URIC-ACID LEVELS IN BLOOD AND PLASMA

BY

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In a survey of over 100 patients on whom routine uric-acid estimations were made at the request of the West London Hospital Rheumatism Clinic it was confirmed that the level of uric acid is higher in plasma than in whole blood (Table I). This difference had been recognized previously (Hawk, 1947), and in the present series

TABLE I.—Blood Uric Acid and Plasma Uric Acid in 114 Patients

	Mean Value	Standard Error
Whole blood	3.52±0.93	0.087
Plasma	4.04±1.55	0.097

Significance ratio = 3.8

was found in 102 out of 114 patients. The high significance ratio shows that there is a real difference between the uric-acid levels of blood and of plasma.

It was also noticed that for any one patient the blood-plasma-uric-acid ratio remained constant over considerable periods, though in one case the actual uric-acid figures varied greatly (Table II).

TABLE II.—Blood/Plasma Ratio of Uric Acid

Patient	Blood Uric Acid mg./100 ml.	Plasma Uric Acid mg./100 ml.	Blood/Plasma %	Date
Mr. A (leukaemia)	10.0	12.9	78	28/7/48
	7.6	9.6	79	5/8/48
	16.0	21.0	76	13/6/49
Mr. B (gout)	5.0	5.1	98	
	5.2	5.4	96	
Mr. C.	4.8	5.0	97	Over four weeks
	5.4	5.6	96	

This observation suggested that one or more factors which remain reasonably constant in any one individual affected either the actual amount of uric acid present in the blood and plasma or the chemical reactions by which uric acid is estimated in Folin's method (Folin, 1933), which was employed in all estimations.

It was thought that interfering substances might be responsible. Ergothioneine and glutathione, both sulphhydryl-containing reducing substances, which occur in minute quantities in the red cells, were found to increase "uric-acid values"—that is, they produced an increase in the depth of colour given by uric acid which would be interpreted as excess uric acid.

The addition of 100 mg. of glutathione per 100 ml. produced an increase of about 1 mg. of uric acid per 100 ml. in standard solutions of uric acid, and the rise due to the same amount of ergothioneine was about 4 mg. of uric acid per 100 ml.

However, in the amounts in which these substances occur in the erythrocytes they do not have an appreciable effect on uric-acid reagents. They are therefore not responsible for any difference between blood and plasma.

In fact, if they interfered with the estimation they would raise the apparent uric-acid level in whole blood, thus tending to obliterate the difference.

Molybdenum was alleged to reduce the uric-acid reagents, thus giving rise to apparently higher uric-acid values. Using King's (1937) and Folin's methods and running parallel series of estimations with molybdenum-free and not specially purified reagents we found good agreement between the two series, provided that the standard was treated in exactly the same way as the test solution—that is, with the same reagents.

After eliminating these chemical factors, the initial measurement of blood and plasma was questioned. There might be a discrepancy between the volume of blood and plasma delivered by the same pipette, owing to the higher viscosity of the blood. If a less than nominal volume of blood is delivered, while the correct amount of plasma can be obtained, a higher plasma uric acid would, of course, result. As whole blood presumably becomes more viscous as its cell content increases, it was thought that some measure of the "drainage factor" might be obtained by correlating the packed cell volume with blood and plasma uric-acid levels. In over 100 cases blood and plasma uric acid were measured and the packed cell volume recorded. The results are shown in Table III.

TABLE III.—Blood and Plasma Uric-acid Levels and Packed Cell Volume

Blood/Plasma Uric Acid %		Packed Cell Volume
Mean	Error	Mean
90.5±5.3	0.71	Above 40% .. 45.5%
97.5±4.7	0.71	Below 40% .. 34.2%

This analysis by cell volume can be interpreted to show two other possibilities. First, there may be a natural difference between the uric-acid content of red cells and plasma. Uric acid may not be able to diffuse freely across the cell membrane, and a slight excess remains permanently in the plasma. Secondly, uric acid may be adsorbed on the protein precipitated by tungstic acid. A larger precipitate will adsorb more uric acid and therefore give rise to a lower uric-acid value in the filtrate. As the precipitate from whole blood is larger than that of plasma, a difference in the results may be expected on this assumption. A low cell volume would produce a smaller precipitate and tend to cancel out the difference.

In conclusion, it can be stated that there is a distinct difference between blood and plasma uric-acid levels. The higher uric acid in the plasma may be an artifact inherent in the technique, but the possibility of a real difference has not been ruled out.

REFERENCES

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