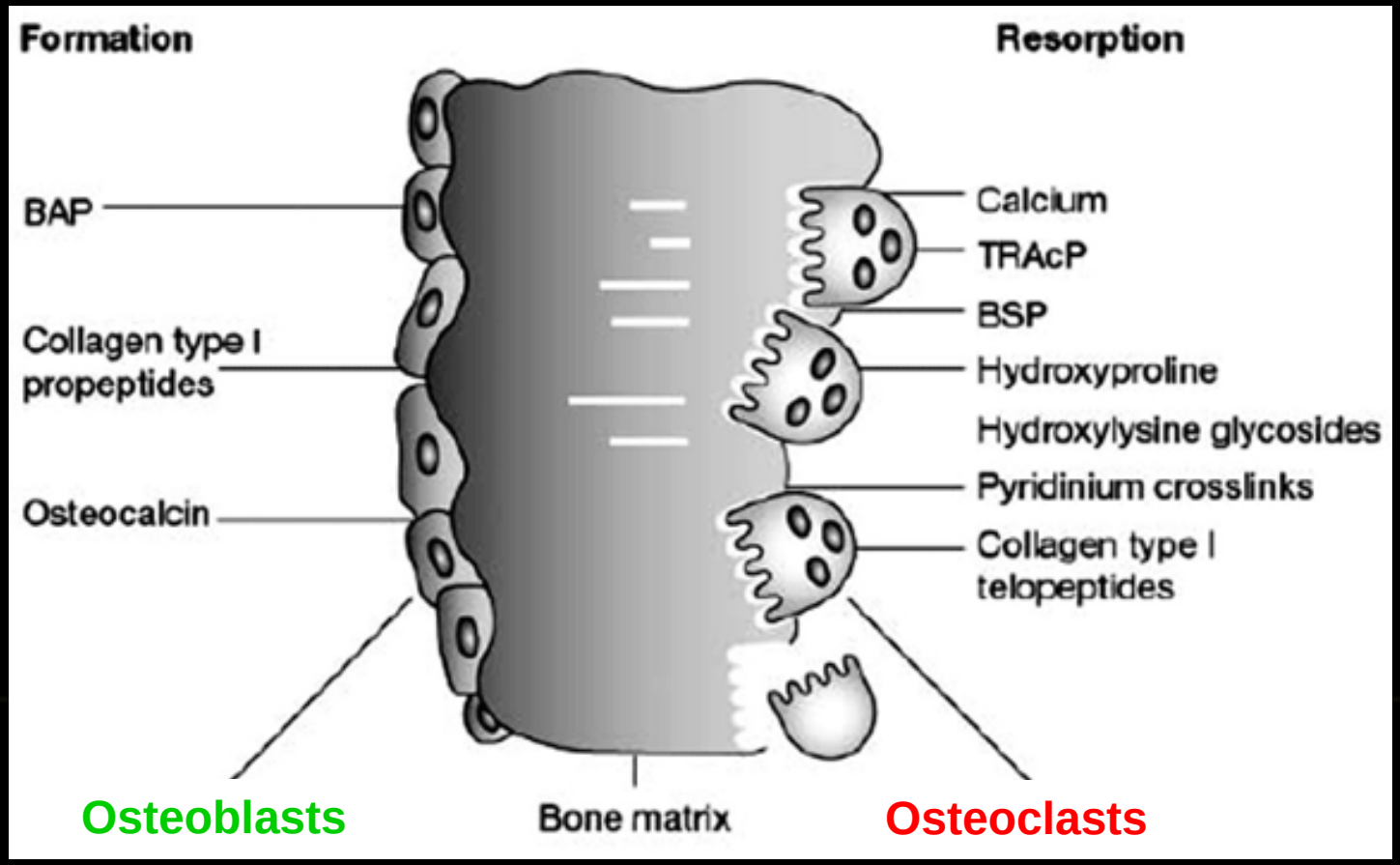
BONE STRUCTURE

- Normal bone is living tissue
- It is constantly being broken down and built back up



BONE METABOLISM

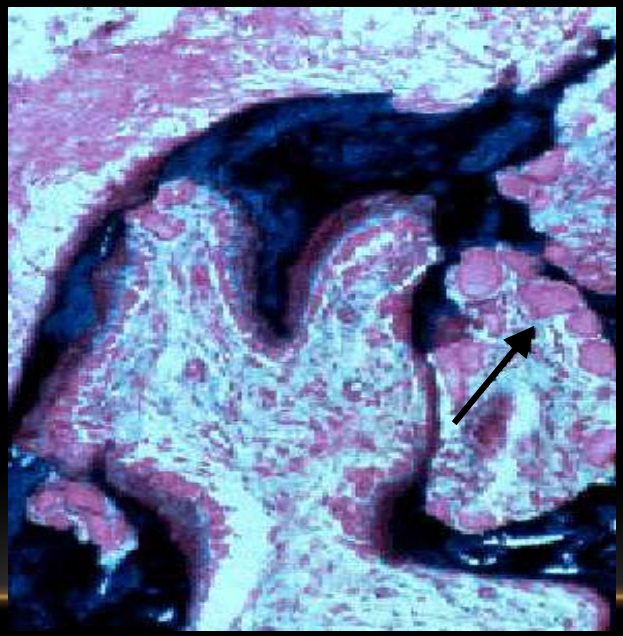
- Osteoblasts form new bone
- Osteoclasts break bone down



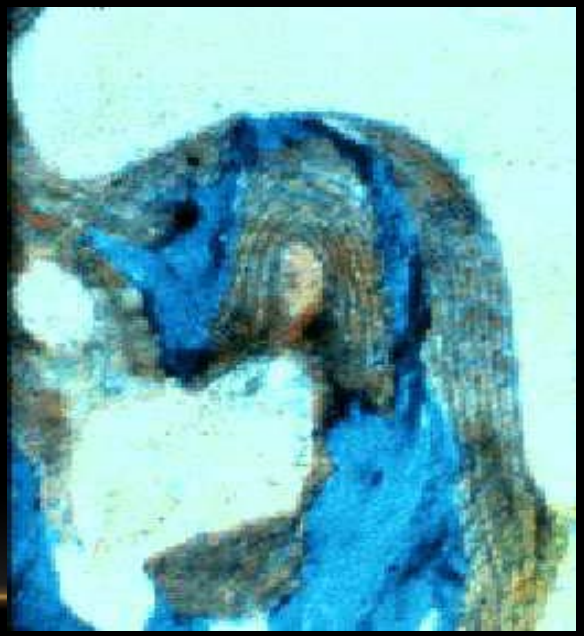
RENAL OSTEODYSTROPHY

- 2 Main types:
  - High-turnover (Osteitis Fibrosa Cystica) ↑ **PTH**
  - Low-turnover (Adynamic or Osteomalacia) ↓ **PTH**

Normal Bone



High Turnover (↑PTH)



Adynamic (↓PTH)

RENAL OSTEODYSTROPHY

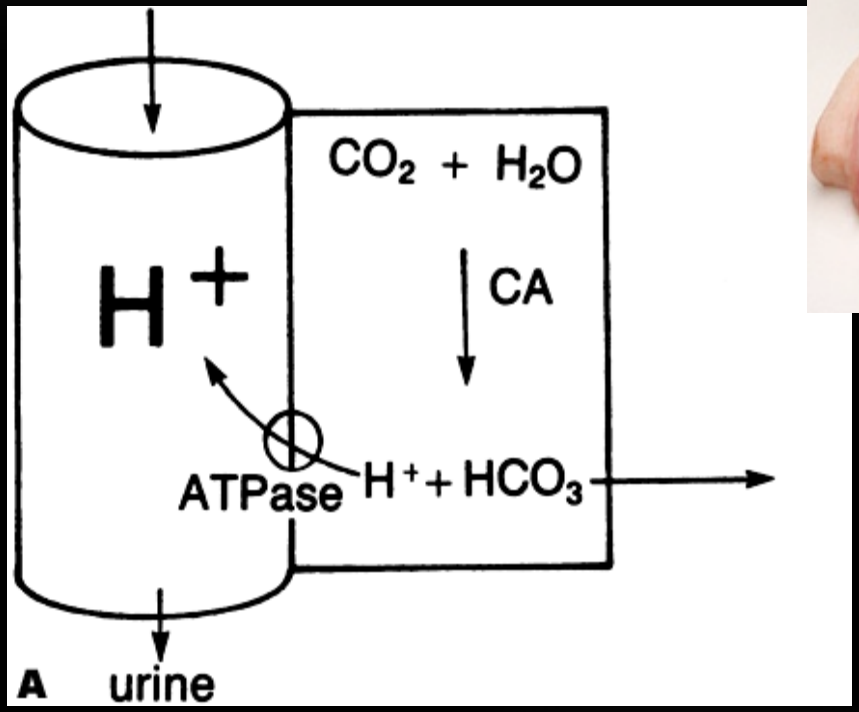
- Both main types of R.O.D. are associated with increased fracture rates
- “Mixed” Renal Osteodystrophy occurs when high-turnover disease is then over-treated
- Early identification and treatment are essential

METABOLIC ACIDOSIS

- The kidney excretes metabolic acid as needed
- As CKD worsens, acid retention can occur
- Chronic acidosis can cause:
  - Fatigue
  - Abdominal pain, anorexia, nausea
  - Shortness of breath
  - Bone damage

METABOLIC ACIDOSIS

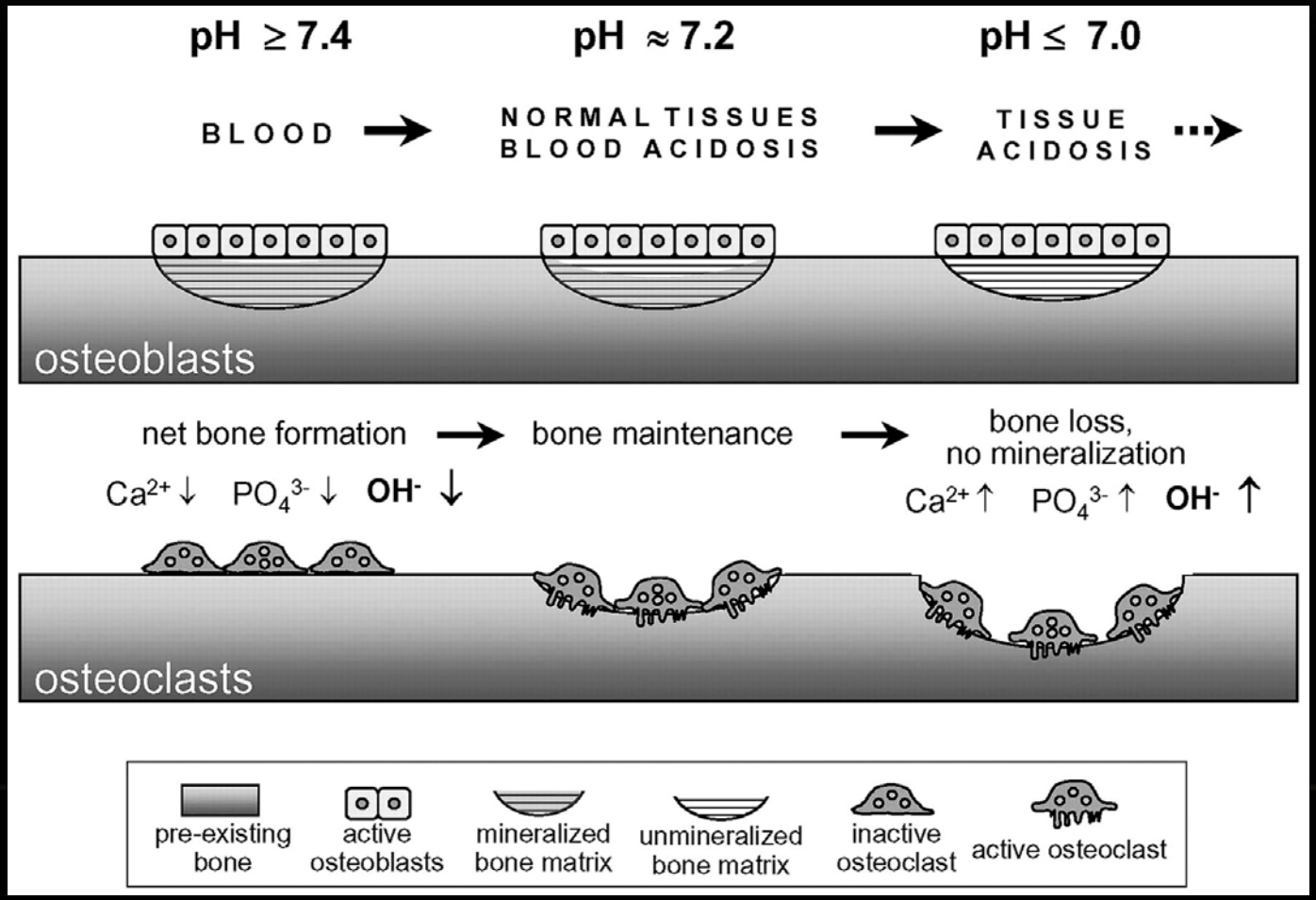
- Animal protein = ↑ acid load



- CKD = ↓ renal acid secretion

METABOLIC ACIDOSIS

- Chronic acidosis can cause bone demineralization

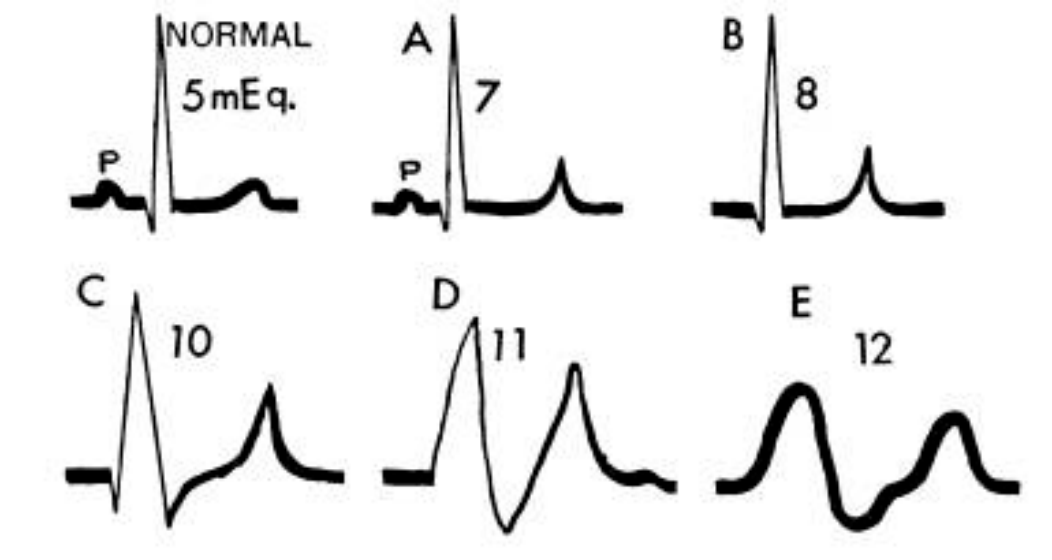


METABOLIC ACIDOSIS

- Treat with oral alkali (sodium bicarbonate)
- Treatment appears to slow CKD progression
- Treatment decreases bone demineralization
- There is little or no effect of sodium bicarbonate on blood pressure (i.e. the sodium load is negligible)

HYPERKALEMIA

- Incidence and severity vary
- Tends to occur at later CKD stages
- Often necessitates medication and/or diet changes
- Can be lethal if it becomes severe

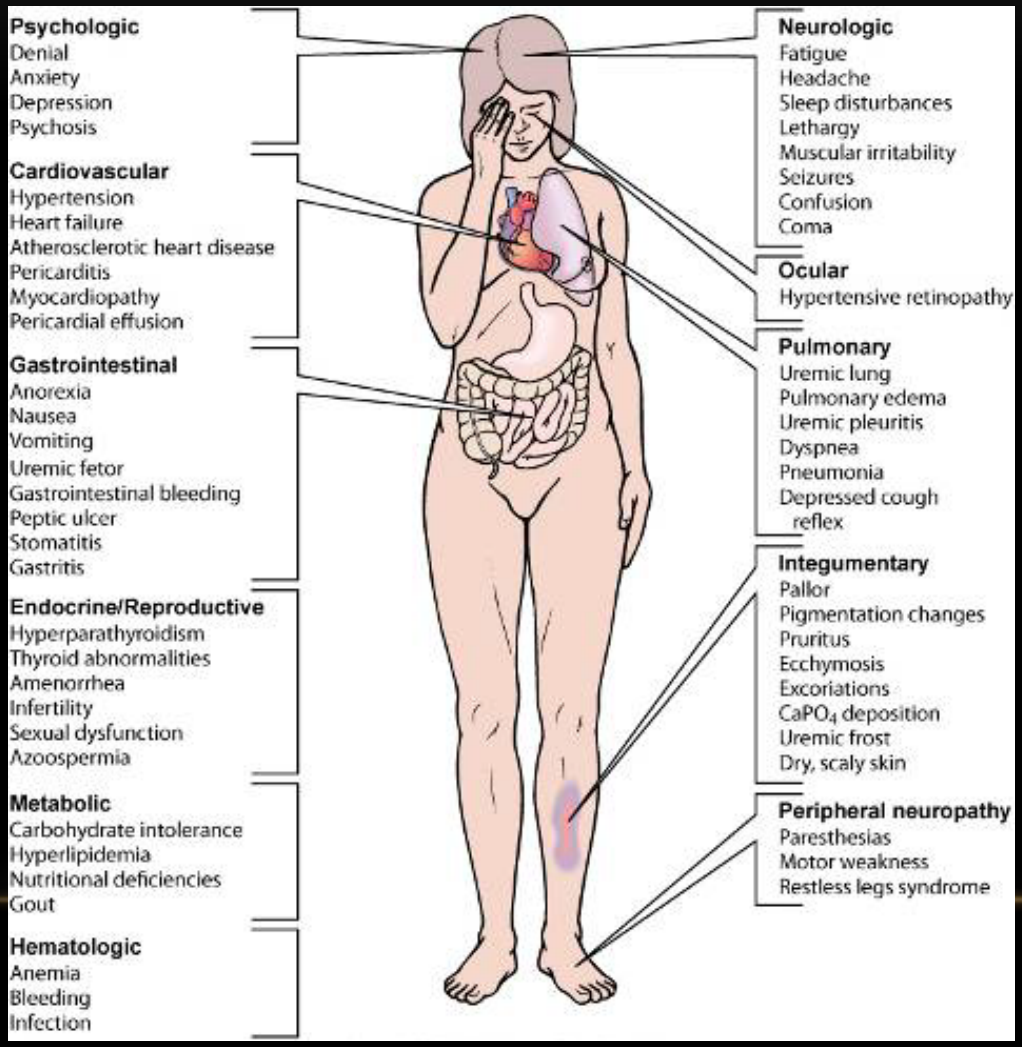


CKD SYMPTOMS

- Early
  - Fatigue
  - Difficulty concentrating
  - Cold Intolerance
  - Aversion to animal protein
  - Restless leg syndrome
- Late (Uremic)
  - Anorexia
  - Nausea/Vomiting
  - Dysgeusia
  - Pruritus
  - Fluid retention
  - Easy bruising/bleeding
  - Chest pain
  - Bone pain
  - Confusion/Coma

UREMIA

- A syndrome that results from retention of nitrogenous wastes in the body



UREMIC SYMPTOMS

- Fatigue

- Difficulty Concentrating

UREMIC SYMPTOMS

- Anorexia

- Nausea

- Dysgeusia

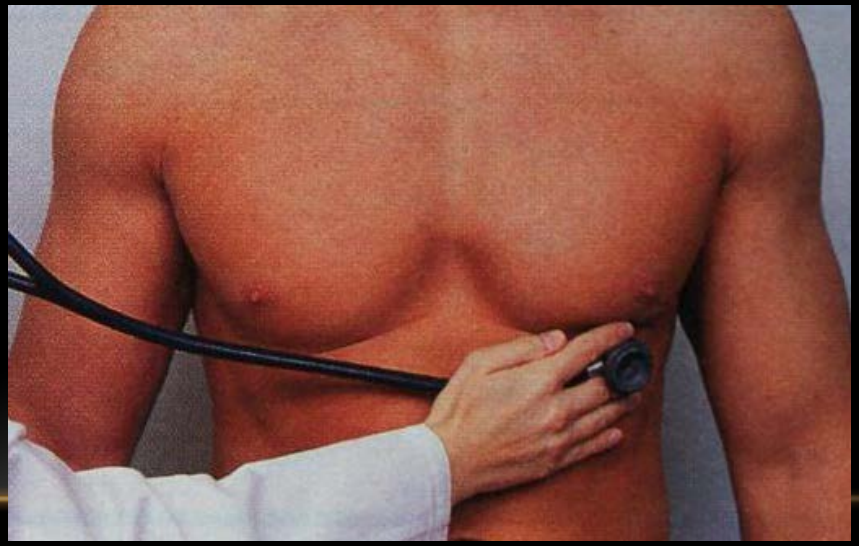
UREMIC SYMPTOMS

- Pruritus
- Chest Pain
- Shortness of Breath

UREMIC SIGNS

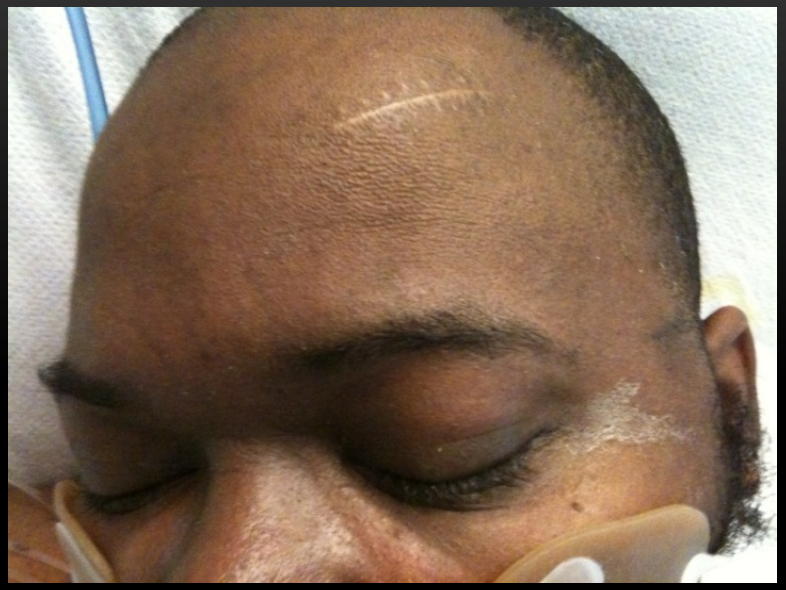
- Uremic Fetor

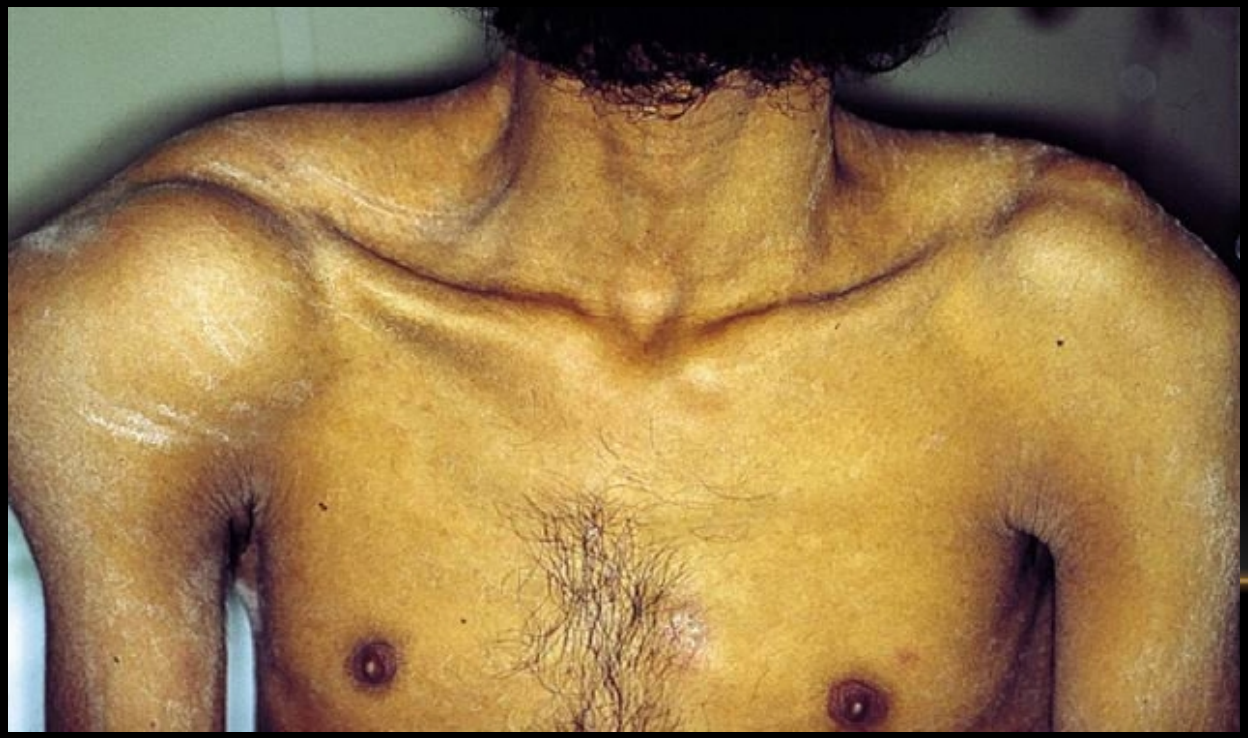
- Pericardial Friction Rub



UREMIC SIGNS

- Sallow Complexion
- Uremic Frost





CKD TREATMENT GOALS

- Prevention
- Early detection
- Treatment to slow progression
- Management of sequelae
- Education/preparation for renal replacement therapy, if needed

BASIC CKD MANAGEMENT

- Minimize Proteinuria
- Promote Adequate Nutrition
- Strict Blood Pressure Control
  - In particular, use of RASIs (ACE or ARB)
- Avoid Nephrotoxic Exposures
  - NSAIDs
  - Smoking
  - Iodinated contrast

WHEN TO REFER? – SOME SUGGESTIONS

1. The CKD is already stage IV or worse
2. The etiology for the CKD requires special treatment
3. The patient develops CKD sequelae that you aren't comfortable treating
4. You cannot identify the etiology of the CKD
5. The patient demonstrates rapid progression of their renal disease
6. You cannot control the patient's hypertension
7. There are unexpected metabolic abnormalities
8. The patient has nephrotic syndrome

CASE #1

- A 68 year old woman with a longstanding history of fibromyalgia and hypothyroidism presents for a check-up. She is asymptomatic except for mild arthralgias which are controlled with gabapentin 300 mg TID and meloxicam 15 mg daily. Her physical exam is unremarkable. Routine lab work reveals a potassium of 4.9, a BUN of 13 and a Creatinine of 1.6 (was 1.2 a year ago.)
- 1. What is the most likely cause of her elevated creatinine?
- 2. What is the appropriate workup?

CASE #2

- A 25 year old male presents with complaints of nocturia x 1 week. He has no past medical or surgical history. He has no other complaints or urinary abnormalities. He is not sexually active and denies drug use. He has not seen a doctor in over 6 years. Routine lab work shows normal electrolytes, BUN 34, Creatinine 5.91. UA reveals 4+ protein.
- 1. What is the most likely diagnosis?
- 2. What is the most appropriate next step?

CASE #3

- A 64 year old woman with HTN, type 2 DM, anemia, hyperlipidemia and CKD presents for a checkup. She has been feeling more fatigued and has been having trouble sleeping. Her baseline serum creatinine has been slowly worsening over the last 3 years and is now 2.6. Her electrolytes are normal. Hemoglobin is 9.2 g/dL, iron level 28, transferrin saturation 19%.
- 1. What is the most likely cause for her fatigue?
- 2. What is the most likely cause for her anemia?

THANKS FOR YOUR ATTENTION!