UREA TESTS OF RENAL EFFICIENCY. I.

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The urea tests of renal efficiency commonly mentioned in the literature include (a) simple estimation of blood urea concentration, (b) determination of urine urea concentration following ingestion of urea, and (c) observations on the relationship between blood and urine urea concentrations. From a comparative study of these three methods, the general conclusion reached in this hospital (1) was that in renal lesions associated with azotemia or any other evidence of impairment in excretion of nitrogenous substances, the ratio of urine urea to blood urea concentration was the most sensitive index of renal efficiency.

All urea tests are based upon the clinical observation that when the kidneys become impaired the rate of excretion of urea diminishes. If the rate of excretion cannot keep pace with the rate of production urea accumulates in the blood. Rate of excretion of urea in the urine, and degree of retention of urea in the blood are therefore regarded as indices of kidney function. The assumption that these tests estimate the ability of the kidneys to do work connotes that excretory ability of the kidneys is the only, or at least predominant, factor influencing urea excretion. Ambard, Marshall, and Davis, Pepper and Austin, and Addis and his coworkers have recorded their observations on the effects of blood urea concentration. In 1921, Van Slyke and his coworkers demonstrated the influence of urine volume output (2). For normal individuals these authors presented a mathematical expression for the relationship of these factors. Thus, \( K = \frac{D}{B \sqrt{VW}} \) where \( D \) represents gm. urea and \( V \), volume urine output per 24 hours, \( W \) represents body weight (expressed in kilos), and \( B \), blood urea concentration (gm. per liter). The value for \( K \) (called
the urea secretory constant) was found to be $7.5 \pm 3$ for normal individuals. Because of the wide variations noted in normal subjects, these authors concluded that blood urea concentration and urine volume output were not the only factors, aside from kidney excretory ability, governing the rate of urea excretion. For this reason they stated that their "urea secretory constant" must be regarded as "an object of investigation rather than an aid in the clinic." It might appear that the latter view would also apply to the "urea concentration factor." Especially so, since in the calculation of the latter no account is taken of urine volume output. The "urea concentration factor" represents merely the ratio of urine urea to blood urea concentration. Thus "factor"

$$= \frac{U}{B},$$

where $U$ represents mg. urea per 100 cc. urine, and $B$ represents mg. urea per 100 cc. blood. The latter has, however, in the great majority of instances yielded results consistent with the clinical picture, and has also been applied in a quantitative determination of the work done by the kidneys (kilogrammeter per gm. urea excreted), with fairly consistent results (3). It appears, therefore, necessary to attempt a logical explanation why the factor is a fairly accurate index of the excretory ability of the kidneys.

Since urine volume output and blood urea concentration affect urea excretion, it appears reasonable to assume that, if these variables be reduced to the minima, variations in the rate of urea excretion will be due chiefly to kidney excretory ability. The necessity of restricting fluids for 12 hours prior to the factor test, and discarding those tests in which a polyuric response is noted has been repeatedly emphasized (4). Under such conditions the volume output of urine rarely exceeds the rate corresponding to the minimum value of the "augmentation limit."1 Austin, Stillman, and Van Slyke (2) have shown that the augmentation limit in normal subjects varied between 2.5 and 6 liters per 24 hour unit time. Also under the set of conditions for the test, the effect of blood urea concentration can hardly be great. It has been shown (1) that following ingestion of 15 gm. urea the mean increase in blood urea nitrogen was 9 mg. per 100 cc. blood. In a normal individual this would correspond, approximately, to a

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1 By the term "augmentation limit" is meant the maximum urine volume output necessary to produce the maximum rate of urea excretion.
50 per cent increase in blood urea concentration. The influence of such an increase may be judged from the data of Addis and Drury (5).

That these variables are controlled under the conditions of the test may be found in a comparative study of the "urea secretory constant" and the "urea concentration factor" obtained in the same individuals by the same procedure. Such study was made of twenty normal subjects and forty with albuminuria. The procedure of the test has been repeatedly described (1, 2, 4).

In each case the values of \(\frac{U}{B}\) and \(\frac{D}{B\sqrt{VW}}\) were found. In the calculation of the latter the additional data necessary were urine volume and body weight. The normal and pathological cases were separately grouped.

### TABLE I.

<table>
<thead>
<tr>
<th>Group No.</th>
<th>(\frac{U}{B})</th>
<th>(\frac{D}{B\sqrt{VW}}) (mean value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>41 to 50</td>
<td>6.3</td>
</tr>
<tr>
<td>2</td>
<td>31 &quot; 40</td>
<td>4.5</td>
</tr>
<tr>
<td>3</td>
<td>21 &quot; 30</td>
<td>3.1</td>
</tr>
<tr>
<td>4</td>
<td>11 &quot; 20</td>
<td>2.7</td>
</tr>
<tr>
<td>5</td>
<td>1 &quot; 10</td>
<td>1.1</td>
</tr>
</tbody>
</table>

A statistical study was made of the normal group. The arithmetical mean, the standard deviation about the true value, and the coefficient of variation were calculated. The forty cases of albuminuria were divided into five groups according to the factor. Thus, Group 1 consisted of Factors 41 to 50, Group 2 consisted of 31 to 40, etc. In each group the value of the mean of the corresponding "constants" was found.

The factors and their corresponding constants (mean value) of the different groups of cases of albuminuria are recorded in Table I. The individual results are graphically recorded in Chart 1. The continuous line represents the values of \(\frac{U}{B}\) plotted from highest to lowest. The dots represent the corresponding values of \(\frac{D}{B\sqrt{VW}}\). The parallelism between the values for \(\frac{U}{B}\) and \(\frac{D}{B\sqrt{VW}}\) is noted.
In normal subjects when no urea was given the value of $\frac{D}{B\sqrt{VW}}$ was 7.5 ± 3 (2). When urea was administered the value of the coefficient of variation was not only less, but was practically identi-
cal with that found for the factor, $\frac{U}{B}$. The mean value for the factor was 47.3 and the standard deviation about the true value was 6.9. The mean value for the constant was 9.8, and the standard deviation about the true value 1.4. Table II briefly tabulates the results. It would appear from the table that the administration of urea affects the variables. It is interesting here to note that Van Slyke\(^2\) found that when urea is given there is less varia-

\[\begin{array}{|c|c|c|}
\hline
\text{When urea is given} & \frac{U}{B} & 47.3 \\
\hline
\text{“ “ “ “} & \frac{D}{D\sqrt{VW}} & 9.8 \\
\hline
\text{“ no urea is given} & \frac{D}{B\sqrt{VW}} & 7.5 \\
\hline
\end{array}\]

\[\begin{array}{|c|c|c|}
\hline
\text{Date} & \text{Weight.} & \text{Blood urea-nitrogen.} & \text{Urine. 2nd hr. specimen.} & \frac{D}{B\sqrt{VW}} & \text{Remarks} \\
\hline
\text{June 9} & 65.4 & 38 & 46 & 00 & 1.51 & 10.9 & 2.0 \\
\text{“ 14} & 65.7 & 34 & 43 & 55 & 1.44 & 17.4 & 2.5 \\
\text{“ 19} & 65.0 & 35 & 41 & 85 & 1.24 & 15.2 & 2.7 \\
\text{July 4} & 64.7 & 28 & 42 & 105 & 1.00 & 21.3 & 4.2 \\
\text{“ 15} & 64.0 & 24 & 31 & 95 & 0.94 & 14.2 & 3.0 \\
\text{“ 21} & 64.6 & 22 & 27 & 70 & 0.96 & 18.3 & 2.9 \\
\text{“ 28} & 64.6 & 21 & 37 & 95 & 2.76 & 44.4 & 8.3 \\
\text{Aug. 2} & 62.5 & 21 & 32 & 50 & 2.28 & 40.2 & 5.5 \\
\text{“ 8} & 61.8 & 22 & 35 & 45 & 2.76 & 45.2 & 6.0 \\
\hline
\end{array}\]

\(^2\) Personal communication.
tion in the relationship between blood urea concentration and urea excretion.

The following case is cited in illustration of (a) the parallelism between the factor and constant and (b) between the latter and the clinical picture.

Hospital No. 2155, male, age 27 years, was admitted to the Medical Service of Dr. A. H. Gordon, with a diagnosis of acute nephritis. The complete laboratory data are recorded in Table III.

A low factor and a low constant are noted during the acute stage of the illness. During the stage of convalescence they approach the normal values. Until July 21, though the patient appeared well for over 2 weeks previously, there was no alteration in the factor and in the constant. The only evidence of disease clinically was the persistence of isolated red blood cells in the urine. Following the disappearance of the blood from the urine, both the factor and the constant increased in value. A parallelism between the clinical picture and factor, and between the factor and constant is thus noted.

RÉSUMÉ.

When urea was administered by mouth to normal individuals, previously restricted from fluids for at least 12 hours, and tests showing polyuric responses, above the rate equal to the minimum value of the "augmentation limit" (2.5 liters per 24 hours), were discarded, the coefficient of variation in the case of the factor was practically identical with that of the constant. Under the same set of conditions a parallelism was also noted between the values of the factor and constant in forty cases of albuminuria.

Since urine volume output is essential in calculating the constant and is not taken into consideration in the calculation of the factor, and in view of the above observations, its effect on urea excretion is practically negligible under the set of conditions described. Excretory ability of the kidneys thus appears to be the predominant factor influencing the value of the ratio $\frac{U}{B}$. The ratio has, therefore, a sound basis as a test of renal efficiency.

BIBLIOGRAPHY.

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