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# HIGH PREVALENCE OF HIGH-LEVEL $\beta$ -AMINO-ISOBUTYRIC ACID EXCRETORS IN MICRONESIANS

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**D**IFFERENTIAL excretion of  $\beta$ -amino-isobutyric acid is under genetic control, and family data indicate that a single major gene pair is responsible for most of the variation<sup>1,2</sup>. High excretors are homozygous for a single recessive gene and low excretors either heterozygous or homozygous for the dominant allele. Striking differences in the prevalence of high excretors in various populations have been demonstrated and it appears that this genetic polymorphism may be of considerable value in anthropogenetic investigations<sup>3,4</sup>.

We are particularly interested in utilizing this trait to explore the genetic relationships and origins of various Pacific peoples and this report extends our observations on excretion of  $\beta$ -amino-isobutyric acid to the Micronesians inhabiting the Marshall Islands. The fact that some of the Micronesians were exposed to considerable radiation in 1954 is of special interest here. It is known that radiation exposure can temporarily at least increase  $\beta$ -amino-isobutyric acid excretion<sup>5</sup>, and the Marshallese population permits an examination of possible long-term effects of such exposure on  $\beta$ -amino-isobutyric acid excretion.

The following information on the radiation exposure and present status of the inhabitants of Rongelap and Utrik was obtained from the reports of the Brookhaven National Laboratory<sup>6</sup>, and from Dr. R. A. Conard of Brookhaven National Laboratory.

Micronesian inhabitants of Rongelap and Utrik atolls, Marshall Islands, were accidentally exposed to fallout in March 1954, following the detonation of a high-yield thermonuclear device during experiments at Bikini Atoll in the Pacific Proving Grounds.

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Sixty-four inhabitants of Rongelap received an estimated dose of 175 r. whole-body  $\gamma$ -radiation. 18 Rongelap people on Ailingnae received about half this dosage, and 157 of the people on Utrik received about 14 r. whole-body radiation. The exposed people were evacuated to radiation-free islands in the Marshalls. The Utrik inhabitants were repatriated soon after their evacuation when it was determined that the island was safe for habitation. The exposed Rongelapese, as well as some 150 unexposed relatives, were returned to Rongelap in July 1957 when the radiological hazard was judged to have been terminated. There was, however, slight residual radioactivity remaining on the island, and the body burdens of radioactive substances, particularly of caesium-137 and zinc-65, and urinary excretion of nucleotides has risen in the Rongelapese since their return. Both the originally exposed and the unexposed people now have increased body burden, with no significant differences between the two groups. The body burden of these radionuclides is below the maximum permissible levels.

Rongelap is in the western (Ralik) chain and Utrik in the eastern (Radak) chain of the Marshall Islands. Some differences in language and customs prevail between these two groups, but for most purposes the people of Rongelap and Utrik may be considered to be closely related racially.

Rongelap urines from 65 exposed (including 12 urines from individuals exposed on Ailingnae), 119 unexposed and 4 unidentified people were collected in plastic bottles containing thymol preservative. The sample represents 75.7 per cent of the population of the village at the time of the visit. The sexes were equally represented, and the ages of the subjects varied from 3 years to more than 70 years. In some cases, several members of the same family were included, and some kinships suitable for genetic analysis were available. Eighteen samples randomly selected on Utrik were also studied. The urines were kept at 4° C. and shipped in refrigerated containers to Seattle for analysis. Studies were completed 2-3 weeks after collection of specimens. Determinations of  $\beta$ -amino-isobutyric acid were carried out by high-voltage electrophoresis on paper<sup>7</sup> and creatinine was determined by the alkaline-picrate method.

During the course of the medical evaluation of the Rongelapese by Conard and his associates, the body burdens of nucleotides were determined<sup>8</sup>. Through the courtesy of Dr. S. Cohn of the Brookhaven National Laboratory, who performed these measurements, the body burdens of caesium-137 and zinc-65

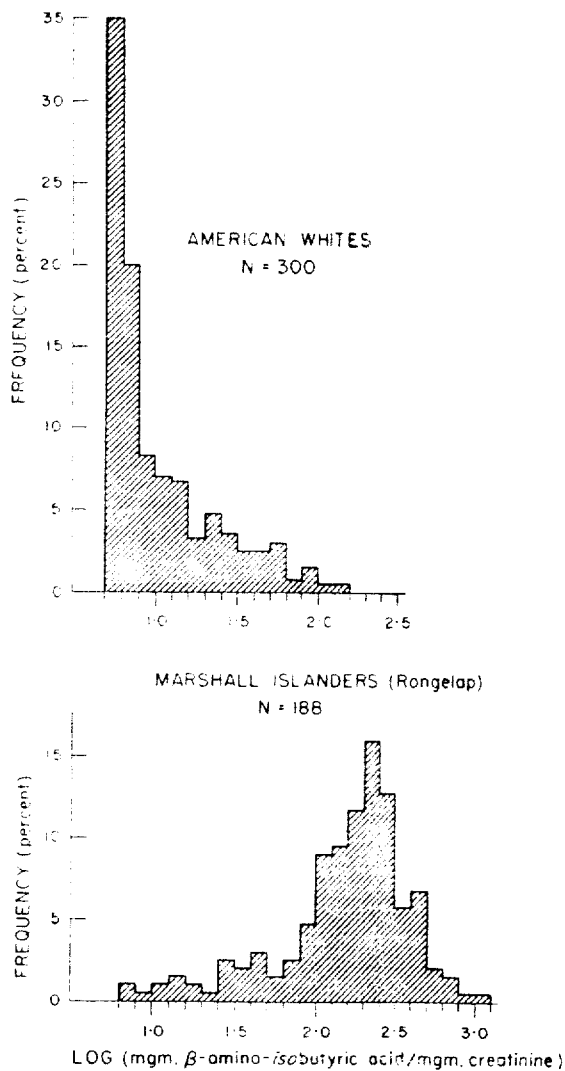


Fig. 1. Frequency distributions of urinary excretion-rates of  $\beta$ -amino-isobutyric acid of Marshall Islanders (Rongelap) and U.S.A. Whites

of the individuals on whom determination of  $\beta$ -amino-isobutyric acid had been made were supplied to us. The availability of these data gave us an opportunity to determine if these low levels of radioactivity had any effect on the excretion of  $\beta$ -amino-isobutyric acid.

In Fig. 1 the frequency distribution of  $\beta$ -amino-isobutyric acid excretion for the Rongelapese is presented. A similar histogram for a New York City white population is included for comparative purposes. The two distributions are essentially complementary to one another, and if superimposed exhibit bimodality with the mode in the neighbourhood of 1.75. Taking this point as the division between high and low excretors, it is estimated that nearly 96 per cent of the Rongelapese are high excretors. A breakdown of this population into exposed and unexposed groups shows almost identical mean  $\beta$ -amino-isobutyric acid excretion values for the two categories (exposed  $2.07 \pm 0.06$  and unexposed  $2.10 \pm 0.04$ ). A scatter plot between calcium-137 levels and  $\beta$ -amino-isobutyric acid-level shows no correlation (Fig. 2), and a similar plot between zinc-65 levels and  $\beta$ -amino-isobutyric acid shows no correlation either. The mean  $\beta$ -amino-isobutyric acid excretion level for 18 Micronesians, who were on Utrik at the time of the atomic explosion and therefore not exposed to significant radiation, was  $2.21 \pm 0.13$ , which is extremely close to the mean value reported for the Rongelapese (i.e. 83 per cent of the Utrik people were high excretors, and this is not significantly different from the prevalence in the Rongelap group. A number of families are included in the Rongelap data (that is, father, mother and at least one child), and of these, the high excretor by high excretor matings are the only ones with significant genetic information. There were 11 such matings with a total of 31 offspring (29 high excretors and 2 low excretors). One of the low excretor offspring was illegitimate, as determined by blood group data, leaving one unexplainable exception to genetic hypothesis.

Rubini *et al.*<sup>5</sup> have recently demonstrated that  $\beta$ -amino-isobutyric acid excretion can be a sensitive indicator of radiation exposure. The mechanism involved is probably the same as that underlying the effect of nitrogen mustard on  $\beta$ -amino-isobutyric acid excretion<sup>6</sup>. Such agents markedly increase breakdown of deoxyribonucleic acid: the thymine thus released is effectively converted to  $\beta$ -amino-isobutyric acid in man<sup>7,8</sup> and excreted into the urine since no appreciable tubular re-absorption of  $\beta$ -amino-isobutyric acid occurs<sup>9</sup>. It is unlikely that the high prevalence of high-level  $\beta$ -amino-isobutyric acid excretors found in Rongelap is due to radiation. The identical average  $\beta$ -amino-isobutyric acid values in the exposed and unexposed group precludes the possibility that the elevation is due to the fallout exposure in