# A Further Study of the Response of the Opossum Kidney, *Didelphys virginiana* to injury. (18244)

W. deB. MacNider.

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

In previous communications(1,2) consideration has been given to changes in the opossum kidney of an atypical order, resulting from an injury of an unknown nature, which resulted in the establishment of a cytological reaction on the part of these organs which would fall in the category of a chronic type of nephropathy very largely confined to the glomeruli. To the total number of 58 opossums previously studied, there must now be added observations on 5 additional animals. The present investigation is based not only on the study of the kidneys of the 5 new animals but on a critical review of the histological material representing the group as a whole; 63 adult animals of unknown age. In both of the above referred to studies as well as in this further study, the observation of dominant interest has been in the reaction of the glomeruli of 19 of these animals to an injurious agent. In the kidneys of such animals there occurs a variable number of glomeruli larger in diameter than unaffected structures in which the capsule is lined by a parietal layer of Bowman's membrane consisting of high, usually discrete, columnar epithelial cells. These cells decrease in height and the degree of cellular differentiation as the base of the glomeruli is reached. At this point there is a sharp transition of this order of columnar cell to the flattened, squamous type of cell normal for the glomerular membrane which is reflected as the visceral layer of epithelium over the capillary tufts. Such capillary networks are usually definitely abnormal in structure with thickened walls which frequently have the appearance of syncytial layers of endothelial tissue. Fig. 1 and 2.

In the previous studies(1,2) no explanation was offered for the development of these atypical glomeruli. A suggestion, however, was offered for the transition in cell type between the parietal and visceral layers of epithelium as occurs in such atypical structures. Such an explanation was found in the assumption that the flattening of the visceral

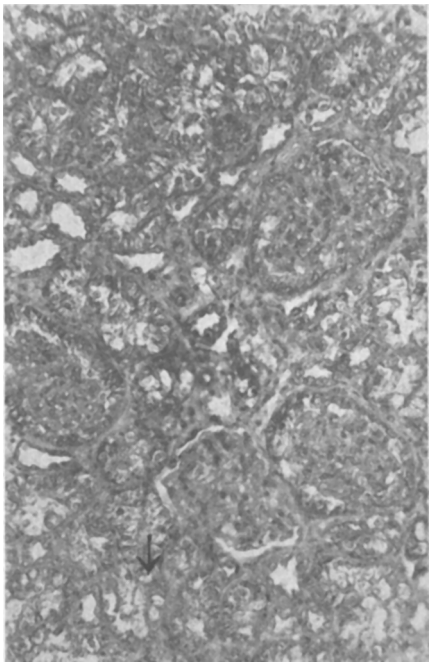

FIG. 1.

Microphotograph. Zeiss ×150, H & E. The figure is from the cortical area of an adult opossum kidney. Four glomeruli are included in the figure. The lower of these 4 structures is normal in size and cytological structure. Both the parietal and visceral layers of Bowman's membranes are formed by a flattened, squamous type of epithelial cell. The capillary tufts are distended and uniformly fill the space enclosed by Bowman's capsule. The upper 3 glomeruli in the figure are of larger size than the structure just described. In each one of them the parietal layer of Bowman's membrane if formed by cells which vary in height from a columnar order of cell to those of a flattened, squamous type. The flattening out process leading to a transition in cell form has not occurred uniformly over the surface of the parietal layer of the membrane. The capillaries of the glomerular tuft vary in their patency and degree of distension.

1. MacNider, Wm. deB., PROC. SOC. EXP. BIOL. AND MED., 1927, v25, 130.

2. MacNider, Wm. deB., *J. Elisha Mitchell Scientific Soc.*, 1945, v61, 165.

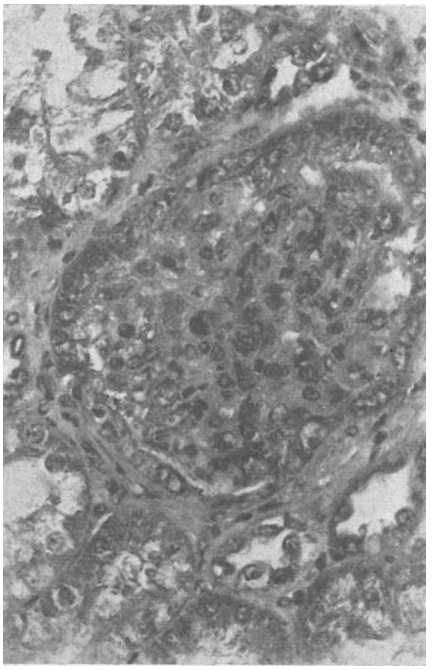

FIG. 2.

Microphotograph. Zeiss ×350., H & E. The figure shows one glomerulus under high magnification from the cortical area of the kidney. The cells of the parietal layer of Bowman's membranes though varying in height are of the columnar type of cell with pale nuclei and only in one area show evidence of the compression or flattening out process leading to the squamous order of cell. The capillary loops of the glomerulus are not discrete but appear fused, poorly differentiated and imperfectly distended with blood. Bowman's capsule is thickened and gives in general a hyaline appearance.

layer of cells was in part due to the pressure exerted on them with each ventricular systole as the capillary loops of such glomeruli became distended with blood and under pressure impinged upon and stretched the visceral layer finally resulting in a permanent flattening out of such cells. The delayed flattening of the columnar order of cell which constitutes the parietal layer of Bowman's membrane is likely due to the initial distension of the capillary loops having dissipated the force within these vessels before they fill the space encompassed by the glomerular capsule and impinge upon the atypical cells forming the parietal layer of Bowman's membrane. The explanation is strengthened by the observation that the columnar type of cell in the parietal layer of this membrane is not evenly or uniformly changed as it makes its transition to a flattened order of cell but is associated with the ability of capillary loops in a given area of the glomerulus to impinge and exert pressure upon a given section of the cells forming the parietal layer of the membrane. Those capillary loops showing endothelial thickening with partial or complete loop occlusion correspond to the areas on the parietal layer of Bowman's membrane which show the

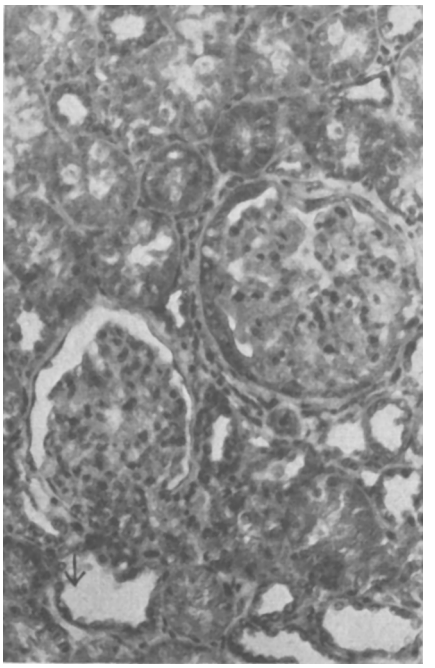

FIG. 3.

Microphotograph. Zeiss ×188, H & E. This figure from the cortex of the opossum kidney presents 2 glomeruli. The lower structure though increased in size is of normal cellular composition. The parietal layer of Bowman's membrane is uniformly formed by a normal order of flattened, squamous type of epithelium which when reflected over the glomerular capillaries maintains this same characteristic. The capillaries show imperfect lobulation and are not distended with blood. The upper glomerulus in this figure is greatly increased in size and appears distended by its capillary loops. In this structure are shown at various areas of the parietal layer of Bowman's membrane different types of epithelium in their transition from a columnar order of cell to the flattened type normal for the membrane. In those two areas in the glomerulus at which the capillaries fail to impinge upon the parietal layer of the membrane the cell type remains of a higher order in its configuration.

least change in cell type. Fig. 3.

In the kidneys of 2 of the 5 opossums studied in the present report and in 6 of those animals subjected to a critical review, structures have been observed, which with reservation may be designated atypical glomeruli in the process of formation. The existence of such atypical structures developing only in an injured kidney of an adult animal in a process of repair may in part explain the origin of those glomeruli which have been previously described as having an epithelial lining of an abnormal cellular design. The site of formation of these bodies has followed no definite pattern but have in general been more frequently observed in the cortico-medullary area of the kidney. The development of such structures is brought about by one arterial vessel, variable in diameter, impinging against the wall of the renal tubule and invaginating this wall so as to form a double layered sac. The course of events is suggestive of the process involved in the usual embryological formation of the glomeruli. The walls of such an arterial vessel responsible for a given tubular invagination show the presence of smooth muscle cells. Such vessels are usually distended with blood and at the point of impact against the tubular wall undergo a sharp reduction in caliber. As the process of invagination progresses such vessels break into capillary structures containing blood cells. This vascular development would constitute the afferent element in the glomerular mechanism. In only 2 instances has it been possible to delineate clearly the efferent vessel arising from the capillary glomerular bed while at the same time maintaining in focus the afferent vessel. The circulation through such abnormal structures, comprising as they must a part of the general renal circulation has not been ascertained. For such an elucidation an appropriate injection technique would have to be employed preferably before the animal was sacrificed. The epithelial cells lining this two layered structure in the process of development by a process of invagination have not shown much difference in size or configuration. In general it would appear that the cells covering that part of the tubule which is in the process of becoming invaginated and therefore corresponding in a normal glomerular structure to its visceral layer, are of a lower and more flattened nature than similar cells on that portion of the tubule receiving the invagination. Fig. 4. The following measurements are from one of these atypical glomerular like bodies:*

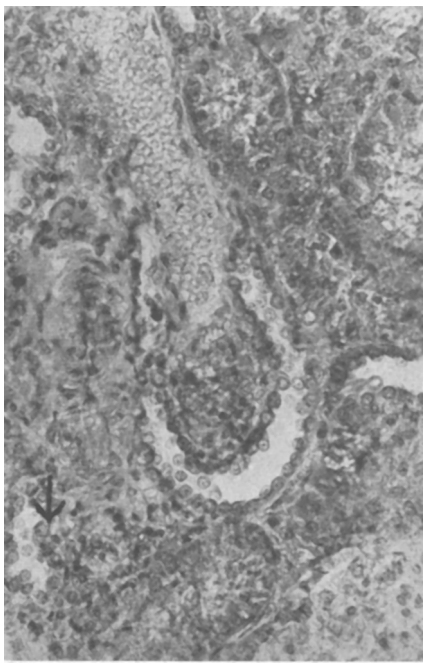

FIG. 4.

Microphotograph. Zeiss ×250, H & E. The figure shows a glomerular like structure from the cortex of the opossum kidney in the process of formation. A vessel, arterial in character, with smooth muscle cells in its wall has impinged upon a renal tubule and is in the process of inverting one wall of the tubule with the formation of a 2-layered sac. Capillaries in the process of formation are covered by what would correspond in the normal glomerulus to the visceral layer of Bowman's membrane. These structures as a whole are encompassed by the outer layer of the invaginated tubule which in turn would correspond to the parietal layer of Bowman's membrane. The cells in the outer layer of the invaginating structure, though poorly differentiated, appear in general to have a greater height than those cells forming the inner layer of the same structure.

The measurements included in the body of this paper were made from the atypical glomerulae like structure of Fig. 4.

* I desire to thank Professor Edward C. Pliske, formerly of the Department of Anatomy of the University of North Carolina, for his courtesy and care in obtaining these values

| | M |
|---|---|
| Long diameter of tubule bow | 185.0 |
| Short diameter of tubule bow | 111.0 |
| Long diameter of glomerular knot | 148.0 |
| Short diameter of glomerular knot | 61.5 |
| Arterioles of knot | 7.5 |
| Maximum epithelial height | 9.0 |
| Minimum epithelial height | 4.5 |

*Discussion.* For a number of years research in this laboratory has very largely concerned itself with a study of the processes of epithelial repair in the kidney and the liver when these organs were effecting such a process as a result of either slight or severe mechanical or chemical injury(3-7). The observation has been made that the factor of tissue difficulty, strain, as these organs attempt their cytological restoration influences the morphological characteristics, the type of epithelial cell, which either transitorially or permanently establishes the process of repair. A slight injury is followed by the reappearance of a normal order of cell for the location in which the injury has occurred. A very severe injury registers its influence in the process of repair by a reversion to an embryonic order of epithelial tissue, frequently syncytial in nature and showing no or very poor cellular differentiation. In a certain number of instances such an order of repair remains over months or even years as a permanent morphological transition while in other instances there would appear to remain in this embryonic order of tissue of repair the urge to return to the differentiated type of cell normal for this area that has participated in the severe injury.

The injury which has been described for the opossum kidney shows itself in a dominant fashion, not in the tubular epithelium of this organ, but to a similar tissue (epithelium) found in the glomeruli. In a certain number of these ancestrally old animals, the marsupials, it would appear that the repair process may also revert to an embryonic status not only in the type of cell which is found in the two layers of Bowman's membrane but furthermore and rarely, this reversion may take on structural proportions with an attempt to form new bodies atypically glomerular in their configuration.

3. MacNider, Wm. deB., *J. Med. Research,* 1911, v20, 369.

4. MacNider, Wm. deB., *J. Med. Research.,* 1916, v29, 177.

5. MacNider, Wm. deB., *J. Exp. Med.,* 49:387.409; Harvey Society Lecture 1928-29.

6. MacNider, Wm. deB., *J. Pharm. and Exp. Therap.,* 1936, v56, 359.

7. MacNider, Wm. deB., *J. Pharm. and Exp. Therap.,* 1937, v59, 393.

Received September 1, 1950. P.S.E.B.M., 1950, v75.

## Differential Effect of Desoxycorticosterone and the Sodium Hormone on Eosinophil Count in the Mouse. (18245)

J. KIMBALL SCOTT. (Introduced by Frank A. Hartman)

*From the Department of Physiology, The Ohio State University, Columbus.*

Certain steroids from the adrenal cortex cause a reduction in the number of circulating eosinophils. Seventeen-hydroxy-11-dehydrocorticosterone and related compounds are most potent. Desoxycorticosterone in large doses will cause eosinopenia(1). Meyer and Speirs(2) have recently modified the Thorn(3) test for the assay of the compounds. It occurred to us that this might be another means of comparing desoxycorticosterone and the sodium hormone. We have been able to show that the sodium hormone is without effect on the eosinophils, while we

1. Speirs, R. S., and Meyer, R. K., *Endocrinol.,* 1949, v45, 403.

2. Meyer, R. K., and Speirs, R. S., *Anat. Rec.,* 1950, v106, 249.

3. Thorn, G. W., The diagnosis and treatment of adrenal insufficiency. Charles C. Thomas, Springfield, Ill., 1949.