

Biomarkers of bone diseases

By
Dr. Gouse Mohiddin Shaik

Biomarkers of bone diseases

- **Introduction**
- Bones as part of skeleton provides structure, integrity and strength to the body
- Protect vital organs
- Home for bone marrow... source of many cells
- Play role is Ca^{++} homeostasis
- Stores minerals like Ca^{++} , Mg^{++} P.....
- roughly 1-2 kg of calcium and almost 1 kg of phosphate is stored in a average adult
- Biomarker availability changes throughout the day

Biomarkers of bone diseases

- **Introduction**
- General sources of biomarkers includes
- Serum – bone turnover biomarkers
- Urine – bone turnover biomarkers
- Synovial fluid – arthritis...



Biomarkers of bone diseases

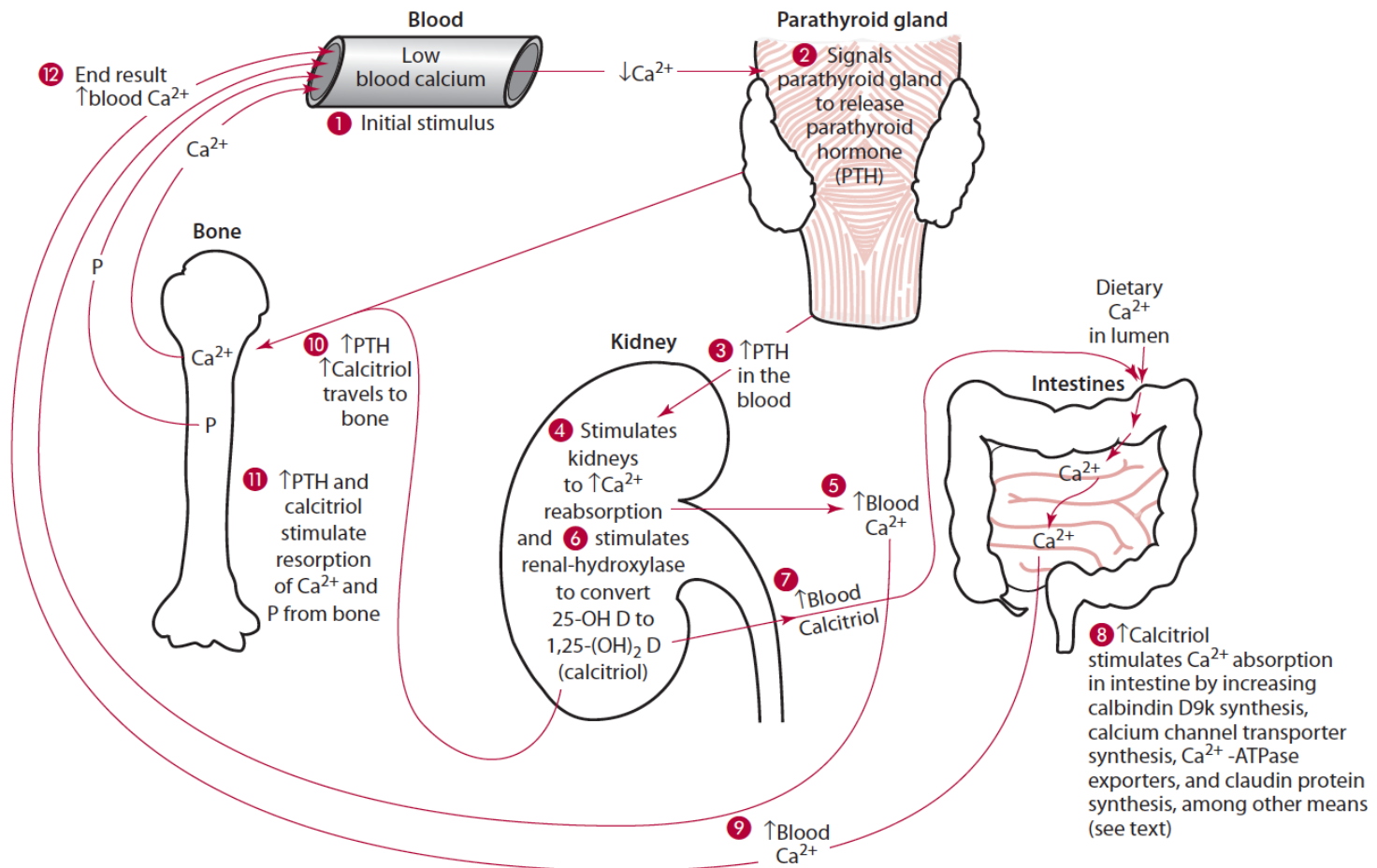
- Introduction

Bones	Vital Organs Protected
Skull	brain, ears, eyes, nose
Ribs	heart, lungs, internal organs
Short and long bones	marrow
Vertebrae	Spinal cord
Pelvic girdle	reproductive organs



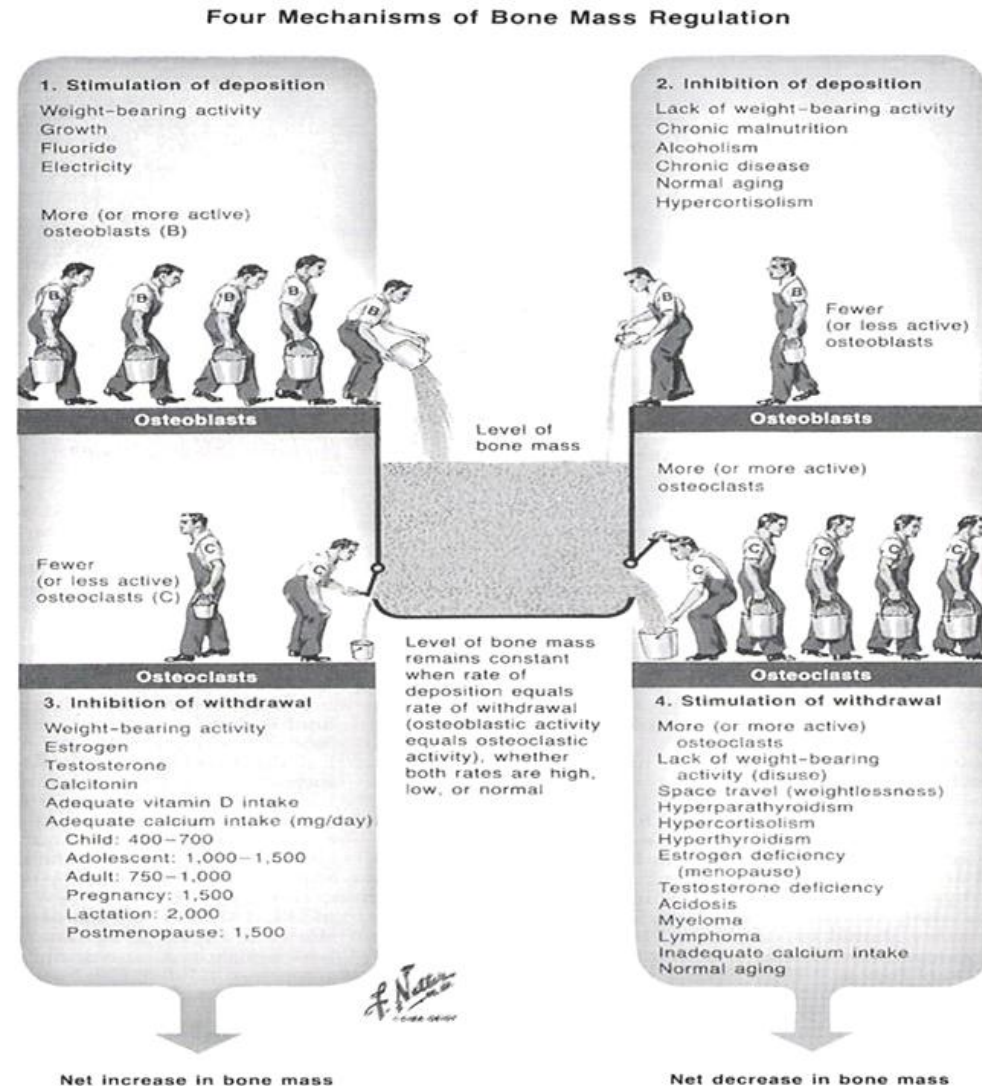
Biomarkers of bone diseases

- Calcium homeostasis



Biomarkers of bone diseases

Bone mass regulation Osteoblasts vs osteoclasts



Brinker, M. R. (2000). Basic sciences. In M. D. Miller & M. R. Brinker (Eds.), Review of orthopaedics (pp. 1-40). Saunders, Philadelphia

Biomarkers of bone diseases

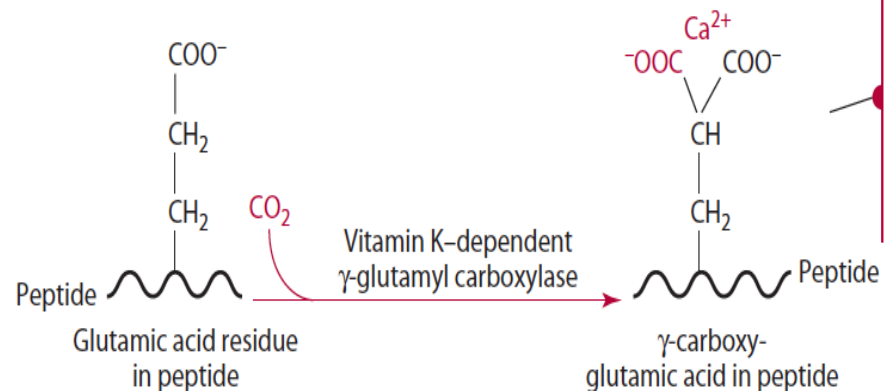
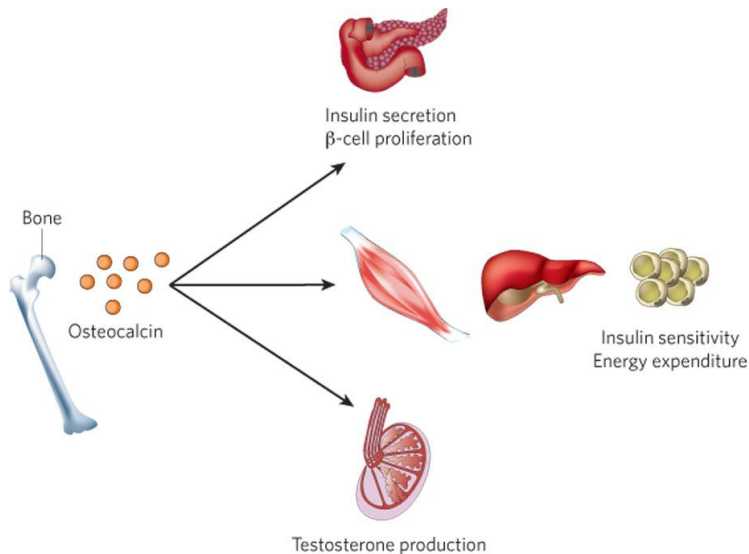
- Markers of bone formation
- Bone alkaline phosphatase (BAP)
- Glycoprotein expressed on the osteoblasts (bone forming cells) membrane
- Reflects the biosynthetic activity of osteoblasts
- BAP different from other ALP in glycation
- Sensitive ELISA tests specific to BAP can be done in blood
- Increased levels can serve as biomarker of bone cancers, broken bones...

Biomarkers of bone diseases

- Markers of bone formation
- Osteocalcin
- Solely secreted by osteoblasts
- Contains GLA (γ -carboxyglutamic acid) residues
- Vitamin K is essential to produce GLA
- Levels are directly co related with bone mineral density
- Acts as prediction biomarker of osteoporosis during treatment
- Can also effect insulin production and sensitivity

Biomarkers of bone diseases

- Markers of bone formation
- Osteoclastin
- GLA (γ -carboxyglutamic acid)



Gla-proteins can bind Ca^{2+} , which then reacts with other cell components like phospholipids to affect blood clotting and bone mineralization, among other processes.

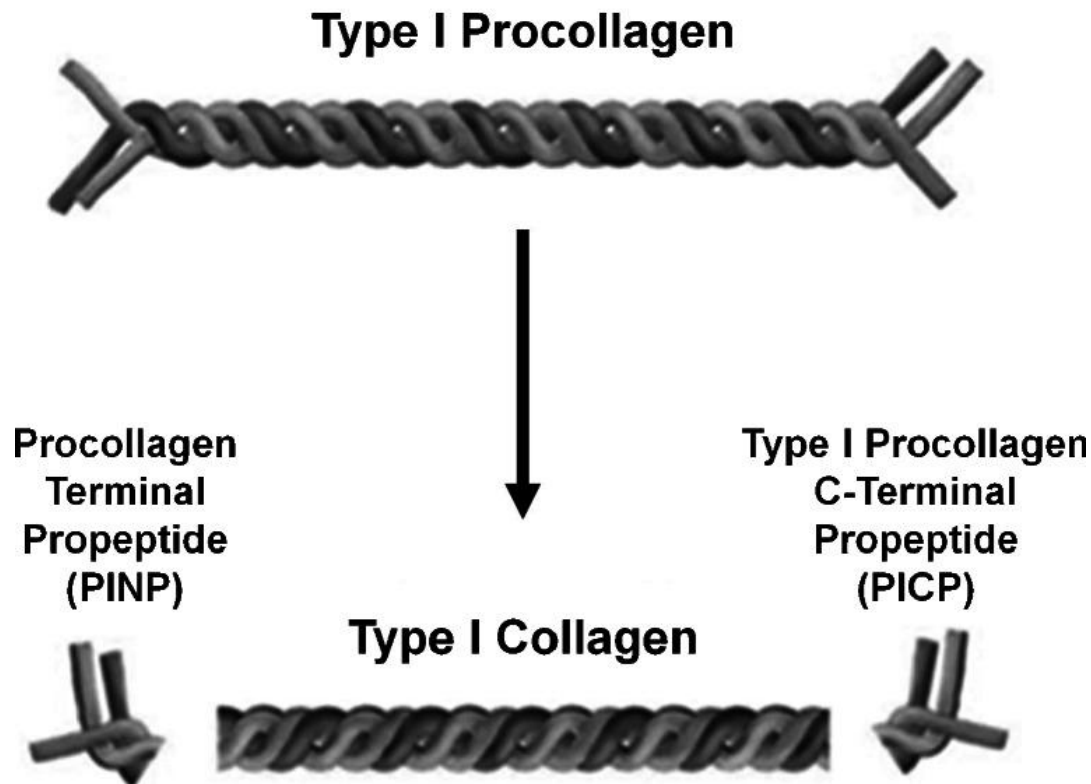
Biomarkers of bone diseases

- Markers of bone formation
- Pro-collagen type-1 pro-peptides
- These pro-peptides are cleaved from the ends of collagen type-1 molecule and can be detected in blood
- Depending on the terminus cleaved 2 types
- P1NP and P1CP (N and C terminus)
- Other tissues like skin, tendons, blood vessels.. Also produce. But bone is the main source
- Level of pro-peptides directly reflect amount of newly synthesized collagen

Biomarkers of bone diseases

- Markers of bone formation
- Pro-collagen type-1 pro-peptides

Bone Collagen Synthesis

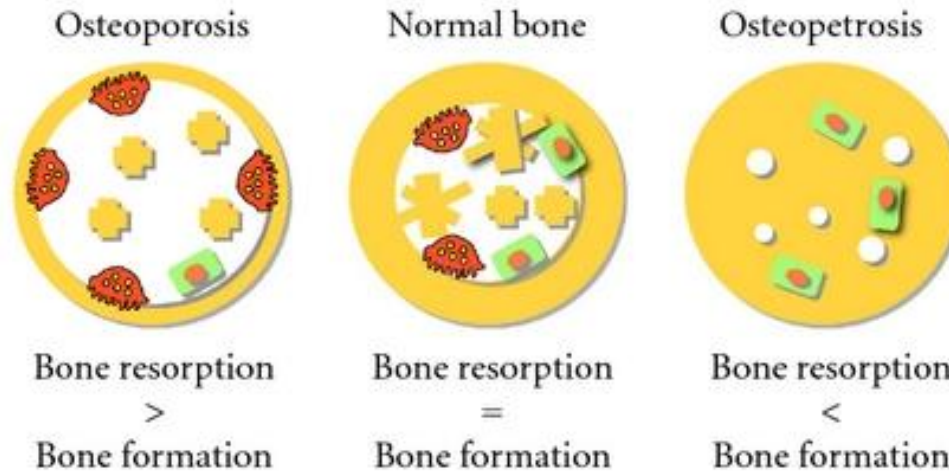
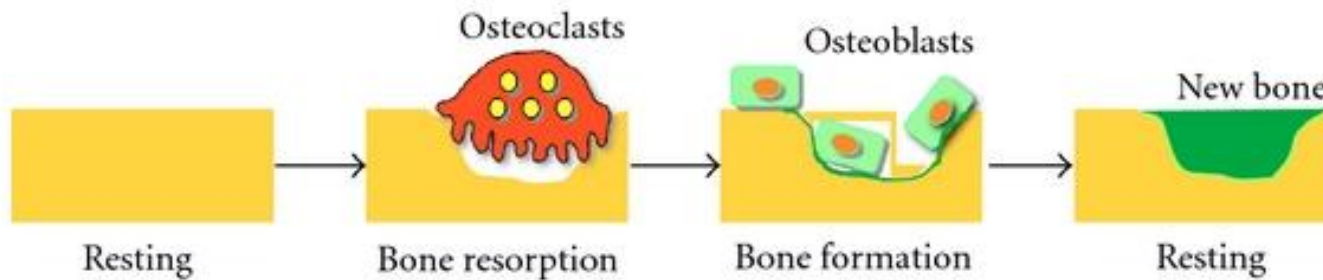


Biomarkers of bone diseases

- **Markers of bone resorption**
- Bone resorption is the process of breaking down the bones into its mineral and collagenous constituents
- Osteoclasts are key players
- Bone remodeling and Ca^{++} homeostasis are the main reason for bone resorption
- Post-menopause women tend to have more osteoclasts activity leading to more bone resorption
- As long as resorption is equal to formation healthy bone is maintained

Biomarkers of bone diseases

- Markers of bone resorption

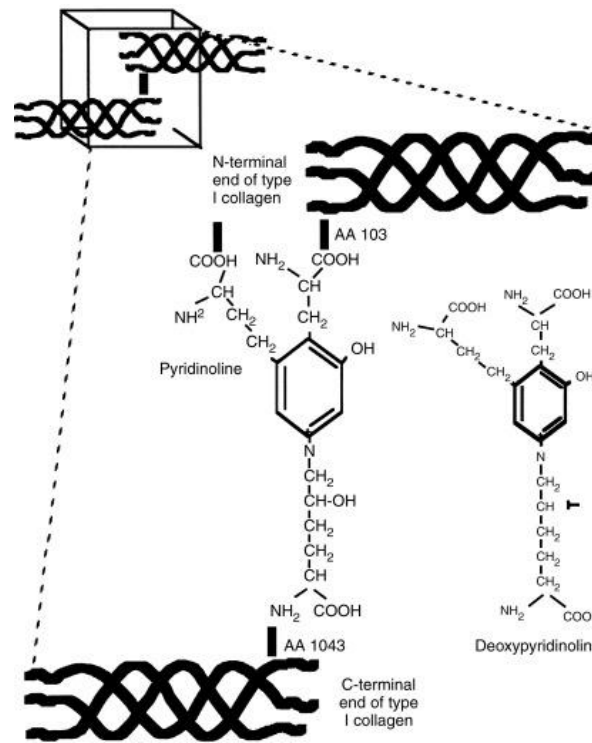


Biomarkers of bone diseases

- Markers of bone resorption
- Hydroxy proline
- Urinary hydroxy proline test is the classical test for bone resorption
- Although not specific... useful some times
- Other classical test being urinary calcium
- As it is also not specific to bones not used now a days

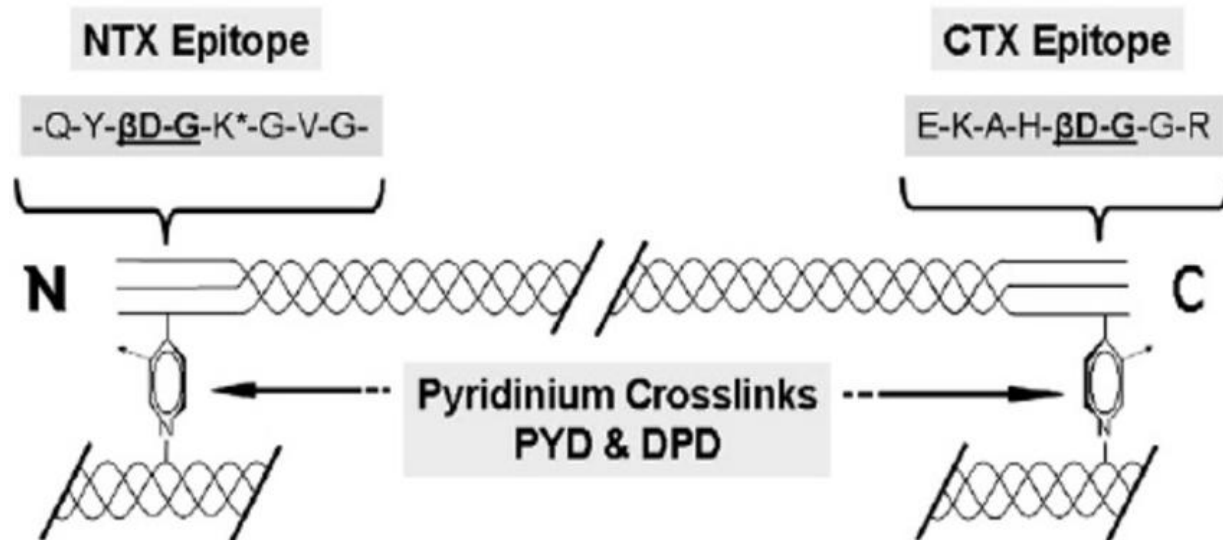
Biomarkers of bone diseases

- Markers of bone resorption
- Pyridinoline or Hydroxylysylpyridinoline (PYD)
- A cross linking compound of collagen
- Pyridinoline and deoxypyridinoline are released in to blood during bone resorption and can be found in urine



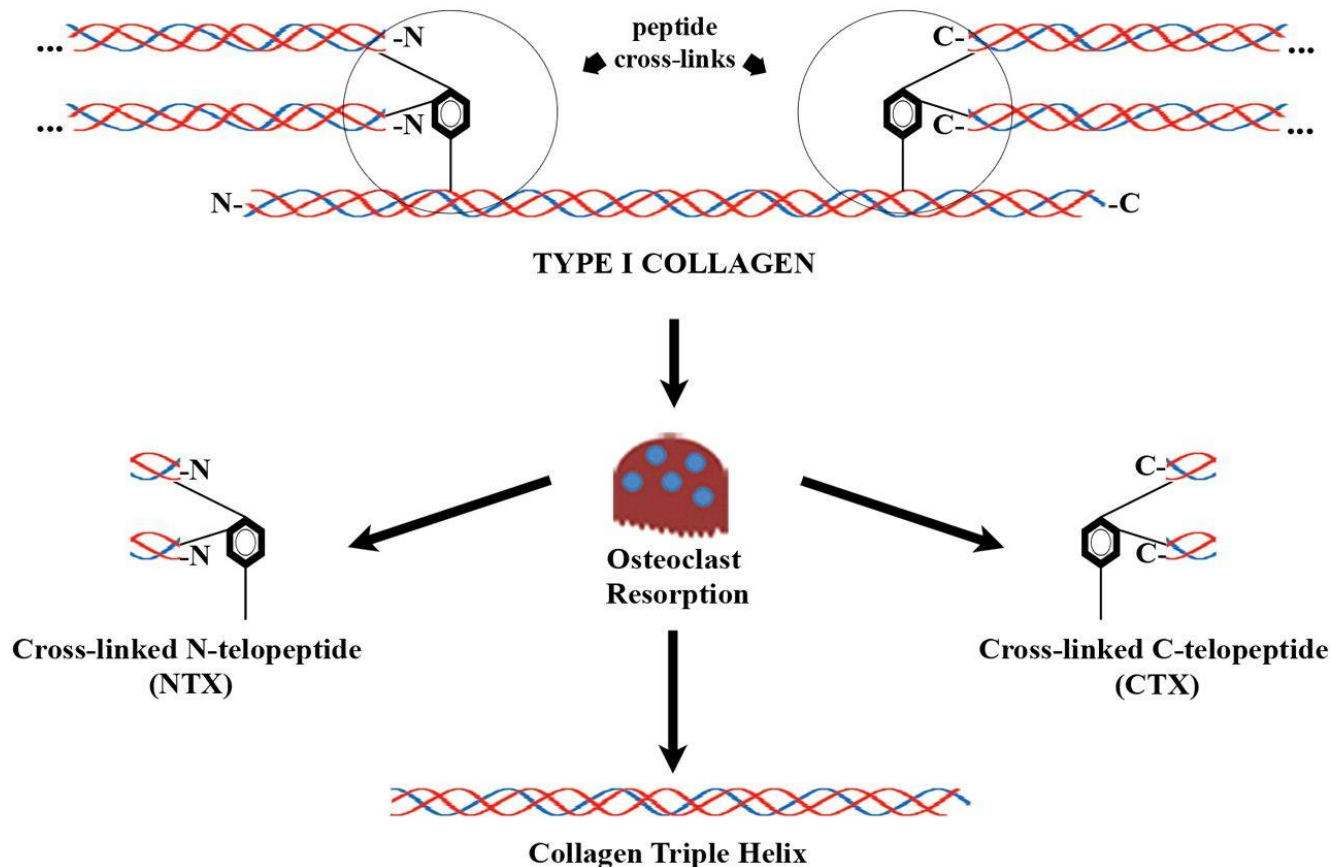
Biomarkers of bone diseases

- Markers of bone resorption
- Telopeptides of type-1 collagen (NTx / CTx)
- Along with PYD telopeptides are also released during bone resorption
- Both N-terminal and C-terminal are released
- Epitope specific antibodies can be used in ELISA



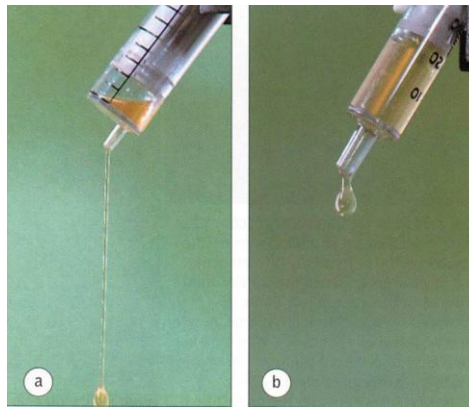
Biomarkers of bone diseases

- Markers of bone resorption
- Telopeptides of type-1 collagen



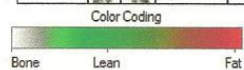
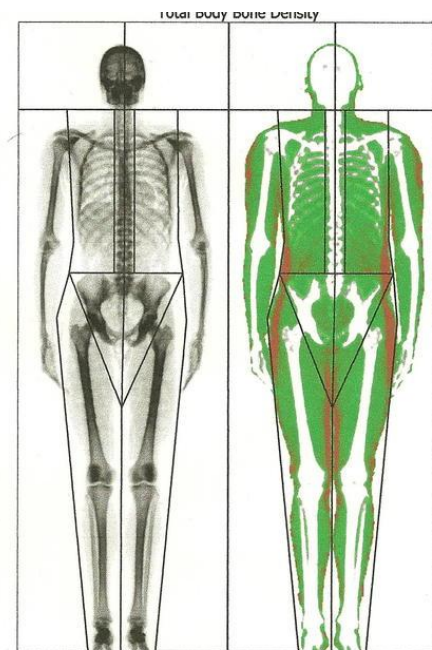
Biomarkers of bone diseases

- Other biomarkers of bone diseases
- Rheumatoid arthritis (RA)
- A complex inflammatory disease effects joints
- Preliminary symptoms are joint pains and swelling
- Systemic biomarkers like TNF- α rises
- Localized biomarkers like viscosity of synovial fluid decreases (assessed by **string test**)

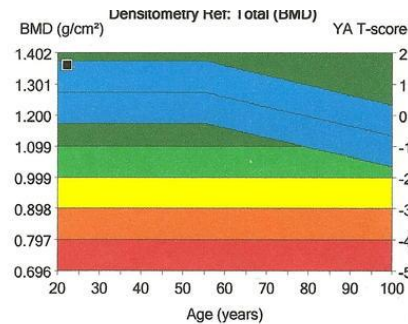


Biomarkers of bone diseases

- Imaging biomarker of bone diseases
- Dual x-ray absorptiometry
- Inexpensive and precise method to analyze bone mineral density



COMMENTS:



Densitometry (Enhanced Analysis)					
Region	¹ BMD (g/cm ²)	² Young-Adult (%) T-score		³ Age-Matched (%) Z-score	
Head	2.076	-	-	-	-
Arms	1.201	-	-	-	-
Legs	1.440	-	-	-	-
Trunk	1.194	-	-	-	-
Ribs	1.058	-	-	-	-
Spine	1.273	-	-	-	-
Pelvis	1.280	-	-	-	-
Total	1.364	111	1.6	105	0.9

T-Score	% of Bone Loss
0.0	0
-1.0	10%
-2.0	20%
-2.5	25%
-3.0	30%
-4.0	40%

Next class

- Next class.....
 - Biomarker detection techniques