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# Multiple Myeloma and Hypophosphatemia

## CLINICAL PRESENTATION

A 60-year-old man with chronic alcoholism presented after a fall with head trauma and confusion. Multiple myeloma had been diagnosed 2 months earlier, but he had not yet begun therapy. On physical examination, he appeared confused, orthostatic, and dyspneic, with no focal neurologic deficits. Laboratory testing was significant for a total protein level of 9.5 g/dL, albumin level of 2.4 g/dL, calcium level of 8.2 mg/dL and inorganic phosphorus level $<$ 1 mg/dL. Serum urea nitrogen level was 8 mg/dL, creatinine level was 0.87mg/dL (corresponding to estimated glomerular filtration rate of 90 mL/min/1.73 $m^2$ as calculated by the 4-variable MDRD [Modification of Diet in Renal Disease] Study equation), bicarbonate level was 27 mEq/L, and pH was 7.46. After an unremarkable computed tomographic scan of the head and a lumbar puncture, he was treated for hyperviscosity and severe hypophosphatemia. Further laboratory tests showed $\beta_2$-microglobulin level of 3,353 ng/mL and quantitative immunoglobulin G (IgG) level of 7,274 mg/dL, with IgGλ protein on serum immunofixation. The patient's clinical status failed to improve, and serum inorganic phosphorus values were again $<$1 mg/dL despite intravenous replacement. 25-Hydroxyvitamin D level was 14.2 ng/mL, and intact parathyroid hormone level was 51.6 pg/mL. On a spot urine sample, phosphorus level was 180.7 mg/dL, and creatinine level was 186 mg/dL.

- **What electrolyte abnormities are commonly encountered in multiple myeloma?**
- **What are the clinical manifestations of hypophosphatemia?**
- **What are the causes of hypophosphatemia?**
- **What is the evaluation of hypophosphatemia in this patient?**

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# QUIZ PAGE SEPTEMBER 2016 ANSWERS

## DISCUSSION

### What electrolyte abnormities are commonly encountered in multiple myeloma?

Paraproteinemia can cause tubular syndromes, including proximal and distal renal tubular acidosis and nephrogenic diabetes insipidus.[1] Hyponatremia can occur with overhydration, proteinuria, or syndrome of inappropriate antidiuretic hormone excretion.[2] Spurious results from altered water concentration are now minimized with the use of direct ion-selective electrodes. Hypercalcemia is caused by increased osteoblastic bone destruction[3] and rarely by calcium binding to the abnormal immunoglobulin associated with normal ionized calcium. Hyperphosphatemia usually occurs with reduced glomerular filtration rate, tumor lysis syndrome, and less frequently, factitious measurements from paraprotein interfering with the colorimetric assay.[4-6]

### What are the clinical manifestations of hypophosphatemia?

A wide spectrum of signs and symptoms have been described and include neurologic symptoms with paresthesia, irritability, confusion, delirium, seizures, and coma. Myopathy can result in proximal weakness, ileus, dysphagia, diaphragm dysfunction with respiratory failure, heart failure, and rhabdomyolysis. In addition, increased cell rigidity can predispose to hemolysis and thrombocytopenia.[7,8]

### What are the causes of hypophosphatemia?

Hypophosphatemia can result from decreased intestinal absorption and from urinary wasting with hyperparathyroidism, Fanconi syndrome, and other rare acquired and hereditary syndromes of isolated phosphaturia. It also occurs with an intracellular shift in acute respiratory alkalosis, during acute volume expansion with normal saline solution, with insulin therapy in diabetic ketoacidosis states,

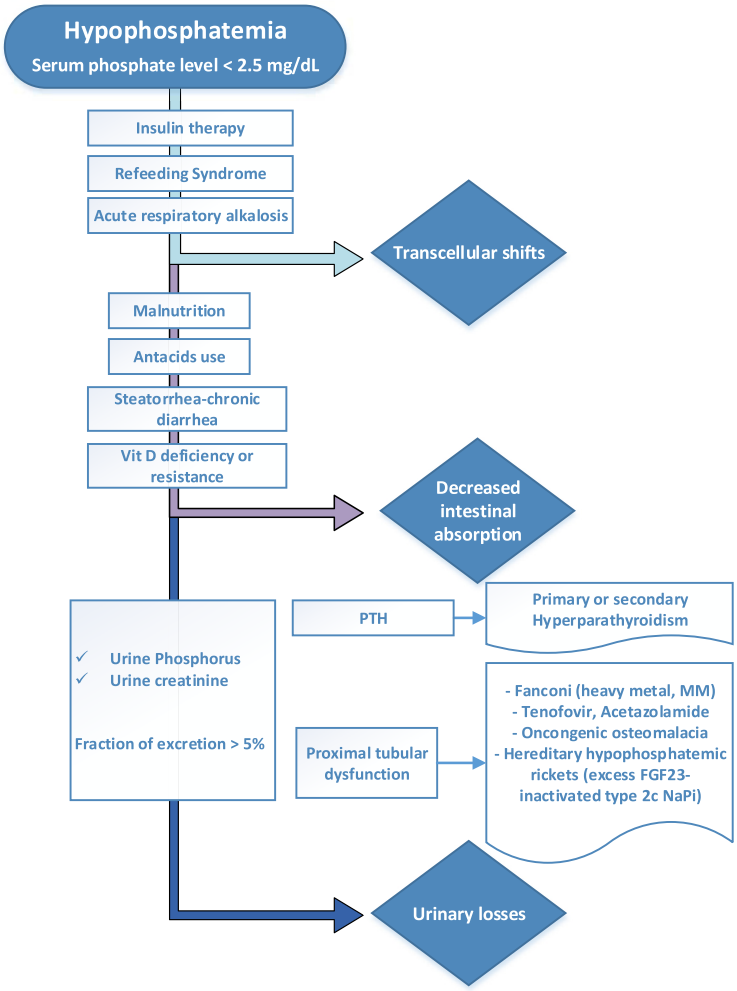


**Figure 1.** Causes of hypophosphatemia. Abbreviations: FGF23, fibroblast growth factor 23; NaPi, sodium phosphorus cotransporter; PTH, parathyroid hormone; MM, multiple myeloma. Based on information from Subramanian and Khardori,[7] Brunelli and Goldfarb,[8] and Tenenhouse and Murer.[12]