Selection, Gene Migration and Polymorphic Stability in a U. S. White and Negro Population

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IN ANY POPULATION the frequencies of the alleles associated with a polymorphic locus are related to the total genetic constitution of the population and the environment in which it is situated; changes in either would result in corresponding changes in allelic frequencies. Since polymorphic traits provide an opportunity for rapid evolutionary changes (Ford, 1960), their distributions in appropriate populations can be used to study the directed (gene migration, selection, mutation) and non-directed (chance, drift) forces which have produced the recent evolutionary trends in man (Motulsky, 1960; Blumberg, 1961; Allison, 1962).

In American Negro populations, admixture with European Whites has altered the genetic constitution (Glass and Li, 1953; Stern, 1953; Glass, 1955; Roberts, 1955) and the change in their environment, by movement from Africa to North America, could have altered the adaptive values at the polymorphic loci. In this paper, frequencies of several polymorphic traits in Negroes and Whites living in the same Southern U. S. community will be compared with the frequencies of the same traits in contemporary West African Negroes in order to help evaluate the relative roles of selection, gene migration and drift in producing the present frequencies of the traits in the American Negroes. This comparison should also indicate which polymorphisms, if any, in the American Negro population are unstable; that is, traits with significantly different adaptive values in the two populations which have not reached stable frequencies, or traits which have adaptive disadvantage in the American Negroes, but are still present because of prior advantage in Africans (transient polymorphisms). The studies were conducted in Evans and Bullock Counties, Georgia. Claxton is the county seat of Evans, and the populations, for convenience, have been called the Claxton populations. A description of the populations studied and a discussion of the techniques used for identification of the phenotypes are given elsewhere in this issue. (Cooper, Blumberg, Workman and McDonough, 1963).

ANALYSIS OF THE DATA

The frequencies of the polymorphic traits studied in the Claxton populations are presented in table 1, together with estimates of the frequencies of the same traits in other Negro and White populations and in West Africans. We have assumed that the remote ancestors of the American Negroes were mainly from West Africa (see, for example, Herskovits, 1941; Fage, 1959) and that the West African frequencies obtained from recent studies closely approximate those

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in the African populations from which the American Negroes have descended. While drift and mutation have probably had little effect on the African frequencies in the period since the Negroes came to North America, is is possible that changes in the selective values of particular traits in West Africa have caused corresponding changes in the gene frequencies in that period. Any conclusions drawn from the data must be considered with these restrictions in mind.

As seen in table 1, the frequencies of the traits in the Claxton White population are, in general, quite similar to those observed in other U. S White and English populations, the greatest differences being approximately 5 per cent. The frequencies in the Claxton Negro differ from other U. S. Negro populations by at most 4 per cent for the majority of the alleles considered. A comparison of the frequencies given in table 1 permits the assumption that genetic drift has had no appreciable effect upon the distribution of the polymorphic traits in either the Negro or the White population in Claxton. In addition, approximately 12 to 15 generations, or 350 years, have elapsed since the arrival of the first Negroes in North America (Glass and Li, 1953; Fage, 1959); and both the Negro and White populations in Evans County each contain more than 2,400 individuals (Cooper *et al.*, 1963). From theoretical considerations, for this population size and time interval, it is unlikely that drift or mutation

TABLE 1. FREQUENCIES OF ALLELES STUDIED IN THE CLAXTON POPULATIONS COMPARED TO FREQUENCIES FROM OTHER STUDIES

Allele or Segment	West African Negro	Claxton Negro	Other American Negro	Claxton White	Other U. S. and English White
R^o(cDe)	.594[4]	.535	.438[4]	.037	.026[6]—.028[4]
R^1(CDe)	.069[4]	.103	.158[4]	.426	.408[6]—.420[4]
R^2(cDE)	.086[4]	.108	.109[4]	.148	.141[6]—.150[4]
r(cde)	.211[4]	.230	.264[4]	.358	.384[4]—.389[6]
A	.148[4]	.158	.141—.188[8]	.246	.23 —.29[8]
B	.151[4]	.129	.093—.147[8]	.050	.057 —.09[8]
O	.704[4]	.713	.674—.733[8]	.704	.66 —.70[8]
M	.476[4]	.485	.476—.532[7]	.508	.533 —.547[7]
S	.134[4]	.155†	.160[6]—.186[4]	.281†	.327[6]—.377[4]
Fy^a	.0[6]	.046	.053[6]	.422	.414[6]—.434[7]
P	.780[4]	.757	*	.526	.542[6]
Jk^a	.783[4]	.743	.732[4]	.536	.514[6]—.523[7]
K	.009[6]	.005	.018[7]	.042	.046[6]—.066[7]
Lu^a	.036[6]	.044	*	.036	.039[6]
Js^a	*	.122	.103[1]	.002	.0[1]
Di^a	.0[13]	.03	.00[14]	.0	.0[14]
G6PD	.18—.21[11]	.118	.11[10]	.0	.0[11]
Hb^s	.08—.14[9]	.043	.02—.06[7]	.0	.0[7]
Hp^1	.60—.78[11]	.520	.531[3]—.539[2]	.41	.43[3]
Tf^{D1}	.035—..088[11]	.049	.055[12]	.01	.0
T	.795[5]	.670	.697[5]	.527	.455[5]

*No suitable estimate could be found.
†Estimated by $S = 1 - \sqrt{S(-)}$ for purposes of comparison with West African data.

[1]Giblett and Chase, 1954
[2]Giblett and Steinberg, 1960
[3]Sutton *et al.*, 1959
[4]Glass, 1955
[5]Glass and Li, 1953
[6]Race and Sanger, 1958
[7]Mourant, 1954
[8]Mourant *et al.*, 1958
[9]Allison, 1956
[10]Beutler, 1959
[11]Allison and Blumberg, 1962
[12]Parker and Bearn, 1961
[13]Gershowitz, 1959
[14]Layrisse, 1958

has had an appreciable effect on gene frequencies, (Kimura, 1956; Moran, 1962).

The unlikelihood of significant admixture between the American Negro and the American Indian population was discussed by Glass (1955). His conclusions are supported by our finding the *Di*^{a} allele, relatively common in American Indians (Layrisse, 1958), in only one of 188 Claxton Negroes.

If the assumptions discussed above are correct, then the frequency differences between the Claxton and West African Negroes can be ascribed almost totally to the effects of gene migration resulting from admixture between the American White and the American Negro population and to differences in the adaptive values of the traits in the West African and American Negro populations.

Selection and Migration

In order to evaluate the relative effects of selection and migration, estimates have been made of the total amount of gene migration from the American White into the Claxton Negro population using the method of Bernstein (1931) which assumes that the observed differences are due to migration alone. In the following calculations is is assumed that the frequencies of the traits in the Claxton Whites are representative of the frequencies in the White population which has contributed to the Negro gene pool. If q_W, q_N, and q_{Af} are the frequencies of an allele in the Claxton White, Claxton Negro and West African populations respectively, then the total amount of gene migration, m, is given by

$$m = \frac{|q_N - q_{Af}|}{|q_W - q_{Af}|}.$$

Such an estimate of gene migration, m, for a given locus or segment, is equivalent to an estimate of the admixture, or hybridization, which has occurred between two populations only if: (a) there is no assortative or preferential mating between the two populations with respect to the locus considered; (b) the gene migration is entirely from one population into the other; (c) individuals whose genotype is derived from both populations have no special bias with respect to fertility, social factors, geographic mobility, and other factors which would affect their contribution to the gene pool of the population. For example, for an organism in which the hybrids between two populations are not viable, no amount of admixture will result in gene migration. For the present study, since we shall assume only that there has been no preferential mating with respect to the traits under consideration, the relation between the estimates of gene migration and the actual amount of admixture can not be considered. In the absence of differences in the adaptive values of the traits in West Africa and in the United States the estimates of m, computed for each of the loci, should be equal. Then, an alteration of the adaptive values of the alleles resulting either from change in environment or from modification of the gene pool by admixture would result in differences between the m values calculated for the alleles. Small variation in the m values could be ascribed to sampling accidents, drift, or small inaccuracies in the estimates of the allelic frequencies in the West African population, as well as to small changes in the

adaptive values. However, significantly different estimates of m must be the result of significant differences in the adaptive values of the alleles in the two populations.

Estimates of gene migration (m) have been calculated only for those alleles where reliable West African frequencies are obtainable and where the difference between the frequencies of the alleles in the Claxton White and West African populations, $|q_W - q_{Af}|$, is sufficiently large that the sampling error of the ratio is small. We have considered only those alleles for which $|q_W - q_{Af}|$ is at least .09. Table 2 gives the alleles considered and the corresponding values of $|q_W - q_{Af}|$ and m. The alleles or chromosome segments not suitable for this kind of analysis, for one or both of the above reasons, were *O*, *M*, R^2, *K*, Lu^a, Di^a, and Js^a.

DISCUSSION

The most striking feature of the analysis is the apparent separation of the polymorphic traits into two distinct groups. In the larger group (Group I), including all the red blood cell antigens, the m values have a range from .094 (*P*) to .218 (*B*) and a mean value of .131. The other group (Group II), which includes Hp^1 (haptoglobin), Hb^s (sickle cell hemoglobin), G6PD, *T* (PTC-taste test) and possibly the Tf^{D1} (transferrin) alleles, has m values which range from .34 to .70, all considerably greater than those in the first group.

In order to determine which of the two groups contains alleles whose frequencies have been primarily altered by gene migration, we should consider estimates of m obtained from alleles whose frequencies would have remained approximately constant in the West African and American White populations over the past 300 years, and for which $|q_W - q_{Af}|$ is large. Since the frequencies of Rh alleles (which all fall in Group I) are considered to be quite stable over

TABLE 2. COMPUTED VALUES OF M AND $|q_w - q_{AF}|$

Allele or Segment	$\lvert q_w - q_{Af} \rvert$	m
	Group I	
R^o	.562	.113
Fy^a	.422	.109
R^1	.357	.095
P	.266	.094
Jk^a	.247	.167
r	.147	.129
S	.147	.143
B	.101	.218
A	.098	.107
	Group II	
T	.268	.466
Hp^1	.19—.38	.42—.70
G6PD	.18—.21	.34—.44
Hb^s	.08—.14	.46—.69
Tf^{D1}	.074	.495*

*The West African frequency for Tf^{D1} which was used (.088) was based on only two samples. See text for discussion.

a period of several hundred years (see, for example, Mourant, 1954) we have assumed that the m values of the Group I alleles, in the Claxton Negroes, reflect primarily the effects of gene migration. The mean of the m values for R^0 ($|q_W - q_{Af}| = .562$) and R^1 ($|q_W - q_{Af}| = .357$), namely m = .104, can be considered the best estimate of m in the Claxton Negro population. The variation in the m values estimated for the Group I traits (*i.e.*, the red blood cell antigens) could result from either small differences in the adaptive values of the traits in West Africa and Claxton, sampling error or genetic drift. For the Group I traits the environmental selective forces appear to be similar in West Africa and in the Southern United States. This implies that they are mantained by selective forces which operate in both ecological settings. They are, however, balanced at different levels as shown by the gene frequencies for Africans and Whites in table 1, indicating probable differences between the gene pools of the given populations. Thus, barring unknown cyclic changes which could have occurred during the generations since the movement of the Africans to North America, or selective forces which have uniformly affected the m values for the Group I alleles, gene migration, resulting from admixture between the Claxton Negroes and the American Whites, appears to be the chief cause for the differences in the frequencies of these alleles in the West African and Claxton Negro populations.

For the Group II polymorphisms, gene migration alone cannot account for the m values which are all significantly larger than .104. Nor, as noted above, could either mutation or drift have significantly influenced the frequencies of these alleles. If the contemporary West African frequencies accurately reflect the population from which the Claxton Negroes are descended then these Group II traits must have significantly different adaptive values in West Africa and Claxton. Evidence from other studies supports this hypothesis. It has been suggested that heterozygotes for either Hb^s or G6PD have an adaptive advantage in a malarial environment (Allison, 1956; Motulsky, 1960). Selection against the heterozygotes for Hb^s or G6PD would lead to a rapid decrease in the frequency of the alleles. The *T* allele has been considered in relation to thyroid disorders (Kitchin *et al.*, 1959). There is evidence from studies on Greek populations that the Hp^1 allele may be positively correlated with the thalassemia trait (Blumberg, 1963).

The Group II polymorphisms, *T*, G6PD, Hb^s, and possibly Hp^1 and Tf^{D1}, have values of m ranging from .34 to .70, indicating that these polymorphisms were, and probably still are, unstable. Since the G6PD and Hb^s alleles are almost completely absent in U. S. Whites, these traits may represent transient polymorphisms, present in the U. S. Negro because of a former adaptive advantage in the West Africans.

The present data do not provide any interpretation of the nature of the adaptive factors operating on the polymorphisms included in Group II. It should be stressed that the statistical analysis can only provide correlations between environmental conditions and allelic frequencies. Any valid interpretation of the differences in adaptive values must derive from medical or biochemical studies.

The statistical analysis of the data could be extended to a consideration of either the rate of gene migration per generation (Glass and Li, 1953; Saldanha, 1957) or the adaptive values for the traits. Such analysis would, however, entail assumptions such as constant rates of migration and fixed adaptive values, which are most unlikely, and the numbers produced would be of dubious worth.

The estimation of m for the Hp^1 gene is based on estimates of West African frequencies derived from populations in which many of the sera could not be typed because of absent or low haptoglobin levels (Allison, Blumberg and ap Rees, 1958). Although some ahaptoglobinemia is due to genetic causes (Giblett and Steinberg, 1960), much of it is probably due to the environment. Furthermore, in cases which have been recorded as ahaptoglobinemia at one time, but typable at another, the serum is often type 2-2 (Blumberg and Gentile, 1961). Hence the West African surveys may over-estimate the Hp^1 frequency. For example, if in the West African population sampled by Blumberg and Gentile (1961) half of the sera classified as type O were in fact type 2-2, the value of $|q_W - q_{Af}|$ would be too small to permit an accurate calculation of m. Furthermore, it is now known that there are at least three alleles commonly segregating at the *Hp* locus (Hp^{1F}, Hp^{1S}, Hp^2) (Smithies, Connell and Dixon, 1962) and the frequency of Hp^1 is actually the sum of Hp^{1F} and Hp^{1S} frequencies.

The calculation of m for the Tf^{D1} allele is based on only a small number of West African studies. Recently several slow moving transferrin variants determined by alleles other than Tf^{D1} have been reported and in some cases the transferrin phenotypes may have been misclassified in the earlier studies. Hence the Tf^{D1} frequencies reported may be high. Furthermore, it is not unlikely that the slow moving variants reported in non-Africans are determined by different alleles. The m value calculated for Tf^{D1} must be considered tentative.

Values of m greater than .20 have been reported by Glass (1955) and Roberts (1955) from comparisons between other American Negroes and Whites. Unfortunately, they compared the frequencies of polymorphisms in Negroes and Whites who did not live in the same community and used different populations to compare different alleles. Hence, from their studies it is impossible to analyze the variation in the m values which could reflect variation in the populations considered, different amounts of admixture, or in the influence of social factors as well as adaptive differences, drift, and so forth. The frequencies of the R^0 and R^1 alleles in the Claxton Negroes are closer to the West African frequencies than are those reported by Glass (1955); Pollitzer (1958), in a study of Negroes from Charleston, South Carolina, found frequencies almost equal to those in West Africa. This variation suggests that there may be significant differences in both the amount of admixture and the amount of gene migration in different U. S. Negro populations. That is, the high estimates of m obtained from studies on Negroes living in large Northern cities could reflect either different rates of admixture or a similar rate of admixture but differential rate of geographic movement of Negroes with a high proportion of white ancestry. In Pollitzer's (1958) study, both the gene frequencies and his anthropological studies on the relative isolation of the populations suggested a low rate of admixture.

The simultaneous analysis of the distribution of several polymorphic traits has served to isolate four (or five, including the Tf^{D1}) alleles whose frequencies are, or have been, significantly altered by selective pressures which are different in the West African and Claxton populations. Additional statistical and biological studies are required to determine the nature and amount of the adaptive differences of these alleles. Similar studies in other populations should reveal additional traits which are undergoing rapid evolutionary change. The same populations, and in fact the same blood samples, may be used to determine if newly-discovered polymorphisms are balanced (Group I) or unstable (Group II). Such studies are being undertaken with the serum Gm (gamma globulin), Gc (group specific) and beta lipoprotein groups.

The variation within the group least affected by adaptive differences (Group I) should be further analyzed not only in other American Negro populations, but in populations throughout the world. In this way, the loci most stable over many generations and in different populations could be determined and used for anthropological or historical studies in these populations.

SUMMARY

The frequencies of more than 15 polymorphic traits were studied in an American Negro and White population living in the same rural Southern U. S. community and compared with the frequencies of the same traits in West African Negroes and other American Negro and White populations. It is suggested that neither genetic drift nor mutation were likely causes of the variability observed. By estimation of the total amount of gene migration, m, from the Whites to the Negroes, (under the assumption of no selection) the polymorphic traits can be separated into two distinct groups. In Group I, the larger group, which contains the red blood cell antigens, the estimates of m (.1 to .2) are consistent with the hypothesis that migration alone can account for the differences in gene frequencies between the West African and the American Negro populations. The best estimate of m was found to be .104. In Group II, containing the G6PD, Hb^s, and T alleles (and possibly Hp^1 and Tf^{D1}) the significantly higher estimates of gene migration (.4 to .7) were concluded to result from both gene migration and different adaptive values of the traits in the West African and American environments.

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