Selenium and Vitamin E

Deficiency in horses, cattle and small ruminants

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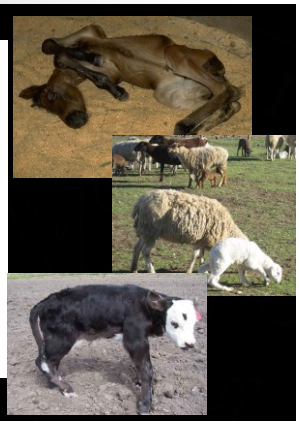
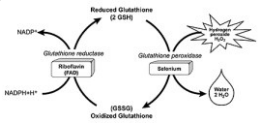


Selenium-definition and function

- Essential micronutrient/trace mineral
- Selenium functions through selenoproteins, which contain the amino acid selenocysteine.
- Functions

1) Cell membrane protection, Glutathione peroxidases and some Thioredoxin reductases

2) Conversion T4 to T3, Iodothyronine deiodinases



3) Other functions e.g.
biosynthesis of dNTPs for DNA, redox regulation transcription factors, regulation of apoptosis, immunomodulation, protein folding

[1, 2]

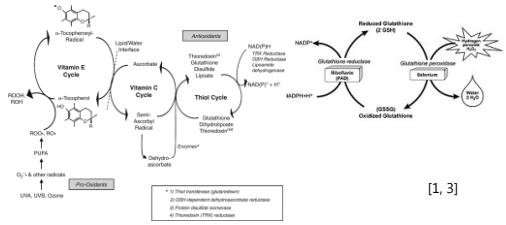
Selenium deficiency overview

- **Most important function** is in glutathione peroxidase **protection of cell membranes**
- **Too low levels cannot prevent oxidation** of cell membranes
- **Muscle membranes rupture** and leak cellular enzymes
- These damaged muscles **become non-functional and turn white, hence the name "white muscle disease"**

[1, 2]

Vitamin E deficiency may affect selenium deficiency severity

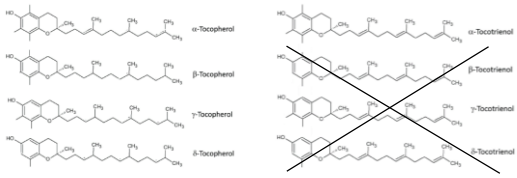
Vitamin E works with the selenium-containing enzyme **glutathione peroxidase** and other vitamins, and trace-element-containing enzymes **in protecting the cells surface** against oxidative damage caused by free radicals.



[1, 3]

Vitamin E

- **Eight** naturally **occurring forms**, two groups saturated or unsaturated side chain
- **Four saturated** named α-, β-, γ-, δ-tocopherol, α-form most biologically active
- 1 IU of vitamin E = specific activity of 1 mg of synthetic all-racemic-tocopherol acetate. [1, 3]



http://pharmacology.imedpub.com/a-brief-journey-of-tocotrienols-as-anticancer-agents.php?aid=19824

Vitamin E-other functions

- Plays a role for the **immune system** (increased dosages may reduce mastitis occurrence in dairy cows)
- Vitamin E is an **enzyme activity regulator**, f. ex. by playing a role in **deactivation of protein kinase C to inhibit smooth muscle growth**.
- Vitamin E can also **affect gene expression**, f. ex. by **downregulation** of the expression of the **CD36** scavenger receptor gene and **modulate** the expression of **connective tissue growth factor**.

[1, 3]

Vitamin E- sources

- Storage capacity is limited →Large and regular intake [1, 3]
- Green fodders, grains are good sources [1]
- Animal products relatively poor source [1]

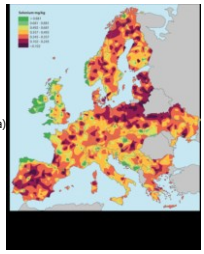
- Young grass > mature herbage[1]
- Leaves >stems[1]
- Leaching or excessive storage →oxidation of Vit E [4]
- Cereal grains, wheat and barley α-, while maize also γ- [5]
- Note: Vitamin E sensitive to freezing [5]

Selenium-sources

- Narrow range from deficient, essential and toxic doses [1]
- Selenium is not essential for plants

Content depends upon soil content, 0.01-0.3 mg/kg forage [6,7]

- Exceptions that accumulate Se
  Locoweed/Swainsona (North America and Australia)
  Broccoli, mushrooms and Brazil nut [1]
- Animal products and byproducts are in general high in Se [1]



Selenium-soil levels decrease

Intensive plant production in many countries [6]

Acid rain that reduces Se bioavailability, and acidic soil also has **reduced bioavalability** [6]

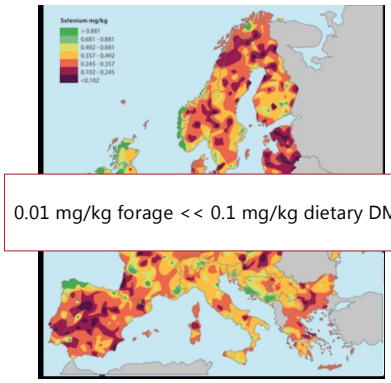
Selenium is added **in some commercial fertilizers**, however, only a small fraction is taken up by plants [6,7]

Selenium deficiency will likely manifest with **increasing frequency** in the future [6,7]

Selenium and Vitamin E requirements

Species	Se requirement	Vitamin E requirement
Horse	0.1 mg/per kg dietary DM [8]	1-2 IU/kg BW* [8]
Dairy cattle	0.3 mg/per kg dietary DM [9]	15 IU/kg dietary DM [9] 0.8 IU/kg BW lactating cow 1.8 IU/kg BW dry period
Beef cattle	0.1 mg/per kg dietary DM [10] max 2mg/per kg dietary DM	200-500 IU/head/day [11] growing and finishing
Sheep	0.1-0.2 mg/per kg dietary DM[12] max 2mg/per kg dietary DM	15 IU/head/day ewes and [12] finishing lambs

*assumed total daily dietary forage intake 2-2.5% of BW



0.01 mg/kg forage << 0.1 mg/kg dietary DM

So what are the consequences of selenium deficiency?

White muscle disease (WMD) in horses

- Most **commonly** in **foals** from **birth to 60 days** of age, but cases have been encountered in **foals up to 1 year** of age [14]
- Disease in **older foals and yearlings** often precipitated by **exercise after a period of confinement** [14]
- **High mortality 30-45%** [13,14]
- **No sex or breed predilection**
- **Seasonal occurrence corresponds to the foaling season** (February to June) in the Northern hemisphere [14]
- Single case or several affected foals in a herd [14]

Presenting signs of WMD in horses

Peracute form

Death due to **cardiovascular collapse** and **pulmonary oedema** within hours

- Clinical signs: sudden recumbency, tachypnea, dyspnea and arrhythmias

Subacute form

Marked **progressive muscular weakness** and associated **metabolic derangements** (hyperkalemia, hyponatremia, hypocalcemia, hypochloremia)

- Clinical signs: inability to stand, weakness, dysphagia, trismus and muscle fasciculations

[14]

Differential diagnosis depends on the clinical signs

Dysphagia

Cleft palate, pharyngeal paralysis, inflammation, other malformation, or botulism

Pigmenturia and weakness

Hemolytic anemia (neonatal isoerythrolysis)

Weakness and decreased muscle tone

Tick paralysis (where Dermacenter ticks are endemic), botulism

Stiff, awkward gait

Spinal cord disease (meningitis, herpersvirus 1, myeloencephalopathy, rabies), cerebellar disease, tetanus , or septic arthritis

Tachypnea and dyspnea

Pneumonia, or heart failure [14]

White muscle disease -diagnosis

- Clinical pathology:
  - Myopathy
  - Nutritional myopathy can be supported by low Se plasma levels, serum glutathione-peroxidase (GSHPx) and Vit E levels
- At **necropsy**, affected **muscle** groups appear **pale or exhibit pale striations**
- Muscles **with high physiological motion activity** are **most severly affected**
  - F.ex. diaphragm, intercostal muscles, gluteal muscles, the tongue, masticatory muscles and the myocardium
- Histopathology polyfocal degeneration and necrosis with hyalinization, fragmentation and mineralization of myofibres [14]

Treatment

- **Selenium IM 0.06 mg/kg BW divided** and injected at two separate sites, may be **repeated after 3 and 8/10 days**
- **Injectable 300 IV vitamin E/mL** as D-α-tocopherol, used **if disease is suspected to be related to Vit E deficiency**
- **Other treatment** depends on the **presentation**, e.g.
  - Fluids to correct electrolyte disturbances
  - Feeding tube recumbent or dysphagic
  - Plasma transfusion if failure of passive transfer through colostrum
  - In cases of septicaemia or aspiration pneumonia antibiotics

[14]

WMD may also depend on Vitamin E levels

- Higuchi et al. (1989) found **foals with WMD** (n=21) to have **approx. normal tocopherol** levels (430.2±121.7 µg/dl), **low selenium levels** (0.32±0.17µm/l) and **low GSH-Px**
- Vitamin E levels therefore may play a role of WMD in horses and broodmares should probably be supplemented if needed
- **E and selenium levels were measured** in serum simultaneously, and found a **weak but significant correlation**

Feeding lower than recommended levels does not always cause white muscle disease

- Brummer et al. (2013) fed a **low selenium diet** 0.06 mg/kg DM to **adult horses for 196 days** compared to a
- V
  E **recommended intake**

⇒None of the horses had clinical signs

In non-reproducing non-performing horses the selenium requirement is probably lower than the NRC min req 0.1 mg Se/kg DM

Increased requirement in pregnant mares

- Karren et al. (2010), **supplementing mares** during **last trimester increased Se** levels in new borne **foals**

>0.1 mg Se/kg DM to pregnant mares in the last trimester may be required for optimal immune function in foals

antibodies in foals from mares receiving 3 mg Se/day compared to 1 mg/day

Increased requirement performing horses

- **Exercise** is associated with **increased production** of **reactive oxygen species**

Increased Se supplementation may be beneficial for mitigating oxidative muscle damage and aiding in postexercise recovery

- White et al. (2016) found **0.3 mg Se/kg DM** vs. 0.1 mg Se/kg DM in untrained horses, **increased GPx activity**, and **lessened lipid peroxidation following exercise**

What about calves, lambs and kids?

The **typical presentation of WMD** is the **same as in horses**, more likely to occur early in life

In 1958 Muth et al. **first described** the effect of Se and Vit E supplementation on selenium responsive ill-thrift (WMD) in **calves** [23]

Slow-release devices are available and can provide **selenium supplementation for 200–360 days** for livestock that is **rarely handled** [24]

Selenium can also be **applied to pasture through the fertilizer** application rate of 10 g Se/ha, provide adequate levels **7-12 months** [24]

What about other animals??

- Most common in livestock and **rarely in pigs** [1]
- Can occur in **wild herbivores** has been described in lesser kudu, nyala and giraffe [25-27]
- **Rarely** seen in **dogs and cats** [1]
- Some curious cases
  - Lion cubs [28]
  - Sea lion [29]

What about humans?

Very rare in well-nourished populations

Certain regions with low selenium
- Keshan disease (China)

Selenium deficiency is rarely the sole cause in the diseases described in humans

Genetic mutations to the selenoproteins

Selenium deficiency may also be a risk factor in:
Cardiovascular disease, renal failure, brain disorders with increased oxidative stress, autoimmune disease, diabetes, hypothyroidism, male infertility, cancer

[2,30]

Selenium deficiency other diseases- humans

Disease	Cause	Symptoms	ref
Keshan disease	low selenium diet and *Coxsackie*virus infection	Juvenile cardiomyopathy: necrotic lesions, inflammatory areas, calcification through myocardium	30, 31
Kashin-Beck	Possibly low selenium, mycotoxins and fulvic acid contaminated water	Osteoarthritis (degeneration and necrosis cartilage) children 5-13 y	2
Nutritional myotonic dystrophy	low selenium diet or parenteral/enteral nutrition	muscle pain and weakness	32
Chronic muscle disorder associated with oxidative stress	alcohol HIV infection (increased demand?)	muscle pain and weakness	32
Rigid spine muscular dystrophy			32
Multiminicore disease			32
Mallory body-like desmin-related myopathy	mutations in the selenoprotein N gene	hypotonia, mostly axial muscle weakness, scoliosis, sarcomeric disorganization,...	32
Dropped head syndrome			32

Other Selenium and/or Vitamin E deficiency related diseases in animals

Disease	Species	Cause	Signs	Ref
Nutritional muscular dystrophy	Chicken, turkey salmon	Low selenium diet	Cardiac and muscle affections	32
Exudative diathesis	Chicken	Combined selenium and vitamin E deficiency	Generalised oedema of the subcutaneous fat,	1
Rigid lamb syndrome	Sheep	Combined selenium and vitamin E deficiency	Rigidity of the limbs and spine	32
Fatal myopathy	Guinea pig	Combined selenium and vitamin E deficiency	muscle affection, lipid peroxidation, low glutathione peroxidase	32

Other Selenium and/or Vitamin E deficiency related diseases in animals

Disease	Species	Cause	Signs	Ref
Equine motor neuron disease (EMND)	Horse	Vitamin E deficiency minimum 18 months Genetic?	Muscle wasting, muscle fasciculations, recumbency	33
Neuroaxonal Dystrophy/ Equine Degenerative Myeloencephalopathy (NAD)	Horse	Vitamin E deficiency similar pathophysiology to EMND	Symmetric ataxia most severe pelvic limbs, proprioceptive def.	33
Vitamin E deficient myopathy	Horse	Vitamin E deficiency Other factors?	Similar to EMND but no neurogenic atrophy, moth eaten mitochondria	33
Mulberry heart disease	Pigs	Vitamin E and/or selenium deficiency Other unknown causes possibly viral or other traceminerals	Sudden cardiac failure, enlarged liver, microangiopathy, hepatosis dietetica or exudative diathesis	34
Nutritional encephalomalacia ("crazy chick disease")	Chickens	Vitamin E	Inability to walk or stand, haemorrhage and necrosis brain cells	1

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