

Uric acid, joint morbidity, and streptococcal antibodies in Maori and European teenagers

Rotorua Lakes study 3

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Stanhope, J. M., and Prior, I. A. M. (1975). *Annals of the Rheumatic Diseases*, **34**, 359–363. **Uric acid, joint morbidity, and streptococcal antibodies in Maori and European teenagers. Rotorua Lakes study 3.** Two hundred and ninety-four New Zealand secondary school students were examined by questionnaire, and physical and biochemical methods. The sample contained almost equal numbers of Maoris and Europeans. The findings related to joint conditions are presented. Past injury and rheumatic disease accounted for some of the reported morbidity, but no important sex or race differences in these factors emerged. There were, however, significant differences in serum uric acid levels with the Maori having higher levels than the Europeans. A significant correlation with body mass was present in both race and sex groups but a correlation with haemoglobin was present only in the European females. While hyperuricaemia was not associated with morbidity in this young sample, ethnic differences anticipated the higher prevalence of gout already observed in Maori men.

Studies among New Zealand Maori and European adults have shown significantly higher serum uric acid levels and rates of clinical gout in the Maori (Rose and Isdale, 1963; Rose and Prior, 1963; Prior and Rose, 1966; Evans, Prior, and Morrison, 1969). This predisposition to hyperuricaemia and gout is associated with high rates of obesity, hyperglycaemia, and hypertriglyceridaemia, and represents a complex metabolic problem which contributes to morbidity and mortality in Maori adults (Prior, Rose, Harvey, and Davidson, 1966).

The present study was undertaken in a New Zealand secondary school, which contained almost equal numbers of Maori and Europeans aged 13 to 16 years, to find out if ethnic differences similar to those seen in adults could be shown in serum uric acid concentration, joint symptoms, smoking habits, respiratory health, and coronary risk factors including lipid levels. Serum uric acid levels are reported.

In addition we present data relating to joint conditions in the sample, examining the quantity and distribution of joint symptoms and signs, with a view to estimating the contribution of rheumatic, hyper-

uricaemic, and traumatic components to joint morbidity.

Rheumatic fever and rheumatic heart disease have a notably higher morbidity and mortality rate in Maori than in Europeans (Stanhope, 1975) and are presumably related to a higher rate of streptococcal infection or to the presence of some other conditioning factors. The antistreptolysin O and anti-hyaluronidase titres were estimated to detect race differences.

In a previous paper we described smoking habits, respiratory health, and related variables (Stanhope and Prior, 1975a), and the differences in the pattern of coronary risk factors will also be reported (Stanhope and Prior, 1975b).

Methods

Each subject was studied by means of questionnaires, examinations, and laboratory determinations in November 1972. The school enrolment was 298, and the response rate was over 98%. The samples reported comprise 83 Maori males and 74 European males, 53 Maori females and 61 European females. Owing to small numbers, the ethnic categories 'part-Maori' (less than half) and 'other' (neither European nor Maori) have been excluded.

A joint symptom score was established as a measure of past joint morbidity. Joints were considered in seven groups: shoulders, elbows, hands, hips, knees, feet, and back. Each joint group was scored 1 for stiffness or swelling only at any time in the past; 2 for any two of stiffness, swelling, and pain; and 3 for all three symptoms. Pain not associated with any other symptom was scored 0, because it was felt that it could be arising from nonjoint structures, or was too subjective a complaint. Current joint morbidity was assessed by the presence of signs and symptoms on clinical examination.

A rheumatic score was established as a measure of the likely contribution of rheumatic disease to joint morbidity. Questions asked of the subject with parental help were, 'Have you ever been admitted to hospital? If so, why?' (Yielding relevant positive responses up to a second admission); 'Has a doctor ever told you you had heart disease? joint trouble? rheumatic fever?'; 'Are you taking any medicines regularly? Penicillin?'. A hospital admission for rheumatic fever was given a weight of 3 and a report of rheumatic fever or of regular penicillin therapy was given a weight of 2, relative to the other items. Questions asked of the subject only were, 'Have you ever had stiff, swollen, or painful joints during an illness?' and 'Did the doctor give you medicine for it?', each positive answer receiving a weight of 1. Among findings on examination, mitral stenosis was scored 3, mitral or aortic incompetence 2, and aortic stenosis 1, excluding cases in which a nonrheumatic valvular abnormality was considered probable.*

An injury score was established as a measure of the likely contribution of injury to joint morbidity. Questions were equally weighted, and were (with relevant positive replies), 'Have you ever had any serious injuries? Cause?' (falls, sports, road accidents); 'Did they leave any permanent damage?' (recurrent backache, loss of power, loss of limb); 'Have you ever been admitted to hospital? If so, why?' (any condition classifiable as injury, yielding positive responses up to a fifth admission); 'Have you ever had stiff, swollen, or painful joints after playing sport or games?'

* The weighting of these items was decided in consultation with Dr. B. L. J. Treadwell, Rheumatology Unit, Wellington Hospital.

Antistreptolysin O (ASO) and antihyaluronidase titres (AHT) were determined by the micromethod of the Centre for Diseases Control, Atlanta, Georgia, U.S.A.

Serum uric acid (SUA) levels were determined by a phosphotungstic carbonate method using an autoanalyser (after Crowley and Alton, 1968). Quality control methods included use of commercial standards. Comparison in our laboratory between the autoanalyser and uricase method using the Beckman Glucose Analyser Uric Acid Accessory Kit on 63 fresh unfrozen samples showed that the autoanalyser method gave values, on average, 0.39 mg higher than the uricase method, comparable with the 0.4 mg/100 ml difference reported by Crowley and Alton.

Statistical methods included Student's 't' test for comparing relatively unskewed distributions, Mann Whitney U test for comparing skewed distributions, and Kruskal-Wallis one-way analysis of variance for detecting heterogeneity among more than two groups. Pearson's correlation was used for comparisons between two relatively unskewed variables, otherwise Spearman's rank correlation was used.

None of the joint-related variables were correlated significantly with age in any of the four major sex/race groups, or in the whole sample, so that age divisions were not required in the analysis.

Results

SUA AND BODY BULK

The mean levels of SUA by age and for the combined ages are given in Table I. Both sex and race differences are shown. Among boys, Maoris had higher levels than Europeans by approximately 0.0595 mmol/l (1 mg/100 ml) ($P < 0.0001$); whereas among girls the difference was approximately half as much ($P = 0.0015$). Boys had higher levels than girls among both Maori ($P = 0.0003$) and Europeans ($P < 0.0001$). SUA was not significantly correlated to joint symptom score ($P = 0.79$).

Our group previously reported a positive relationship between SUA and body bulk in two groups of

Table I Serum uric acid levels by sex, race, and age

Age (year)	Male		Female	
	Maori	European	Maori	European
13	*6.27 ± 0.24(10) (0.373 ± 0.014)	5.37 ± 0.53(9) (0.32 ± 0.032)	5.90 ± 0.40(2) (0.351 ± 0.024)	4.83 ± 0.30(11) (0.287 ± 0.018)
14	6.49 ± 0.17(37) (0.386 ± 0.010)	5.17 ± 0.15(39) (0.308 ± 0.009)	5.19 ± 0.15(36) (0.309 ± 0.009)	4.71 ± 0.14(25) (0.280 ± 0.008)
15	6.37 ± 0.21(32) (0.379 ± 0.012)	5.76 ± 0.27(23) (0.343 ± 0.016)	5.49 ± 0.29(15) (0.327 ± 0.017)	4.81 ± 0.15(25) (0.286 ± 0.009)
16	6.02 ± 0.44(4) (0.358 ± 0.026)	5.23 ± 0.13(3) (0.311 ± 0.008)	— (0)	— (0)
Total	6.39 ± 0.11(83) (0.380 ± 0.007)	5.38 ± 0.13(74) (0.320 ± 0.008)	5.30 ± 0.13(53) (0.315 ± 0.008)	4.77 ± 0.10(61) (0.284 ± 0.006)
Skewness (g)	+0.35	+0.61	+0.14	+0.34
Correlation with body bulk (r)	+0.368	+0.285	+0.412	+0.315
Correlation with haemoglobin (r)	+0.046	+0.202	+0.002	+0.289

* Mean ± standard error in mg/100 ml (no. of subjects in subgroup in parentheses), and in mmol/l in parentheses underneath.

Table II Sex and race differences in various factors

	Male		Female		Summary comment
	Maori	European	Maori	European	
Sample size	83	74	53	61	
Joint symptom score (mean)	0.47	0.18	0.36	0.54	European males low
Injury score (mean)	0.79	0.45	0.49	0.39	—
Rheumatic score (mean)	0.34	0.04	0.60	0.13	Maori higher than Europeans
ASO titre (geometric mean)	192	181	194	184	
AHT (geometric mean)	561	319	395	239	Maori higher than Europeans, boys higher than girls

Polynesian adults, and reviewed literature which described similar findings in European and other populations (Evans, Prior, and Harvey, 1968). The present study confirmed this relationship in Maori and European adolescents. Measurements of body bulk were chosen so as to be uncorrelated with height; in boys this was I_3 (weight/height³); in girls it was I_2 (Quetelet's index, weight/height²); as described elsewhere (Stanhope and Prior, 1975b). The correlation of SUA level with body bulk is significant in all four subgroups and was higher in the Maoris than Europeans (Table I). SUA level was significantly correlated with haemoglobin level only in European girls (Table I).

JOINT SYMPTOM SCORE, INJURY SCORE, AND RHEUMATIC SCORE

The observed range of the joint symptom score was 0–6 out of a possible 21 (Table II), 82% of subjects remembering no symptoms; this was significantly related neither to race ($P = 0.21$) nor to sex ($P = 0.23$) alone. In analysis of heterogeneity, European males were low scorers ($P = 0.0237$).

The observed injury score range was 0–6 out of a possible 9. 64% of subjects recalled no relevant injuries. Again, neither race ($P = 0.053$) nor sex ($P = 0.18$) was significantly related to the injury score, although it was correlated with the joint symptom score ($P < 0.0001$).

The observed rheumatic score range was 0–10 out of a possible 17. 89% of subjects had 0 scores. Rheumatic score was unrelated to sex ($P = 0.34$), but was significantly higher in Maoris than in Europeans ($P = 0.0426$), and was correlated with the joint symptom score ($P = 0.0027$).

CURRENT JOINT ABNORMALITY

Abnormal joint signs and symptoms were present in eleven subjects, three Maori boys, two European

boys, one Maori girl, and five European girls. They included 1 case of hallux valgus, 2 mild scoliosis, 3 late effects of injury, and 5 nonspecific complaints. There were no significant sex and race differences.

Current joint abnormality was not significantly correlated with injury score ($P = 0.077$), rheumatic score ($P = 0.053$), or SUA ($P = 0.63$).

ASO TITRE

The distribution of ASO titre was of log-normal type, without significant skewness when transformed into logarithms. There were no significant sex or race differences. The mean \log_{10} ASO titre was 2.2748, standard deviation 0.2438. Thus, the geometric mean titre was 188 Todd units. ASO titre was not correlated significantly with rheumatic score ($P = 0.29$) or joint symptom score ($P = 0.22$).

AHT

AHT also had a log-normal distribution, without significant skewness when transformed into logarithms. Analysis of variance showed that there were both sex and race effects, but no sex-race interaction. The titres of Maori subjects were on average 1.72 times those of Europeans, and boys' titres were on average 1.38 times those of girls. The overall mean \log_{10} AHT was 2.5723, standard deviation 0.4773, corresponding to a geometric mean titre of 374 units. AHT was correlated with ASO titre ($P = 0.0031$), but not with rheumatic score ($P = 0.29$) or joint symptom score ($P = 0.95$).

Discussion

Defining higher levels of SUA in both male and female Maori teenagers than in Europeans has confirmed findings already reported in adults aged 20 years and over. Showing high uric acid levels and hyperuricaemia in other Polynesian groups, including

Cook Island Maori (Prior and Rose, 1966) and Tokelau Islanders (Prior, Stanhope, Evans, and Salmond, 1974) in the Pacific, suggests an important genetic contribution to this disorder.

Previous reports have shown that SUA is a continuous variable, and this is again confirmed with no evidence of bimodality in the four sex/race groups of the present study and so suggests a polygenic basis for the disorder.

In adult studies previously reported, a relationship between SUA level, body weight, body mass, and adiposity has been shown (Evans and others, 1968) and this is an obvious factor in the present study in male and female Maori and European teenagers. Greater muscle mass and trunk fat mass have been found in the Maori adolescents than in the Europeans in this study (Stanhope and Prior, 1975b). Weight loss in obese subjects can lead to lower uric acid levels (Nicholls and Scott 1972) and to a decrease in total uric acid pool (Emmerson, 1973). This important finding clearly has major public health implications if it is accepted that long-term hyperuricaemia is potentially harmful.

The adult studies in New Zealand have shown a widening separation of Maori and European weights, and body mass and fat measures with increasing age (Prior, 1974). Further information on the dynamic relationships between increasing body bulk, uric acid levels, clinical gout, diabetes, renal function, and blood pressure levels is being sought in prospective adult Maori samples studied over a period of 10 years.

Rheumatic fever shows striking geographic and ethnic heterogeneity in its incidence in New Zealand (Frankish, 1974; Kirschner and Gallagher, 1950) and is a cause of prolonged ill health and disruption to

schooling in youth, as well as being a precursor of valvular heart disease in adulthood. In our study a score based on symptoms and signs suggestive of past rheumatic fever distinguished between the two ethnic groups. ASO titre did not confirm this difference, correlating neither with rheumatic score nor with joint symptom in general, and agrees with published findings that the ASO titre falls 8–10 weeks after recovery from uncomplicated streptococcal infection, or 6 months after a rheumatic fever episode. The 95% confidence limits (63–566) of our mean level 188 Todd units are compatible with Bennett's statement that the highest titres are seen in schoolchildren where 80% may exhibit titres of from 184 to 333 Todd units (Bennett, 1968).

AHT, while not correlating with rheumatic score either, did show an ethnic difference consistent with greater experience of or reaction to invasive streptococcal infection in the Maori child.

Morbidity and mortality differences attributed to rheumatic fever are being studied through a case register in the high-risk Wairoa area of the east coast of the north island of New Zealand. This, coupled with a proposed survey of a large teenage sample, will permit more active prevention.

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References

- BENNETT, C. W. (1968) In 'Clinical Serology', revised 1st ed., p. 136. Thomas, Springfield
- CROWLEY, L. V., AND ALTON, F. I. (1968) *Amer. J. clin. Path.*, **49**, 285 (Automated analysis of uric acid)
- EMMERSON, B. T. (1973) *Aust. N.Z. J. Med.*, **3**, 410 (Alteration of urate metabolism by weight reduction)
- EVANS, J. G., PRIOR, I. A. M., AND HARVEY, H. P. B. (1968) *Ann. rheum. Dis.*, **27**, 319 (Relation of serum uric acid to body bulk, haemoglobin and alcohol intake in two south Pacific Polynesian populations)
- , PRIOR, I. A. M., AND MORRISON, R. B. I. (1969) *N.Z. med. J.*, **70**, 306 (The Carterton study: 5. Serum uric acid levels of a sample of New Zealand European adults)
- FRANKISH, D. J. (1974) *Ibid.*, **80**, 48 (Rheumatic fever on the east coast, north island)
- KIRSCHNER, L., AND GALLAGHER, D. J. A. (1950) *Ibid.*, **49**, 118 (Studies on the pathogenesis of rheumatic fever)
- NICHOLLS, A., AND SCOTT, J. T. (1972) *Lancet*, **2**, 1123 (Effect of weight-loss on plasma and urinary levels of uric acid)
- PRIOR, I. A. M. (1974) *N.Z. med. J.*, **80**, 245 (Cardiovascular epidemiology in New Zealand and the Pacific)
- , AND ROSE, B. S. (1966) *Ibid.*, **65**, 295 (Uric acid, gout and public health in the south Pacific)
- , ROSE, B. S., HARVEY, H. P. B., AND DAVIDSON, F. (1966) *Lancet*, **1**, 333 (Hyperuricaemia, gout and diabetic abnormality in Polynesian people)
- , STANHOPE, J. M., EVANS, J. G., AND SALMOND, C. E. (1974) *Int. J. Epidemiology*, **3**, 225 (The Tokelau Island migrant study)
- ROSE, B. S., AND ISDALE, I. C. (1963) In 'Epidemiology of Chronic Rheumatism' vol. 1, ed. J. H. Kellgren, M. R. Jeffrey, and J. Ball, p. 156. Blackwell Scientific Publications, Oxford
- , AND PRIOR, I. A. M. (1963) *Ann. rheum. Dis.*, **22**, 410 (A survey of rheumatism in a rural New Zealand Maori community)

- STANHOPE, J. M. (1975) *N.Z. med. J.*, in press (New Zealand trends in rheumatic fever 1885–1971)
- , AND PRIOR, I. A. M. (1975a) *N.Z. med. J.*, in press (Smoking behaviour and respiratory health in a teenage sample: the Rotorua Lakes study 1)
- , AND PRIOR, I. A. M. (1975b) Submitted for publication (Coronary risk factors in New Zealand adolescents: the Rotorua Lakes study 2)