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SERUM BETA-CROSSLAPS (BETA-CTX) A BONE TURNOVER MARKER

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The measurement of bone mineral density is essential for the diagnosis of osteoporosis, but it does not allow us to monitor the rate of bone loss at a point in time. Biochemical markers of bone turnover include markers of bone formation and bone resorption. They are useful to determine whether there are abnormalities in the process of bone remodeling and can be used to monitor the rate of bone loss in various metabolic bone disorders. Importantly, they allow us to monitor the efficacy of drug therapy for osteoporosis and other bone disorders.

Human bone turnover or remodeling is a balanced process of bone formation and bone resorption. Most of the organic matrix of bone consists of Type I collagen. This is a helical protein that is cross-linked at both the C-terminal and N-terminal ends of the molecule. A fragment of collagen at its C-terminal end changes its nature as bone ages, whereby its constituent alpha form of aspartic acid converts to the beta form. This fragment or telopeptide is called Beta-CTx.

During bone resorption proteases degrade collagen and Beta-CTx is released into the circulation. It is a specific marker for the degradation of Type I collagen. Increased levels of Beta-CTx are found in serum in states of increased bone resorption and may return to normal levels during resorption-inhibiting therapy.

The most common causes of unbalanced bone turnover are age and menopausal related osteoporosis and osteopaenia. Disease related causes of unbalanced bone turnover include hyperparathyroidism, hyperthyroidism, Paget's disease, bone metastases, multiple myeloma and rickets.

Sensitive serum markers for bone formation include osteocalcin, bone-specific alkaline phosphatase and PINP (procollagen type I N-terminal propeptide). Serum markers of bone resorption include Beta-CTx and ICTP (carboxy-terminal cross-linked telopeptide). Urine markers for bone resorption include NTX (amino-terminal cross-linked telopeptide of Type I collagen) and pyridinolines. In earlier studies, assays of most bone resorption markers, in particular NTX and pyridinolines, were confined to urine.

The major disadvantage of urinary measurements is the inherent variation associated with urine collection and the degree to which the sample may be diluted or concentrated. Correction for this using urine creatinine measurement is not always reliable and may be influenced by muscle mass and/or impaired renal function.

A serum marker (Beta-CTx) is currently available for assessment of bone resorption and replaces the previous urine markers. Serum Beta-CTx measurement is commercially available as the Roche-B-Crosslaps assay. This is a highly specific assay using two monoclonal antibodies which recognise the ß form of aspartic acid at the C-terminal end of Type I collagen.

In assessment of response to therapy with anti-resorption medications, a decrease after 3-6 months of greater ≥25% of basal values is indicative of an adequate therapeutic response.

Acceptable samples:

- serum collected in standard tubes (gold/SST)
- plasma from K3-EDTA (purple) or Heparin (green) tubes

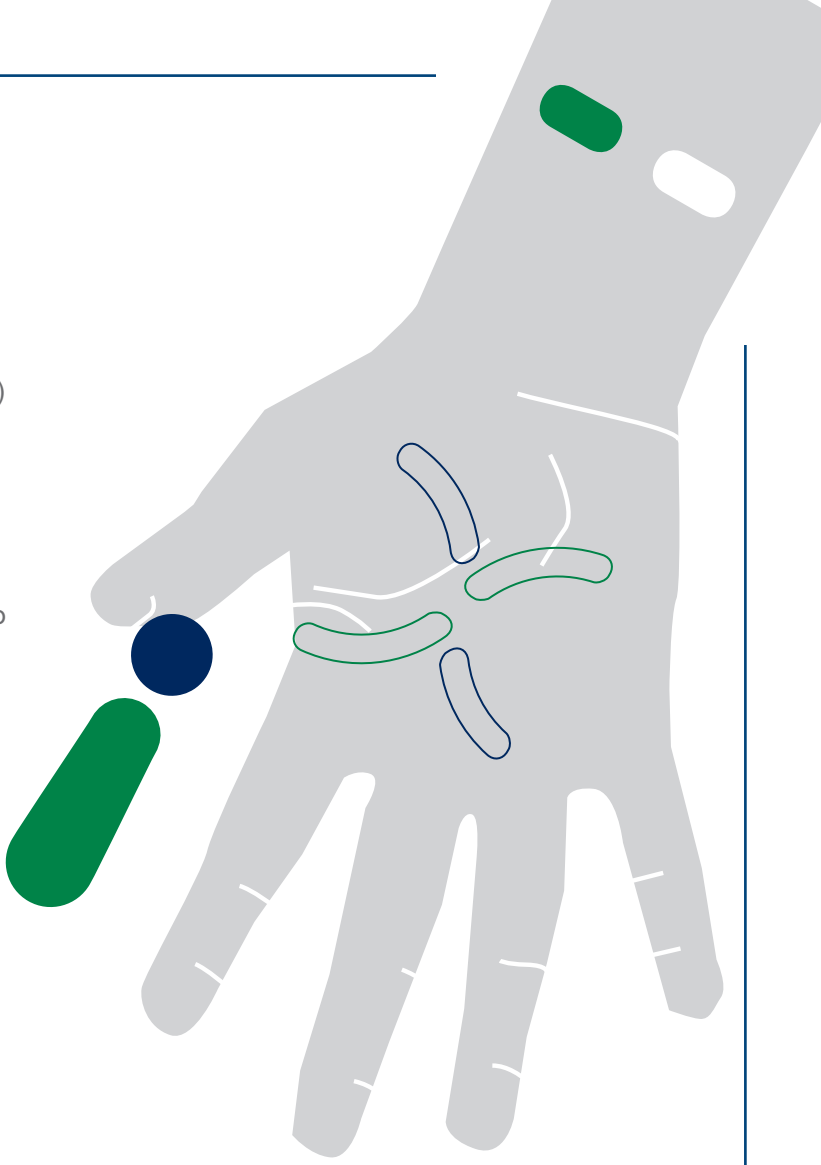
It is recommended to draw blood as fasting morning samples due to a circadian rhythm of Beta-CTx release. All follow up samples should also be taken in the fasted state.

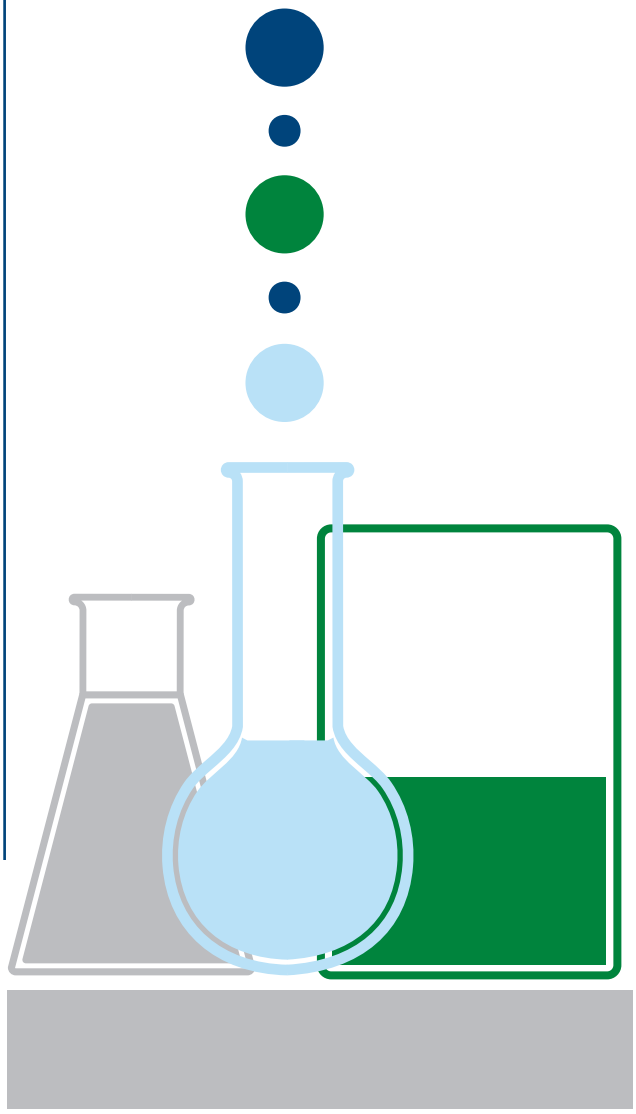
Tests available for bone formation:

- serum Osteocalcin
- bone-specific alkaline phosphatase

Tests available for bone resorption:

serum Beta-CTx





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