MINERAL METABOLISM

- Minerals

- Are essential for normal growth & maintenance of body
- If daily requirement > 100mg - Major elements or macrominerals
- If daily requirement < 100mg - Trace elements or microminerals

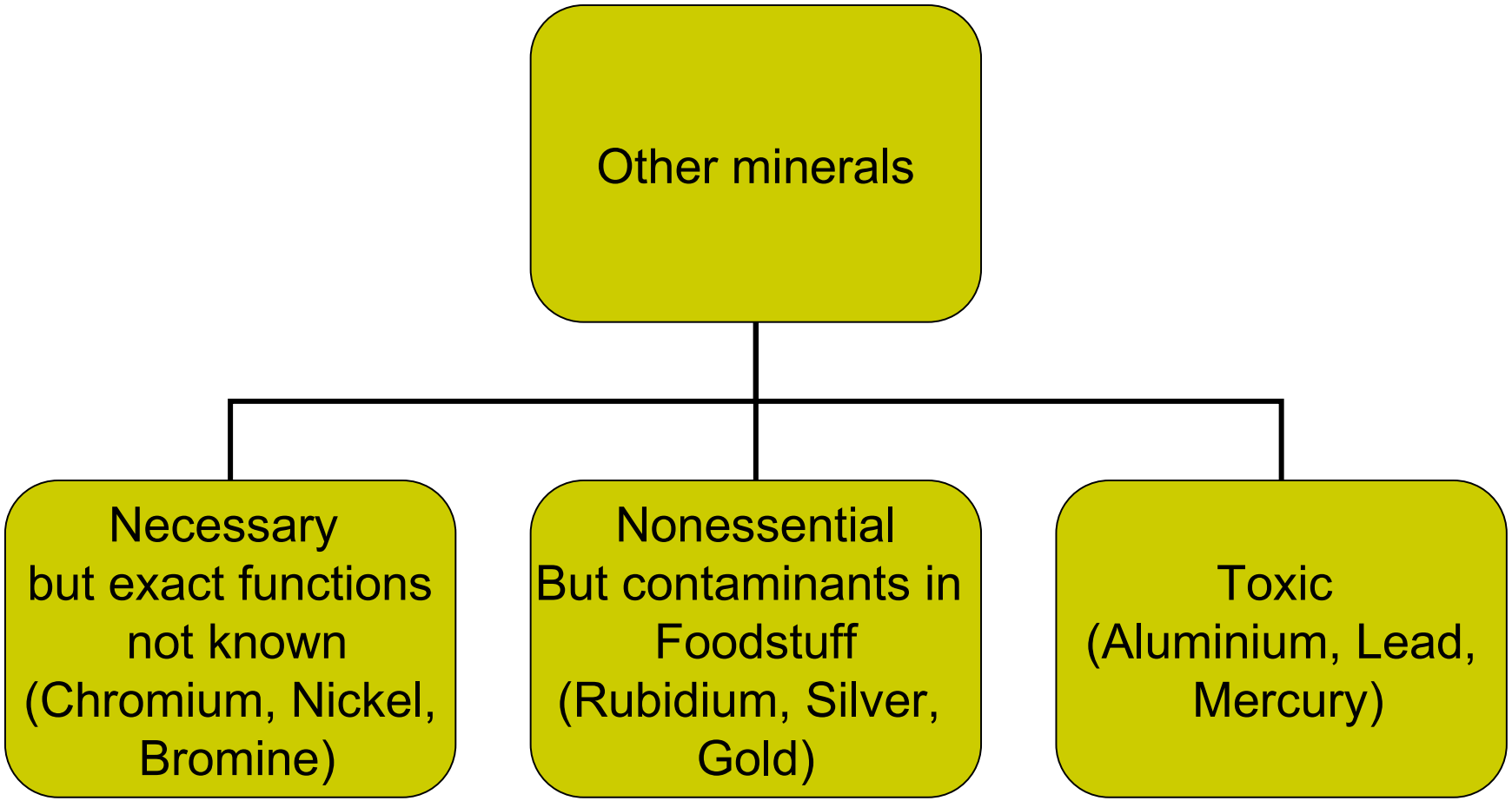
Minerals

- Major elements

1. Calcium
2. Magnesium
3. Phosphorus
4. Sodium
5. Potassium
6. Chloride
7. Sulfur

- Trace elements

1. Iron
2. Iodine
3. Copper
4. Manganese
5. Zinc
6. Selenium
7. Molybdenum
8. Fluoride


Other minerals
Necessary
but exact functions
not known
(Chromium, Nickel,
Bromine)
Nonessential
But contaminants in
Foodstuff
(Rubidium, Silver,
Gold)
Toxic
(Aluminium, Lead,
Mercury)

CALCIUM

CALCIUM

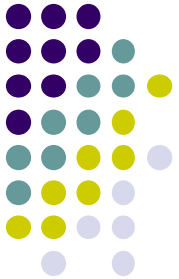
Total body calcium content

1 – 1.5kg

Distribution

Bones	**99%**
ECF	**1%**

CALCIUM



Sources :

Milk – good

Egg, Fish & vegetables –Medium

Cereals – small amount of Ca

CALCIUM

Requirements :

Adult – 500mg/day

Child – 1200mg/day

Pregnancy & Lactation – 1500mg/day

After 50 yrs of age – 1500mg/day + Vitamin D- 20µg/day

CALCIUM

Absorption :

From duodenum

Against conc. Gradient

Requires energy & a carrier protein- divalent metal ion transporter (DMT)

It is a calcium dependent ATPase

CALCIUM

Factors which ↑ Absorption :

a. **Vitamin D – Calcitriol induces Calbindin in intestinal epithelial cells**

b. **Parathyroid hormone – indirect effect through vit D, PTH↑ 1 α hydroxylase activity**

c. **Acidity**

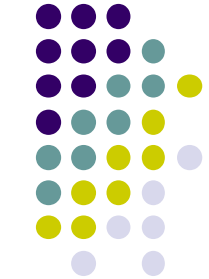
d. **Amino acids – Lys & Arg**

CALCIUM

Factors which ↓ Absorption :

a. **Phytic acid – present in cereals, fermentation & cooking ↓ phytates**
b. **Oxalates – Present in leafy vegetables, form insoluble calcium oxalate**
c. **Phosphate – precipitation of calcium phosphate**
d. **Malabsorption syndrome – FA not absorbed , calcium salt of FA is formed**

Functions of Calcium



1. **Bone & teeth formation :**

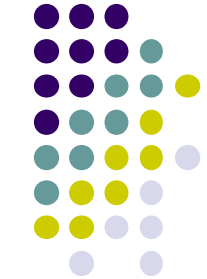
- **Bulk qty used for this**
- **Bones are reservoir for calcium**
- **Osteoblasts induce bone deposition**

Functions of Calcium

2. Muscles :

- **Mediates excitation/ contraction of muscle fibres**
- **Ca – troponin C interaction – muscle contraction**
- **Upon getting neural signal, Ca released from SR**
- **Ca activates ATPase**
- **Increases action of actin & myosin & facilitates excitation-contraction coupling.**
- **Decreases neuromuscular irritability**
- **Ca deficiency – tetany**

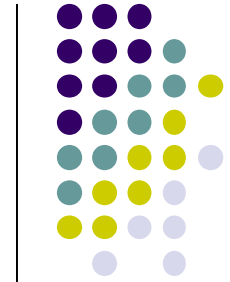
Functions of Calcium



3. Coagulation :

- **Factor IV in coagulation cascade**
- **Chelates to γ carboxy Glu residues during thrombin formation**

Functions of Calcium



4. Nerve conduction :

- **Transmission of nerve impulse from pre synaptic to post synaptic region**

Functions of Calcium

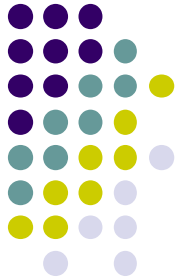
5. Secretion of hormones :

- **Mediates secretion of insulin, PTH, calcitonin, Vasopressin from cells**

Functions of Calcium

6. Second messenger :

- **In systems involving G proteins & Inositol triphosphate**



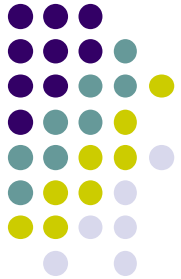
- Some hormones use ca as 2nd messenger, instead of cAMP

Functions of Calcium

7. Vascular permeability :

- **Decreases passage of serum through capillaries**
- **Clinically used to reduce allergic exudates**

Functions of Calcium



8. Activation of enzymes :

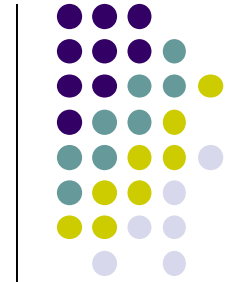
- **By binding to a regulatory protein – Calmodulin (4 Ca^{2+} ions)**
- **Ca-Calmodulin**
- **↓**
- **Kinase -> Active kinase**
- **↓**
- **Enzyme -> Enzyme – P**
- **↓**
- **Biological effect**

Functions of Calcium

9. Myocardium :

- **Prolongs systole**
- **So care should be taken when Ca is administered intravenously**

Functions of Calcium

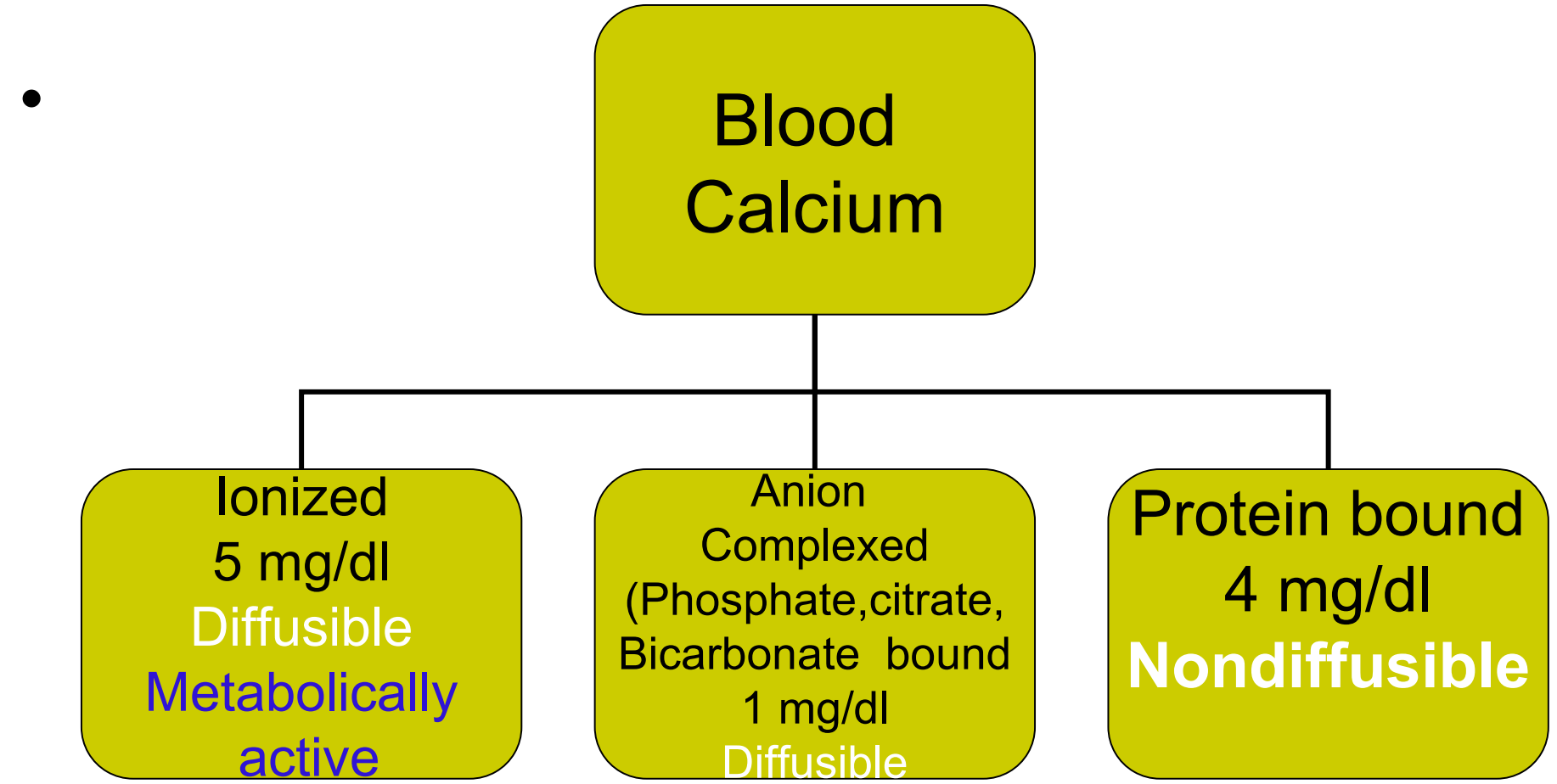


10. Calpains :

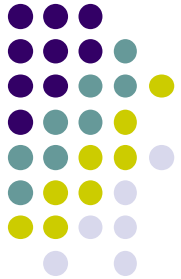
- **Calcium dependent Cys proteases**
- **Involved in cell mobility, cell cycle progression.**

- **CALCIUM HOMEOSTASIS or Maintenance of blood calcium level**

Calcium in blood
Normal level – 9-11mg/dl



Factors regulating blood Calcium level



. **Normal level – 9-11 mg/dl**

3 hormones that regulate calcium level in blood are

a. **Calcitriol - ↑ serum calcium**

b. **PTH - ↑ serum calcium**

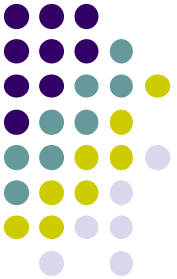
c. **Calcitonin - ↓ serum calcium**

A. Vitamin D :

a. in intestine –

- Promotes Ca & P absorption
- By ↑ synthesis of calcium binding protein – Calbindin
- Thus ↑ blood calcium levels

Factors regulating blood Calcium level



. A. Vitamin D :

b. in bone –

- ↑ Number & activity of osteoblasts
- Stimulates them to secrete ALP
- Thus causes ↑ in local conc. of phosphate
- ↑ ionic product of Ca & P
- Thus ↑ bone mineralization
- Helps osteoclastogenesis – remodeling of bone

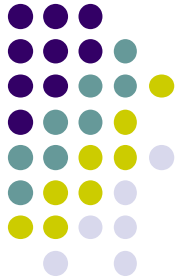
Factors regulating blood Calcium level

. A. Vitamin D :

c. In renal tubules -

- **↑ reabsorption of Ca & P**

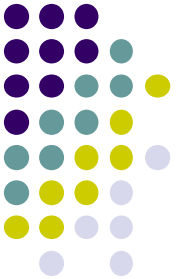
Factors regulating blood Calcium level



. B. Parathyroid hormone : secreted by parathyroid glands as prepro PTH (115 aa) – in ER & GA broken to form PTH (84 aa)

Release of PTH mediated by cyclic AMP

Factors regulating blood Calcium level

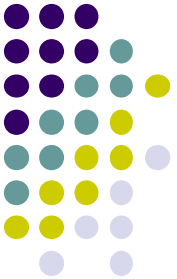


. B. Parathyroid hormone :

a. In bones -

- **Causes demineralization / decalcification**
- **↑ number of osteoclasts**
- **induces Pyrophosphatase in osteoclasts**
- **Osteoclasts release lactate into surrounding medium -> solubilizes Ca**

Factors regulating blood Calcium level

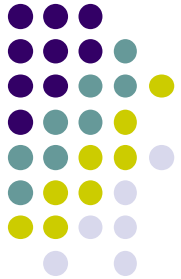


. B. Parathyroid hormone :

b. In kidney -

- **↑ reabsorption of Ca , so conserves Ca**
- **↑ excretion of phosphates**

Factors regulating blood Calcium level

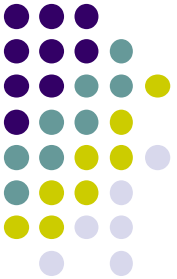


. B. Parathyroid hormone :

c. In intestine -

- **Increases vitamin D by stimulating 1 α hydroxylase in kidney**
- **Thus indirectly ↑ absorption of Ca**

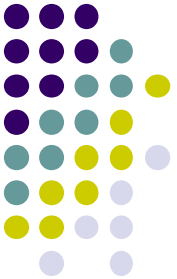
Factors regulating blood Calcium level



. C. Calcitonin : secreted by thyroid parafollicular cells. Secretion stimulated by

- **High Serum calcium**
- **Glucagon**
- **Gastrin**

Factors regulating blood Calcium level

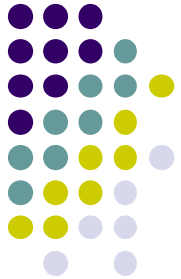


. C. Calcitonin :

a. In bone -

- ↑ activity of osteoblasts
- ↓ activity of osteoclasts
- Inhibits bone resorption
- Thus ↓ serum calcium level
- Calctonin & PTH are antagonistic
- Together promote bone growth & remodeling

Factors regulating blood Calcium level

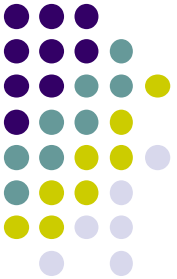


. C. Calcitonin :

b. In kidney -

- **↑ Phosphorus excretion (III to PTH)**

Factors regulating blood Calcium level

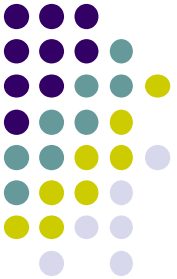


Calcitonin, Calcitriol & PTH act together :

When blood Ca ↓

- **PTH secretion stimulated**
- **Calcitonin inhibited**
- **Bone demineralization -> entry of Ca in blood & renal Ca excretion ↓**

Factors regulating blood Calcium level

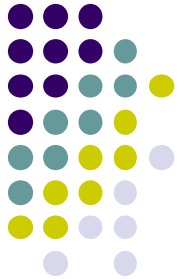


Calcitonin, Calcitriol & PTH act together :

When blood Ca ↑

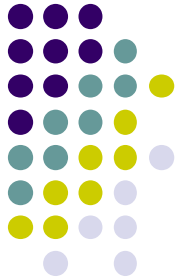
- **PTH secretion inhibited**
- **Calcitonin stimulated**
- **causes entry of Ca into bone**

Factors regulating blood Calcium level



- Clinical significance : CT is a tumor marker
- Calcitonin increased in medullary carcinoma of thyroid

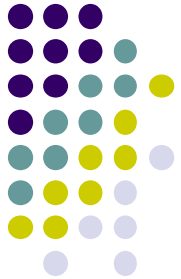
Factors regulating blood Calcium level



D. Phosphorus :

- **Reciprocal relationship bt Ca & P**
- **Ionic product of Ca & P in serum is constant**
- **Ca= 10mg/dl X P= 4mg/dl ; ionic product = 40**
- **In renal insufficiency, P excretion ↓ -> serum P ↑ -> Ca level lowered -> may lead to tetany**

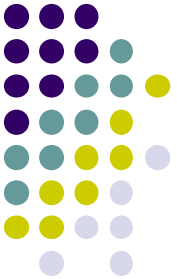
Factors regulating blood Calcium level



E. Serum proteins :

- **In hypoalbinemia, total Ca ↓**
- **No deficiency manifestations although total calcium low, since ionized form is normal**

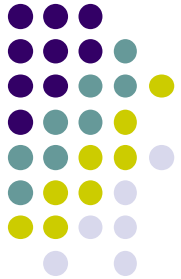
Factors regulating blood Calcium level



F. Alkalosis & acidosis : (pH)

- **Acidosis favors ionization of calcium**
- **Alkalosis favors formation of protein bound Ca -> ↓ ionized Ca -> may lead to Ca deficiency manifestations**

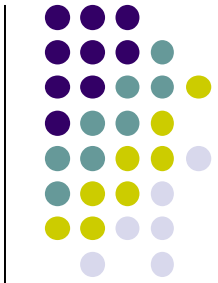
Factors regulating blood Calcium level



G. Children :

- **Ca level higher**
- **Ionic product of Ca & P in serum is constant 50 (instead of 40 in adults)**

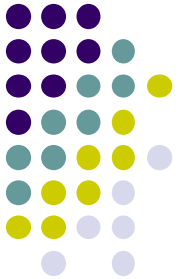
Factors regulating blood Calcium level



H. Renal threshold :

- **Is 10mg/dl**

Hypercalcemia



Plasma Calcium level > 11 mg/dl

Causes:

- **Primary hyperparathyroidism**
- **Paget's disease**
- **Multiple myeloma**
- **Metastatic carcinoma of bone**

Hypercalcemia

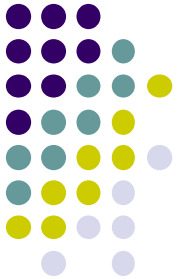
Symptoms :

- **Osteoporosis**

- **Punched out areas of bone resorption in X-ray**

- **Pathological fracture of bone**

Hypercalcemia



Symptoms :

- **Anorexia, nausea, vomiting**
- **Polyuria, polydypsia**
- **Calcium precipitation in urine – Renal stones**
- **Ectopic calcification - renal tissue, pancreas, arterial walls & muscle tissues**
- **Confusion, depression**

Hypercalcemia

Biochemical findings :

- **↑ serum calcium**
- **↓ serum phosphate**

Hypercalcemia

Management :

- **Adequate hydration**
- **I V normal saline**
- **Promote Ca excretion**
- **Treat underlying cause**

Hypocalcemia

Serum calcium < 8.8 mg/dl

- **If < 8.5 mg/dl -> mild tremors**
- **If < 7.5 mg/dl -> tetany**

Hypocalcemia

Causes :

- **Deficiency of Vitamin D (rickets) - no tetany, marginal decrease in serum calcium**
- **Deficiency of parathyroid (**
- **↑ Calcitonin**
- **Malabsorption, alkalosis**

Hypocalcemia

Symptoms :

- **Tetany**
- **Carpopedal spasm**
- **Laryngeal spasm & stridor**
- **Chvostek's sign – facial contraction on tapping over facial nerve**
- **Trousseu's sign – carpopedal spasm on BP cuff inflation for 3min**


nu107020 www.fotosearch.com

Ask the patient to relax his facial nerves. Next, stand directly in front of him and tap the facial nerve either just anterior to the earlobe or below the zygomatic arch and the corner of the mouth. A positive response varies from twitching of the lip at the corner of the mouth to spasm of all facial muscles, depending on the severity of hypocalcaemia


Finger tap

Hypocalcemia

Symptoms :

- **Neuromuscular irritability, muscle twitchings**
- **Muscle cramps**
- **Paresthesia**
- **Seizures**
- **Bradycardia**
- **Q-T interval in ECG ↑**

Hypocalcemia

Biochemical findings :

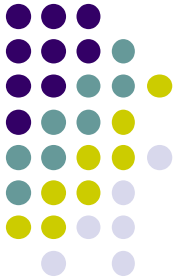
- **↓ serum calcium**
- **↑ serum Phosphate**

Hypocalcemia

Management :

- **oral calcium with Vit D supplementation**
- **Tetany - I V Calcium**
- **Treat underlying cause**

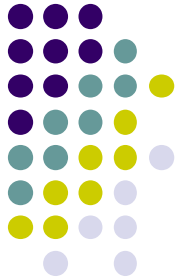
Bone markers



- serum Ca, P, Mg, ALP, acid phosphatase

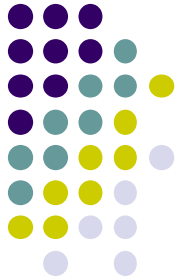
- Urine Ca & P

Osteoporosis



- **Characterized by bone demineralization resulting in progressive loss of bone mass**
- **Results in frequent bone fractures**
- **Occurrence – elderly people – over 60 yrs – both sex & post-menopausal women**
- **Causes –**
- **reduced Ca & vit D absorption**
- **reduced levels of sex hormones**
- **increased Ca excretion**

Osteopetrosis

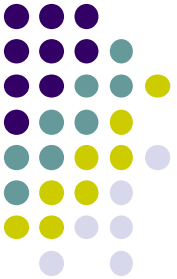


- **Also called marble bone disease**
- **due to inability of bone resorption**
- **increased bone density**

Renal osteodystrophy

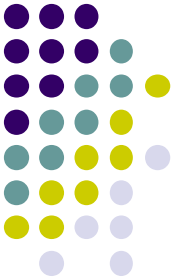
- Occurs in chronic renal failure
- 1 alpha hydroxylation doesn’t occur
- Sec. hyperparathyroidism
- Demineralisation - Fractures,

Phosphorus



- Total body phosphate – 1 kg
- 80% in bone & teeth
- 10% in muscles
- Phosphate is an intracellular ion

Functions of phosphate ion

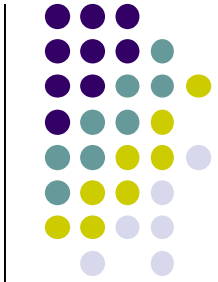


- Bone & teeth formation
- Production of high energy phosphate compounds - ATP, CTP, GTP & creatine P
- Synthesis of nucleoside co-enzymes like NAD & NADP

Functions of phosphate ions

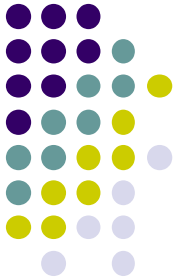
- Phosphodiester backbone in DNA & RNA
- Formation of phospholipids, phosphoproteins
- in enzyme regulation – covalent modification
- Phosphate buffer system in blood

Phosphorus



- **Requirement**
- 500mg/day
- **Sources** –
- Milk – good
- Cereals, nuts & meat – moderate
- **Serum level** –
- Adults – 3-4 mg/dl
- Children – 5-6 mg/dl
- Fasting level ↑ than Post prandial since P used for metabolism

Maintenance of P level in bood



-by PTH

↑ **Calcium & phosphate release from bone**

↑ **Phosphate loss in urine**

Causes of

Hypophosphatemia	Hyperphosphatemia
↓ absorption of phosphate (Vit D deficiency)	↑ absorption of phosphate (Vit D excess)
↑ urinary excretion (Hyper parathyroidism, Hypo phosphatemic rickets)	↓ urinary excretion (Hypo parathyroidism, renal impairment)
Intracellular shift (insulin therapy, respiratory alkalosis)	↑ cell lysis (comes out of cells) (chemotherapy)