ABSENCE OF ABNORMAL VARIANTS OF CHOLINESTERASE (E.C.3.1.1.1.8) IN A MALAYSIAN POPULATION WITH THREE MAJOR RACIAL GROUPS

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SYNOPSIS

Surveys in a number of European and American populations have found the frequency of occurrence of the heterozygotes for the gene for the dibucaine-resistent variant of Cholinesterase (E.C.3.1.1.8) to be relatively constant. Similar surveys in Oriental population have shown low incidences of the same gene. This study done on a multi-racial population consisting of 3 major groups shows an absence of the gene for the dibucaine resistent variant of cholinesterase. This is supported by the clinical experience in the use of Suxamethonium as a single dose in more than 25,000 individuals.

INTRODUCTION

The presence of the genetically determined a typical cholinesterase (E.C.3.1.1.8. Acylcholine Acylhydrolase) in human plasma has long been recognised as one of the causes of delayed recovery from Suxamethonium induced neuromuscular paralysis (Kalow and Staron 1957). Other causes of delayed recovery have been attributed to low cholinesterase levels as in liver disease, in patients with cancer receiving cytotoxic drugs such as AB-132, severe malnutrition and in patients with glaucoma receiving Ecothiopate iodide and during late pregnancy (Foldes *et al*, 1956 Wong and Ross 1963, Waterlow 1950, Gesztes 1966 and Robertson 1966).

Using dibucaine and sodium fluoride as inhibitors, it is possible to detect at least 4 genes, controlling the formation of the different enzyme types, the usual (E_1^u); the dibucaine resistant (E_1^a); the fluoride resistant (E_1^f) and the silent (E_1^s). They combine to form 10 genotypes of which 6 are associated with increased sensitivity to succinylcholine as shown as prolonged apnoea after its administration.

The population distribution of the common atypical allele E_1^a has been studied in various parts of the world. The frequency of E_1^a heterozygotes in populations of European origin varies from 2·5% to 3·8% (Kalow 1964, Goedde and Altland 1963 and Szeinberg *et al*, 1963). The oriental Jewish population has the highest incidence so far reported of E_1^a (9% Iraqi Jews, 11% Iranian Jews), (Szeinberg *et al*, 1966). The frequency of the clinically significant homozygote which corresponds to heterozygote frequencies of 3% and 10% are 1/2500 and 1/400 respectively. However the rarity of the abnormal gene in population of African origin, with a somewhat higher frequency in American negroes which could be accounted for by admixture with Caucasians has been reported (Motulsky and Morrow 1968). The gene is extremely rare in populations of Oriental origin such as Japanese (Omato and Goedde, 1965). A high frequency of the silent gene with 1·5% of the population being homozygotes (suggesting a heterozygote frequency of 20%) has also been reported among the Alaskan Eskimos (Gutsche *et al*, 1967).

In Malaysia a single dose of Suxamethonium during anaesthesia in about 25,000 patients in a population with 3 major racial groups (the urban distribution of which is Chinese 49·4%; Indians 29·3%; Malays 18·6% and Eurasians, Europeans, Japanese and Koreans forming the remainder 2·7%), no Suxamethonium sensitive individuals showing as prolonged apnoea, have been observed or reported, indicating a possible absence of any of the 6 genotypes. As the heterozygote enzyme ($E_1^uE_1^a$) could produce clinically unrecognisable apnoea (up to 7 minutes), population screening was done to

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study the existence of any abnormal variants of cholinesterase E.C.3.1.1.8.

MATERIAL

A total of 947 volunteers, comprising the 3 major racial groups from Singapore and Malaysia were screened (472 Chinese; 205 Indians and 270 Malays).

METHODS

The rapid screening Agar-diffusion test (Harris, Robson 1963) was done in duplicate on the 368 volunteers (147 Chinese, 30 Indians and 191 Malays). The dibucaine numbers were determined in duplicate according to the spectrometric method (Kalow and Genest 1957) in 579 volunteers (325 Chinese, 175 Indians and 79 Malays).

RESULTS

1. Agar Diffusion Test

No difficulty was encountered during this test and all the volunteers so screened gave a clear indication on the agar plates that their sera belonged to the 'usual' type. The readings were done independently by both authors and the finding agreed. However, the failure to detect atypical esterase by this method however is 0·1% to 0·2% (Simpson and Kalow, 1965).

2. Dibucaine Numbers (D.N.)

The distribution of the D.N. of 579 individuals are shown in Fig. 1. It is noted that the modes of the distribution of the D.N. for the three racial groups all fell on 75 and all the 3

Fig 1

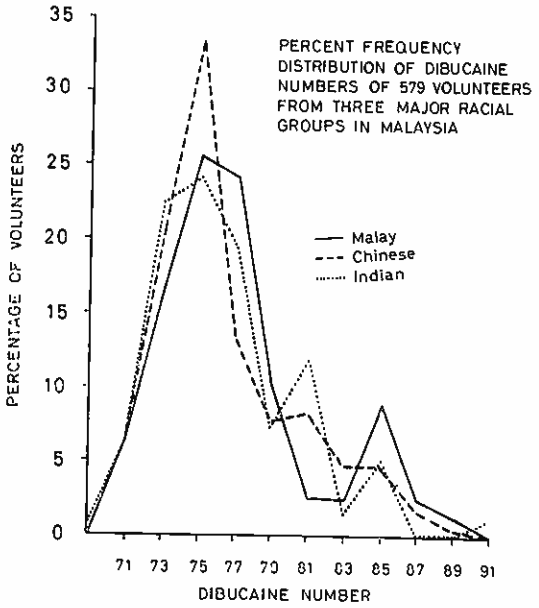

Fig. 1. The Absence of Abnormal variants of cholinesterace (E.C.3.1.1.8) in a Malaysian Population with three Major Racial Groups.

curves are skewed to the right, i.e. there are more values to the right of the modal value than to the left.

Table I shows the mean D.N. of 579 individuals from the three major racial groups; and the 95% confidence intervals for the 3 racial groups. When the D.N. of all the 579 individuals are considered together, their mean value is 76·48 with 95% confidence interval of 76·17 to 76·79.

By means of analysis of variance (Table II) it is found that the variance ratio F is less than

TABLE I

Racial Groups	Number of Samples	Dibucaine Numbers		
		Mean	Standard Error	95% Confidence Interval
Malays	79	76·95	0·47	76·03 to 77·87
Chinese	325	76·42	0·21	76·00 to 76·84
Indians	175	76·37	0·30	75·79 to 76·93
All Groups	579	76·48	0·16	76·17 to 76·79

TABLE II

Sources of Variation	Degrees of Freedom	Sum of Squares	Mean Square	Variance Ratio, F
Between groups	2	20·49	10·25	$\frac{10·25}{15·35} = 0·668$
Within groups	576	8843·49	15·35	

1 and hence the mean D.N. of the three racial groups are certainly not significantly different from one another. Therefore the 3 racial groups may be considered as samples drawn from the same population.

In view of the clinical absence of Suxamethonium sensitive individuals in over 25,000 patients on whom the drug was used and in the absence of the heterozygote $E_1^a E_1^u$ in the 947 multiracial volunteers tested both by the rapid screening method, and by the Spectrometric (D.N.) method, there is an absence of the heterozygote for the Dibucaine resistant gene. This finding is similar to that of other workers who have described the rarity of this gene in population of Oriental origin.

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