Micronutrients: Phosphorus

Dr. Ritamarie Loscalzo
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Phosphorus General Info

✓ Essential **macromineral**
✓ 2\textsuperscript{nd} most abundant mineral in the body, after calcium
✓ Makes up about 1% of your body weight
✓ Stored mostly in the bones and teeth – about 85%
✓ **Phosphorus functions:**
  - Bone mineralization
  - Energy production
  - Acid/alkaline homeostasis
  - Manages kidney function and filters waste
✓ First isolated in 1669 in urine during alchemy trials
✓ The name is derived from the Greek “Phos” (light) and “Phoros” (bearer), meaning “bringer of light”
✓ Phosphoric acid in soda drinks can lead to bone issues
Chemistry of Phosphorus

✓ 15th element in the periodic table – symbol P
✓ A vital part of all living things
✓ A non-metal; part of the nitrogen family
✓ As a gas, it’s colorless
✓ As a solid, it’s silvery white or red, depending on how it is bonded
✓ Burns when exposed to air, so is stored under water
✓ At least 3 allotropic forms:
  ➢ White (yellow)
  ➢ Black
  ➢ Red
Phosphorus in Living Organisms

✓ Component of adenosine triphosphate (ATP)
✓ Phosphorylation *activates enzymes, hormones, and cell-signaling molecules*
✓ Human bones are made up of mostly calcium *phosphate* \( \text{Ca}_3(\text{PO}_4)_2 \)
✓ Binds to hemoglobin in red blood cells and *regulates oxygen delivery* to the tissues of the body
Phosphorus Functions

✓ Major **structural component of bone** in the form of a calcium phosphate salt called hydroxyapatite
✓ Phospholipids (e.g., phosphatidylcholine) are major structural components of **cell membranes**
✓ **Energy production and storage** depends on phosphorylated compounds, such as adenosine triphosphate (ATP) and creatine phosphate
✓ **DNA and RNA** are long chains of phosphate-containing molecules
✓ Helps maintain body’s **acid-base balance (pH)** by acting as an important buffer
Phosphorus Digestion

✓ Most absorbed in organic form
  ➢ Hydrolyzed enzymatically in small intestine lumen
  ➢ Released as inorganic phosphate

✓ Phospholipase C
  ➢ Zinc-dependent enzyme
  ➢ Hydrolyzes the glycerophosphate bond in phospholipids

✓ Alkaline phosphatase
  ➢ Zinc-dependent enzyme
  ➢ Activity is stimulated by calcitriol
  ➢ Functions at the brush border of the enterocyte to free phosphorus from some bound forms
  ➢ It cannot free phytate-bound phosphorus
Phosphorus Absorption

Phosphorus is readily absorbed in the small intestine

Phosphate intake from food 32 mmol

Fecal excretion 11 mmol

Net intestinal absorption 21 mmol

Formation 8 mmol

Reabsorption 8 mmol

Extracellular fluid phosphorus 22 mmol

208 mmol  187 mmol

Phosphorus excreted in urine 21 mmol

Source: Nat Rev Neph © 2010 Nature Publishing
Phosphorus Absorption

✓ About 50% - 70% of dietary phosphorus absorbed
  ➢ Animal sources at the upper end of the range
  ➢ Phytate-containing foods at the lower end

✓ Primarily in duodenum and jejunum

✓ In its inorganic form throughout small intestine

✓ Occurs by two processes:
  ➢ A saturable, carrier-mediated active transport system dependent on sodium and enhanced by calcitriol
  ➢ Concentration-dependent passive diffusion process
## Influences on Phosphorus Absorption

### Decreases
- Leaky gut and other GI issues
- Excessive magnesium, calcium, and aluminum
- Phytates in wheat bran & dried beans
  - Absence of phytase in digestion
  - Phytase – phosphate esterase – frees phosphate from phytic acid
- Iron
- Smoking
- Alcohol

### Increases
- Vitamin D3
  - Stimulates absorption in the duodenum and jejunum
- Vitamin K
- Vitamin C
- Vitamin E
- Boron
Phosphorus Transport

✓ Quickly absorbed from intestine into blood
✓ Appears in blood within about an hour after ingestion
✓ Found in blood in both organic and inorganic forms

- 70% - organic phosphate: phospholipids in lipoproteins
- 30% as HPO$_4^{2-}$ and H$_2$PO$_4^-$ and trace amounts PO$_4^{3-}$

Inorganic phosphates associated with:
  - Calcium
  - Magnesium
  - Sodium
Phosphorus Storage

- Found in all cells of the body; majority in:
  - Bone
  - Muscle

- Circulating phosphate is in equilibrium with skeletal and cellular inorganic phosphate

- Inorganic phosphorus
  - Ultrafilterable phosphate
  - Plasma ranges: 2.5 – 4.5 mg/dL

- Organic phosphates formed in intermediary metabolism

- Variability of serum phosphate concentration as a result of:
  - Dietary phosphate
  - Age and stage growth
  - Time of day
  - Various hormones
  - Renal function
Phosphorus Excretion

✓ Excess excreted by kidneys, regulated by hormones:
  ➢ Parathyroid hormone (PTH)
  ➢ Vitamin D
  ➢ Fibroblast growth factor-23 (FGF-23)

✓ Slight drop in blood calcium levels sensed by parathyroids
  ➢ → Increased secretion of PTH
  ➢ → ↓ Urinary excretion of calcium
  and ↑ urinary excretion of phosphorus
  ➢ → Stimulates bone resorption
Regulation of Phosphorus: 1

✓ Concentrations are tightly controlled
  ✓ Intracellularly
  ✓ Extracellularly

✓ Blood levels maintained between 3.0 and 4.5 mg/dL

✓ Blood levels not indicative of optimal levels in bone
Regulation of Phosphorus: 2

**Diagram:**

- **Ca**
  - + PO4
  - + Vitamin D
  - + Ca and PO4 absorption

**PTH**
- + FGF-23
- PTH effect:
  1. Ca reabsorption
  2. PO4 reabsorption
  3. 1,25 Vit. D

**FGF-23 effect:**
1. PO4 reabsorption
2. 1,25 Vit. D

**Increase serum calcium**
**Decrease serum phosphorus**

**Source:** J Am Board Fam Med © 2009 American Board of Family Medicine
Phosphorus Drug Interactions

- **Aluminum-containing antacids** form aluminum phosphate, which is not absorbable
- **Proton pump inhibitors** may also limit the efficacy of phosphate-binder therapy in patients with kidney failure
- **Excessively high doses of 1,25-dihydroxyvitamin D** or its analogs, may result in hyperphosphatemia
- **Potassium supplements or potassium-sparing diuretics** taken with phosphorus supplements may result in high blood levels of potassium (hyperkalemia), resulting in life-threatening heart rhythm abnormalities
- **HRT in postmenopausal women** is associated with higher urinary phosphorus excretion and lower serum phosphorus levels in treated compared to untreated women
Phosphorus Deficiency

✓ Inadequate phosphorus intake rarely results in abnormally low serum phosphorus levels (hypophosphatemia) because renal reabsorption of phosphorus increases to compensate for decreased intake

✓ Found in cases of near-starvation

✓ Inherited disorders, such as Renal Phosphorus Wasting disease, can lead to deficiency

✓ **Deficiency symptoms include:**
  • Loss of appetite
  • Muscle weakness
  • Bone fragility
  • Numbness in the extremities
Bone Mineralization

✓ **85% of body phosphorus found in bone**

➢ Of prime importance in development of skeletal tissue

➢ **Found in amorphous calcium phosphate forms**
  
  • $\text{Ca}_3(\text{PO}_4)_2$
  • $\text{CaHPO}_4 \cdot 2\text{H}_2\text{O}$
  • $\text{Ca}_3(\text{PO}_4)_2 \cdot 3\text{H}_2\text{O}$,
  • Hydroxyapatite: $\text{Ca}_{10}(\text{PO}_4)_6 (\text{OH})_2$
    – crystalline form laid down on collagen in ossification of bone formation

✓ **Ratio of calcium to phosphorus**

➢ 13:1

➢ Similar to extracellular fluid

➢ Crystalline bone – 1.5:1
Bone Metabolism Influenced by

✓ Parathyroid hormone (PTH)
  ➢ Stimulates resorption of phosphate from bone, same as calcium
  ➢ Stimulates excretion of phosphorus in urine
  ➢ PTH-induced urinary excretion of phosphorus
    • Sufficient to override bone resorption of phosphorus
    • Effects a net decrease in plasma phosphate

✓ Calcitriol
  ➢ In conjunction with PTH enhances phosphate resorption from bone
  ➢ Stimulates phosphate absorption in the intestine
    • Through enhanced alkaline phosphatase activity

✓ Calcitonin
  ➢ Promotes bone mineralization

✓ Phosphorus that is not part of the bone
  ➢ Found either in extracellular fluids such as blood or soft tissue
  ➢ Within cells, major anion involved with other processes
Nucleotide/Nucleoside Phosphates

✓ Important component of nucleic acids DNA and RNA
✓ Alternates with pentose sugars to form the linear backbone
✓ Intermediary metabolism of energy nutrients in the form of high-energy phosphate bonds
  ➢ Nucleotide adenosine triphosphate (ATP)
  ➢ Creatine phosphate (phosphocreatine) - synthesized in muscle from ATP and creatine
  ➢ Can provide energy to muscles as needed (e.g., exercise)
    • Transferring its PO₄ to ADP via creatine kinase
✓ Uridine triphosphate (UTP)
  ➢ Activate substances in intermediary metabolism
  ➢ Hydrolysis provides for the coupling of uridine monophosphate and glucose 1-phosphate to form uridine diphosphate (UDP)-glucose
  ➢ UDP-glucose is critical for the synthesis of glycogen
Phosphorus Intracellular Second Messenger

✓ Functions as second messenger to affect cellular metabolism

✓ Part of cyclic adenosine monophosphate (cAMP)
  ➢ Acts within cells by activating certain protein kinases
  ➢ Generated in response to the binding of certain hormones to cell receptors
  ➢ Derived from ATP

✓ Inositol triphosphate (IP$_3$)
  ➢ Second messenger to trigger intracellular calcium release
  ➢ Actions mediated by protein kinases
Phosphoproteins

- Intermediary metabolism of the energy nutrients through the phosphorylation of different substrates in the body
- **Protein kinases activated by cAMP**
  - Function to phosphorylate specific target proteins within the cell
  - Changes cellular activities
Phospholipid Structural Roles

- Cell membranes contain phospholipids
- Important to the bilayer structure of cell membranes → Polar and nonpolar regions
- Examples:
  - Phosphatidylcholine
  - Phosphatidylinositol
  - Phosphatidylserine
Acid-Base Balance

✓ Phosphate functions in acid-base balance
✓ Main intracellular buffer within cells
✓ Filtered phosphate reacts with secreted hydrogen ions in kidneys
  ➢ Releases sodium ions
  ➢ Removes free hydrogen ions
  ➢ Increases pH
✓ Actions can be reversed to lower pH
Assessing Phosphorus Status

✓ Serum phosphorus is generally part of routine blood chemistry

- Serum phosphorus is a poor reflection of body stores because <1% is in extra cellular fluid
- Hypophosphatemia (< 3.0 mg/dl)
- Hyperphosphatemia (>4.5 mg/dl)
- Vitamin D3
- Protein status
- Parathyroid hormone (PTH)
- PTH-related peptide (PTHrP)
- Renal function labs (GFR<20-25 mL/min)

***Serum indicates little about phosphorus status

✓ Functional Tests:
  - SpectraCell
  - NutrEval by Genova / Metametrix
  - NTX or Osteonex – for bone turnover

✓ Questionnaires and good history taking for signs and symptoms

No routine biochemical method appears to assess phosphorus status accurately
## Table 1. Recommended Dietary Allowance (RDA) for Phosphorus

<table>
<thead>
<tr>
<th>Life Stage</th>
<th>Age</th>
<th>Males (mg/day)</th>
<th>Females (mg/day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infants</td>
<td>0-6 months</td>
<td>100 (AI)</td>
<td>100 (AI)</td>
</tr>
<tr>
<td>Infants</td>
<td>7-12 months</td>
<td>275 (AI)</td>
<td>275 (AI)</td>
</tr>
<tr>
<td>Children</td>
<td>1-3 years</td>
<td>460</td>
<td>460</td>
</tr>
<tr>
<td>Children</td>
<td>4-8 years</td>
<td>500</td>
<td>500</td>
</tr>
<tr>
<td>Children</td>
<td>9-13 years</td>
<td>1,250</td>
<td>1,250</td>
</tr>
<tr>
<td>Adolescents</td>
<td>14-18 years</td>
<td>1,250</td>
<td>1,250</td>
</tr>
<tr>
<td>Adults</td>
<td>19 years and older</td>
<td>700</td>
<td>700</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>18 years and younger</td>
<td>-</td>
<td>1,250</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>19 years and older</td>
<td>-</td>
<td>700</td>
</tr>
<tr>
<td>Breast-feeding</td>
<td>18 years and younger</td>
<td>-</td>
<td>1,250</td>
</tr>
<tr>
<td>Breast-feeding</td>
<td>19 years and older</td>
<td>-</td>
<td>700</td>
</tr>
</tbody>
</table>
## Hyperphosphatemia

### Tolerable Upper Intake Level (UL) for Phosphorus

<table>
<thead>
<tr>
<th>Age Group</th>
<th>UL (mg/day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infants 0-12 months</td>
<td>Not possible to establish*</td>
</tr>
<tr>
<td>Children 1-3 years</td>
<td>3,000 (3.0 g)</td>
</tr>
<tr>
<td>Children 4-8 years</td>
<td>3,000 (3.0 g)</td>
</tr>
<tr>
<td>Children 9-13 years</td>
<td>4,000 (4.0 g)</td>
</tr>
<tr>
<td>Adolescents 14-18 years</td>
<td>4,000 (4.0 g)</td>
</tr>
<tr>
<td>Adults 19-70 years</td>
<td>4,000 (4.0 g)</td>
</tr>
<tr>
<td>Adults 71 years and older</td>
<td>3,000 (3.0 g)</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>3,500 (3.5 g)</td>
</tr>
<tr>
<td>Breast-feeding</td>
<td>4,000 (4.0 g)</td>
</tr>
</tbody>
</table>

*Source of intake should be from food and formula only.
Hyperphosphatemia Risk

✓ Kidney disease or stones
✓ Low PTH
✓ Kidney trauma/injury
✓ Transplant recipients
✓ Dialysis
✓ Consumption of excessive soft drinks or highly processed foods
✓ Excessive use of enemas or laxatives containing phosphates
Hyperphosphatemia Symptoms

✓ Hyperphosphatemia typically asymptomatic
✓ If acute, symptoms result from hypocalcemia:
  ➢ Joint pain
  ➢ Muscle cramps and spasms
  ➢ Fatigue
  ➢ Perioral numbness
  ➢ Bone pain
  ➢ Pruritus
  ➢ Nausea
  ➢ Vomiting
  ➢ Rash
Excessive Phosphate Intake: Adverse Effects on Health
Assessing Bone Mineral Density

Test for those especially at risk for osteoporosis

✓ DEXA aka DXA
  - Dual-energy X-ray absorptiometry is one of the best tools
  - Scan specific sites at two different energy levels

✓ CT scans:
  - Less precise and accurate than DEXA
## Dietary Sources of Phosphorus

<table>
<thead>
<tr>
<th>Plant</th>
<th>Animal</th>
</tr>
</thead>
<tbody>
<tr>
<td>✓ Cashews</td>
<td>✓ Chicken</td>
</tr>
<tr>
<td>✓ Sunflower Seeds</td>
<td>✓ Turkey</td>
</tr>
<tr>
<td>✓ Lentils</td>
<td>✓ Beef</td>
</tr>
<tr>
<td>✓ Almonds</td>
<td>✓ Halibut</td>
</tr>
<tr>
<td></td>
<td>✓ Sardines</td>
</tr>
<tr>
<td></td>
<td>✓ Salmon</td>
</tr>
<tr>
<td></td>
<td>✓ Tuna</td>
</tr>
<tr>
<td></td>
<td>✓ Dairy</td>
</tr>
</tbody>
</table>
Herbs High In Phosphorus

✓ Poppy seed
✓ Mustard seed
✓ Caraway
✓ Celery seed
✓ Dill weed
✓ Cumin
✓ Coriander
✓ Fennel seed
✓ Chervil
✓ Anise
✓ Parsley
✓ Onion powder
✓ Paprika
✓ Curry
✓ Chili powder
✓ Fenugreek
✓ Marjoram
✓ Tarragon
✓ Spearmint
✓ Basil
✓ Turmeric
✓ Nutmeg
✓ Saffron
✓ Thyme
✓ Cardamom
✓ White pepper
✓ Ginger
# Food Sources of Phosphorus

## Phosphorus content by food group (organic sources)

<table>
<thead>
<tr>
<th>Food Group</th>
<th>P (mg)</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grains (1 oz.)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Whole</td>
<td>85</td>
<td></td>
</tr>
<tr>
<td>Refined</td>
<td>33</td>
<td></td>
</tr>
<tr>
<td>Vegetables (1/2 cup)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dark-green</td>
<td>39</td>
<td></td>
</tr>
<tr>
<td>Red &amp; orange</td>
<td>25</td>
<td></td>
</tr>
<tr>
<td>Beans &amp; peas</td>
<td>119</td>
<td></td>
</tr>
<tr>
<td>Starchy</td>
<td>43</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>21</td>
<td></td>
</tr>
<tr>
<td>Fruit and juices (1/2 cup)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>17</td>
<td></td>
</tr>
<tr>
<td>Milk (1 cup)</td>
<td>247</td>
<td></td>
</tr>
<tr>
<td>Meat &amp; beans (1 oz.)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>63</td>
<td></td>
</tr>
<tr>
<td>Oils (1 tsp.)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Discretionary calories</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Added sugars</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Solid fats</td>
<td>1</td>
<td></td>
</tr>
</tbody>
</table>

- Whole grains > refined grains
  - Phytates reduce absorption
- Protein-rich foods have phosphorus

Forms of Phosphorus Supplementation

✓ **Elemental phosphorus:** Highly toxic; only used as a homeopathic treatment

✓ **Inorganic phosphates:** Not toxic at typical doses:
  - Dibasic potassium phosphate
  - Monobasic potassium phosphate
  - Dibasic sodium phosphate
  - Monobasic sodium phosphate
  - Tribasic sodium phosphate
  - Phosphatidylcholine
  - Phosphatidylserine
Topical Phosphorus

✓ Phosphate is the drug (salt) form of phosphorus – combines w/other compounds
  ➢ E.g: Clindamycin phosphate topical - used to treat acne by decreasing the number of acne lesions. Clindamycin is an antibiotic; phosphates allow penetration.

✓ Phosphates in enemas as laxatives

✓ Athletes use phosphate supplements before competitions or heavy workouts to help reduce muscle pain and fatigue
Phosphorus/Calcium Ratio

Optimal Intake:

- Ratio of serum calcium to phosphorus 10:4
- A high ratio of phosphorus to calcium sensitizes the body and increases inflammatory tendencies

- Phosphorus level too high:
  - Frequent colds and flu
  - Sensitive skin
  - Caries near gum line
  - Red-rimmed eyes
  - Low blood pressure
  - Sensitive to pain and noise
Resources

✓ Advanced Nutrition and Human Metabolism – Gropper, Smith and Groff

✓ Better Bones Blog – Dr. Susan A. Brown, PhD
http://www.drritamarie.com/go/BetterBones

✓ Dr. Edward Group DC, NP, DACBN, DCBCN, DABFM
http://www.drritamarie.com/go/PhosphorusFoods

✓ Last, Walter, DC; The Calcium/Phosphorus Ratio
http://www.drritamarie.com/go/CalciumPhosphorusRatio

✓ Linus Pauling Institute:
http://www.drritamarie.com/go/LPIPhosphorus

✓ University of Maryland Medical Center:
http://www.drritamarie.com/go/UofMarylandPhosphorus