Hyperuricemia in Filipinos: Interaction of Heredity and Environment

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IN PREVIOUS STUDIES from this department, hyperuricemia and an increased frequency of gout have been described in Filipinos living in the United States (Decker and Lane, 1959; Decker *et al.*, 1962). In the latter report, the mean serum uric acid level (SUA) of 113 adult Filipino males living in Seattle and working in the Alaska salmon canneries was 6.3 mg/100 ml. Sixty Filipino patients in the Hawaii State Psychiatric Hospital had a mean SUA of 6.1 mg/100 ml (Healey *et al.*, 1966). The mean SUA for Caucasians and other races in these two studies was 5.1 mg/100 ml.

In light of these findings, it seemed surprising that clinical gout was not noticed more often in the Philippine Islands, since the prevalence of gout parallels the presence of hyperuricemia. Manahan (1963) estimated the incidence of gout in admissions to the Philippine General Hospital, Manila, as 0.01%, compared to a race-specific incidence of 0.68% for Filipinos admitted to the Queen's Hospital, Honolulu (Rosenblatt *et al.*, 1966).

In this study, the SUA of adult male residents of the Philippine Islands was measured. The results show that the mean serum uric acid level of these Filipinos is not elevated.

MATERIAL AND METHODS

The study was limited to adult males to avoid known SUA variations with age and sex and to facilitate comparison with the previous studies in Seattle and Hawaii. For reasons which are discussed below, it was considered important to obtain samples from inhabitants of different geographic locations. The composition of the sample is shown in Table 1. It included students and employees of the University of The Philippines College of Medicine in Manila,

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TABLE 1. MEAN SERUM URIC ACID AND PLACE OF ORIGIN OF 483 NATIVE ADULT FILIPINO MALES

Number	Place	Language group	Serum uric acid (mg/100 ml) mean ± SD
140	Manila	Tagalog	5.3 ± 1.4
146	Cebu	Visayan	5.1 ± 1.2
115	Bacnotan, La Union	Ilocano	5.3 ± 1.3
82	Pugo, La Union	Ilocano	5.3 ± 1.3
483			5.2 ± 1.3

TABLE 2. MEAN SERUM URIC ACID OF U. S. CAUCASIANS, NATIVE FILIPINOS, AND U. S. FILIPINOS

Number	Race	Location	Serum uric acid (mg/100 ml) mean ± SD
88	Caucasian	Seattle	5.0 ± 1.1
43	Caucasian	Hawaii	5.2 ± 1.3
483	Filipino	Philippine Islands	5.2 ± 1.3
113	Filipino	Seattle	6.3 ± 1.4
60	Filipino	Hawaii	6.1 ± 1.3

outpatients attending a dermatology clinic in Cebu, and cement plant workers and farm laborers from two small towns in the province of La Union.

All the men were asked the date and place of their birth, and the majority were asked the birthplaces of their parents. Blood was obtained by venipuncture in the postabsorptive state. The serum was separated, frozen, and flown to Seattle, where the uric acid level was determined by the enzymatic spectrophotometric method (Liddle *et al.*, 1959). This same method was used in the previous studies. Repeated measurements have shown that frozen storage and several thawings do not significantly alter the uric acid value.

RESULTS

The men ranged in age from 21 to 87 years. The total number tested was 483. The number in each group and the mean SUA are shown in Table 1. The SUA ranged from 1.8 to 10 mg/100 ml with a mean of 5.2 mg/100 ml. The mean for each group did not differ significantly from the total mean.

DISCUSSION

These data indicate that hyperuricemia is not characteristic of Filipinos living in the Philippine Islands. The mean SUA of the men in this study is not different from that of the Caucasian groups in the previous studies in Seattle and Hawaii (Table 2). This value of 5.2 mg/100 ml is also the same as the mean SUA of adult Caucasian males in the Tecumseh, Michigan, survey (Mikkelsen *et al.*, 1965). By contrast, it is significantly lower than the values found in the Filipinos in Seattle and Hawaii in the previous studies cited (Table 2). The distribution curves of the SUA for the Filipinos in this study

and the Caucasians in the U. S. (Decker *et al.*, 1962) are not different when compared by the Kolmogorov-Smirnov two-sample test.

The Filipinos are believed to be Malayan in origin with later admixtures of Chinese and Spanish. Although no distinct anthropologic or genetic differences have been recognized, clear-cut distinctions are drawn between the inhabitants of various regions based on language differences. Lexicostatistical studies indicate that Iloko speakers, for example, have been separate from the Tagalog and the Visayan people for about 2,000 years (Dyen, 1965).

Because most of the Filipino immigrants to Hawaii and mainland United States came from the Ilocano area of Luzon, we thought that the hyperuricemia might be present only in the inhabitants of this area of the Philippine Islands. Steuermann (1963) had previously made a similar suggestion because he found hyperuricemia and gout in Filipino plantation workers in Hawaii and did not find it in a group of army inductees in Manila. However, the present study shows there is no difference between the mean SUA of the Ilocanos in La Union province and the other Filipinos studied. The men we tested in Manila were predominantly Tagalog and those from Cebu were Visayan (Fig. 1). These are the three largest language groups in the Philippines.

Thus it is clear that Filipinos who were born in the Philippine Islands and have immigrated to the United States show a high frequency of hyperuricemia and of gouty arthritis. In contrast, racially identical Filipinos who have not left the Philippine Islands are neither hyperuricemic nor gouty. The difference is not based upon artifact, such as drug ingestion or associated disease, nor is it due to differences in body size. The contrast must be due to some environmental cause.

One possibility is that the U. S. Filipinos are exposed to factors that raise the SUA that are not present in the environment of their counterparts in The Philippines. As a corollary, the factors which lead to hyperuricemia in the U. S. Filipinos do not similarly affect people of other races, specifically Caucasians.

One environmental difference between the hyperuricemic and normouricemic groups appears to be the diet. The Filipinos in the United States eat more meat than those in The Philippines, whose main staple is rice. While an increased intake of proteins and purines, the uric acid precursors, offers an explanation for the different SUA levels in Filipinos, it does not explain why the U. S. Filipinos have a higher SUA than Caucasians. The diet of the Filipinos in the United States does not include more meat or purine-rich foods than the usual Caucasian diet. This point was well demonstrated in the study in the Hawaii State Hospital, where all patients received the same diet but the Filipinos had a significantly higher mean SUA.

One hypothesis is that many Filipinos have, as a racially determined characteristic, an inability to handle the higher purine loads imposed by the diet taken in the United States. The trait would be expressed (as hyperuricemia) only upon challenge as, for example, erythrocyte glucose-6-phosphate dehydrogenase deficiency is expressed (as hemolytic anemia) only upon challenge. Neither the site nor the nature of this postulated defect in the purine economy of the Filipino is known. However, since uric acid is a metabolic

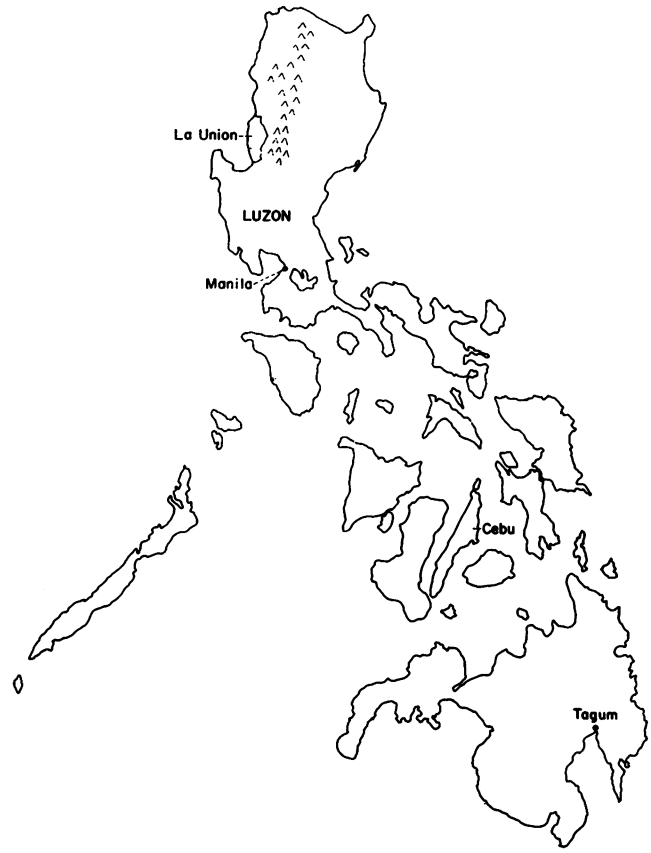

FIG. 1. Map of the Philippine Islands indicating the locations of the different groups where uric acid levels were studied.

end product, the defect may represent a renal tubular inability to increase uric acid excretion in response to the additional load. Such a defect has been postulated in some patients with primary hyperuricemia and gout (Nugent and Tyler, 1959; Seegmiller *et al.*, 1962).

The alternate possibility that environmental factors in the Philippine Islands either reduce uric acid production or facilitate its excretion seems remote, since the mean SUA of the Filipinos living there is the same as the mean for U. S. Caucasians, and this is considered to be the normal level.

SUMMARY

The mean serum uric acid of 483 Filipino men living in the Philippine Islands was 5.2 mg/100 ml. This value is the same as the mean for U. S. Caucasians and in sharp contrast with the mean for U. S. Filipinos of 6.1 mg/100 ml found previously.

We suggest that these findings may be due to a heritable renal tubular defect which is expressed as hyperuricemia when stressed by an increased dietary intake of uric acid precursors.

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REFERENCES

DECKER, J. L., AND LANE, J. J. 1959. Gouty arthritis in Filipinos. *New England J. Med.* 261: 805–806.

DECKER, J. L., LANE, J. J., AND REYNOLDS, W. E. 1962. Hyperuricemia in a male Filipino population. *Arthritis Rheum.* 5: 144–155.

DYEN, I. 1965. Lexicostatistical classification of the Austronesian languages. *Internat. J. Amer. Ling.* 31, No. 1 (Suppl.), p. 31.

HEALEY, L. A., CANER, J. E. Z., AND DECKER, J. L. 1966. Ethnic variations in serum uric acid. I. Filipino hyperuricemia in a controlled environment. *Arthritis Rheum.* 9: 288–294.

LIDDLE, L., SEEGMILLER, J. E., AND LASTER, L. 1959. The enzymatic spectrophotometric method for determination of uric acid. *J. Lab. Clin. Med.* 54: 903–913.

MANAHAN, L. A. 1963. Rheumatic diseases in the Philippines. *Proc. Austral. Rheum. Cong.*, pp. 20–22.

MIKKELSEN, W. M., DODGE, J. J., AND VALKENBURG, H. 1965. The distribution of serum uric acid values in a population unselected as to gout or hyperuricemia, Tecumseh, Michigan, 1959–1960. *Amer. J. Med.* 39: 242–251.

NUGENT, C. A., AND TYLER, F. H. 1959. The renal excretion of uric acid in patients with gout and in nongouty subjects. *J. Clin. Invest.* 38: 1890–1898.

ROSENBLATT, G., DECKER, J. L., AND HEALEY, L. A. 1966. Gout in hospitalized Filipinos in Hawaii. *Pacific J. Med. Surg.* 74: 312.

SEEGMILLER, J. E., GRAYZEL, A. I., HOWELL, R. R., AND PLATO, C. 1962. The renal excretion of uric acid in gout. *J. Clin. Invest.* 41: 1094–1098.

STEUERMANN, N. 1963. In *Epidemiology of Chronic Rheumatism,* Kellgren, J. H., Jeffrey, M. R., and Ball, J. (eds.), Vol. 1. Oxford: Blackwell Scientific Publications, pp. 170–175.