XVI. NOTE ON THE EXCRETION OF PHOSPHATE DURING WATER DIURESIS.

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In the course of some experiments on exercise we had occasion to examine the excretion of inorganic phosphate during a copious diuresis—500 to 1500 cc. per hour—produced by drinking water. The consistent results obtained have an important bearing on several current theories of phosphate excretion.

Details of sampling and analysis are given in a previous paper [Havard and Reay, 1925]. The whole blood phosphate figures are assumed in this discussion to be identical with those for plasma [Zucker and Gutman, 1922].

Table I.

Exp. 1. A.C.

Time a.m.	Urine cc.	Water rate cc. per hour	P (mg.) per 100 cc.	P (mg.) per hour	P (mg.) per 100 cc. blood	Urea (g.) per litre	Urea (g.) per hour	Sulphates (mg. SO_4'') per 100 cc.	Sulphates (mg. SO_4'') per hour
A. 9.30–10.20	140	168	10·40	17·5	10.55 a.m. 3·60				
B. 10.20–10.45	355	852	1·46	12·5.	11.20 a.m. 3·67				
C. 10.45–11.20	680	1168	1·14	13·3	—				
D. 11.20–11.35	663	652	1·70	11·1	—				
Exp. 2. H.K.B.O.									
A. 9.50–10.21	202	391	2·7	10·6	—	4·25	1·66	—	—
B. 10.21–10.47	524	1210	0·733	8·9	10.45 a.m. 2·97	0·90	1·09	7·82	94·6
C. 10.47–11.11	518	1270	0·840	10·6	11.0 a.m. 2·97	0·95	1·20	7·61	96·6
						Average blood-urea value 0·3 g. per litre		Average blood-sulphate value 2·3 mg. SO_4'' %	

Table I gives figures for two typical experiments taken from a series of fifteen. Some more figures are given in the previous paper. In Exp. 1, showing the onset of diuresis, the kidney is at first concentrating phosphate from 3·6 mg. P per 100 cc. plasma to 10·4 mg. P per 100 cc. urine. As the diuresis develops, the kidney dilutes phosphate first to 1·46 mg. P per 100 cc. and later to 1·14 mg. P per 100 cc., whilst sulphates and urea are being concentrated. This fall in urinary P below plasma level has been noted in 44 different samples of urine.

Yet all the while the rate of phosphate excretion is comparatively constant, and actually falls, as the diuresis develops, from 17·5 to 12·5 mg. P per hour. In fact the figures for the rate of phosphate excretion are even more accurately constant during a heavy diuresis, when phosphate is being greatly diluted below the plasma value, than during a moderate diuresis when dilution is less or even absent.

In Exp. 2 it is well seen that the greater the diuresis, the greater is the dilution, so that the resulting rate of excretion is very accurately constant.

From these data, then, we may conclude that, given a constant plasma phosphate, and in the absence of disturbing factors such as acidosis and alkalosis, the kidney in excreting phosphate can maintain a constant rate of excretion quite independent of whether in so doing it has to concentrate or dilute the phosphate.

This result is not reconcilable with the theory that the urine is produced by glomerular filtration and reabsorption, as recently stated by Mayrs [1922], unless phosphate is considered to be a "threshold" substance. Mayrs holds that "absorption in the case of 'no-threshold' bodies is negligible, and may be regarded merely as evidence of renal inefficiency." This is obviously inconsistent with the very accurate regulation of the urinary phosphate percentage below the plasma value, while sulphates and urea are still being concentrated. By no process of merely passive "leaking back" could the percentage of phosphate in the glomerular filtrate be reduced 50 % below that of the plasma. At least, if this were anything but a definitely regulated activity of the kidney, we should expect that the greater the speed at which the glomerular filtrate traverses the tubules the nearer would the percentage of phosphate approach the plasma value. In fact, the reverse is found to be the case and the phosphate percentage falls even lower as the diuresis increases [cf. White, 1925]. It seems, then, that on the reabsorption theory phosphate must leave the category of "no-threshold" bodies along with urea [Mayrs, 1922], ammonia and creatinine [Marshall and Crane, 1924], which leaves only sulphates and foreign bodies. It has previously been suggested by Wigglesworth and Woodrow [1924] that there is probably a threshold value for plasma phosphate at about 2·4 mg. %.

Another possible explanation is suggested in a paper by Eichholtz and Starling [1925]. They conclude from perfusion experiments on the isolated kidney that a great part of the phosphates present in normal plasma is present as a non-ionised colloidal calcium compound to which the glomerular membrane is normally impermeable. "If this be true," they continue, "the secretion of phosphates in normal urine must be due to processes of excretion by the tubular cells." These conclusions are supported by work by Barkus [1924] on the excretion of parenterally introduced phosphates in sheep, and by work by Addis, Meyers and Bayer [1924], on anaesthetised rabbits; Bock and Iversen [1921] as a result of experiments on water diuresis and purine diuresis, came to the conclusion that phosphate is excreted by the tubules.

Our own results fit in most easily with this conception of phosphate excretion. If the glomerular membrane is normally impermeable to phosphates and the rate of excretion is governed solely by the processes of secretion by the tubule cells, then the rate of excretion will naturally be quite independent of any change in the flow of water through the glomerular membrane.

The main difficulty in accepting this theory unreservedly is in the statement by Cushny [1919] that the phosphate in the blood is freely filterable through a collodion membrane. Eichholtz and Starling, however, found that cyanide made the glomerular membrane permeable to the colloidal phosphate before the proteins, so possibly the particles may pass a collodion membrane.

Our results are not inconsistent with the idea of a glomerular filtrate being modified as it passes down the tubules by reabsorption of phosphate or secretion of water. Certainly it is difficult to picture clearly the regulation of the processes in the tubule cells in turning over from concentrating to diluting the glomerular filtrate as the diuresis increases, while maintaining accurately a constant rate of excretion. Nevertheless, this sometimes happens in the case of chlorides, and these are almost universally considered to be filtered through the glomerulus. On the whole, however, our results are more easily accounted for by the idea suggested by Eichholtz and Starling than by any previous theory.

Summary.

1. The rate of phosphate excretion is independent of the water rate even when, owing to copious diuresis, the urinary phosphate is below the level of the plasma phosphate.

2. It is shown that this is inconsistent with the view that phosphate is a "no-threshold" substance as represented in Cushny's theory of kidney secretion.

3. The bearing of this result on other theories of kidney secretion is briefly discussed.

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