Minerals

University Of Fallujah
College Of Medicine

Lecture : (4)

Stage : 2th Stage

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Department: Chemistry and Biochemistry

Date:

Minerals Part 4

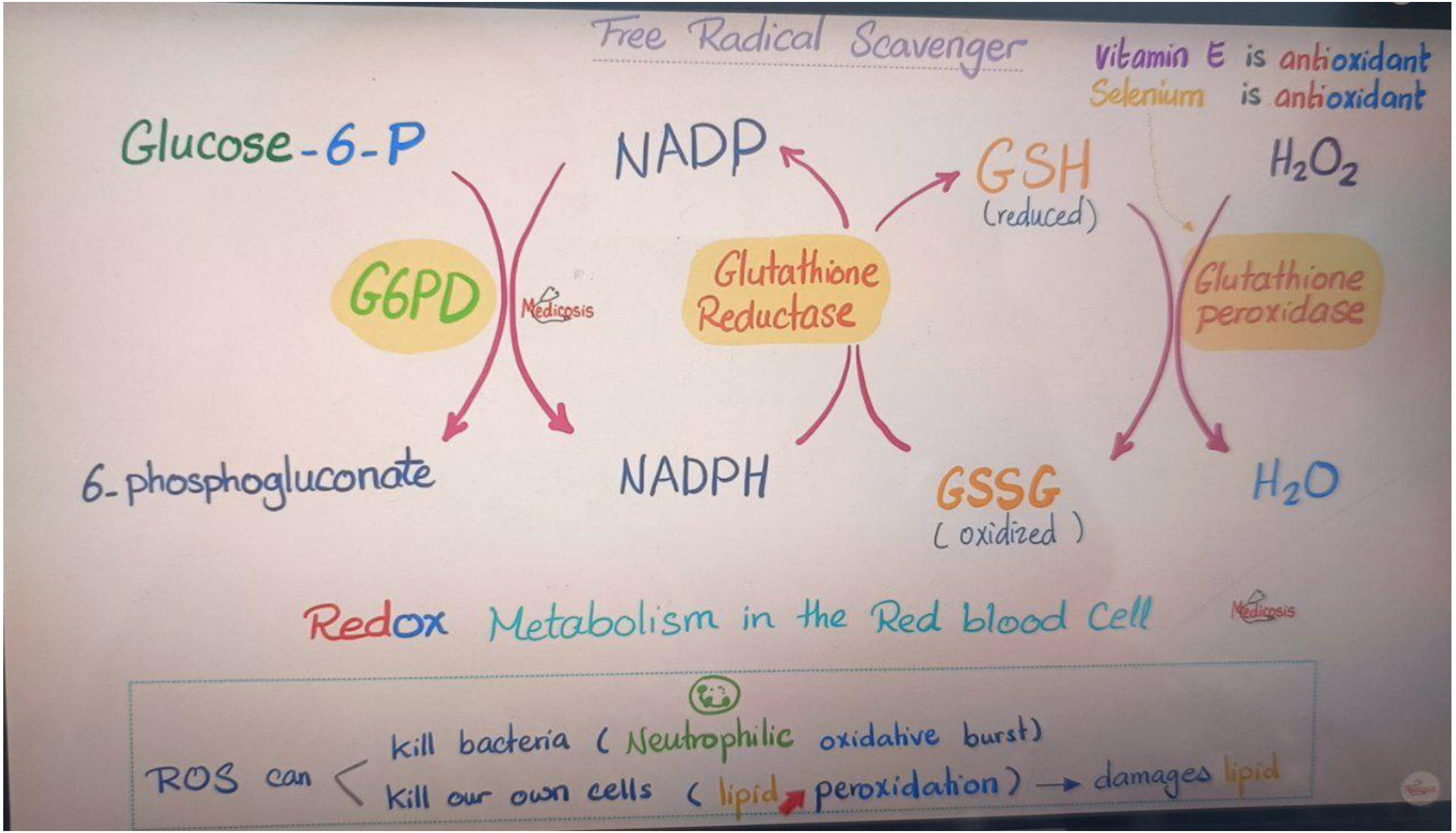
Selenium, Cobalt and Manganese

Learning Objectives

- ❑ Describe the Biological Importance of Each Trace Element
- ❑ Identify Dietary Sources and Requirements
- ❑ Explain the Absorption, Transport, and Storage Mechanisms
- ❑ Summarize Excretion and Homeostatic Regulation
- ❑ Correlate Deficiency and Toxicity States with Biochemical Findings
- ❑ Apply Biochemical Knowledge to Clinical and Laboratory Contexts

❑ Selenium

- Selenium is a trace mineral.
- **Source of Se:** Seafood, meats, Brazil nuts, cereals, poultry and eggs.
- **Body requirement daily:** 50-70 mcg/day.
- **Normal level of Se in blood:** 70to 150 ng/mL.
- **Function:** it is essential component of various enzymes and proteins to make DNA, protect against cell damage and infections, It is good antioxidant; and its action is complementary to Vitamin E. involved in reproduction and metabolism of thyroid hormones


Free Radical Scavenger
Vitamin E is antioxidant
Selenium is antioxidant
Glucose-6-P
NADP
GSH
(reduced)
H_2O_2
G6PD
Medicosis
Glutathione Reductase
Glutathione peroxidase
6-phosphogluconate
NADPH
GSSG
(oxidized)
H_2O
Redox Metabolism in the Red blood Cell
Medicosis
ROS can
Kill bacteria (Neutrophilic oxidative burst)
Kill our own cells (lipid peroxidation) → damages lipid

❑ Absorption of Selenium

- **Absorption:** Selenium is notable for its high intestinal absorption efficiency. The specific compound form influences the exact rate:
- **Selenomethionine (Organic):** ~90% absorbed. This form utilizes the same transport mechanisms as the amino acid methionine.
- **Selenite/Selenate (Inorganic):** ~80% absorbed.

- **Metabolic Activation:** Simply absorbing selenium is not enough.

The critical step that controls its overall bioavailability is its subsequent conversion inside cells into the biologically active form, selenocysteine, which is incorporated into essential selenoproteins.

- **Excretion:** The kidneys are the principal organs responsible for regulating selenium levels, with excess primarily excreted in the urine.

❑ Selenoproteins

- Selenium's biological role is executed through selenoproteins, which are vital for combating oxidative stress and regulating metabolism.
- **Antioxidant Defense:**
  - **Glutathione Peroxidases (GPx):**
    - **Function:** Catalyze the reduction of hydrogen peroxide and lipid hydroperoxides to water and harmless alcohols.
    - **Mechanism:** They use **glutathione (GSH)** as a reducing agent, converting it to its oxidized form (GSSG). This is a primary defense against oxidative damage.
- **Redox System Regeneration:**
  - **Thioredoxin Reductase (TR):**
    - **Function:** Regenerates reduced thioredoxin, which is crucial for maintaining other antioxidant proteins and controlling transcription factors.
- **Thyroid Hormone Metabolism:**
  - **Iodothyronine Deiodinases (DIO):**
    - **Function:** Activate thyroid hormone by converting thyroxine (T4) to the biologically active triiodothyronine (T3).

❑ Se deficiency

- Two conditions are associated with severe selenium deficiency:
  - **Keshan disease**, a type of cardiomyopathy, or disease of heart muscle.
  - **Kashin-Beck disease**, a form of osteoarthritis (degenerative joint disease.(

❑ Groups with a Higher Risk of Deficiency:

✓ **Individuals in Low-Selenium Regions:**
- Especially those relying on a **local, plant-based diet**, as crops grown in selenium-poor soil do not provide adequate levels.

✓ **Patients with HIV/AIDS:**
- The disease can cause **chronic diarrhea, malabsorption, and reduced appetite**, all of which contribute to poor selenium status.

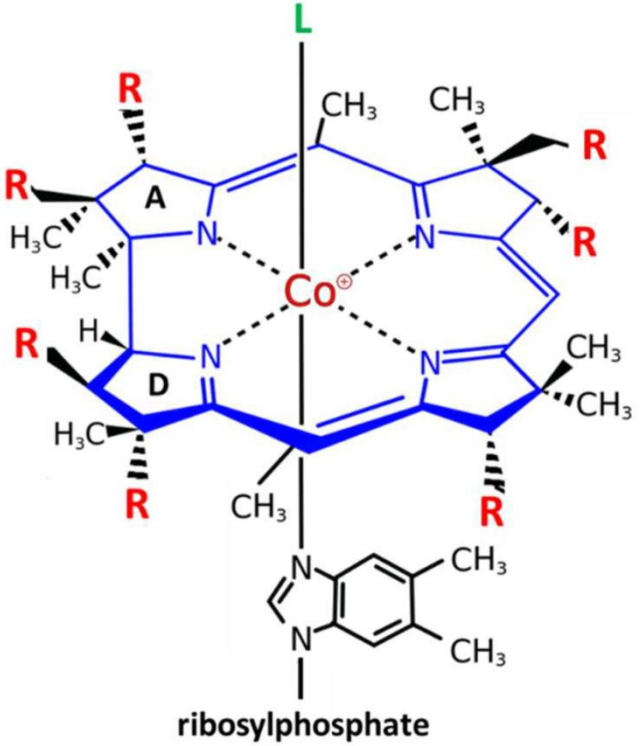
✓ **Patients Undergoing Hemodialysis for Kidney Failure:**
- **Dialysis:** The mechanical filtration process can **directly remove selenium** from the bloodstream.
- **Diet:** They are often placed on a **highly restricted diet**, which further limits their selenium intake.

❑Toxicity of Selenium

- Chronically high intakes of selenium can lead to health problems.
  - **Symptoms:**
- **Metallic taste, bad breath, nausea and diarrhea**
- **Hair loss**
- **Nail brittleness or discoloration**
- **Skin rash or lesions and flushing**
- **Fatigue**
- **Muscle tenderness**
- **Heart attack**
- **Respiratory distress**
- **Kidney failure**

Cobalt

- **Body requirement daily:** 1.5 micrograms of vitamin B12 / day.
- **Normal level of Co in blood:** <1.8 µg/L.
- **Function:** Co is the active center of a group of compound called cobalamins, Vitamin B.12



❑ Cobalt

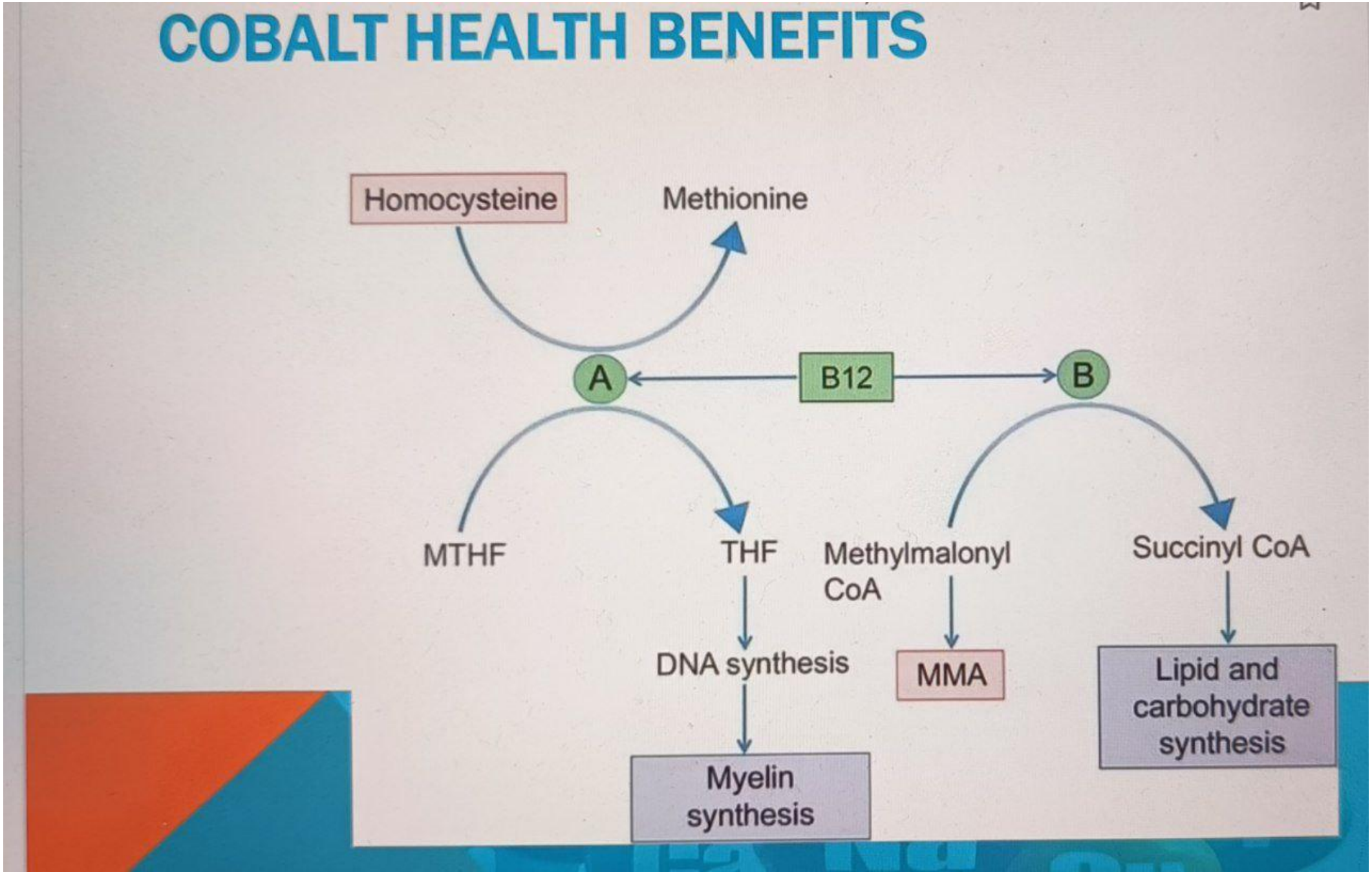
Cobalt (Co) Pharmacokinetics

- **Absorption:** Can occur via the:
  - Gastrointestinal tract
  - Lungs (inhalation)
  - Skin (dermal contact)
- **Distribution & Function:**
  - Its essential function is as the core component of **Vitamin B12 (Cobalamin)**.
  - Transported in the blood, frequently bound to **albumin**.
  - Distributed throughout the body, with the highest concentrations stored in the **liver** and **kidneys**.
- **Excretion:**
  - Primarily eliminated via the **urine** and **feces**.

COBALT IN THE BODY

Absorption	• 5-40% through Gut • 30% through Lungs
Storage	• Liver • Spleen • Kidney • Muscles • Fat
Excretion	• 80% through Urine • Remaining through Faeces

COBALT HEALTH BENEFITS



❑Pathology of Vitamin B12 Deficiency

- **I. Hematological Complication: Megaloblastic Anemia**
- **Pathophysiology:** Disruption of DNA synthesis leads to ineffective production of large, immature red blood cells (megaloblasts).
- **Key Symptoms:**
  - Severe fatigue and generalized weakness
  - Unexplained weight loss
  - Glossitis (inflamed, sore tongue)
- **II. Neurological Complication: Subacute Combined Degeneration (SCD)**
- **Pathophysiology:** Demyelination and degeneration of the spinal cord, primarily affecting the **dorsal** (sensory) and **lateral** (motor) columns.
- **Key Symptoms:**
  - **Peripheral:** (paresthesia).
  - **Motor:** Weakness, poor coordination, and ataxia (balance problems).
  - **Cognitive/Psychiatric:** Memory impairment, depression, and irritability.
- **III. Effects on Infants**
- Failure to thrive
- Significant developmental delay and regression

❑ Manganese (Mn)

- **Biological Functions of Manganese**
- Manganese acts as an essential **cofactor** for numerous enzymes through two primary mechanisms:

- **Enzyme Activator:** Directly binds to and activates enzymes.

- **Metalloenzyme Component:** A structural and functional part of specific enzymes.

❑ Enzyme activator

- Manganese activates enzymes responsible for the utilization of: biotin, thiamin, vit C and choline.
- It acts as a **catalyst in the synthesis of fatty acids and cholesterol**, facilitates **protein and carbohydrate metabolism**, and plays a key role in the **production of sex hormones**..

❑ Manganese Metalloenzymes and Their Functions

- **Arginase:** Primarily in the liver, it catalyzes the final step in the **urea cycle**, converting arginine into urea and ornithine to eliminate toxic ammonia.

- **Glutamine Synthetase:** Crucial for **nitrogen metabolism**, it synthesizes the amino acid glutamine from glutamate and ammonia.

- **Phosphoenolpyruvate Carboxykinase (PEPCK):** A key enzyme in **gluconeogenesis**, it helps convert precursors like lactate and amino acids into new glucose, thereby regulating blood sugar levels.

- **Manganese Superoxide Dismutase (Mn-SOD):** Located in the mitochondria, it is a vital **antioxidant** that protects cells from oxidative damage by converting superoxide free radicals into hydrogen peroxide.

❑ Mn- Toxicity Symptoms

- Most cases of manganese toxicity are seen in the industrial workers who are exposed to manganese dust.
- These workers develop nervous system problems similar to Parkinson's disease.

- Manganese toxicity is most likely to occur in people with chronic liver disease, as the liver plays important role in eliminating excess manganese from the body [in addition it can be excreted in a significant amounts through sweat.

❑ Hypomanganesemia:

- **Cause:**

Usually results from *inadequate intake*, *malabsorption*, or *prolonged parenteral nutrition* lacking manganese supplementation.
Can also occur in genetic transporter defects (e.g., mutations in *SLC39A8*).

- **Early Effects:**

Reduced activity of manganese-dependent enzymes such as **superoxide dismutase (Mn-SOD)**, **arginase**, and **pyruvate carboxylase**.
Leads to impaired antioxidant defense and energy metabolism.

- **Clinical Manifestations:**

Skeletal abnormalities (bone deformities, poor growth).
Neurological symptoms such as tremors, ataxia, or seizures.
Metabolic disturbances, including altered glucose and lipid metabolism.