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## **Vitamin D deficiency in rabbits**

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**The topic of the “vitamin of sun” or vitamin D is brought up again and again. This vitamin has an active role in the health of bone, muscles and immunity and plays a preventive role against certain diseases and cancers.**

Vitamin D is not present naturally in the body of mammals and man in spite of its important role. It is also absent in most food, or present in small quantities only. Only ultraviolet sunrays (270–300 nm) of minimal index 3 strength can activate the transformation of the 7-dehydrocholesterol precursor, which is present in keratinocytes into – cells of the superficial layer of the skin, or fur hairs of mammals and convert these into a molecules that the body can absorb: vitamin D<sub>3</sub> (vit. D). In birds and most mammals, the skin is covered by feathers or fur that prevents UVB to reach the skin. As a consequence, vit. D<sub>3</sub> is not synthesized in the skin, but within oily secretions covering the feather and hairs. Vitamin D is ingested when the birds or animals groom themselves. Excessively produced vitamin D is rapidly excreted by the body.

The transformation of the vit. D precursor (7-dehydrocholesterol) by UVB has been

discovered in 1923 by Harry Goldblatt and Katherine Soames, research that was later developed by Alfred Fabian Hess and Mildred Weinstock. In 1930, Adolf Windaus (University of Gottingen, Germany) was given the Nobel Prize for his research on sterols and their relation with vitamins. He continued his research on the structure of vit. D. In fact, this molecule is named wrongly as it is a hormone.

In man, and more often in elderly persons, vit. D deficiency is widespread. Over the last years, I have had the opportunity to study numerous blood test results (CBC and biochemistry panel) of rabbits in Switzerland, in Europe and in the USA. To my surprise, the lack of vit. D is also common in rabbits. When not treated, the effect on their health can have grave consequences. Over the last years, I had the opportunity to analyze blood panels from rabbits in Switzerland, Europe and the USA (n=5), and some with a follow-up over 12 to 36 months. Different stages of vit. D deficiency stages were observed. When left untreated, it can have devastating effects on the health of these rabbits.

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CBC - Female spayed rabbit n°2, 3 years old						
	July 2012		June 2013		Reference	Remarks
White blood cells		5.2	Low	3.9	5-12K/ul	
Heterophils			Low	1560	2275-9759/ul	
Monocytes				263	0-850/ul	
Lymphocytes		30%		1872	1500-7000/ul	Infection/inflammation
Eosinophils		0%	High	168	0-100/ul	Inflammation or presence of parasites
Red blood cells	Low	4.7		5.4	5.0-8.0 10 <sup>6</sup> /ul	
Hemoglobin		10.5		12.2	10-15 g/dL	
Hematocrit	Low	31		38	36-48%	Mirrors RBC results
MCV		65			65-75 mm <sup>3</sup>	Sign of deficient iron metabolism
MCH			High	22.6	12.5-17.5 pg	Mirrors MCV
Platelets		440		463	200-500 K/ul	Sign of deficient iron metabolism
Biochemical parameters						
ALP	High	40	High	37	4-20 IU/l	If ALP only is elevated = not a liver problem. A sole elevation of ALP = bone disease, demineralization of the bones. This is confirmed by the low level of phosphorus. Also heart failure. Suggests a possible vit. D deficiency
ALT	Low	39		71	48-70 U/l	Insignificant or malnutrition
AST	Low	19	Low	17	33-99U/l	Insignificant or malnutrition
BUN	Low	16	Low	15	17-24 mg/dL	Insignificant or malnutrition
Glucose		136	High	202	108-160mg/dL	Frequent cause in rabbits : stress
Cholesterol	Low	21		33	24-65 mg/dL	
Bilirubin		0.2	Low	0.1	0.2-0.8 mg/dL	
Albumin	High	4.2	High	5.9	2.7-3.6 g/dL	Possible chronic dehydration ?
Globulin	Low	2.1	Low	2.3	2.9-4.9 g/dL	
Calcium		12		15.6	8-15.5 mg/dL	
Phosphorus		4.5	Low	3.4	4.4-7.2	See ALP
Potassium		4.5		5.4	4.3-5.8 mEq/l	

**Table 1:** Modified values of the blood panels of spayed female n°2 (3 years old) that has never been given the opportunity to get sun exposure. She presents an early stage of vit. D deficiency with signs of osteoporosis. The owner confirmed that her rabbit has no access to sun light

### Special calcium metabolism

Vit. D regulates the absorption of calcium and phosphorus in the intestine in order to ensure a good mineralization of the bones. In most mammals, the absorption of calcium in the intestine is linked to the metabolic needs of the body, while in rabbits; absorption of this mineral depends on the amount present in the food and less so

about the metabolic needs and vit. D. The levels of calcium in the blood are also different. While they are relatively stable and range between 5.0-6.4 mg/dL in mammals, they are superior by 30 to 50% in rabbits: 13-15 mg/dL. The urinary elimination of calcium varies accorded to the amount ingested by the rabbits, unlike mammals. In order to facilitate this process,

the amount of calcium filtered by the kidney glomeruli is high: 40 to 60% (less than 2% for mammals). When the metabolic needs in calcium increase (growth, gestation, lactation), the amount of calcium excreted in the urine decreases. This particularly efficient calcium metabolism of rabbits is necessary to insure the lifetime growth of incisors and cheek teeth (2 to 4 mm/week).

### Blood biochemistry

Caged and indoor (house) rabbits don't

have the opportunity to nibble fresh grass or to hop on a natural soil. Arguments used to keep rabbits inside are the presence of predators, the possible infection with parasites, summer heat or the possibility to develop a special bond with the animal. Yet, keeping a rabbit exclusively inside and non-exposure to UVB ultraviolet rays carry their lot of problems: vit. D deficiency, which is not compensated by food (Table 1, 2, 3).

The biochemical analysis of blood of these rabbits shows invariably the same change.

CBC - Female rabbit n°5, unknown age					
	May 2013		September 2013		Reference
WBC	Low	3.5			5-12K/ul
Monocytes	High	8.0			0-2%
Lymphocytes		56%	Low	432	1500-7000/ul
Eosinophils		1%	High	208	0-100/ul
RBC		5.31			4-7 10 <sup>6</sup> /ul
Hemoglobin	Low	11.5	Low		10-15 g/dL
Hematocrit	Low	33.4	Low	32	36-48%
MCV	Low	63	Low	62	65-75 mm <sup>3</sup>
MCH		21.7	High	20.5	12.5-17.5 pg
Platelets		232	High	1053	200-500 K/ul
Biochemical parameters					
ALP	High	53	High	168	4-20 IU/l
ALT	Low	33	Low		48-70 U/l
AST	Low	18	Low		33-99U/l
Creatin kinase	High	1231			140-372U/l
BUN	Low	15	Low	8	17-24 mg/dL
GGT	Low	4			50-140 U/l
Glucose	High	263			108-160mg/dL
Cholesterol	Low	19			24-65 mg/dL
Bilirubin	Low	0.1			0.2-0-8 mg/dL
Albumin	High	3.9	High		2.7-3.6 g/dL
Globulin	Low	1.8			2.9-4.9 g/dL
Albumin/Globulin	High	2,2			0.7-1.9
Phosphorus			Low	2.4	4.4-7 mmol/l
Potassium			Low	3.3	4.3-5.8 mg/dL

**Table 2:** Blood panel values of the female rabbit n°5 (age unknown) suffering from vit. D deficiency over a longer period of time, with a deficient iron metabolism and possible cardiovascular problems. The owner confirmed that his rabbit lives in a relatively dark apartment, with access to sun light. See also Figure 2.

The level of enzymes hydrolyzing a phosphate group off organic molecules – alkaline phosphatase (ALP) is very elevated. These enzymes are indicative of the liver function or bone disease. If the other tests of the hepatic function (AST, ALT, GGT, and albumin) have all normal results, the problem has an osseous origin. Two other tests return low levels: serum phosphate and calcium phosphate. All in all, the abnormal levels of ALP, phosphate and glucose) are indicative of vit. D deficiency.

In rabbits these changes are usually accompanied by a high blood level of glucose while that of cholesterol is

extremely low. The level of one of the 2 serum proteins – globulin, is also very low; that of the other protein – albumin, is normal. Creatinine phosphokinase (CK) are sometimes elevated. An elevated level of this enzyme, which is secreted by certain tissues, accompanied by a low level of cholesterol and abnormal levels of ALP, phosphorus and calcium point out muscular weakness. These animals often develop heart pathology.

### Hematological analyses (CBC)

A chronic vit. D deficiency also leads to changes in the complete blood count. Two

CBC – Male neutered rabbit n°3, 4 years old							
	2008		2010		2012		Référence
WBC		7.8		5.8		5.7	5-12K/ul
Heterophils		-	Low	2262		3249	2275-9759/ul
Monocytes		116		156		456	0-850/ul
Lymphocytes		5304		3828		1938	1500-7000/ul
Eosinophils		0		0		57	0-100/ul
Globules rouges		6.6		5.8		6.6	5.0-8.0 10 <sup>6</sup> /ul
Hemoglobin		13.8		12.2		14.2	10-15 g/dL
Hematocrit		39	Low	35		43	36-48%
MCV	Low	60	Low	59		65	65-75 mm <sup>3</sup>
MCH	High	21	High	20.8	High	21.8	12.5-17.5 pg
Platelets		-		-		-	200-500 K/ul
Biochemical parameters							
ALP	High	54	High	89		46	4-20 IU/l
ALT	Low	39		21		21	48-70 U/l
AST	Low	13	Low	17		12	33-99U/l
BUN		19		24		20	17-24 mg/dL
Glucose	High	174		116		115	108-160mg/dL
Cholesterol		35		40		33	24-65 mg/dL
Bilirubin	Low	0.1	Low	0.1	Low	0.1	0.2-0.8 mg/dL
Albumin	High	3.7	High	4.2		3.8	2.7-3.6 g/dL
Globulin	Low	1.8	Low	1.7	Low	2.1	2.9-4.9 g/dL
Calcium		12.3		13.7		12.9	8-15.5 mg/dL
Phosphorus	Low	3-3		4.5	Low	3.9	4.4-7.2
Potassium		4.3		5.2		5.0	4.3-5.8 mEq/l

**Table 3:** Modified blood panel values in castrated male rabbit n°3, 4 years old, that has no exposure to sunlight. He presents an early stage of vit. D deficiency, with early signs of bone disease.

results are noteworthy: a very low level of hemoglobin (anemia) that is caused by a deficient iron metabolism and a very high platelet count (Table 1, 2, 3). The latter are responsible for blood coagulation; a high level of platelets leads to cardiovascular problems.

Lack of vit. D also affects white blood cells, cells of the immune system that protect against exterior aggressions. Lymphocytes are very low. There is also an inverted proportionality between vit. D and the level of eosinophil cells in man. The worse the vit. D deficiency, the higher is the level of eosinophil cells. Such a correlation is also observed in rabbits (Table 1, 2, 3). One should thus not hastily conclude that a high level of eosinophils is linked to the presence of parasites, but a sign of inflammation.

In conclusion, vit. D deficiency as similar



**Figure 1:** "Indian feather" pattern on the incisors of a female rabbit suffering from metabolic bone disease.

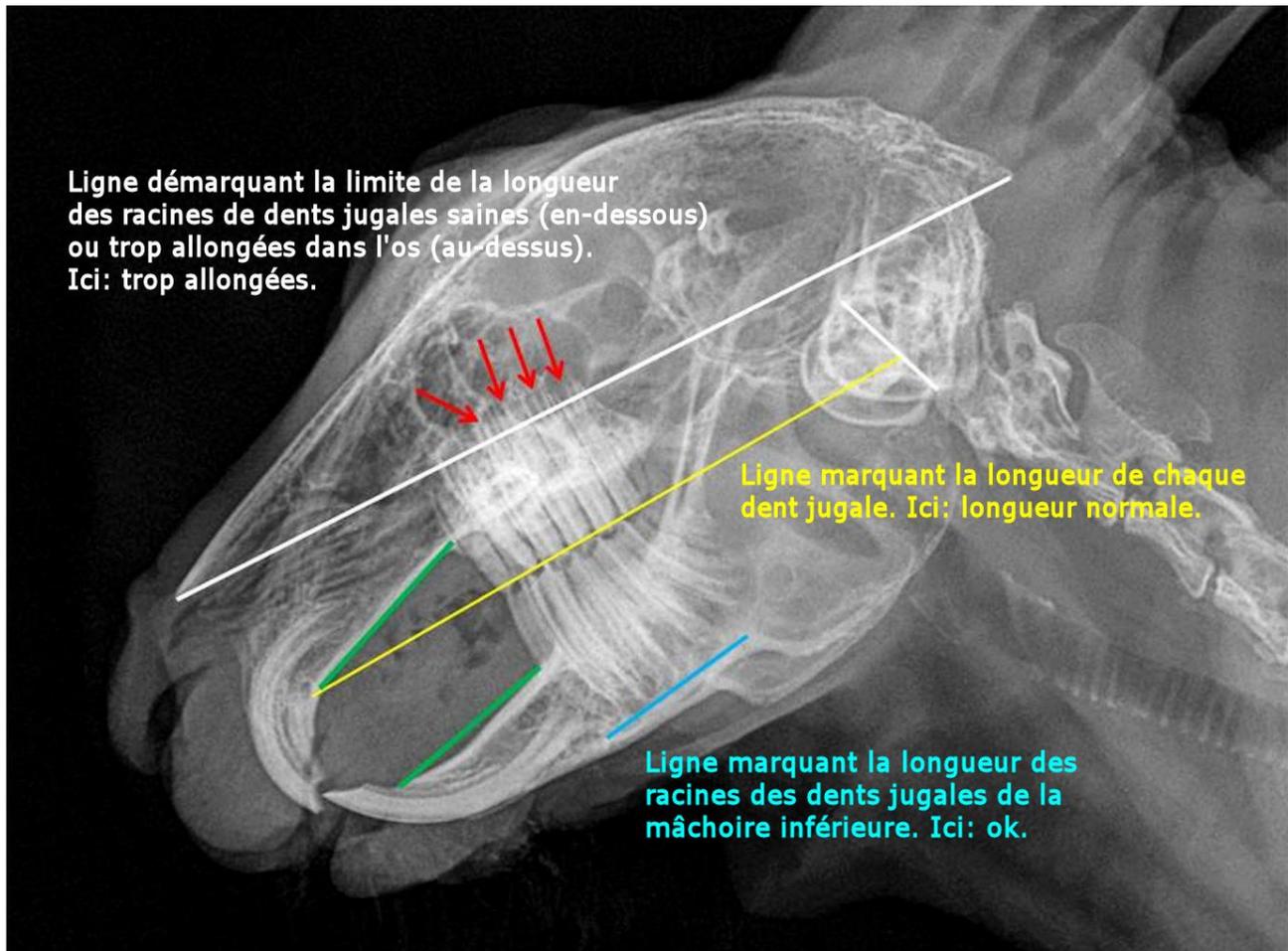
consequence on the health of man and that of rabbits: demineralization of bones, deficient iron metabolism and anemia, effect on the immune system and inflammation, muscular weakness and cardiovascular.

### **Bone and dental problems**

A rabbit that lives in an environment without sun exposure and is fed a diet deficient in vit. D with develop metabolic bone disease. "Indian feather" pattern on the incisors of a female rabbit that developed metabolic disease, due to a lifetime refusal to eat her cecal droppings.

The quality of bone is poor (osteomalacia). The skull is also affected by bone demineralization (osteoporosis), more particularly the upper and lower jaw bones. The volume of the alveolar bone surrounding and keeping the incisors and cheek teeth in their sockets decreases. Teeth start to move and growth irregularly. Malocclusion develops as a result. Roots of teeth can grow into the bone, into the ocular cavity or can pass through the lower jaw bone. This is called "acquired dental disease", irreversible and evolutionary. Treatment depends on the stage of the disease; it is usually difficult and expensive. Vitamin supplements exist but should be dosed carefully as rabbits are very sensitive to vit. D overdoses, dangerous too.

A sun exposure and a varied diet remains the best cure. Food that is high in energy should be avoided. Instead, it is possible to collect fresh grass during the spring, summer or fall months. Dandelion and clover are rich in calcium. Alfalfa is rich in calcium too, but not all rabbit enjoy its taste. Sun dried hay contains varying concentration of vit. D. It provides furthermore fibers that allow a good wear for teeth and a good digestion. Pellets should be of good quality, and enriches with minerals and vit. D.



**Figure 2:** Elongation of cheek teeth roots (arrows) in rabbit n°5, which suffer from a more advanced stage of vit. D deficiency, with osteomalacia and possible cardiovascular problems.

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