

THE RELATIONSHIP OF BLOOD URIC ACID CONTENT TO THE STATE OF RENAL FUNCTION IN NEPHRITIS

Christopher Johnston

J Clin Invest. 1931;9(4):555-559. <https://doi.org/10.1172/JCI100320>.

Research Article

Find the latest version:

<https://jci.me/100320/pdf>



THE RELATIONSHIP OF BLOOD URIC ACID CONTENT TO THE STATE OF RENAL FUNCTION IN NEPHRITIS.

By CHRISTOPHER JOHNSTON

(From the Hospital of the Rockefeller Institute for Medical Research, New York)

(Received for publication July 14, 1930)

In a recent paper from this laboratory (1) the blood urea clearance test was compared in nephritic subjects with other measures of renal function, namely, the concentrations of urea, creatinine, and hemoglobin in the blood, and the two-hour excretion of phenolsulphone-phthalein. In the present paper the blood urea clearance test is similarly compared with the concentration of uric acid in the blood.

After the introduction of Folin's micro methods of blood analysis, some evidence accumulated to show that in the course of a progressive nephritis, uric acid was the first nitrogenous waste product to be increased in the blood, and that its estimation could be used as the most delicate indicator of early impairment of renal function (2, 3). At the same time, it was appreciated that in the terminal stages of nephritis the increase of uric acid did not parallel the increase of the creatinine, nonprotein nitrogen, or urea (4). It was subsequently shown that in patients with essential hypertension the blood uric acid was often distinctly elevated, and bore no prognostic significance (5). Hitzemberger and Richter-Quittner (6) found in two such patients that the endogenous excretion of uric acid was slightly above normal, and that they responded to high purine diets by the prompt excretion of large amounts of uric acid.

Further doubt was then cast on the validity of the blood uric acid determination as an index of renal function by reports of its increase in many unrelated conditions. Gout, leukemia, and pneumonia had for many years been known to cause this increase, but newer work indicated that in addition, a rise in the level of blood uric acid could be found in pernicious anemia (7), carbon monoxide poisoning (8), toxemias of pregnancy (9), erythemia (10), eczema (11), and during

the first few days of life (12). Umeda (13) had shown that normal individuals excreted only small amounts of uric acid when on excessively high fat diets, but it remained for Lennox (14, 15) and Harding (16) and his collaborators to show that this decreased excretion was accompanied by a remarkable increase in the blood uric acid either during starvation, or as the result of a ketogenic diet.

Folin, Berglund and Derick (17), injected uric acid into normal men and found that the excretion period following injection varied be-

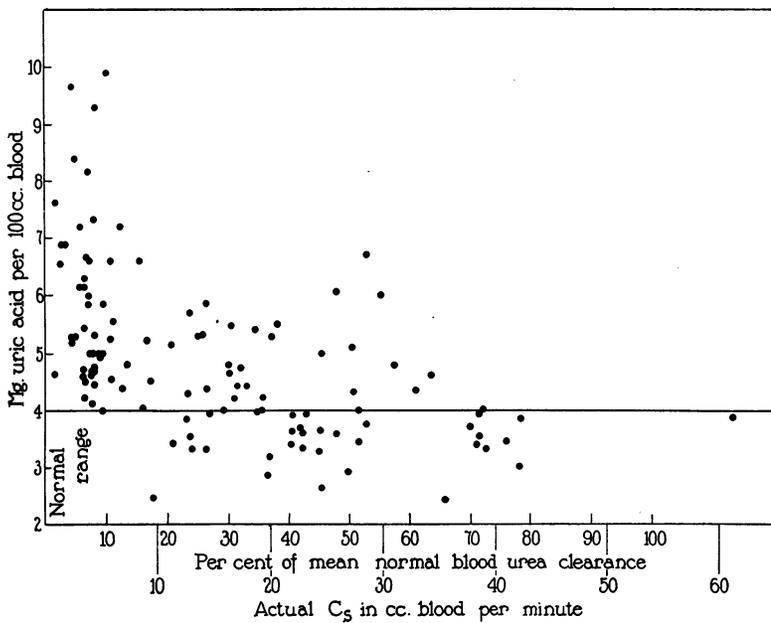


FIG. 1

tween one and four days. They were able to recover from 30 to 90 per cent of the amount injected, the remainder being apparently destroyed.

Although the estimation of blood uric acid as an aid to estimating the state of renal function in nephritis has apparently been abandoned in many clinics, its use has been so general that it still appears desirable to report a comparison of blood uric acid contents with determinations of the blood urea clearance, which has shown itself to be especially reliable and sensitive as a measure of renal function (1).

The urea nitrogen of blood and urine was determined in our cases by the Van Slyke-Cullen urease aeration method (18) (the gasometric urease methods had not yet been introduced). The uric acid was determined in whole blood filtrate by the method of Benedict (19).

Figure 1 presents the data obtained from 117 tests on 30 patients. Twenty-one of these patients had chronic hemorrhagic Bright's disease, and the remainder were distributed as follows: acute hemorrhagic, 2; chronic degenerative, 3; arteriosclerotic, 3; cardiac failure, 1. The approximate upper limit of normal, taken as 4 mgm. of uric acid per 100 cc. of blood, is indicated by the horizontal line drawn at that level across the chart.

The data in figure 1 indicate the following:

1. Normal blood uric acid (2 to 4 mgm. per cent) occurs in a large proportion of nephritic cases with urea excreting power from normal down to 20 per cent of normal.

2. Moderately increased blood uric acid (between 4 and 6 mgm. per cent) may accompany either slight renal damage or the most extreme loss of function.

3. Blood uric acid over 7 mgm. per cent appears to be caused by nephritis only when the latter has reached an advanced stage with urea excreting function less than one-fifth normal. Since similar uric acid values may be caused by other pathological conditions, however, even such high values may not always be accepted as evidence of renal damage.

The irregular correlation of blood uric acid to renal function is what might be anticipated from the fact that uric acid is removed from the human body only partly by excretion, part being destroyed.

Of the two exceptional cases, in which the uric acid rose above 6 mgm. per cent while the clearance was approximately 50 per cent of normal, severe cardiac decompensation was present in one and acute streptococcic pharyngitis in the other. In this connection it may be said that the records of all patients with urea clearances above 20 per cent of normal, together with abnormally high values for blood uric acid, were carefully examined. They were all receiving diets with 40 grams or more of protein daily, adequate in both carbohydrates and total calories, so that starvation acidosis could not have been present as a complicating factor.

SUMMARY AND CONCLUSIONS

The concentration of uric acid in the blood of 30 patients with renal disease has been compared with the standard blood urea clearance determined simultaneously.

The determination of blood uric acid as an indicator of renal function appears to be of little value. Normal blood uric acid may occur despite 80 per cent loss of urea excreting power. When rise of blood uric acid does occur there is, except in some terminal cases, little correlation between the extent of rise in blood uric acid and the extent of fall in renal function.

BIBLIOGRAPHY

1. Van Slyke, D. D., McIntosh, J. F., Möller, E., Hannon, R. R., and Johnston, C., *J. Clin. Invest.*, 1930, viii, 357. *Studies of Urea Excretion. VI. Comparison of the Blood Urea Clearance with Certain Other Measures of Renal Function.*
2. Myers, V. C., Fine, M. S., and Lough, W. G., *Arch. Int. Med.*, 1916, xvii, 570. *The Significance of the Uric Acid, Urea and Creatinin of the Blood in Nephritis.*
3. Baumann, L., Hansmann, G. H., Davis, A. C., and Stevens, F. A., *Arch. Int. Med.*, 1919, xxiv, 70. *The Uric Acid Content of the Blood Compared with the Renal Dietary Test.*
4. Folin, O., and Denis, W., *Arch. Int. Med.*, 1915, xvi, 33. *The Diagnostic Value of Uric Acid Determinations in Blood.*
5. Krauss, E., *Deut. Arch. f. klin. Med.*, 1922, cxxxviii, 340. *Der Harnsäuregehalt des Blutes bei Erkrankungen der Niere im Vergleich zum Reststickstoff und Kreatinin.*
6. Hitzengerger, K., and Richter-Quittner, M., *Wien. Arch. f. Inn. Med.*, 1921, ii, 189. *Ein Beitrag zum Stoffwechsel bei der Vaskulären Hypertonie.*
7. Gettler, A. O., and Lindeman, E., *Arch. Int. Med.*, 1920, xxvi, 453. *Blood Chemistry of Pernicious Anemia.*
8. Czoniczer, G., *Münch. Med. Wchnschr.*, 1920, lxxvii, 1121. *Ueber Urikämie bei Kohlenoxydvergiftung.*
9. Williams, J. L., *J. Am. Med. Assoc.*, 1921, lxxvi, 1297. *Increased Amount of Uric Acid in the Blood in the Toxemias of Pregnancy.*
10. Isaacs, R., *Arch. Int. Med.*, 1923, xxxi, 289. *Pathologic Physiology of Polycythemia Vera.*
11. Schamberg, J. F., and Brown, H., *Arch. Int. Med.*, 1923, xxxii, 203. *The Relationship of Excess of Uric Acid in the Blood to Eczema and Allied Dermatoses.*
12. Kingsbury, F. B., and Sedgwick, J. P., *J. Biol. Chem.*, 1917, xxxi, 261. *The Uric Acid Content of the Blood of New-borns.*

13. Umeda, N., *Biochem. J.*, 1915, ix, 421. The Influence of Fat and Carbohydrate in the Excretion of Endogenous Purines in the Urine of Dog and Man.
14. Lennox, W. G., *J. Am. Med. Assoc.*, 1924, lxxxii, 602. Increase of Uric Acid in the Blood During Prolonged Starvation.
15. Lennox, W. G., *J. Biol. Chem.*, 1925, lxvi, 521. A Study of the Retention of Uric Acid During Fasting.
16. Harding, V. J., Allin, K. D., Eagles, B. A., and Van Wyck, H. B., *J. Biol. Chem.*, 1925, lxiii, 37. The Effect of High Fat Diets on the Content of Uric Acid in the Blood.
17. Folin, O., Berglund, H., and Derick, C., *J. Biol. Chem.*, 1924, lx, 361. The Uric Acid Problem.
18. Van Slyke, D.D., and Cullen, G. E., *J. Biol. Chem.*, 1916, xxiv, 117. The Determination of Urea by the Urease Method.
19. Benedict, S. R., *J. Biol. Chem.*, 1922, li, 187. The Determination of Uric Acid in Blood.