INE INSTITUTE OF NUTRITIONAL ENDOCRINOLOGY

# Micronutrients: Selenium

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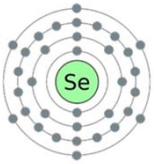
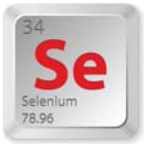
## Selenium General Info

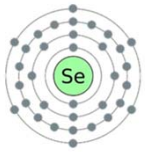
- ✓Essential micromineral; essential in small amounts, toxic at high levels
- ✓Very frequently deficient in modern diet
- ✓Vital for over a number of key enzymes in human body
  - ➢Selenoproteins
  - ➢5-prime deiodinase



## What We Will Cover

- ✓ Why selenium is so important
- ✓ Signs and symptoms of deficiency
- ✓ What happens when excess is consumed
- ✓ Where to find selenium in food supply
- ✓ When to supplement and best types
- ✓ Factors that help or hinder absorption
- ✓ When to use lab testing



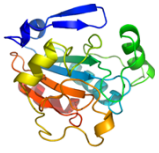

## Selenoproteins

- ✓ **25 Selenoproteins identified**
- ✓ **Selenoprotein synthesis**
  - ➢ Selenocysteine is incorporated into amino acid sequence
  - ➢ Forms a functional protein
- ✓ **Only half of the 25 have the metabolic function identified**
  - ➢ Glutathione peroxidases
  - ➢ Thioredoxin reductase
  - ➢ Iodothyronine deiodinases (thyroid hormone deiodinases)
  - ➢ Selenoprotein P
  - ➢ Selenoprotein W
  - ➢ Selenophosphate synthetase
  - ➢ Methionine-R-sulfoxide reductase
  - ➢ 15 kDA selenoprotein (Sep15)
  - ➢ Selenoprotein V
  - ➢ Selenoprotein S

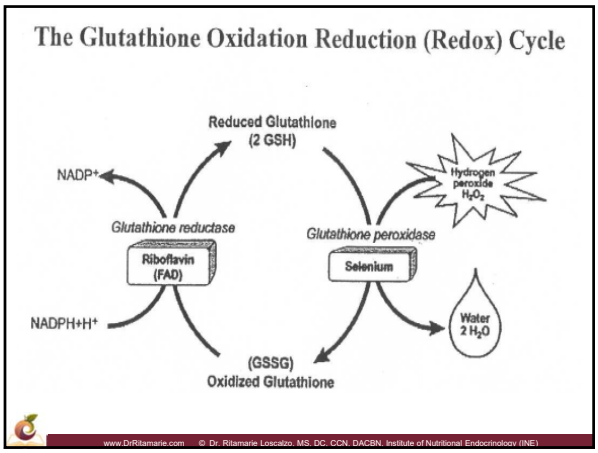



## Glutathione Peroxidases

- ✓ Five selenium-containing glutathione peroxidases (GPx) have been identified
  - ➢ Cellular or classical GPx
  - ➢ Plasma or extracellular GPx
  - ➢ Phospholipid hydroperoxide GPx
  - ➢ Gastrointestinal GPx
  - ➢ Olfactory GPx

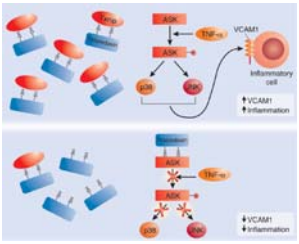


- ✓ Each GPx is a distinct selenoprotein
  - ➢ Reduce potentially damaging reactive oxygen species, such as hydrogen peroxide and lipid hydroperoxides, to water and alcohol by coupling their reduction with the oxidation of glutathione
  - ➢ Sperm mitochondrial capsule selenoprotein protects developing sperm from oxidative damage and later forms a structural protein required by mature sperm




## Thioredoxin Reductase

- ✓ Regeneration of thioredoxin and several antioxidants along with Vitamin C
- ✓ Reduced thioredoxin is important for regulating cell growth and viability

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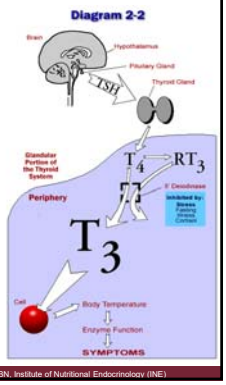
## Iodothyronine Deiodinases

- ✓ The thyroid gland
  - ➢ T3 is created by removal of one iodine atom from T4 in a reaction caused by selenium-dependent deiodinase enzymes
- ✓ Three different selenium-dependent iodothyronine deiodinases (types I, II, and III)
  - ➢ Activate and inactivate thyroid hormone by acting on T3, T4, or other thyroid hormone metabolites
- ✓ Selenium is essential for normal development, growth, and metabolism

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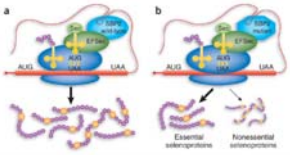
## Selenoprotein P

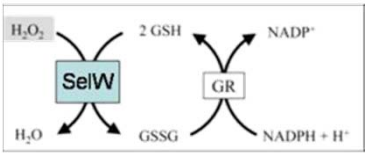
- ✓ Found in plasma
- ✓ Associated with vascular endothelial cells (cells that line the inner walls of blood vessels)
- ✓ Primary function is transport for selenium
- ✓ Also an antioxidant that protects endothelial cells from damage induced by such compounds as peroxynitrite, a reactive nitrogen species (RNS)






## Selenoprotein W

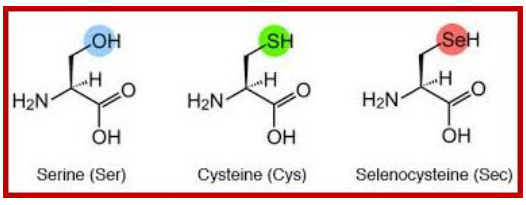
- ✓ Found in muscle
- ✓ Plays a role in muscle metabolism
- ✓ There is about 80% commonality of this selenoprotein with six different species of animals





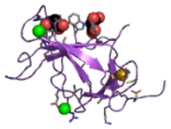

## Selenophosphate Synthetase

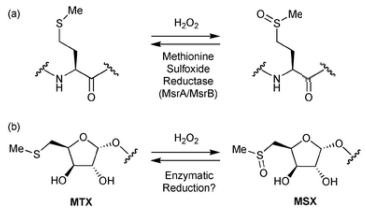
- ✓ Required by the genetic code to incorporate selenocysteine into selenoproteins



## Methionine-R-sulfoxide Reductase

- ✓ Reduction of oxidized methionine residues, using thioredoxin as a reductant
- ✓ Two forms of this selenoprotein

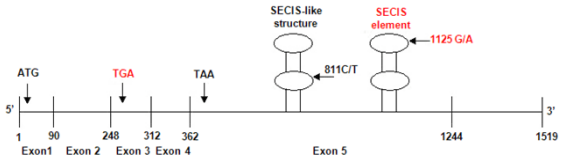







## 15 kDA Selenoprotein

- ✓ Mammalian protein
- ✓ Located in the endoplasmic reticulum
- ✓ Has a redox function and is also implicated in cancer prevention



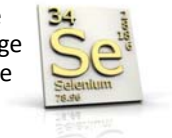



## Selenoproteins V and S

- ✓ **Selenoprotein V:** In testes for spermatogenesis
- ✓ **Selenoprotein S:** Also involved in inflammatory and immune responses

## Antioxidant Nutrient Interaction with Selenium

- ✓**Copper and zinc:** Superoxide dismutase
- ✓**Iron:** Catalase
- ✓**Vitamin C:** Thioredoxin reductase maintains the antioxidant function of vitamin C by catalyzing its regeneration from its oxidized form, dehydroascorbic acid
- ✓**Vitamin E (α-tocopherol):** Limits the oxidation of lipids, preventing damage from vitamin E deficiency in oxidative stress






## Seelnium and Iodine Interactions

- ✓Selenium deficiency may exacerbate the effects of iodine deficiency
- ✓Iodine is essential for the synthesis of thyroid hormone
  - ➢Selenium supplementation decreases plasma T4
  - ➢Increased deiodinase activity
  - ➢Increased conversion of T4 to T3




## Selenium Deficiency

- ✓Results in decreased activity of the glutathione peroxidases and other thioredoxin reductase and thyroid deiodinases
- ✓Isolated selenium deficiency does not usually result in obvious clinical illness
- ✓Selenium-deficient individuals appear to be more susceptible to additional physiological stresses

## Risks of Selenium Deficiency

- ✓ Chronically ill people who receive total parenteral nutrition without added selenium for prolonged periods of time
- ✓ People who have had a large portion of the small intestine surgically removed
- ✓ Those with severe gastrointestinal problems, such as Crohn's disease ➔ Impaired absorption
- ✓ Specialized medical diets used to treat metabolic disorders, such as phenylketonuria (PKU), are often low in selenium




## Selenium Deficiency and Kashin-Beck Disease

- ✓ Characterized by the degeneration of articular cartilage between joints (osteoarthritis)
- ✓ Associated with selenium-deficient status
- ✓ Affects children between the ages 5 and 13 years
- ✓ Severe forms of the disease may result in joint deformities and dwarfism



## Selenium Deficiency and Immune Function

- ✓ Selenium supplementation
  - ➢ Stimulates the immune response
  - ➢ 200 mcg/day of selenium as sodium selenite enhanced immune cell response to foreign antigens
- ✓ Plays a role in regulating the expression of cell-signaling molecules called cytokines, which orchestrate the immune response
- ✓ IV sodium selenite used in alternative cancer centers

## Selenium Deficiency and Viral Infection

- ✓ Enhanced progression of some viral infections
- ✓ Oxidative stress induces changes in the expression of some viral genes
- ✓ Cellular glutathione peroxidase protects against myocarditis resulting from mutations in the genome of a previously benign virus
- ✓ Decreased activity of glutathione peroxidase
  - ➢ Increases oxidative damage and the likelihood of mutations in the viral genome



## Selenium and Cancer

- ✓ Selenium supplementation
  - ➢ At high levels reduces the incidence of cancer
  - ➢ Significantly reduces tumor incidence
  - ➢ Methylated forms of selenium are the active species against tumors
- ✓ Low plasma selenium concentrations
  - ➢ Even greater risk of liver cancer
  - ➢ Associated with an increased risk of lung cancer
- ✓ Low dietary selenium intake
  - ➢ Associated with increased risk of prostate cancer
  - ➢ IV sodium selenite used as part of alternative cancer treatment

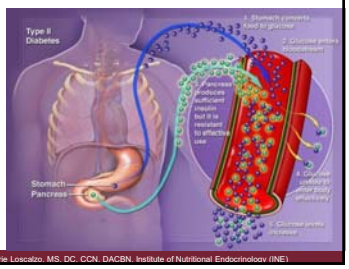


## Selenium Deficiency and Cardiovascular Disease

- ✓ Optimizing selenoenzyme activity
  - ➢ Decreases the risk of cardiovascular disease
    - Decreases lipid peroxidation
    - Influences the metabolism of cell-signaling molecules known as prostaglandins
- ✓ Low levels of selenium increases the risk of cardiovascular disease

## Selenium Deficiency and Type 2 Diabetes Mellitus

- ✓ Insufficient dietary: can interfere with the body's ability to effectively use insulin
- ✓ Selenium can promote diabetes
- ✓ Supplementary selenium decreases risk






## Selenium Deficiency and HIV/AIDS

- ✓ Interaction between selenium and the HIV that causes AIDS
- ✓ Declining selenium levels in HIV-infected individuals
  - ➢ Sensitive markers of disease progression and severity
  - ➢ Even before malnutrition becomes a factor
  - ➢ Associated with a significantly increased risk of death from HIV
- ✓ Adequate selenium nutritional status
  - ➢ May increase resistance to HIV infection
    - Enhances the function of T cells
    - Modifies T cell production of cytokines
- ✓ In HIV infection, increased oxidative stress appears to favor viral replication
  - ➢ Activates specific transcription pathways
  - ➢ Selenium plays an important role in decreasing oxidative stress in HIV-infected cells
  - ➢ Suppresses the rate of HIV replication
- ✓ HIV may be capable of incorporating host selenium into viral selenoproteins that have glutathione-peroxidase activity
- ✓ The immune system and the activity of the virus are affected by selenium nutritional status




## Selenium Excess

- ✓ Garlic breath
- ✓ Nausea
- ✓ Diarrhea
- ✓ Skin rashes
- ✓ Irritability
- ✓ Metallic taste in the mouth
- ✓ Brittle hair or nails
- ✓ Loss of hair or nails
- ✓ Discolored teeth
- ✓ Nervous system problems

## Recommended Dietary Allowance

Based on the amount of dietary selenium required to maximize the activity of the antioxidant enzyme glutathione peroxidase in plasma

**Table 1: Recommended Dietary Allowances (RDAs) for Selenium [6]**

| Age | Male | Female | Pregnancy | Lactation |
|---|---|---|---|---|
| Birth to 6 months | 15 mcg* | 15 mcg* | | |
| 7–12 months | 20 mcg* | 20 mcg* | | |
| 1–3 years | 20 mcg | 20 mcg | | |
| 4–8 years | 30 mcg | 30 mcg | | |
| 9–13 years | 40 mcg | 40 mcg | | |
| 14–18 years | 55 mcg | 55 mcg | 60 mcg | 70 mcg |
| 19–50 years | 55 mcg | 55 mcg | 60 mcg | 70 mcg |
| 51+ years | 55 mcg | 55 mcg | | |

*Adequate Intake (AI)



## Food Sources

### Animal Based

- Tuna
- Halibut
- Sardines
- Ham
- Shrimp

### Plant Based

- Brazil nuts 100 mcg each nut
- Wild mushrooms
  - Pine mushrooms
  - Porcini mushrooms
- Reishi/chaga powders
- Chia seeds
- Mustard seeds



## Supplements

- ✓ Sodium selenite and sodium selenate
  - Inorganic forms
  - Selenate is almost completely absorbed
    - Significant amount is excreted in the urine before it can be incorporated into proteins
  - Selenite is only about 50% absorbed but is better retained than selenite
- ✓ Selenomethionine
  - Organic form of selenium that occurs naturally in foods
  - About 90% absorbed
- ✓ Selenium-enriched yeast
  - Mainly supplies selenomethionine
  - The consumer should be aware that some forms of selenium yeast on the market contain yeast plus mainly inorganic forms of selenium
- ✓ Both inorganic and organic forms of selenium can be metabolized to selenocysteine by the body and incorporated into selenoenzymes

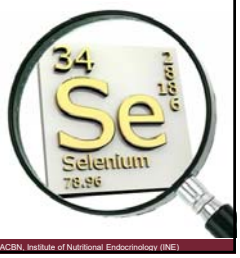
## Drug Interactions

- ✓The anticonvulsant medication valproic acid has been found to decrease plasma selenium levels
- ✓Supplemental sodium selenite decreases the toxicities of the antibiotic nitrofurantoin and the herbicide paraquat



## Selenium Assessment

- ✓Signs and symptoms
- ✓Family history and health history
- ✓Taste test
- ✓Organic acids test
- ✓Toxic and essential elements



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