## The Role of Vitamin D in Fracture and Nonunion Healing

I. Serum vitamin D [25(OH)D] levels
   A. "Normal" levels debatable
      1. 20-50 ng/mL (Institute of Medicine)
      2. 30-100ng/mL (Endocrine Society)
   B. Hypervitaminosis D
      1. Upper normal threshold defined by adverse effects related to hypercalcemia
      2. >50 – 100 ng/mL
      3. Incidence: evidence for the possibility of toxicity (resultant symptomatic hypercalcemia) is limited to case reports and small series
   C. Hypovitaminosis D
      1. Lower threshold defined by increasing parathyroid hormone and impaired calcium absorption
      2. Vitamin D insufficiency: 12-19 ng/mL vs. 21-30 ng/mL
      3. Vitamin D deficiency: <12ng/mL vs. <20 ng/mL
      4. Incidence in orthopaedic trauma population approximately 70-85%

II. Basic science evidence (potential but unproven effects on fracture healing)
   A. combination of *in vivo* and *in vitro* studies show that vitamin D can increase production of VEGF, PDGF, BMP3, osteocalcin and osteopontin, FGF-23, and TNAP
   B. vitamin D can increase osteoblast differentiation towards osteogenesis and osteoclastogenesis for remodeling

III. Clinical evidence
   A. Common Limitations
      1. Definitions used for hypovitaminosis D are debatable not consistent throughout literature
      2. Vitamin D serum concentration is often considered dichotomous categorical variable (sufficient vs. deficient) but its physiologic effects on bone healing are likely not that simple
   B. Effects/associations of hypovitaminosis D
      1. Acute fracture healing – incidence of hypovitaminosis D similar in orthopaedic trauma population and patients with nonunions
      2. Effects of vitamin D supplementation – treatment regimens during acute fracture healing not standardized
         1. Normalizing vitamin D levels: many supplementation regimens have been studied and they generally all can improve vitamin D levels within a few weeks but not necessarily to normal levels.
         2. Fracture healing – Despite improvement of vitamin D levels with supplementation, researchers have failed to show significant decreased nonunion incidence with vitamin D supplementation
         3. Nonunion healing
            a. Current recommendations are to treat patients with hypovitaminosis D regardless of the presence of nonunion
            b. No studies comparing healing success for surgically treated nonunions with and without vitamin D supplementation