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Pathological Changes in the Dog Kidney Resembling Normal Histological Structure in the Aglomerular Fish Kidney, Opsanus Tau.*

WILLIAM DE B. MACNIDER.

From the Laboratory of Pharmacology, the University of North Carolina.

During the past 10 years investigations[1, 2, 3] have been in progress in this laboratory which have been concerned with the acute changes of a degenerative character which may be induced in the dog kidney by the use of suitable subcutaneous injections of uranium nitrate, and with the histological changes arising as processes of repair in the kidneys of animals which survive such injections that result in the development of a pathological state which may be designated a chronic nephritis.

This preliminary report is based on the study of the kidneys of 6 dogs with a chronic nephritis developing from the use of uranium, the duration of which has varied from 4 years to 6 years and 8 months. In addition to the usual routine functional studies which have been made of the blood and urine of these animals, histological studies have been undertaken of biopsy material removed from the kidneys before the commencement of the uranium intoxications, during the acute degenerative phase of the renal injury and at intervals of 3 months during the periods of repair which have resulted in the establishment of a chronic nephritis.

The biopsy material obtained for study has been in the form of wedge shaped pieces of tissue taken from both poles and the outer convex border of the kidneys. Such material has represented a cortical surface 1-1.5 cm. in width with a depth extending into the substance of the kidney of 0.5-1.5 cm. The exposed renal surfaces caused by the removal of such material were closed with cat gut chromicised sutures. The tissue was fixed in corrosive-acetic, cut in serial sections and stained with haematoxylin and eosin.

The primary injury to the kidney from uranium, as has been emphasized by Suzuki,[4] is to the convoluted tubule epithelium. The processes of degeneration and repair to this tissue have been de-

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1 MacNider, W. deB., *J. Exp. Med.*, 1929, **49**, 384.

2 MacNider, W. deB., *J. Exp. Med.*, 1929, **49**, 411.

3 MacNider, W. deB., *Science*, 1931, **73**, 103.

4 Suzuki, L., *Morphologie der Nierensekretion*, Jena, 1912.

scribed.[1, 2] The glomerular injury which is delayed in its development, results during a period of years in inducing either a partial or complete structural obliteration of these structures so that areas exist in the kidneys of such animals, as shown in serial sections, in which the glomeruli are either destroyed by a process of connective tissue formation with a secondary hyalinization or they exist as relatively avascular units in which one or more capillary loops remain open for blood distribution.

In certain areas the largely hyalinized glomeruli give the appearance of having become canalized for the passage of blood. In such spaces blood cells with normal staining reactions can be demonstrated. In such zones of glomerular degeneration and obliteration, the epithelium in the convoluted tubule areas, though changed morphologically, has shown an unusual degree of preservation. Such tubules have become separated by an increase in intertubular connective tissue in which is found a degree of vascularity which can not be explained as arising from an inflow of blood through those glomeruli which may yet show some degree of patency. Furthermore, the study of serial sections made from biopsy material from the kidneys of these animals during the fourth, fifth, and sixth years of the existence of a chronic nephritis has shown areas in which the glomeruli have undergone complete obliteration, and yet in such zones a modified type of convoluted tubule epithelium has been preserved. Such areas resemble the normal structure first described by Marshall[5] for the aglomerular fish, *Opsanus tau.*

The source of the intertubular blood supply in such aglomerular areas and in zones, the seat of advanced glomerular degeneration is now the object of investigation in which the whole kidney is studied following appropriate methods of injection. In serial sections now available, vessels may be traced growing into the renal cortex from the medulla, which apparently arise from those vessels which take their origin from the arcuate arteries and passing down into the medulla furnish this tissue with a portion of its blood supply.[6] On the cortical side of such areas there has occurred an ingrowth of vessels through adhesions formed between the surface of the cortex and surrounding tissue, the formation of which resulted from the stripping of the kidney from its bed of perirenal fat and the operative injury necessitated by the removal of biopsy material.

These observations suggest 2 possibilities: (1) that an organ, the

[5] Marshall, E. K., Jr., *Bull. Johns Hopkins Hosp.*, 1929, **45**, 95.

[6] MacNider, W. deB., *J. Med. Research*, 1911, **19**, 425.

seat of processes of degeneration followed by repair, may as a result of the latter process revert back to a type of structure normal for a remote ancestral form; (2) the possibility of inducing an ingrowth of vessels into the kidney through the cortex in an attempt to maintain function in a relatively aglomerular structure.

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Further Studies on the Cultivation of Mycobacterium Leprae.

EARL B. MC KINLEY AND ELIZABETH VERDER.

From the Department of Bacteriology, Hygiene and Preventive Medicine, School of Medicine, George Washington University.

We[1] have previously reported the cultivation of *Mycobacterium leprae* in minced chick embryo suspended in Tyrode's solution direct from leprous nodules containing acid-fast organisms. Evidence of growth and multiplication was obtained in as few as 5 days although subsequent experience has shown that better growth occurs in from 10 days to 2 weeks. The leprosy nodules were digested with 3% sodium hydroxide to free the organisms from the tissue and to destroy contaminants and, following neutralization, the tissue medium was inoculated. Human embryonic tissue (spleen, liver, lung) has also been employed and more experience with this tissue leads us to believe that it is a better medium than chick embryo, contrary to our previous report, although it is, of course, more difficult to obtain.

Leprosy nodules which have been treated as described above, the acid-fast organisms from which have been seeded in minced embryonic tissue suspended in Tyrode's solution, have been found to contain acid-fast organisms which are unquestionably alive. After carrying such cultures in the tissue medium through several generations we wished to test the viability of these acid-fast organisms by placing them on a solid medium, such as the hormone glycerol agar, under a gaseous tension of CO_2 and oxygen. Such cultures were prepared and were incubated under these conditions for 3 months. In one series of 10 cultures of this type we have found 6 to be positive as judged by definite micro-colonies of acid-fast organisms (quite similar to those which have been described for *B. tuberculosis*

[1] McKinley, E. B., and Verder, E., PROC. SOC. EXP. BIOL. AND MED., 1933, **30**, 659.