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Urea and Creatinine Concentration in the Blood; a Statistical Study.

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The relationship between the accumulation of urea and creatinine in the blood has held considerable interest since Myers[1] reported evidence which tended to show that in nephritis urea increased in the blood before creatinine did. It seemed probable that data obtained in a clinic where most of the patients were undergoing treatment for chronic diseases might show some relationships between these compounds which would be of value. Results obtained over a period of eight years were therefore tabulated and studied. All cases where analyses of both compounds in the same sample of blood were available were utilized. Such studies were not made on all patients, but blood was obtained from most of those in whom the presence of renal insufficiency was suspected. During the greater part of the period creatinine determinations were done on all specimens where a urea nitrogen concentration greater than 20 mg. per 100 cc. was found, but were generally omitted when the concentration was lower than this figure. During the earlier part of the period both substances were determined in most specimens submitted. The method of Folin and Wu[2] was used for the creatinine determination. During the last two years an unpublished method of Folin and Sumner was used for determining the urea nitrogen; before that time the technique recommended by Van Slyke and Cullen[3] was followed.

The average results are given in the table. The two halves of the table are alike except that in the right hand portion normal and slightly increased values are given at smaller intervals than in the left hand part. It is evident that, except when the urea nitrogen concentrations were low, the urea and creatinine values tended to vary together. Holbrook and Haskins[4] have recently reported similar findings in a series of selected cases. When the urea nitrogen concentration was slightly increased the ratio between creatinine and urea was approximately the same as when the urea was mark-

Urea Nitrogen	No.	Creatinine	Ratio	Urea Nitrogen	No.	Creatinine	Ratio
0.0 to 4.9	3	1.33	0.333	0.0 to 8.0	25	1.44	0.213
5.0 to 9.9	60	1.43	0.172	8.0 to 8.9	16	1.36	0.163
10.0 to 14.9	239	1.51	0.119	9.0 to 9.9	22	1.45	0.153
15.0 to 19.9	190	1.61	0.095	10.0 to 10.9	30	1.44	0.136
20.0 to 24.9	128	1.82	0.083	11.0 to 11.9	56	1.51	0.131
25.0 to 29.9	86	2.03	0.075	12.0 to 12.9	50	1.54	0.123
30.0 to 34.9	49	2.51	0.075	13.0 to 13.9	42	1.50	0.112
35.0 to 39.9	29	2.81	0.076	14.0 to 14.9	61	1.53	0.107
40.0 to 44.9	22	2.92	0.069	15.0 to 15.9	56	1.54	0.100
45.0 to 49.9	22	3.37	0.071	16.0 to 16.9	64	1.64	0.100
50.0 to 54.9	19	2.68	0.052	17.0 to 17.9	22	1.66	0.095
55.0 to 59.9	12	4.42	0.077	18.0 to 18.9	31	1.64	0.089
60.0 to 64.9	14	5.55	0.089	19.0 to 19.9	17	1.63	0.084
65.0 to 69.9	14	5.34	0.081	20.0 to 20.9	30	1.66	0.081
70.0 to 74.9	6	4.32	0.059	21.0 to 21.9	32	1.84	0.086
75.0 to 79.9	3	6.83	0.088	22.0 to 22.9	24	1.95	0.088
80.0 to 84.9	4	6.28	0.075	23.0 to 23.9	26	1.83	0.079
85.0 to 89.9	2	4.15	0.047	24.0 to 24.9	16	1.86	0.076
90.0 to 94.9	3	8.13	0.089	25.0 to 25.9	28	1.91	0.075
95.0 to 99.9	2	8.35	0.085	26.0 to 26.9	13	2.04	0.077
100.0 to 104.9	2	8.95	0.088	27.0 to 27.9	17	2.01	0.073
105.0 to 109 9	5	10.14	0.094	28.0 to 28.9	19	2.08	0.073
110 0 to 114.9	4	7.78	0.070	29.0 to 29.9	9	2.40	0.082
115.0 to 119.9	3	10.03	0.084	30.0 to 34.9	49	2.51	0.075
120.0 to 124.9	6	9.35	0.077	35.0 to 39.9	29	2.81	0.076
125 0 to 129.9	1	13.30	0.103	40.0 to 49.9	44	3.15	0.070
135.0 to 139.9	3	7.30	0.054	50.0 to 59.9	31	3 35	0.062
140 0 to 144.9	1	14.50	0.101	60.0 to 69.9	28	5.44	0.085
150.0 to 154.9	2	9.35	0.062	70.0 to 79.9	9	5.16	0.069
155.0 to 159 9	1	16.00	0.101	80.0 to 89.9	6	5.57	0.066
160.0 to 164.9	1	15 00	0.092	90.0 to 99.9	5	8.22	0.087
170 0 to 174.9	2	9.75	0.057	100.0 to 109 9	7	9.66	0.090
175.0 to 179.9	1	10.30	0.059	110.0 to 119.9	7	8.74	0.076
180.0 to 184.9	1	13 30	0.073	120.0 to 129.9	7	9 91	0.081
200 0 to 204.9	2	9.90	0 050	130.0 to 149.9	4	9.10	0.067
215.0 to 219.9	1	4.60	0 021	150.0 to 174.9	6	11.53	0.071
235 0 to 240.0	2	13.00	0.054	175.0 to 199.9	2	11.80	0.066
290.0 to 294.9	1	18.40	0.063	200.0 to 299.9	6	11.47	0.050

Urea nitrogen and creatinine determinations are expressed as mg. per 100 cc. blood.
The ratio was obtained by dividing the creatinine by the urea nitrogen.

edly abnormal. There is no evidence that there was a group of patients with slight increases in urea nitrogen but with normal creatinine values, as would be expected if the kidney was more permeable to creatinine than to urea.[5] A study of the distribution of individual urea and creatinine values confirmed the impression given by the averages.

Cases where the results of more than one study upon the same patient were available were also analyzed. There were 230 successive determinations of this sort. When both the urea and creatinine increased the urea tended to increase faster than did the creatinine, but when both decreased the urea also tended to decrease more rapidly. Almost all of the relationships observed could be explained on the basis of variations in the urea concentration similar to those known to take place in intestinal obstruction. It seems more logical to attribute these variations to changes in the rate of formation rather than of elimination of urea. Such variations in the rate of formation would, of course, cause greater changes in the blood urea concentration when kidney function is impaired than when it is normal. Such a hypothesis would explain better the very high blood urea nitrogen values accompanied by normal creatinine concentrations than does the assumption of a different permeability of the kidney for these two compounds. Part of the figures could be explained by introducing a time factor into the conception. The urea may accumulate earlier in the blood than does creatinine, and the creatinine later rise fairly rapidly to a comparable level. Such an explanation can be applied only with difficulty to much of the data obtained in successive determinations on the same patient; for instance, to the facts that there was a more rapid fall of urea than of creatinine when both were decreasing, and that where the urea was constant there were as many cases which showed a drop as showed a rise in creatinine (although the average per cent rise was greater than the average fall). The evidence in favor of variations in the rate of creatinine formation was at least as slight as was that in favor of the proposition just stated. It seems best not to press explanations which apply only to a very small proportion of the determinations analyzed, but rather to conclude that, in our series, composed almost wholly of chronic cases, with acute nephritis very meagerly represented, urea and creatinine concentrations in the blood paralleled each other; that there was not infrequently evidence of rather sudden changes in urea concentration probably associated with variations in the rate of urea formation; and that there was a small number of cases where some additional factor or factors seemed to be affecting the results.

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Calcium Content of Maternal and Foetal Blood Serum Following Injection of Parathyroid Extract in Foetuses in Utero.

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In considering the changes in the maternal organism during pregnancy many observers from the time of Rokitansky have noted alterations in the teeth and skeletal tissues.[1] In this connection, Seitz[2] has pointed out that "of all the mineral substances, calcium passes in the greatest amount from the mother to the foetus" during gestation. It has been found also that about the time of very active development of bone in the foetus, which probably necessitates the mobilization of a considerable supply of calcium in the foetal body, the parathyroid glands of the embryo are already differentiated morphologically.[3] Of immediate interest, however, are the recent investigations of Collip,[4] as a result of which there is available an extract of the parathyroid glands which exerts a powerful influence on the mobilization of calcium in the blood. By means of this highly concentrated parathyroid substance, the old problem of the mechanism which is involved in the exchange of calcium from mother to foetus is reopened to experimental inquiry from a new angle. The possibility of the escape of active parathyroid substance from the foetus to the mother across the placental boundary, can be tested by direct observation.

In the present experiments, parathyroid extract was injected into foetuses *in utero*. Observations were made upon the calcium content of the maternal blood serum at intervals of about 4 hours, in order to detect any changes in the calcium level of the maternal blood, such as might be produced by the escape of parathyroid substance into the maternal circulation. About 17 to 22 hours after the injection of the foetuses, the uterus was opened and blood samples for calcium determinations were taken from all of the foetuses. The