

## Atypical Cholinesterase:

### Frequency in a Puerto Rican Population

Carlos H. Garcia, M.D.,\* and Pedro M. Diaz, M.D.†

In a population of 1,739 Puerto Ricans screened for atypical serum cholinesterase, there were 35 heterozygotes for the atypical gene. No homozygotes for the atypical or the "silent" gene were found. The frequency of the atypical gene in this population was 0.0100, and the estimated incidence of the homozygous  $q^2$  was 1/10,000.

SUCCINYLDICHOLINE (SDC) is hydrolyzed by the plasma enzyme cholinesterase (acyl-choline acyl-hydrolase 3.1.1.8; I.U.B. Commission on Enzymes). This enzyme is controlled by four genes, probably allelic:  $E_1^u$  for the usual esterase;  $E_1^a$  for atypical esterase or esterase which is resistant to dibucaine inhibition;  $E_1^r$  for a sodium fluoride-resistant type; and  $E_1^s$  for the "silent" gene, which produces no detectable activity of esterase.<sup>1</sup> Patients with the abnormal variants of cholinesterase show sensitivity to SDC in various degrees.

The various combinations of the four allelomorphous genes can result in ten genotypes and seven phenotypes. This is because of the inability of present laboratory methods to detect heterozygotes for the silent gene.

The atypical enzyme is the commonest of the abnormal variants. About 4 per cent of Caucasian populations of Europe and North America are heterozygous for the atypical gene. The reported frequency among Caucasian populations range from 2 per cent in Moroccan Jews to 8.5 per cent among Czechoslovakians.<sup>2</sup> These differences are not statistically significant and could be the result of the small samples used in most of these studies.

The frequency of the atypical gene appears

to be lower in non-Caucasian populations. The trait was absent in 125 Ituri pygmies,<sup>3</sup> 700 Thais,<sup>4</sup> 511 Japanese,<sup>3,4</sup> and 291 South American Indians.<sup>5</sup> Lisker *et al.*<sup>6</sup> found an frequency of 1.9 per cent heterozygotes in Mexican Indians. Motulski *et al.*<sup>7</sup> have reported a significantly lower frequency among Seattle Negroes (1.05 per cent heterozygotes) and Congolese Negroes (0.22 per cent heterozygotes). They attribute the higher incidence among Seattle Negroes to Caucasian admixture. Simpson and Kalow,<sup>7</sup> however, reported a 2.8 per cent incidence of heterozygotes in 2,138 Brazilians estimated to have a gene pool of 48 per cent Caucasian, 34 per cent Negro, and 18 per cent Indian. This figure is not significantly different from the 3.8 per cent frequency found by Kalow in 2,017 Caucasian Canadians.<sup>7</sup>

The prevalence of the atypical gene among Caucasian and mixed populations, therefore, is still in doubt. For this reason, we report here the results of screening a large Puerto Rican population for the atypical gene.

#### Methods

Blood samples were obtained from unselected patients who came for operation at the Puerto Rico Medical Center. Samples were collected in glass tubes without anticoagulant, centrifuged, and the serum transferred to a second tube and frozen until analyzed. Hemolyzed samples were discarded. The sera were tested with a rapid screening method described by Morrow and Motulski.<sup>8</sup> The samples were read visually by two observers.

All sera with positive or doubtful results, except two because the amounts available were inadequate for testing, were saved and later analyzed by the standard method of Kalow and Genest<sup>9</sup> and/or the method described by Liddell *et al.*,<sup>10</sup> using R02-0683 (dimethylcarbamate of 2-hydroxy-5-phenylbenzyl trimethylammonium bromide, Roche Laboratories) as

\* Instructor.

† Assistant Professor. Present address: Department of Anesthesiology, University of Miami School of Medicine, Miami, Florida.

Received from the Section of Anesthesiology, Department of Surgery, University of Puerto Rico School of Medicine, San Juan, Puerto Rico. Accepted for publication July 29, 1971. Supported in part by USPHS Grants NS 07719 and 5501-RR05419.

TABLE 1. Incidence of Atypical Cholinesterase in a Puerto Rican Population

Number of People Tested	Normal Homozygotes	Heterozygotes	Atypical Homozygotes	Per Cent Heterozygotes	Incidence of Atypical Gene
1,739	1,704	35	0	2.01	0.0100

the inhibitor instead of dibucaine. These tests were read in a Beckman DU spectrophotometer.

### Results

Of a total of 1,739 patients, 1,704 were normal homozygous and 35 (2.01 per cent) heterozygous for the atypical gene. There were no homozygotes for the atypical or the silent gene (table 1).

Any samples with the genotypes  $E_1^f E_1^f$  and  $E_1^f E_1^*$  were classified as heterozygous for the atypical gene, since we did not examine for fluoride numbers. For the same reason, those with the  $E_1^u E_1^f$  genotype were classified as normal homozygous. Since these genotypes are rare, no serious error should arise.

### Discussion

The results of this study imply that the incidence of the atypical gene is low in our population. The 2.01 per cent heterozygotes is lower than, but not significantly different from ( $\chi^2 = 2.79$ ;  $P > 0.05$ ), the 2.8 per cent reported by Simpson *et al.*<sup>7</sup> in 2,138 Brazilians. However, it is significantly lower ( $\chi^2 = 8.56$ ,  $P < 0.005$ ) than the 3.8 per cent reported by Kalow<sup>2</sup> in 2,017 Caucasian Canadians. It is higher than the frequency in the Negro and Oriental populations reported by Motulsky *et al.*<sup>3</sup>

The Puerto Rican gene pool consists of Caucasian, Negro, and Indian genes, in decreasing order of frequency. There are no Oriental genes. The exact proportions of the above genes in this pool, however, are not known. Lisker<sup>11</sup> reported a frequency of 1.8 per cent heterozygotes in a sample of 469 Spaniards living in Mexico, with a 0.011 frequency for the atypical gene (there was one  $E_1^*$   $E_1^*$  in this group). We could not find any other similar studies in Spanish populations.

The lower frequency of the atypical gene in the Puerto Rican population could be the result of a lower frequency of the gene in Span-

ish populations or admixture with Negro or Indian genes, or a combination of these factors. Our findings suggest that prolonged apnea after succinylcholine may be expected to occur less often among Puerto Ricans than among other people of European stock. Based on our data, the estimated frequency of the homozygous  $q^2$  is 1/10,000.

### References

1. Lehman II, Lidell J: Human cholinesterase (pseudocholinesterase): Genetic variants and their recognition. *Brit J Anaesth* 41:235-244, 1969
2. Kalow W: Pharmacogenetics and anesthesia. *ANESTHESIOLOGY* 25:377-387, 1964
3. Motulsky AG, Morrow A: Atypical cholinesterase gene  $E_1^*$ : Rarity in Negroes and most Orientals. *Science* 159:202-203, 1968
4. Alland K, Epple F, Gredde HW: Pseudocholinesterase—variants in Thailand and Japan. *Humangenetik* 4:127-129, 1967
5. Arends T, Davies DA, Lehmann H: Absence of variants of usual serum pseudocholinesterase in South American Indians. *Acta Genet (Basel)* 17:13-15, 1967
6. Lisker R, Del Moral C, Loria A: Frequency of the atypical pseudocholinesterase in four Indian (Mexican) tribes. *Nature* 202:815, 1964
7. Simpson NE, Kalow W: Comparison of two methods for typing of serum cholinesterase and prevalence of its variants in a Brazilian population. *Amer J Hum Genet* 17:156-162, 1965
8. Morrow AC, Motulsky G: Rapid screening method for the common atypical pseudocholinesterase variant. *J Lab Clin Med* 71:350-356, 1968
9. Kalow W, Genest K: A method for the detection of atypical forms of human serum cholinesterase. Determination of dibucaine numbers. *Canad J Biochem Physiol* 35:339-346, 1967
10. Lidell J, Lehmann H, Davies D: Harris and Whittaker's pseudocholinesterase variant with increased resistance to fluoride: A study of four families and identification of the homozygote. *Acta Genet (Basel)* 13:95-108, 1963
11. Lisker R, Loria A, Zarate C: Studies on several genetic hemotological traits of the Mexican population. 13. Red cell and serum polymorphism in Spanish immigrants. *Acta Genet (Basel)* 17:524-529, 1967