# Minerals

**University Of Fallujah**
**College Of Medicine**

**Lecture : ( 3 )**

**Stage : 2th Stage**

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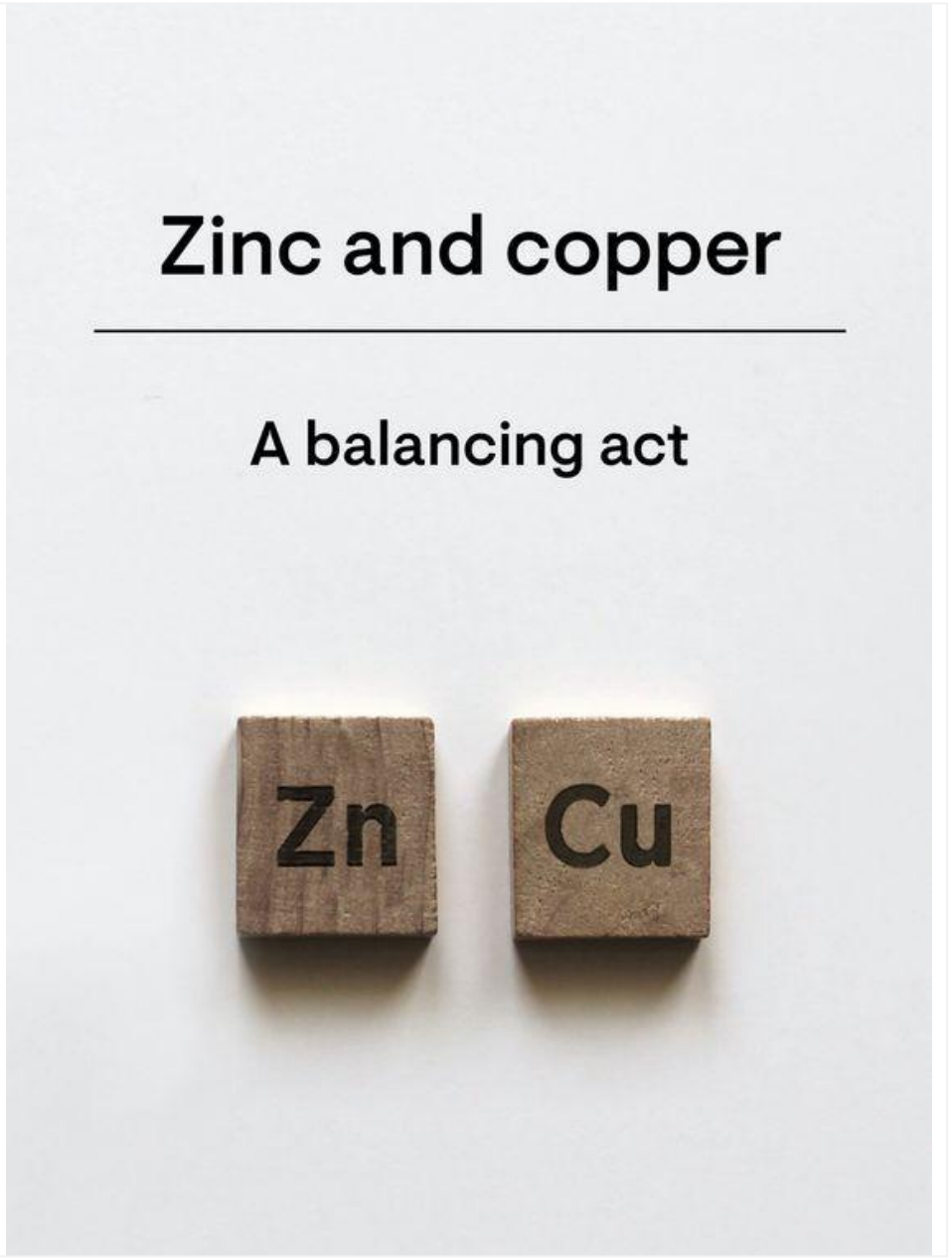
**Date:**

# Zinc and Copper



# *Learning Objectives*

- ❑ Describe the Biological Importance
- ❑ Outline the Sources and Requirements
- ❑ Explain the Absorption and Transport
- ❑ Summarize the Storage and Excretion
- ❑ Discuss the Clinical Aspects
- ❑ Apply Biochemical Understanding to Clinical Scenarios

- **Zn :** plays important structural and catalytic functions in the body.
- Zinc fingers are super secondary structures in proteins (for example, transcription factors) that bind to DNA and regulate gene expression., Hundreds of enzymes require Zn for activity.

- Examples include alcohol dehydrogenase, which oxidizes ethanol to acetaldehyde.
- **Carbonic Anhydrase:** Central to the bicarbonate buffer system for maintaining blood pH.
- **Porphobilinogen Synthase (ALAD):** Essential for heme synthesis; its inhibition by lead (which displaces zinc) is a key mechanism of lead poisoning.
- **Superoxide Dismutase (Cu/Zn-SOD):** A major antioxidant enzyme that requires both copper and zinc to neutralize harmful free radicals

# ❑ Zinc (Zn)

- **Source of Zn:** oysters, red meat, beans, nuts, seafood and dairy products .

- **Body requirement daily:** 10 up to 20 mg/ day.

- **Normal level of Zn in blood:** 0.66 to 1.10 mcg/mL. or (66-110)mg/d

## ❑Sites and Mechanisms of Absorption

- **Primary site:** Jejunum (and to a lesser extent ileum).
- **Mechanisms:**
  - ✓ **Carrier-mediated transport:** via *ZIP4* (apical transporter on enterocyte brush border).
  - ✓ **Intracellular binding:** to metallothionein (MT), which regulates intracellular zinc levels.
  - ✓ **Basolateral export:** via *ZnT1* transporter into the portal blood.

## ❑Factors Affecting Absorption

- **Enhancers:**
- Animal proteins (cysteine, histidine)
- Organic acids (citric acid)
- Adequate zinc status (upregulates ZIP4)
- **Inhibitors:**
- Phytates (in cereals, legumes)
- Iron and calcium in high doses
- Chronic alcohol intake
- Malabsorption syndromes (e.g., celiac disease)

## ❑Zinc Deficiency: Causes and Symptoms

- **Causes:**
  - **Drugs:** Certain medications, like penicillamine, can bind to (chelate) zinc and cause deficiency.
  - **Genetic Disorder:** A rare genetic defect in the intestinal zinc transporter causes **Acrodermatitis Enteropathica**, which prevents zinc absorption.
- **Symptoms:** The consequences of severe zinc deficiency include:
  - Dermatitis (skin rashes, especially around extremities)
  - Diarrhea
  - Impaired growth and development in children
  - Weakened immune system
  - Vision problems (due to zinc's role in Vitamin A metabolism)

# ❑ Zn- deficiency

**Clinical feature:**

- Growth retardation, delayed sexual and bone maturation, skin lesion, diarrhoea, alopecia, impaired appetite, ↑ susceptibility to infections.

❑ **Laboratory Assessment and Pre-Analytical Considerations:**

- **Primary Biomarker:** The definitive biochemical test for assessing zinc status is the measurement of **plasma or serum zinc concentration**.
- **Critical Pre-Analytical Requirement:** Sample integrity is paramount. The specimen **must be collected free from hemolysis**.
- **Rationale:** Erythrocytes have a high intracellular zinc concentration (~10x that of plasma). Hemolysis releases this cellular zinc, leading to a **falsely elevated or normal** result, which can mask a true deficiency and produce a clinically misleading report.

# ❑ Groups at Risk of Zinc Inadequacy

- **People with gastrointestinal and other diseases** such as ulcerative colitis, GI-surgery, malabsorption syndrome, chronic liver disease, chronic renal disease, sickle cell disease, diabetes, malignancy and chronic diseases all lead to increase Zn loss.
- **Vegetarians**
- **Pregnant and lactating women:** due to high fetal requirements for Zn.
- **Older infants (**aged 7–12 months**) who are exclusively breastfed:**
- **People with sickle cell disease:** because RBCs are continuously being broken down and they lose Zn.
- **Alcoholics:** up to 50% of alcoholics have low Zn status because ethanol consumption decreases intestinal absorption and increases urinary excretion.

# ❑ Copper

## ❑ Copper (Cu) in Human Nutrition and Health

### 1. Dietary Sources

Copper is obtained from a variety of dietary sources, including:

- Organ meats (e.g., liver)
- Shellfish
- Whole grains and cereals
- Nuts and seeds
- Legumes
- Dark chocolate

### 2. Body Requirements & Normal Levels

**Recommended Dietary Allowance (RDA):**

Adults: **900 µg/day**

Infants (at birth): ~200 µg/day

**Normal Serum/Plasma Concentration: 63.5 – 158.9 µg/dL**

- **Biological Functions**
  Copper serves as an essential cofactor for numerous enzymes involved in critical physiological processes:
- **Energy Production:** Key component of cytochrome c oxidase in the mitochondrial electron transport chain.
- **Iron Metabolism:** Required by ceruloplasmin for the oxidation and mobilization of iron for hemoglobin synthesis.
- **Connective Tissue Formation:** Essential for lysyl oxidase in the cross-linking of collagen and elastin.
- **Antioxidant Defense:** Central to the function of superoxide dismutase (Cu/Zn-SOD), which neutralizes superoxide free radicals.
- **Neurotransmitter Synthesis:** Required by dopamine β-hydroxylase for the production of norepinephrine.
- **Other Roles:** Melanin production (pigmentation), immune function, and regulation of gene expression.

| Cu-REQUIRING ENZYME | FUNCTION |
| --- | --- |
| *Cytochrome c oxidase* | Transfers electrons from cytochrome c to oxygen in the ETC (see p. 75) |
| *Dopamine β-hydroxylase* | Hydroxylates dopamine to norepinephrine (see p. 286) |
| *Ferroxidases* | Oxidize iron (see. p. 403) |
| *Lysyl oxidase* | Forms cross-links in collagen and elastin (see pp. 48–49) |
| *Tyrosinase* | Synthesizes melanin (see p. 288) |
| *Superoxide dismutase* (nonmitochondrial form; also requires zinc) | Converts superoxide to hydrogen peroxide (see p. 148) |

# ❑ Copper homeostasis

## 1. Absorption

- Approximately 40% of dietary copper is absorbed, primarily in the **stomach and duodenum**.
  - The efficiency of absorption is influenced by:
    - ✓ The chemical form of copper in the diet.
    - ✓ The presence of **dietary antagonists**, such as high levels of **zinc, iron, or calcium**, which can compete for absorption and reduce copper uptake.

## 2. Transport and Distribution

- Upon absorption, copper is transported in the **portal blood** bound to **albumin** and other small molecules for delivery to the liver.
- In the **liver**, copper is incorporated into **ceruloplasmin**, its primary transport protein.
- Approximately **90-95% of circulating copper** in the blood is bound to ceruloplasmin, which serves as the main mechanism for distributing copper to peripheral tissues.

# ❑ Groups at Risk of Copper Inadequacy

- **People with Celiac Disease:** due to intestinal malabsorption.
- **People taking high doses of Zinc supplements:** high dietary intakes of Zn can interfere with copper absorption.
- **People with Menkes Disease**

# ❑ Menke’s syndrome

- Menkes’ steely hair syndrome is a sex-linked inherited metabolic disorder in which serum and tissue copper levels are very low due to a defect in absorption.

## ❑ Cause and Genetics:

- Inheritance: It is an X-linked recessive disorder. This means the defective gene is located on the X chromosome.
- **Gene**: The mutation is in the ATP7A gene.
- Mechanism: This gene is responsible for transporting copper from the intestines into the bloodstream and then across the blood-brain barrier. A defect here leads to severe copper deficiency, despite adequate intake.

# ❑ Copper and Health

- Two diseases in which copper might play a role: cardiovascular disease (CVD) and Alzheimer's disease.

1. **Cardiovascular Disease:** Copper deficiency leads to changes in blood lipid levels, a risk factor for atherosclerotic CVD.
2. **Alzheimer's Disease:** dietary copper deficiency plays a role in the etiology and pathophysiology of Alzheimer's disease.

# ❑ Copper toxicity

- Chronic exposure to high levels of copper can result in liver damage and gastrointestinal symptoms (e.g., abdominal pain, cramps, nausea, diarrhea, and vomiting).
- **Wilson's disease:** is an inherited metabolic disorder affecting copper metabolism .

  although it's a ceruloplasmin protein deficiency, the copper that should be attached is in the serum and liver due to blockage of its (Cu) excretion from the liver to bile or serum،

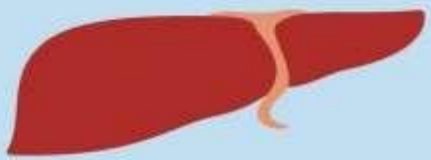
  this accumulation in liver can go into hepatitis, then a fibrosis, then a cirrhosis.

- **How is it a genetic deficiency and the cause is a deficiency in the ceruloplasmin protein????"**

- **Inheritance: Autosomal Recessive** (both parents must be carriers).
- **Defective Gene:** The **ATP7B** gene on chromosome 13.
- **The Job of the ATP7B Protein:** It acts as a **"Copper Transport Pump"** in the liver cells (hepatocytes).
- Its crucial roles are:
  - To load copper onto **Ceruloplasmin** for safe transport in the blood.
  - To pump excess copper into the **bile** for elimination from the body.

# Symptoms of Wilson Disease

## Liver



Abdominal pain.

Dark urine or a light stool color.

Jaundice.

## Brain

Mood changes.

Anxiety and depression.

Disruptive thoughts and feelings.

## Eye

Rings around the edge of your corneas.

## Nervous system

Tremors.

Stiff muscles.

Problems with coordination.

# Thank you