



# Bone Mineral Metabolism Fact Sheet

**American  
Nephrology  
Nurses'  
Association**

*Developed by:  
ANNA Hemodialysis  
Special Interest Group*

## **ANNA's Mission Statement**

*ANNA will promote excellence by advancing nephrology nursing practice and positively influence outcomes for individuals with kidney disease.*

**Additional Information:**

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# ***I. Overview***

In this fact sheet:

- Pathophysiology of Bone Mineral Metabolism
- Diagnostic Testing
- Treatment Interventions
- Complications of Bone Mineral Metabolism

Disorders of mineral metabolism in chronic kidney disease (CKD) have been associated with higher mortality than anemia and inadequate dialysis (Block et al., 1998).

In this fact sheet, you will gain insight regarding:

- Development of the disease.
- Testing used to diagnose.
- Treatment regimens, including diet and medications.
- Complications that may occur.

In normal renal function, the kidneys play an active role in regulating the excretion of waste products and maintaining a delicate balance of minerals in our bodies, while also secreting hormones, which impact other body systems.

## ***Disease Manifestation and Possible Symptoms***

### **Clinical Progression of Bone Mineral Disorder in CKD**

- Phosphorus excretion diminishes, leading to an increase in serum phosphorus.
- Calcium is not reabsorbed, leading to decreased serum calcium.
- Vitamin D is not activated, leading to hypertrophy and hyperplasia of the parathyroid glands with increased secretion of parathyroid hormone.
- Both decreased serum calcium levels and increased serum phosphorus levels stimulate excessive secretion of PTH.

An elevated PTH increases both the number and activity of osteoclasts (cells that break down bone). As osteoclasts break down bone, calcium and phosphorus are released into the serum, causing an elevation in phosphorus levels. This leads to demineralized (weakened) bones, which are subject to easy fractures, and calcification of the heart, vasculature, and soft tissues.

Under normal conditions, the kidney plays the following roles:

- Excretion of phosphorous and calcium.
- Acid base balance.
- Activation of vitamin D.

The following disease process occurs as renal function decreases when GFR is less than 60:

- Decreased urinary phosphorous excretion.
- Decreased vitamin 1,25 D levels due to the kidney's ability to convert 25 D into 1,25 D, which is the biologically active form.
- Increased PTH secretion as a response to stimulate calcium absorption in the intestines.
- Decreased calcium excretion.

As CKD progresses into Stages 3 and 4, the worsening condition and exacerbation of the above four processes induces serum changes in:

- Phosphorus (increases).
- PTH (increases).
- Calcium imbalance (decreases in response to the drop in Vitamin 1,25D decrease).

This condition may be present and undetected for a long period of time prior to the initiation of renal replacement therapy. If left uncontrolled, clinical evidence has demonstrated mortality in CKD patients. The clinical manifestations may include:

- Exacerbated hyperphosphatemia.
- Secondary hyperparathyroidism.
- Potential for calcium overload (Block et al., 2004; Craver et al., 2002).

If a patient's pathology is enough to mediate physical symptoms, the patient may experience:

- Itching (due to increased phosphorous or PTH levels).
- Reddened eyes (due to capillary deposition of minerals).
- Bone pain and/or be at risk for fractures.

## **II. Diagnostic Testing**

In CKD Stage 5 patients on dialysis:

- Serum phosphorus ( $\text{PO}_4$ ): 3.5 – 5.5 mg/dL
- Serum calcium (Ca): 8.4 – 9.5 mg/dL
- Calcium/phosphorus  $\text{CaPO}_4$  Product < 55  $\text{mg}_2/\text{dL}_2$
- PTH: Biointact PTH 75 – 150 pg/mL or Intact PTH 150 – 300 pg/mL

In 2009, global recommendations were published by the Kidney Disease: Improving Global Outcomes Group (KDIGO). The following clinical practice guidelines were recommended based on clinical evidence review:

### **Stage 3 (GFR 30 to 59)**

PTH – Greater than the upper limit of normal for the assay used

Phosphorous: Maintain normal

Calcium: Maintain normal

### **Stage 4/5 (GFR 15 to 29)**

PTH – Greater than than the upper limit of normal for the assay used.

Phosphorous: Maintain normal.

Calcium: Maintain normal.

### **Stage 5D (or on Replacement Therapy)**

PTH – 2 to 9 times the upper limit of normal for the assay used.

Phosphorous: Treat toward normal

Calcium: Maintain normal

**Source:** KDIGO CKD-MBD Work Group, 2009.

Other laboratory tests that may be useful:

- Alkaline phosphatase: 20 – 140 international units/L
- $\text{CO}_2$ : > 22 mEq/L
- Aluminum levels: < 20 mcg/L
- Vitamin D levels (rarely measured)

Other testing:

- Bone X-rays for suspected fractures
- Bone biopsy from the iliac crest
- Dual imagery X-ray absorptiometry (DXA) to visualize bone lesions
- Radiographs to detect possible calcifications
- EKG

### III. Complications of Mineral Imbalance

#### Vascular

- Cardiovascular problems resulting in arteriosclerosis, vascular calcification, valvular calcification, and cardiomyopathy.
- Progressing cardiovascular disease may in turn lead to cardiovascular problems, such as myocardial infarction, peripheral vascular disease (which presents as calciphylaxis and ulcers in the torso and extremities), and cerebrovascular disease in the form of transient ischemic attacks and cerebrovascular accidents.

#### Osteodystrophy (Bone Disease)

- Determined by bone biopsy and estimated with monitoring of serum levels.
- High turnover bone diseases:
  - Mixed uremic osteodystrophy with varying degrees of mineralization defects and hyperparathyroid changes.
  - Osteitis fibrosa is an abnormal bone reabsorption, formation, and marrow fibrosis.
- Low turnover bone diseases:
  - Adynamic bone disease suppresses bone formation secondary to hypercalcemia and/or over suppression of PTH.
  - Osteomalacia produces large amounts of unmineralized bone, and it may be aluminum or non-aluminum-related. Osteomalacia has decreased substantially since aluminum binder use has diminished.

### IV. Interventions

Interventions to prevent and treat disorders of bone/mineral metabolism include diet, medications, and dialysis. The patient may require surgical intervention if these methods are unable to be controlled.

#### Diet

Due to a high need for protein consumption, it is virtually impossible to eat a phosphorus-free diet; therefore, phosphorus is restricted, and phosphate binders must be used. Patients should also be instructed to check food labels for potassium, calcium, or phosphorus, which may impact their overall health.

K/DOQI suggests the following guidelines for daily mineral intake:

Phosphorus: 800 – 1,000 mg/day.

Calcium:  $\leq$  2000 mg/day from all sources (including phosphate binders).

High-phosphorus foods that should be restricted include:

- Dairy products.
- Dried beans.
- Nuts.
- Chocolate.
- Dark colas.
- Whole grains.
- Baked goods made from a mix.
- Foods containing phosphorus additives.

**Source:** Fennema, 1987.

#### Medications

##### *Phosphate Binders*

Phosphate binders work by binding phosphorus in the digestive system, beginning in the small intestine and eliminated in the stool. It is imperative that the binders be administered with food or as per the package insert. Phosphate binders should not be administered with any other medications. Adherence to prescribed regimens is crucial.

Patients should be screened for any underlying GI pathology prior to administration of any phosphate binder because the prevalence of these disorders in patients with CKD can be as high as 57%. The most commonly reported side effects from the use of any phosphate binder are GI disturbance and constipation (Murtagh, Addington-Hall, & Higginson, 2007).

The following recommendations have been stated in the KDOQI and KDIGO guidelines in regard to the discontinuation of calcium-based binders in patients with CKD in the presence of:

- Serum calcium greater than 10.2 (KDOQI).
- PTH less than 150 (KDOQI).
- Signs of calcification on radiographs or other diagnostic reports (KDIGO).

*Calcium-Based Binders:*

Calcium carbonate (Tums<sup>®</sup>, Tums<sup>®</sup> EX, Phoslo<sup>®</sup>).

*Non-Calcium, Non-Metal-Based Binders:*

Sevelamer carbonate (Renvela<sup>®</sup>), sevelamer hydrochloride (Renagel<sup>®</sup>) (Genzyme, 2007).

*Metal-Based Binders:*

Lanthanum carbonate (Fosrenol<sup>®</sup>).

Aluminum (Alucaps<sup>®</sup>, Alternagel<sup>®</sup>, and Basogel<sup>®</sup>).

\*The use of aluminum-based binders is recommended only as a short-term therapy due to concerns regarding aluminum toxicity (National Kidney Foundation, 2003).

*Magnesium-Based Binders:*

MagneBind<sup>®</sup> – This binder requires monitoring of magnesium levels and contains calcium as well.

*Vitamin D Analogs Include:*

- Calcijex<sup>®</sup> (calcitriol injection) is indicated in the management of hypocalcemia in patients undergoing chronic renal dialysis. It has been shown to significantly reduce elevated PTH levels. Reduction of PTH has been shown to result in an improvement in renal osteodystrophy (Abbott Laboratories, 2004a).
- Rocaltrol<sup>®</sup> (calcitriol capsules and oral solution):
  - Pre-dialysis patients: Rocaltrol is indicated in the management of secondary hyperparathyroidism and resultant metabolic bone disease in patients with moderate to severe chronic renal failure (Ccr 15 to 55 mL/min) not yet on dialysis for hyperparathyroidism.
  - Dialysis patients: Rocaltrol is indicated in the management of hypocalcemia and the resultant metabolic bone disease in patients undergoing chronic renal dialysis.
  - Hypoparathyroidism patients: Rocaltrol is also indicated in the management of hypocalcemia and its clinical manifestations in patients with post-surgical hypoparathyroidism, idiopathic hypoparathyroidism, and pseudohypoparathyroidism (Roche Laboratories, 2004).
- Hectorol<sup>®</sup> (doxercalciferol injection) is indicated for the treatment of secondary hyperparathyroidism in patients with chronic kidney disease on dialysis (Genzyme Corporation, 2006b).
- Hectorol<sup>®</sup> (doxercalciferol capsules):
  - Dialysis patients: Hectorol is indicated for the treatment of secondary hyperparathyroidism in patients with CKD on dialysis.
  - Pre-dialysis patients: Hectorol is indicated for the treatment of secondary hyperparathyroidism in patients with Stage 3 or Stage 4 CKD (Genzyme Corporation, 2006a).
- Zemplar<sup>®</sup> (paricalcitol injection) is indicated for the prevention and treatment of secondary hyperparathyroidism associated with Stage 5 CKD (Abbott Laboratories, 2004b).
- Zemplar<sup>®</sup> (paricalcitol capsules) are indicated for the prevention and treatment of secondary hyperparathyroidism associated with Stages 3 and 4 CKD (Abbott Laboratories, 2005).

*Calcimimetic agents (Cinacalcet [Sensipar<sup>®</sup>])*

Indicated for the treatment of secondary hyperparathyroidism in patients with CKD on dialysis and for the treatment of hypercalcemia in patients with parathyroid carcinoma. It increases the sensitivity of the calcium-sensing receptors on the parathyroid gland to calcium. Available in tablets.

## Dialysis

Dialysate is phosphorus-free to remove the maximum amount of phosphorus. If phosphorus remains elevated, longer or more frequent dialysis may be recommended. The recommended dialysate calcium concentration is 2.5 mg/dL with tailoring to individual patients as needed (National Kidney Foundation, 2003).

## Parathyroidectomy

Recommended in patients with severe hyperparathyroidism (iPTH persistently > 800 pg/mL) with hypercalcemia and hyperphosphatemia, and non-responsive to medical therapy.

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## Additional Reading

Burrows-Hudson, S., & Prowant, B. (2005). *Nephrology nursing standards of practice and guidelines for care*. Pitman, NJ: American Nephrology Nurses' Association.

### Other Questions:

For questions and/or concerns please contact us at 1-888-600-2662.

**For more information about nephrology nursing, dialysis, transplantation or other renal disorders check out the American Nephrology Nurses' Association (ANNA) Web site at [www.annanurse.org](http://www.annanurse.org).**

