# Biocultural Adaptation To Disease In The Caribbean: Case Study Of A Migrant Population

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The concept of "adaptation" has been appropriated, misappropriated, discovered, and rediscovered by generations of cultural and medical anthropologists. This term has been utilized to depict short-term population and individual responses to various environmental or social "stresses." In contrast, geneticists have consistently defined adaptation as a long-term genetic response to the environment through natural selection (Lewontin, 1978). Recently this concept of adaptation through natural selection and its relationship to disease has been presented as a "new" paradigm in medical anthropology (Williams and Neese, 1991; Wiley, 1992), even though it has long been realized that in humans biology and culture interact, especially in the case of disease.

This paper examines the complexity of biocultural adaptation to a geographically widespread disease: malaria. Against a backdrop of the evolutionary history of the population, the interactions among the molecular, cellular, and organismic responses to the causative deadly parasite (*Plasmodium falciparum*) are examined. A case study from Caribbean populations, traced over several hundred years, reveals the complex mechanisms involved in the populational response to the disease. On the organismic level, it has been demonstrated that individuals with malarial protective genes (e.g., hemoglobin AS—the sickle cell trait) are parasitized by *Plasmodium falciparum* but experience a less severe form of the disease and lower mortality (Allison, 1954a; Wilcox *et al.*, 1983). The mechanisms usually invoked to explain this reduced mortality and morbidity include an increased tendency to sickling by Hb AS (sickle cell trait) individuals, which hampers the growth of the parasite (Friedman, 1978). These mechanisms are involved in resistance to malaria, but do not explain the absence of microcirculatory obstruction in individuals with the abnormal hemoglobins (hemoglobinopathies). Recently, it has been suggested that the interactions between carbohydrate receptors within the ABO blood group system, certain hemoglobin variations (e.g., sickle-cell trait, hemoglobin AE, alpha- and beta- thalassemia), and the rosetting ability of red blood cells (the binding ability of uninfected RBCs to Plasmodium-infected ones) all play important roles in the development of cerebral malaria, the survival of the organism, and ultimately the action of natural selection on the population (Carlson *et al.*, 1994).

## THE DISEASE

It has been estimated that malaria is still the most prevalent parasitic disease worldwide, affecting more than 270 million people and killing 1 to 2 million children yearly (WHO, 1990). The Anopheles mosquito and the transmission of the Plasmodium parasite exist where the average temperature exceeds 59° F (15° C) for at least one month a year. Malaria cannot thrive at altitudes above 9,900 feet (3,000 meters) nor in temperate climes.

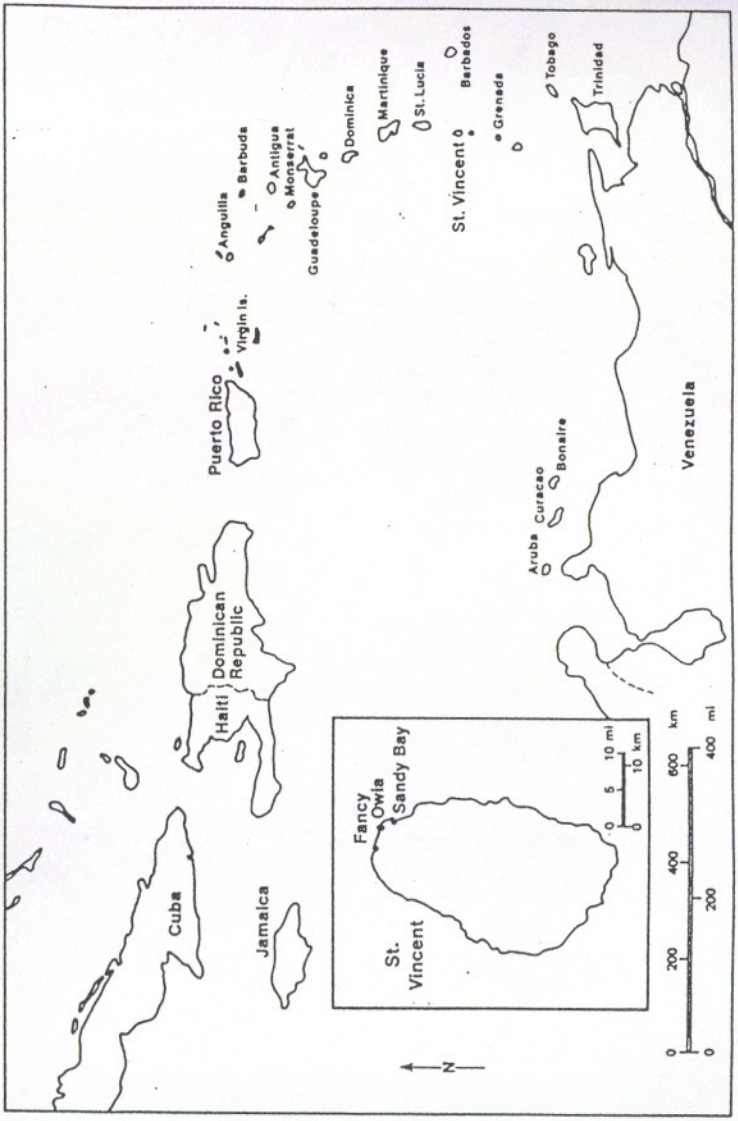
In addition, tranquil bodies of water allow successful breeding of the mosquito that transmits this parasite to humans. During one phase of its life cycle and development, sporozoites of Plasmodium migrate from the gut of the infected mosquito to the salivary glands, from whence they are passed to the human host during the collection of a blood meal by the female mosquito. Four human malarial parasites (*Plasmodium falciparum, P. vivax, P. malaria, and P. ovale*) require two hosts for the transmission of the disease: the human organism and the female Anopheles mosquito. The deadliest form of malaria, cerebral malaria, is caused by *Plasmodium falciparum* which kills the human host if the parasites circulating in the blood sequester in the brain.

Until recently, Black Caribs (also known as the Garifuna) of Central America and the Caribbean have been under heavy malarial parasitization by *Plasmodium falciparum* and *Plasmodium vivax*, carried by two mosquito species, *Anopheles darlingii* and *Anopheles albinamus*. During 1973-1978 in the Province of Colon, Honduras, 80,822 persons were tested for malaria with 22.7% diagnosed positive for *P. vivax*, while only 0.49% were parasitized by *P. falciparum* (Custodio and Huntsman, 1984). This study indicated that despite the extensive cultural intervention in the form of insecticide spraying programs designed to eradicate the Anopheles mosquito, the Garifuna continued to suffer from malaria.

## THE POPULATION

The origin of the Black Caribs (Garifuna) can be traced to St. Vincent Island of the Lesser Antilles (see Figure 1). This island, located approximately 21 miles southwest of St. Lucia, is presently inhabited by an amalgam of Island Carib/Arawak Indians with West Africans. The descendants of the few Black Carib families who avoided deportation by the British currently reside in three villages located on the northern slopes of St. Vincent (these villages are shown in Figure 1). In addition, an African/European hybrid subpopulation, termed Creole, is distributed throughout the island. St. Vincent was initially settled by Arawak Amerindians from Venezuela in approximately 100 AD. Between 1200 AD and European contact, another Amerindian group (the Caribs) expanded from Venezuela and intermixed with the original inhabitants of St. Vincent Island. Archaeological evidence (mostly ceramic motifs) has been interpreted by Rouse (1976) to indicate an invasion by the Caribs, followed by the extermination of the Arawak males and hybridization with the Arawak females. However, on the basis of linguistic evidence, Gullick (1979) has argued in favor of a relatively small Island Carib contingent moving into the Caribbean and hybridizing on a smaller scale with the Arawaks.

**Figure 1**
**Caribbean with inset of St Vincent**



From 1517 to 1646, an African component was added to St. Vincent's gene pool and most likely malaria was introduced to the island. The origin of this African contribution to the island has been explained by several theories: (1) runaway slaves from Barbados, an adjoining island and a center of the Caribbean slave trade; (2) raids on the European settlements, by the Caribs of St. Vincent resulted in their return to St. Vincent Island with African slaves; (3) the shipwreck off the coast of St. Vincent Island. This African component, intermixed with Amerindians to produce what has been called the Black Carib (Garifuna) population of St. Vincent Island, is an exceptionally successful group that was deported by the British in 1797 to the Bay Islands and eventually settled in coastal Central America. The Spanish navy transported the Garifuna to the Gulf of Honduras from whence the Black Caribs colonized most of the eastern coast of Central America.

Prior to European contact and colonization, no census records or reliable enumerations exist for the Amerindians residing on St. Vincent Island. Gullick (1984) estimated the island population at contact as approximately 5,000 persons. This number included both the Island Caribs and Africans, even though the Amerindian component was put at a few hundred. After the second Carib war (1795–1805) approximately 2,000 Black Caribs were deported by the British to the Bay Islands. Gonzalez (1984) has argued that a total of 4,200 Black Caribs surrendered to the British occupation forces in July 1796, but only 2,026 Black Caribs actually arrived in Roatan of the Bay Islands. Gonzalez attributes this numerical discrepancy (between the British captain's log and the numbers imprisoned) to a devastating epidemic, ostensibly from typhus, during the nine-month internment of the Black Caribs on Balliceaux Island while awaiting deportation. In addition, there must have been some deaths in the ship's hold en route from Balliceaux to Roatan.

Although 2,026 Black Caribs were deported from St. Vincent Island, some chose to remain on Roatan. The remainder of the Black Caribs were relocated from the Bay Islands to Honduras and their numbers grew exponentially in a short time. From a single village in Honduras at the turn of the 19th century, the Black Caribs colonized much of the coast of Central America, presently residing in 56 villages, plus several "satellite communities" in New York and Miami. The total population of Black Caribs increased from fewer than 2,000 persons in 1800 to currently more than 100,000 persons living in Central America (Crawford, 1983). This is an unprecedented evolutionary success story. Adapting to the malarially infested coastal environments, they colonized Belize, Guatemala, Honduras, and Nicaragua. Both genetic and cultural factors contributed to the Garifuna success.

## BIO-CULTURAL FACTORS OF GENETIC ADAPTATION

At the time of Black Carib relocation, malaria was responsible for the depopulation of much of coastal Central America. African slaves, infected with *Plasmodium falciparum,* had been brought to work the fruit plantations of the coastal regions of Central America. Because of the presence of the Anopheles mosquito in Central America, the malarial parasite (brought

from Africa) was able to enter the local vectors and infect the Amerindians. *Anopheles albinamus* and *Anopheles darlingii* transmitted malaria to both the Amerindians (causing extensive morbidity, mortality, and depopulation) and the uninfected Africans (many of whom were genetically resistant to malaria). With some exceptions, surviving Amerindian groups moved from the malarially-infested coastal regions to the malaria-free highlands. This populational movement left vast unoccupied coastal tracts to the rapidly expanding Garifuna.

In addition to their genetic resistance to malaria, the Black Caribs were uniquely "predisposed" to the successful colonization of diverse environments because their gene pool is exceptionally diverse (as measured by mean per locus heterozygosity), resulting from the tri-racial, multi-ethnic origin of the founding population of St. Vincent Island. In addition to heterogeneous Amerindians, consisting of Arawak and Carib genes, African slaves most likely constituted a cross-section of several West African groups. A European component was added to the Garifuna gene pool by admixture with the Creole populations, a European-African hybrid(speaking creolized languages) brought to the coast of Central America. There is also some evidence of gene flow from the highland Maya groups to the coastal Garifuna (Crawford *et al.*, 1984).

The presence of a serum protein variant called albumin Mexico in the Central American Black Carib populations and its absence on St. Vincent Island suggests a Central American origin of the gene (Crawford, 1987). This albumin variant could not have been introduced into the Black Carib gene pool by the Carib or Arawak Indians because of its absence in South American indigenous populations. The economic and social contacts between the Maya Indians of Belize and the immigrant Black Caribs and Creoles of Stann Creek, Punta Gorda and Belize City have resulted in some gene flow between these groups. The greater geographic isolation of the Livingston and Hopkins Black Carib communities from the Amerindian groups would explain the lower incidence of the albumin variant in their populations.

Measures of genetic admixture based upon an assortment of blood groups, serum and red blood cell proteins confirm a tri-racial origin of the Black Carib gene pool (Crawford *et al*, 1984). Based upon the frequencies of immunoglobulin gene complexes or allotypes (the most sensitive serum genetic markers for the study of admixture), Schanfield, *et al.* (1984) estimated that on average approximately 76% of the genes in the coastal Black Carib gene pools were of African origin. The Amerindian component in the Garifuna gene pool was approximately 20%, and the remaining 4% of the genes were from European gene flow. In contrast, the Black Carib gene pool of St. Vincent Island contained 46% African genes, 16% European admixture, and approximately 38% Amerindian genes. These measures of admixture indicate that the gene pools of the Garifuna of Central American are much more African than the Black Carib gene pools of St. Vincent Island.

A geographically expanding, colonizing population such as the Black Caribs would encounter an assortment of environmental conditions (Crawford, 1983). Thus, the Black Caribs, with their extreme intra-populational

genetic variation and an amalgam of Amerindian and African cultures and adaptive strategies, would be better able to adapt to the unique ecological conditions they encountered (Crawford, 1987). Given a colonizing population with a gene pool containing many variant genes, it is likely that some of these genes may prove to be protective against diseases that may be encountered in new environments.

This high level of Black Carib biodiversity was maintained and possibly further increased through various social and demographic mechanisms. For example, an analysis of the mate selection system revealed that the majority of Garifuna households practiced traditional serial monogamy (several consecutive unions) instead of "permanent pair bonding," which resulted in the rapid "reshuffling" of genes within their gene pool (Crawford, 1987). The typical Black Carib matrilineal household consisted of a mother, a grandmother, children by a number of different males, and a resident adult male. High migration rates between Black Carib villages and Maya communities helped maintain genetic diversity, with 12% of all matings in small villages being exogamous and 3% inter-ethnic. Approximately 20% –30% of the children born in large communities had parents of differing ethnicities (Kerns, 1984). Thus, gene flow has further elevated the high level of genetic diversity observed among Garifuna populations (Crawford *et al*, 1981).

High fertility rates have characterized both large Black Carib communities and small villages. Firschein (1984) described an average rate of 5.84 children per woman over 60 years of age in the towns of Punta Gorda and Stann Creek. However, in rural villages of Honduras Brennan (1983) observed 10.9 live births per woman 45 years of age or older, an exceptional level of achieved reproduction. Firshein (1961) has argued that in a malarial environment Black Carib women with the sickle-cell trait (Hb AS) produce more liveborn children than do women who possess normal hemoglobin (Hb AA). This argument was the cornerstone of the theory that natural selection maintains the Hb AS as a "balanced polymorphism" through differential fertility rather than differential mortality, as Allison (1954a) had proposed. Later studies by Custodio and Huntsman (1984) and Madrigal (1989), however, found no fertility differential between Hb AA and Hb AS females.

In a holoendemic malarial environment, the cost of maintaining protective genes (such as sickle cell) is the mortality associated with sickle cell anemia (Hb SS). It has been suggested that the clinical affects of this anemia may be in part-ameliorated through cultural means, i.e., the consumption of cyanogen-rich cassava or manioc in the diet (Houston, 1973). Dietary organic cyanogens consist of sublethal cyanide (CN-) and its metabolites thiocyanate (SCN-) and cyanate (CNO-). When ingested, these cassava-derived cyanogens combine with an assortment of proteins, including hemoglobin plus various essential proteins of the malarial organism (Jackson, 1990). These cyanide derivatives chemically bond with hemoglobin S, inhibiting sickling and improving the oxygen carrying capacity of hemoglobin. There is in-vitro evidence to suggest that when these ingested cyanide derivatives combine with proteins of *Plasmodium falciparum* its growth and development are severely retarded (Nagel *et al.*,

1980). In the past, cyanates were used in the United States for clinical treatment of crises associated with sickle cell anemia.

The Black Caribs are both cultivators and consumers of cassava. In its untreated form, cassava contains massive quantities of cyanogens that, if ingested, will seriously poison or kill. Grating cassava, followed by an extensive leeching process, eliminates most of the deadly cyanides. Cassava flour contains the richest known food source of organic cyanogens with 70–80 mg per 100 grams of flour (Houston, 1973). At this level of cyanogens in the flour, the consumption of over 1 kilogram of bread made from the cassava flour would be necessary to provide a Black Carib with one gram or more cyanogens per day. However, Black Carib children are often fed a gruel of cassava containing greater amounts of cyanogens, possibly decreasing the likelihood of the sickling crises during critical stages of their growth and development.

Jackson (1990) has proposed two alternative evolutionary models to explain the observed levels of cassava consumption and the incidence of HB*S gene in Liberian populations that experience holoendemic malaria. One model focuses on the ingestion of lower dosages of cyanogens (0.3 mg CN-/kg body wt/day) which inhibits sickling of red blood cells and maintains high frequencies of hemoglobin S in the gene pool. The alternative model stresses higher dietary intake of cyanogens (1.5 mg CN-/kg body wt/day) which affects the survival of the *Plasmodium falciparum* organism in the red blood cells and, reduces the effects of the disease, but is associated with lower frequencies of HB*S. Both of these evolutionary models are reliant upon the biocultural adaptation of Liberian populations to malaria.

## GENETIC FACTORS

The Black Caribs of Central America exhibit a high level of genetic variation, resulting in part from the tri-racial, multi-ethnic origin of the founding populations. Out of 29 standard genetic traits tested for genetic variation, 26 were polymorphic and only three were monomorphic, i.e., invariable (Crawford *et al*, 1984). The mean per-locus heterozygosity (D), a measure of average genetic variation, for the Caribs of Central America was 45%, which reflects the complex origins of the populations. Since some of the immunoglobulin variation is limited to specific geographical populations, hybridized groups exhibit many new combinations of gene complexes. For example, while European populations normally exhibit 10 to 12 immunoglobulin forms (phenotypes), the Black Caribs of St. Vincent Island had 42 such phenotypes (Schanfield, *et al*, 1984). These new gene complexes, introduced by gene flow, would be "tested" by natural selection during exposure to different environmental conditions.

The evolutionary success of the Garifuna and other African-derived populations can best be understood by both their cultural and genetic charcteristics. The high genetic variation, coupled with the presence of genetic variants that provide varying degrees of genetic resistance to malaria, has contributed to the population explosion of the Black Caribs of Central America (Crawford, 1983).

## ADAPTATION TO MALARIA

### Protective Genes

A suite of genetic variants or mutations protect human populations against malaria. These protective genes include: Gerbich negative blood group, ovalocytosis, glucose-6-phosphate dehydrogenase deficiency (G-6-PD -), Duffy blood group (FY*C), human leukocyte antigens (HLA), and the various hemoglobinopathies mentioned earlier (HB*S, HB*C, HB*D, HB*E, and alpha- and beta thalassemia). To date only one study has attempted to characterize the presence of most of these malaria protective genes (using molecular genetic techniques) in a single human population, the Wosera of Papua New Guinea (Wagner, 1995).

### Gerbich Blood Group

Gerbich is a blood group antigen expressed on the surface of the erythrocyte (red blood cell). In most human populations the absence of the Gerbich antigen rarely occurs. However, in Papua, New Guinea, the frequency of the Gerbich negatives (Ge-) is high and a relationship has been observed between malarial endemicity and the distribution of Gerbich negative individuals (Booth and McLoughlin, 1972). Serjeantson (1989a) confirmed this relationship by showing that Ge- individuals were significantly less parasitemic for *Plasmodium falciparum* and *P. vivax*. To date the Black Carib populations have not been tested for the Gerbich negative genes. It would be interesting to determine whether this purported relationship between the distribution of Ge- individuals and endemic malaria is limited only to Melanesia, or whether other populations had adaptively responded to malaria by selecting for the Gerbich negative phenotypes.

### Ovalocytosis

In hereditary ovalocytosis the red blood cells appear oval in shape, oval macrophages are present, and the RBCs fail to sediment (Wagner, 1995). This condition is rare in most human populations, but occurs at relatively high frequencies in parts of Southeast Asia and Melanesia (Booth *et al.*, 1977). There is a relationship between ovalocytosis and lower P. falciparum parasite densities, suggesting that this condition may offer resistance to malarial infection (Serjeantson *et al.*, 1977). Serjeantson *et al.* (1992) have presented a possible mechanism for the decreased parasite numbers, involving the rapid depletion of intracellular ATP (a molecule involved in cellular energy production). Presently no data are available on the incidence of ovalocytosis in Black Carib populations.

### Glucose-6-phosphate dehydrogenase deficiency (G-6-PD-)

The gene for the G-6-PD enzyme is located on the X-chromosome; deficiencies occur mostly in males. To the malarial organism this enzyme is important for survival because G6PD is involved in the metabolism of glucose. Since RBCs lack nuclei, the absence of the G6PD enzyme in erythrocytes is more critical than in nucleated cells, because it affects the detoxification of products of oxygen metabolism and may result in cellular death (Beutler, 1990). Motulsky (1960) demonstrated that the geographical distribution of G6PD deficiency parallels the world-wide distribution

of endemic malaria. Weymes and Gershowitz (1984) reported the frequency of the G6PD A- phenotype in Black Caribs to be 7% for Hopkins and 6% for Stann Creek. To date the Black Carib populations have not been screened for molecular variants of G6PD and their adaptive roles in genetic resistance to malaria have not been investigated.

**Duffy Blood Group**

The Duffy blood group system has two different genetically determined protein variants called A and B which are distributed on a worldwide basis. Miller, *et al.* (1976) demonstrated that individuals who lack the A and B antigens of the Duffy system (called FY*C instead of FY*A or FY*B) are more resistant to infection from *Plasmodium vivax*, because this malarial organism utilizes the Duffy antigens as attachment points during invasion of the erythrocyte (Miller, 1994). The absence of FY*A and FY*B antigens has been attributed to the actions of natural selection operating against malaria. The FY*C gene occurs at close to 100% in parts of Africa, while it is entirely absent in other human populations. Because of the African component in the Black Carib gene pool, the FY*C gene occurs from 93% in Roatan, Honduras, to 85% in Stann Creek. Judging from the high frequency of the FY*C mutation in Black Carib populations, the majority of individuals are resistant to invasion by *Plasmodium vivax*.

**Human Leukocyte Antigens (HLA)**

HLA antigens, because they bind "foreign" proteins and present them to the immune system, play a major role in susceptibility to infectious diseases (Tiwari and Terasaki, 1985). Evidence of the association between HLA and malaria in Sardinia was first presented by Piazza, *et al.* (1972). One HLA variant, B53, has been found in lower frequency in Gambian children with severe malaria than in the general population (Hill, *et al.*, 1991). This HLA molecule contains a groove that presents the antigen to the T-cell receptor, and may be a target for the T-cell action (Miller, 1994). Unfortunately, because of the difficulties of maintaining viable white cell samples under field conditions, to date none of the HLA genes have been characterized among any of the Black Carib populations. However, with the recent development of DNA-based HLA typing, several new molecular techniques may be employed in the identification of HLA markers that will establish their relationship to malarial susceptibility.

**Hemoglobinopathies**

Disorders of the synthesis of the globin portion of the hemoglobin molecule have collectively been termed hemoglobinopathies. These disorders are divided into two categories (Wagner, 1995): 1) thalassemias that are caused by the underproduction of globin chains (either the alpha- or beta-); 2) hemoglobin variants that produce a mutated form of the molecule (e.g., HbS, HbC, HbE. HbD). The primary focus of this paper is on the hemoglobin variants among the Black Caribs of the Caribbean and Central America.

No aboriginal human population contains all these protective genes; instead the particular array of genes is dependent on which chance mutations

may have occurred and whether the population experienced gene flow from groups that were parasitized by malaria. The frequencies of these protective genes are determined by the population's evolutionary history —particularly the action of natural selection — and possible gene flow. Because Amerindian populations were not exposed to malaria until the 17th or 18th centuries (the introduction of African slaves) New World natives do not display any malarial-protective genes above recurrent mutation levels (Livingstone, 1967). Those portions of the Garifuna gene pool derived from Africans however, contain several hemoglobino- pathies (hemoglobin variants such as hemoglobin S and C), G-6-PD deficiency, and Duffy variants.

**Table 1.** Incidence of Genes Known to be Involved in Resistance to Malaria in Central American Black Carib Populations

| Genes | Range of Frequencies |
|---|---|
| Sickle cell (HB*S) | 3% to 24% |
| Hemoglobin C (HB*C) | 0 to 5% |
| Duffy null (FY*C) | 78% to 93% |
| G-6-PD (GPD*A-) | 6% to 10% |

**Hemoglobin Variants**

In Black Carib populations the HB*S gene ranges from 3% to 24% (see Table 1). This range reflects the amount of African admixture, the possible local actions of natural selection, and the sizes of the samples collected from these populations over a period of several generations. The highest incidence of HB*S was observed in Seine Bight, Belize, by Firschein in 1961. Approximately one generation later, Custodio *et al.* (1984) sampled the same village but found an HB*S gene frequency of only 7.5% (a statistically significant difference of 16%). Similarly, Firschein reported that in 1956 the frequency of HB*S in Stann Creek was 11%, while my investigations in 1976 revealed a frequency of 8%.

My studies of the Black Carib and Creole populations of Central America and St. Vincent Island provided a unique opportunity for determining the reasons behind the sampling deviations in gene frequencies over a 20 year period (Crawford *et al.*, 1984). Table 2 summarizes the gene frequencies for the hemoglobin variations for the Black Caribs (CA) and Creoles (CR) of Belize and Guatemala. On average, the Black Caribs have a higher frequency of HB*S (0.069) than do the Creoles (0.052). In all the Black Carib communities compared, there is a marked reduction of HB*S between 1956 and 1978, with the frequency decreasing from 11.1 to 8% in Stann Creek, 23.6% to 7.5% in Seine Bight, and 13% to 3% in Hopkins (Firschein, 1961; Weymes and Custodio, 1984). In contrast, two independent surveys conducted a few years apart in Livingston, Guatemala, showed no observable differences.

The observed difference of 0.16 cannot be explained by the relaxation of selection for one or two generations. In addition, by combining the total

Black Carib sample and subdividing it into three generations (under 20 years of age, 20 years to 39.9 years of age, and 40 and above), a chi square comparison of the hemoglobin distributions failed to reveal any significant differences among the generations.

**Table 2.** Gene frequencies of hemoglobins in population samples from Belize and Guatemala (CR = Creoles; CA = Caribs).

| | Populations | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Belize City | Stann Creek | | Punta Gorda | | Livingston | Total | |
| Allele | CR | CA | CR | CA | CR | CA | CA | CR |
| HB*A | 0.949 | 0.917 | 0.929 | 0.945 | 0.940 | 0.923 | 0.928 | 0.941 |
| HB*S | 0.043 | 0.80 | 0.071 | 0.053 | 0.040 | 0.077 | 0.069 | 0.052 |
| HB*C | 0.009 | 0.003 | 0.000 | 0.002 | 0.020 | 0.000 | 0.003 | 0.007 |

WILL BE FIXED

The role of random sampling error was tested as the possible explanation for the disparity in gene frequencies described by Firschein (1991), Crawford (1984), and Weymes and Gershowitz (1984). Sampling error was tested using standard methods based upon the size of the sample and the frequency of the gene. Given the observed gene frequencies of HB*S, and the large sample sizes employed in this study, the random sampling error was only 0.0001 (Li, 1961). Thus, it is highly unlikely that the differences in gene frequencies between the two samples of Seine Bight could be explained by random error. The most likely explanation is that Firschein (1961) used a biased sample of females attending a prenatal clinic of the local hospital and that these females had histories of health problems and conceptions associated with the hemoglobinopathies.

## INTERACTION ON THE CELLULAR LEVEL

### Rosette Formation

How do the various protective genes ameliorate the effects of the deadly disease *Plasmodium falciparum*? Friedman (1978) hypothesized that in Hb AS (sickle cell trait) individuals the parasitized red blood cells (PRBCs) would sequester in the blood vessels for a prolonged period of time and would sickle because of low oxygen level and low acidity (pH). The sickling causes the cell membrane to leak potassium, the absence of which kills the parasite. The death and elimination of a proportion of the infecting parasites would give the Hb AS individual's body an opportunity to develop an immune response. However, this model fails to explain why those individuals with the protective genes rarely contracted the more severe cerebral malaria and died.

Recent investigations have revealed that genes for two lethal hemoglobin diseases, thalassemia and sickle cell anemia, when inherited in combination with the gene for normal hemoglobin, protect against cerebral malaria through their impaired ability to bind PRBCs (Carlson et al, 1994). Normally, PRBCs form rosettes with normal red blood cells and adhere to

endothelial cells of the blood vessel. This mass of cells obstructs the blood vessels resulting in tissue damage and eventual death. Individuals with alpha- and beta-thalassemia and HbAS have a diminished capability of producing rosettes. Excessive binding of PRBCs and RBCs is usually associated with cerebral malaria. Inhibition of rosetting is asociated with the small size of the thalassemic red blood cells and with the mechanical properties of cells bearing HbS (Carlson *et al.*, 1994). Scholander *et al.* (1996) have revealed that the binding capacity of PRBCs is influenced by immunoglobulins in the formation of fibrillar strands. Blood group antigen O was found to be associated with significant resistance to cerebral malaria. Thus, antigens A and B are thought to play an active role in the rosetting process (Hill, 1992).

## CONCLUSION

Genetic adaptation to malaria is a complex organismic and populational response based upon numerous genetic systems, the evolutionary history of the population, its social organization, nutrition patterns, and cultural practices associated with the disease. Not only is the hemoglobin type involved in controlling the numbers of parasites, but blood group antigens, adhesiveness of red blood cells, define the probability of survivorship or death. Unique historical events such as admixture or gene flow of resistant genes may accelerate the selective processes. Genetic variation such as in immunoglobulins may play an active role in survivorship. Thus, genetic adaptation of a population is not usually based on a single gene combination but on a complex polygenic/cultural interaction of variables.

The Black Caribs of Central America and the Caribbean represent a unique evolutionary success story. This success was made possible by an exceptional level of genetic variation, a genetic adaptation against malaria, and an appropriate extractive efficiency for this geographical region. The Black Caribs have successfully managed to colonize much of the coast of Central America, numerically expanding in two centuries from fewer than 2,000 persons in 1800 to over 80,000 persons in the 1990s. At the heart of this success is their genetic adaptation to a deadly disease—malaria.

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