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John H. Talbott

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# SERUM URATE IN RELATIVES OF GOUTY PATIENTS<sup>1, 2</sup>

By JOHN H. TALBOTT

(From the Medical Clinic of the Massachusetts General Hospital and the Fatigue Laboratory, Harvard University, Boston)

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Though the hereditary nature of gouty arthritis has been recognized for centuries, systematic studies of afflicted families are rare. Of several items which are pertinent to such studies, there are at least two significant ones. These concern (a) the hereditary transmission of gout and (b) the pathogenesis of its clinical manifestations. If the hereditary data are obtained from routine clinical records without painstaking study of the living relatives, the familial incidence appears to be low. Diligent medical and social investigation of gouty families, however, discloses evidence which indicates a high familial incidence and supports the hypothesis that gout is an hereditary malady (1, 2, 3, 4, 5). Such a survey which has been conducted by us has shown, in addition, that an elevated serum urate may be observed in relatives of gouty patients even though they, the relatives, display no other clinical evidence of gout or gouty arthritis.

## EXPERIMENTAL OBSERVATIONS

These data were obtained during the past five years from the investigation of one hundred and thirty-six blood relatives of twenty-seven patients with gout. A clinical diagnosis of gout (6, 7) was apparent in each of the patients. Twenty-three of the twenty-five males had x-ray evidence of gouty arthritis. The two females had proved urate tophi. The concentration of serum urate (8) was determined four or more times. In all except one sample from one patient it was greater than 6.0 mgm. per 100 cc. In the absence of renal insufficiency or leukemia, an elevation of serum urate above 6.0 mgm. constitutes important evidence in support of a diagnosis of gouty arthritis in patients with unexplained joint disease.

<sup>1</sup> This investigation was aided by a grant from the Corn Industries Research Foundation.

<sup>2</sup> The results of this investigation were presented at the meeting of the American Society for Clinical Investigation, Atlantic City, New Jersey, May 2, 1938.

Exceptions to this may be noted in patients over 60.

No one of the one hundred and thirty-six relatives appeared to be suffering from gout or gouty arthritis. Fifty-eight per cent of the group were males. The ages varied from 6 to 86. Most of them were in either the 3rd, 4th or 5th decade of life. The kinship to the gouty patients included parent, sibling, child, grandchild, niece, nephew and cousin. Two had rheumatoid arthritis, six degenerative joint disease, and two rheumatic heart disease. The remainder of the group were in apparent good health.

X-rays of the feet were taken in one hundred and ten subjects. Changes considered to be consistent with gout were not observed in any. The concentration of serum urate was determined one or more times in each relative. One hundred and two had a concentration less than 6.0 mgm. per 100 cc. In a few instances the determinations were repeated and the normal values were checked. The average for the one hundred and two subjects was 4.6 mgm. This is slightly higher than the average for a similar number of non-gouty subjects (9). The concentration of serum non-protein nitrogen was less than 35 mgm. per 100 cc. in each member of this group.

The remaining thirty-four relatives had a serum urate greater than 6.0 mgm. per 100 cc. The serum values ranged from 6.1 to 10.8 mgm. per 100 cc. (Table I). The average was 7.3 mgm. The determination was repeated in thirteen subjects one or more times within four years of the original observation and found elevated. The ages of these subjects ranged from 14 to 86. Eighty per cent were males. The genealogical trees of two families are given in Figures 1 and 2.

The serum nonprotein nitrogen concentration was less than 35 mgm. per 100 cc. in each instance. Intravenous phenolsulphonphthalein and urine concentration tests were studied in a few. The tests were normal. Other causes of increased serum urate were excluded tentatively by the

medical history and by physical examination. It is apparent that an elevated serum urate may be observed in members of gouty families who present no other evidence of gouty arthritis. It is concluded that such an elevation is intimately associated with the constitutional gouty diathesis and is not the result of renal disease.

It is of interest that, during the eighteen to thirty-six months that have elapsed since this communication was prepared for publication, three of the thirty-four have had one or more attacks of acute arthritis. Their ages at the time of the acute attacks were 40, 46, and 47, respectively. One or more joints of the feet were involved. X-ray changes or subcutaneous tophi were not demonstrable subsequently. A presumptive diagnosis of gout in these three subjects is justified probably on the basis of family history, elevated

TABLE I  
*Experimental observations on twenty-seven gouty families*

| Family    | Relatives with a normal concentration of serum urate Number | Relatives with an increased concentration of serum urate |  |  |
|-----------|---|--|--|--|
|           |   | Age  | Sex  | Serum urate<br><i>mgm. per 100 cc.</i> |
| An.....   | 13  | 17<br>20<br>21<br>25<br>43                               | Male<br>Male<br>Female<br>Female<br>Female | 6.3-6.9<br>7.7<br>6.2<br>10.7<br>7.0   |
| Br.....   |   | 38   | Male                                       | 8.0                                    |
| Bu.....   | 5   | 17<br>20<br>37<br>42<br>47                               | Male<br>Male<br>Male<br>Female<br>Male     | 7.0<br>6.6<br>6.1<br>7.0<br>6.2-6.7    |
| Caf.....  | 3   |  |  |  |
| Can.....  | 2   |  |  |  |
| Cent..... | 3   | 37   | Male                                       | 6.5                                    |
| Char..... | 3   |  |  |  |
| Chas..... | 5   |  |  |  |
| Col.....  | 8   | 18   | Male                                       | 9.4-6.6-8.8                            |
| Cora..... |   | 40   | Male                                       | 9.5-6.2-7.4                            |
| Cron..... | 14  | 46   | Male                                       | 6.6-6.1                                |
| Di.....   |   | 24   | Male                                       | 7.4                                    |
| Fa.....   |   | 37   | Female                                     | 6.4                                    |

TABLE I—Continued

| Family    | Relatives with a normal concentration of serum urate Number | Relatives with an increased concentration of serum urate |                      |  |
|-----------|---|--|----------------------|--|
|           |   | Age  | Sex                  | Serum urate<br><i>mgm. per 100 cc.</i> |
| He.....   | 1   | 72   | Male                 | 7.7                                    |
| McG.....  | 1   |  |                      |  |
| Mor.....  | 2   | 54<br>63   | Male<br>Male         | 7.4<br>6.8                             |
| Mort..... |   | 48   | Male                 | 6.3-9.5-7.1                            |
| Na.....   | 5   | 34   | Male                 | 7.3                                    |
| Pe.....   | 7   |  |                      |  |
| Re.....   | 5   | 24<br>29<br>57   | Male<br>Male<br>Male | 6.8-7.9<br>7.9<br>9.1                  |
| Ri.....   | 5   | 65   | Male                 | 6.1                                    |
| Sa.....   | 1   | 20   | Male                 | 6.1-7.0                                |
| Sch.....  | 1   | 37   | Female               | 6.2                                    |
| St.....   |   | 58   | Male                 | 6.5-6.9                                |
| Ta.....   | 12  | 39<br>46<br>86   | Male<br>Male<br>Male | 6.4-6.7<br>9.6-10.0<br>6.4-6.2-6.3     |
| Tran..... | 5   | 28<br>14   | Female<br>Male       | 6.7<br>6.4-6.4                         |
| Tort..... | 1   |  |                      |  |

serum urate and an acute attack of arthritis. On the other hand, no one of the subjects who had a concentration of serum urate less than 6.0 mgm. per 100 cc. has had any acute attacks which suggested gouty arthritis. Obviously, it is hazardous to predict whether any more of the relatives will develop symptoms of arthritis in the future.

In addition to the blood relatives, the wives of five patients with gout, whose sons had an elevated serum urate, were interviewed. The concentration of serum urate was less than 5.0 mgm. per 100 cc. in each of them.

#### DISCUSSION

Twenty-five per cent of one hundred and thirty-six relatives of gouty patients showed an increase in serum urate above 6.0 mgm. per 100 cc. It is believed that this is a manifestation of a familial

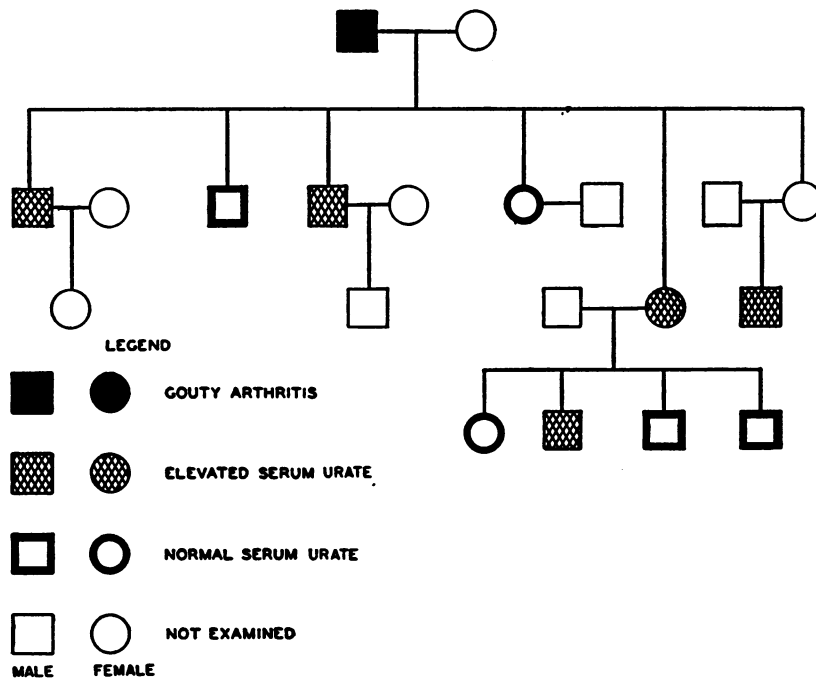


FIG. 1. GENEALOGIC TREE OF FAMILY BU

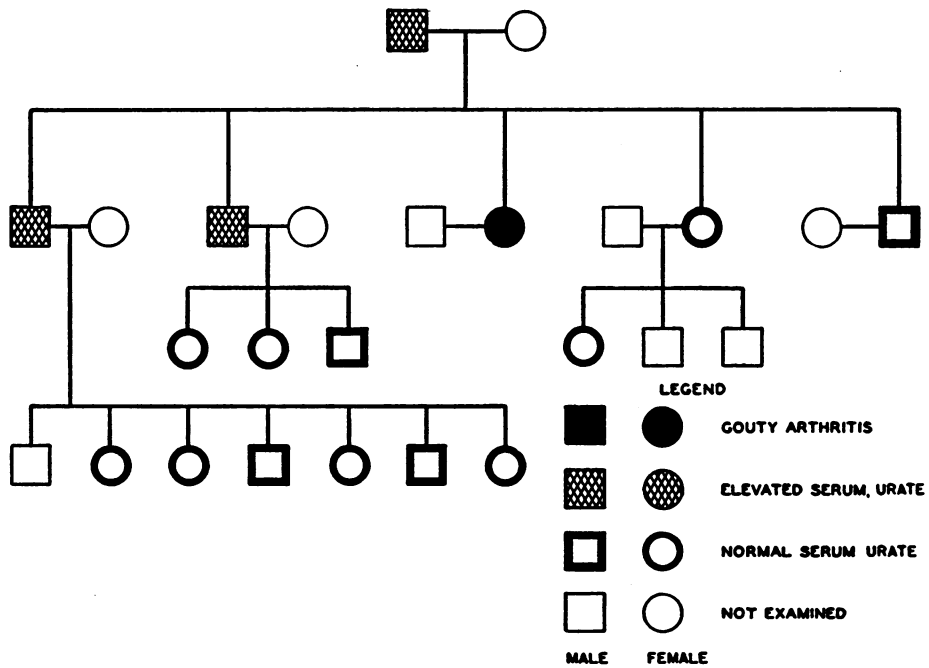


FIG. 2. GENEALOGIC TREE OF FAMILY TA

tendency. If this assumption is correct, it is probable that an increased concentration is present at birth or shortly after, although the youngest age observed by us was 14. The fact that three subjects were older than 70 indicates that an elevated level in the body is compatible with good health and a reasonably long life. The high incidence of males in the group with an elevated serum urate agrees precisely with the sex distribution of clinical gout.

Little is known concerning the etiology of gout other than that it is a metabolic dyscrasia associated with an increased concentration of urate in the body. It is the belief of the writer that an increased formation of urate is the most significant factor in the gouty diathesis (10). If this hypothesis is correct, cases of gouty arthritis may appear in gouty families regardless of mode of living or environment. The finding of an increased concentration of serum urate in non-gouty relatives of gouty patients lends additional support to the hypothesis that gout is a defect of purine metabolism, this defect being one of increased formation of urate.

#### SUMMARY

A study has been made of one hundred and thirty-six relatives of twenty-seven patients with gouty arthritis. At the time of their first examination no one of the relatives had had any symptoms or x-ray evidence of acute or chronic gout. The serum urate was normal in one hundred and

two of the group; the average was 4.6 mgm. per 100 cc. In the remaining thirty-four, the concentrations varied from 6.1 to 10.8 mgm. per 100 cc.; the average was 7.3 mgm. per 100 cc. Eighty-three per cent of these subjects were males. It is concluded that an elevated serum urate, an essential component of the gouty diathesis, may be observed in symptom-free members of gouty families.

The following persons assisted in this study: Dr. F. S. Coombs, Mrs. E. A. Gall, Mr. W. V. Consolazio, and Mr. L. J. Pecora.

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