Extraction of amino acids from and their addition to renal blood plasma

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SHALHOUB, R., W. WEBBER, S. GLABMAN, M. CANESSA-FISCHER, J. KLEIN, J. deHAAS, AND R. F. PITTS. Extraction of amino acids from and their addition to renal blood plasma. Am. J. Physiol. 204(2): 181-186. 1963. Twenty paired samples of arterial and renal venous plasma, collected simultaneously from dogs in ammonium chloride acidosis, were analyzed by column chromatography for 23 \( \alpha \)-amino acids. Fifteen additional paired samples from dogs in acute metabolic alkalosis were similarly analyzed. In ammonium chloride acidosis, glutamine plus asparagine, glycine, citrulline, tryptophan, and proline are extracted from renal blood plasma. Alanine, serine, glutamic acid, cystine, and ornithine are added to renal venous plasma. The addition of glutamic and aspartic acids amounts only to 4\% of the extraction of glutamine plus asparagine. It is, therefore, probable that both \( \alpha \)-amino and amide nitrogens are removed from the parent amide molecules. In acute metabolic alkalosis, the extraction of glutamine plus asparagine is halved, on an average. The extraction of glycine and the addition of alanine and serine are essentially unchanged. Therefore, only the extraction of glutamine plus asparagine varies to a quantitatively significant degree with changes in acid-base balance which markedly alter the rate of excretion of ammonia.

In 1921 Nash and Benedict (1) observed that the rate of urinary excretion of ammonia greatly exceeds the rate at which preformed ammonia is presented to the kidneys in arterial blood. Indeed, ammonia is added to rather than extracted from renal blood. Accordingly, ammonia must be produced within the kidneys from one or more nitrogenous precursors. Urea (2, 3), amino acids (4), and the amide groups of plasma proteins (5) were subsequently suggested as source materials.

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1 This study was aided by grants from the National Heart Institute and the Life Insurance Medical Research Fund.

2 The automatic analyzer used in this study was purchased on a grant from the National Science Foundation.

3 National Heart Institute Trainee.

4 Public Health Service Fellow.

5 Guggenheim Foundation Fellow.

In 1943 Van Slyke and his colleagues (6) observed that glutamine is extracted from renal arterial blood in amounts sufficient to account for some 60\% of the ammonia produced by the kidneys. In some experiments the extraction of small amounts of \( \alpha \)-amino nitrogen sufficed to account for the remainder. Increased urinary excretion of ammonia in consequence of the infusion of glutamine and certain, but not all, amino acids (7, 10) has been cited as evidence confirming the derivation of ammonia from the amide and \( \alpha \)-amino groups of circulating amino acids. The high concentration of renal glutaminase and the adaptive increase in enzyme activity which occurs in chronic acidosis (11-14), no less than the high rate of extraction of the amide, have focused attention on glutamine as the major precursor. However, it has been inferred that certain amino acids, including alanine, histidine, aspartic acid, glycine, leucine, methionine, and cysteine, all of which increase ammonia excretion when infused intravenously, are normal precursors of at least minor significance.

Utilizing methods of column chromatography we have measured the concentrations of 23 \( \alpha \)-amino compounds in arterial and renal venous plasma of dogs in chronic ammonium chloride acidosis and in acute metabolic alkalosis. In confirmation of the results of Van Slyke et al. (6) we have observed that glutamine\(^6\) is extracted from renal blood plasma in acidosis in far greater amounts than are other amino acids. Lesser but significant quantities of glycine, citrulline, tryptophan, and proline are also extracted. In contrast, alanine, serine, glutamic acid, cystine, and ornithine are added to renal venous plasma. Since, in acidosis, the glutamic and aspartic acids added to renal venous plasma are equivalent only to 4\% of the glutamine plus asparagine extracted and, since negligible amounts of the acids are excreted, it is probable that the \( \alpha \)-amino as well as the amide nitrogens of glutamine plus asparagine are removed from the parent molecules.

\(^6\) The sum of glutamine and asparagine was actually determined chromatographically. Most of the material in plasma is glutamine.
In acute metabolic alkalosis, the only change of quantitative significance in the renal metabolism of amino acids is a reduction in the extraction of glutamine. The extraction of glycine from and the addition of alanine and serine to renal blood are essentially unchanged. We conclude that a change in the extraction of glutamine from renal blood plasma is the major correlate of change in rate of ammonia production. However, production of ammonia from the large stores of free amino acids present in tubular cells may account in quantitative significance in the renal metabolism of ammonia.

Our experiments were initiated to determine the relationship between total renal production of ammonia, namely, that excreted plus that added to renal venous blood for a lack of correlation between extraction of nitrogenous compounds and formation of ammonia.

Our experiments were performed using more reliable methods. Balances obtained in this latter series are reported in an accompanying paper (15). Amino acid values derived from 8 of these experiments have been combined with the original 12 and are reported in this paper.

**TABLE 1. Renal plasma concentrations of amino acids in metabolic acidosis**

<table>
<thead>
<tr>
<th>Amino Acid</th>
<th>Arterial</th>
<th>Venous</th>
<th>Arterial—Venous</th>
<th>$P_{(A-V)}$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>S.D.</td>
<td>Mean</td>
<td>S.D.</td>
</tr>
<tr>
<td>Glutamine—Asparagine</td>
<td>0.450 ± 0.093</td>
<td>0.294 ± 0.081</td>
<td>0.156 ± 0.061</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Glutamine</td>
<td>0.276 ± 0.120</td>
<td>0.324 ± 0.116</td>
<td>0.046 ± 0.032</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Glutamine</td>
<td>0.142 ± 0.050</td>
<td>0.178 ± 0.051</td>
<td>0.036 ± 0.034</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Glutamine</td>
<td>0.169 ± 0.046</td>
<td>0.146 ± 0.042</td>
<td>0.034 ± 0.012</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Glutamine</td>
<td>0.024 ± 0.010</td>
<td>0.031 ± 0.012</td>
<td>0.007 ± 0.006</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Glutamine</td>
<td>0.034 ± 0.010</td>
<td>0.027 ± 0.010</td>
<td>0.007 ± 0.004</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Glutamine</td>
<td>0.070 ± 0.005</td>
<td>0.054 ± 0.006</td>
<td>0.016 ± 0.011</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Glutamine</td>
<td>0.129 ± 0.061</td>
<td>0.137 ± 0.069</td>
<td>0.008 ± 0.016</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Glutamine</td>
<td>0.224 ± 0.113</td>
<td>0.230 ± 0.112</td>
<td>0.004 ± 0.017</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Glutamine</td>
<td>0.141 ± 0.047</td>
<td>0.137 ± 0.047</td>
<td>0.004 ± 0.014</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

**TABLE 2. Renal plasma concentrations of amino acids in metabolic alkalosis**

<table>
<thead>
<tr>
<th>Amino Acid</th>
<th>Number of Experiments</th>
<th>Arterial</th>
<th>Venous</th>
<th>Arterial—Venous</th>
<th>$P_{(A-V)}$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>S.D.</td>
<td>Mean</td>
<td>S.D.</td>
<td>Mean</td>
</tr>
<tr>
<td>Glutamine—Asparagine</td>
<td>0.383 ± 0.069</td>
<td>0.306 ± 0.075</td>
<td>0.077 ± 0.029</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Glutamine</td>
<td>0.187 ± 0.069</td>
<td>0.227 ± 0.064</td>
<td>0.038 ± 0.029</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Glutamine</td>
<td>0.093 ± 0.029</td>
<td>0.125 ± 0.037</td>
<td>0.032 ± 0.026</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Glutamine</td>
<td>0.125 ± 0.029</td>
<td>0.107 ± 0.031</td>
<td>0.018 ± 0.009</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Glutamine</td>
<td>0.019 ± 0.007</td>
<td>0.029 ± 0.013</td>
<td>0.010 ± 0.012</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Glutamine</td>
<td>0.030 ± 0.010</td>
<td>0.032 ± 0.011</td>
<td>0.002 ± 0.005</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Glutamine</td>
<td>0.034 ± 0.010</td>
<td>0.032 ± 0.012</td>
<td>0.008 ± 0.008</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Glutamine</td>
<td>0.038 ± 0.010</td>
<td>0.039 ± 0.013</td>
<td>0.001 ± 0.004</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Glutamine</td>
<td>0.080 ± 0.026</td>
<td>0.085 ± 0.004</td>
<td>0.003 ± 0.013</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Glutamine</td>
<td>0.019 ± 0.008</td>
<td>0.020 ± 0.006</td>
<td>0.001 ± 0.005</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Glutamine</td>
<td>0.077 ± 0.028</td>
<td>0.076 ± 0.052</td>
<td>0.001 ± 0.019</td>
<td>&lt;0.001</td>
<td></td>
</tr>
</tbody>
</table>

**METHODS**

Our experiments were performed on mongrel dogs, of either sex, weighing over 20 kg. Under pentobarbital anesthesia, a catheter was introduced into the right renal vein by way of the saphenous vein. Its position was verified fluoroscopically, checked by a quick test of p-aminophenylaurate (PAH) extraction and observed directly at autopsy. Both ureters were catheterized through a midline incision just above the symphysis. Urine was collected only from the right catheter. Arterial blood was obtained from a retention needle in the femoral vessel.

In a typical experiment, 10 g ammonium chloride/day was administered orally for 3 days prior to an experiment. Creatinine and PAH were incorporated in an infusion made two-thirds isotonic with sodium sulfate and given intravenously at a rate of 5 ml/min. Urine collection periods were of 20-min duration. Blood, for the determination of glomerular filtration rate, renal plasma flow, and hematocrit, was drawn at the beginning and end of each urine collection period. Midperiod values were interpolated. Blood for the quantification of amino acids was drawn slowly over an interval of 1 min at the midpoint of each urine collection period.
changed to one containing creatinine, PAH, and 1.0% sodium bicarbonate. One or more 5-g priming doses of sodium bicarbonate were administered to alkalinize the urine. After 30 min, a second series of clearance observations were made. In five experiments, data were obtained only in acidosis.

Blood samples were centrifuged at once in a cold room and the plasma separated. Creatinine and PAH were determined by the methods of Phillips (16) and Bratton and Marshall (17), respectively. True renal plasma flows were calculated from measured extraction and excretion of PAH according to the formula of Wolf (18). For free amino acid determinations, plasma proteins were precipitated by 1:6 dilution with 1% picric acid. Excess picric acid was removed by passing 50 ml filtrate through a column of Dowex 2 X 10 resin. The column was washed five times with 3-ml portions of 0.02 N HCl and the eluate plus washings concentrated to a small volume in a flash evaporator at 30 C. After neutralization, the fluid was allowed to stand at room temperature for 4 hr to oxidize cysteine to cystine. After reacidification, the filtrates were evaporated to dryness and the flasks were stored at -10 C. For analysis, the residue was dissolved in 10 ml of pH 2.2 buffer and an aliquot representing 2.5 ml plasma was analyzed for amino acids and amides in the course of preparation of filtrates. The extent of interconversion or loss or gain of free amino acids and amides in the course of preparation of filtrates is unknown. One step in addition to those involved in preparation of plasma filtrates was necessary to prevent interference by glutathione, namely, treatment with alkaline sodium sulfite.

Plasma carbon dioxide content was measured by the method of Van Slyke and Neill (20) and pH of whole blood and urine was measured at 38 C with a radiometer-Copenhagen micro glass electrode. Hematocrits were determined in capillary tubes spun down in an International micro capillary centrifuge and measured on an International micro capillary reader.

RESULTS

The concentrations of 23 amino acids in 20 paired arterial and renal venous plasma samples obtained from dogs in ammonium chloride acidosis are summarized in Table 1. The compounds are tabulated in order of diminishing statistical significance of arteriovenous difference. The small number of paired analyses of tryptophan resulted from the absence of this amino acid in samples prepared by ultrafiltration, as well as from its occasional inadequate separation on the column from other basic compounds. Less than 20 paired analyses of other amino acids result from inadequate column separation.

It is evident that glutamine plus asparagine are extracted from arterial plasma in greatest absolute amounts. The confidence limit that the arteriovenous difference is greater than zero is well below one-tenth of 1% (P = <0.001). Glycine is also extracted in significant amounts and with high probability. In all 20 experiments glutamine plus asparagine were extracted; in 19 of 20 experiments, glycine was extracted. Serine was added to renal blood in all 20 experiments and in 19 of them alanine was added. If one accepts a confidence

7 Glutamine plus asparagine were eluted from the 150-cm column with buffer of pH 3.25 at 20 C in 6-9 hr. The statement of Stein and Moore (19) that glutamine is unstable on the column applies to conditions of chromatography different from those utilized in this study.

8 Since both amides are eluted at the same volume, analytical separation on the column is impossible. More than 90% of the total in plasma is glutamine (16).
TABLE 4. Relation of extraction to reabsorption of glutamine + asparagine in acidosis

<table>
<thead>
<tr>
<th></th>
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<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>μM/ml</td>
<td>ml/min</td>
<td>μM/min</td>
<td>μM/ml</td>
<td>ml/min</td>
<td>μM/ml</td>
<td></td>
</tr>
<tr>
<td>0.471</td>
<td>15.2</td>
<td>7.16</td>
<td>0.136</td>
<td>94.1</td>
<td>12.79</td>
<td>562</td>
</tr>
<tr>
<td>0.399</td>
<td>42.1</td>
<td>16.80</td>
<td>0.194</td>
<td>157</td>
<td>30.46</td>
<td>-13.66</td>
</tr>
<tr>
<td>0.258</td>
<td>40.0</td>
<td>10.37</td>
<td>0.130</td>
<td>144</td>
<td>18.77</td>
<td>-8.40</td>
</tr>
<tr>
<td>0.535</td>
<td>25.9</td>
<td>13.86</td>
<td>0.128</td>
<td>170</td>
<td>21.76</td>
<td>-7.90</td>
</tr>
<tr>
<td>0.390</td>
<td>21.8</td>
<td>8.50</td>
<td>0.133</td>
<td>98.4</td>
<td>13.09</td>
<td>-4.59</td>
</tr>
<tr>
<td>0.264</td>
<td>38.8</td>
<td>10.24</td>
<td>0.064</td>
<td>174</td>
<td>11.14</td>
<td>-0.90</td>
</tr>
<tr>
<td>0.466</td>
<td>31.2</td>
<td>14.54</td>
<td>0.066</td>
<td>146</td>
<td>9.64</td>
<td>4.90</td>
</tr>
<tr>
<td>0.465</td>
<td>30.3</td>
<td>14.09</td>
<td>0.094</td>
<td>127</td>
<td>11.94</td>
<td>2.15</td>
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<tr>
<td>0.409</td>
<td>28.0</td>
<td>11.45</td>
<td>0.163</td>
<td>121</td>
<td>19.72</td>
<td>-8.27</td>
</tr>
<tr>
<td>0.491</td>
<td>26.1</td>
<td>12.82</td>
<td>0.283</td>
<td>96.0</td>
<td>27.17</td>
<td>-14.35</td>
</tr>
<tr>
<td>0.417</td>
<td>50.6</td>
<td>21.10</td>
<td>0.101</td>
<td>244</td>
<td>24.64</td>
<td>-3.54</td>
</tr>
<tr>
<td>0.544</td>
<td>50.0</td>
<td>32.10</td>
<td>0.266</td>
<td>218</td>
<td>57.98</td>
<td>-25.00</td>
</tr>
<tr>
<td>0.456</td>
<td>49.6</td>
<td>22.62</td>
<td>0.181</td>
<td>185</td>
<td>33.49</td>
<td>-10.87</td>
</tr>
<tr>
<td>0.420</td>
<td>43.2</td>
<td>18.14</td>
<td>0.154</td>
<td>161</td>
<td>24.79</td>
<td>-6.65</td>
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<tr>
<td>0.474</td>
<td>55.0</td>
<td>26.07</td>
<td>0.184</td>
<td>232</td>
<td>42.69</td>
<td>-16.52</td>
</tr>
<tr>
<td>0.605</td>
<td>51.9</td>
<td>31.40</td>
<td>0.199</td>
<td>174</td>
<td>34.63</td>
<td>-3.23</td>
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<tr>
<td>0.440</td>
<td>55.5</td>
<td>24.47</td>
<td>0.210</td>
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<td>-16.34</td>
</tr>
<tr>
<td>0.431</td>
<td>41.6</td>
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<td>0.111</td>
<td>120</td>
<td>13.32</td>
<td>4.61</td>
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<tr>
<td>0.440</td>
<td>48.0</td>
<td>21.12</td>
<td>0.114</td>
<td>345</td>
<td>39.33</td>
<td>-18.21</td>
</tr>
<tr>
<td>0.633</td>
<td>44.9</td>
<td>28.42</td>
<td>0.220</td>
<td>177</td>
<td>38.94</td>
<td>-10.52</td>
</tr>
<tr>
<td>0.450</td>
<td>39.9</td>
<td>18.2</td>
<td>0.157</td>
<td>169</td>
<td>26.4</td>
<td>-8.19</td>
</tr>
<tr>
<td>0.009</td>
<td>12.4</td>
<td>7.5</td>
<td>0.061</td>
<td>59</td>
<td>5.13</td>
<td>7.92</td>
</tr>
</tbody>
</table>

Probability that reabsorbed – extracted differs from zero = <0.001. * = Mean; ^ = SD.

The relation of extraction to reabsorption of glutamine + asparagine in acidosis is summarized in Table 4. The order in which these compounds are listed is the same as that of Table 1. The most striking difference in renal amino acid metabolism in acute metabolic alkalosis is the reduction in extraction of glutamine plus asparagine. In all 15 experimental periods glutamine plus asparagine were extracted. However, extraction was roughly halved. The extraction of glycine from and the addition of alanine and serine to renal blood plasma are nearly the same in alkalosis and acidosis. In fact, the only statistically significant changes in arteriovenous difference which resulted from acute alteration of acid-base balance were those of reduced extraction of glutamine plus asparagine (P < 0.001) and reduced addition of cystine (P < 0.02). The only quantitatively significant change is the reduction in extraction of glutamine plus asparagine. It is therefore apparent that acute transition from acidosis to alkalosis affects mainly extraction of the two amides.

The concentrations of free α-amino compounds in renal tissue under conditions of normal acid-base balance and in ammonium chloride acidosis are summarized in Table 3. Each datum is the average of analyses performed on the kidneys of two dogs. Because concentrations differed in tissue samples removed from the two dogs in the same state of acid-base balance, it is probable that the apparent differences in mean values in acidosis and in alkalosis are not significant. However, the fact that the concentrations of most free amino acids are much greater in renal tissue than in plasma is significant. The most striking absolute tissue concentrations, as well as tissue to plasma concentration ratios, are those of glutamic acid. Obviously, in the course of reabsorption, the several amino acids must be actively pumped from tubular fluid into tubular cells. Transport from cells to peritubular blood could occur by passive diffusion down gradients of concentration. Those amino acids which are negatively extracted, i.e., added to renal venous plasma, must in addition be produced within tubular cells.

Under conditions of our experiments, insignificant fractions of the filtered loads of the various amino acids are excerted. Rates of exceration have been measured in six of the experiments of this series and in a number of other experiments from this laboratory. Because of their very low values, they have not been routinely measured nor are they reported in this paper. Disregard of rates of excretion introduces errors not exceeding 2.0%. It follows that rates of reabsorption are essentially equal to rates of filtration. The latter variable has been measured in all experiments and is considered equivalent to the former. With the exception of glutamine plus asparagine, rates of filtration and reabsorption of α-amino compounds exceed rates of extraction. As illustrated in Table 4, the two amides are extracted in acidosis in amounts significantly greater than their rates of reabsorption (P < 0.001). Therefore, they must not only be pumped from tubular fluid into tubular cells, but also from peritubular plasma into cells. In acute alkalo-
addition of serine and alanine to renal blood plasma are
alter markedly the rate of excretion of ammonia.
unrelated to acute changes in acid-base balance which
tissue are greatly in excess of those in plasma and
of the animal. The extraction of glycine from and the
asparagine is significantly related to the acid-base state
of glutamine -/- asparagine in alkalosis
RENAL METABOLISM OF AMINO ACIDS
asparagine. Only the extraction of glutamine plus
ations are far less significant than that of glutamine plus
line, tryptophan, and proline, although their contribu-
thine. Also contributing to this pool are glycine, citrul-
in lesser amounts, as glutamic acid, cystine, and orni-
thine. Also contributing to this pool are glycine, citrul-

DISCUSSION

In confirmation of the results of Van Slyke et al. (6),
we have observed that the extraction of glutamine plus
asparagine from renal blood plasma in metabolic
acidosis greatly exceeds the extraction of other a-amino
acids. Extraction of these amides is reduced in acute
metabolic alkalosis, but remains significantly above zero
for the brief duration of the experiments. Since glutamine
disappears into the kidney and glutamic acid is neither
excreted nor added to renal venous blood in appreciable
amounts, it follows that both amino and amide nitrogens
are contributed to a renal nitrogen pool. From this pool
may be derived the ammonia added to renal venous
blood and excreted in the urine and the a-amino groups
added to renal venous blood as alanine and serine and
in lesser amounts, as glutamic acid, cystine, and ornithine.
Also contributing to this pool are glycine, citrulline, trypotphan, and proline, although their contributions
are far less significant than that of glutamine plus
asparagine. Only the extraction of glutamine plus
asparagine is significantly related to the acid base state
of the animal. The extraction of glycine from and the
addition of serine and alanine to renal blood plasma are
unrelated to acute changes in acid-base balance which
alter markedly the rate of excretion of ammonia.

Since the concentrations of most amino acids in renal
tissue are greatly in excess of those in plasma and

glomerular filtrate, they must be pumped from tubular
fluid into cells against concentration gradients. Further
transport into peritubular blood could occur passively
by diffusion. In acidosis glutamine plus asparagine are
extracted from renal blood plasma in amounts greater
than those filtered and reabsorbed. Hence these amides
must be pumped into tubular cells, not only from tubular
fluid, but also from peritubular blood. One might
reasonably conclude that, in so far as glutamine, asparagine, glycine, citrulline, trypotphan, and proline
contribute nitrogen to the formation of ammonia, all must
be pumped into cells of distal tubules and collecting
ducts from peritubular blood. This follows from the
generally accepted view that reabsorption is essentially
complete within the proximal segments of the nephrons
(21, 22) and that ammonia is added to the urine in the
distal tubules and collecting ducts (23, 24). If this were
literally true then reabsorption and extraction would be
completely independent, the former occurring proximally,
the latter distally. However, Glabman and Giebsch,
in unpublished experiments on rats in chronic
metabolic acidosis, have observed that a highly significant
fraction of the urinary ammonia of the rat is added to
tubular fluid in the proximal segments. Therefore,
ammonia is formed, at least in part, in this segment from
amides and/or amino acids, possibly in the course of
their transport from tubular urine to peritubular blood.
Proximal urine of the rat is appreciably more acid than
blood plasma in metabolic acidosis (25, 26). Thus, a pH
gradient exists which favors proximal diffusion and
trapping of ammonia. However, it is thoroughly pos-
sible that the several amino acids are pumped into cells
of all renal segments from peritubular blood as well as
from tubular urine. Once in the cell their fate is deter-
mined by factors other than portal of entry.

The fact that most of the free amino acids are more
concentrated in renal tissue than in plasma suggests that
moment-to-moment utilization need not vary in precise
accord with extraction. Data to be presented in an
accompanying paper (15) indicate that the extraction of
glutamine plus asparagine in acute metabolic alkalosis,
superimposed on mild chronic alkalosis, may be reduced
disproportionately to rate of cellular production of
ammonia.

We have implied that the amino acids, serine, alanine,
etc., which are added to renal blood plasma, are pro-
duced in the kidney by amination of intermediates from
an intracellular nitrogen pool largely established by the
extraction of glutamine plus asparagine. It is, of course,
possible that they arise from the action of tissue proteases
on plasma proteins which are filtered in small amounts
and reabsorbed. If such is their origin, then most of the
amino acids must be added as peptides, for those added
as free amino acids are not in the proportions nor is the
pattern that of the constituents of plasma albumin. No
information on this point is available.

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REFERENCES


