

Oral Biology
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Lecture - 10
Mineralization dynamics - Part 1

Today here we are to learn about Mineralization dynamics and I am here Doctor Ramya to present you about the Mineralization dynamics.

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Lecture outline


- Mineralization – What is it
- Composition of Bone
- Mineralization – Process overview
- Promoters of mineralization
- Inhibitors of mineralization
- Theories of mineralization
- Markers of bone turnover




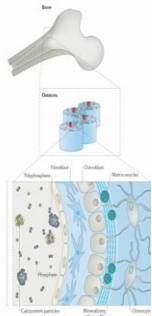
So, this lecture outline would be covering upon all the aspects of mineralization which consists of what is mineralization all about, the composition of bone, the mineralization process overview, promoters of mineralization, inhibitors of mineralization and then we move on to theories and markers of bone turnover.

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Mineralization – What is it




- Mineralization is the process by which mineral crystals are deposited in an organized fashion onto the organic ECM.
- Mineralization is one of the important steps in the formation of hard tissues of the body, that is bone, enamel, dentin and cementum.

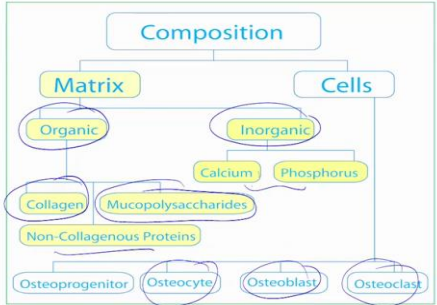


So, first we have to learn about what mineralization is all about. What is it about? And mineralization is the process by which mineral crystals are deposited in an organized fashion in the organic extracellular matrix. So, that is the most important statement and it is one of the most important steps in the formation of hard tissues of the body; the hard tissues of the body being the bone, the cementum, the enamel and the dentin.


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Composition of bone





- The mineral content (inorganic portion) of all the hard tissues of the body is mainly in the form of *calcium hydroxyapatite* crystals, $\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2$.



So, here before we step on to knowing about the mineralization we have to learn about the composition of bone which is the most representative hard tissue in the body or the

more widely present hard tissue in the body. So, knowing about the composition would just give an overview of what the hard tissues are all about. So, any hard tissue would have a basic structure that is the matrix and then the mineral component.

we have overview that is your organic and then your inorganic component. So, the organic matrix is the one which would be laid first and following which the mineralization steps happen in a sequence of events.


So, this organic component has the collagen which is the most important part of the bone and this collagen in the bone mostly is type 1. So, type 1 is actually the predominant collagen in the hard tissues and further we have mucopolysaccharides and other non collagenous proteins which are mentioned as NCP's.

There are cellular elements in the matrix as well. So, the cellular elements mean bone formative cells that is your osteoblast and then we have the bone resorptive cell that is your osteoclast and then the resting osteoblast is called as the osteocyte and then for all these to form there are progenitor cells. And then we move on to the inorganic composition; the inorganic composition again are made up of many ions the predominant ions of the bone are your calcium and phosphorus.

So, they form the most important vital component and this inorganic portion is actually in the form of calcium hydroxyapatite and this calcium hydroxyapatite is actually the principal crystal which is present in the hard tissues of the body name it the bone, the enamel, the dentin and the cementum.

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Non collagenous proteins



Noncollagenous protein	Structural features	Function
Osteopontin	RGD amino acid sequence, phosphorylation	Cell attachment, HA binding
Bone sialoprotein	RGD amino acid sequence, sulfation of tyrosines	Cell attachment
Bone acidic glycoprotein	Polyaspartic acid	Mineralization
Thrombospondin	RGD amino acid sequence, EGF homology	Cell attachment
Biglycan	Leucine repeat structure, two GAG chains near NH ₂ terminus	Cell-cell or cell-protein interactions
Decorin	Leucine repeat structure, one GAG chain near NH ₂ terminus	Binds collagen, regulates fibril formation
Osteonectin	EF hand motif, NH ₂ -terminal domain rich in asparagines and glutamate	Ca ²⁺ and hydroxyapatite binding, cell spreading
Osteocalcin	Gamma carboxylation of glutamic acid	Bone turnover




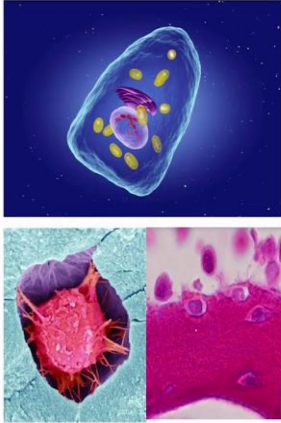
And then further we have the non collagenous proteins. So, the non collagenous protein as already mentioned are also shortly mentioned as NCP's and these are very important and they play a very vital role in the bone metabolism, regulation and the remodeling status of the bone.

So, to quickly go through the non collagenous proteins we have the osteopontin, the bone sialoprotein, glycoprotein, thrombospondin, biglycan, decorin, osteonectin and osteocalcin and these have a wide variety of function ranging from cell attachment mineralization cell attachment and fibril formation, calcium binding, cell spreading and bone turnover.

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Osteoblasts

- Osteoblasts are active bone forming cells.
- abundant cytoplasm filled with rough endoplasmic reticulum
- Synthesize collagen primarily of the type I variety
- Two types of osteoblasts
 1. Mesenchymal osteoblast - surrounded completely by randomly oriented collagen fibrils and is thus responsible for the synthesis of woven bone.
 2. Surface osteoblasts - line up along the surface of preexisting bone tissue & involved in the direct synthesis of lamellar bone.
- Newly formed bone secreted by osteoblast - osteoid
- Osteoblast encased in the mineralized - osteocyte.
- Regulated by Cbfa1 (osteoblast-specific transcription factor) BMP and vitamin D₃.



So, the first thing here the most important one the most important formative cell that is the osteoblast. The most important cell in the bone or any hard tissue or specifically the hard tissue which is bone and dentin and cementum have some formative cell called as osteoblast whereas, it is different in case of enamel where it is called as ameloblast. So, this osteoblast actually has a very prominent polygonal outline and this polygonal outline is actually actively bone forming cells and it is actually very prominent and plump in appearance.

It is polygonal and it has an abundant cytoplasm and numerous cellular organelles present good enough to be secretory in nature or to secrete the bone component. The main predominantly secretory material which the bone actually secretes is the type 1 collagen and that is what is the most important organic component of the hard tissues and then we see that osteoblast as the name implies which is the formative cell of the bone.

There are two types of osteoblasts the mesenchymal and the surface. As the word indicates mesenchymal osteoblasts are those which are actually surrounded by the collagen fibers or it is intermingled between the collagen fibers and are responsible for formation of woven bone. Whereas, your surface osteoblasts are the one which have present on the surface of the bone and are involved in direct synthesis of lamellar bone.

So, the moment being you are hearing the word woven bone and lamellar bone; woven bone is a newly formed bone whereas, your lamellar bone is actually the matured bone

which is sheet like in appearance. And then we have another important term which is actually should be remembered as the osteoblast secretes the bone it actually secretes bone around this area and then gets entrapped in its own matrix and after it gets entrapped in its own matrix it loses many of its secretory cellular organelles and that goes into a resting phase called as osteocyte.

During that process there are some it actually develops lot of processes so that it can actually derive nutrition from the external source. So, this picture is actually an osteocyte and this is what is actually seen in the histopathological image. So, the one which is outside is called as a surface osteoblast and here it is started secreting the bone matrix and it gets entrapped in its own matrix and you can see an osteoblast getting into a resting phase that is your osteocyte.

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Osteoclast

- Osteoclasts are specialized multinucleated giant cells that resorb bone.
- Osteoclasts are giant cells derived from monocyte fusion and have from about 2 to 12 nuclei per cell.
- Intimately associated with the surface of bone and use a structure called a *ruffled border* to bind matrix adhesion proteins and produce resorption pits called *Howship's lacunae*.
- It secretes acid and proteases across the ruffled border, and these dissolve the mineral of bone and destroy the organic matrix
- Osteoclasts can be differentiated histologically by immunohistochemical stains for tartrate-resistant acid phosphatase.
- They closely attach to the bone matrix by binding its surface integrins to a bone protein called vitronectin.

And then further we move on to osteoclast which is actually very important. The osteoclast as the name indicates it is actually involves in the resorption of the bone. And this osteoclast is also called as giant cells because of the size and also because of many number of nucleus present in the cytoplasm.

So, the number of nucleus is very high and there are almost more than 2 to 12 nuclei per cell and the structure of the osteoclast has a periphery which is ruffled in appearance which is thrown into folds and that actually increases the surface area of the osteoclast to

get attached to the bone and at the same time derive lot of activity or conduct lot of activity because of that ruffle the system present there.

And this osteoclast is actually present on the bone surface in an area called as Howship's lacunae. And then we can see that this particular osteoclast is getting attached to the bone at a point through a molecule called as vitronectin and this vitronectin is very important so that it actually helps to seal establish a tight seal on the surface of the bone so that the acid proteases that are secreted from the osteoclast do not escape onto the adjacent area.



It is very clearly more precisely focused in the area where the resorption has to take place. So, that is how it happens and then further we can see that these osteoclasts can be very easily histologically identified and also specifically identified by advanced methods that is immunohistochemistry through tartrate resistant acid phosphatase enzyme staining.

So, this acid phosphatase is actually a very important enzyme which is secreted by the osteoclast and it is an important diagnostic marker. So, to be more specific the tartrate resistant type of acid phosphatase enzyme is actually the one which is very importantly regulating the osteoclast itself and it helps to for the osteoclast to conduct its resorptive activity.

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Regulation of Osteoclast

Osteoclast Inhibition	Osteoclast activation
<ul style="list-style-type: none">• Osteoprotegerin (OPG)• Calcitonin• Estrogen• Transforming Growth Factor Beta (TGF Beta) (Via Increase In OPG)• Interleukin 10 (IL-10)	<ul style="list-style-type: none">• RANKL (ligand) is secreted by osteoblasts and binds to the RANK receptor on osteoclast precursor and mature osteoclast cells• PTH• Interleukin 1 (IL-1)• 1,25 dihydroxy vitamin D• Prostaglandin E2• IL-6 (myeloma)



And this important thing is that the osteoclast has an array of inhibitors and activators as well. So, the regulation of osteoclasts is so closely governed by array of activators; the activators include the RANKL ligand which binds on to the RANK receptor on the osteoclast and then we have the most important hormone here the parathyroid hormone, Interleukin 1 and we have your vitamin D here, prostaglandins and Interleukin 6 to be more precise and then further we have osteoclast inhibition happening from because of osteoprotegerin, calcitonin, estrogen, TGF beta and Interleukin 10.

So, all these are very important regulators which either activate or which inhibit. So, there are a series of molecules or an array of molecular molecules which are responsible to regulate the osteoclastic activity.

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Osteoblast & Osteoclast interaction

- Osteoblasts, osteocytes, and osteoclasts influence each other in a paracrine manner to maintain the balance of bone formation and bone resorption.
- Osteoblasts activate osteoclast formation by expressing M-CSF, RANKL, and WNT5A and inhibit osteoclast activity through OPG.
- Osteocyte-derived SOST inhibits osteoblast differentiation and stimulates osteoclastogenesis.
- Osteoclasts also secrete coupling factors such as BMP6, CTHRC1, EFNB2, S1P, WNT10B, SEMA4D, and CT-1 to act on osteoblasts and osteocytes and thereby influence bone formation.

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Han, Y., You, X., Xing, W. *et al.* Paracrine and endocrine actions of bone—the functions of secretory proteins from osteoblasts, osteocytes, and osteoclasts. *Bone Res* 6, 16 (2018). <https://doi.org/10.1038/s41413-018-0019-6>

And then further we have an important understanding to know here is that the osteoblast and the osteoclast do interact with each other. So, how do they interact? They act through a system called as paracrine signaling. So, this paracrine signaling is when there is a release of the signaling agents or the molecular signals to the neighboring cells that is a paracrine activity.

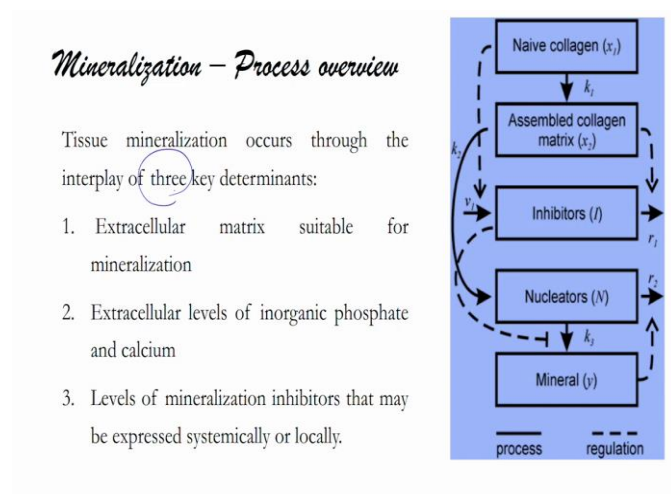
So, here we can see that the osteoblast trigger paracrine activity through your colony stimulating factor, RANKL, WNT pathway and also inhibit osteoclastic activity through your osteoprotegerin. So, that is what you can see they are closely associated with so many molecules and then there is an interplay of molecules here. Osteocyte which is

actually resting also has lot of molecules which actually take care of that particular resting cell.

So, why is that important see as the bone is formed and it is in the resting phase still at any time the particular resting osteocyte has to come into play and then take care of the bone remodeling process. So, for that to happen there are again a lot of genetic events or genetic factors involved and then we also have SOST which inhibits osteoblast differentiation and stimulates osteoclastogenesis.

So, it is all a very tightly regulated interplay of network of molecular events which controls the osteoblast and the osteoclast interaction. And then further osteoclast is actually controlled by your BMP and then we have your CTHRC1 and EFBNT, S 1 IP and then we have WNT and CT which is acting on the osteoblast and the osteocytes and all are very very important for influencing the bone formation.

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So, as an overview of bone formation we can see that the tissue mineralization occurs through most important three key determinants. So, this is the most important point over here three key determinants are important for mineralization. So, what are those key determinants? So, the first one is your matrix. So, that is the ground substance, the foundation, the template over which you have your inorganic phosphates and calcium getting deposited.


And then how much of it has to get deposited is controlled by the mineralization inhibitors those can be locally acting or they can be systemically acting. So, those that is about the process overview. So, to repeat the process overview we have three important determinants the matrix, the ions and then the inhibitors.

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Process Of Mineralisation



- *Spontaneous precipitation* (crystallisation) of calcium phosphate does not occur during the process of formation of hard tissues, even though the tissue fluid contains calcium, phosphate and other minerals.
- This is because of the presence of substances inhibiting crystal formation and also because of the formation of an unstable, inadequate mass of crystal that cannot initiate the mineralisation process.



So, the process of mineralization happens by the most important spontaneous precipitation; precipitation or crystallization of calcium phosphate and occurs in the formation of your hard tissues. And even it occurs even if the particular surrounding extra cellular fluid does not contain enough ions it happens through a very tightly regulated system.


So, this is because of there are some substances which are actually inhibiting the crystal formation and then there are some substances which are actually promoting the crystal formation. So, spontaneous precipitation actually does not occur during the process of formation of hard tissues even though the tissue fluids are containing calcium and phosphate and other minerals.

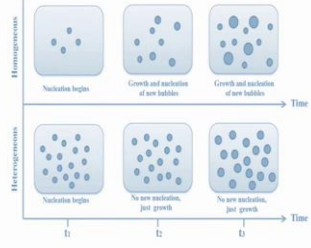
So, it is all tightly regulated.


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Process Of Mineralisation

- Mineralisation occurs by aggregation of ions to form crystals. This process is termed as nucleation. Nucleation is of two types:
 - **Homogenous nucleation:** When local increase in the concentration of minerals allows the formation of sufficient ionic crystals required for mineralisation, it is called homogenous nucleation. Nucleation refers to the first aggregation of ions to form a crystal.
 - **Heterogenous nucleation:** When the presence of nucleating substances (nucleators), which could act as a template for crystal formation, initiates the process of mineralisation even in the absence of an increase in the ionic concentration, it is called heterogenous nucleation.





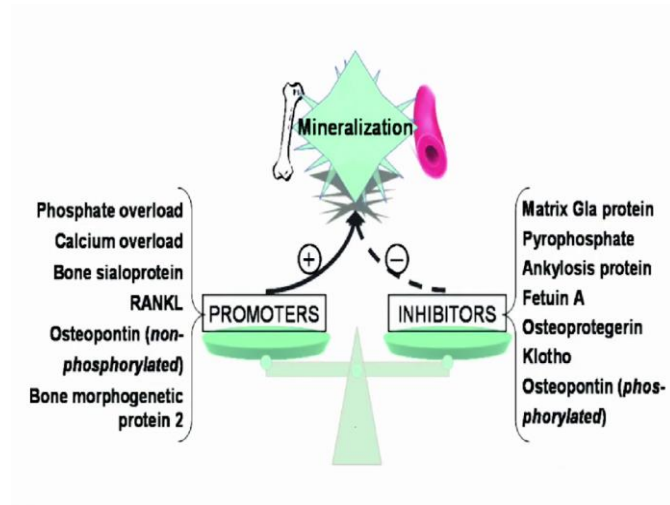


The process in overview is actually of two types that is your homogeneous nucleation and heterogeneous nucleation. So, homogeneous nucleation is very simple to understand as the name suggests it is the increase in the concentration of mineral allowing the formation of sufficient ionic crystals required for mineralization. So, nucleation refers to the first aggregation of ions to form a crystal.

So, this actually happens because of local increase in concentration of minerals. Then we have the heterogeneous mineralization where the presence of nucleating substances are important and that acts as a template for crystal formation. So, what happens is even in the absence of an increased ionic concentration there is crystallization and this is called as heterogeneous nucleation this can happen only when the nucleators are there.

So, again there are two types of crystallization the homogeneous and the heterogeneous. Homogeneous is actually a very low due to local increase in the ionic content the homogeneous crystallization takes place whereas, the heterogeneous nucleation takes place because of the presence of a nucleator agent and then there is deposition of ions even in the absence of a adequate concentration. So, that is your heterogeneous nucleation.

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This again is a very nice overview of what mineralization is all about there are promoters and inhibitors. So, which are the promoters and which are the inhibitors? So, phosphate overload definitely is a promoter and then we have calcium overload and then bone sialoprotein which is shortly called as BSP's and then we have the RANKL, osteopontin and bone morphogenetic protein.

So, we have six promoters and then inhibitors we have Matrix Gla Protein as called as MGP, pyrophosphate, ankylosis protein, fetuin, osteoprotegen, klotho, osteopontin.

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Calcium

The total body content of calcium in an adult is approximately 1.1 kg, of which around 98-99% is present in bone and teeth alone.

FUNCTIONS OF CALCIUM

- Helps in the stability of cell membranes
- Helps in muscle contraction
- Helps in exocytosis in secretory cells
- Helps in blood clotting
- Helps in the development of bone and teeth

The diagram shows a Calcium atom with a central nucleus labeled "Ca" and four concentric electron shells. The outermost shell contains two electrons.

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Then in one by one the most important promoter agents are the first to know is your calcium. So, calcium is given lot of importance here in today's lecture also because that forms a most important role in mineralization.


So, the total body content of calcium I mean is about 1.1 kg and it accounts to almost 98 to 99 percent which is present in bone and teeth. So, in addition to mineralization it also actually helps in stability of cell membrane, muscle contraction, exocytosis in secretory cells, blood clotting and development of bone and teeth.


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Calcium

DIETARY INTAKE

- Daily requirement of calcium is around 300 mg but more has to be consumed because only 60% of what we take is absorbed.
- Milk, vegetables, cheese and fruits are some of the main sources of calcium.
- The recommended dietary allowance (RDA) for calcium is 0.5-0.8 g/day. During pregnancy, the calcium intake should be around 1.5 g/day, and in lactating mothers, it should be 2 g/day for the healthy growth of the infant.





Dietary calcium intake here is again a very important point to remember here in mineralization dynamics because the part of calcium gets complete once you know how much of dietary intake has to be there. So, around at least minimum of 300 milligrams is expected to be consumed and those are available as milk, vegetables, cheese and fruits. And then we have the recommended RDA allowance that is very important to be calculated per kilogram requirement of the human body that is 0.5 to 0.8 grams per day.

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Calcium

CALCIUM ABSORPTION

- Calcium is absorbed in the duodenum.
- Factors such as vitamin D, fat, citrates, protein diet and low pH in the gastrointestinal tract increase the absorption of calcium.
- Phytic acid and oxalic acid decrease absorption by forming insoluble calcium phytate and calcium oxalate.
- Calcium enters the cells by passive diffusion and binds to the calcium-binding proteins within the cell.
- From the cells, the calcium is passed out by active calcium pumps on the cell membrane.

The diagram illustrates the calcium cycle. It shows the flow of calcium between the gut, extracellular fluid, cells, and bones. Key values include: Calcium intake (1000 mg/day), Absorption (950 mg/day), Secretion (250 mg/day), Feces (600 mg/day), Urine (100 mg/day), Cells (15,000 mg), Extracellular fluid (1,200 mg), Reabsorption (880 mg/day), Deposition (500 mg/day), and Bone (1,000,000 mg).

CALCIUM EXCRETION

- Calcium is excreted in faeces and in urine.
- In the faeces, it is excreted through the exfoliated gastrointestinal tract cells, and in the urine, it is excreted as calcium phosphate and calcium chloride.

And the requirement actually increases when there is a increased demand. And then calcium absorption and excretion are very important. So, you can see that the calcium is getting absorbed in the duodenum and then there are so many factors which are helping in absorption or favoring absorption that is your vitamin D, fat, citrates, protein diet and low pH in the gastrointestinal tract.

Further the phytic acid and oxalic acid decrease absorption by forming insoluble calcium phytate and calcium oxalate and calcium also enters the cell by passive diffusion and then further you can see that calcium is excreted in the urine and the faeces. So, this is actually excreted through the exfoliated gastrointestinal cells and it is excreted as calcium phosphate and calcium chloride.

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Calcium

- The normal blood calcium level is maintained between 9 and 11 mg/100 mL.
- Blood calcium may be in a free state or may be complexed with hydrogen carbonate and citrates and in some cases, bound to plasma proteins.
- Blood calcium level is maintained by two hormones and vitamin D.
 - **Parathyroid hormone:** Secreted by the chief cells of the parathyroid gland
 - **Calcitonin:** Secreted by the parafollicular cells of thyroid gland
 - **Vitamin D:** Acts like a third hormone in this regulatory process

The diagram illustrates the homeostatic regulation of blood calcium levels. A central box indicates the 'Homeostatic: Blood Ca²⁺ level (about 10 mg/100 mL)'. When the level falls (stimulus), the parathyroid gland releases PTH, which stimulates calcium release from bones and increases calcium uptake in the kidneys. Active vitamin D also stimulates calcium uptake in the kidneys and increases uptake in the intestines. When the level rises (stimulus), the thyroid gland releases calcitonin, which stimulates calcium deposition in bones and reduces calcium uptake in the kidneys.

And then we have the calcium ions here the normal calcium ions is about 9 to 10 or 11 milligrams per 100 ml and the blood calcium is usually as in a free state or it might be in a conjugated with hydrogen carbonate and citrates. And the blood calcium level is actually maintained by most important hormones which was already said that is the parathyroid hormone and the calcitonin.

There are other hormones as well which we will be quickly reading through in addition to vitamin D.

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Phosphate


- Although Ca²⁺ and P_i are both integral parts of bone mineral, genetic experiments in mice suggest that circulating P_i may have a more prominent role in the regulation of bone mineralization.

The diagram shows the chemical structure of a phosphate ion (PO₄³⁻). It consists of a central phosphorus atom (P) bonded to four oxygen atoms (O). One oxygen is double-bonded to the phosphorus, and the other three are single-bonded, each with a negative charge. A legend identifies the colors: yellow for Phosphate and red for Oxygen.


And the most important inorganic ion next to calcium is your phosphate and these are also very important and play a very dominant role in forming the mineralized inorganic component of the hard tissues.

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Parathyroid Hormone



<ul style="list-style-type: none">• The main function of parathyroid hormone (PTH) is to increase the blood calcium level.• The action of PTH is both by its direct effect on bone and kidney and by its indirect effect on intestine through vitamin D.• The secretion of PTH varies inversely with the level of calcium in blood. Parathyroid hormone acts in the following ways:<ul style="list-style-type: none">• Effect of PTH on kidney<ul style="list-style-type: none">• Increases the reabsorption of calcium• Increases phosphate excretion• Increases the conversion of 25-hydroxy-cholecalciferol to its active form <i>1,25-dihydroxycholecalciferol</i> (calcitriol) which enhances calcium absorption in the intestine	<ul style="list-style-type: none">• Effect of PTH on bone<ul style="list-style-type: none">• Increases osteoclastic activity on bone, thereby mobilizing calcium from bone to plasma• Decreases osteoblastic activity and new bone formation, thereby decreasing utilization of blood calcium• Effect of PTH on intestine<ul style="list-style-type: none">• Increases the absorption of calcium and phosphorus by indirectly increasing the renal production of <i>1,25-dihydroxycholecalciferol</i> (calcitriol)
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The next important part of this promoters of your mineralization is that now we are going to look into the hormonal part. So, parathyroid hormone is actually secreted by the parathyroid gland and these are very important hormones which are acting through the kidney on the bone and on the intestine to maintain adequate levels of calcium in the blood. So, these actually are very important regulators of your mineralization mechanism.

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Calcitonin

The modes of action of calcitonin are as follows:

- When the blood calcium level increases, calcitonin reduces the number of active osteoclasts and inhibits bone resorption, thereby reducing the amount of calcium mobilized to blood.
- It prevents the distal tubular reabsorption of calcium, thereby increasing the excretion of calcium and reducing the blood calcium level.

Calcitriol

- Calcitriol is responsible for all the effects of vitamin D on calcium metabolism. Calcitriol increases the blood calcium level by its effect on the intestine, kidneys and bone. The functions of calcitriol are as follows:
- Calcitriol increases the formation of calcium binding proteins, which in turn cause increased absorption of calcium from the intestine and also enhance calcium transport.
- Calcitriol increases osteoclastic activity and increases mobilisation of calcium from bone to blood.
- Calcitriol increases renal reabsorption of calcium and decreases phosphate reabsorption.


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And then the next two important hormones are your calcitonin and calcitriol. So, what happens with calcitonin is that the blood calcium level increases, if it increases calcitonin reduces the number of osteoclast and inhibits bone resorption. So, the main activity of calcitonin is that it actually reduces the bone resorption, whereas calcitriol is responsible for all the effects of vitamin D and calcium metabolism and increases the formation of calcium binding proteins.


So, calcitriol increases osteoclastic activity and increases mobilization of calcium from blood into the bone.

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Vitamin D



- The most active metabolite of vitamin D is calcitriol, which is formed in the kidney and is considered a hormone.
- The active form of vitamin D is formed from vitamin D₂ or ergocalciferol and vitamin D₃ or cholecalciferol. Vitamin D₃ is made in the skin when 7-dehydrocholesterol reacts with ultraviolet light.
- Ergosterol is derived from diet. Cholecalciferol is hydroxylated in the liver to form 25-hydroxycholecalciferol. This reaction is catalysed by the microsomal enzyme present in the liver, hepatic 25-hydroxylase.
- It is further transported to the proximal tubules of the kidneys, where it is hydroxylated to form calcitriol (1,25-dihydroxycholecalciferol).
- This product is the active form of vitamin D, which mediates most of the physiologic actions of the vitamin.



And further we have the vitamin D the most active part of vitamin D is your calcitriol and which is formed in the kidney and it is considered as a hormone. So, this vitamin D again is a very very important vital or vital agent in mineralization and we know that just getting exposed to sun itself would give you an ample amount of vitamin D to your body. So, it is a very very important body to stay very strong because this vitamin D is what actually helps in strengthening your mineralization.

So, the most active metabolite of vitamin D is calcitriol and this calcitriol is actually very important part and mediates the physiological action of the vitamin.

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Other Hormones

- **Growth hormone:** It increases absorption of calcium from intestine and also enhances protein synthesis in bone.
- **Insulin:** It is an anabolic hormone that favours bone formation.
- **Sex hormones:** They increase calcium absorption, decrease calcium excretion and enhance bone mineralisation. Oestrogen has direct effect in reducing bone resorption.
- **Prolactin:** It increases calcitriol production, thereby increasing calcium absorption during lactating period.
- **Thyroid hormone:** Increase in levels of thyroid hormone is accompanied by osteoporosis and hypercalcaemia.



Other hormones in addition to what we saw till now that is your parathyroid hormone and then we saw calcitonin, calcitriol, vitamin D additionally we have the growth hormone, insulin, the sex hormone especially the oestrogen, prolactin and thyroid hormone which are very important and have a significant role on the mineralization of the hard tissues.

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Proteins of the SIBLING family

- Proteins of the SIBLING (small, integrin-binding ligand N-linked glycoprotein) family
- sialoprotein [BSP], dentin sialoprotein, dentin matrix protein-1 [DMP-1], and matrix extracellular glycoprotein [MEPE])
- Play key roles in mineralization
- Genes coding for members of the SIBLING protein family are similarly organized and are all located on human chromosome 4q21-23

