Selenium and/or vitamin E deficiencies Nutritional (enzootic) muscular dystrophy in farm animals (NMD), White muscle disease.

Selenium and/or vitamin A deficiencies or deficiency of either selenium or vitamin E alone or in combination, usually in association of predisposing (contributing) factors such as high levels of dietary polyunsaturated fatty acids, unaccustomed exercise, and rapid growth of young animals cause nutritional (enzootic) muscular dystrophy in farm animals (cattle, sheep, goats, and horses), and mulberry heart disease and hepatosis dietetica in pigs. These diseases are also known as selenium-vitamin E-responsive diseases because selenium and vitamin E are important in etiology, treatment and control of such diseases. Selenium and vitamin E deficiencies may be involved in reproductive performance, retained placenta in cattle, resistance to infectious diseases like bovine mastitis, controversial.

Recently, the term selenium responsive disease had been created in some regions of the world, particularly in New Zealand, and in parts of Australia and North America, the diseases such as ill-thrift in sheep and cattle, bone marrow abnormalities in sheep, because these diseases respond beneficially to selenium administration alone.

Selenium and/or vitamin E deficiency disease	Selenium-responsive disease	Selenium and vitamin E deficiency disease (Controversial)
1-Nutritional (enzootic) muscular dystrophy in farm animals **2-Mulberry heart disease in pigs.** **3-Hepatosis dietetica in pigs**	**1-Ill-thrift in sheep and cattle.** **2-Bone marrow abnormalities in sheep**	**1-Poor reproductive performance in sheep and cattle.** **2-Resistance to bovine mastitis.** **3-Retained placenta in cattle**

Nutritional Muscular Dystrophy (NMD); enzootic muscular dystrophy, enzootic nutritional muscular dystrophy in farm animals, White muscle disease in growing calves, stiff-lamb disease in young lambs.

The disease occurs in all farm animal species but most commonly in young, rapidly growing calves, lambs, kids, and foals born rom dams that have been fed for long periods (usually during winter months) on diets low in selenium and vitamin E with or without conditioning factors. There are two forms or two major syndromes of the disease:

Acute form (myocardial dystrophy), which occurs most commonly in young calves, lambs and kids, and occasionally in foals.

Subacute form (skeletal muscle dystrophy), which occurs in older calves, lambs, and yearling cattle.

EPIDEMIOLOGY:

Goats kids may require more selenium than lambs or calves, which may explain the higher incidence of the disease in kids, and the high mortality in goat kids from birth till 3 months of age.

NMD in horses occurs most commonly in foals to about 7 months of age, and occurs sporadically in adult horses.

NMD in cattle, occurs most commonly in young calves exposed to stressors such as being turned outdoors after winter housing, walking long distances, jostling and movement associated with vaccination and dehorning procedures, after weaning, and may occurs in steers (12 – 18 months of age) under feedlot conditions, and heifers at time of parturition.

ETIOLOGY:

- The selenium- and vitamin E-responsive or deficiency diseases of farm animals caused by diets deficient in selenium and/or vitamin E, with or without the presence of conditioning factors such as an excessive quantity of polyunsaturated fatty acids in ration.:

Selenium deficiency:

- Selenium deficiency is an endemic in some areas of the world such as in some states of USA (the pacific northwest and northeastern, and southeastern), Canada (eastern provinces, Atlantic provinces as the soils pH is acidic and consequently, the forages are deficient in selenium; < 0.10 mg/kg DM), United Kingdom. Several factors influence the availability of soil selenium to plants, such as:
    - Soil pH: acidity reduce selenium availability to plant while alkalinity encourage selenium absorption by plants.
    - High level of sulfur in soil, which competes for absorption sites with selenium in both plants (plants deficient in selenium and causing primary selenium deficiency in animals), and in animals (causing secondary selenium deficiency) as sulfur reduces availability of selenium.
    - Seasonal conditions of pasture, the content being lowest in spring and when rainfall is heavy.
    - ***In general, forages and grains contains ≥ 0.10 mg/kg DM is considered adequate, and soils contains < 0.5 mg/kg is likely to yield crops deficient in selenium.***

Vitamin E deficiency:

- NMD can occur in ruminants with vitamin E deficiency and an adequate selenium status.
- Vitamin E deficiency occurs most commonly when animals are fed inferior quality hay or straw or root crops as these are deficient in vitamin E content. On the other hand, cereal grains, green pasture, and well-cured fresh hay contain adequate amounts of the vitamin E. the levels of α-tocopherol (vitamin E) in pasture declines by up to 90 % as it matures or after harvesting, consequently if the animals feed on it causing primary vitamin E deficiency.
- Preservation of grains with propionic acid and sodium hydroxide (as a method of inexpensive storage and protection from fungal growth) will lead to marked reduction in their vitamin E content lead to primary vitamin E deficiency in animal fed them.
- High levels of fat or polyunsaturated fatty acids in animal diet will associated with loss of naturally occurring antioxidants such as tocopherols on the diet leading to secondary vitamin E deficiency (but simultaneously with selenium level of diet < 0.05 mg/kg DM).

Conditioning factors:

I. Myopathic agents in the animal diet, such as: -
    a. Polyunsaturated fatty acids (PUFAs) in diet: diets rich in PUFAs such as cod liver oil, other fish oils, fishmeal used as protein concentrate, lard, linseed oil, soybean and

corn oils have been implicated in the production of NMD, as they consuming natural antioxidant contents of the diet such as tocopherols lead to low level vitamin E content in diet.

b. The oxidation during rancidification of the oil or the fat contents of diet causes destruction of the vitamin content.
c. Lupinosis-associated myopathy in sheep is mainly skeletal muscular myopathy recorded in weaner sheep grazing lupin stubbles infected with fungus.

II. Unaccustomed exercise, such in: -
   a. Calves (2 – 4 months of age), that raised indoors and turned out onto pasture in spring also in lambs (1 – 3 weeks of age) when turned out with their ewes for the first time after lambing.
   b. Vigorous exertion associated with running and suckling may lead to acute form of the disease on deficient pastures or lambs derived from deficient ewes.
   c. Driving calves or lambs for long distances.
   d. Wandering and bellowing that occurs in calves weaned at 6 – 8 months of age
   e. Jostling and movement associated with vaccination and dehorning procedures

Selenium-responsive diseases:

- These are a group of diseases recorded in selenium deficient areas (such as New Zealand). These diseases respond beneficially to administration of selenium. These include: -
  - Ill-thrift in lambs and calves on pasture.
  - Infertility in ewe (whose blood selenium is < 10 µg/mL).
  - Diarrhea in older calves and lactating ewes.
  - These diseases are recorded in areas where soil selenium < 0.45 mg/kg, the pasture selenium content is < 0.02 mg/kg DM, and the mean blood selenium levels in affected animals is ≤ 1.0 µg/mL, (normal blood selenium level ~ 2.0 µg/mL, doubtful 1.1 – 1.9 µg/mL).

I-The relation between selenium-vitamin E-status and reproduction performance in farm animals:

- The published information on the effect of vitamin E and selenium deficiency or supplementation of the diet with selenium and/or vitamin E on reproductive performance of farm animals are conflicting and controversial. As some studies showed that IM injection of dairy cattle with selenium and vitamin E 3 weeks prepartum did not have any effect on the average days to first estrus or first service, average days to conception, services per conception, or number of uterine infusions required, while other studies stated that the IM injection of selenium and vitamin E 3 weeks prepartum increased the percentage of cows pregnant to first service, reduce the number of services per conception, decreased the incidence of retained placenta, and reduced the interval from calving to conception.
- Some data indicating that using of intraruminal pellet of selenium may increase milk production and decrease somatic cell count of milk in dairy cattle.
- There is a high incidence (> 10 %) of retained fetal membranes has been associated with marginal levels of selenium, and injection of selenium to pregnant cows increases the level

of selenium in the blood and reduces incidence of retained placenta. For this reason, a dietary level of 0.1 mg/kg DM selenium as well as vitamin E supplementation are recommended to minimize the incidence of retained placenta in cattle.

II- Relation of selenium- vitamin E status and resistance to infectious diseases:

- The status of the selenium and vitamin E in an animal can alter or impair: -
    A. Antibody response.
    B. Phagocytic function.
    C. Lymphocytic response.
    D. Resistance to infectious diseases.
- Vitamin E can stimulate the immune defense mechanisms in laboratory animals and cattle. As vitamin E supplementation can enhances both cellular and humoral immunity and lymphocyte stimulation indices.
- A deficiency of selenium leads to inhibit: -
    A. Resistance to viral and microbial infections.
    B. Neutrophil functions.
    C. Antibody production.
    D. Proliferation of T and B lymphocytes in response to mitogens.
    E. Cyto-destruction of T lymphocytes and natural killer lymphocytes.
- In general, selenium-vitamin E deficiency result in immunosuppression and supplementation with selenium and vitamin E augment the immunological functions and they have interactive effects on lymphocyte response. It was suggested that blood selenium levels over 100 µg/L are necessary to maintain optimum immunocompetence in growing beef cattle

Selenium-vitamin E status and mastitis in dairy cattle:

- There is some evidence that vitamin E and selenium deficiency may be associated with an increase in incidence of mastitis in dairy cattle, particularly in the early stage of lactation because vitamin E prevents the suppression of blood neutrophils and macrophages functions during postpartum period.
- Selenium and vitamin E supplementation beginning on dry period (last 14 days) and continuing for up to 8 weeks after parturition is important to reduce incidence of mastitis in dairy cattle because they enhance the macrophage and neutrophil functions as well as the phagocytic function in the mammary gland.

PATHOGENESIS:

Selenium is an essential nutrient for animals as: -

1. Selenium is a biochemical component of the enzyme glutathione peroxidase (GSH-PX).
    a. The plasma GSH-XP protects cellular membranes and lipid containing organelles from peroxidative damage (of free radicals) by inhibiting and destruction (reducing them) of the endogenous peroxides (such as hydrogen peroxide, certain organic hydroperoxides, which are derived from glutathione during process of redox cycling) converting them to non-toxic hydroxy fatty acids materials.
    b. There are two types of the GSH-PX enzymes in the tissues and blood, which are selenium-dependent GSH-PX and non-selenium-dependent GSH-PX. The non-sele-

nium-dependent enzyme does not contain selenium and does not react with hydrogen peroxide but show activity towards organic hydroperoxides. The spleen, cardiac muscle, erythrocytes, brain, thymus, adipose tissue, and striated muscles (skeletal muscles) contain only the selenium-dependent GSH-PX. The liver, lungs, adrenal glands, testes, and kidneys contain both enzymes. The hepatic tissue contains the highest level of non-selenium-dependent enzyme. Consequently, certain tissues or sub-cellular components may not be adequately protected from oxidant damage because they are inherently low in GSH-PX-dependent selenium, even with adequate dietary selenium and vitamin E, and variation in the activity of GSH-PX among certain tissues such as liver, myocardial and skeletal muscles would explain the variations in the severity of lesions between tissues (and also between species, i.e. in young calves, lambs, foals affected by NMD; myocardial and skeletal muscles severely affected, while in pigs affected by mulberry heart disease and hepatosis dietetica).

c. The activity of the enzyme in erythrocytes is positively related to the blood concentration of selenium in animals so it is a useful aid for diagnosis of selenium deficiency in animals, as the enzyme from the erythrocytes of both cattle and sheep contains 4 g atoms of selenium per mol of enzyme.

2. Selenium also protect ***non-membrane proteins*** against oxidative damage. In this context, *protection against oxidative damage to susceptible non-membrane proteins by dietary selenium, but not by vitamin E (acts only in lipid), may explain why some nutritional diseases respond to selenium but not to vitamin E.*
3. Selenium is a component of type-I iodothyronine deiodinase, which catalyzes the conversion of thyroxine (T4) to a more active tri-iodothyronine (T3), so animals with low selenium diets have high level of circulating T4 and low level of circulating T3 (this may explain the reduction in growth rate, and wool and hair abnormalities associated with selenium deficiency particularly in sheep, in addition to selenium improve iodine absorption).
4. Selenium play a role in enhancing the immune system, particularly phagocytic function in the mammary gland of dairy cattle (*as shown above*).
5. Selenium is a component of other proteins, such as seleno-protein of muscle, seleno-flagellin, selenium-transport proteins, formate dehydrogenase, and glycine reductase.
6. Selenium facilitates significant changes in the metabolism of many drugs and toxic substances (counteract the toxicity arsenic, cadmium, mercury, copper, silver, and lead)

Function of Vitamin E (Tocopherols):

1. Vitamin E is an antioxidant that prevent oxidative damage (prevent lipoperoxidation by preventing fatty acid hydroperoxide formation) to sensitive membrane lipids, especially membranes rich in unsaturated fatty acids such as mitochondria, endoplasmic reticulum, plasma membranes and cell wall.
2. Vitamin E plays important role in immune system (enhances both cellular and humoral immunity and lymphocyte stimulation indices, *as shown above*).

The function of sulfur-containing amino acids:

1. Sulfur containing amino acids act as precursors of glutathione, which in turn act as substrate for GSH-PX and maintain sulfhydryl groups in the cells.

The relationship between selenium, vitamin E and sulfur-containing amino acids:

1. There is important interrelationship exists among selenium, vitamin E and sulfur-containing amino acids in preventing some of the nutritional diseases caused by their deficiency.
    a. Vitamin E prevent oxidative damage or lipoperoxidation of the lipid containing organelles by preventing fatty acid hydroperoxide formation, intracellular.
    b. Selenium is a component of GSH-PX, which preventing oxidative damage of the endogenous lipo-peroxides by inhabiting and destructing peroxides.
    c. containing amino acids act as precursors of glutathione which act as substrate for GSH-PX.

N.B.:

- The endogenous peroxides and hydroperoxides are called free radicals that derived from glutathione during redox cycling (metabolic end-products), when are accumulated in the tissue lead to oxidative damage.

When the diet is deficient in selenium and/or vitamin E:

2. There is a widespread tissue lipoperoxidation leading to hyaline degeneration and calcification of muscle fibers (cardiac & skeletal).
3. Abnormal calcium retention in the muscle fibers, which is one of the earliest changes.
4. Muscular degeneration allows the release of intracellular enzymes of muscle fibers into circulation such as lactate dehydrogenase, creatinine phosphokinase, AST, which of importance in diagnosis.
5. Muscular degeneration allows the release of myoglobin into the blood circulation, which results in myoglobinamia, myoglobinuria and nephrosis. This more common in horses, older calves and yearling cattle than in young calves whose muscles have a lower concentration of myoglobin. Hence, the tendency to myoglobinuria will vary depending on the species and age of the affected animal.
6. Dysfunctions of the affected muscles (myocardial and diaphragm dysfunction lead to heart failure, while skeletal muscles dysfunction leads to locomotor abnormalities). In calves, lambs, and foals, the major muscles involved are the skeletal, myocardial and diaphragmatic muscles. The myocardial and diaphragmatic form of the disease (acute form) occurs most commonly in young calves, lambs, kids and foals, resulting in acute heart failure and severe respiratory distresses, and this form does not respond to treatment. The skeletal form (subacute form) of the disease occurs more commonly in older calves, yearling cattle, older foals, results in weakness and recumbency, that form is less severe and respond well to treatment.
7. The degeneration of the skeletal muscle is rapidly and successively followed by invasion of phagocytes and regeneration, while in myocardial muscle, replacement by fibrosis in chronic cases and acute heart failure and death in extensive acute cases.
8. During clinical and subclinical white muscle disease in calves and yearling cattle there is a significant increase in both the osmosis and the peroxidative hemolysis of erythrocytes, which making erythrocytes highly susceptible to hemolysis following exposure to hypotonic saline. This defect is due to alterations in the integrity of the cell membranes of which to-

copherols are an essential component. Increase in the hemolytic susceptibility of the erythrocytes may provide a basis for a single functional test for vitamin E deficiency in sheep and cattle.

CLINICAL FINDINGS:

IN CASE OF ENZOOTIC MUSCULAR DYSTROPHY

There are three forms of enzootic muscular dystrophy in calves:

A- **Acute enzootic muscular dystrophy.**
B- **Subacute enzootic muscular dystrophy**.
C- **Subclinical muscular dystrophy**.

A-Acute enzootic muscular dystrophy: the case fatality may reach to 100 %.

1. Collapse and sudden death may occur in affected animals after exercise without any other previous signs (excitement during hand feed of young calves and lambs may precipitate the condition).
2. In calves under close observation, the following signs can be noticed:
3. Sudden onset of dullness, and severe respiratory distress, accompanied by a frothy or bloody-stained nasal discharge in some cases.
4. The affected animal usually in lateral recumbency and unable to assume sternal recumbency even when assisted.
5. Their neurological reflexes are normal, as their sight and mental attitude are normal.
6. The animal is usually thirsty and can swallow unless the tongue is affected.
7. Increase heart rate up to 150 – 200/min, and often with arrhythmia, and respiratory rate is high up to 60 – 70/min, with loud breath sounds over the entire lung fields.
8. The body temperature is usually normal or slightly elevated, and become subnormal before death.
9. The affected animal commonly dies within 6 – 12 hours after onset of signs in spite of therapy.

B-Subacute enzootic muscular dystrophy:

1. Locomotor abnormalities in the form
    a. Some of affected animals may be found in sternal recumbency unable to stand, and may some of them may make attempts to stand.
    b. Some animals may be still in stand position, but reluctant to move, with stiffness gait, and trembling in limbs, unable to stand for only few minutes. The gait in calves is associated with rotating movements of hocks, and in lambs, the gait is associated with stiffness, goose-stepping gait.
    c. Muscular tremor is evident when the animal is forced to stand for more than a few minutes.
2. Symmetrical enlargement and firmness on palpation of the dorso-lumber, gluteal, and shoulder muscle masses, although this is difficult to detect.
3. Most of the affected animals retain their appetite and able to suck well if held up to the dam or eat if hand-fed.
4. If the diaphragm and intercostal muscles are involved, signs of dyspnea and abdominal type respiration occur. And the heart rate may be elevated without arrhythmia.

5. The body temperature is usually within normal range, but there is may transit fever may be due to the effect of myoglobinamia and pain.
6. The affected animal responds to treatment within a few days, and able to stand and walk normally within 3 – 5 days.

Subclinical muscular dystrophy:

1. It occurs in apparent normal animals in herds at the time of clinical cases are present.
2. There is only elevation in the activities of serum creatine phosphokinase for several days before the onset of clinical signs, and if the animal treated the activities of the creatine phosphokinase returns to normal.

In yearling cattle (18 – 24 months of age), selenium and/or vitamin E deficiency may cause:

1. The upper borders of the scapula protrude above the vertebral column and widely separated from the thorax (this called flying scapula), due to bilateral rupture of the serratus ventralis muscles. This is also recorded in red deer.
2. Sometimes, the toes of the animal are spread and there is relaxation of carpal and metacarpal joints or knuckling at the fetlocks and standing in tip-toe.
3. Inability to rise head, inability to swallowing or inability to use tongue.
4. Paralytic myoglobinuria, may occurs in yearling cattle with a history of recent turning out to pasture or unaccustomed exercise, as stiffness gait, lameness, recumbency, myoglobinuria, and severe cases may die within a few days.

Subcapsular liver rupture lambs:

- The disease occurs in young lambs usually under 4 weeks of age, due to vitamin E deficiency. The affected lamb is suddenly collapsed and recumbent, weak and die within a few minutes or after several hours of recumbency and weakness.

Muscular dystrophy in foals:

1. The disease most commonly during the first few months of life, and is common in the first week.
2. The affected foal is unable to suck, recumbency, difficult in rising and trembling if the foal forced to stand.
3. The tachypnea, tachycardia, and normal body temperature.

Generalized steatitis, fat necrosis, yellow fat disease:

1- The disease is recorded in farm animals, and more common in foals under 2 months of age or recently weaned foals. The selenium and/or vitamin E deficiency may be incorporated as a cause.
2- The common signs are cachexia due to steatitis alone, or as primary myopathy or myositis with steatitis secondary.

CLINICAL PATHOLOGY:

1-Plasma creatine phosphokinase (CK/CKP):

- CK is the most commonly used laboratory aid in the diagnosis of NMD in animals.
- The enzyme is highly specific for cardiac and skeletal muscle, and is released into blood following unaccustomed exercise or myodegeneration.
- Its half-life is 2 – 3 hours, but remains as a good indicator for muscle damage for about 3 days.

Serum CK IU/L	Cattle	Sheep	Horse	NMD
	26±5	52 ±10	58 ± 6	5000 - 10000

2-Aspartate aminotransferase (AST):

1- AST is used as an indicator of muscular and liver damage.
2- The activity of the enzyme remains elevated for 3 – 10 days after their release into blood, because its half-life is longer than CK.

Serum AST U/L	Cattle	Sheep	Horse	NMD
	78 - 135	60 - 280	220 - 600	300 - 3000

3-Selenium status:

Serum selenium	Cattle	Sheep	Horse	NMD
Adult	70 – 100 ng/L	120 – 150 ng/L	130 -160 ng/L	
Young	50 – 80 ng/L	50 – 80 ng/L	70 – 90 ng/L	

Selenium	liver	kidney
Normal level	1.2 – 2.0 µg/g DM	3.5 – 5.3 µg/g DM
Deficiency	0.07 – 0.60 µg/g DM	0.6 – 1.4 µg/g DM

4-Glutathione peroxidase activity (GSH-PX) in blood and plasma:

- There is a direct relationship between the GSH-PX activity of the blood and the selenium levels of blood and tissues of cattle, sheep, horses, and pigs.
- The GSH-PX activity is a sensitive indicator of the level of dietary selenium intake and the response to selenium administration (oral or parenteral).
- *Because selenium is incorporated into erythrocyte GSH-PX only during erythropoiesis, an increase in the enzyme activity of blood will not occur for 4 – 6 weeks following administration, but the plasma or serum GSH-PX increase rapidly with selenium administration because it is not dependent on incorporation of selenium into erythrocyte.*

In cattle	Blood selenium level	GSH-PX activity
Normal or adequate level	>100 ng/mL	> 60 mU/mg hemoglobin
Marginal selenium deficiency	50 – 100 ng/ mL	30 – 60 mU/mg hemoglobin
Deficiency	< 50 ng/mL	< 30 mU/mg hemoglobin

5-Vitamin E status:

- Tocopherol levels in the blood and liver provide a good information about the vitamin E status in the animal, but because of the difficulty of laboratory assays of tocopherols, they are not commonly used.

α-tocopherol level	Cattle	sheep	Horse
In liver NORMAL Critical level below which deficiency occurs	20 mg/kg WW < 5 mg/kg WW	6 mg/kg WW < 2 mg/kg WW	Mean plasma vitamin E levels 2.8 µg/mL
In serum critical level	< 2 mg/L		

NECROPSY FINDINGS:

Gross lesions:

- The lesions of affected group of skeletal muscle (biceps femoris muscle, dorso-lumber, gluteal, and shoulder muscles) are bilaterally symmetrical, and contain localized white or graying areas of degeneration. These areas may be in streaks, involving a large group of muscle fibers that run through the center of the apparently normal muscle, or as peripheral boundary around a core of normal muscle.
- In the diaphragm, the distribution of the damaged bundles gives the tissue a radially striated appearance.
- The affected muscle is friable and edematous (cocked appearance) and may be mineralized.
- When the heart is affected, white areas of degeneration are visible, particularly under the endocardium of the left ventricle in calves and both ventricles in lambs. The lesions may extend to involve the entire ventricular septum and papillary muscles.
- Pulmonary congestion and edema are common.

Microscopical lesions:

- The lesions of the muscle are non-inflammatory, hyaline degeneration is followed by coagulative necrosis and variable degree of calcification.
- In generalized steatitis in foals under 2 months of age: there is yellow-brown fat consists of necrotic fat infiltrated with neutrophils, macrophages, and giant cells

TREATMENT:

- In all previous described conditions, the recommended treatment is using a combined mixture of selenium and α-tocopherol because of the synergistic functions of selenium and vitamin E and because it is not always possible to the know the cause of the conditions (selenium and /or vitamin E).
- Selenium is used in the form sodium or potassium selenite, and α-tocopherol is used in the form of DL-α-tocopherol (α-tocopherol is the most potent form of the tocopherols; 1 IU of vitamin E = 1 mg synthetic racemic α-tocopherol acetate and 1 mg DL- α-tocopherol acetate = 0.92 IU vitamin E

In treatment of NMD in calves, lambs, and foals:

1. Using a mixture of 3 mg selenium (as sodium or potassium selenite) + 150 IU of DL-α-tocopherol acetate/ mL.
2. The dose is 2 mL/ 45 kg BW. One treatment is usually effective and sufficient in case of skeletal form (subacute form), while in case of myocardial form (acute form) or when the myocardium is severely involved will usually not respond to treatment.
3. In case of herd, all the contact animals should be treated with the same dose for prophylaxis (the contacts have subclinical form, as previously mentioned).
4. All the animals of the herds, particularly clinical cases should be rested and handled carefully during treatment to avoid excitation and muscular exercise that may aggravate the condition causing acute muscular dystrophy.
5. The clinical cases (subacute skeletal form) will usually begin to improve by the 3rd day after treatment and animals able to stand and walk normally within 5 – 7 days.

N. B.: *Most injectable vitamin E and selenium preparations are adequate in selenium but insufficient in vitamin E (vitamin E is more expensive and less stable)*

CONTROL:

- All diseases caused by selenium and/or vitamin E deficiency can generally be controlled and prevented by provision of both nutrient to susceptible animals fed on deficient rations or in deficient soils.

Provide selenium and vitamin E:

- Both selenium and vitamin E should be provided when the diets (or the soil in grazing animals) are deficient in both nutrients, but this may not apply in every situation.
- For selenium supplementation the following points should be noticed: -

1-Maternal transfer to newborn:

- The diseases caused by selenium deficiency in neonates could be prevented by the provision of selenium (oral or parenteral supplementation) to the dam during pregnancy or directly to the young growing animals, because selenium of the dam can pass through placenta to the fetus and provides protection for neonates, as well as it will rise the selenium content of the colostrum, but by the 7^{th} day after parturition, the selenium level of the milk may be inadequate to maintain adequate serum level of the neonate.

2-Selenium potentially toxic:

- Selenium is *toxic* (for animal and human, and may be *carcinogen* for man), and any treatment and control program using it must be monitored.
- Selenium injected into or fed to animals concentrates in liver, kidney, skeletal muscles, and other tissues (*kidney and liver appear accumulate 3 – 4 mg/ kg of selenium*), so *withdrawal periods* before slaughter must be allowed.
- The use of selenium in the diet of lactating dairy cattle may possible adulteration of milk supplies. However, addition of selenium to the diets of lactating dairy cattle at levels that are protective against deficiency diseases does not result in levels in milk that are hazardous for human consumption. The feeding of excessive quantities of selenium to dairy cattle would cause toxicity before levels became toxic for man.

3-Dietary requirement of selenium:

- For all animal species (both ruminants or non-ruminants), the selenium dietary requirement is 0.1 mg/ kg DM.
- Take in consideration, even within a region of high selenium concentration, some feeds may contain levels of selenium < 0.1 mg/ kg DM.
- Selenium and vitamin E supplementation should be provided continuously in the selenium deficient areas because the feeds grown in them are known to be deficient in selenium.

Different methods of selenium and vitamin E supplementation:

Selenium and vitamin E supplementation can be achieved by:

1. Dietary supplementation in feed and water supplies.
2. Parenteral injection individually.
3. Oral administration.
4. Pasture top-dressing in deficient areas.

The method used for supplementation depend on:

1. Circumstances of the farm.
2. The ease of the administration.
3. The labor available.
4. The coast.
5. The severity of the deficiency that exist.
6. Whether or not the animals being dosed regularly for other diseases such as parasitism.

1-Dietary supplementation:

- Selenium and vitamin E supplementation in the diets or in salt and mineral mixes is successful in preventing the diseases caused by deficiencies of these two nutrients.
- For preventing NMD of calves and lambs: providing selenium and vitamin E:

-I***n the diets of as:***

	Selenium (elemental/actual)	Vitamin E (α-tocopherol)
Cattle during pregnancy	0.1 – 0.3 mg / kg DM/cow	1 g / day/ cow
Ewes during pregnancy	0.1 mg / kg DM/ ewe	75 mg / day / ewe

-***In the salt-mineral mixture***: to feed *ad libitum*.

	Selenium (elemental/actual)	Vitamin E (α-tocopherol)
Cow and ewe during pregnancy	14.8 mg / kg DM	2700 IU/ kg

2-Individual parenteral injection

1-Injection of Selenium:

- The *generally recommended dose of selenium* is 0.1 mg /kg BW SC, every 2 months or 0.2 mg/ kg BW, SC every 4 months. The recommended dose rates of repeated injections at monthly intervals are: 1 mg of selenium to lamb, 5 mg to ewe, 10 mg to calf, and 30 mg to adult cattle. The injections are administered 1 month before the anticipated dangerous period.
- In dairy cattle, using sodium selenate at dose rate 0.10 or 0.15 mg/ kg BW SC will maintain the blood selenium level and activity of GSH-PX up to 6 months after injection. The current label dose of injectable selenium is 0.055 mg selenium/kg BW.
- Slow-release preparation of Barium selenate is used by SC injection is used now in sheep and cattle before breeding and parturition.
- 1 mg selenium is equivalent to 2.2 mg anhydrous sodium selenite, 2.4 anhydrous sodium selenate, or 4.7 mg hydrated sodium selenate

2-*Injection of vitamin E in pregnant animals* a few weeks before parturition will increase the level of vitamin E levels in the serum of dam and neonate and in colostrum.

3-*Injection of vitamin E and selenium* have been used successfully for prevention and control selenium and vitamin E deficiency diseases in animals.

4-In the horse:

Daily requirement for horses	Selenium	Vitamin E (as DL-α-tocopherol)
	2.4 µg/ kg BW/day	600 – 1800 mg/day

3-Oral administration:

- For control and preventing selenium and vitamin E deficiency diseases in animals, particularly in selenium-deficient areas or pastures, oral administration of selenium is achieved in a regular basis, as:
  1. ***Intraruminal selenium pellet or sustained-released intraruminal bolus.***
  2. ***Oral administration of sodium selenite programs in severely selenium-deficient areas.***
  3. ***Oral selenium and anthelmintics or vaccines administration.***

i. *Intraruminal selenium pellets or sustained-released selenium intraruminal bolus:* this is designed to settled in the forestomach of the ruminants (rumen or reticulum), and release selenium in the GIT (about 1mg/ day), that will be absorbed and produce satisfactory blood selenium for up to more than 2 years in cattle, and 4 years in ewes. The pellet is usually administered during last trimester of pregnancy in pregnant dams (last three months of pregnancy in cattle), which will rise the selenium levels in serum and milk of dams, and selenium status of the neonates sufficient to prevent NMD. In sheep, the pellet is composed of 0.5 g elemental selenium and finely divided metallic iron, and in cattle, the pellet contains 10 % selenium and 90 % iron grit.

ii. Oral administration of sodium selenite programs in severely selenium-deficient areas and usually using a dose rate of 0.044 mg/ kg BW, the programs of sodium selenite administration used in ewes and lambs are:

	1st dose	2nd dose	3rd dose	4th dose
In ewe	Before mating	At mid-gestation	3 weeks before lambing	----------
Dose rate	(5mg/kg BW)	(5mg/kg BW)	(5mg/kg BW)	
In lambs	At docking	At weaning	3 months interval	3 months interval
Dose rate	1mg/ kg BW	2mg/ kg BW	2mg/ kg BW	2mg/kg BW

iii. *Oral selenium combined with anthelmintics or vaccines administration:* this is an oral dosing of sodium selenite combined with the administration of anthelmintics or vaccines in selenium-deficient areas. ***A 100-day controlled-release anthelmintic capsule*** containing 13.9 mg selenium is available now that will protect lambs from selenium deficiency for at least 180 days.

4-Pasture top-dressing by selenium:

- It is an economical, alternative to individual animal dosing, particularly in severely deficient areas with a high stocking rate.
- The application of sodium selenate as a top-dressing is now used in some countries where selenium-deficient areas such as pumice soil.
- 10 g selenium/hectare (may be added to super-phosphate fertilizers) gives an effective protection for 12 months.