

# THE RELATION OF SERUM URIC ACID TO HAEMOGLOBIN LEVEL IN PATIENTS WITH CARDIAC AND RESPIRATORY DISEASE

BY

J. G. LEWIS AND J. E. GARDNER

*From the Department of Chemical Pathology, the Brompton Hospital, London*

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An investigation was made of the serum uric acid in 130 male patients with long-standing cardiac or pulmonary disease. The mean serum uric acid was 4.66 mg. per 100 ml. with a standard deviation of  $\pm 0.99$ .

The serum uric acid increased parallel with a rise in the haemoglobin level. The coefficient of correlation was +0.5, which was nearly six times the standard error.

The frequency of hyperuricaemia (over 6 mg. per 100 ml.) was 11 times in 47 patients with a haemoglobin level above 110% as compared with twice in 83 patients when the haemoglobin level was below this figure.

The highest levels of serum uric acid were seen in patients with cyanotic congenital heart disease.

Two of the patients with hyperuricaemia gave a suggestive history of gout, and this was believed to have been caused by the secondary polycythaemia.

Serum uric acid levels were significantly higher, as were the haemoglobin concentrations, in the obese compared with the patients who were not obese.

This study originated from a clinical impression that in certain patients a moderate elevation of the haematocrit or haemoglobin concentration was associated with a high average, or above normal, level of serum uric acid (Goldthwait, Butler, and Stillman, 1958; Beckett and Lewis, 1960). These subjects were not known to have polycythaemia rubra vera, a condition in which hyperuricaemia is not uncommon (Lawrence, Berlin, and Huff, 1953).

The purpose of this investigation was to test the validity of this impression by relating the serum uric acid to different levels of the haemoglobin. The patients studied had chronic cardiac or respiratory disorders which are known at times to have an accompanying secondary polycythaemia, and hence could be expected to show a wider range of haemoglobin readings than normal subjects. At the same time the opportunity was taken to study the frequency of hyperuricaemia in patients with chronic chest disease, and some of the factors which appeared to influence the level of the serum uric acid.

## Material and Methods

The serum uric acid was measured in selected male patients with long-standing chest disease attending the Brompton Hospital. The method of estimation

was that of Folin (1922) modified by Folin and Trimble (1924). The range of normal accepted was 1.5 to 6.0 mg. per 100 ml., and the standard deviation of duplicated tests by this method was  $\pm 5\%$ . Individual values of the serum uric acid were correlated with the haemoglobin level, type of chest disease, and the presence of obesity. Patients were excluded from the study if they were treated with anticoagulant therapy, salicylates, or corticosteroids at the time of the test. They were also not included if they had chronic renal disease with proteinuria, primary polycythaemia, acute pneumonia, or were having radiation therapy.

The haemoglobin level was measured by the oxyhaemoglobin method using a photoelectric colorimeter, with a neutral grey solution as a standard. A haemoglobin value of 100% was taken to equal 14.6 g. per 100 ml.

## Results

One hundred and thirty patients were investigated, and their mean serum uric acid was 4.66 mg. per 100 ml. with a standard deviation of  $\pm 0.99$ ; the values ranged from 2.8 to 8.5 mg. per 100 ml. The correlation of the serum uric acid with the percentage haemoglobin is shown in Table I and Fig. 1, and it will be seen that there is an increase in average values with rise of haemoglobin concentration. The coefficient of

TABLE I  
SERUM URIC ACID RELATED TO HAEMOGLOBIN LEVEL  
IN 130 PATIENTS WITH CHEST DISEASE

	Percentage Haemoglobin				
	<90	90-	100-	110-	>120
No. of patients ..	10	31	42	34	13
Mean serum uric acid (mg./100 ml.)	3.84	4.1	4.7	5.08	5.4
No. with hyperuricaemia ..	—	—	2 (5%)	7 (21%)	4 (31%)

correlation was +0.5, and was of significance as it was nearly six times the standard error. The frequency of hyperuricaemia is also given in Table I for the different haemoglobin ranges, and it appears that serum uric acid values above normal were uncommon when the haemoglobin concentration was below 110%.

All the 130 male patients had symptoms or signs of chronic cardiac or respiratory disease, and most required admission to hospital for treatment. Within this group the highest values of haemoglobin and serum uric acid were seen in those with cyanosis, especially if caused by congenital heart disease, or cor pulmonale. The

clinical features of the 13 patients with hyperuricaemia are shown in Table II. Two of the patients with hyperuricaemia and a high haemoglobin value gave a history of joint pain which clinically resembled gout.

TABLE II  
CLINICAL STATE OF 13 PATIENTS WITH HYPERURICAEMIA

Patient	Age	Disease	Serum Uric Acid (mg./100 ml.)	Haemoglobin Level (%)
B. C.	18	Pulmonary stenosis with right to left shunt ..	8.5	140
P. D.	22	Atrial septal defect, anomalous venous drainage ..	7.5	120
C. H.*	58	Emphysema, cor pulmonale ..	6.9	128
J. P.	70	Bronchitis, emphysema, coronary disease, obesity ..	6.8	118
R. H.	42	Asthma, obesity ..	6.7	106
P. W.*	37	Patent ductus with pulmonary hypertension, heart failure, and tuberculosis ..	6.6	148
S. B.	66	Bronchitis and emphysema ..	6.5	116
E. W.	59	Emphysema with cyanosis ..	6.5	100
H. C.	66	Emphysema, cor pulmonale ..	6.1	112
F. B.	57	Cor pulmonale, emphysema ..	6.0	120
J. L.	53	Bullous emphysema ..	6.0	118
G. Y.	55	Emphysema with cyanosis ..	6.0	115
W. B.	52	Chronic rheumatic carditis ..	6.0	112

\* Gout.

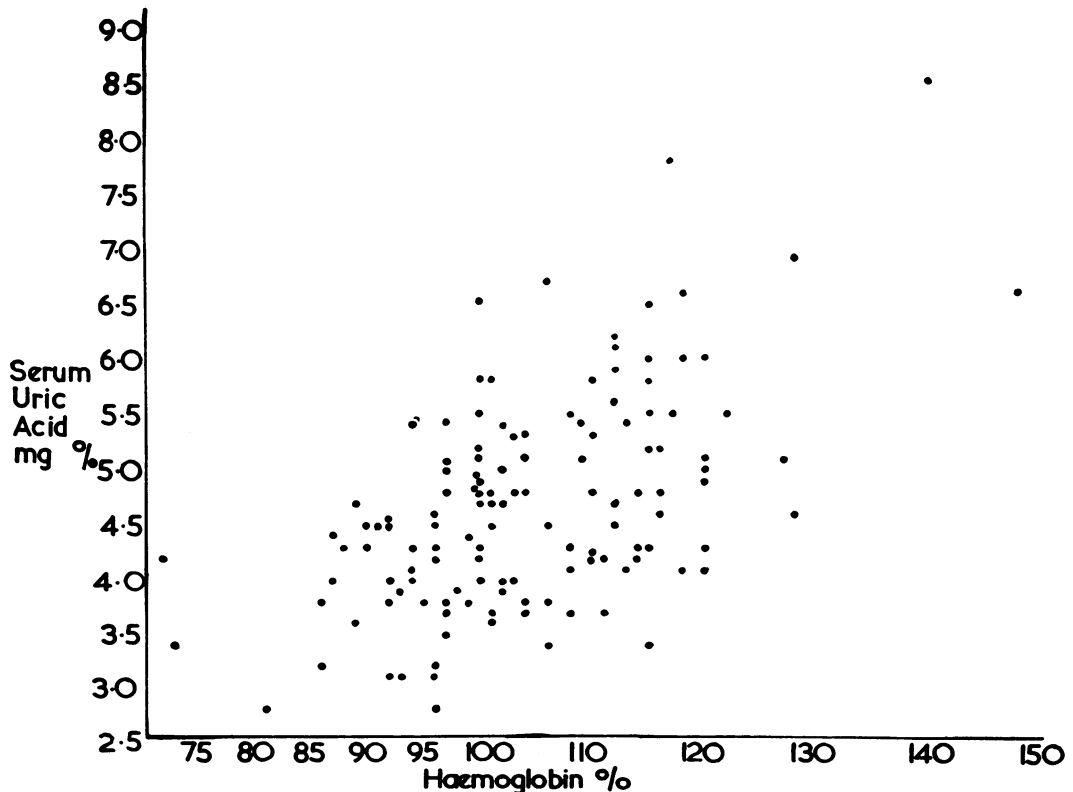


FIG. 1

The relation of the serum uric acid and haemoglobin level to body weight is shown in Table III. The diagnosis of obesity was based on the known weight and appearance of the patient, taking into account the sex, height, and age. In only 89 patients were the clinical details

TABLE III  
SERUM URIC ACID AND HAEMOGLOBIN LEVELS IN 85  
PATIENTS RELATED TO BODY WEIGHT

	Overweight	Not Overweight
No. of patients .. ..	37	52
Average serum uric acid level (mg./100 ml.) .. ..	5.0	4.23
Standard deviation .. ..	0.88	0.67
Average haemoglobin level ..	106	99.4
Standard deviation .. ..	11	9.0

such that an assessment could be made of the presence or absence of obesity. The mean values of the serum uric acid and haemoglobin were significantly higher in the overweight patients than in those not overweight ( $P < 0.01$ ). There was no increase of the serum uric acid with age.

### Discussion

The study showed that there was an association between the haemoglobin level in its higher ranges and the serum uric acid. High haemoglobin concentrations may reflect a number of conditions such as an absolute increase in red cells due to secondary polycythaemia, a relative polycythaemia caused by a contraction of the plasma volume (Berlin, Lawrence, and Gartland, 1950), or a shift in the distribution of red cells (Blum and Zbar, 1959).

There are several possible reasons why an absolute or relative increase in haemoglobin concentration may be associated with a corresponding rise in the serum uric acid. First, the augmented production of red cells and nucleoproteins in secondary polycythaemia leads to an increased total of uric acid in the body, and hence serum levels will rise to an extent which depends on renal excretion. Second, in patients with compensatory polycythaemia a high haemoglobin level is the consequence of anoxia, which may also interfere with cardio-renal function, and so cause retention of uric acid. Third, in relative polycythaemia the plasma volume is correspondingly decreased, and a proportionate reduction may also be seen in patients with an increased red cell mass (Berlin *et al.*, 1950; Lawrence *et al.*, 1953; Blum and Zbar, 1959). This diminution in available solvent might be expected to contribute to a secondary rise in the concentration of

serum uric acid. Finally there is the factor that when respiratory disease is associated with secondary polycythaemia heart failure is often present as well (Cournand, 1950; Wilson, Borden, and Ebert, 1951), and these patients often need diuretic therapy which may itself cause the serum uric acid to rise.

The average serum uric acid of the men studied may not be representative of those with chronic cardiac or respiratory disease, since there was a bias towards patients with a high haemoglobin level. The incidence of hyperuricaemia (10%) compared with the 3 to 6% expected in a random selection (Gertler, Garn, and Levine, 1951; Goldthwait *et al.*, 1958). Persistently high levels of serum uric acid were infrequent in those with long-standing respiratory disease in the absence of a significantly raised haemoglobin, and it is not unexpected that patients with anoxia, cyanosis, and cor pulmonale should have higher average serum uric acid levels than those with healed tuberculosis, minor respiratory disease, or normal subjects.

Hyperuricaemia, on the other hand, is not uncommon in cardiological practice, for it is prevalent in those with premature coronary artery disease (Gertler *et al.*, 1951). The highest values of serum uric acid in the present study were observed with congenital heart disease. The view that an elevated serum uric acid is mainly a reflection of an increased red cell production may apply especially to cyanotic congenital heart disease since secondary polycythaemia is most extreme in this condition (Whitby and Britton, 1950). The resulting hyperuricaemia is clinically important since secondary gout may occur as shown by Yü, Wasserman, Benedict, Bien, Gutman, and Stetten, (1953), and probably by two of the patients in this study.

Significantly higher haemoglobin levels were seen in the obese patients. It is known that obesity can cause cardiorespiratory disease with anoxia and so lead to a compensatory increase in blood volume (Arnott, 1960), but this only occurs in extreme examples. Polycythaemia may also be present in patients with obesity even though the oxygen tension is normal (Weil, 1955). Certain workers, such as Huff and Feller (1956), have shown that the mass of circulating red cells is significantly related to fat as well as lean tissue. It is thus tempting to ascribe, at least in part, the higher average serum uric acid of the obese patient with cardiorespiratory disease to an increased production of red cells as compared with those not overweight. This might also explain why higher average serum uric acid levels

are seen in the normal endomorphic subject, and those of similar build with coronary artery disease (Gertler *et al.*, 1951), and diabetes mellitus (Beckett and Lewis, 1960) as compared with ectomorphs.

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