GLUTAMINE AS SOURCE MATERIAL OF URINARY AMMONIA

Sirs:

Nash and Benedict\(^1\) in 1921 showed that ammonia excreted in the urine is formed in the kidneys. The source material has been in dispute; at first it was believed to be urea, then amino acids.

Dogs have been prepared with kidneys explanted by the technique of Rhoads,\(^2\) which renders it possible without anesthesia to draw blood from the renal vein by skin puncture. The renal blood flow was estimated from the creatinine excretion by the principle of Van Slyke, Rhoads, Hiller, and Alving.\(^3\) The cc. of renal blood flow per minute were calculated as \(\frac{\text{mg. of creatinine excreted per minute}}{\text{mg. removed from 1 cc. of renal blood}}\). The amount removed from renal blood was calculated as the difference in creatinine content per cc. between arterial and renal venous bloods. From the renal blood flow thus obtained and the arterio-renal-venous differences of other substances, such as urea and \(\alpha\)-amino nitrogen, the amounts of such substances removed from the blood by the kidneys per minute could be calculated.

All the urea thus found to be removed from the blood by the kidneys was excreted unchanged in the urine. Even when the ammonia excretion was made greater than the urea, by giving HCl and a low protein diet, none of the urea extracted from the blood by the kidneys was used to make ammonia. The same was true of adenosine and adenylic acid. Of \(\alpha\)-amino N,\(^4\) sometimes none was removed from the blood by the kidneys and sometimes small amounts, inadequate to provide nitrogen for the ammonia excreted.

The amide nitrogen of glutamine, demonstrated by one of the writers\(^5\) in blood, was removed from the blood plasma in much greater amounts than appeared in the urine; the excess sufficed to provide (a) the ammonia removed from the kidney via the renal vein\(^1\) and (b) 60 per cent or more of the ammonia excreted in the urine. Administration of glutamine to a dog in hydrochloric acid acidosis markedly increased the ammonia excretion. Depressing the ammonia excretion by changing from hydrochloric acid acidosis to bicarbonate alkalosis was accompanied by a corresponding decrease in removal of glutamine from the renal blood. The glutamine

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analyses were duplicated by two methods: (1) measuring the decrease in α-amino N caused by heating at pH 6.5; (2) measuring the NH₃ formed by action of a glutaminase prepared by one of the writers (R. M. A.) from kidney tissue. In some experiments in which the amount of glutamine amide nitrogen removed from the blood did not suffice to account for all of the urinary ammonia, the small amounts of α-amino N removed sufficed to make up the difference. Some results indicating the relation between glutamine and ammonia are given in the table.

<table>
<thead>
<tr>
<th>Condition</th>
<th>Renal blood plasma flow cc. per min.</th>
<th>Urine ammonia N mg. per min.</th>
<th>Glutamine amide N removed from renal blood mg. per min.</th>
<th>Preformed NH₃ N in blood Arterial mg. per 100 cc.</th>
<th>Preformed NH₃ N in blood Renal venous mg. per 100 cc.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acidosis</td>
<td>245 0.562 0.33</td>
<td>0.02</td>
<td>0.10</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>268 0.605 0.39</td>
<td>0.02</td>
<td>0.10</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>262 0.615 0.41</td>
<td>0.04</td>
<td>0.10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alkalosis</td>
<td>178 0.005 0.02</td>
<td>0.034</td>
<td>0.075</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>200 0.004 0.02</td>
<td>0.039</td>
<td>0.075</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>191 0.004 0.04</td>
<td>0.042</td>
<td>0.063</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

It appears that the data reported provide the first direct evidence by experiments in vivo of a physiological function of glutamine in animals.

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