

Gout in a New England town

A prevalence study in Sudbury, Massachusetts

J. B. O'SULLIVAN

Diabetes and Arthritis Field Research Unit, Boston; Center for Disease Control, Atlanta, Georgia

An accurate prevalence rate for gout has proven difficult to obtain from population samples, partly because of the low frequency of the condition but also because of the imprecision resulting from dependence on evidence obtained from medical histories. The frequent occurrence of hyperuricaemia also complicates the problem by contributing to faulty diagnoses in the presence of joint pain from other causes. In fact, recent recommendations for standardization of the diagnosis of gout have suggested that further progress in our understanding of the epidemiology of gout might not be made without additional reports showing its prevalence determined by diagnoses made independently of the serum uric acid level (New York, 1968).

A study of the adult population of Sudbury, Massachusetts, was initiated in 1964. The information concerning the prevalence of gout obtained during the initial survey is the subject of this report. The effect of two recommended criteria used to define gout on the outcome of the study is also analysed (Rome, 1963; New York, 1968).

Material and methods

SUBJECTS

The town of Sudbury was chosen as a suitable site for an epidemiological survey on the basis of its size, the relative stability of its population, the cohesive strength provided by its civic organizations, and our prior favorable assessment of the support that might be provided by townspeople and physicians in the area. This town was immortalized by Longfellow's 'Tales of a Wayside Inn' and, more recently, has been historically documented by Powell's Pulitzer-Prize-winning 'Puritan Village'. The town's 1964 census listed 6,071 legal residents who were 15 years of age and over on January 1, 1964. Residents objecting for religious reasons and non-residents who maintained a technical legal residence in the town were excluded from all study tabulations. Medical questionnaires were mailed to the remaining 5,976 defined residents. These forms were filled out at home, returned, and reviewed by the physician at the time of the examination. Towards the end of the study, house-bound persons were visited by a nurse and a physician.

METHODS

Participants were examined in the afternoon or evening by

a physician and their sample of whole blood was allowed to clot for 30 minutes before refrigeration. Serum was carefully separated the next morning for uric acid assay. Uric acid levels in Sudbury were determined by an automated colorimetric procedure (AutoAnalyzer *n*-method) (O'Sullivan, Francis, and Kantor, 1965). The standard deviation (S.D.) of the differences for duplicate determinations by this method was determined to be 0.07 mg. per 100 ml. Samples of a serum control pool, introduced intermittently throughout the study under various false names, gave a mean and S.D. of 5.24 ± 0.13 mg. per 100 ml. A close agreement of results was obtained when a 5 per cent. random subsample of the specimens was also analysed by the uricase method, with the AutoAnalyzer showing a mean and standard deviation of the distribution of 4.93 ± 1.29 mg./100 ml. for 169 individuals, and the Uricase method showing 4.77 ± 1.26 mg./100 ml. for the same samples. All patients with serum uric acid levels above the population's 95th percentile had blood smears which showed no evidence of myeloproliferative conditions (O'Sullivan, 1966).

DIAGNOSIS

The diagnosis of gout was based alternately on the recommendations to two international symposia, held in Rome (1963) and New York (1966), sponsored by the Council for International Organizations of Medical Sciences (C.I.O.M.S.), established under the joint auspices of UNESCO and WHO, with partial support from the National Institute of Arthritis and Metabolic Diseases and the Arthritis and Rheumatism Foundation. These criteria are summarized in Table I. Demonstration of urate crystals in synovial fluid is given greater emphasis in the 1966 New York criteria, but this has little effect on the outcome of epidemiological studies since the procedure is not applicable in such situations and medical histories do not indicate that many patients receive diagnostic arthrocentesis. Otherwise the two sets of criteria differ in that the New York criteria require two attacks of swelling in joints other than the great toe; in that a point is added for a good response to colchicine therapy; and in that the serum uric acid level is omitted as a diagnostic criterion.

Results

A total of 4,626 persons (77 per cent.) from the eligible population of 5,976 responded for examination.

Table I Diagnostic criteria for gout*

1963 (Rome) Criteria	1966 (New York) Criteria*
1. Painful joint swelling Abrupt onset, clearing in 1-2 weeks initially	1. Two attacks of painful limb joint swelling. Abrupt onset and remission in 1-2 weeks initially
2. Serum uric acid: ≥7 mg. in males, ≥6 mg. in females	2. An attack involving a great toe—as described in 1
3. Presence of tophi	3. Presence of a tophus
4. Presence of urate crystals in synovial fluid	4. Response to colchicine—major reduction in inflammation within 48 hrs

* Two or more of the criteria in each set is required for diagnosis. The 1966 criteria (published 1968) allow the diagnosis of gout independently of these criteria if synovial urate crystals are demonstrated.

Confidence in determining the prevalence rate for gout required an assessment of the possible biasing effects of non-response. Accordingly, several sources of information were reviewed. These sources included questionnaires that were returned by people who did not report for testing, telephone information from the non-respondent or a resident member of his family, and a survey of the records in the four surrounding community hospitals. No additional cases of gout were uncovered and one woman stating she had gout did not describe a characteristic medical history. For these reasons the age-specific results reported here will use the total population figures as the more appropriate denominator.

Fifty of the study participants stated that a physician had told them that they had gout. These fifty persons were evaluated by the criteria outlined and, where possible, verified by contacting the physician who made the initial diagnosis. Finally, 22 were accepted as cases of gout. All satisfied one or both of the recommended criteria outlined in Table I. The prevalence rate for gout in the population of Sudbury is, then, of the order of 3.7 cases per thousand.

Table II displays age- and sex-specific prevalence rates for gout. The sex ratio is approximately 7:1, with the rate for males at 6.6 and females 1.0 cases per thousand. There is also a definite increase in prevalence rates with advancing age between 35 and 74

years, and no cases were found below 37 or above 75 years. The highest prevalence rate is for the 65-to-74-year group, being 24.4 and 16.3 cases per thousand for males and females respectively.

The role of the diagnostic criteria in the outcome of this prevalence study is analysed in Table III. Ten of the 22 patients with gout satisfy both the New York and the Rome criteria, while eight satisfy the Rome and four the New York criteria only. The overall prevalence rate can thus be seen to be the highest estimate of the condition in the town of Sudbury.

Table III Effect of diagnostic criteria on number of persons classified as having gout, by sex

Criterion	Male	Female	Total
Rome only	6	2	8
New York only	4	0	4
Both	9	1	10
Total	19	3	22

Table IV (overleaf) contrasts characteristics of the gouty patients with those of the responding population. The patients with gout are seen to be a considerably more overweight group than the general

Table II Verified cases of gout, by age and sex

Sex	Male		Female			
	Total	Cases of gout		Total	Cases of gout	
		Number	Per cent.		Number	Per cent.
15-24	549	0	0	533	0	0
25-34	659	0	0	807	0	0
35-44	904	6	0.66	833	0	0
45-54	457	5	1.09	382	0	0
55-64	206	5	2.43	243	1	0.41
65-74	123	3	2.44	123	2	1.63
>75	46	0	0	111	0	0
Total	2,944	19	0.66	3,032	3	0.10

Table IV *Characteristics (per cent.) of persons with gout in Sudbury*

Characteristic	Persons with gout (22)	Remaining population (4,604)
Family history of gout	27.3	4.9
Tophi	13.6	0.1
Kidney stones	22.7	2.8
Relative body weight (median per cent.)	125	107

population and to have a higher frequency of a family history of gout, tophi, and kidney stones.

The distribution of sex-specific uric acid levels in the population has been published (O'Sullivan, 1968). The mean uric acid for each age group shows essentially no increase by age in males (24-74), while females clearly show a shift to a higher level during the menopausal years (Table V). The median values were between 0.1 and 0.2 mg. per 100 ml. lower than the mean uric acid levels and were also unaffected by age in male participants. The small variations observed will be explored in a later analysis, although data at hand reveal these to be due to the different distributions of body weight in each of the age groups. The proportion of the population with hyperuricaemia in excess of the limits set by the Rome criteria ranges from 10 to 20 per cent. in males and 2 to 31 per cent. in females (Table V). The age trend by those cutting points are essentially compatible with the results shown by the mean serum uric acid levels.

Discussion

The antiquity of gout and the classical nature of its clinical appearance would suggest that knowledge of its frequency in the population must be a secure statistic. There are, however, remarkably few publications with credible data. Most of the reported investigations are hospital or clinic based and propose, for example, that the prevalence of gout is approximately 5 per cent. of all cases of arthritis (Hench, 1935)—without acknowledging the unresolved prob-

lem in determining the prevalence of other specific arthritides (Cathcart and O'Sullivan, 1970) and the even greater one of identifying *all* cases of arthritis. The study reported here, on the other hand, is based on a total pre-enumerated community, 77 per cent. of whom responded, and included attempts to assess the incidence of gout among the non-respondents. The findings support the rarity of classical gout, giving a prevalence rate of three to four cases per thousand. These findings are compatible with the low frequency documented in samples of the populations of Wensleydale and Leigh (Popert and Hewitt, 1962) and are not at variance with a study performed in conjunction with the Framingham Heart Study that showed thirteen patients with gout initially—a rate of two cases per 1,000 of the population (Hall, Barry, Dawber, and McNamara, 1967). Although showing a low prevalence rate, the Sudbury results were not considered overstated on the basis of secondary gout, particularly in view of the absence of evidence of myeloproliferative diseases as judged by blood smears obtained from the hyperuricaemic participants. Similarly, pseudogout was discounted, since nineteen of the 22 accepted cases of gout gave a history of podagra and fifteen responded to colchicine, both events being unlikely in chondrocalcinosis. A remarkable finding is that in approximately two-thirds of the patients who stated that a doctor told them they had gout, the diagnosis could not be substantiated by history, data, or verification of records by hospital or personal physician. It appears likely that a casual reference to the condition during preliminary differential diagnosis provided an easy explanation for the patient with an otherwise non-specific arthralgia or arthritis.

The prevalence of gout increases with age. The absence of cases among both the young and the old simply reflects the comparatively lower prevalence of the condition of these age groups. Otherwise, the age-dependence observed is in marked contrast to the absence of any clear age-trend in male uric acid levels between 25 and 74 years—the lower levels outside these age groups being consistent with the findings in other studies (Dodge and Mikkelsen,

Table V *Mean uric acid levels and hyperuricemia in Sudbury*, by age and sex*

Age group (yrs)	Male			Female		
	No.	Mean (mg./100 ml.)	≥ 7 mg/100 ml. (Per cent.)	No.	Mean (mg./100 ml.)	≥ 6 mg./100 ml. (Per cent.)
15-19	371	5.7	10.0	390	4.1	1.8
25-34	530	6.0	17.9	707	4.1	2.1
35-44	739	5.9	15.8	700	4.2	4.3
45-54	318	6.0	18.2	301	4.6	7.3
55-64	132	6.1	20.5	170	4.8	19.4
65-74	76	5.9	19.7	89	5.3	28.1
≥75	19	5.7	0	51	5.5	31.4

* Excluding 22 persons with verified gout.

1970). Although the genetic background of hyperuricaemia and gout is as yet unresolved, the contrasting prevalences of uric acid levels and gout with age show no indication of an increasing population susceptibility to gout. This conclusion assumes that an upward shift in uric acid levels is predictive of gout. In these circumstances, any sizable increase in preclinical gout in the population might be expected to cause an increase in serum uric acid levels with age. This was not found, and mean and median uric acid levels showed no evidence of increasing skewness with age.

The reported prevalence rate for gout in Sudbury is a maximal figure. The lower figures that would have been obtained had this report been based on either the Rome or the New York criteria rather than on both combined can be calculated from Table III. The study does serve to emphasize many of the reasons why the criteria are still inadequate, at least for epidemiological use. Patients experiencing classical episodic attacks in the big toe can be excluded by the Rome criteria if the intermittent gout is not accompanied by hyperuricaemia, or if the initial uric acid level can not be located for documentation. Furthermore, the use of uricosuric agents after the initial attack may hinder the documentation of hyperuricaemia, as was seen in two of the cases reported here who met the New York but not the Rome criteria. The advantage of the New York criteria in this regard, on the other hand, is offset by the lack of uniformity with which a diagnostic colchicine test is performed. The high prevalence of hyperuricaemia, as defined at the Rome symposium, clearly demon-

strates the possibilities of misclassification in persons with forms of arthritis other than gout. Therefore, until these practical diagnostic problems are resolved, it appears likely that our ability to define the full spectrum of the clinical variants of gout with any degree of certainty will be a continuing problem.

Summary

- (1) The prevalence of gout in the town of Sudbury was found to be 3.7 cases per thousand with a 7:1 male to female ratio. Additional patients, exceeding slightly the number with verified gout reported a history of gout but failed to meet the criteria, and evidence for an alternative diagnosis was found in most of them.
- (2) The role of two recommended criteria for gout determining these results is assessed and their respective deficiencies identified.
- (3) In men, the increase in prevalence rates for gout by age, excluding the extreme age groups, was not matched by a corresponding rise in mean serum uric acid levels. This finding is taken to imply that no increasing susceptibility to gout exists in the population.

This study would not have been possible without the cooperation of the residents of Sudbury and their steering committee (Chairman, Mr. Ronald Adolph). I am indebted to Miss Clare M. Mahan for assistance in data retrieval, to other members of the examining team, and to the physicians from Sudbury and the surrounding communities.

References

- CATHCART, E. S., AND O'SULLIVAN, J. B. (1970) *New Engl. J. Med.*, **282**, 421 (Rheumatoid arthritis in a New England town)
- C.I.O.M.S. Criteria, Rome (1963) In 'The Epidemiology of Chronic Rheumatism', ed. J. H. Kellgren, M. R. Jeffrey, and J. Ball, p. 327. Blackwell, Oxford
- C.I.O.M.S. Criteria, New York (1968) In 'Population Studies of the Rheumatic Diseases', Proc III int. Symp., 1966, ed. P. H. Bennett and P. H. N. Wood, p. 457 (Int Congr. Ser. No.148) Excerpta Medica Foundation, Amsterdam
- DODGE, H. J., AND MIKKELSEN, W. M. (1970) *J. chron. Dis.*, **23**, 161 (Observations on the distribution of serum uric acid levels in Tecumseh, Michigan)
- HALL, A. P., BARRY, P. E., DAWBER, T. R., AND MCNAMARA, P. M. (1967) *Amer. J. Med.*, **42**, 27 (Epidemiology of gout and hyperuricaemia)
- HENCH, P. S. (1935) *Med. Clin. N. Amer.*, **19**, 551 (A clinic on some diseases of the joints)
- O'SULLIVAN, J. B. (1968) In 'Population Studies of the Rheumatic Diseases', Proc. III Int. Symp., 1966, ed. P. H. Bennett and P. H. N. Wood, p. 371 (Int. Congr. Ser. No. 148). Excerpta Medica Foundation, Amsterdam
- , FRANCIS, J. O'S., AND KANTOR, N. (1965) *Clin. Chem.*, **11**, 427 (Comparison of a colorimetric (automated) with an enzymatic (manual) uric acid procedure)
- POPERT, A. J., AND HEWITT, J. V. (1962) *Ann. rheum. Dis.*, **21**, 154 (Gout and hyperuricaemia in rural and urban populations)