CALCIUM

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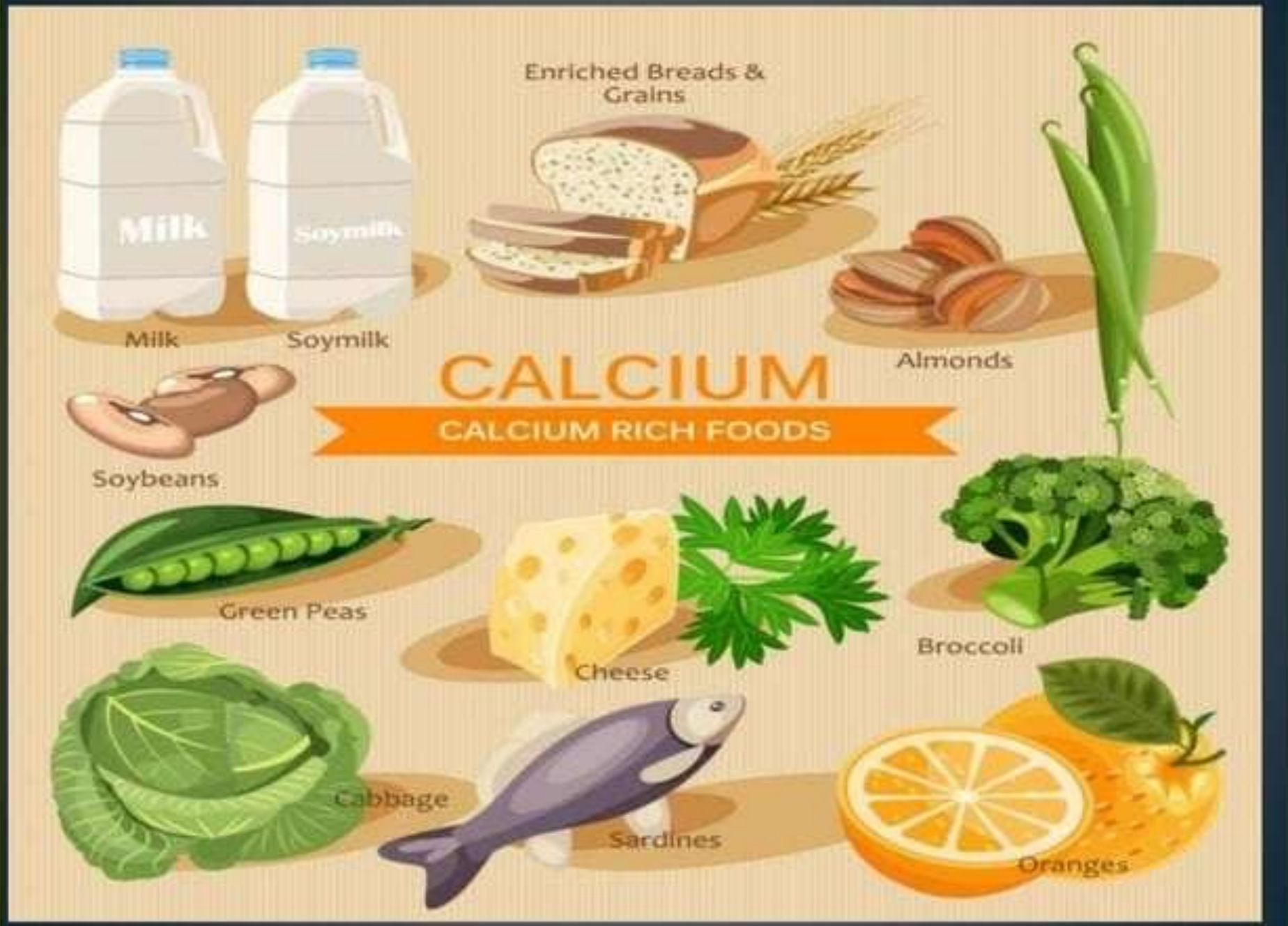
Content

- Introduction to calcium
- Sources
- Dietary requirement
- Calcium absorption
- Biochemical function
- Calcium in blood
- Calcium estimation
- Factors regulating calcium level in blood
- Disease states

Introduction

- Most abundant among minerals in the body.
- Total content in adult man=about 1-1.5kg.
- 99% of calcium is present in bone and teeth.
- 1% calcium found outside the skeletal muscles, perform a wide variety of function.


Milk
Soymilk
Enriched Breads & Grains
Almonds
CALCIUM
CALCIUM RICH FOODS
Soybeans
Green Peas
Cheese
Broccoli
Cabbage
Sardines
Oranges

CALCIUM CONTENT OF COMMON FOODS

Milk
300 mg per 1 cup

Salmon (with bones)
241 mg per 4 ounces

Sardines (with bones)
213 mg per 2 ounces

Bok choy, cooked
190 mg per 1/2 cup

Collard greens, cooked
179 mg per 1/2 cup

Spinach, cooked
145 mg per 1/2 cup

Kale, raw
137 mg per 1 cup

Figs
135 mg per 5 figs

Turnip greens, cooked
104 mg per 1/2 cup

Almonds
93 mg per 1/2 cup

Orange
52 mg per medium orange

Sesame seeds
51 mg per 1 tablespoon

Arugula, raw
32 mg per 1 cup

Mushrooms
18 mg per 2 ounces

www.thepaleomom.com

sources

- Best sources:milk and milk products.
  - Calcium content of cow's milk is about 100mg/100ml.
  - Human milk is 30mg/dl

- Good sources:beans, leafy vegetables,fish, cabbage ,egg etc.
  - Cereals contain small amount of calcium.

Dietary requirements

- Adult men and women = 800mg/day
- During pregnancy,lactation and post-menopause= 1.5gm/day
- Children(1-18yrs)= 0.8-1.2g/day
- Infants(<1yrs)= 300-500mg/day

Calcium absorption

- Calcium absorption mainly occurs in duodenum by an energy dependent active process.

- Factors promoting calcium absorption:

1. Vitamin D (through its active form calcitriol) induce the synthesis of calcium binding protein in the intestinal epithelial cells and promote calcium absorption.

2. Parathyroid hormone enhance calcium transport from the intestinal cells.

3. Acidity is more favourable for calcium absorption.

4. Lactose promote calcium uptake by intestinal cells.

5. The amino acid lysine and arginine faciliate calcium absorption.

Factors inhibiting calcium absorption.

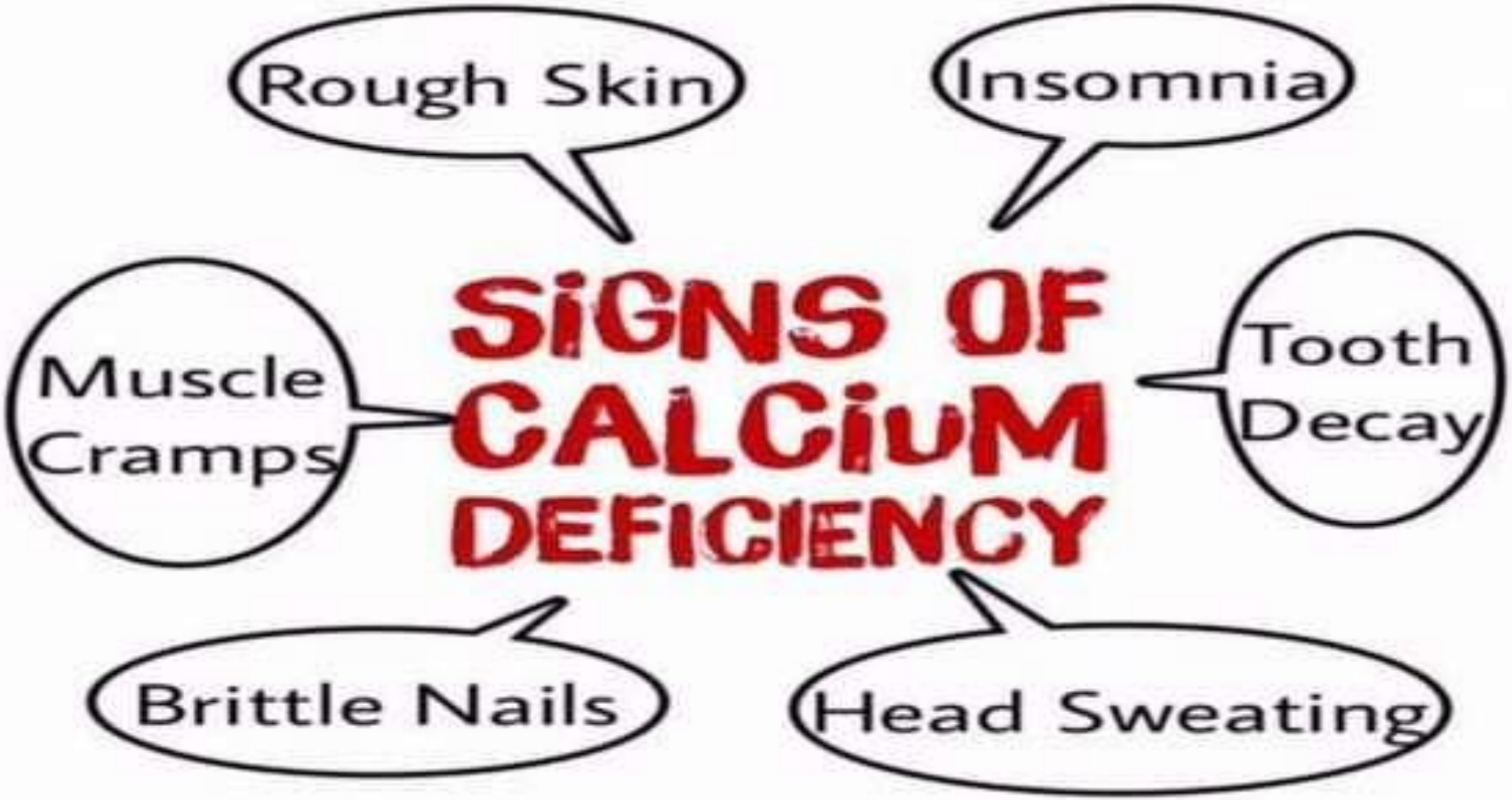
1. Phylates and oxalate form insoluble salts that interfere ca absorption.

2. High content of dietary phosphate forms insoluble calcium phosphate and prevents ca uptake.the dietary ratio of ca and P-1:2 and 2:1 is ideal for optimum ca absorption by intestinal cells.

3. High content of dietary content interfere with ca absorption.

4. The free fatty acids react with ca to form insoluble ca soaps. Paticularly observed when the fat absorption is impaired.

5. Alkaline condition is unfavourable for ca absorption.


Rough Skin
Insomnia
SIGNS OF CALCIUM DEFICIENCY
Muscle Cramps
Tooth Decay
Brittle Nails
Head Sweating
www.TheOrangePetals.com

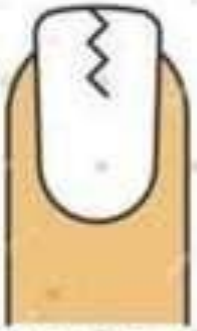
Calcium Deficiency Symptoms:

Fatigue

Memory Loss

Depression

Tooth Decay



Brittle Nails

Biochemical function

1. **Development of bone and teeth:**

- Bulk quantity of calcium is required for bone and teeth formation.

- Bones act as a reservoir for calcium in the body.

- Osteoblast induce bone deposition and osteoclast produce demineralisation.

2. **Nerve transmission:**

- Ca is necessary for nerve impulse transmission.

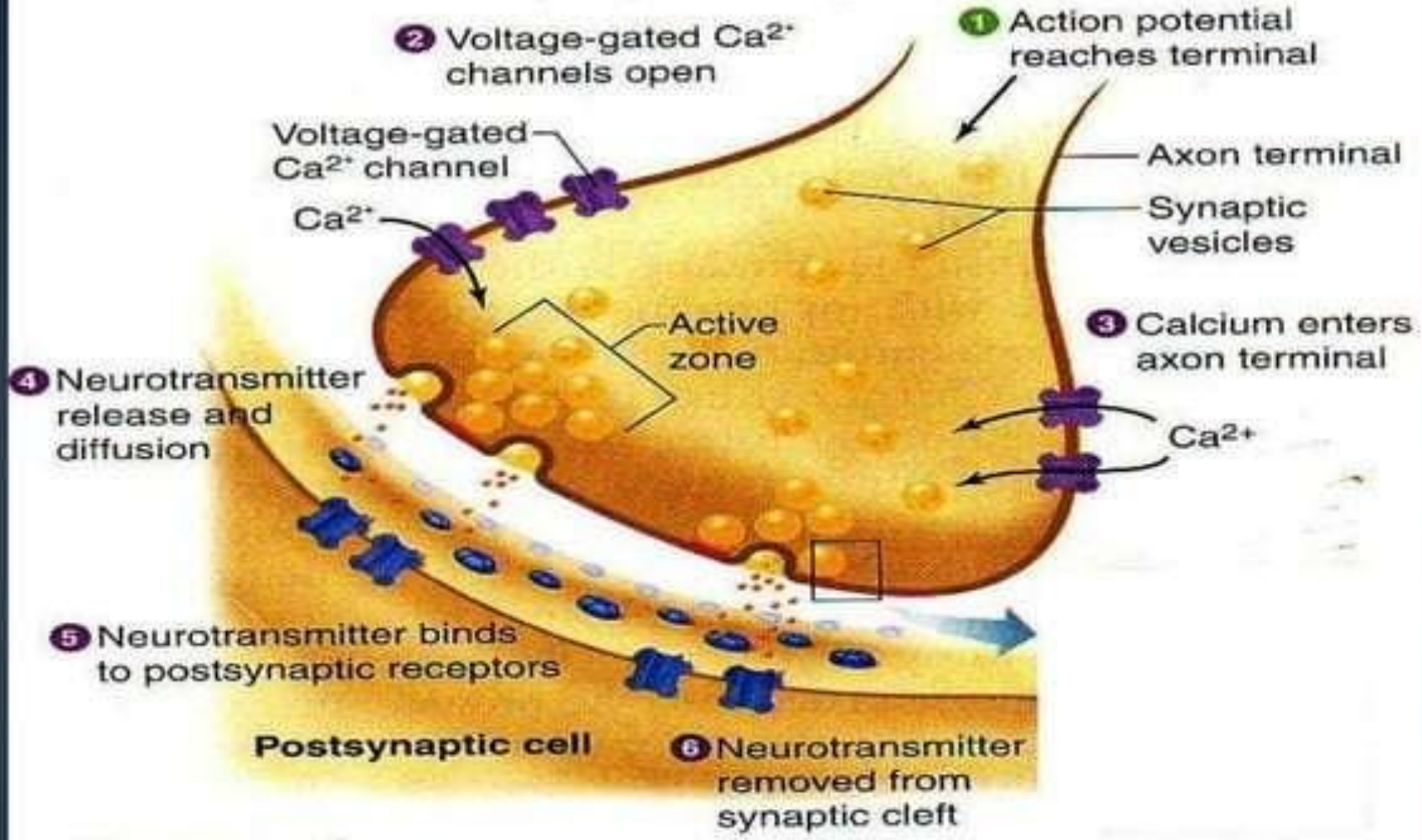


FIGURE 6–27

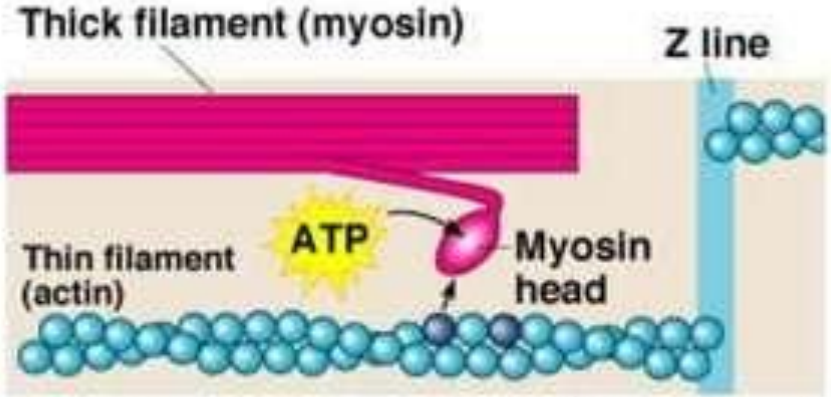
Neurotransmitter storage and release at the synapse and binding to the postsynaptic receptor. Voltage-gated calcium channels in the terminal open in response to an action potential, triggering release of neurotransmitter.

3. **Muscle contraction and excitation:**

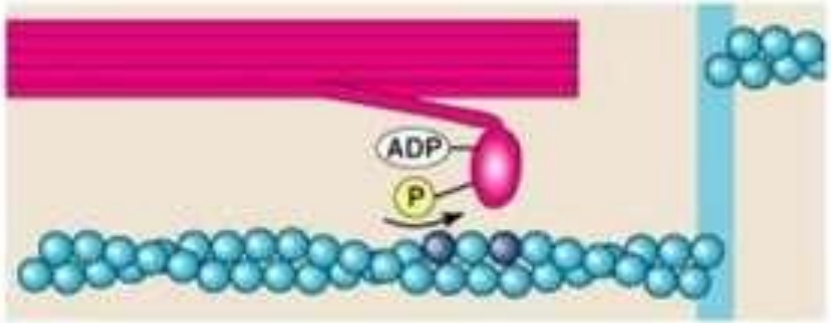
- Ca mediates excitation and contraction of muscle fibers.

- Ca also activates ATPase, increase reaction of actin and myosin and faciliates excitation- contraction coupling.

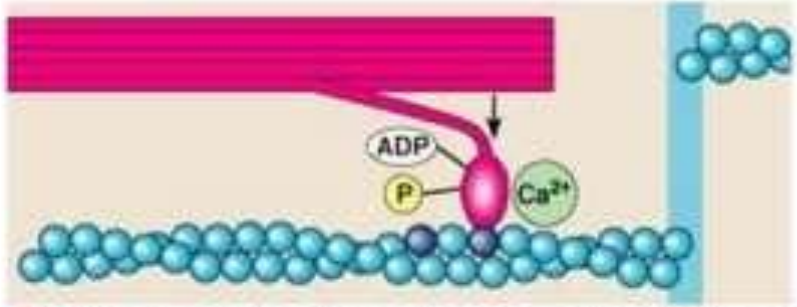
- The inactive myosin kinase is made active by calcium ions.



1 ATP binds to a myosin head, which is released from an actin filament.

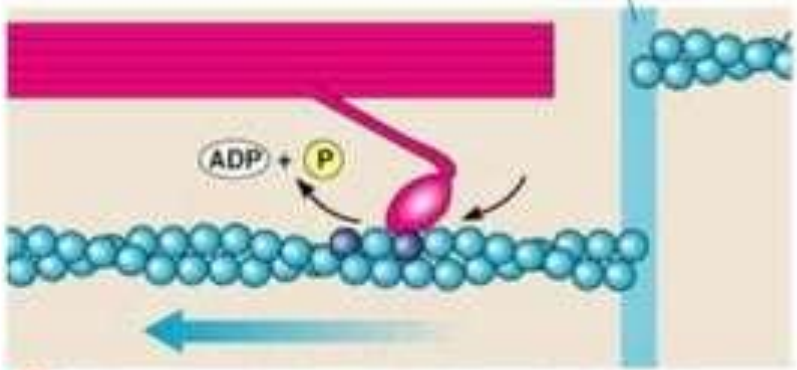


2 Hydrolysis of ATP cocks the myosin head.



3 The myosin head attaches to an actin binding site, with the help of calcium.

New position of Z line



4 The power stroke slides the actin (thin) filament.

4. **Calcium-calmodulin complex:**

- Calmodulin(mol.wt. 170000)is a ca binding regulatory protein.

- Ca –calmodulin complex activates certain enzymes e.g.adenylate cyclase, ca dependent protein kinase.

- It regulates microfilament mediated processes such as degranulation of secretary vesicles, endocytosis, cell motility etc.

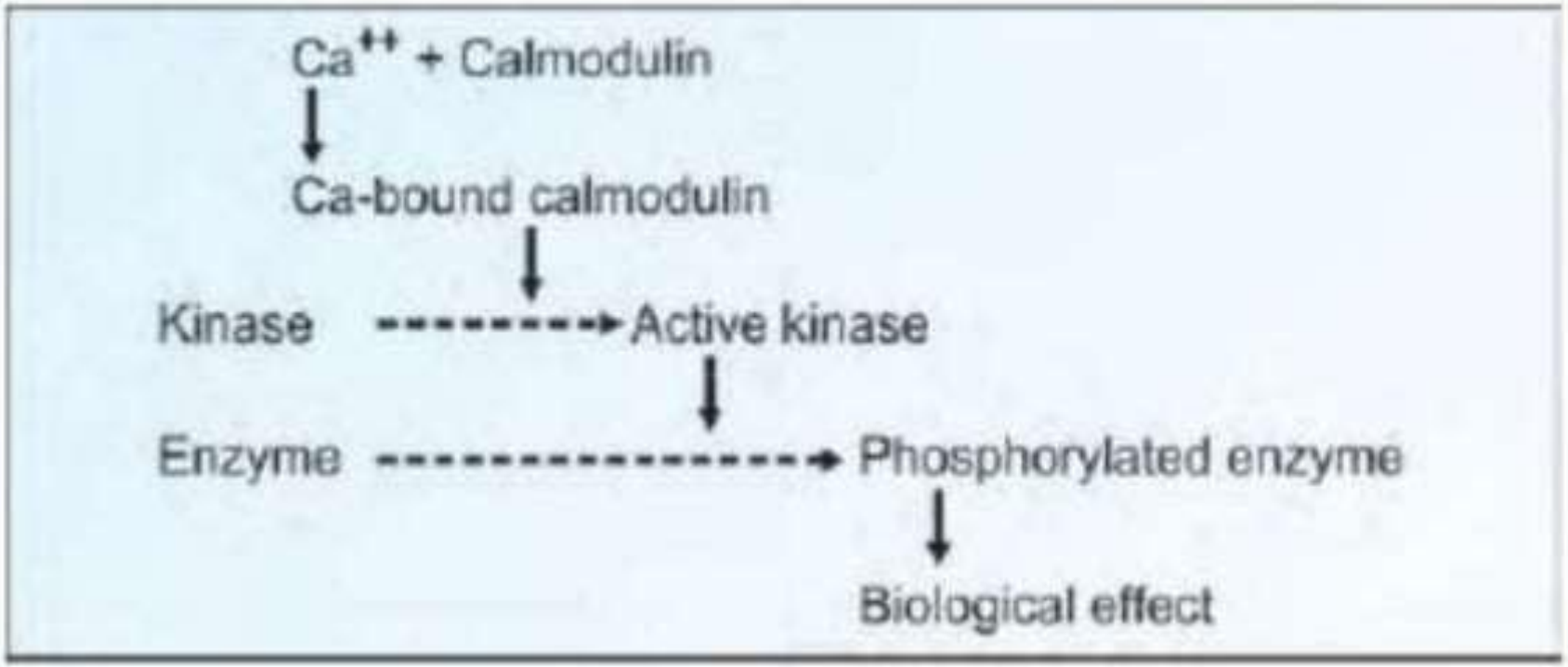
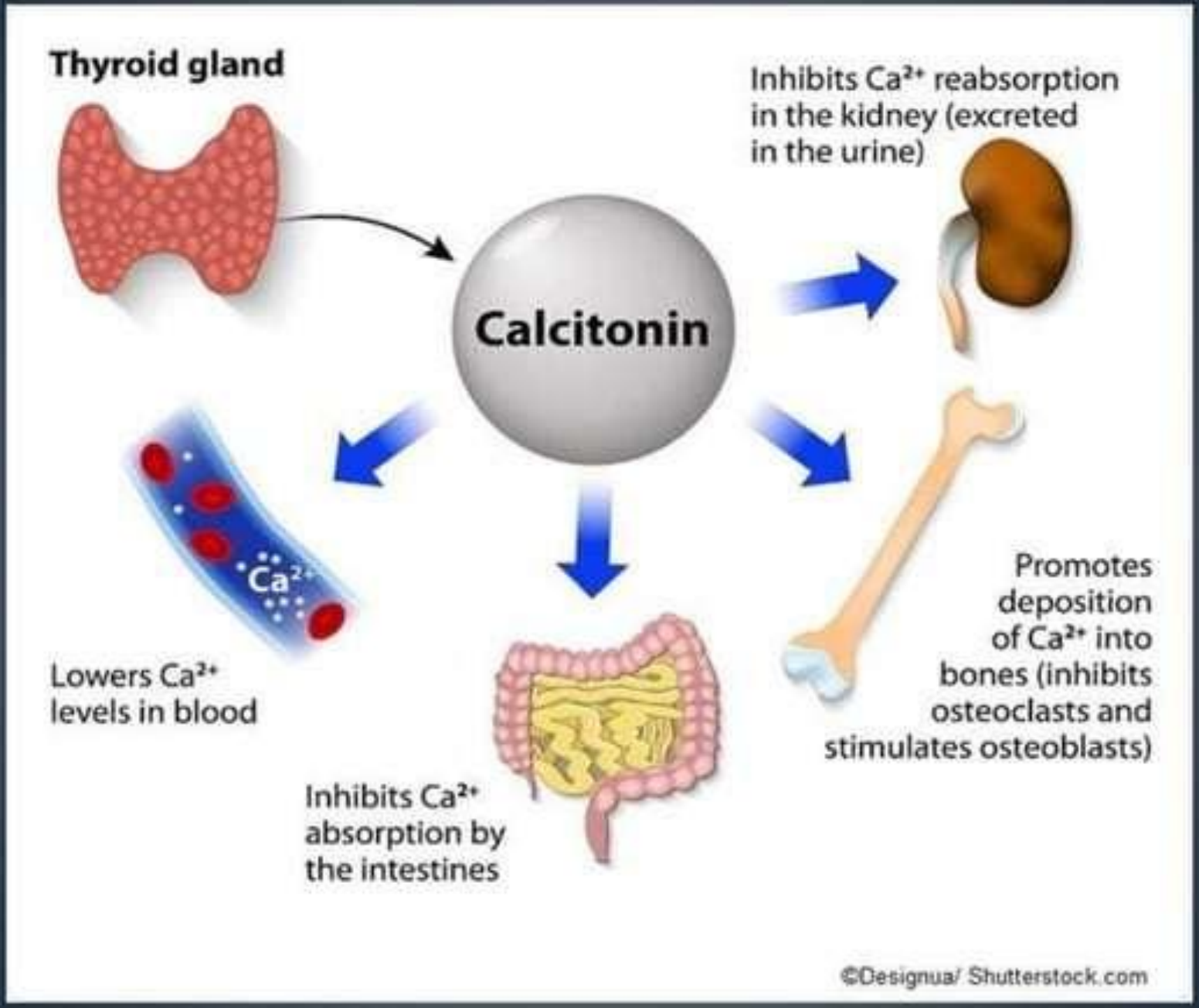


Fig. 39.3: Mechanism of action of calmodulin

5. **Secretion of hormones:**

- Ca mediate secretion of insulin, calcitonin, parathyroid hormone, vasopressin etc. from the cells.


Thyroid gland
Inhibits Ca^{2+} reabsorption in the kidney (excreted in the urine)
Calcitonin
Ca^{2+}
Lowers Ca^{2+} levels in blood
Inhibits Ca^{2+} absorption by the intestines
Promotes deposition of Ca^{2+} into bones (inhibits osteoclasts and stimulates osteoblasts)
©Designua/ Shutterstock.com

6. **Activation of enzymes:**

- Ca is needed for the direct activation of enzymes such as lipase ATPase and succinate dehydrogenase.

7. **Membrane integrity and permeability**

- Ca influence the membrane structure and transport of water and several ions across it.

8. **vascular permeability:**

- Ca decrease the passage of serum through capillaries.

- Thus, ca is clinically used to reduce allergic exudates.

9. Ca as intracellular messenger:

- Certain hormones exert their action through the mediation of ca instead of CAMP.

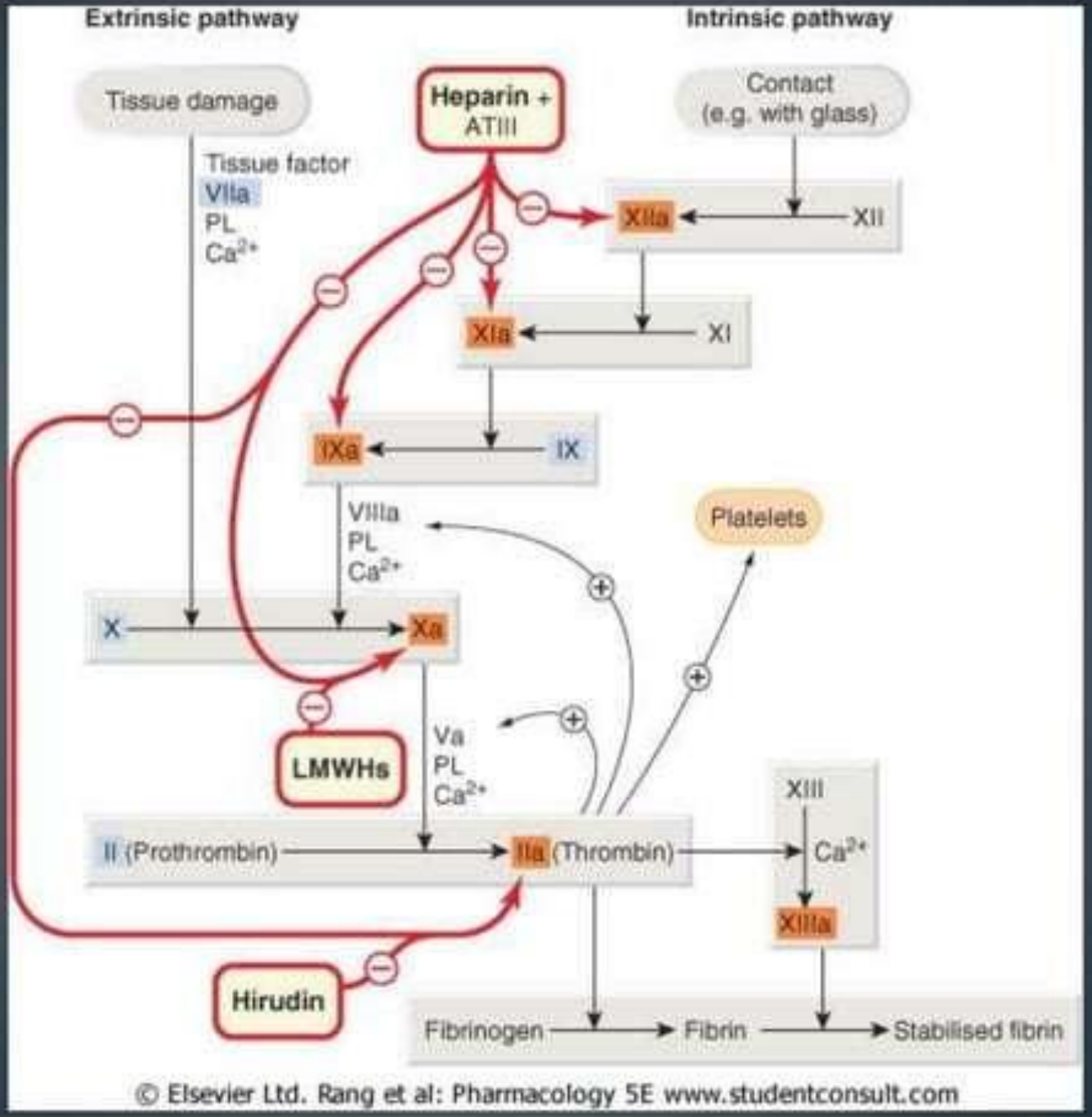
- It is regarded as 2nd messenger for such hormonal action.e.g epinephrine in liver glycogenolysis.

- Ca serves as 3rd messenger for some hormone. Eg antidiuretic hormone acts through CAMP, and then ca.

10. Blood coagulation:

- Ca k/a factor IV in blood coagulation cascade.

- Prothrombin contains gamma-carboxy glutamate residues which are chelated by ca during the thrombin formation.


Extrinsic pathway
Intrinsic pathway
Tissue damage
Heparin + ATIII
Contact (e.g. with glass)
Tissue factor
VIIa
PL
Ca2+
XIIa
XII
XIa
XI
IXa
IX
VIIIa
PL
Ca2+
Platelets
X
Xa
LMWHs
Va
PL
Ca2+
XIII
II (Prothrombin)
IIa (Thrombin)
Ca2+
XIIIa
Hirudin
Fibrinogen
Fibrin
Stabilised fibrin
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11. Myocardium:

- In myocardium ca2+ prolongs systole.
- In hypercalcemia cardiac arrest is seen in systole.
- Therefore, when ca2+ is administered intravenously, it should be given very slowly.

12. Contact inhibition:

- Ca2+ is believed to be involved in cell to cell contact and adhesion of cells in a tissue.
- The cell-cell communication may also require ca2+.

Blood level of calcium

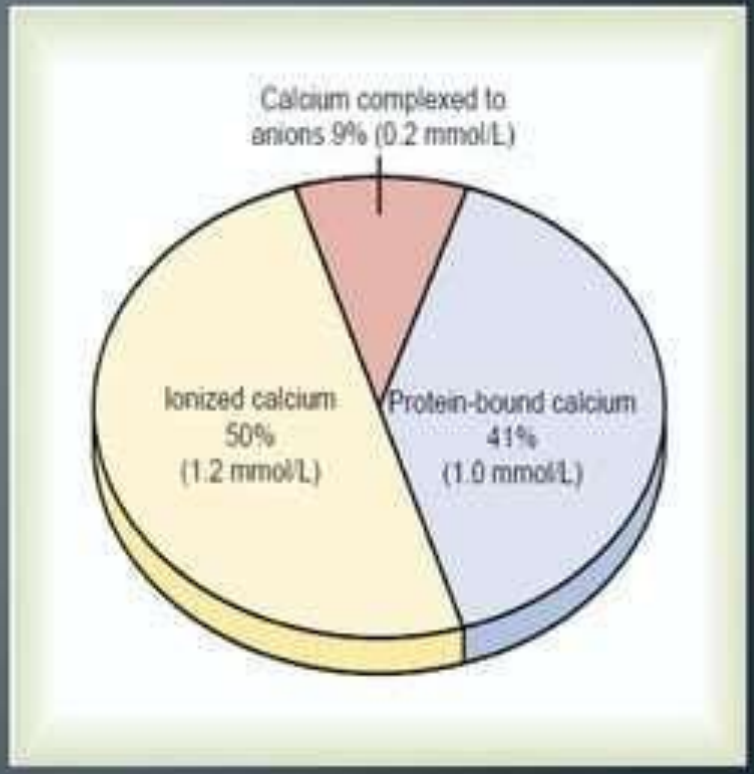
- Normal calcium level in blood is **9-11**mg/dl.

- Three physiochemical states:

✓ free/ ionised- 50%

✓ Protein bound- 41%

✓ Complexed - 9%



- Free form is the biologically active form.
- Proteins-mostly with albumins and to some extent, with globulins.
- Complexed – with small diffusible organic and inorganic anions eg. HCO_3^-, $H_2PO_4^-$, citrate, lactate.

Measurement of total calcium methods

- Chelation with o-Cresolphthalein complexone (colorimetric)
- Atomic Absorption Spectrophotometry(AAS)
- Flame photometer

Chelation with o-cresolphthalein

- Ca is estimated by treating serum with orthocresolphthalein, which produce a violet colour with **ca** in alkaline medium.

- Ca also can be estimated by ion selective electrode method.

Sulkowitch test,is a bedside screening test for urinary ca.

✓The reagent contains oxalic acid, acetic acid, ammonium oxalate .

✓Equal quantity of reagent is added to urine.

- ✓If no precipitate, then blood ca level is 7.5mg/dl (hypocalcemia).
- ✓Fine cloudy precipitate, blood ca level is at normal level 9-11mg/dl.
- ✓Heavy precipitate indicates hypercalcemia (and result hypercalciuria).

Factors regulating blood calcium level

- Major factors that help to maintain blood ca level in normal range (9-11mg/dl) includes :

1. **Vitamin D**

- Calcitriol the active form of vit.D induces the synthesis of specific ca binding protein in the intestinal cells.

- This protein increases the intestinal absorption of ca as well as phosphate.

- Thus blood ca level is increased by calcitriol.
- Calcitriol stimulates ca uptake by osteoblast of bone and promote calcification or mineralization (deposition of ca phosphate) and remodelling.

2. **Calcitonin :**

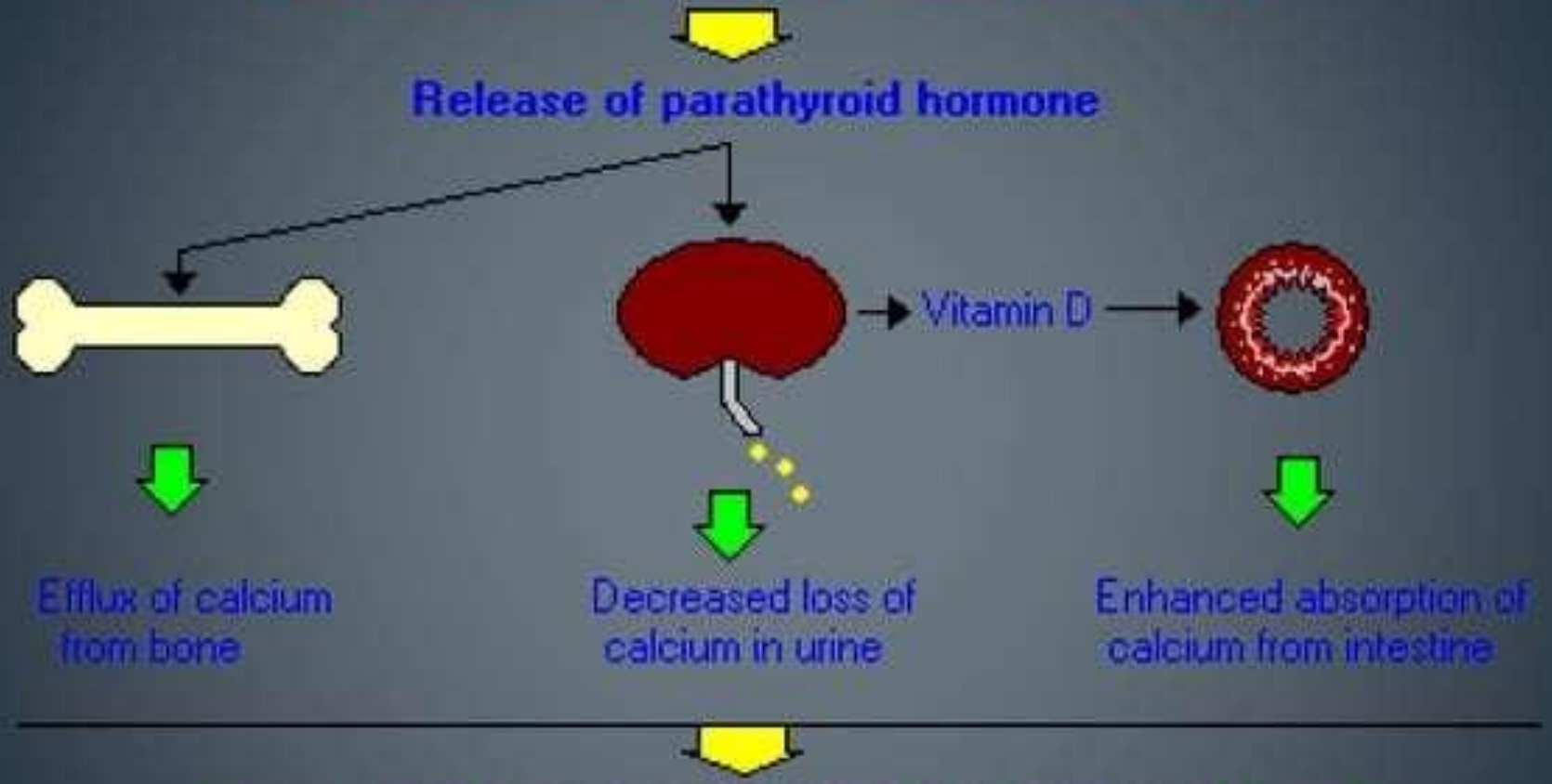
- A peptide containing 32 amino acids.
- Secreted by parafollicular cells of thyroid gland.
- Its action on ca metabolism is antagonist to that of PTH.

- Thus calcitonin promotes calcification by increasing the activity of osteoblast.
- It decreases bone reabsorption and increases the excretion of ca in urine,ultimately decreasing blood ca level.

3. **Parathyroid hormone**:(mol.wt=95000)

- PTH is secreted by 2 pairs of parathyroid glands that are closely associated with thyriod glands.

- Storage of PTH is only for about 1hrs.
- Release of hormone is mediated by cyclic AMP.
- The normal PTH level in serum is 10-60ng/L.
- In primary hyperthyroidism ,increased to 100ng/l.


Low concentration of calcium in blood
Release of parathyroid hormone
Vitamin D
Efflux of calcium from bone
Decreased loss of calcium in urine
Enhanced absorption of calcium from intestine
Increased concentration of calcium in blood

Mechanism of action of PTH

- PTH binds to the membrane receptor protein on the target cells and activate adenylate cyclase to liberate CAMP.
- This increases intracellular ca that promotes the phosphorylation of protein(by kinases)which finally bring about the biological action.
- PTH has 3 dependent tissues-bone, kidney and intestine-to exert its action.
- PTH prime function is to elevate serum ca level.

Action on bone

:

- PTH causes decalcification or demineralization of bone, a process carried out by osteoclast.
- This is brought about by increased activity of enzyme pyrophosphatase and collagenase; stimulated by PTH.
- This enzyme result in bone resorption.
- Demineralization ultimately result in increase blood ca level.

Action on kidney:

- PTH increase ca reabsoption by kidney tubules.
- It's the most rapid action of PTH to increase blood ca level.
- PTH promote the production of calcitriol(1,25DHCC) in the kidney by stimulating 1-hydroxylation of 25-hydroxycholecalciferol.

Action on the intestine:

- Action of PTH on intestine is indirect.

- It increases intestinal absorption of ca by promoting the synthesis of calcitriol.

others factors regulating blood ca level

4. **Phosphorus** :Its increase levels, lowers ca levels.

5. **Serum proteins**:Abt. 0.8mg/dl of ca is reduced with each g/dl lowering of albumin.

6. **Alkalosis and acidosis**: Acidosis favours ionization and vice versa.

7. **Children, pregnancy**:In children ca level at upper limit(abt.50); in pregnancy and lactation at lower limit.

- Excretion of calcium from body:

1. Sweat loss: 0.3 mmol/24 hrs

❖Increased in extreme environmental conditions

2. Urinary excretion: 6mmol/ 24 hrs

❖Increased in hypercalcemia, phosphate deprivation, acidosis

❖Decreased by PTH, some diuretics, vitamin D

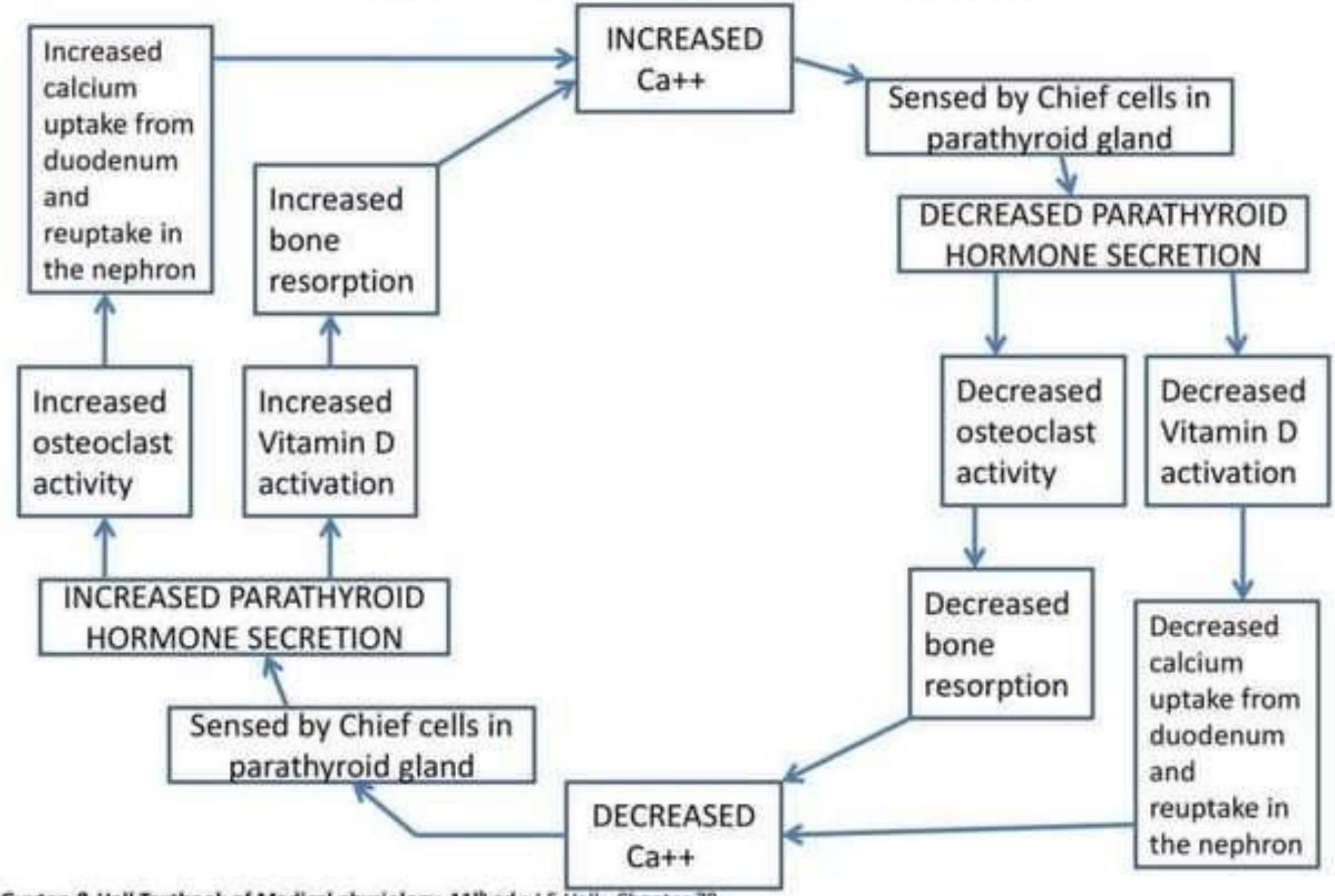
3. **Fecal loss:**

- 19 mmol/24 hrs
- Increased in vitamin D deficiency

Importance of ca:phosphorus ratio

- plasma ca:p ratio important for calcification of bone.
- Product of ca & P is around 50(in child),around 40(in adult)and is less than 30 in rickets.

Calcium homeostasis



Guyton & Hall Textbook of Medical physiology, 11th ed.; J.E.Hall; Chapter 79

Diseases states

1. **Hypercalcemia:**

- Elevated serum ca level (>11mg/dl)

- Associated with hyper parathyroidism, caused by increased activity of parathyroid gland.

- There is osteoporosis and X-ray shows punched out areas of bone resorption.(osteitis fibrosa cystica generalictica or von Recklinghaysen's diseases).

- Pathological fracture of bone may result.
- In urine, ca is excreted, which may cause inhibition of elimination of chloride and that may lead to hypercholerimic acidosis.
- Ca may be precipitated in urine,leading to recurrent bilateral urinary calculi.

- Ectopic calcification may be seen in renal tissue, pancreas, arterial walls and muscle tissues.

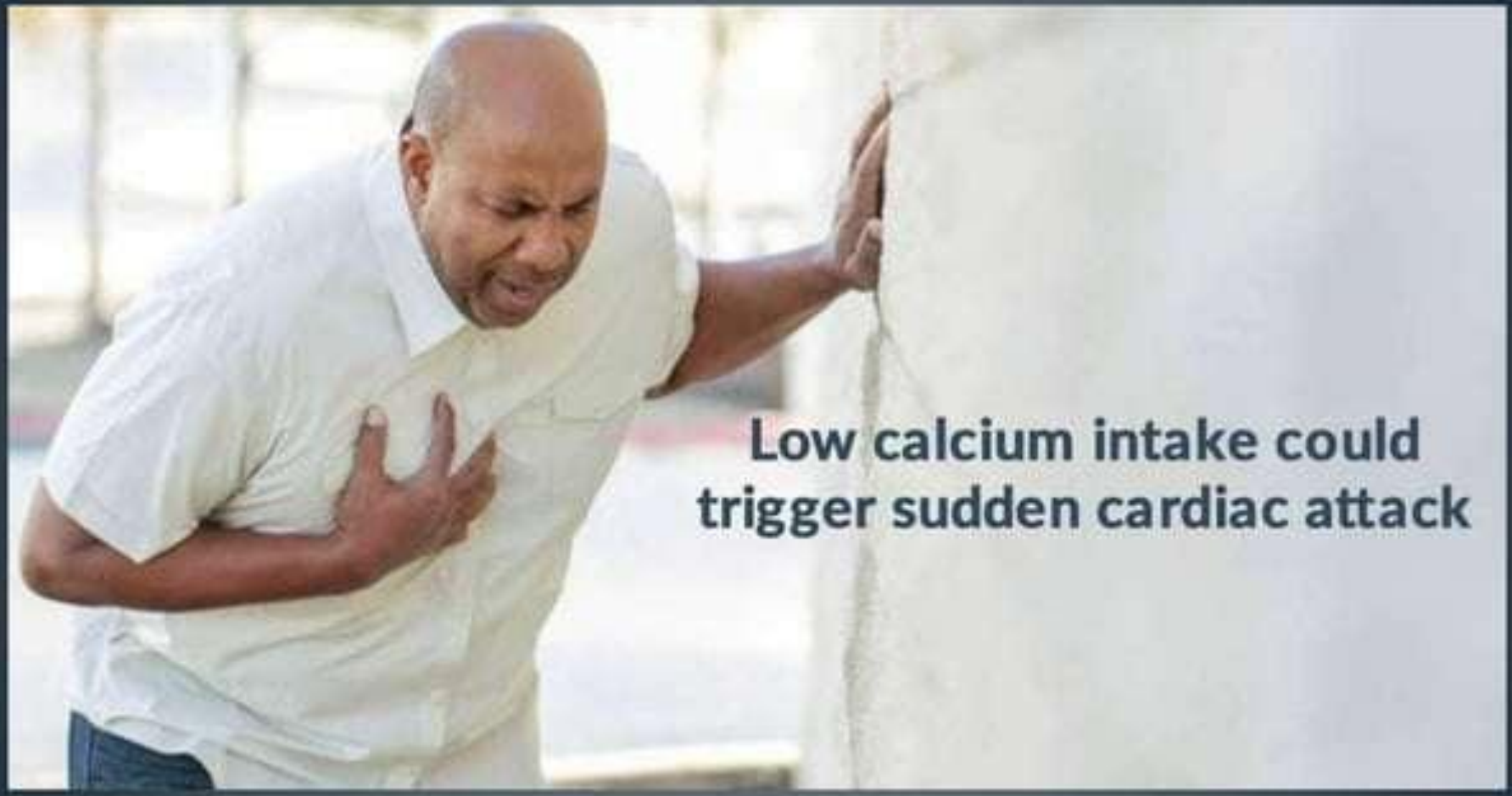
- Symptoms of hypercalcemia include:

- Lethargy, muscle weakness, loss of appetite, constipation, nausea, increased myocardial contractility and suseptibility to fracture.

- Other minor causes of hypercalcemia;
  - In multiple myeloma, paget's diseases and metastatic carcinoma of bone, there will be bone resorption and mild hypercalcemia.
  - Increased absorption of ca from intestine is seen in milk-alkali syndrome and vit.D toxicity.
  - Lithium therapy and thiazide diuretics may also causes mild hypercalcemia.

2. **Hypocalcemia**:

- Condition where ca level is < 8.8 mg/dl.
- If,ca level < 8.5 mg/dl, there will be mild tremors.
- If ,ca level <7.5 mg/dl, tetany a life threatening condition result.


Low calcium intake could
trigger sudden cardiac attack

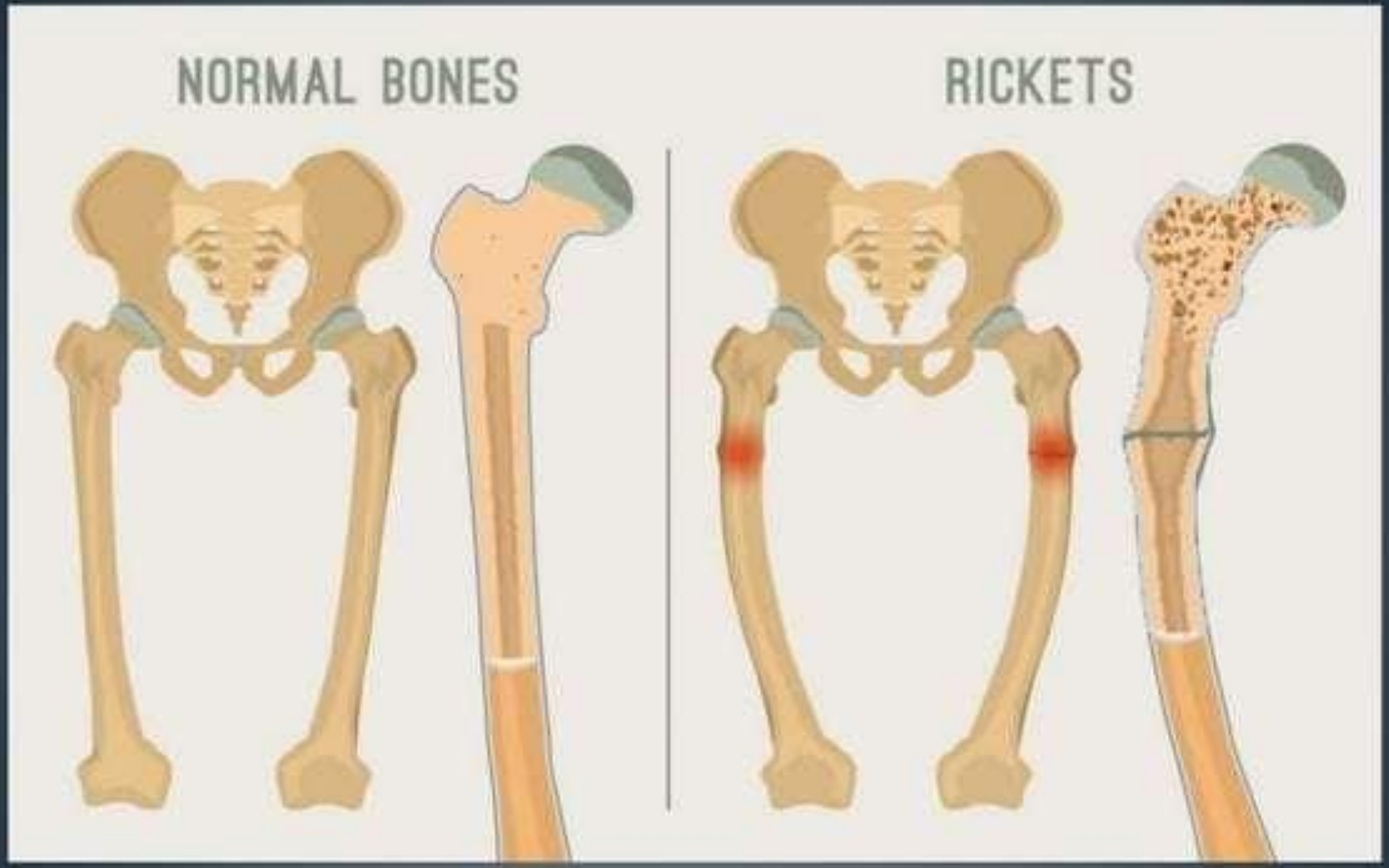
- Tetany may be due to accidental surgical removal of parathyroid glands or by autoimmune diseases.
- Main manifestation are carpopedal spasm ; laryngismus and stridulus.
- Laryngeal spasm may lead to death.

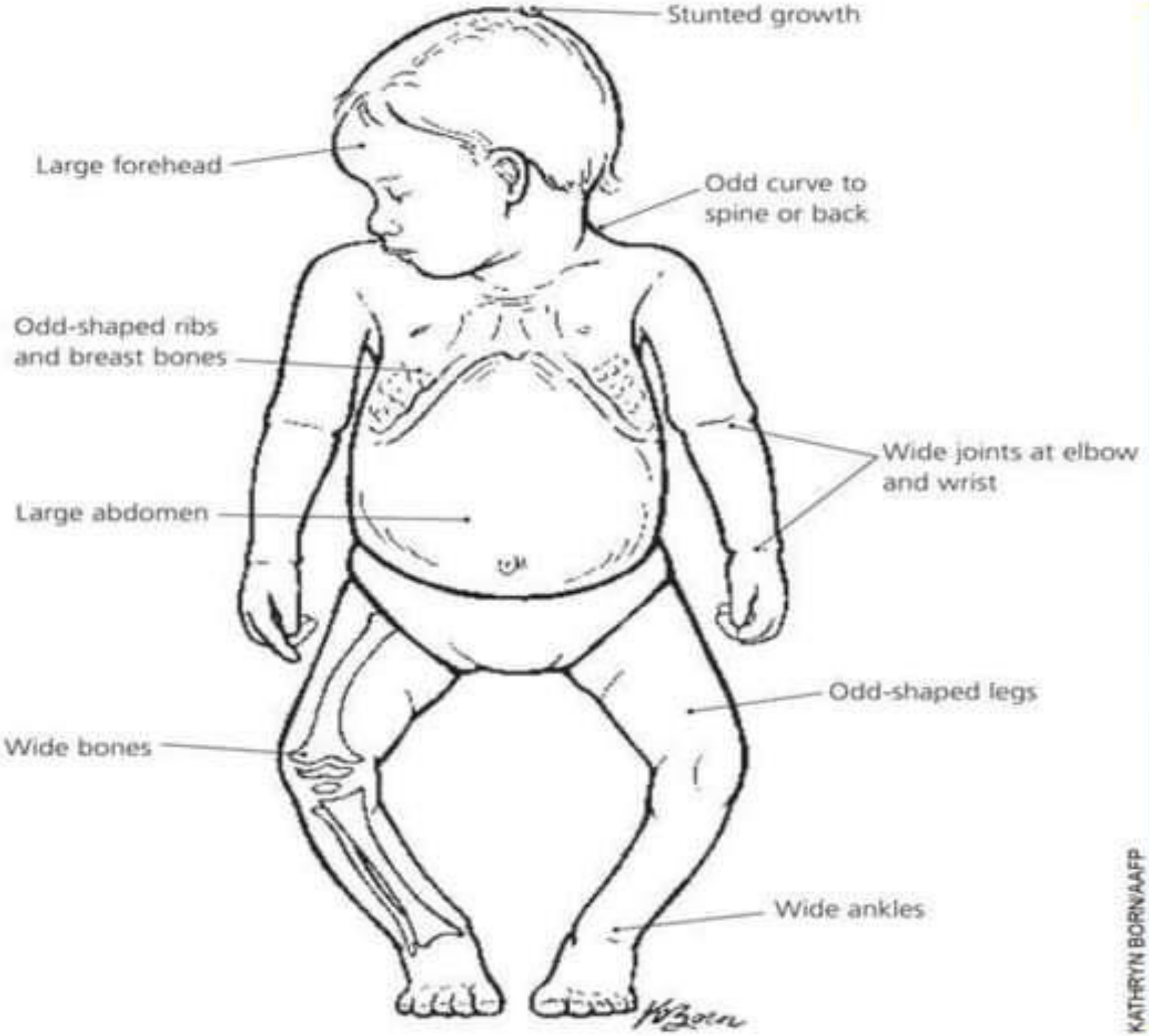
Fig. 39.6: Carpopedal spasm in tetany

- Clinical signs are chovstek's sign(tapping over 5th cranial nerve causes facial contraction) and Trousseu's sign(inflation of B.P cuff causes carpopedal spasm.)
- Increased Q-T interval in ECG.
- Urinary excretion of both ca and P is decreased.
- Treatment: Give intravenous injection of ca salts.

3. **Rickets:**

- Disorder of defective calcification of bone.
- Due to low level of vit.D in body or due to dietary deficiency of ca and P –or both.
- Characteristic feature of rickets-increased activity of alkaline phosphatase activity.


NORMAL BONES
RICKETS

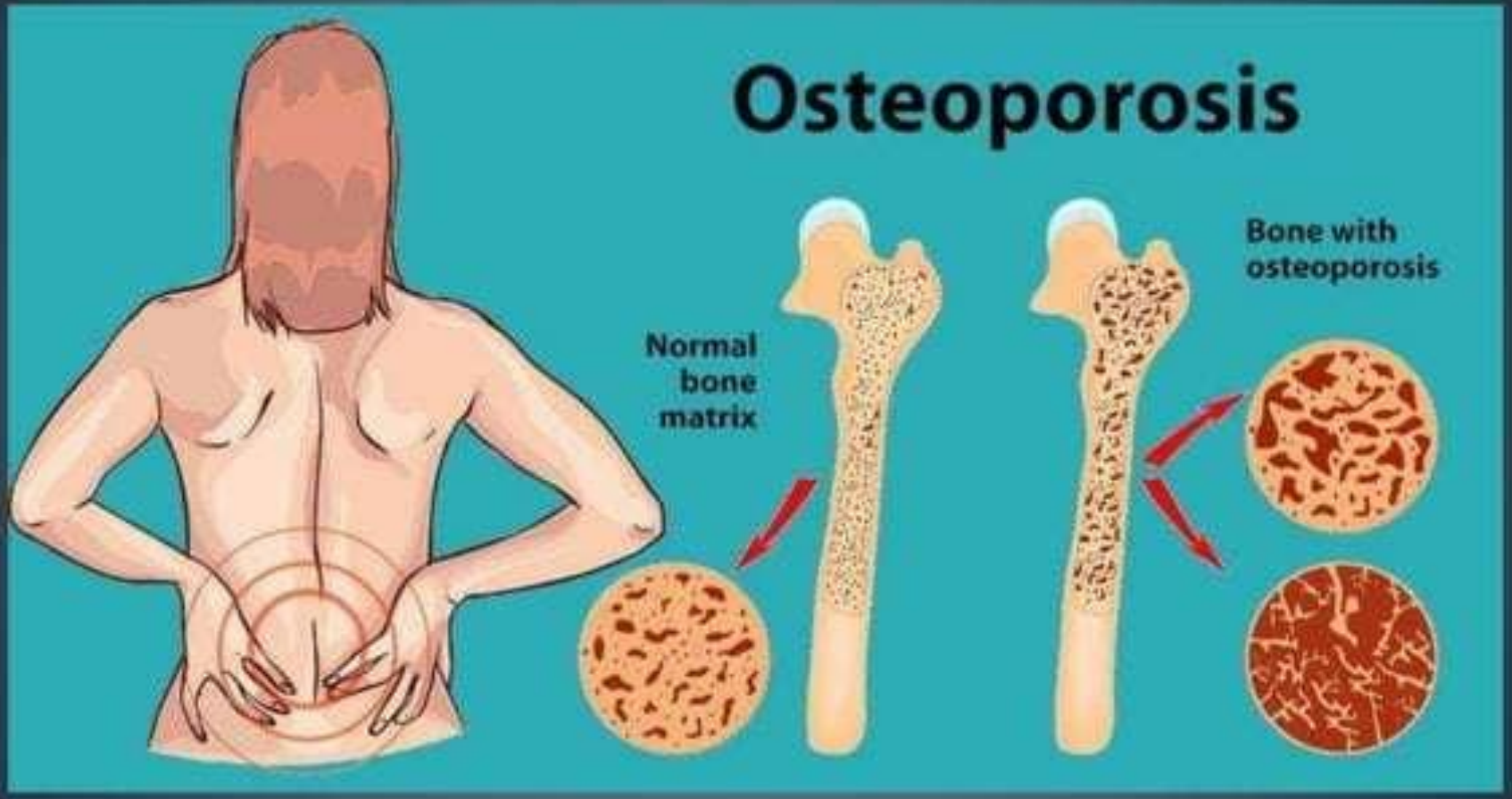

Stunted growth
Large forehead
Odd curve to spine or back
Odd-shaped ribs and breast bones
Wide joints at elbow and wrist
Large abdomen
Odd-shaped legs
Wide bones
Wide ankles
KATHRYN BORN/AAFP

- **Renal rickets**, associated with damage to renal tissue;causing impairment in the synthesis of calcitriol. (A/k vit.D resistant rickets.)

4. **osteoporosis**: Charecterized by demineralisation of bone resulting in the progressive loss of bone mass.

- Occurrence: Elderly people(over 60 yrs) of both sexes are at risk; however >post menopausal women.

- Osteoporosis result in frequent bone fracture which is the main cause of disability in elderly people.


Osteoporosis
Normal bone matrix
Bone with osteoporosis

- Etiology:

- Believed that several causative factors may contribute to it.

- The ability to produce calcitriol from vit.D is reduced with age, particularly in postmenopausal women

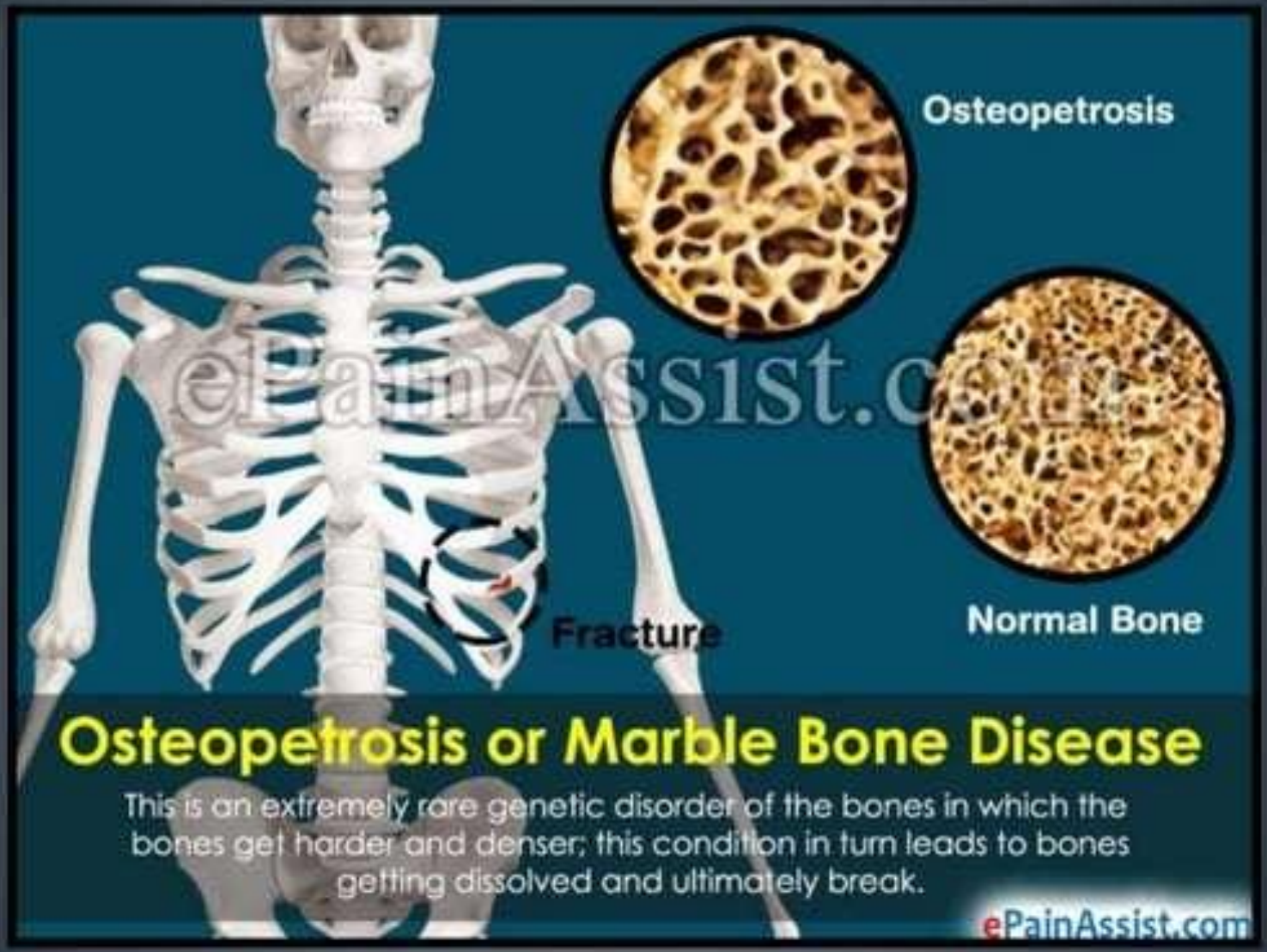
- Immobilized or sedentary individual tend to decrease bone mass while those on regular exercise tend to increase bone mass.

- Deficiency of sex hormones (in women) has been implicated in the development of osteoporosis.

- Treatment:
  - Estrogen supplementation along with ca (in combination with vit.D) to postmenopausal women reduces risk of fracture.
  - Higher dietary intake of ca (abt.1.5 g/day) is recommended for elderly people.

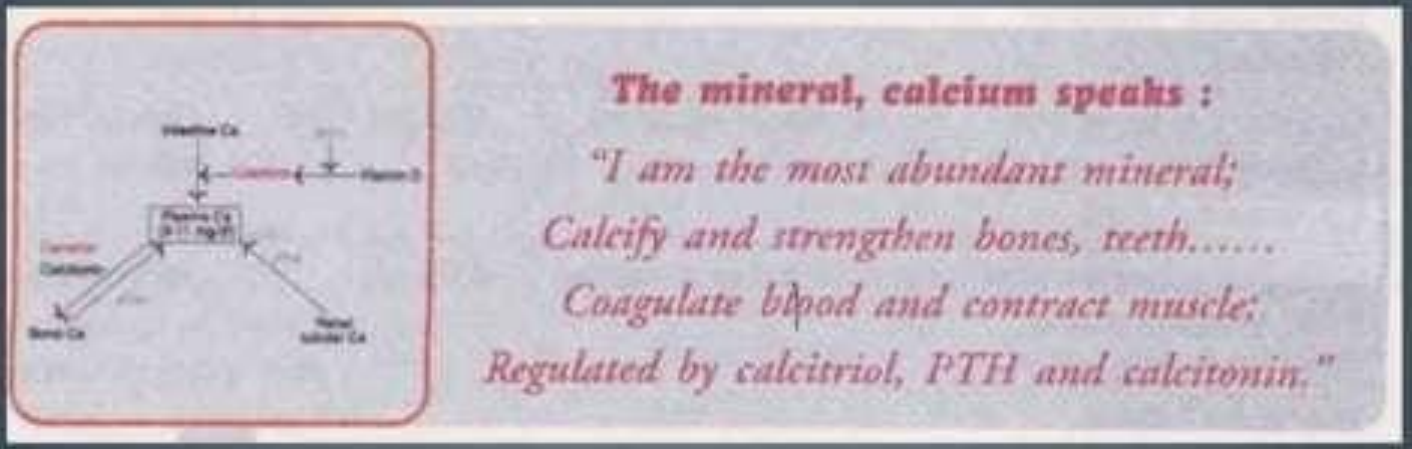
5. **Osteopetrosis**(marble bone diseases):

- Charecterized by increased bone density.
- Mainly due to inability to resorb bone.
- Disorder mainly associated with renal tubular acidosis(due to defect in the enzyme carbonic anhydrase) and cerebral calcification.


Osteopetrosis
Normal Bone
Fracture
Osteopetrosis or Marble Bone Disease
This is an extremely rare genetic disorder of the bones in which the bones get harder and denser; this condition in turn leads to bones getting dissolved and ultimately break.
ePainAssist.com

Reference:
Textbook of biochemistry (DM Vasudevan)
Biochemisty Satyanarayan
Biochemistry Harpers
Source of images:Internet..

Thank you


The mineral, calcium speaks :
"I am the most abundant mineral;
Calcify and strengthen bones, teeth.....
Coagulate blood and contract muscle;
Regulated by calcitriol, PTH and calcitonin."