

Vitamin A, mysterious and often neglected

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Vitamin A protects the skin, soft tissues, bones, teeth, vision and contributes to immunomodulation and to the reproduction. All the beneficial properties of this molecule are, however, not known yet.

In spite of the important role played by vitamin A (vit A), it is not naturally present in the body of mammals and man. In coprophage animals too, bacteria living in

the caecum do not synthetize vit A either, only vitamins B and K. Vit A is also absent in plants. The latter only contains carotenoid precursors in the form of provitamin A



Figure 1: Young giant Flemish rabbits that present an abnormal ear position when temperatures increase, which is characteristic of vitamin A deficiency.

(β -cryptoxanthin, α -, β - and γ -carotene) or xanthophyll's (lycopene, zeaxanthine). Their properties are different but all can be converted into vit Α by mammals. β -carotene is the most efficient as it will split into 2 molecules of vit A. When rabbits live on a diet composed of grains, hay stocked longer than 6 months and fodder plants, they can develop a vit A deficiency. Feeding food rich in carotenoids at regular intervals is thus very important.

Complex metabolism of carotenoids

The absorption of provitamin A carotenoids and their metabolism is not fully understood to this day. The process starts in the stomach and in the duodenum (Figure 2). Carotenoids are separated from the ingesta and solubilized in lipid droplets. Further down in the small intestine, the addition of bile salts and pancreatic hydrolyzing enzymes leads to the formation of aggregated lipid vesicles - micelles, which contain the carotenoids. A passive diffusion mechanism enables the migration of carotenoids from the micelles to the enterocyte cells of the intestinal epithelium, which is part of the mucosal membrane of the large intestine. β -carotene – the most abundant precursor in rabbits, will be transformed into retinal, one of the vit A forms. This conversion is done only in the enterocytes of the intestinal epithelium. Indeed, no traces of β -carotene have been detected in the blood and in other organs of rabbits, proving that enterocytes play a fundamental role in the transformation of carotenoids into vit A. The rate of conversion is high in rabbits compared to

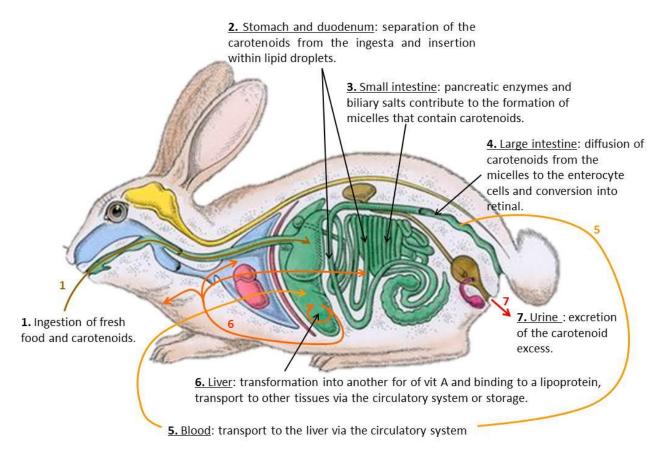


Figure 2: Cycle of carotenoids and vit A in rabbits.

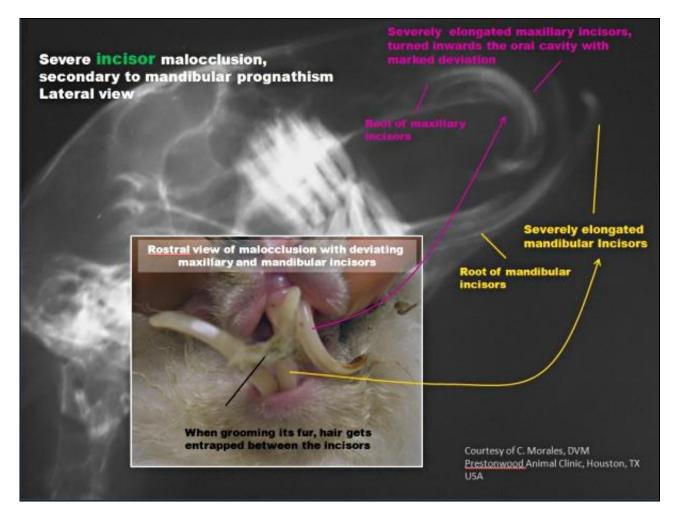


Figure 3: Severe malocclusion of incisors as well as cheek teeth in a rabbit that was found starved and underweight. (Photo and radiography: Dr C. Morales)

that of other mammals, and is close to that of chickens. Blood circulation helps transport the newly formed retinal from the intestine to the liver, where it will be converted into another form of vit A – retinol, then it will be attached to a transport lipoprotein. This allows its transport via the blood circulatory system to other organs. The liver thus regulates the blood level of vit A. Vit A excess is stored in the liver, adipose tissue, kidneys and in the lungs.

Role of vit A in immunity

A liver or biliopancreatic disease or an inflammation caused by parasitic worms or coccidia can lead to the malabsorption of carotenoids in the intestine. One of the main roles of vit A is precisely to maintain the integrity of the epithelial membranes and of the mucosa as they serve as physical barriers against pathogen agents in the gastro-intestinal system, the oral cavity, the respiratory airways, the urogenital system and also the eye. Vit A indeed influences the secondary immune response against the pathogen by activating and modulating T and B lymphocytes. This immune system is much slower than the innate immune system, which includes the immediate activation of defense mechanisms. If mucosal tissues are damaged, the presence of vit A will limit or inhibit cell death (apoptosis) and help restore the integrity and functionality of the membrane. These properties are particularly interesting in rabbits that suffered from respiratory diseases digestive dysfunction like or



Figure 4: Another characteristic of vit A deficiency in rabbits is curving of the ear tips.

enterocolitis or intestinal stasis, from parasitic worms or that suffer from the congenital disorder megacolon.

Avitaminosis and malformations

Vit A is involved in numerous metabolic reactions and contributes to the growth and strength of bones and cartilage, to the development of eyes and vision, and to reproduction. Young rabbits that suffer from a lack of vit A have a retarded or halted growth that may be fatal. They are often sick as the epithelial membrane covering organs that are in contact with the outside environment is deficient and does not function as its protective barrier. Respiratory and digestive diseases are frequent. The poor ossification also affects teeth and dental problems like malocclusion are observed on a regular basis (Figure 3). Cartilaginous tissues are defective and weak and it cannot support the weight of the ears, which fall to the side and/or have their tip bend (Figures 1, 4). This characteristic is

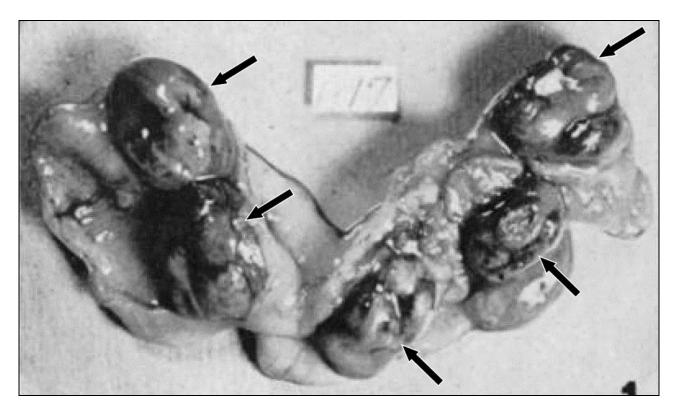
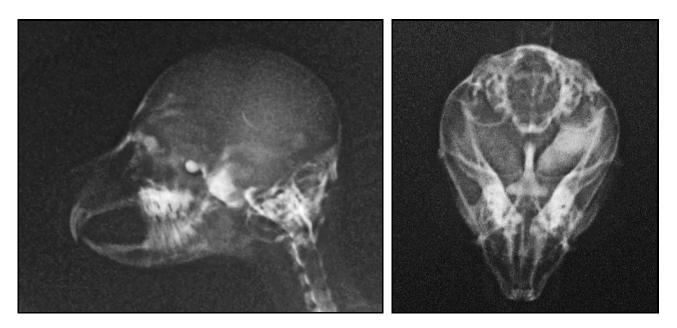


Figure 5: Uterus of a female that suffered from vit A deficiency, showing the resorption of her 5 fetuses (arrows). (Photo: Lamming et al., 1953)



<u>Figure 6</u>: Hydrocephalic newborn, congenital malformation that is frequently observed in does suffering from a vit A deficiency. (Radiographs: Dr I. Aizenberg)

more apparent with warmer temperatures. Few adult rabbits also develop uncoordinated muscular movements (ataxia), become paralyzed or blind. Pregnant females have a tendency to abort or resorb the fetuses in the uterine horns (Figure 5) and produce less milk. A vit A deficiency in a pregnant female rabbit is all the more tragic in that it leads to a poor ossification of the bones during the



Figure 7: A rabbit newborn born with a congenital encephalocele, a malformation that may be caused by an excess of vitamin A (Photo: M. Gruaz)

intrauterine life of the fetus. As a result, hydrocephaly is a frequent complication (Figure 6). The poor hardening of the skull bones and the blockage of the flow of cerebrospinal fluid, which protects the brain against concussion, lead to the accumulation of this fluid in the brain. The generated high pressure within the skull and the weakening of bones induces a deformation of the dome of the skull (calvaria) and can lead to damages to the brain and the nervous system.

Too much vit A is toxic and harmful

Intake of an excessive amount of vit A is as harmful as a deficiency. Rabbits develop signs of toxicity that look like those of a deficiency. They lack vitality, their appetite is reduced and they lose weight. Youngsters may suffer from muscular dystrophy and paresis. Fertility decreases in females; they tend to abort or give birth to newborn with malformations, e.g. newborn with encephalocele (hernia of the brain) (Figure 7). Changes are also observed at the level of organs, such as calcification of the blood vessels, of tendons and of ligaments. Vit A also seems to be an antagonist of vit D, as it causes a demineralization of bones and the destruction of the matrix of cartilaginous tissue. Addition of vit A in the food is not recommended as the margin between beneficial doses and toxic doses is very narrow in rabbits. The combined administration of alfalfa, rich in provitamin A and pellets enriched in vit A should also be avoided. Indeed, the concurrent feeding of these 2 products can elevate the vit A level to toxic levels. It is safer to provide rabbits with a healthy diet, with rapidly dried good quality hay and fresh vegetables that are rich in carotenoids like (among others) spinach, broccoli, dandelion, carrots or pumpkin. Carotenoid excess will be excreted through the urine. If a toxicosis appears in spite of all taken precautions, a vit E treatment has been proven effective in rabbits.

Acknowledgements

Many thanks to Mr. M. Gruaz (Switzerland), to Dr I. Aizenberg (Hebrew University of Jerusalem, Israel) and to Dr C. Morales (Prestonwood Animal Clinic, USA) for the permission to use their pictures. A Big thanks also to Dr. R. degli Agosti (University of Geneva, Switzerland) and Mrs. B. Salt (USA) for their support.

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