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PHYSIOLOGY

Inactivation of Isoniazid in Burmese Subjects

INACTIVATION by acetylation of the anti-tuberculosis drug isoniazid *in vivo* is subject to genetic polymorphism[1–3]. Studies of the gene frequency for rapid inactivation in different regions have revealed considerable racial variations[4–7]. Because of the association of isoniazid neuropathy with slow inactivation of the drug in therapeutic practice[8,9], the recording of gene frequencies among different races and in different countries is of practical importance. It is also of ethnological value in studies of population migrations. This communication reports such an investigation among Burmese subjects.

Isoniazid (10 mg/kg orally) was administered to 121 Burmese subjects, seventy-nine males and forty-two females, aged between 18 and 38. Venous blood samples were taken 6 h later, the serum was separated and extracted and the concentration of isoniazid was estimated by a vanillin condensation method[10]. Internal standards were added to serum taken from untreated subjects. The distribution of concentrations found (Fig. 1) was bimodal with an antimode at 3 μg/ml. Calculation on the basis of the seventy-six rapid and forty-five slow inactivators thus separated yields a gene frequency of 0·390 for rapid inactivation. A scatter diagram on a logarithmic scale (Fig. 2) suggested that eighteen of the rapid inactivators were homozygotes and the remaining fifty-eight heterozygotes. This distribution yields a gene frequency for rapid inactivation of 0·388 (Chi squared = 0·0094, $P > 0.99$).

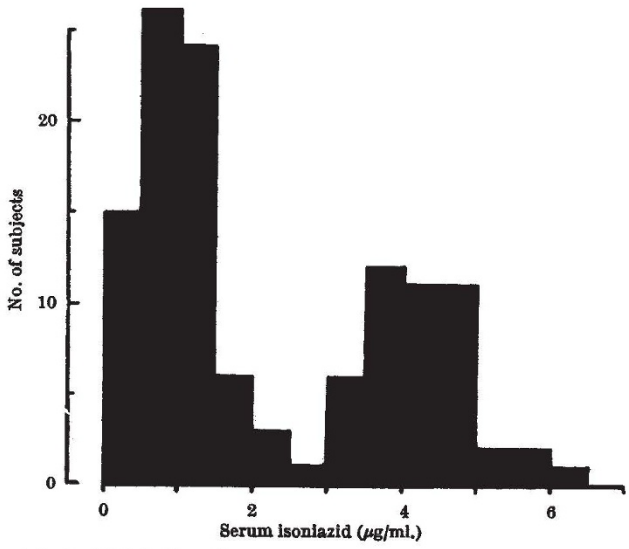

Fig. 1. Distribution of serum isoniazid concentrations in 121 Burmese subjects, 6 h after oral dose of 10 mg/kg.

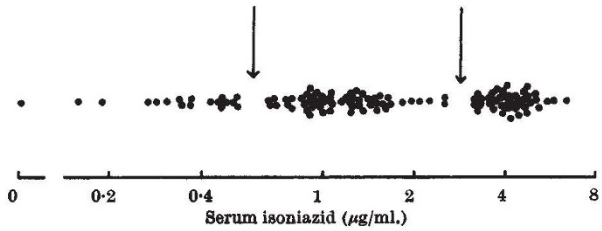

Fig. 2. Scatter diagram of serum isoniazid concentrations in 121 Burmese subjects, 6 h after oral dose of 10 mg/kg.

The gene frequency found indicates that approximately 37 per cent of Burmese subjects would carry the risk of neuropathy if clinically treated with isoniazid. This frequency is intermediate between those found among Thai[5] and South Indian[6] subjects, as might be expected both geographically and ethnologically (Table 1). The results of the present investigation are therefore consistent with current opinion of the Mongoloid origin of the gene responsible for the hepatic acetyltransferase involved.

Table 1. GENE FREQUENCIES FOR ISONIAZID INACTIVATION IN DIFFERENT POPULATIONS

Race	No. studied	Gene frequency Rapid	Slow	Reference
Caucasian and Negro	485	0·28	0·72	2
Caucasian	105	0·24	0·76	7
Negro	116	0·27	0·73	
Japanese	209	0·71	0·29	
Japanese	1,808	0·66	0·34	5
Ainu	86	0·69	0·31	
Korean	65	0·67	0·33	
Ryukyan	124	0·60	0·40	
Thai	108	0·46	0·54	
Burmese	121	0·39	0·61	This work
S. Indian	321	0·22	0·78	6

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