127. The Seat of Elimination of Drugs in the Kidney.

By Shohei OZAWA.

Department of Pharmacology, Tokyo Imperial University.


It was found recently by Tamura and his co-workers that some urinary constituents such as water and chloride are eliminated only from the glomeruli and the others from both the glomeruli and tubules, and also that some dyes such as carmine are eliminated only from the glomeruli and some others like indigocarmine from both the glomeruli and tubules.

In my experiments it was intended to determine the seat of elimination in the kidney of alkaloids and aromatic compounds. The Tamura method was applied on the toad, for the separate investigation of the glomerular and tubular functions. In this method the toad’s kidney on one side is perfused with oxygenated saline solution through one of the renal arteries, others are all ligatured. The perfused glomeruli are thus in activity and consequently a certain amount of urine can be obtained from the treated kidney. By investigating this urine we can directly know whether or not any urinary substances are to be excreted through the tubules.

We can also infer the function of the glomeruli by comparing the urine from the control kidney with that from the treated.

Quite recently, Tamura and his co-workers have modified the method. This “modified Tamura method” was adopted to compare the amount of excretion from the glomeruli with that from the tubules. The operation is performed as follows: The treated kidney is perfused with oxygenated saline solution through one or two renal arteries, all others being ligatured; on the control side the same number of arteries are left circulating, the rest being all ligatured. In this way, we can obtain about the same amount of urine on both sides, and by analysing these two samples of urine we are able to know in what proportion the glomeruli and the tubules take part in the excretion.

By applying these two methods above mentioned the following results have been obtained:

I) Among alkaloids the following are eliminated from both glomeruli and tubules.
Morphine, Apomorphine, Atropine, Cocaine, Antipyrine, Adrenaline, Quinine, Strychnine, Nicotine, Pilocarpine, Physostigmine, Hydrastine, Veratrine, Colchicine, Choline acetylate.

II) Among aromatic compounds salicylic acid, benzoic acid, cinnamic acid and gallic acid are eliminated only from glomeruli and carbolic acid, resorcin, pyrocatechin, pyrogallol and protocatechuic acid from both glomeruli and tubules; the first four acids contain carboxyl and when this radical is substituted by hydrogen, the resultant substances such as carbolic acid and pyrogallol are eliminated not only from glomeruli but also from tubules.

III) Several drugs which are excreted from both glomeruli and tubules have been investigated concerning the ratio in which they are excreted from glomeruli and tubules respectively. For this purpose the modified Tamura method was carried out on the toad and the drug in question was injected intravenously. After a definite interval the reaction of that drug in the urine on each side was tested, and when the test proved positive, the urine was diluted gradually till at last no more positive reaction was noticeable. Thus by comparing the degree of dilution, the proportion in which glomeruli and tubules participate in the excretion can be decided. For instance, if the reaction of the drug in the urine fades away when diluted ten times on the control side, and two times on the treated side, the amount of excretion from the control kidney is five times as much as that from the treated kidney. As the amount of excretion from the control kidney is the total sum from both glomeruli and tubules, while the amount from the treated kidney is excreted through tubules alone, the ratio can be estimated by the following formula:

\[
\text{The ratio } \frac{\text{Excretion from glomeruli}}{\text{Excretion from tubules}} = (5-1) : 1 = 4 : 1
\]

The following table shows the proportion of excretion from glomeruli and tubules:

<table>
<thead>
<tr>
<th>Drug</th>
<th>Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphine</td>
<td>7:1</td>
</tr>
<tr>
<td>Antipyrine</td>
<td>1:1</td>
</tr>
<tr>
<td>Adrenaline</td>
<td>3:1</td>
</tr>
<tr>
<td>Pyrogallol</td>
<td>2:1</td>
</tr>
<tr>
<td>Atropine</td>
<td>3:1</td>
</tr>
<tr>
<td>Physostigmine</td>
<td>1:1</td>
</tr>
<tr>
<td>Colchicine</td>
<td>7:1</td>
</tr>
</tbody>
</table>

From this table I can infer that many drugs are excreted mainly from glomeruli and partly from tubules.
Bibliography.

2) Cushny, The Secretion of the urine, 1926.
3) Gadamer, Lehrbuch d. chem. Toxikologie, 1924.
5) Schmidt, Pharmakologische Chemie, organische Chemie II. 1923.