

REVIEW ARTICLE

Effect of Vitamin D on Performance of Ruminant Animal: A Review

Hamed AminiPour*

Department of Agriculture, Payam Noor University Of Karaj, Karaj,Iran.

Email: h.aminipor@gmail.com

ABSTRACT

Vitamin D is thought of as the “sunshine vitamin” because it is synthesized by various materials when they are exposed to sufficient sunlight. The 2 major natural sources of vitamin D are cholecalciferol and ergocalciferol. In this chapter, the term vitamin D in the absence of a subscript will imply either vitamin D₂ or vitamin D₃. Under modern farming conditions, some animals, especially poultry are raised in total confinement with little or no exposure to natural sunlight. Even though with enough sunlight exposure, vitamin D is not needed in the diet, it still fits the definition of a vitamin in all respects for animals and humans that are confined indoors away from the sun. In recent years vitamin D receptors have been found in tissues not associated with the traditional role of calcium metabolism. The additional role of vitamin D awaits further elucidation.

INTRODUCTION

Vitamins are defined as a group of complex organic compounds present in minute amounts in natural foodstuffs that are essential to normal metabolism and lack of which in the diet causes deficiency diseases.

Vitamins are required in trace amounts in the diet for health, growth, and reproduction. Omission of a single vitamin from the diet of a species that requires it will produce deficiency signs and symptoms. Many of the vitamins function as coenzymes; others have no such role, but perform certain essential functions. Some vitamins deviate from the preceding definition in that they do not always need to be constituents of food. Certain substances that are considered to be vitamins are synthesized by intestinal tract bacteria in quantities that are often adequate for body needs. However, a clear distinction is made between vitamins and substances that are synthesized in tissues of the body. Ascorbic acid, for example, can be synthesized by most species of animals, except when they are young or under stress conditions. Likewise, in most species, niacin can be synthesized from the amino acid tryptophan and vitamin D from action of ultraviolet light on precursor compounds in the skin. Thus, under certain conditions and for specific species, vitamin C, niacin, and vitamin D would not always fit the classic definition of a vitamin.

Classically, vitamins have been divided into two groups based on their solubility's in fat solvents or in water. Thus, fat-soluble vitamins include A, D, E, and K, while vitamins of the B-complex and C are classified water soluble. Fat-soluble vitamins are found in foodstuffs in association with lipids. The fat-soluble vitamins are absorbed along with dietary fats, apparently by mechanisms similar to those involved in fat absorption.

CHEMICAL STRUCTURE

Vitamin D designates a group of closely related compounds that possess anti rachitic activity. It may be supplied through the diet or by irradiation of the body. There are about 10 provitamins that, after irradiation, form compounds having variable antirachitic activity. The two most prominent members of this group are ergocalciferol (D₂) and cholecalciferol (D₃). Chemical structures of ergocalciferol and cholecalciferol and their precursors, ergosterol and 7-dehydrocholesterol, are shown in Fig 1. All sterols possessing vitamin D activity have the same steroid nucleus; they differ only in the nature of the side chain attached to carbon 17.

Ergocalciferol is derived from a common plant steroid, ergosterol, and is the usual dietary source of vitamin D. Cholecalciferol is produced exclusively from animal products. 7-Dehydrocholesterol is derived from cholesterol or squalene, which is synthesized in the body

and present in large amounts in skin, intestinal wall, and other tissues. Vitamin D precursors have no anti rachitic activity until the ring is opened between the 9 and 10 positions by irradiation and a double bond is formed between carbons 10 and 19 to form vitamin D. There is negligible loss of crystalline cholecalciferol over 1 year of storage in amber evacuated.

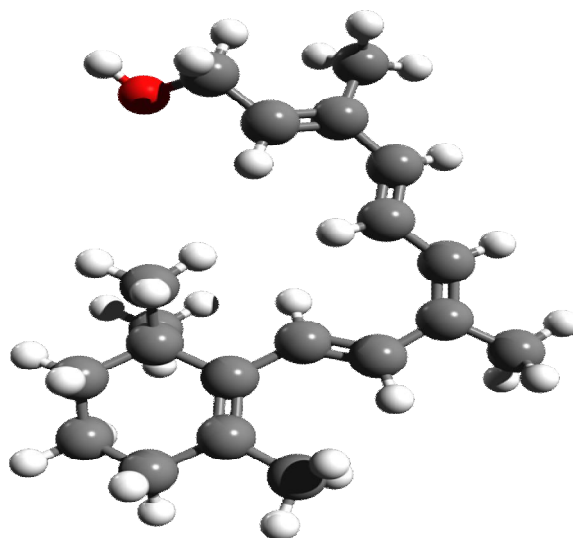


Fig. 1: Vitamin D₂ (ergocalciferol), vitamin D₃, (cholecalciferol), and their precursors in animal (7-dehydrocholesterol) and plant (ergosterol) tissues, from www.Wikipedia.com.

Physical and chemical methods of vitamin D analysis include UV absorption, colorimetric procedures, fluorescence spectroscopy, gas chromatography/mass spectroscopy, competitive binding assays, and high-pressure liquid chromatography (HPLC). The HPLC procedure is very promising, with the separation process resulting in an exceedingly high resolving capability and increased sensitivity [24, 27 and 42].

A major advantage of HPLC is that compounds are not altered by the heat of gas-liquid chromatography, so they may be detected as the actual known compounds. Other benefits of using HPLC are the reduced labor and time required to separate vitamin D and its metabolites. Compounds may be identified by the retention time of either an internal or external standard and a new technique of stop flow in which the UV spectrum of the molecule separated may be examined.

METABOLISM

Absorption and Transfer

Vitamin D obtained from it is absorbed from the intestinal tract, with conflicting reports as to which portion of the small intestine serves as the primary absorption site. It has also been suggested that the largest amount of dietary vitamin D is more likely to be absorbed in the ileum because of longer retention time of food in the distal portion of the intestine [14, 22, 25, and 42]. Vitamin D is absorbed from the intestinal tract in association with fats, as are all the fat-soluble vitamins. Like the others, it requires the presence of bile salts for absorption. Because it is fat soluble, vitamin D is absorbed with other neutral lipids via chylomicra into the lymphatic system of mammals or the portal circulation of birds and fishes. It has been reported that only 50% of a dose of vitamin D is absorbed. However, considering that sufficient vitamin D is usually produced by daily exposure to sunlight, it is not surprising that the body has not evolved a more efficient mechanism for dietary vitamin D absorption [1, 5, 18, 38 and 42].

Cholecalciferol is produced by irradiation of 7-dehydrocholesterol with UV light either from the sun or from an artificial source. Cholecalciferol is synthesized in the outer skin layers. Presence of the pro vitamin 7-dehydrocholesterol in the epidermis of the skin and sebaceous secretions is well recognized.

In poultry, Tian et al. [42, 61] reported that in the chicken, the skin of legs and feet contains about 30 times as much 7-dehydrocholesterol (pro vitamin D₃) as the body skin. Vitamin D is

Hamed AminiPour

synthesized in the skin of many herbivores and omnivores, including humans, rats, pigs, horses, poultry, sheep, and cattle. However, little 7-dehydrocholesterol is found in the skin of cats and dogs (and likely other carnivores), and therefore little vitamin D is produced in the skin [4, 17, 20, 42].

During exposure to sunlight, the high-energy UV photons penetrate the epidermis and photolyze 7-dehydrocholesterol (pro vitamin D₃) to pre vitamin D₃. Once formed, pre vitamin D₃ undergoes a thermally induced isomerization to vitamin D₃ that takes 2 to 3 days to reach completion. In poultry, the time course revealed a fourfold increase in the circulating concentration of vitamin D₃, with a peak about 30 hours post radiation [42, 61 and 65].

Approximately 15% of pro vitamin D₃ in human skin exposed to 10 minutes of simulated sunlight is converted in the stratum basale to vitamin D₃ [42, 44]. Longer exposure times do not significantly increase D₃ concentrations in the epidermis.

Heuser and Norris [19, 27, 42, 53] showed which 11 to 45 minutes of sunshine daily were sufficient to prevent rickets in growing chicks, and that no further improvements in growth were obtained under these conditions by adding cod liver oil. During initial exposure to sunlight, pro vitamin D₃ in the human epidermis is efficiently converted to pre vitamin D₃. However, because pre vitamin D₃ is also labile to sunlight, once it is formed, it begins to photolyze to additional photoproducts, principally lumisterol and tachysterol. The net result is that prolonged exposure to sunlight does not significantly increase the pre vitamin D₃ concentration above about 15% of the initial pro vitamin D₃ concentrations [6, 9, 42].

More than 90% of pre vitamin D₃ synthesis in skin occurs in the epidermis. The cholecalciferol formed by irradiation of the 7-dehydrocholesterol in the skin is absorbed through the skin and transported by the blood to the lipids throughout the body. Clearly, absorption can take place, because rickets can be successfully treated by rubbing cod liver oil on the skin. Once vitamin D₃ is formed, it is transported in the blood. Some of the vitamin D₃ formed in and on the skin ends up in the digestive tract as many animals consume the vitamin as they lick their skin and hair.

FUNCTIONS

The general function of vitamin D is to elevate plasma Ca and P to a level that will support normal mineralization of bone as well as other body functions. The active form of vitamin D, 1, 25-(OH)₂D, functions as a steroid hormone. The hormone is produced by an endocrine gland, circulated in blood bound to a carrier protein (DBP), and transported to target tissues.

In the target tissue, the hormone enters the cell and binds to a cytosolic receptor or a nuclear receptor. 1,25-(OH)₂D regulates gene expression through its binding to tissue-specific receptors and subsequent interaction between the bound receptor and the DNA [11, 40, 42, 59].

The receptor hormone complex moves to the nucleus, where it binds to the chromatin and stimulates the transcription of particular genes to produce specific mRNAs, which code for the synthesis of specific proteins. Evidence for transcription regulation of a specific gene typically includes 1, 25-(OH)₂D-induced modulation in mRNA levels. Additionally, evidence may include measurements of transcription and/or the presence of a vitamin D-responsive element within the promoter region of the gene (Hannah and Norman, 1994).

Recent research provides evidence that a membrane-bound receptor, in addition to nuclear receptors, exists [29, 42].

The 1, 25-(OH)₂D₃ receptor has been extensively characterized, and the DNA for the human receptor has been cloned (Baker et al., 1988). The 1,25-(OH)₂D₃ receptor is a protein with a molecular weight of about 67,000 daltons. The nucleotide sequence of the bovine vitamin D₃ receptor has been reported [26, 42].

Common vitamin D receptor gene alleles have been shown to contribute to the genetic variability in bone mass and bone turnover; however, the physiological mechanisms involved are unknown. The vitamin D receptor alleles are associated with differences in the vitamin D

endocrine system and may have important implications in relation to the pathophysiology of osteoporosis [32, 42].

Recent studies have identified a heterodimer of the vitamin D receptor (VDR) and a vitamin A receptor within the nucleus of the cell as the active complex for mediating positive transcriptional effects of 1, 25-(OH)₂D. The two receptors (vitamins D and A) selectively interact with specific hormone response elements composed of direct repeats of specific nucleotides located in the promoter of regulated genes. The complex that binds to these elements actually consists of three distinct elements: the 1,25-(OH)₂D₃ hormonal ligand, the vitamin D receptor, and one of the vitamin A (retinoid) X receptors [42, 55].

Since the late 1980s, it has become apparent that 1, 25-(OH)₂D₃ also has the potential to generate biological actions through mechanisms not dependent on regulation of gene transcription [30, 42].

Research suggests that 1,25-(OH)₂D₃ may also generate biological responses via signal transduction mechanisms that are independent of the nuclear VDRs, that are termed nongenomic pathways. Nongenomic responses can include stimulation of membrane lipid turnover, activation of Ca²⁺ channels, and elevation of intracellular Ca²⁺ concentrations, all of which have been shown to occur within seconds after addition of 1,25-(OH)₂D₃. Progress has been made in identifying and purifying an integral protein of the basal lateral membrane that may be a receptor for 1, 25-(OH)₂D₃ [28, 42].

These studies have provided definite correlations between binding to the solubilized membrane receptor and the ability to initiate transcaltachia (the rapid hormonal stimulation of Ca transport). The involvement in genomic and nongenomic signal transduction pathways is not unique to the steroid hormone 1,25-(OH)₂D₃; these same pathways are also utilized by virtually all steroid hormones [16, 42].

Tetany in humans and animals results if plasma Ca levels are appreciably below normal. Two hormones—thyrocalcitonin (calcitonin) and parathyroid hormone (PTH)—function in a delicate relationship with 1,25-(OH)₂D to control blood Ca and P levels. Production rate of 1, 25-(OH)₂D is under physiological control as well as dietary control. Calcitonin, contrary to the other two, regulates high serum Ca levels by (1) depressing gut absorption, (2) halting bone demineralization, and (3) reabsorption in the kidney. Vitamin D brings about an elevation of plasma Ca and P by stimulating specific pump mechanisms in the intestine, bone, and kidney. These three sources of Ca and P thus provide reservoirs that enable vitamin D to elevate the levels of Ca and P in blood to levels that are necessary for normal bone mineralization and for other functions ascribed to Ca.

Intestinal Effects

It is well known that vitamin D stimulates active transport of Ca and P across intestinal epithelium. This stimulation involves the parathyroid hormone directly and the active form of vitamin D.

Parathyroid hormone indirectly stimulates intestinal Ca absorption by stimulating production of 1, 25-(OH)₂D under conditions of hypocalcemia. As the human body becomes vitamin D insufficient, the efficiency of intestinal Ca absorption decreases from approximately 30 to 50% to no more than 15%.

The mechanism whereby vitamin D stimulates Ca and P absorption is still not completely understood.

Evidence [42, 64] indicates that 1, 25-(OH)₂D is transferred to the nucleus of the intestinal cell, where it interacts with the chromatin material. In response to the 1,25-(OH)₂D, specific RNAs are elaborated by the nucleus, and when these are translated into specific proteins by ribosomes, the events leading to enhancement of Ca and P absorption occur [42, 49].

In the intestine, 1,25-(OH)₂D promotes synthesis of Ca-binding protein (calbindin) and other proteins and stimulates Ca and P absorption. Vitamin D has also been reported to influence magnesium (Mg) absorption as well as Ca and P balance [42, 60].

Administration of 1, 25-(OH)₂D₃ to rachitic animals has been shown to stimulate the

incorporation of [^3H] leucine into several proteins of the intestinal mucosa. This apparent increase in protein synthesis was accounted for at least in part by the discovery that $1,25\text{-(OH)}_2\text{D}$ induces synthesis of a specific intestinal protein that has been identified as calbindin. Calbindin is not present in the intestine of rachitic chicks but appears after vitamin D treatment. Intestinal Ca transport relies on the integrated effects of both genomic and nongenomic mechanisms of hormone action. Two kinds of mucosal proteins are dependent on vitamin D: (1) calbindin and (2) intestinal membrane Ca-binding protein (IMCal). IMCal is a membrane component of the translocation mechanism rather than a cytosol constituent [42, 56].

It is proposed that the primary nongenomic mechanism by which $1,25\text{-(OH)}_2\text{D}$ regulates Ca transport across the luminal membrane of the enterocyte involves inducing a specific alteration in membrane phosphatidylcholine content and structure, which leads to an increase in membrane fluidity and thereby to an increase in Ca transport rate. The size of the villus and the microvilli increases upon $1, 25\text{-(OH)}_2\text{D}_3$ treatment. The brush border undergoes noticeable alterations in structure and composition of cell surface proteins and lipids, in a time frame corresponding to the increase in Ca^{2+} transport mediated by $1,25\text{-(OH)}_2\text{D}_3$ [42, 41 and 51].

In addition to inducing calbindin and IMCal, $1, 25\text{-(OH)}_2\text{D}_3$ has been shown to increase levels of several other proteins in the intestinal mucosa. These include alkaline phosphatase; Ca stimulated ATPase, and Phytase enzyme activities [3, 42].

Once Ca is transported to the basolateral membrane, it is extruded from the cell against a 1,000-fold concentration gradient by Mg-dependent Ca-ATPase, which is also increased by $1,25\text{-(OH)}_2\text{D}_3$ [13, 42].

Originally, it was believed that vitamin D did not regulate P absorption and transport, but in 1963, it was demonstrated, through the use of an in vitro inverted sac technique, that vitamin D does in fact play such a role [24, 42].

Little is known about the actual mechanism of phosphate transport, but phosphate is transported against an electrochemical potential gradient involving sodium in response to $1, 25\text{-(OH)}_2\text{D}_3$.

Bone Effects

Vitamin D plays roles both in the mineralization of bone as well as demineralization or mobilization of bone mineral. $1,25\text{-(OH)}_2\text{D}$ is one of the factors controlling the balance between bone formation and resorption. In young animals during bone formation, minerals are deposited on the matrix. This is accompanied by an invasion of blood vessels that gives rise to trabecular bone. This process causes bones to elongate. During vitamin D deficiency, this organic matrix fails to mineralize, causing rickets in the young and osteomalacia in adults. $1,25\text{-(OH)}_2\text{D}_3$ brings about mineralization of the bone matrix, and Wasserman et al. [65] provided evidence that $1,25\text{-(OH)}_2\text{D}_3$ is localized in the nuclei of bone cells. Also, there is some indication that $24, 25\text{-(OH)}_2\text{D}_3$ and possibly 25-OHD_3 may have unique actions on bone. Vitamin D also plays a role in the mobilization of Ca from bone to the extracellular fluid compartment. This function is shared by PTH [42, 63].

However, little is known about the mechanism of bone reabsorption in response to these factors, although it may be similar or identical to the intestinal transport system. It is an active process requiring metabolic energy, and presumably it transports Ca and phosphate across the bone membrane by acting on osteocytes and osteoclasts.

Rapid, acute plasma Ca regulation is due to the interaction of plasma Ca with Ca-binding sites in bone mineral since blood is in contact with bone. Changes in plasma Ca are brought about by a change in the proportion of high- and low-affinity Ca-binding sites, access to which is regulated by osteoclasts and osteoblasts, respectively [42, 45].

These cells, in turn, respond to hormonal signals by shape changes. Contraction of osteoclasts and corresponding expansion of osteoblasts make more high-affinity sites available, whereas osteoblast contraction and osteoclast expansion, make more low-affinity

sites available, leading to a decrease or an increase in the blood Ca level, respectively.

Another role of vitamin D has been proposed in addition to its involvement in bone; namely, in the biosynthesis of collagen in preparation for mineralization [23, 42].

A vitamin D deficiency causes inadequate cross-linking of collagen as a result of low lysyl oxidase activity, which is involved in a condensation reaction for the collagen cross-linking. This may be a direct effect of vitamin D or a result of mineral changes in blood; it is not considered a major function of vitamin D.

CALCIUM AND PHOSPHORUS ABSORPTION BY RUMINANTS

Calcium

There is clear evidence that sheep and cattle absorb Ca from their gut according to need and that they can alter the efficiency of absorption to meet a change in requirement.

For example, Braithwaite and Riazuddin [2, 37, and 39] showed which youth sheep by a high Ca requirement absorb Ca at a higher rate and with greater efficiency than mature animals with a low requirement. An increase in both absorption and efficiency of absorption also occurs in mature sheep when their requirement for Ca is increased through pregnancy or lactation or after a period of Ca deficiency [5, 42, 48].

Studies in cattle have given similar results. Thus, the efficiency of absorption of Ca in the small intestine of the dairy cow has been shown to rise in response to a reduction in dietary Ca intake and to the onset of lactation [12, 21, 42, and 54].

Calcium absorption has also been shown to be directly related to milk production, though in early lactation, when the demand for Ca is greatest, the increase in absorption falls short of the requirement, with the deficit being met by increased bone resorption [8, 42, 52, 58].

The mechanism by which Ca is adjusted in response to requirement has received much attention. In this sequence, a fall in plasma Ca concentration resulting from an increase in demand leads in turn to an increase in parathyroid hormone release. This then stimulates the increased production by the kidney of 1,25-(OH)₂D, which acts on the gut to increase the production of calbindin and so accelerates Ca absorption. In a reverse manner, an increase in plasma Ca concentration causes suppression of parathyroid hormone release, a reduction in 1,25-(OH)₂D production, and reduced Ca absorption. Although all aspects of this system have not yet been fully examined in ruminants, it appears that the same mechanism operates, in that an increase in circulatory 1, 25-(OH)₂D level has been found to precede the increase in Ca absorption that occurs in cattle soon after parturition [42, 43, 46, 62].

EFFECT OF DIETARY

Ruminants

The outstanding disease of vitamin D deficiency is rickets, generally characterized by a decreased concentration of Ca and P in the organic matrices of cartilage and bone. The signs and symptoms are similar to those of a lack of Ca or P or both, as all three are concerned with proper bone formation. In the adult, osteomalacia is the counterpart of rickets and, since cartilage growth has ceased, is characterized by a decreased concentration of Ca and P in the bone matrix. Osteoporosis is defined as a decrease in the amount of bone, leading to fractures after minimal trauma. In osteoporosis, bone mineral and protein matrix are lost, resulting in less overall bone but normal composition. Osteomalacia is also characterized by inadequate bone mineralization; however, in contrast to osteoporosis, persons with osteomalacia have normal protein matrix that is not fully mineralized. When bone mass becomes too low, mechanical support and skeletal integrity cannot be maintained, and fractures can occur with minimal trauma.

Clinical signs of vitamin D deficiency are seen mainly in the young. General consequences of deficiency can appear as inhibited growth, weight loss, and reduced or lost appetite before characteristic signs that relate primarily to the bone system become apparent. The role of vitamin D in the adult appears to be much less important except during reproduction and lactation. Congenital malformations in newborns result from extreme deficiencies in the diet of the mother during gestation, and the mother's skeleton is injured as well.

The same disruption of the orderly processes of bone formation with vitamin D deficiency occurs in animals as it does in humans and includes the following characteristics [15, 47]:

1. Failure of Ca salt deposition in the cartilage matrix.
2. Failure of cartilage cells to mature, leading to their accumulation rather than destruction.
3. Compression of the proliferating cartilage cells.
4. Elongation, swelling, and degeneration of proliferative cartilage.
5. Abnormal pattern of invasion of cartilage by capillaries.

Although there appear to be differences between species in the susceptibility of different bones to such degenerative changes, differences that probably reflect bodily conformation and stance there is nevertheless an apparent common pattern.

Spongy parts of individual bones, and bones relatively rich in spongy tissue, are first and worst affected. As in simple Ca deficiency, the vertebrae and the bones of the head suffer the greatest degree of resorption. Next come the scapula, sternum, and ribs. The most resistant bones are the metatarsals and the shafts of long bones.

Clinical signs of vitamin D deficiency in ruminants are decreased appetite and growth rate, digestive disturbances, rickets, stiffness in gait, labored breathing, irritability, weakness, and occasionally tetany and convulsions. There is enlargement of joints, slight arching of the back, and bowing of legs, with erosion of joint surfaces causing difficulty in. Young ruminants may be born dead, weak, or deformed.

Clinical signs involving bones begin with thickening and swelling of the metacarpal or metatarsal bones. As the disease progresses, the forelegs bend forward or sideways. In severe or prolonged vitamin D deficiency, tension of the muscles will cause bending and twisting of long bones to give the characteristic deformity of bone. There is enlargement at ends of bones from deposition of excess cartilage, giving the characteristic "beading" effect along the sternum where ribs attach. The lower jaw bone becomes thick and soft; in severe cases, eating is then difficult. Calves may experience slobbering, inability to close the mouth, and protrusion of the tongue [9, 36, and 42]. Joints (particularly the knee and hock) become swollen and stiff, the pastern straight, and the

Back humped. In more severe cases, synovial fluid accumulates in the joints. Posterior paralysis may also occur as the result of fractured vertebrae. The structural weakness of the bones appears to be related to poor mineralization. The advanced stages of the disease are marked by stiffness of gait, dragging of the hind feet, irritability, tetany, labored and fast breathing, weakness, anorexia, and retardation of growth. Calves may be born dead, weak, or deformed [10, 28, 30, 42, and 44].

Clinical signs of vitamin D deficiency in sheep and goats are similar to those in cattle, including rickets in young animals and osteomalacia in adults. An early report of rickets in Scotland referred to the condition as "bent leg," which occurred in ram lambs 7 to 12 months of age.

The condition was prevented by administration of small doses of vitamin D in the form of cod liver oil. Newborn lambs can receive enough vitamin D from their dams to prevent early rickets if the dams have adequate storage. Newborn kids had rickets if the dam was deficient in vitamin D during pregnancy.

In older animals with vitamin D deficiency (osteomalacia), bones become weak and fracture easily, and posterior paralysis may accompany vertebral fractures. In dairy cattle, milk production may be decreased and estrus inhibited by inadequate vitamin D. Cows fed a diet deficient in vitamin D and kept out of direct sunlight showed definite signs of vitamin D deficiency within 6 to 10 months [34, 42].

Functions that deplete vitamin D are high milk production and advancing pregnancy, especially during the last few months before calving. The visible signs of vitamin D deficiency in dairy cows are similar to those of rickets in calves. The animal begins to show stiffness in limbs and joints, which make it difficult to walk, lie down, and get up. The knees, hocks, and other joints become swollen, tender, and stiff. The knees often spring forward, the posterior joints straighten, and the animal is tilted on its toes. The hair becomes coarse and rough, and the animal has an overall appearance of unthriftiness [7, 34, and 51].

Hamed AminiPour

As the deficiency advances, the back often becomes stiff, humped, bent, and flexed. In vitamin D-deficient herds, calving rates are lower and calves have been born dead or weak. Milk fever is a paralyzing metabolic disease caused by hypocalcemia near parturition and initiation of lactation in high milk-producing dairy cows. Milk fever is an impaired metabolic condition that is related to Ca status, previous Ca intake, and malfunction of the hormone form of vitamin D [1,25-(OH)₂D] and PTH.

Animals that develop milk fever are unable to meet the sudden demand for Ca that is brought about by the initiation of lactation. Milk fever usually occurs within 72 hours after parturition and is manifested by circulatory collapse, generalized paresis, and depression of consciousness. The most obvious and consistent abnormality is acute hypocalcemia, in which serum Ca decreases from a normal 8 to 10 mg/dL to 3 to 7 mg/dL. Early in the onset, the cow may exhibit some unsteadiness as she walks. More frequently, the cow is found lying on her sternum with her head displaced to one side, causing a kink in the neck, or turned into the flank. The eyes are dull and staring and the pupils dilated. If treatment is delayed many hours, the dullness gives way to coma, which becomes progressively deeper, leading to death.

Aged cows are at the greatest risk of developing milk fever. Heifers almost never develop milk fever. Older animals have a decreased response to dietary Ca stress due to both decreased production of 1,25-(OH)₂D and decreased response to the 1,25-(OH)₂D. Target tissues of cows with milk fever may have defective hormone receptors, and the number of receptors declines with age. In older animals, fewer osteoclasts exist to respond to hormone stimulation, which delays the ability of bone to contribute Ca to the plasma Ca pool [25, 27, 31, and 42].

The aging process is also associated with reduced renal 1 α -hydroxylase response to Ca stress, therefore reducing the amount of 1,25-(OH)₂D produced from 25-OHD. Parturient paresis also occurs in ewes. It is a disturbance of metabolism in pregnant and lactating ewes characterized by acute hypocalcemia and the rapid development of hyperexcitability, ataxia, paresis, coma, and death. The disease occurs any time from 5 weeks before to 10 weeks after lambing, principally in highly conditioned older ewes at pasture. The onset can be associated with an abrupt changing of feed, a sudden change in weather, or short periods of fasting imposed by circumstances such as shearing or transportation. The degree of involvement of vitamin D by Ca metabolism in parturient paresis by sheep is unclear.

Vitamin D should be supplied to growing animals that are denied sunlight over extended periods because of cloud cover or confinement housing. In northern latitudes during winter, photochemical conversion of pro vitamin D to its active compound in the skin of ruminants is limited because of insufficient UV radiation.

25-OHD was higher in plasma of cattle in summer than in winter. 25-OHD concentrations of blood plasma were higher if bulls were kept outdoors versus indoors. Vitamin D deficiency may be observed in young ruminants that are closely confined and do not consume sun-cured roughage.

The clinical history of a flock of sheep kept under total confinement which showed a high incidence of an osteodystrophic condition. A form of osteodystrophia has also been produced experimentally in goats.

When grazing ruminants have normal exposure to direct sunlight or are fed normal amounts of sun-cured forage, little chance for vitamin D deficiency exists. However, seasons of minimum sunlight, artificially cured forages, sheep with full fleece, feedlot animals without access to sunlight or sun-cured forages, and high-producing dairy cows with limited access to sunlight or sun-cured forage may lead to the need for dietary supplementation [11, 33, 42, 63].

REFERENCES

1. Abrams, J. T. (1978). In *Handbook Series in Nutrition and Food*, Section E: Nutritional Disorders (M. Rechcigl Jr., ed.), Vol. 2, and p. 179. CRC Press, Boca Raton, Florida.
2. Braithwaite, G. D. (1974). *Br. J. Nutr.* 31, 319.
3. Braithwaite, G. D., and Riazuddin, S. H. (1971). *Br. J. Nutr.* 26, 215.
4. Braithwaite, G. D., Glascock, R. F., and Riazuddin, S. H. (1969). *Br. J. Nutr.* 23, 827.

Hamed AminiPour

5. Braithwaite, G. D., Glascock, R.F., and Riazuddin, S. H. (1972). *Br. J. Nutr.* 27,417.
6. Bronner, F. (1987). *J. Nutr.* 117, 1347.
7. Bronner, F., and Stein, W.D. (1995). *J. Nutr.* 125, 1987S.
8. Brunvand, L., Haga, P., Tangsrud, S. E., and Haug, E. (1995). *Acta Paediatrica*84, 106.
9. Chen, Jr., P.S., and Bosmann, H.B. (1964). *Science* 150, 19.
10. Church, D. C., and Pond, W.G. (1974). *Basic Animal Nutrition and Feeding*. Albany Printing, Albany, New York.
11. Collins, E.D., and Norman, A.W. (1991). In *Handbook of Vitamins* (L.Machlin, ed.) p. 59. Marcel Dekker, New York.
12. Craig, J.F., and Davis, G.O. (1943). *J. Comp. Pathol. Ther.* 53, 196.
13. Doppelt, S.H., Neer, R.M., Daly, M., Bourvet, L., Schiller, A., and Holick, M.F. (1983). *Orthop. Trans.* 7, 512.
14. El-Hag, A.I., and Karrar, Z.A. (1995). *Annals Trop. Pediat.* 15, 69.
15. Elliot, W., and Crichton, A. (1926). *J. Agar. Sci.* 16, 65.
16. Feliciano, E.S., Ho, M., Specker, B.L., Falciglia, G., Shui, Q.M., Yin, T.A., and Chen, X.C. (1994). *J. Trop. Pediat.* y40, 162.
17. Fleet, J.C. (1999). *Nutr. Rev.* 57, 60.
18. Fraser, D.R. (1984). In *Nutrition Reviews, Present Knowledge in Nutrition* (R.E.Olson, ed.), p. 209. Nutrition Foundation, Washington, D.C.
19. Garabedian, M., Tanaka, Y., Holick, M.F., and DeLuca, H.F. (1974). *Endocrinology* 94, 1022.
20. Goff, J.P., Horst, R.L., and Littledike, E.T. (1984). *J. Nutr.* 114, 163.
21. Goff, J.P., Reinhardt, T. A., and Horst, R.L. (1989). *Endocrinology* 125, 49.
22. Goff, J.P., Reinhardt, T. A., and Horst, R.L. (1991b). *J. Dairy Sci.* 74, 4022.
23. Gonnerman, W.A., Toverud, S.V., Ramp, W. K., and Mechanic, G.L. (1976). *Proc. Soc. Exp. Biol. Med.* 151, 453.
24. Guillard, J.C., de Carvalho, M. J. C., Moreau, D., Boggio, V., Lhuissier, M., and Fuchs, F. (1994). *Nutr. Res.* 14, 1317.
25. Harrison, H. C., and Harrison, H. E. (1963). *Am. J. Physiol.* 205, 107.
26. Harrison, H.E. (1978). In *Handbook Series in Nutrition and Food, Section E: Nutritional Disorders* (M. Rechcigl Jr, ed.), Vol. 3, and p. 117. CRC Press, Boca Raton, Florida.
27. Heuser, G.F., and Norris, L.C. (1929). *Poult. Sci.* 8, 89.
28. Hidioglou, M., Prouix, J.G., and Roubos, D. (1979). *J. Dairy Sci.* 62, 1076.
29. Hidioglou, M., Williams, C.J., and Ho, S.K. (1978). *Can. J. Anim. Sci.* 58, 621.
30. Holick, M.F. (1987). *Fed. Proc. Fed. Am. Soc. Exp. Biol.* 46, 1876.
31. Holick, M.F., MacLaughlin, J. A., and Doppelt, S.H. (1981). *Science* 211, 590. Horst, R.L., and Napoli, J.L. (1981). *Fed. Proc. Fed. Am. Soc. Exp. Biol.* 40,898(Abstr).
32. Horst, R.L., DeLuca, H.F., and Jorgensen, N.A. (1978). *Metab. Bone Dis. Relat. Res.* 1, 29.
33. How, K.L., Hazewinkel, H. A. W., and Mol, J.A. (1995). *Proc. Voorjaarsdagen Congress* (H.P. Meyer and H.A.W. Hazewinkel, Ed.) p. 1, Amsterdam.
34. Howard, G., Nguyen, T., Morrison, N., Watanabe, T., Sambrook, P, Eisman, J., and Kelly, P.J. (1995). *J. Clin. Endocrinal. Metab.* 80, 2800.
35. Kliewer, S. A., Umesono, K., Mangelsdorf, D.J., and Evans, R.M. (1992). *Nature*, 355, 446.
36. Kramer, B., and Gribetz, D. (1971). In *The Vitamins* (W.H. Sebrell Jr and R.S. Harris, eds.), p. 259. Academic Press, New York.
37. Lebrun, J.B., Moffatt, M.E.K., Mundy, R.J.T., Sangster, R.K., Postl, B. D., Dooley, J.P., Dilling, L.A., Godel, J.C., and Haworth, J.C. (1993). *Can. J. Public Health* 84, 394.
38. Lester, G.E. (1986). *Fed. Proc. Fed. Am. Soc. Exp. Biol.* 45, 2524.
39. Lowik, M.R.H., Van Den Berg, H., Schrijver J, Odink, J., Wedel, M., and Van Houten, P. (1992). *J. Am. Coll. Nutr.* 11, 673.
40. Mayer, G.P., Ramberg, C.F., and Kronfeld, D.S. (1968). *J. Nutr.* 95, 202.
41. McDowell, L.R. (1997). *Minerals for Grazing Ruminants in Tropical Regions*. University of Florida, Gainesville.
42. McDowell, L.R. (2001).
43. McIntosh, G. H., and Tomas, F.M. (1978). *Q. J. Exp. Physiol.* 63, 119.
44. Miller, E.R., Ullrey, D.E., Zutaut, C. L., Hoeffler, J.A., and Luecke, R.W. (1965). *J. Nutr.* 85, 255.
45. Neibergs, H. L., Bosworth, B. T., and Reinhardt, T.A. (1996). *J. Dairy Sci.* 79, 1313.
46. Nemere, I. (1995). *J. Nutr.* 125, 1695S.
47. Nemere, I., Zhou, I.X., and Norman, A. W. (1993). *Receptor* 3, 277.
48. Norman, A. W. (1995). *J. Nutr.* 125, 1687S.
49. Norman, A. W., and DeLuca, H.F. (1963). *Biochemistry* 2, 1160.
50. Ohnuma, N., Bannai, K., Yamagauchi, H., Hashimoto, Y., and Norman, A. W. (1980). *Arch. Biochem. Biophys.* 204, 387.
51. Quaterman, J., Dalgarno, A. C., Adam, A., Fell, B.F., and Boyne, R. (1964). *Br. J. Nutr.* 18, 65.
52. Richter, V.G.H., Flachowsky, F., Matthey, M., Ochrimenko, W.I., Wolfram, D., and Schade, T. (1990). *Vet. Med.* 45, 227.
53. Rupel, I.W., Bohstedt, G., and Hart, E. B. (1933). *Wisc. Agric. Exp. Stn. Res. Bull.* 115.
54. Schachter, D., and Kowarski, S. (1982). *Fed. Proc. Fed. Am. Soc. Exp. Biol.* 41, 84.
55. Scott, D., and McLean, A.F. (1981). *Proc. Nutr. Soc.* 40, 257.

Hamed AminiPour

56. Scott, K.C., and Latshaw, J.D. (1994). *Anim. Feed Sci. Tech.* 47, 99.
57. Scott, M.L., Nesheim, M.C., and Young, R.J. (1982). Nutrition of the Chicken, p. 119. Scott, Ithaca, New York.
58. Solanki, T., Hyatt, R.H., Kemm, J.R., Hughes, E.A., and Cowan, R.A. (1995). *Age and Aging* 24, 103.
59. Sood, S., Reghunandanan, R., and Reghunandanan, V. (1995). *Indian J. Exp. Biol.* 33, 61.
60. Sutton, R.A.L., and Dirks, J.H. (1978). *Fed. Proc. Fed. Am. Soc. Exp. Biol.* 37, 2112.
61. Tian, X.Q., Chen, T.C., Liu, Z., Shao, Q., and Holick, M.F. (1994). *Endocrinology* 135, 655.
62. Tomas, F.M. (1974). *Aust. J. Agric.* 25, 495.
63. Tomas, F.M., and Somers, M. (1974). *Aust. J. Agric. Res.* 25, 475.
64. Wallis, G.C. (1944). *S.D. Agric. Exp. Stn. Bull. No. 372*. South Dakota State University, Brookings.
65. Wasserman, R.H. (1981). *Fed. Proc. Fed. Am. Soc. Exp. Biol.* 40, 68.
66. www.Wikipedia.com, 2011.