ON RENAL ACTIVITY: A NEW VIEW OF THE FUNCTION OF THE GLOMERULUS

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ALTHOUGH of recent years a considerable amount of attention has been paid to the processes taking place in the kidney during the secretion of urine, opinion is still divided on the question of the mode of action of the glomerulus. It is universally felt that some simple hydrodynamic or physical force must be brought into play in the glomerulus, the correct interpretation of which will explain the very characteristic, anatomical features this structure possesses. Consequently the theory originally proposed by Ludwig, that the glomerulus was merely a minute filter, still receives a great deal of support. The interpretations given to experimental results have, however, been pushed to their greatest extent in order that they may be made to fall into accord with this theory. Before we can hope to make much further progress in our knowledge of renal activity, it is most essential that we should decide once and for all what is the actual meaning of the structure of the glomerulus, and what is the nature of the work it performs.

As regards the latter point, all workers are agreed that the main bulk of the water secreted in the urine is discharged by the glomerulus. The point, however, which is not so easy to settle is whether the fluid separated from the blood at the glomerular surface does or does not possess a saline concentration similar to that of the blood. Ludwig’s theory necessarily assumes this, but as our knowledge has grown, more and more doubt has been thrown upon it, and at the present day there is, in my opinion, abundance of evidence proving quite conclusively that the fluid appearing at the glomerular surface may, under many conditions, be far less concentrated in salts than is the blood plasma. Hence, it follows that that fluid cannot have been filtered through the glomerular surface by the small hydrostatic pressure—the blood pressure—available within the glomerular loops. Consequently we are driven to the conclusion that the cells discharging this fluid must perform work in liberating it or, as we may express it in more concise, though less definite, terms, the glomerulus secretes. If, then, the idea of the glomerulus being a filter must be abandoned, we are again face to face with the problem: what is the meaning of the very character-
istic and peculiar structure? I believe the following conception gives the correct explanation of the glomerular function.

My view is that the glomerulus is, in reality, a means by which there may be set up at the commencement of the tubule a pressure-head sufficient in magnitude to drive the fluid down the tubule. The renal tubule is a very long structure possessing an extremely narrow lumen. If, then, we apply Poisseuille's law governing the flow of fluid along capillary tubes to the kidney tubule, we at once see that a very considerable pressure is required to drive even a small volume of fluid along such a tubule. As we have seen, it is a well-established fact that the watery part of the urine arises mainly, even under certain circumstances, entirely at the glomerular surface, and this fluid is discharged down the tubule. If we could measure the length of the tubule, the diameter of its lumen in its various sections, and then determine the volume of urine flowing along the tubule in a given time, we could, assuming that Poisseuille's law holds for the tubule, determine how great a pressure is required to maintain such a flow. To test the view, I made some experiments of the following type.

A vigorous diuresis was set up in an anæsthetized dog by the injection of a warm, saline solution. The rate at which the urine was discharged from one kidney at the height of this diuresis was then determined, and immediately the renal vessels and ureter were ligatured and the intact organ which thus contained, as far as possible, the whole of its blood and urine at the instant of ligature, was fixed in formalin. After hardening, it was cut into portions, the medulla separated from the cortex, and pieces of the cortex weighed, imbedded, and cut into sections. These were all mounted in series, and then the total number of glomeruli determined by counting. The number of glomeruli in the whole kidney was then calculated from the ratio of the weight of the whole cortex to that of the small piece examined. As there is but one glomerulus for one tubule, we thus learn the total number of tubules in the dog's kidney. In my experiments it averaged 210,000. The lumen of the tubule in its various parts was next measured. We already possessed measurements of the approximate lengths of the various sections of the tubules. With these data we can calculate the pressure-head which must exist within Bowman's capsules.

Taking one experiment as typical, I found that a pressure of as much as 93 mm. of mercury was required to drive the fluid along one of the tubules at the rate observed during the experiment.

The question at once arises: Whence is this pressure-head derived? There are only two possible sources; namely, (1) a secretory pressure set up by the cells in some part of the tubule, presumably at the
glomerulus, since the secretion of water is effected there, or, (2) a direct pressure transmitted through the glomerular surface from the blood-pressure. All attempts made to ascertain whether any of the cells of the renal tubule can set up a secretory pressure analogous to that observed in the case of the sub-maxillary gland, have completely failed. The maximum pressure at which urine can be discharged from the kidney is always some 30-40 mm. hg. less than the arterial blood-pressure. Hence my suggestion is that the pressure-head is derived from the capillary blood-pressure within the glomerulus, that pressure being transmitted in undiminished amount through the glomerular capillary wall and epithelium;—in undiminished amount, because I believe the glomerular epithelium offers no resistance, or at most, but a minute resistance to distension.

To express this view of the hydrodynamic action of the glomerulus, I term the glomerulus a "propulsor."

The recognition of the fact that a very considerable pressure-head is absolutely necessary to drive the fluid from the glomerulus through the tubule, once and for all dispenses of any possibility of filtration as an effective process at the glomerulus surface. For, after we have subtracted the necessary pressure-head, nothing is left where-with to effect filtration. When regarding filtration as the active process at the glomerulus, it is commonly assumed that the glomerular capillary pressure is approximately that of the aortic pressure. This, however, is certainly incorrect. The glomerular capillary pressure is undoubtedly, in many conditions, much higher than an ordinary capillary pressure, such as we find in most of the systematic capillaries, because the afferent vessels to the glomeruli are larger than most arterioles; but still they are small, and the rate of blood-flow through them is so considerable, that a good deal of the energy of the blood must be used up in overcoming the resistance they offer. I estimate it at a loss of pressure-head of about 30 mm. hg., which, with an aortic blood pressure averaging about 120 mm., leaves a glomerular capillary pressure of about 90 mm. hg.

Many of the points which have been adduced in support of the filtration hypothesis are still better interpreted upon this propulsor view. It explains, for instance, the general structure of the glomerulus; namely, that of a series of thin-walled, distensible loops projecting into the interior of a capsule, which latter is not free to expand beyond a certain limit. In the next place, the fact that the afferent vessel is of large diameter is for the purpose of causing but a relatively small loss of pressure-head between the renal artery and the interior of the glomerulus. The fact that the efferent vessel is smaller than the
afferent, thus offering a heightened resistance to the blood-flow at this point, enables us to realize that there is here a rapid loss of pressure-head, so that the pressure in the capillaries around the tubules is much lower than the glomerular capillary pressure. Moreover, this arrangement permits of an expansion of the glomerulus without producing any appreciable loss of pressure within the glomerulus. The propulsor view enables us to explain yet another feature in the anatomy of the kidney; namely, that the organ is surrounded by an inextensible capsule. This is to prevent a dangerous over-distension of any of the more fragile parts, particularly the glomerular loops and Bowman’s capsule.

An important point in confirmation of my view is the fact that the glomerulus is by no means a rigid structure. On the filtration theory, either the glomerulus must possess rigid walls or the loops must be continually pressed against the inner surface of the capsule. This latter condition is by no means always the case, as was proved by the direct microscopic observations of Nussbaum upon the kidney of the newt with the circulation still flowing. He describes them as pulsating, and as varying in size, at times filling up the whole capsule, and then again retracting and leaving the wall of the capsule. The appearance of the kidney after active diuresis also offers many points in favour of my view. Thus the tubules, especially the proximal tubules, are found widely dilated, and the glomerulus can be seen in most instances to have left the wall of the capsule. The dilatation of the tubule is unaccompanied by any increase in the total transverse diameter of the tubule; what does, however, take place is an increase in the total length. Both these conditions are produced by the high pressure of the fluid within the tubule, especially at its upper end. Lastly, the propulsor theory gives a complete explanation of all the observations that have been made upon the ureter pressure. Without entering into detail upon this point, I may state that the maximum ureter pressure simply measures the pressure which the glomerulus is capable of setting up within the capsule, that is, it is a measure of the glomerular capillary pressure. The flow of fluid along the tubule naturally decreases as the pressure at the outlet of the tubule rises, and ceases when it reaches the pressure at the head of the tubule.

There is one other point upon which I would take this opportunity to express my opinion. This is the mode of action of the diuretic substances of the caffeine group. These are so commonly employed as therapeutic agents, that it is especially important we should know upon what structures in the kidney tubule they act. It becomes especially important because a number of observers who have studied the kidney in this respect have drawn the conclusion that caffeine
and its allies only act upon the vascular mechanism, and hence that they are perfectly safe diuretics to give in cases of kidney disease, since they do not act upon the renal epithelium.

My reason for referring to these diuretics at this time is because I think we cannot condemn this view too strongly. Proof has accumulated in a number of directions that while caffeine does act upon the circulatory mechanisms, upon the heart, and upon the blood-vessels, it also exerts a very decided action upon the cells of the renal tubules. Histological examination of normal kidneys after an active caffeine diuresis brings out this point in the clearest possible manner. Experiments in which the gaseous metabolism of the kidney were studied still further emphasized the fact by showing that a greatly increased consumption of oxygen and formation of carbonic acid took place within the kidney when caffeine was administered. Moreover, the study of the chemical composition of urine secreted under the influence of caffeine has shown that under its influence the renal epithelium loses the power of holding back chlorine within the blood after the chlorine content of the blood has fallen to its normal level; whereas a normal kidney at once ceases to excrete chlorine when this occurs. A kidney under the influence of caffeine will, on the other hand, continue to discharge chlorides.

Lastly, experiments upon the frog's kidney, in which it is possible to eliminate the glomeruli and leave the tubules only in activity, have conclusively proved that caffeine can make the tubule cells secrete. There is no doubt whatever, then, that caffeine and other bodies of the purine group are specific stimulants to the cells of the convoluted tubules. In addition, we know that they act upon the renal blood vessels and that, moreover, they do excite a more copious flow of water from the glomerulus. But the point I wish to emphasize is the caution that, in administering caffeine to a patient suffering from nephritis, we must be sure to recognize that the drug acts powerfully upon the tubular epithelium.