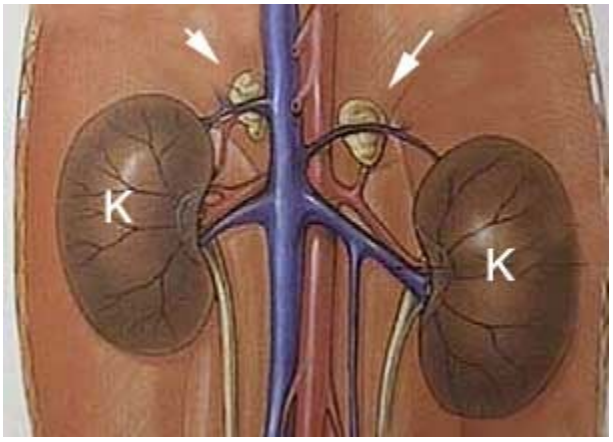
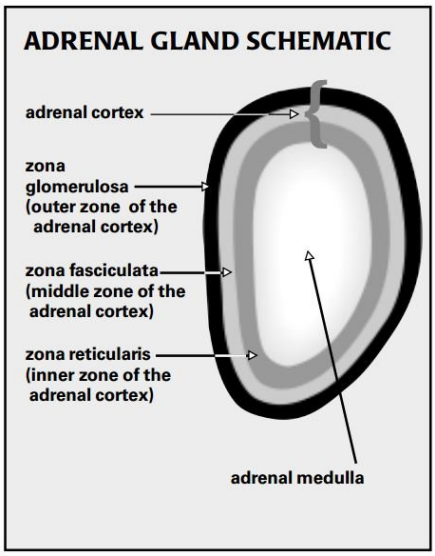
Pathophysiology of Addison's Disease

Addison's disease (hypoadrenocorticism) is an autoimmune disease in which the body makes antibodies against the cells of the adrenal glands. These are hormone producing organs buried in the fat in front of each kidney. The middle of the gland (medulla) makes adrenaline and is not affected by Addison's disease. The outer layer of the glands (cortex) make steroid hormones.





- The cortex has three layers of cell types, the one on the outside (zona glomerulosa) makes the mineralocorticoid aldosterone which acts on the tubules of the kidneys to determine the levels of sodium and potassium in the blood. If these are out of balance, muscle - including the heart - and nerve function are impaired. In Addison's disease the body loses too much sodium and retains too much potassium; this results in slowing of the heart and muscle weakness, it also interferes with movement of the gastrointestinal tract, and slows reaction times. DOCP is a mineralocorticoid drug given to replace the lost aldosterone.
- The next layer of the cortex (zona fasciculata) makes the glucocorticoid hormone cortisol. Cortisol is released in response to stress (physical, physiological or psychological) and reduces inflammation and pain. Cortisol levels in the body are under

the control of the hypothalamus and pituitary gland in the brain. The latter releases a hormone (ACTH) if the body needs more cortisol. All dogs with Addison's disease show a reduced or absent response to ACTH and will need supplementing with a glucocorticoid like prednisone. (Dogs seem to experience fewer side-effects with prednisolone.) Response to ACTH is the diagnostic test for Addison's disease. In this test (called ACTH stim test), samples of blood to measure cortisol are taken before and an hour after a measured dose of ACTH is injected into the dog. In Addisonian dogs the resting cortisol is usually low, and there is little or no increase after ACTH is administered.
    - Some dogs have atypical Addison's and their sodium and potassium levels are normal and they won't need to be treated with Percorten or another mineralocorticoid.
- The most central layer of the cortex (zona reticularis) makes some glucocorticoids but primarily sex steroids - various androgens. These are not affected by Addison's disease, but account for masculinization of spayed bitches, and the retention of some secondary male characteristics in castrated dogs.

Addison's disease has a complex etiology. It has been estimated that up to 40 genes may be involved in some way. The disease is known to be triggered by stress, various drugs and vaccination, and chemicals, as well as many unknown factors in genetically susceptible dogs.

There should be no stigma in the breeding or owning a dog with a health problem like Addison's disease. Most of the diseases which affect our dogs are complex in nature and only through free and open discussion of pedigree and environmental conditions and the sharing of genetic and other material can we find out how to reduce incidence and improve breed health. In the majority of diseases, we are a long way from having that information.

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