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Edwin P. Jordan, Dorothy Gaston

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Research Article

THE BLOOD URIC ACID IN DISEASE

By EDWIN P. JORDAN and DOROTHY GASTON

(From the Department of Medicine of the University of Chicago, Chicago)

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Because of the large number of patients in the University of Chicago Clinics showing high blood uric acid by the Koch [1] modification of the Folin and Benedict methods using the Folin-Wu blood filtrate, it was decided to try a different method. The method which has seemed to to yield most satisfactory results is that described by Folin (1) in which he makes use of unlaked blood filtrate, a cyanide solution stabilized by means of urea, and a uric acid reagent free from phenol reagent. This method has been used for all uric acid determinations in the Medical department since May 1931, and has proved relatively satisfactory as a clinical method. The cyanide solution, which is kept at low temperature, retains its chromophoric power well, and when used with the uric acid reagent has produced no turbid solutions. It was, of course, necessary to determine a new series of normal blood uric acid values by this method, and while the results are not wholly free from unexplained high values (see Table V), it is believed that this method, as compared with the one formerly used, gives more satisfactory results.

For the purpose of comparison a few samples of blood were tested simultaneously for uric acid by the Koch modification formerly used (hereafter called "old method") and by the Folin method at present used. Two samples from a control patient, drawn on different days, gave 7.2 and 9.2 mgm. per 100 cc. by the old method and 3.9 and 3.8 mgm. per 100 cc. respectively by the new method. One sample from a patient with chronic gout gave 12.3 and 5.6 mgm. per 100 cc. by the old and new methods respectively. The uric acid in the blood of a patient with infectious arthritis was 5.3 and 2.1 mgm. per 100 cc. by the old and new methods respectively. There was thus a deviation in all instances in the same direction and to about the same degree, but there also seemed to be less variation in the results given by the method at present in use.

The first and most important consideration for diagnostic purposes in adopting a new method of determining the amount of uric acid in the venous blood was to find an upper limit for normal which would be reasonably satisfactory.

In Table I are a number of uric acid determinations made on disease-free controls. It will be seen that in only two, Case 6, W. C., and Case

[1] Koch, F. C. Modification developed at University of Chicago.

TABLE I

Disease-free controls

Case	Age	Uric acid in mgm. per 100 cc.					
	years						
1. L. C.	30	2.8	3.0				
2. J. G.	30	3.0	2.5				
3. M. H.	31	2.5	2.4				
4. H. H.	28	2.5	2.2				
5. R. H.	39	2.8	3.2				
6. W. C.	43	5.1	4.0	4.3			
7. B. F.	30	3.6	3.2				
8. H. P.	28	3.5	3.4				
9. E. J.	29	3.9	3.8	3.2	3.4	4.8	3.6
10. R. P.	27	3.4					
11. D. G.	27	3.2	2.6				
12. H. V.	36	3.3	2.4				
13. C. M.	41	2.6	3.0				

9, E. J., were any results found higher than 4 mgm. per cent. In one of these (Case 9) the high value obtained was only one of six, the others being normal, and this was interpreted as being of no significance. The other (Case 6) in which the uric acid value remained persistently above 4 mgm. was puzzling. In spite of the fact that this individual is apparently healthy in every way, and is one of the control cases, we are considering the uric acid values as abnormal.

In Table II are given a number of presumably normal uric acid readings and the clinical diagnosis in each case. It will be noted that in none of these is the uric acid above 4 mgm. per 100 cc. As a result this figure —4 mgm. of uric acid per 100 cc.—is considered to be the usual upper limit of normal, subject to the qualifications discussed later.

The problem which prompted our interest in this study was that of gout. Because of several rather dramatic episodes in the diagnosis of this condition it became desirable to determine by the new method the uric acid levels occurring in this disease. Table III gives the amount of uric acid obtained in patients with gout. It was at first intended to attempt the differentiation of acute gout and chronic gout, but because of the tendency for one to shade into the other and because of the complications resulting from diet and medication this was deemed impracticable. It is noteworthy that the uric acid level is in most instances considerably above the upper limit of those believed to be normal as shown in Tables I and II. In none of these patients was the blood uric acid the sole basis of diagnosis, though we have found it an important aid.

It is well recognized (Peters and Van Slyke (2)) that the blood uric acid may be raised above normal in a number of conditions other than true gout. It has been reported that it may or may not be raised in nephritis with impaired kidney function (3), and that has been our ex-

TABLE II

"Normal" blood uric acid

Case	Diagnosis	Age	Uric acid in mgm. per 100 cc.		
		years			
14. W. T.....	Cholelithiasis, colitis	54	2.9		
15. J. C.....	None made, neurologic ?	19	3.4		
16. A. B.....	Postoperative adhesions	69	3.4		
17. M. B.....	None made	33	3.4		
18. F. C.....	Colitis	45	1.6		
19. G. M.....	Carcinoma of pancreas, chronic cystitis	76	2.2		
20. A. C.....	Toxic liver necrosis	48	1.9		
21. V. K.....	Myasthenia gravis	24	3.0		
22. V. D.....	Duodenal ulcer, colitis	48	3.0		
23. J. S.....	Hypertension, myocardial insufficiency	51	2.9		
24. S. H.....	Maxillary sinusitis	45	2.9		
25. M. O'D..	Carcinoma of thyroid	72	1.0		
26. W. D.....	Malignant obstructive jaundice	57	1.5		
27. H. B.....	None made	47	2.4		
28. L. S.....	None made	34	3.8		
29. L. G.....	Acute glomerulonephritis	24	3.7		
30. C. M.....	Acute glomerulonephritis	24	2.2		
31. E. M.....	Chronic glomerulonephritis	23	2.3	2.1	
32. A. D.....	Proliferative arthritis	14	2.6		
33. W. C.....	Proliferative arthritis	64	3.1		
34. S. C.....	Proliferative arthritis	58	2.8	3.0	
35. G. S.....	Proliferative arthritis	48	1.1		
36. J. A.....	Proliferative arthritis	58	2.5		
37. M. A.....	Proliferative arthritis	66	3.3		
38. H. D.....	Proliferative arthritis	26	1.9	1.3	2.3
39. F. H.....	Proliferative arthritis	19	2.8		
40. J. B.....	Proliferative arthritis	52	2.1		
41. H. McC..	Proliferative arthritis	35	3.3		
42. E. D.....	Proliferative arthritis	56	1.7		
43. E. O.....	Proliferative arthritis	31	2.6		
44. S. B.....	Proliferative arthritis	44	3.2		
45. M. H.....	Proliferative arthritis	32	3.7		
46. M. K.....	Traumatic internal derangement of knee	26	2.6		
47. D. R.....	Acute sacroiliac strain	32	2.8		
48. M. B.....	Rheumatic fever ?	21	2.1		
49. E. R.....	Radiculitis	40	3.8		
50. E. S.....	Rheumatic pains, colitis	47	2.2		
51. J. B.....	Osteochondritis desicans	29	2.6		
52. A. W.....	Degenerative arthritis, diabetes	60	3.7		
53. K. J.....	Degenerative arthritis	70	2.9		
54. R. S.....	Acute rheumatic fever	21	1.1		
55. E. F.....	Degenerative arthritis	70	3.0		
56. M. F.....	Degenerative arthritis	65	3.3		
57. M. R.....	Degenerative arthritis, myxedema	55	3.1		
58. N. H.....	Acute myositis, lues latens	50	3.2		
59. B. J.....	Degenerative arthritis, lues latens	43	3.4		

TABLE III

Gout

Case	Age	Uric acid in mgm. per 100 cc.							
	years								
60. F. A.	50	5.2	5.2	4.9	5.0	4.8	7.7	4.5	
61. J. P.	48	4.4							
62. A. S.	66	4.0	6.1						
63. H. H.	48	3.9	4.2						
64. C. H.	46	4.6							
65. F. S.	57	5.7	3.8						
66. D. D.	51	5.6	10.2	7.4					
67. C. L.	57	5.2	5.8	5.8	4.1	4.4	4.4	5.9	
68. J. S.	63	4.5	4.5	4.3	4.8	5.2	4.4	5.1	3.8
69. D. F.	62	4.2	4.3	3.9					
70. H. H.	68	7.1							
71. W. K.	50	5.4							
72. S. L.	45	4.9	4.7	3.6	4.3	5.0			
73. F. W.	48	8.3	4.9	5.2	6.1				
74. L. B.	43	4.7	5.0						
75. Z. B.	46	5.9							
76. H. C.	35	6.7	5.6	5.9					

perience. In Table IV are given the results in a series of patients where the increase in blood uric acid may be explained on a basis other than gout. In Case 85 where one determination was above the expected normal and the others were normal, the diagnosis was not clear and the possibility of visceral gout was considered. Because of the first result the patient was placed on a purine-poor diet and was living on this regime when the other three determinations were made. Many of the results given in Table IV are well within the range of gout, but two are higher than any we have yet found in gout.

It remains to include in Table V those high uric acids which cannot be explained by any information available to us. There have not been many of these. If more tests had been made on these patients it is possible that some of the high values obtained would have been shown to be

TABLE V

Unexplained high uric acids

Case	Diagnosis	Age	Uric acid in mgm. per 100 cc.	
		years		
90. M. H.	Metatarsal fracture	26	5.0	
91. F. L.	Obesity, cholecystitis	50	4.1	
92. M. M.	Migraine ? headaches	48	4.1	
93. K. M.	Proliferative arthritis	59	4.4	3.7
94. G. R.	Still's Disease (quiescent)	14	5.8	
95. N. T.	Proliferative arthritis	68	4.5	
96. V. Z.	Degenerative arthritis ?	51	4.1	
97. E. E.	Tabes, mild diabetes	60	4.2	

TABLE IV

Increased blood uric acid, other than gout

Case	Diagnosis	Age	Kidney function	Uric acid in mgm. per 100 cc.					
		years							
77. F. H.....	Chronic glomerulonephritis	48	Impaired	7.7					
78. G. B.....	Pulmonary tuberculosis; arteriosclerosis	65	Impaired	5.6					
79. M. G.....	Multiple myeloma	57	Not examined	5.0					
80. C. V.....	Melanocarcinoma gallbladder	44	Normal	2.4	4.1				
81. D. J.....	Chronic myelogenous leukemia	45	Not examined	4.6	3.1	3.1	2.6	3.4	3.5
82. R. G.....	Acute yellow atrophy. Death	21	Normal (early)	2.2	4.4				
83. W. P.....	Chronic lymphatic leukemia	27	Not examined	5.0					
84. J. C.....	Chronic glomerulonephritis	24	Impaired—uremia	16.2					
85. C. C.....	No diagnosis made	42	Not examined	5.3	2.7	3.2	2.2		
86. L. W.....	Polycythemia vera	60	Not examined	4.0	3.4				
87. M. T.....	Arteriosclerotic heart disease	70	Impaired	12.6					
88. M. B.....	Uremia			17.4					
89. A. F.....	Lead poisoning ?	53	Not examined	3.88	4.1				

single aberrant tests and of no diagnostic significance. They must, however, be included as indicating flaws in the test as a diagnostic procedure.

DISCUSSION

With the discovery of the uric acid diathesis in gout, attention was focused on purine metabolism. Further studies have indicated that the relationship between uric acid retention and gout is not as simple as at first believed. Observers have reported considerable variation in the amount of blood uric acid under normal conditions as well as in diseases other than gout. The significance of these findings is not as yet thoroughly understood. Although mention of gout in the contemporary American literature is unusual, it has been our experience to find the condition among Chicago patients with greater frequency than was anticipated. Whether a similar incidence of gout occurs in other parts of the country would be a matter of interest.

The amount of uric acid in the blood under normal and pathologic conditions is a matter of basic importance. The more accurately the determinations can be made the sooner will the understanding of purine metabolism approach scientific precision. By Folin's method, here in use, we believe that most, if not all, patients with gout will show blood uric acid values above a range which we accept as normal. The difficulty in diagnosis lies in distinguishing the higher values obtained in conditions other than gout. Most of such high values have occurred in the various conditions already known to be at times associated with high blood uric acid.

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