EXCRETION OF UREA FROM HIGH BLOOD CONCENTRATIONS

V. F. Vasilyeva

From the Department of Physiology (Head - Corresponding Member of the Academy of Medical Sciences, USSR, A. G. Ginetsinsky)
Novosibirsk Medical Institute (Director - Professor G. D. Zalessky)
(Received September 7th, 1956. Presented by Academician L. A. Orbeli)

Of all the precise methods of estimating renal function which are available in a modern clinic, the determination of the urea clearance is the simplest, and therefore, of the greatest practical importance.

In diureses exceeding 2 ml per minute per square meter of body surface, the urea clearance is on the average, 70% of the true filtration, and its value is an indication of renal filtration capacity.

Theoretically this test is based on results which show that the renal tubules are purely passive with respect to urea: it is only filtered in the glomeruli and neither secreted nor reabsorbed actively, and is partially reabsorbed only through simple diffusion as the filtrate passes through the nephron [8,4,5]. The above is the commonly held view concerning the excretion of urea in mammals.

However, certain authors have held a different view. Thus, E. A. Asratyan [1] found in experiments on dogs that with high concentrations of urea in the blood, its clearance in certain cases might be almost twice as great as the total filtration. From this he concludes that there is an additional mechanism for the excretion of urea.

Recently K.M. Shteingardt [2] reached the same conclusion, after having repeated Asrayan's experiments and obtained results agreeing with his in every detail. The conclusions of these authors, which contradict the generally accepted view of the mechanism of the excretion of urea, have been often quoted in Soviet literature, and may cause doubt about the soundness of the method of determining the urea clearance as a means of estimating renal function.

With this in view, we carried out the work reported here.

EXPERIMENTAL METHOD

The experiments were carried out on dogs weighing 8-12 kg with the normal opening of the ureters brought out on to the skin of the belly. For the whole of the period under observation the animals were maintained on their usual liquid and solid diet.

The investigation consisted of a simultaneous determination of the filtration rate (inulin clearance) and urea clearance both with a raised blood urea, and under conditions of rapid diuresis, induced by other osmotically active substances. The animal was given a continuous intravenous injection of a solution containing 2% inulin and 2-10% urea at a rate of 3-5 ml/minute, or 2% inulin with 20-45% glucose solution. Urine and blood samples were taken after the injection had been maintained for 30-40 minutes, when steady concentrations of the substances in the blood had been reached.
Inulin in the urine and plasma was determined using a colorimetric resorption method, and urea – by the urease method as modified by Conway. From these results the filtration rates and urea clearances were calculated. The results were referred to 1m² of body surface, as this allowed comparison of results between dogs of different size and weight.

**EXPERIMENTAL RESULTS**

The results of 33 experiments on 4 dogs have been divided into three groups according to the blood urea concentrations which occurred with the loads used (Table 1).

### TABLE 1

<table>
<thead>
<tr>
<th>Number of experiments in the group</th>
<th>Limits of the observed concentrations of urea in the plasma (mg/ml)</th>
<th>Limits of variation of the ratio urea clearance (C_u) to inulin clearance (C_in)</th>
<th>Average value of ratio C_u/C_in</th>
</tr>
</thead>
<tbody>
<tr>
<td>9</td>
<td>from 0.11 to 0.30</td>
<td>from 0.57 to 0.91</td>
<td>0.72</td>
</tr>
<tr>
<td>11</td>
<td>* 0.31 * 0.50</td>
<td>* 0.60 * 0.97</td>
<td>0.77</td>
</tr>
<tr>
<td>18</td>
<td>* 0.64 * 2.20</td>
<td>* 0.72 * 0.98</td>
<td>0.85</td>
</tr>
</tbody>
</table>

As can be seen from Table 1, the average value of the ratio increases with increase in the concentration of blood urea. However, even with high concentrations up to 220 mg%, i.e. 10 times higher than normal, the ratio C_u/C_in remains less than 1, which shows that no active excretion occurs. At the same time with normal and moderately raised blood ureas this ratio varies considerably, sometimes reaching values of 0.91-0.97. Evidently there is no direct relation between the blood urea and the ratio of the two clearances. The increase in the average value of the ratio with increasing values of blood urea is probably not due to any specific effect of the urea on the tubules, but to the diuretic effect it produces. When diuresis is rapid, and when the rate of flow of the primary urine along the canals increases, conditions are less favorable for the reabsorption of urea, so that its clearance rises and approximates the true filtration rate.

It is known that over very wide limits of diuresis rates the filtration rate in dogs remains constant; however, the rate of flow of fluid along the canals, which clearly will be higher the greater the rate of urine excretion, is entirely determined by the rate of reabsorption of water. A convenient expression for the reabsorption process is the value of the ratio of the inulin content of the urine (u) to that of the plasma (p). The unreabsorbed inulin increases in concentration in proportion to the amount of water reabsorbed, and the ratio u/p increases. We would expect that the ratio C_u/C_in will depend on the ratio u/p.

In order to demonstrate this relationship in general, we altered the amount of water reabsorbed by injecting not only urea but also another osmotic diuretic which changes the value of u/p, namely glucose. The results of the experiment are shown graphically in the figure. The results of the experiments with intravenous injection of urea are shown by the open circles, while the closed circles show the results for glucose. It can be seen that by altering the concentration index of inulin from 40 to 15, the value of C_u/C_in varies from 0.8 to 0.6; however, with a concentration index less than 15, the value of C_u/C_in shows a steady increase, with a value of approximately 1.0 at a u/p ratio of approximately 4.0.

The four points lying above the dotted line must be noted. In these experiments the ratio C_u/C_in exceeds 1.0, and this can only occur if urea is actively excreted.

Table 2 shows the figures corresponding to these four points,