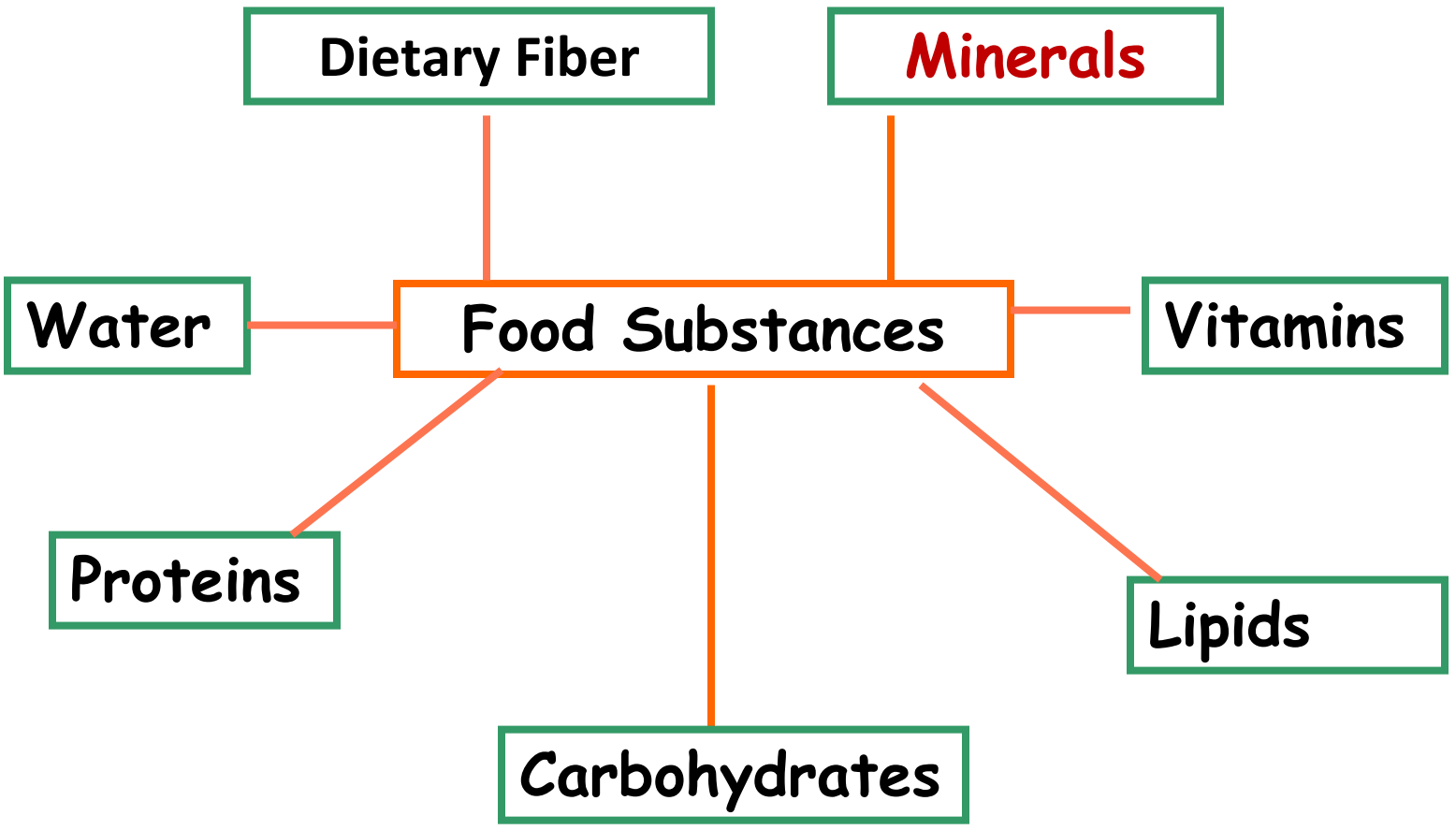
Minerals

- **Minerals are Inorganic elements**
- **Not synthesized** in human body
- Widely distributed in nature
- **Present in foods** of **Plant and Animal** origin

- Minerals in human body **have various structural and functional roles**

- Hence it **is essential to ingest** Minerals **through diet.**

Human Body Ingests Seven Food Nutrients



- **Minerals are classified based on:**
  - ❖ **Functional need to body**
  - ❖ **Its daily requirement**

Two Broad Classes Of Minerals

- **Macro elements**
- **Micro/trace elements-**
- Ultra trace element (required in amounts <u><1 mg/d)</u>

• Macro/Principle/Chief elements

- **Body needs Macro elements relatively in large quantities**
- present in body tissues at concentrations **>50 mg/kg**
- Requirement of these Minerals is **>100 mg/day**

Macro elements

1. Calcium (Ca)
2. Phosphorus (P)
3. Sulfur (S)
4. Magnesium (Mg)
5. Sodium (Na)
6. Potassium (K)
7. Chloride (Cl)

- **Micro Minerals /Trace Elements**

- Body needs Micro Minerals **relatively in less amount**
- Present in **body tissues at concentrations <50 mg/kg**
- **Requirement** of these Minerals is **< 100 mg/day**

Name Of 10 Essential Micro/Trace Elements

1. Iron (Fe)
2. Copper (Cu)
3. Cobalt (Co)
4. Chromium (Cr) (120 µg/d)
5. Fluoride (F)
6. Iodine (I) (150 µg/d)
7. Manganese (Mn)
8. Molybdenum (Mo) (75 µg/d)
9. Selenium (Se) (35 µg/d)
10. Zinc (Zn)

Possibly Essential Elements for Humans (functions not known)

Nickel(Ni), Silicon(Si), tin(Sn), Vanadium(V)

Toxic elements

Arsenic, Lead, Mercury

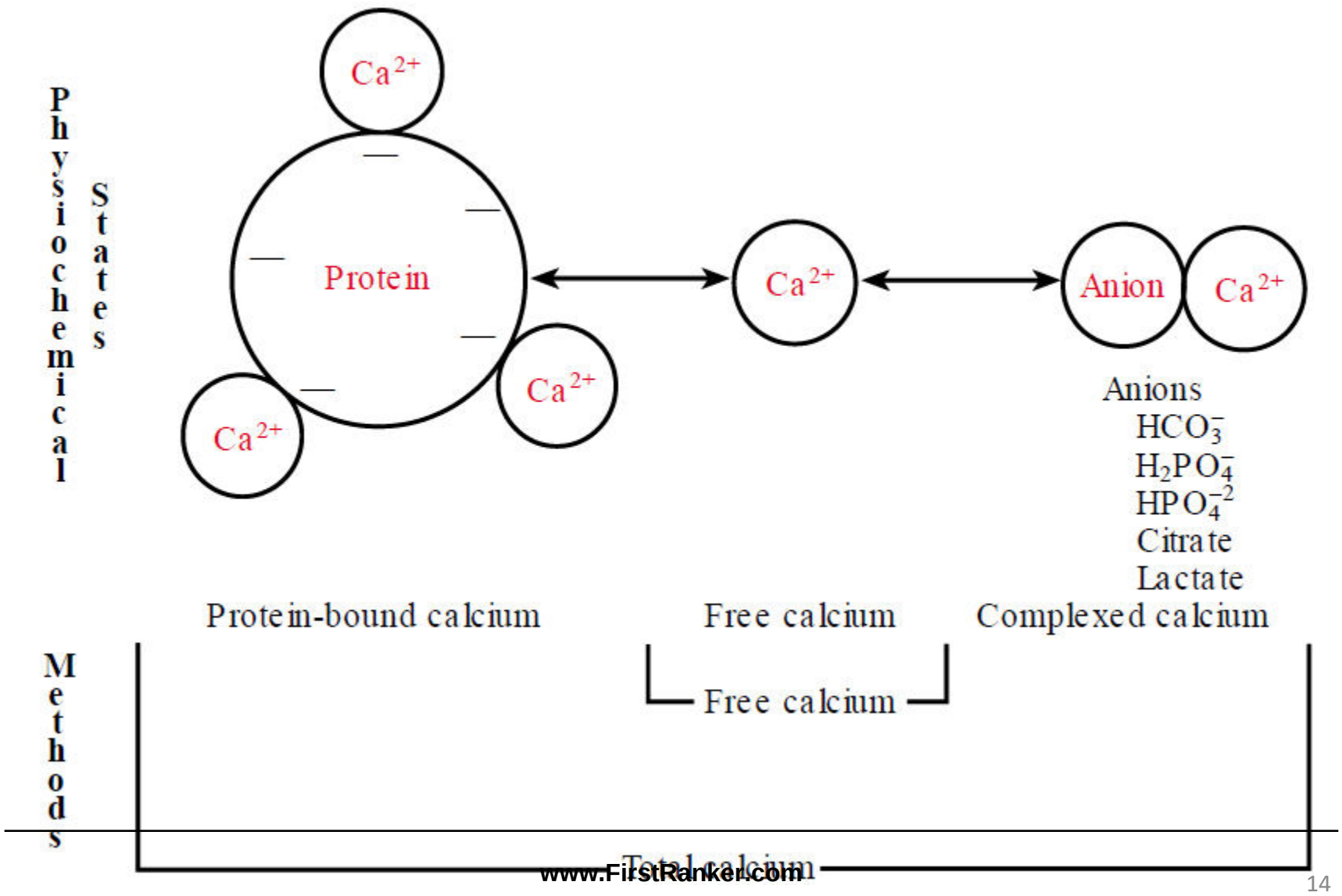
Nutritionally Important Minerals (60Kg)

Macro Minerals		Trace Elements	
Element	g/kg	Element	mg/kg
Ca	15	Fe	20-50
P	10	Zn	10-50
K	2	Cu	1-5
Na	1.6	Mo	1-4
Cl	1.1	Se	1-2
S	1.5	I	0.3-0.6
Mg	0.4	Mn	0.2-0.5
		Co	0.02-0.1

Distribution of Calcium, Phosphate and Magnesium in the Body

Tissue	Calcium	Phosphate	Magnesium
Skeleton	99%	85%	55%
So t tissue	1%	15%	45%
Extracellular fluid	<0.2%	<0.1%	1%
Total	1000 g (25 mol)	600 g (19.4 mol)	25 g (1.0 mol)

Equilibria and determinations of calcium in serum.



Physiochemical States of Calcium, Phosphate, and Magnesium in Normal Plasma

State	Calcium	Phosphate	Magnesium
Free (ionized)	50	55	55
Protein-bound	40	10	30
Complexed	10	35	15
Total (mg/dL) (mmol/L)	8.6-10.3 2.15-2.57	2.5-4.5 0.81-1.45	1.7-2.4 0.70-0.99
Free calcium (mg/dL)	4.6-5.3		

Functions of calcium

<u>Intracellular calcium</u>

1. Muscle contraction
2. Hormone secretion
3. Second Messenger
4. Glycogen metabolism
5. Cell division
6. Enzyme activation

Enzymes regulated by Ca++

Adenyl cyclase
Ca++ dependent protein kinases (PKC)
Ca++ -Mg++ -ATPase
Glycerol-3-phosphate dehydrogenase
Glycogen synthase
Myosin kinase
Phospholipase C
Phosphorylase kinase
Pyruvate carboxylase
Pyruvate dehydrogenase
Pyruvate kinase

Functions of calcium

Extracellular calcium

1. Bone mineralization
2. Blood coagulation

Calcium Dietary Requirements

–**Adult : 800 mg/day**

–**Pregnancy, lactation and post-menopause 1500mg/day**

–**Growing Children:** (1-18 yrs): **1200 mg/day**

–**Infants: (< 1 year): 300-500 mg /day**

Dietary Calcium sources

- **Rich Calcium Sources**

- **Milk and Milk Products**
- Millet (Ragi)
- Wheat-Soy flour
- Black strap molasses

- **Calcium Good sources**

- Yoghurt, sour cream, ice cream
- Tofu
- Guava ,Figs
- Cereals
- Egg yolk
- Legumes

- Green leafy vegetables as collard, kale , Broccolli, Cabbage and raw turnip
- Small Fish as trout, salmon and sardines with bones
- Meat
- Almonds, brazil nuts, dried figs, hazel nuts
- Also soybean flour and cottonseed flour

- Absorption of Calcium occurs in the **Duodenum and proximal Jejunum**
- **Mediated by Calbindin**

(synthesized by mucosal cells)

Factors Promoting Calcium Absorption

❖ **Parathyroid Hormone (PTH) indirectly enhances Ca absorption through the increased activation of Calcitriol**

❖**Calcitriol /activated Vitamin D induces the synthesis of Ca binding protein Calbindin**

❖**Acidity Increases the solubility of calcium salts**

❖**Amino acids Lysine and Arginine form soluble complexes with Calcium**

Factors Inhibiting Calcium Absorption

Phytates and Oxalates present in plant origin diet **form insoluble salts**

The high content of **dietary Phosphates forms insoluble Ca phosphate**
Dietary ratio of Ca : P ---**1:1 / 2:1** is ideal for Ca absorption

The **Free Fatty acids** forms insoluble Ca soaps

Alkaline condition

Low Estrogen levels Estrogen increases Calcitriol levels

High content of **Dietary fiber, Caffeine, Sodium**

Excess Magnesium in diet inhibits Calcium absorption
(Magnesium competes with Calcium for absorption)

Factors Regulating Blood Calcium Levels

- Parathyroid Hormone (PTH)
- Vitamin D- Calcitriol
- Calcitonin

Organs involved for action of PTH

Intestine
Bone
Kidney

PTH Action on the Bone

Stimulating osteoclastic bone resorption-
Indirect effect through local mediators (RANK ligand, tissue growth factor β)
→blood Ca level ↑

This **Inhibits osteoblast function- Directly by interacting with their PTH receptors**

Action Of PTH on the Kidney and Intestine

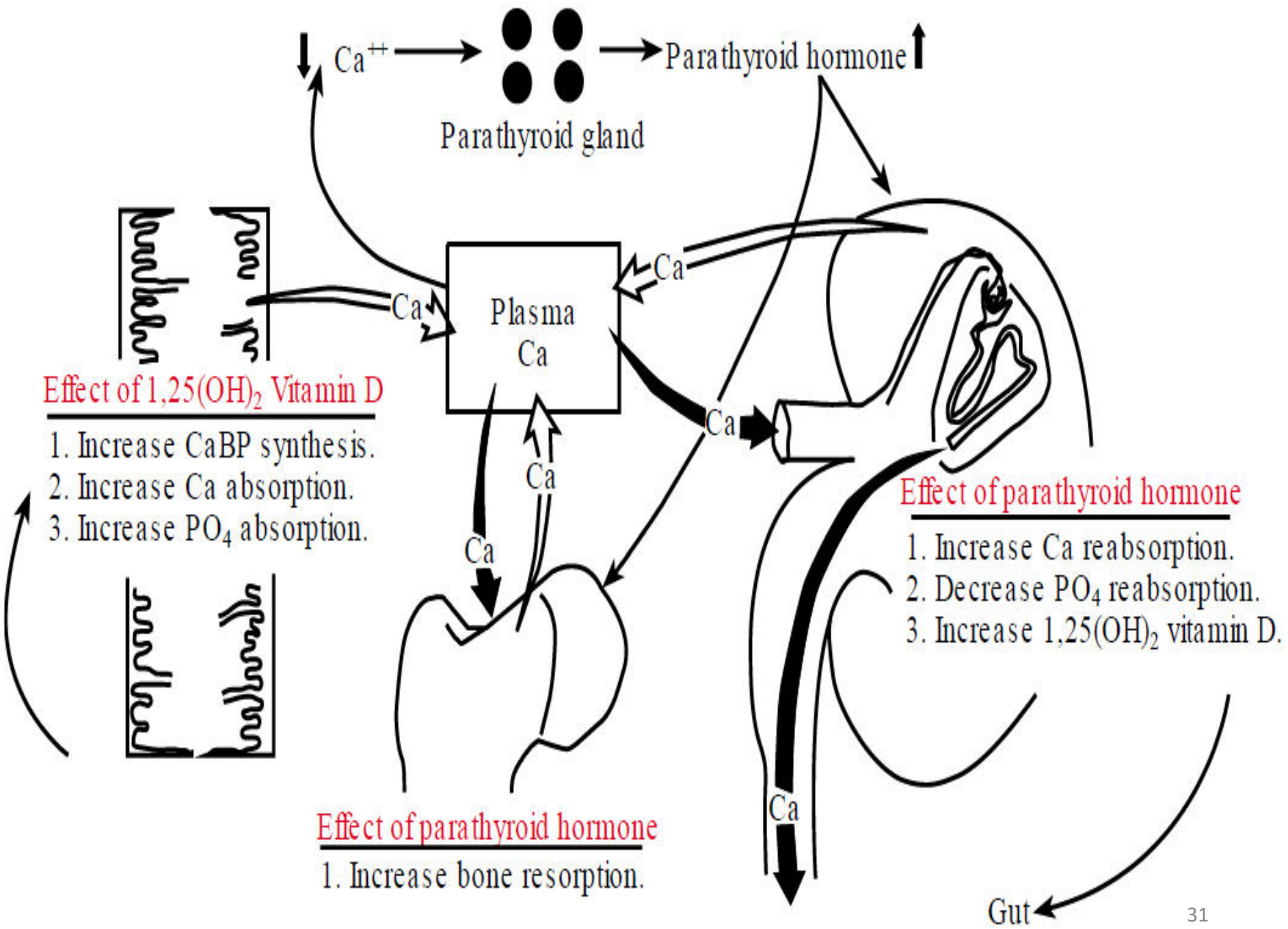
Parathyroid hormone acts on **distal tubule through a cAMP dependent mechanism and Increases renal re absorption of Calcium**
PTH increases phosphate excretion at the proximal tubule by lowering the renal phosphate threshold.

Action on the **Intestine**: **indirect**
PTH is a trophic factor for renal 25(OH)D1α hydoxilase.
Increases conversion of 25(OH)D to the active metabolite 1,25(OH)2D

increases the intestinal absorption of Ca **by promoting the synthesis of Calcitriol**.

Effect of vitamin D

- **Increase calcium binding protein synthesis**
- **Increase calcium absorption**
- **Increase phosphate absorption**



Causes of Hypocalcemia

Hypoalbuminemia
Chronic renal failure
Magnesium deficiency
Hypoparathyroidism
Pseudohypoparathyroidism
Osteomalacia and rickets due to vitamin D def. or resis
Acute hemorrhagic and edematous pancreatitis
Healing phase of bone disease of treated hyperpara and hematological malignancies (hungry bone synd.)

Causes of Hypercalcemia

Primary hyperparathyroidism

Parathyroid adenoma, hyperplasia, carcinoma

Malignancy

Skeletal metastases

Humoral hypercalcemia

PTH-rP

Hematological malignancy

Cytokines (interleukin-1, tumor necrosis factor, etc.)

1,25-Dihydroxyvitamin D (lymphoma)

Familial hypocalciuric hypercalcemia

Causes of Hypercalcemia contd

Idiopathic hypercalcemia of infancy

Vitamin overdose, vitamin D

Granulomatous diseases (e.g., sarcoidosis, tuberculosis)

Renal failure

Chronic, acute (diuretic phase) or after transplant

Chlorothiazide diuretics

Lithium therapy

Milk-alkali syndrome

Immobilization

Increased serum proteins

Hemoconcentration,

Paraprotein

Factors altering the distribution of calcium

Factors altering protein binding of calcium

Altered concentration of albumin or globulin
Heparin
pH
Free fatty acids
Bilirubin
Drugs
Temperature

Factors altering complex formation

Citrate
Bicarbonate
Lactate
Phosphate , Sulphate
Anion gap

Preanalytical Factors in Measurement of Serum Total or Free Calcium

In Vivo

Tourniquet use and venous occlusion (protein bound ca Incrd)
Changes in posture: increase of total calcium on standing
Decrease of total ca on recumbency
Exercise (free ca)
Hyperventilation (free ca)
Fist clenching
Alimentary status
Alterations in protein binding
Alterations in complex formation
Prolonged bed rest (both total and free ca increased)

Preanalytical Factors in Measurement of Serum Total or Free Calcium contd

In Vitro

Inappropriate anticoagulants

Dilution with liquid heparin

Interfering concentrations of
- heparin

Contamination with calcium
- Corks, glassware, tubes

Specimen handling
- Alterations in pH (free calcium)
- Adsorption or precipitation of calcium

Spectrophotometric interference
- Hemolysis, icterus, lipemia

Causes of Hypophosphatemia

- **Shift of phosphate from extracellular to intracellular space**
  - Glucose
  - Insulin
  - Respiratory alkalosis-accelerates glycolisis
- **Renal phosphate wasting**
  - Lowered renal phosphate threshold
    - Primary or secondary hyperparathyroidism
  - Renal tubular defects
    - Familial hypophosphatemia
    - Fanconi syndrome
- **Decreased net intestinal absorption**
  - Increased Loss---Vomiting, Diarrhoea, antacids
  - Decreased absorption
    - Malabsorption
    - Vitamin D deficiency
- **Intracellular phosphate loss**
  - Acidosis
    - Ketoacidosis, Lactic acidosis

Clinical manifestation of serum phosphate depletion depend on length and degree of deficiency

Plasma conc <1.5 mg/dL----produce clinical manifestation

Glycolysis impaired
Muscle weakness
Acute respiratory failure
Decreased cardiac output

Very low serum phosphate (<1 mg/dL)

Rhabdomyolysis
Tissue hypoxia
Mental confusion, Coma

Serum phosphate concentration <0.5 mg/dL

Hemolysis of red blood cells

Causes of Hyperphosphatemia

Decreased renal phosphate excretion

Decreased glomerular filtration rate
Renal failure
Increased tubular reabsorption (increased threshold)
Hypoparathyroidism
Pseudo hypoparathoidism
Acromegaly

Increased phosphate intake

Oral or intravenous administration
Phosphate containing enema

Increased extracellular phosphate load

Transcellular shift
Lactic acidosis, Resp acidosis, DKA
Cell lysis
Rhabdomyolysis
Intravascular hemolysis

Magnesium

Fourth most abundant cation in the body
RBC content of Mg= 3 times of serum
Absorbed from distal small bowel
Excreted mainly through kidney
Daily requirement: 300-350 mg/d (male)
Reference interval 1.7-2.4 mg/dL
Mg is important in neuromuscular excitability
Activator of large number of enzymes:

Alkaline phosphatase, hexokinase, Adenylyl cyclase, cAMP dependent kinase, Squalene synthase, Glutamine synthase

Required for many cellular transport processes:

insulin dependent glucose uptake.

Causes of Magnesium deficiency

GI disorder

Prolonged nasogastric suction
Malabsorption syndrome
Acute and chronic diarrhoea
Protein calori malnutrition

Renal loss

Chronic parenteral fluid therapy
Osmotic diuresis
Glucose (DM)
Mannitol
Urea
Hypercalcemia
Alcohol
Drugs
Diuretics
Aminoglycoside

Metabolic acidosis
Starvation, ketoacidosis
Alcoholism

Causes of hypermagnesemia

Excessive intake

- Orally (usually in the presence of CRF)
  - Antacid
  - Cathartic
- Rectally
  - Purgation
- Parentally
  - Treatment of pregnancy induced HT
  - Treatment of magnesium deficiency

Renal failure

- Chronic usually with administration of magnesium
  - Antacid
  - Cathartic
  - Enema
  - Infusion
- Acute
  - Rhabdomyolysis

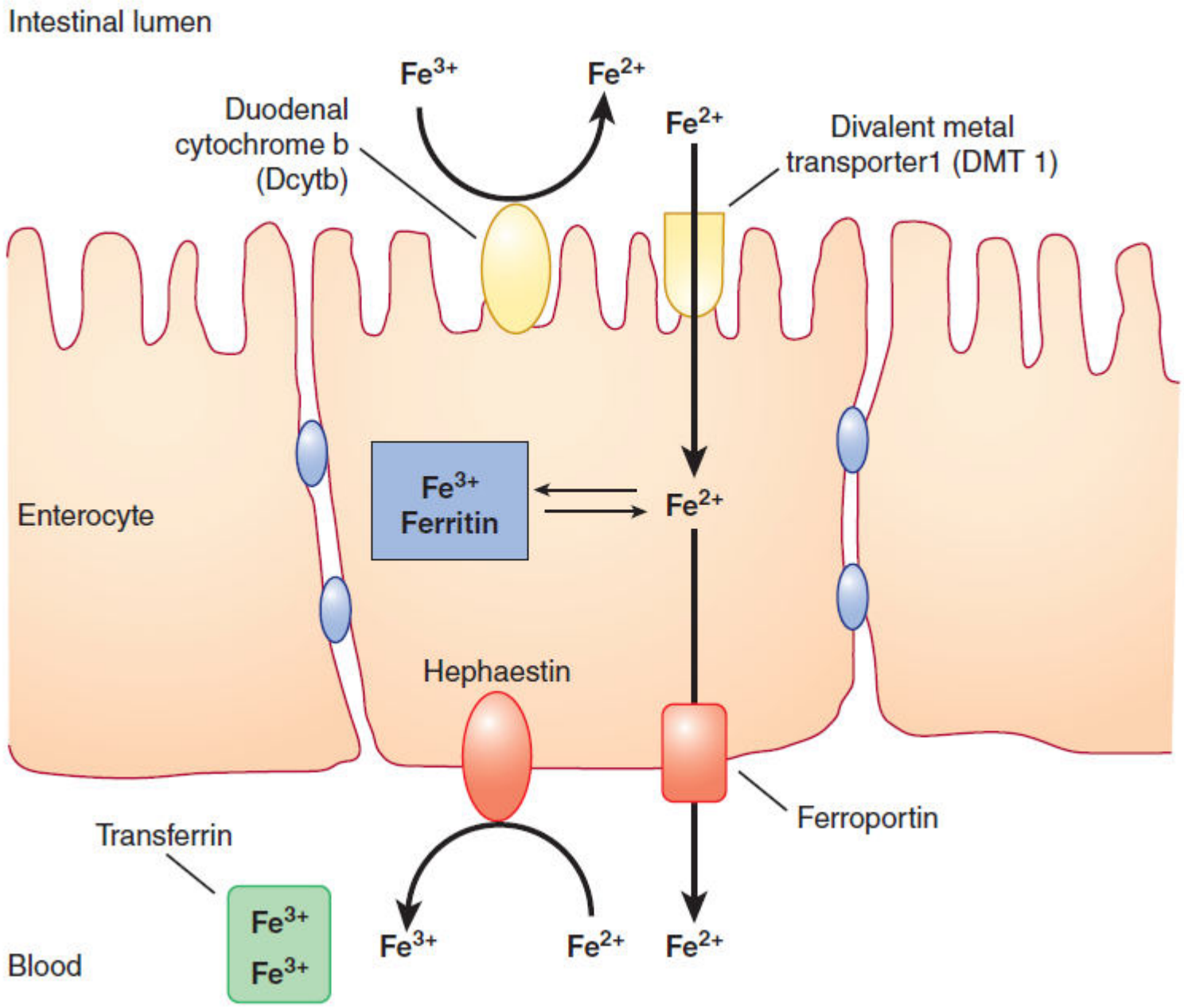
Lithium ingestion

Distribution of Iron in a 70-kg Adult Male

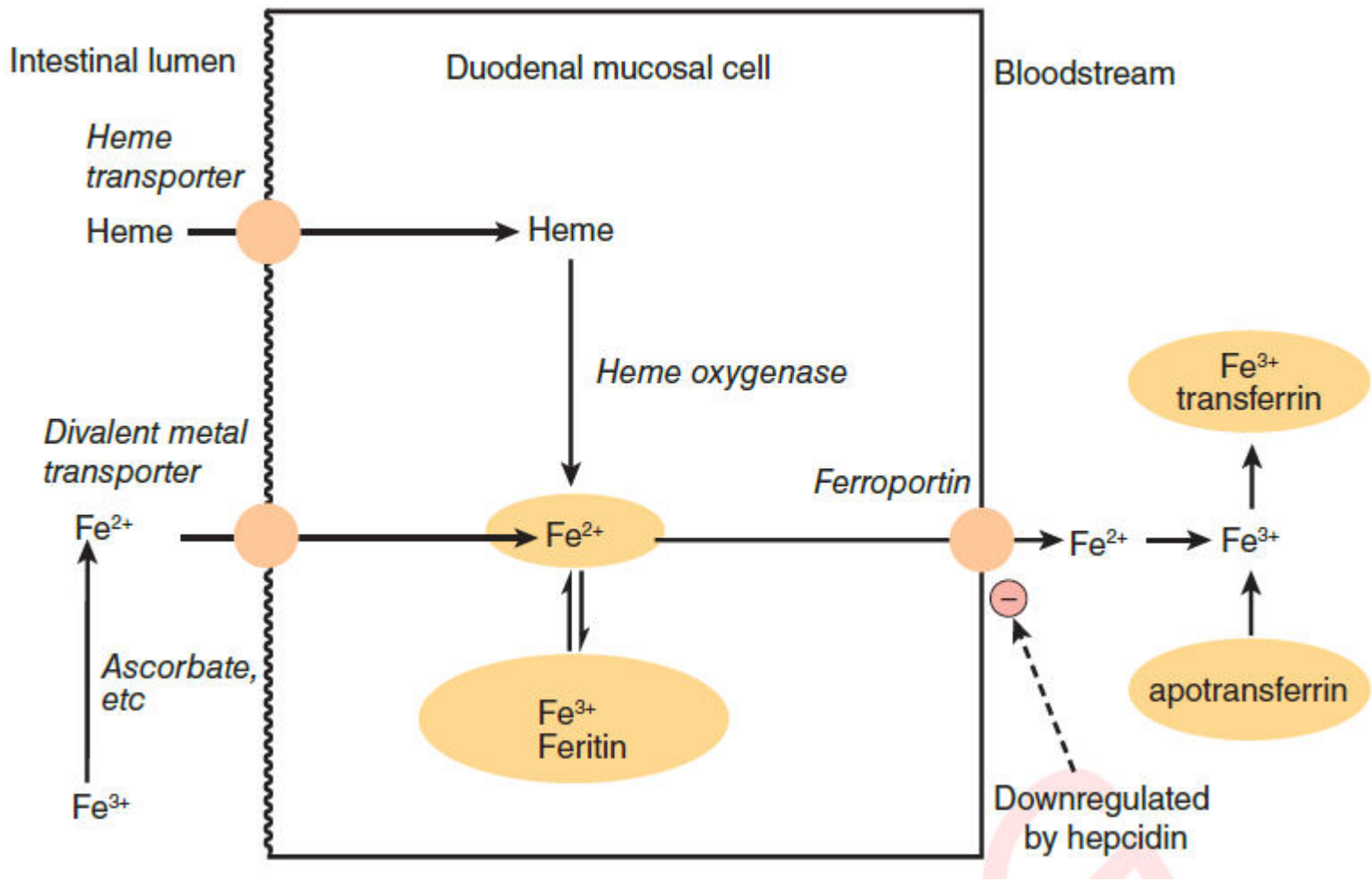
Transferrin	3-4 mg
Hemoglobin in red blood cells	2500 mg
In myoglobin and various enzymes	300 mg
In stores (ferritin)	1000 mg
Absorption	1 mg/d
Losses	1 mg/d

In an adult female of similar weight, the amount in stores would generally be less (100-400 mg) and the losses would be greater (1.5-2 mg/d).

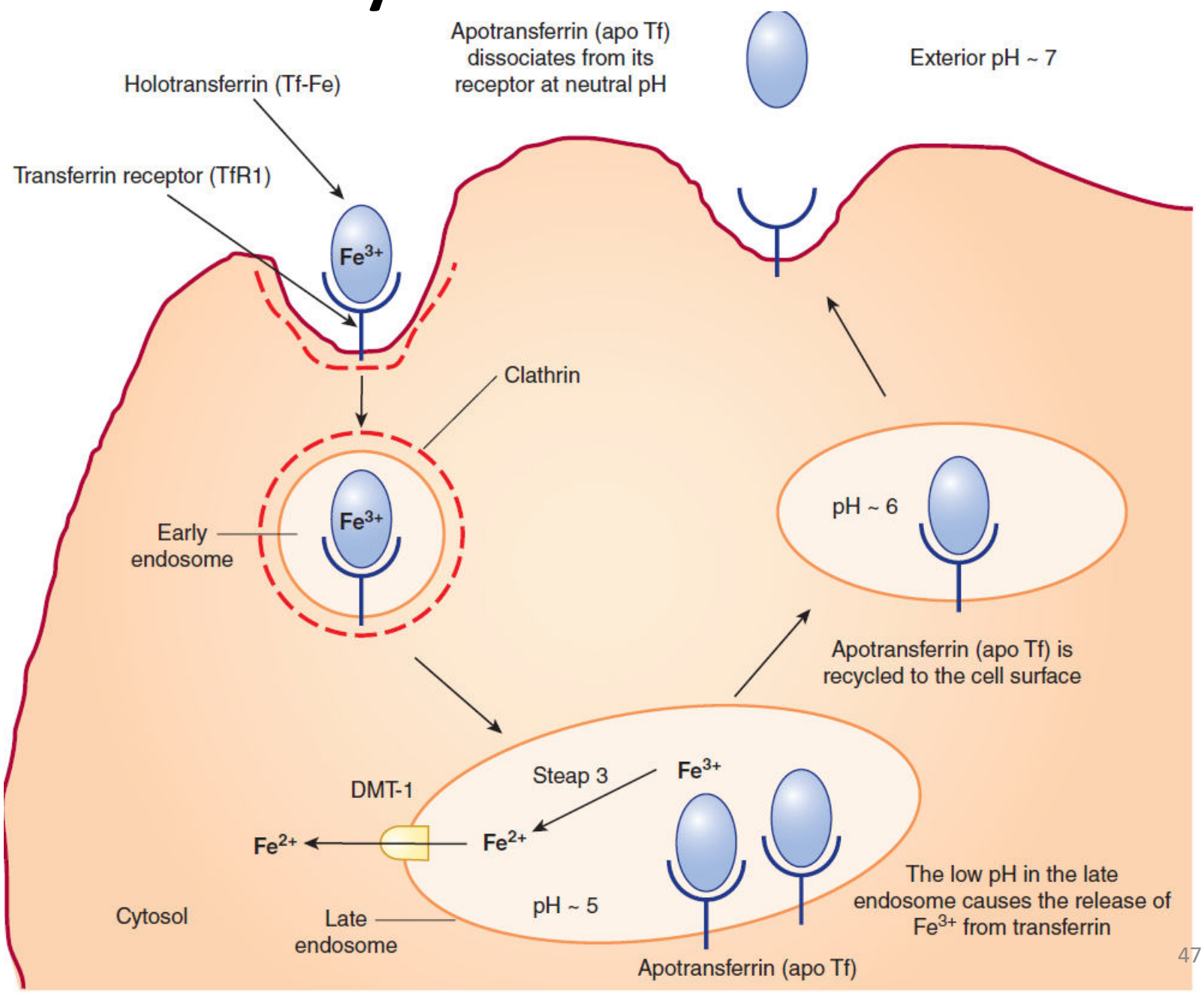
Nonheme iron transport in enterocytes



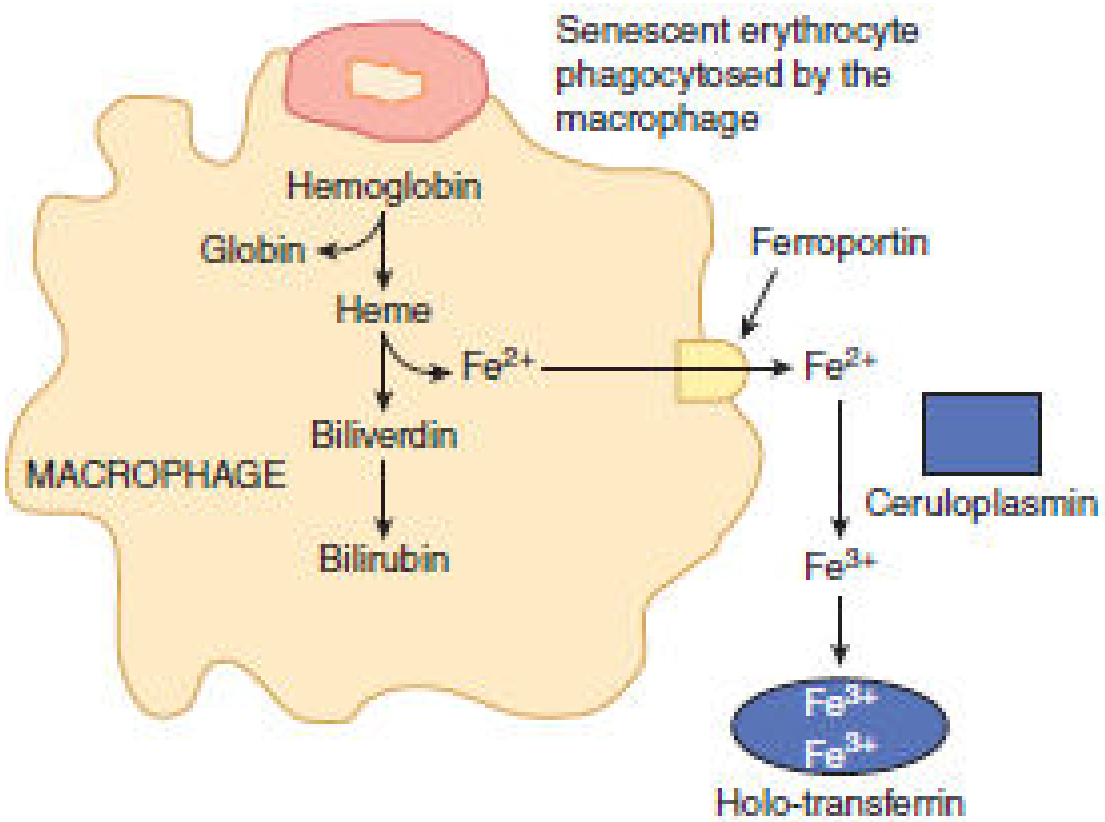
Absorption of iron



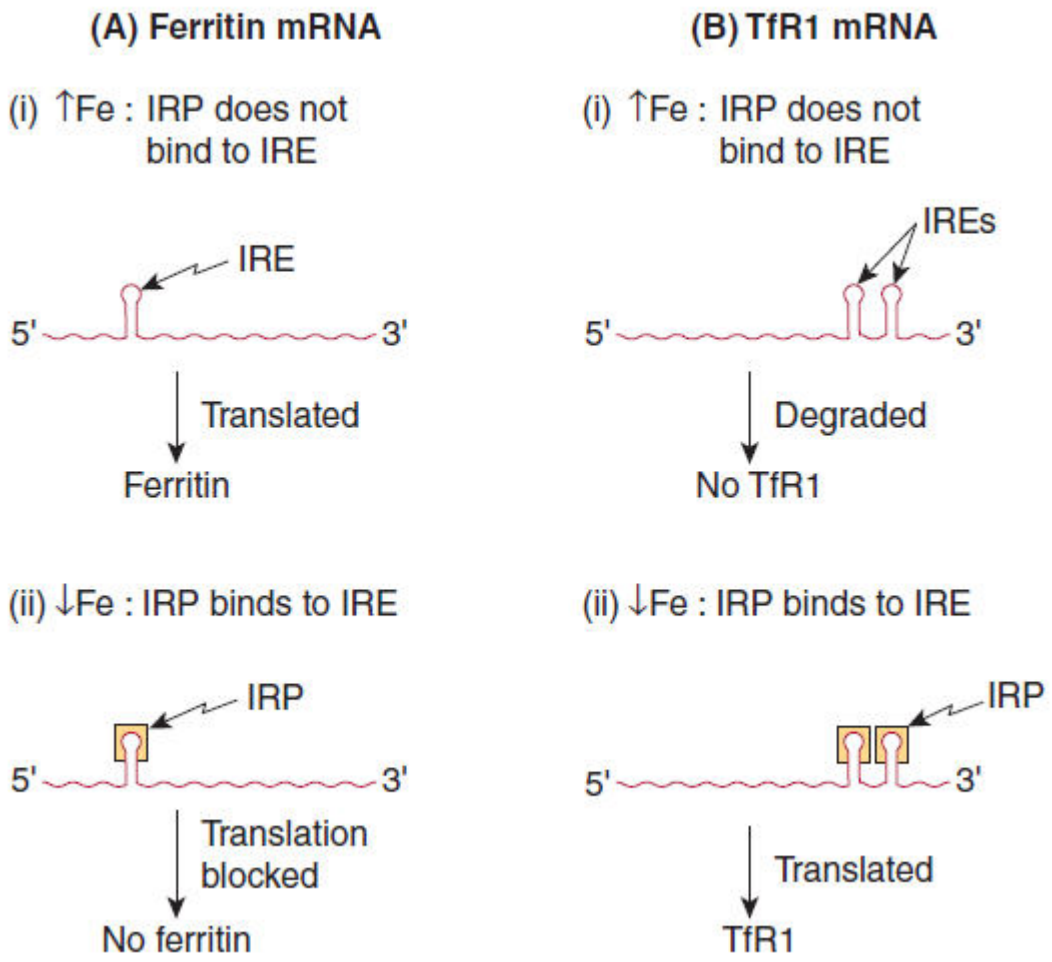
The transferrin cycle



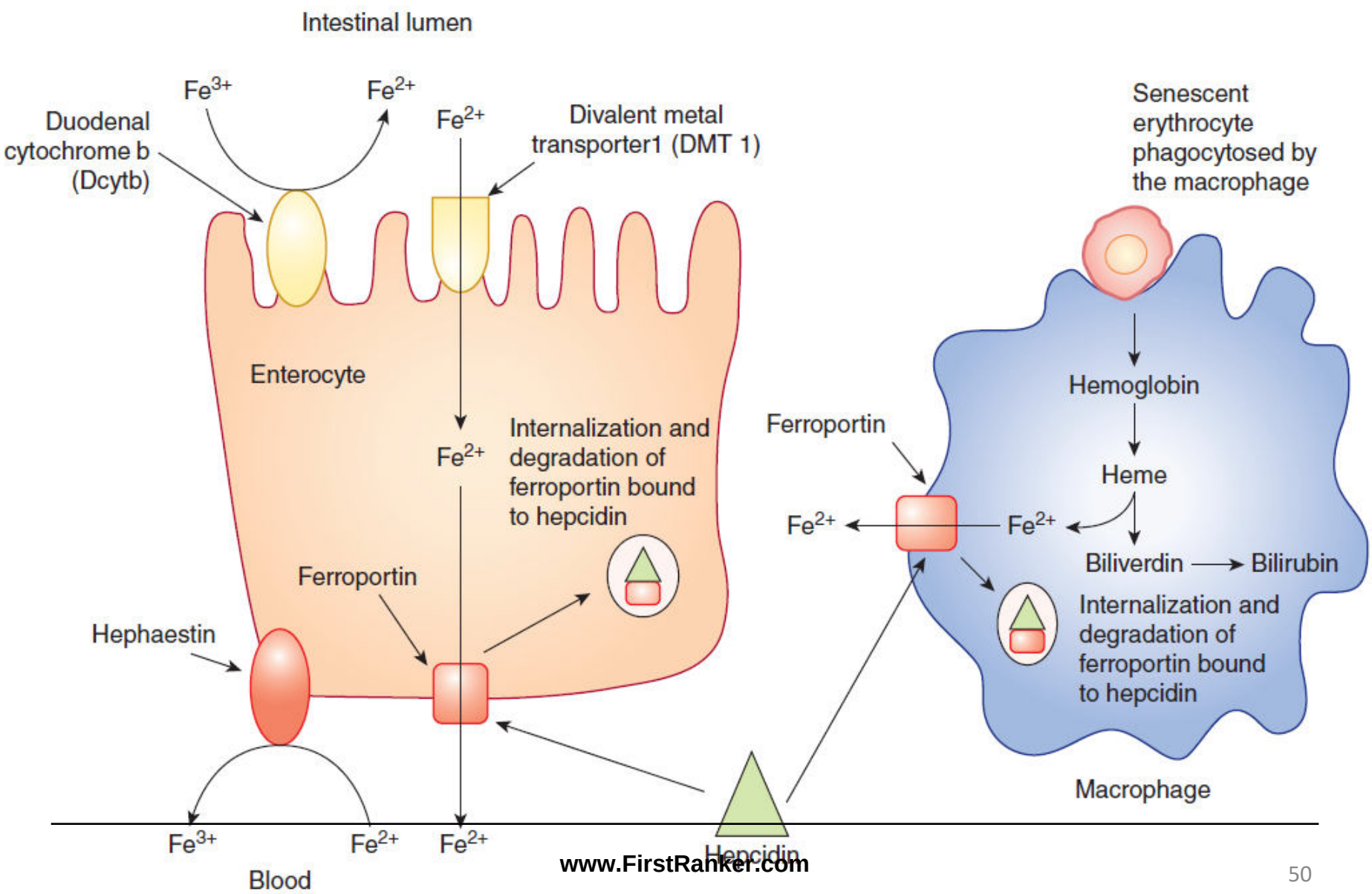
Recycling of iron in macrophages



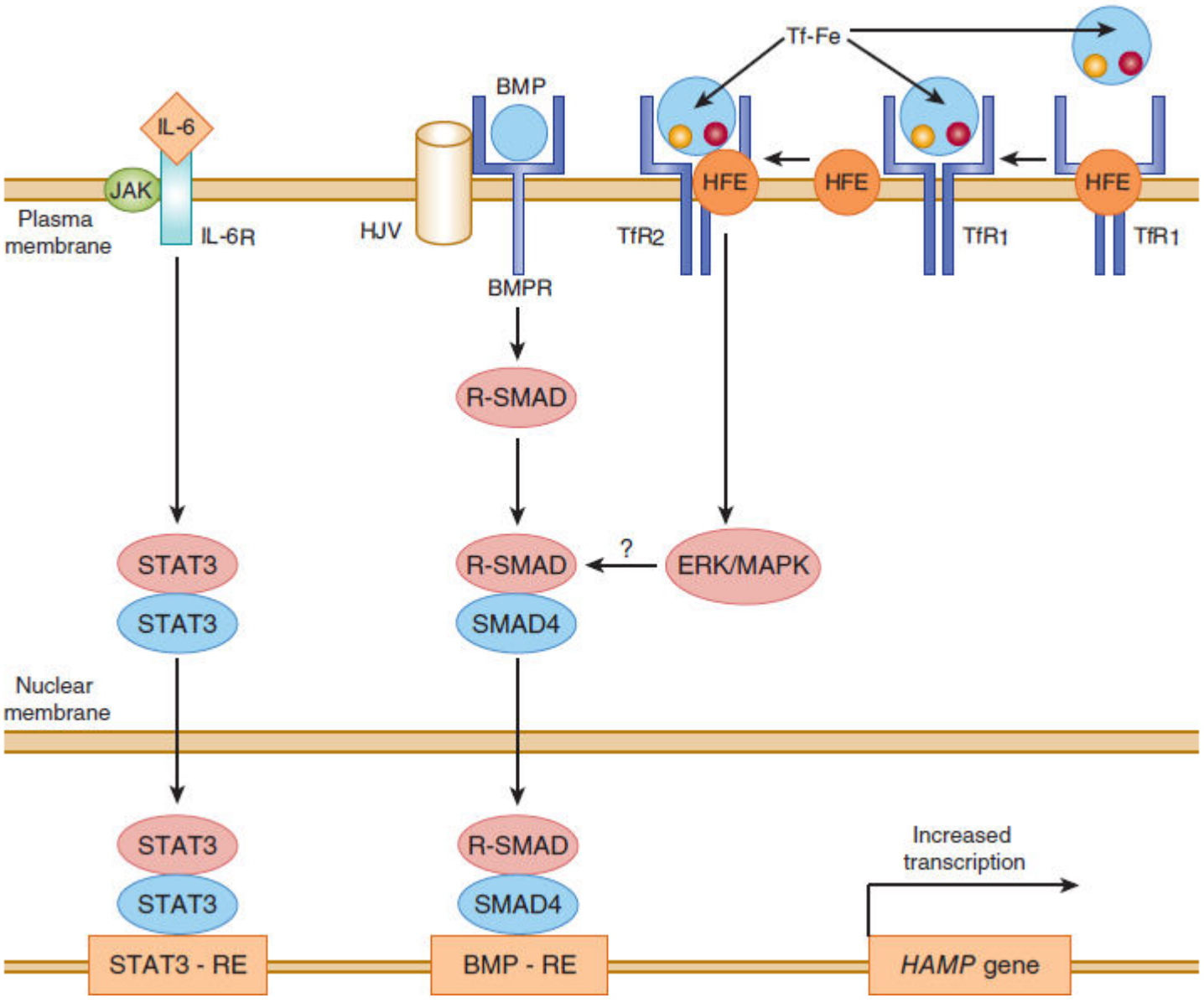
Schematic representation of the reciprocal relationship between synthesis of ferritin and the transferrin receptor (TfR1).



Role of hepcidin in systemic iron regulation



Regulation of hepcidin gene expression



Changes in Various Laboratory Tests Used to Assess Iron-Deficiency Anemia

Parameter	Normal	Negative Iron Balance	Iron-Deficient Erythropoiesis	Iron-Deficiency Anemia
Serum ferritin (µg/dL)	50-200	Decreased <20	Decreased <15	Decreased <15
(TIBC) (µg/dL)	300-360	Slightly increased >360	Increased >380	Increased >400
Serum iron (µg/dL)	50-150	Normal	Decreased <50	Decreased <30
Transferrin saturation (%)	30-50	Normal	Decreased <20	Decreased <10
RBC protoporphyrin (µg/dL)	30-50	Normal	Increase	Increase
Soluble transferrin receptor (µg/L)	4-9	Increase	Increase	Increase
RBC morphology	Normal	Normal	Normal	Microcytic Hypochromic

Diagnosis of Microcytic Anemia

Tests	Iron Deficiency	Inflammation	Thalassemia	Sideroblastic Anemia
Smear	Micro/hypo	Normal micro/hypo	Micro/hypo with targeting	Variable
SI (µg/dL)	<30	<50	Normal to high	Normal to high
TIBC (µg/dL)	>360	<300	Normal	Normal
Percent saturation	<10	10–20	30–80	30–80
Ferritin (µg/L)	<15	30–200	50–300	50–300
Hemoglobin pattern	Normal	Normal	Abnormal	Normal

Zinc

Second most abundant trace element in the body

The most available dietary sources of zinc **: red meat and fish, Germ and whole bran**

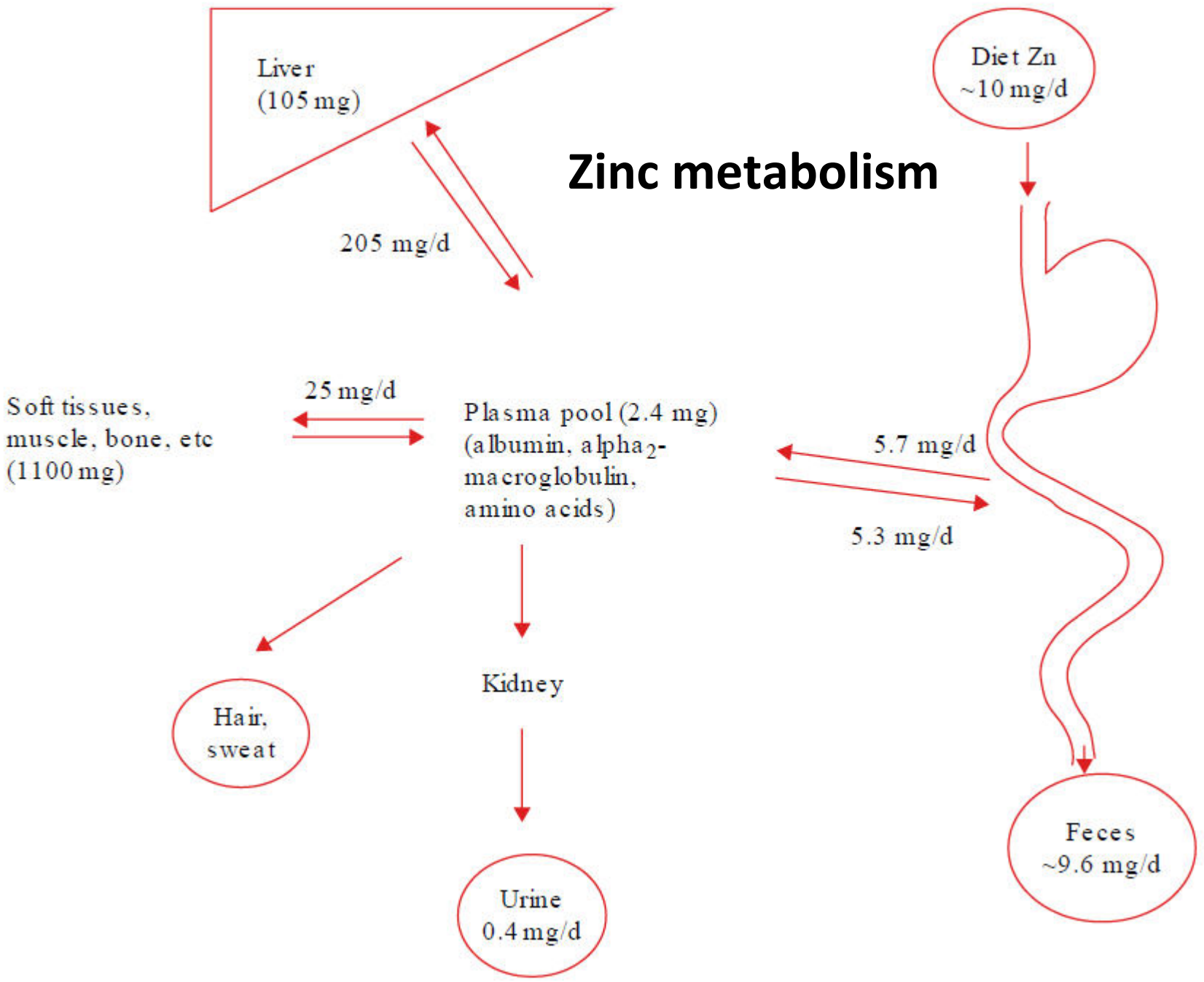
Dietary reference intake

Male: 11 mg/d Female: 8 mg/d

Infants and young children= need small amount

Strict vegetarians= 50% more zinc /d

Zinc in human breast milk is efficiently absorbed because of presence of picolinate and citrate.



Examples of Zinc containing enzymes

Cabonic anhydrase

Alkaline phosphatase

RNA and DNA polymerase

Thymidine kinase and carboxy peptidase

Alcohol dehydranase

Reference interval of zinc

A guidance reference interval: **80-120 μg/dL**

Plasma samples are preferred to serum

Serum concentration is 5% higher than that of plasma

Concentration decreased after food

Concentration is higher in the morning

Clinical deficiency of zinc

Signs and symptoms :

Depressed growth with stunting---cereal based diet

Increased incidence of infection

Diarrhoea

Skin lesions

Alopecia

Acrodermatitits enteropathica

Autosomal recessive inborn error

Mutation on **SLC (solute linked carrier)39a4 gene** on chromosome 8 q24.3

Affects zinc absorption from intestinal mucosa

1. Periorificial dermatitis
2. Alopecia
3. diarrhoea

Role of zinc on immune function

Increase in the activity of serum **thymulin**—
the thymus specific hormone involved in T cell function

Maintain balance develops between Th1 and Th2 helper cells

Increase the lytic activity of natural killer cells

Improve cell mediated immunity

Dietary sources of copper

Organ meats , liver, kidney

Shell fish

Whole grain cereals

Cocoa containing products

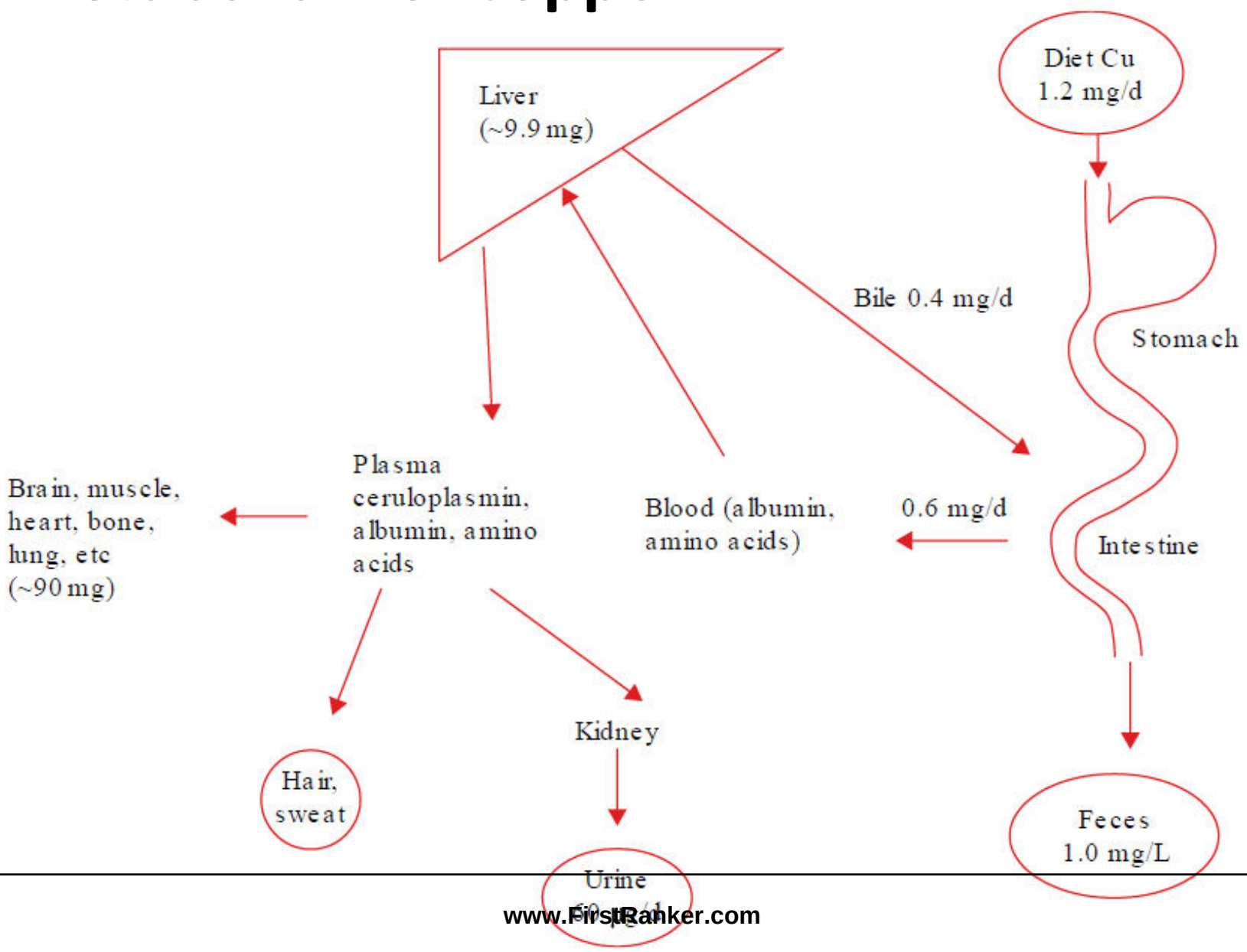
Absorption

The extent of absorption: 20-50%

Absorption reduced by: Zinc, molybdate, iron

Absorption increased by aminoacids

Metabolism of copper



Functions of Copper

In cellular respiration: cytochrome c oxidase-located on mitochondrial membrane

Formation and maintenance of myelin : cytochrome c oxidase

Iron homeostasis: ceruloplasmin

Melanin formation: tyrosinase

Neuro transmitter production : Dopamine β-hydroxylase catalyzes the conversion of dopamine to the neurotransmitter norepinephrine
MAO- catalyzes the metabolism of seroronin
Synthesis of connective tissue: lysyl oxidase- stabilization of extracellular matrix- enzymatic cross linking of collagen and elastin
Protection against oxidants: Superoxide dismutase- protects against free radical damage

Menkes disease

Kinky or steely hair disease

X linked , affects only male infants
Mutations in the gene *ATP7A* gene for a
copper binding P type ATP ase: Responsible for directing the efflux of copper from cells

Copper is not mobilized from the intestine—accumulates
Activities of enzymes are decreased—because of defect of its incorporation into the apoenzyme
Absence of hepatic involvement

Wilson disease

Mutation in a gene encoding a copper binding P type ATPase
Copper fails to be excreted in the bile and accumulates in liver, brain, kidney and RBC
Inhibit the coupling of copper to apoceruloplasmin and leads to low level of ceruloplasmin in plasma
Hemolytic anemia, chronic liver disease, neurologic syndrome

Kayser-Fleisher ring

Liver biopsy should be performed
Treatment:

Major Laboratory tests used in the investigation of diseases of copper metabolism

Test	Normal adult range
Serum copper	10-22µmol/L (70-140µg/dL)
Ceruloplasmin	200-600 mg/L
Urinary copper	<1 µmol (60µg)/24h
Liver copper	20-50 µg/g dry weight

Major Laboratory tests used in the investigation of diseases of copper metabolism

Test	Wilson disease
Serum copper	<8 µmol/L
Ceruloplasmin	<200 mg/L
Urinary copper	>3 µmol/24h
Liver copper	>250 µg/g dry weight

Copper and Anaemia

Interfering iron transport

Part of ALA synthase

Microcytic hypochromic Iron resistant

Selenium

Selenium is an essential element for humans
Constituent of the enzyme **glutathione peroxidse**
The most biologically active compounds contain
Selenocysteine: Selenium is substituted for sulph
in cysteine;
incorporated into protein by specific codon.....
Ingested selenium compounds include
selenate, selenite , selenocysteine,
Selenomethionine
RDA= 55µg/d

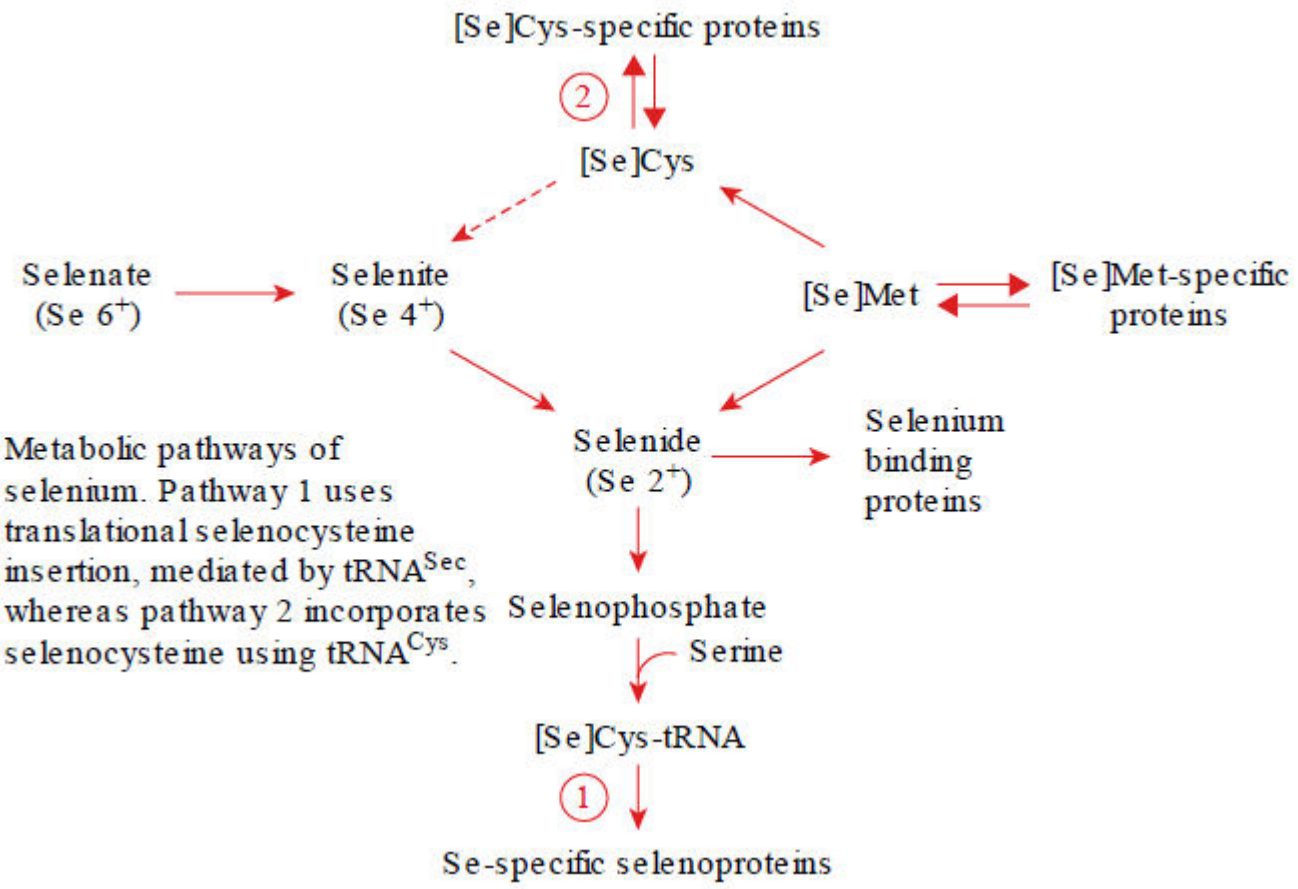
Dietary sources and metabolism of Seleniu

Mainly as selenomethionine from plants

Selenium from Inorganic salts are more
rapidly incorporated than organic sources

50-60% of total plasma selenium- selenoprotein P
30%-- GSHPX-3
Rest- into albumin as selenomethionine
~~Major route of excretion: Urine (20-1000µg/L)~~

Metabolic pathways of selenium



Metabolic pathways of selenium. Pathway 1 uses translational selenocysteine insertion, mediated by $tRNA^{Sec}$, whereas pathway 2 incorporates selenocysteine using $tRNA^{Cys}$.

Functions of Selenium

Glutathione Peroxidase

Remove an oxygen atom from H2O2 and lipid hydroperoxide

1. GSHPx-1 in red cell s, 2. GSHPx-2 in gastrointestina mucosa,
3. blood plasma GSHPx-3,
4. the cell membrane– located GSHPx-4.

Iodothyronine Deiodinase

T4→ T3

Thioredoxin Reductases

Selenoprotein P-transport protein and has antioxidant function

Severe Deficiency

Keshan Disease.
Kashin-Beck Disease

Marginal Deficiencies

Thyroid Function

Immune Function– both cell mediated and B cell function are impai

Reproductive Disorders—necessary for testostereone synthesis and maintenance of sperm viability

Mood Disorders-anxiety, confusion, hostility

Inflammatory Conditions- arthritis, pancreatitis

Viral Virulence—Coxackie virus

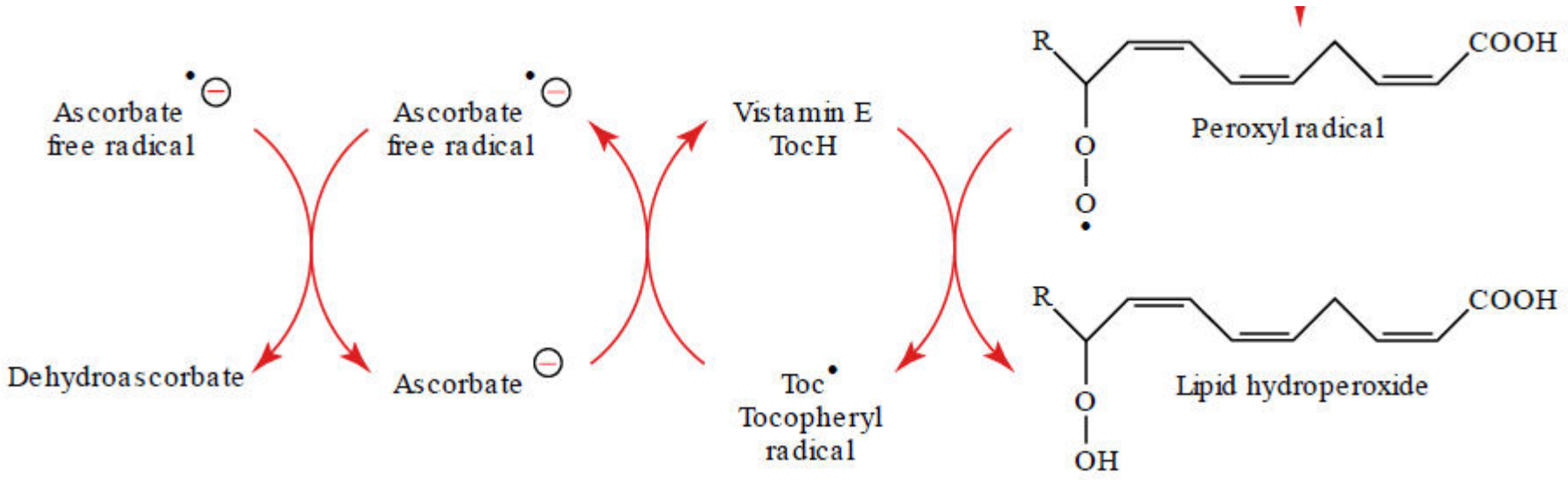
Cancer Chemoprevention

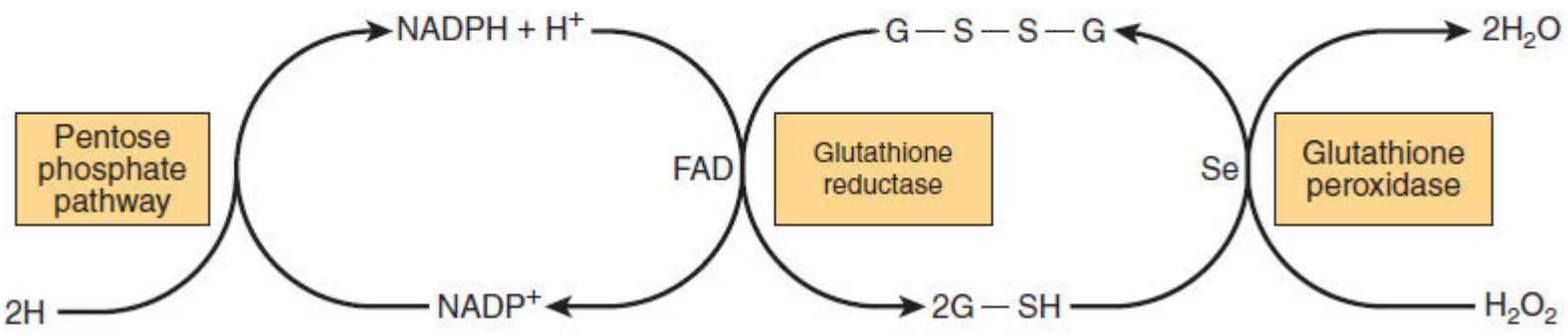
Toxicity of Selenium

Garlic odor
Hair loss
Nail damage
Reference interval: 63-160 µg/L
Selenium depletion: <40µg/L
Tolerable upper limit 400 µg/d

Laboratory assessment: CFAAS (Carbon furnace AAS)
ICP(inductively coupled plasma)-MS

Vitamin E sparing effect of Selenium





Fluoride

Most widely used pharmacologically beneficial trace elements

Supplementation:
Water
Salt
Sugar
Milk

Function of fluoride

The fluoride is exchanged for hydroxil in the crystal structure of apatite, a main component of skeletal bone and teeth.
Stabilizes the regenerating tooth surface.
To reduce decay of the erupting teeth as well as Topical effect on adult teeth.
Pharmacological doses of fluoride may reduce the incidence of bone fracture in patients with osteoporosis.

Absorption, transport, metabolism and excretion of Fluoride

Absorbed from the stomach and the small intestine

Peak increase in blood plasma occurs within 1 hour

Ions are rapidly cleared from plasma into tissues
In exchange with anion e,g. hydoxil, citrate, carbonate
96% of the 2.6 g of total body fluoride is located in bones and teeth
90% of excess fluoride is excreted in urine

Toxicity of Fluoride

Dental fluorosis: The mottling of enamel in the erupting teeth of children
A disfiguring condiition
Caused by ingestion of fluoride containing toothpaste

Skeletal fluorosis: Occupational exposure to inhaled fluoride dust among Cryolite workers during aluminium refining: Bone abnormalities

Laboratory assessment of status of Fluoride

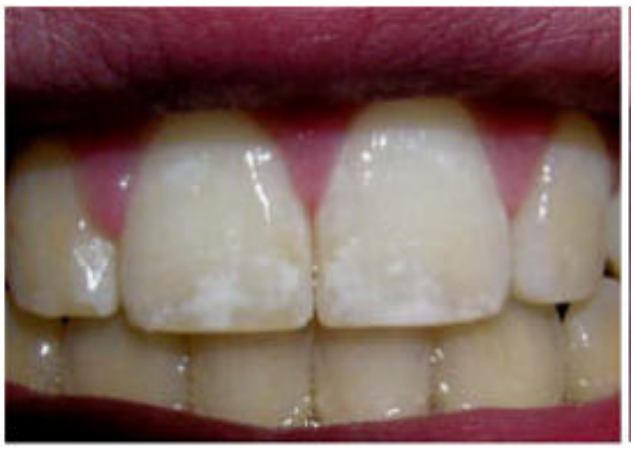
Analysis of drinking water
Determination of fluoride in urine

Direct determination using fluoride specific electrode

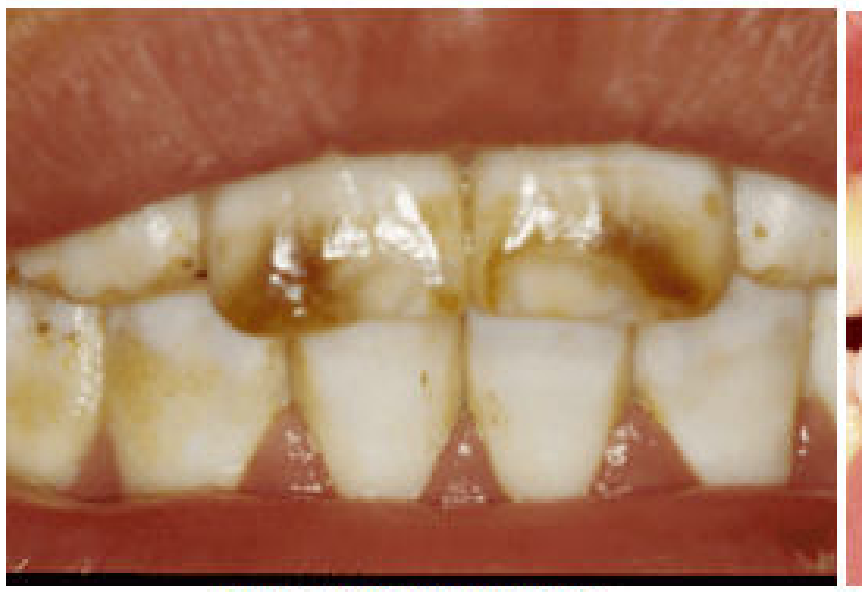
Reference interval of Fluoride

Concentration in body fluids and tissue vary widely

For urine: a guideline interval is: 0.2 – 3.2 mg/L



Mild/Moderate Fluorosis



Moderate/Severe Fluorosis

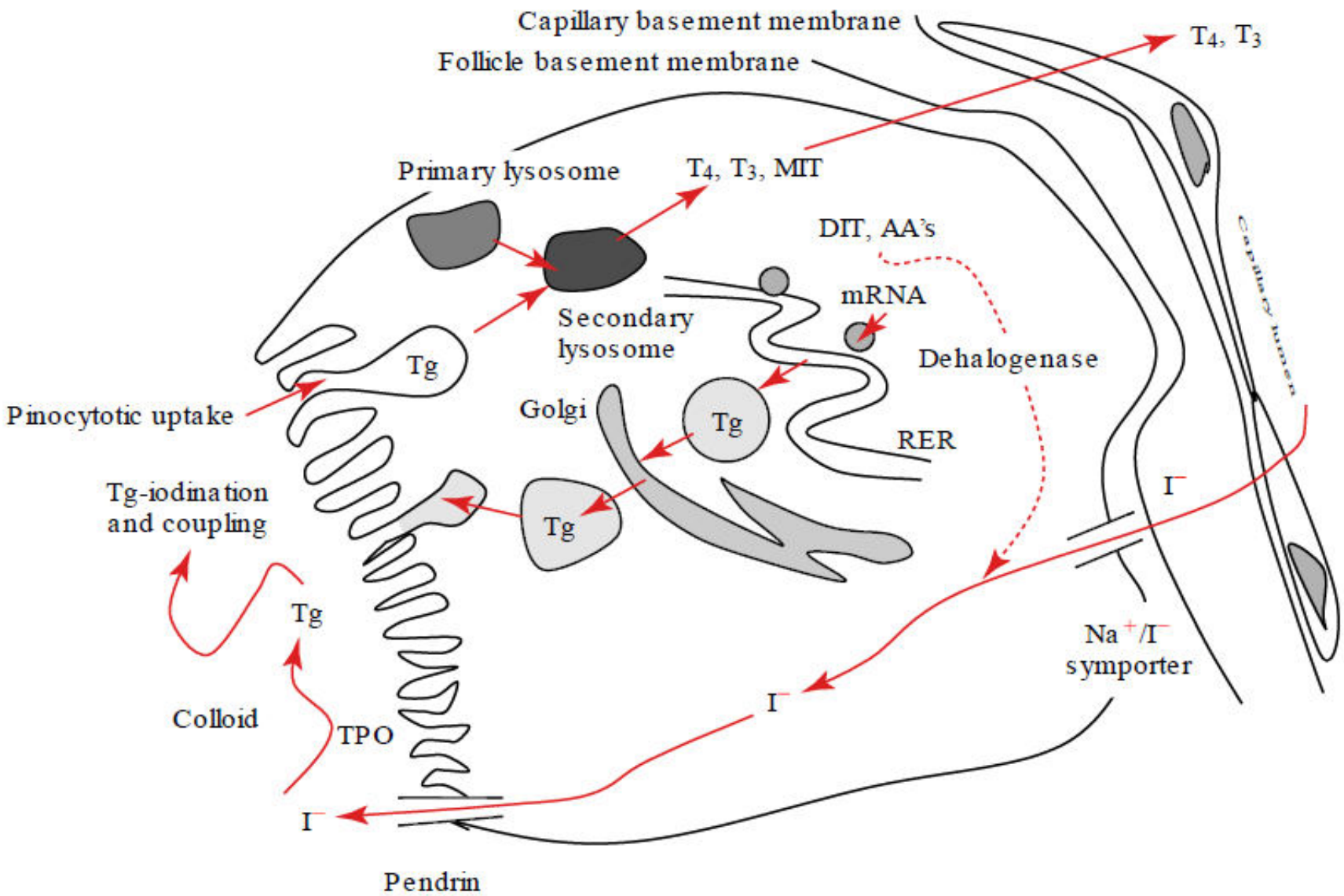
Dental fluorosis

Common sources of dietary iodine

naturally in soil and seawater

Iodized table salt
Cheese
Cows milk
Eggs
Frozen Yogurt
Ice Cream
Iodine-containing multivitamins
Saltwater fish
Seaweed (including kelp, dulse, nori)
Shellfish
Soy milk, Soy sauce
Yogurt

Synthesis o thyroid hormones



Deficiency of iodine

Hypothyroidism

PREGNANCY-RELATED PROBLEMS:
miscarriages, stillbirth, preterm delivery,
congenital abnormalities in their babies

Children of mothers with severe iodine deficiency during pregnancy
mental retardation *(preventable cause)*
problems with growth, hearing, and speech
Cretinism (permanent brain damage, mental retardation,
deaf mutism, spasticity,)

The recommended average daily intake of iodin

Adult: 150 µg/d
children: 90–120 µg/d
pregnant women: 200 µg/d

Urinary iodine is >10 µg/dL in iodine-sufficient populations

MEDIAN POPULATION URINARY IODINE VALUES AND IODINE NUTRITION

MEDIAN URINARY IODINE CONCENTRATION (µg/L)	CORRESPONDING IODINE INTAKE (µg/day)	IODINE NUTRITION
<20	<30	SEVERE DEFICIENCY
20-49	30-74	MODERATE DEFICIENCY
50-99	75-149	MILD DEFICIENCY
100-199	150-299	OPTIMAL
200-299	300-449	MORE THAN ADEQUATE
>299	>449	POSSIBLE EXCESS