

6 Summary

The Influence of several nephropathies and disorders of the excretory passage of kidney on the renal excretion of vitamin A, retinol-binding protein and the Tamm-Horsfall glycoprotein in dogs

Dogs and other carnivores differ from the human being and many other species in their physiological extremely high concentration of retinyl esters, which results in an increased total concentration of vitamin A in blood. The human being and other animal species have similar high values of lipoprotein-bound retinyl esters only within vitamin-A-intoxications. In addition to this, dogs excrete Tamm-Horsfall (THP) glycoprotein lipophil-bound vitamin A with their urine. Several functions of the Tamm-Horsfall protein are known for human beings, but they have only in part been entirely elucidated so far. Up to the present THP has been known as a carrier-protein for dogs and other canides. In human medicine both the THP and the retinol-binding protein (RBP) are used as markers for the functional efficiency of the respective tubule-segment. Numerous studies in the field of human medicine could furnish proof of the influence of kidney diseases on proteins. For the dog only a few studies have been carried out about the influence of diseases on the RBP, the THP and the therewith dependent vitamin-A-metabolism.

For that reason and taking into special consideration the clinical applicability of such a study, it was researched, if kidney diseases, perenal azotaemias or cystitis respectively influence the RBP and the THP as well as the vitamin-A-metabolism in blood and/or in urine. The point in question included the analysis of the renal distribution of the RBP and the THP by means of immunohistological investigations.

Hence, in order to establish their vitamin-A-content and vitamin-A-structure, blood and urine samples of 22 dogs with renal insufficiency, renal-value-modifications or cystitis were tested clinically-chemically as well as by means of reversible phase - high pressure liquid chromatography (RP-HPLC). The electrophoretic separation in the Western-Blot led to the semiquantative evidence of the RBP and the THP in urine. The renal distribution of the RBP and the THP was established immunohistologically on - fixed to formalin and paraplast embedded - histological tissue sections (kidney) of 77 dogs with kidney diseases.

With dogs vitamin-A-metabolism as well as the RBP and the THP are subject to kidney diseases. In this case the plasma-concentration as well as the content of vitamin A, RBP and THP are modified in kidneys and in urine.

Acute renal insufficiencies lead to an increase of vitamin A in blood and in urine; while the

content of retinyl esters is particularly increased, whereas the concentration of retinol is relatively low. Remarkable is the fact, that while the concentration of vitamin A is increased in serum, at the same time more vitamin A excreted through the kidneys. Based on these results can be concluded, that the vitamin-A-homeostasis underlies renal regulatory mechanisms. Dogs with chronic renal diseases evinced only a slight rise of vitamin A in blood, while retinol predominated, whereas the esters were reduced. Dogs with increased renal values due to other diseases had on average the same vitamin-A-values as other comparative healthy dogs. On the other hand it was observed that dogs with cystitis had decreased serum-vitamin-A-concentrations.

As a result of their different localization and metabolic pathways, RBP and THP react to different extent to kidney diseases. If the proximal tubule is affected, the tubular reabsorption is reduced and consequently less RBP is reabsorbed. Therefore an increased amount of RBP is excreted with the urine. Subsequently less RBP can be detected in the epithelial cells of the proximal tubule. If the distal tubule is affected, less THP is produced, which leads consequently to a reduced amount of excreted protein as well as of the accumulated THP.

On account of these mechanisms, the little invasive urine sampling and the subsequent electrophoreses together with the immunohistological and pathological investigations of a kidney biopsy deliver valuable and explicit evidence about the localization of the impairment as well as of the functionality of the tubule.