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Fava Bean Consumption: A Case for the Co-Evolution of Genes and Culture

OVER THE LAST 15 YEARS MY COLLEAGUES AND I HAVE BEEN investigating the interface between human nutritional needs and the traditional cultural food practices that satisfy the nutrient needs of the individual and the population as a whole (Katz and Foulks 1970). For example, we have studied the interrelations between human biology and culture in the traditional preparation and processing of maize into specific foods by American native populations (Katz, Hediger, and Valleroy 1974). In this work we have developed evidence that the traditional cultural practices encompassing the preparation and processing of maize significantly enhance its nutritional quality. Maize was the major food supporting the growth of Meso-American civilization. Alkali treatment almost certainly facilitated the intensification of maize agriculture, which in turn led to substantial modifications in the organization and structure of Meso-American society. These social modifications ultimately had effects on the demography and the ecology of Meso-American populations and hence influenced their genetic composition. Thus, over many centuries there was an indirect link between the cultural processes underlying the development of this technology and biological adaptability and evolution within these societies (Katz, Hediger, Valleroy 1975).

Although maize preparation practices offer considerable insight into the evolution of cultural practices linked to the supply of essential nutrients, their direct effects on the genetic composition of the population, and hence its biological evolution, have not been amenable to further quantitative analyses. In order to take this biocultural evolutionary approach further, we have been attempting to develop models and hypotheses about how food practices influence specific genetic characteristics. Accordingly, this paper considers and extends our work (Katz 1973, 1979; Katz and Schall 1979) on the cultural factors underlying fava bean consumption and the genetics of favism (a severe hemolytic anemia) in the circum-Mediterranean region. Since the genetic condition under-

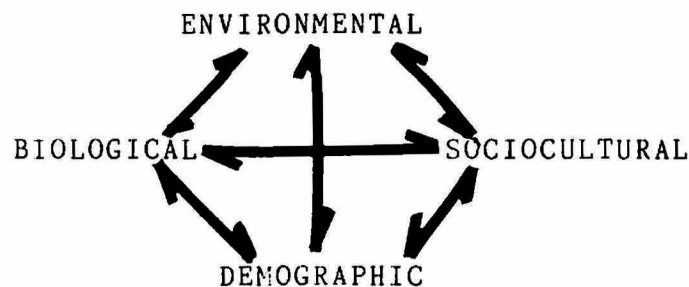
lying favism is already documented, the test case presented in this paper allows for the development of more comprehensive heuristic models that use various human foods to evaluate quantitatively the co-evolutionary interactions between biologically based genetic adaptations and traditional cultural practices.

The consumption of fava beans has been associated with some of the strongest dietary aversions and prescriptions in recorded history. In fact, it is reasonable to hypothesize that there is a direct biocultural evolutionary connection between the traditional aversion to fava bean consumption and its effects on genetically susceptible individuals. To explore and develop this hypothesis, this paper will briefly review some of the salient aspects of biocultural evolutionary theory and then examine fava bean consumption as a test case of some of the important biocultural, ecological, and evolutionary problems confronting the conceptualization of food preferences and aversions.

Food and Biocultural Evolution

The heuristic biocultural evolutionary approach holds that in every human population there is a time-dependent dynamic equilibrium among ecological, sociocultural, human biological, and demographic variables (see Figure 5.1). The

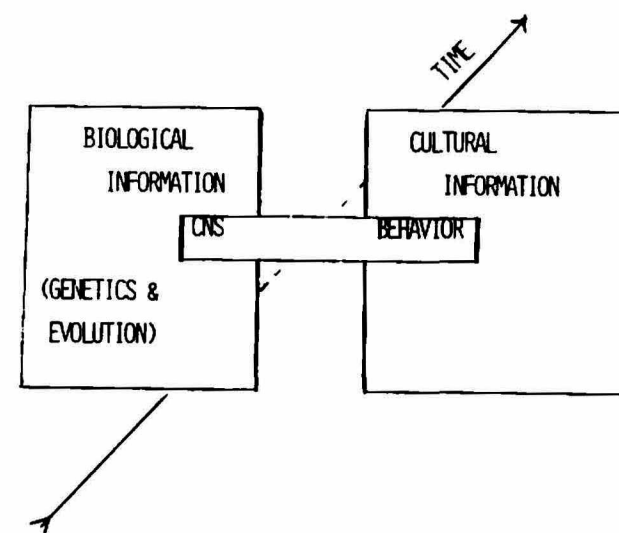
FIGURE 5.1a. The Ecosystems Approach



NOTE: This figure shows the interactions among the following: 1) the biological dimension, which consists of the genetic and phenotypic characteristics of the population; 2) the sociocultural dimension, which consists of the cultural history and the current knowledge or information that is resident in the minds of its members and is accessible to the population as a whole (and includes its material products); 3) the environmental, which includes the non-cultural aspects of the ecosystem in which the population resides; and 4) the demographic dimension, which includes the structure, size, and composition of the population. The interactions are to indicate a dynamic equilibrium where all of the variables are continuously interacting over time and the information content of the system can be continuously changing.

mechanisms of evolution that change the gene pool of a population can also be conceptualized as shifting the genetic "information" pool of the population. Cultural traditions, practices, and knowledge form a "cultural information pool," which complements and supplements the "biological information pool," and these processes of interaction form a dynamic equilibrium over time in any particular ecosystem. This conceptualization of biocultural evolution assists in the testing of hypotheses about the mechanisms of storage, change, and transmission within the biological and sociocultural information pools and particularly about the interactions between the two pools over a wide range of time intervals (Katz and Schall 1979; see also Katz 1973).

FIGURE 5.1b. Information and Biocultural Evolution



NOTE: The mechanisms underlying the evolution of the genetic information changes are understood relatively well, and the mechanisms by which the human central nervous system receives, processes, creates, stores, and sends its information are being successfully investigated. Likewise, there is increasing systematic understanding about the analogous ways in which the sociocultural system develops, changes, stores, transforms, and communicates (i.e., evolves) its information, particularly in response to the needs of the biological system. However, to systematically integrate the knowledge we have concerning evolution of these three interacting systems (i.e., genetic, neurobiological and behavioral, and sociocultural) represents one of the greatest challenges to anthropology. This paper seeks to explore this problem in presenting an integrated approach to the consumption of fava beans, which represents a particularly rich source of data and hypotheses relevant to this topic.

In the context of this broad biocultural evolutionary model, there are some obvious constraints upon the evolution of implicit and explicit knowledge about foods and their consumption within a society. Understanding the full significance and origins of this knowledge could significantly help in our understanding of some aversive food behaviors. Among other factors, we know that there is a biological component accounting for the "fit" between the food consumed and biological needs and processes. These needs can be divided into various categories of nutritional value (such as protein efficiency and related ratios, caloric content, trace elements, vitamins, and so forth). Obviously this fit between food and nutritional value becomes more significant as the food ascends a scale of importance as a source of sustenance within a particular population.

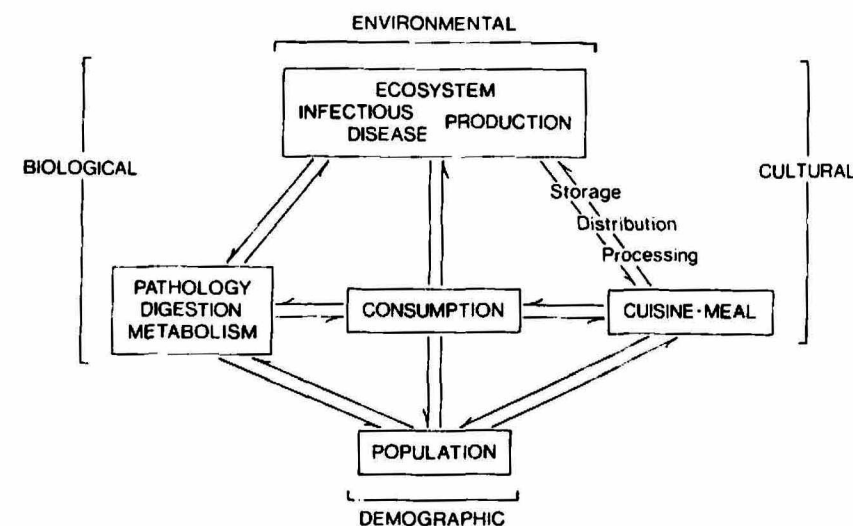
The ecological component is a crucial variable associated with the environmental constraints upon the relative abundance of the food and the ease with which it can be gathered or hunted in the wild state, cultivated, or domesticated. Climatic variables such as rainfall, altitude, sunlight, and temperature, together with soil conditions, all help to establish a possible range of variation. Another component consists of the pharmacological properties of the food. Many edible plants contain highly active toxins, psychoactive drugs, and a wide variety of other compounds whose influence can mimic or even replace the full range of artificially synthesized drugs. Clearly, the special effects of psychoactive drugs synthesized or extracted from plants (e.g., alcohol and coca) must be taken into consideration—for example, their addictive properties. Related to the pharmacological variable is a genetic component, which can limit the fit between populations of consumers and the metabolism and digestibility of the foods they eat. Often the natural constituents of foods contain a factor or factors that may be specifically compatible or incompatible with the genetic constitutions of individuals within the population (Katz 1979).

These biological factors play roles of varying importance in the development and evolution of cultural "knowledge" concerning the processing of food from the raw to a "cooked" state. This leads to several questions about the fit between biological and cultural factors. (1) How close is the fit between the knowledge that accumulates in traditional societies over time and present scientific evidence about optimal patterns of preparation and consumption? For example, to what degree are culturally prescribed food combinations during the same meal or time period nutritionally advantageous? (2) What are the principles by which societies acquire, maintain, and distribute this knowledge of foods over time and space? (3) To what degree is this knowledge about foods linked to other practices within society, and to what extent does it provide an adaptive basis for integrating other aspects of traditional practices, beliefs, myths, and symbols? (4) What are the conditions that favor experimental or nonadaptive uses of foods, whether traditional or nontraditional? (5) What is the nutritional significance of various processing traditions such as heating,

fermentation (with yeasts, molds, bacteria, etc.), sprouting, peeling, drying, mashing, spicing, and the combinations with other foods and chemicals that are associated with the transformation of raw produce into foods? (6) What governs the degree of explicit (as opposed to implicit) knowledge a society accrues about specific foods or food in general? (7) What role do food aversions play in this evolutionary process?

Not only could answers to these and other questions provide the basis for more cogent theoretical developments on the relationship between food and biocultural evolution; they could also have an immediate impact upon our specific understanding of such contemporary human food behaviors as aversions and consumption generally. More theoretically, this kind of conceptualization of the evolutionary feedback relations between and among the elements of the human food chain for any particular population can provide useful heuristic models for the understanding of human ecology. One such conceptualization of the important variables and their relations is presented in Figure 5.2 (see Katz 1982). As our knowledge about any particular food source increases, we can use this kind of heuristic model as a potential resource for formulating addi-

FIGURE 5.2. The Human Food Chain



NOTE: This chain presents a more complex model based on a more detailed development of Figure 5.1a. The dimensions are designed to show some of the relations among the important variables in the human food chain. The environmental, the sociocultural, and the biological are all developed more completely to show the continuity of relationships throughout the chain.

tional questions. The aim of the remainder of this paper is to exemplify the utility of this approach for examining the interface between biological evolution and adaptation and the cultural beliefs and practices that shape human food behaviors, using fava beans as an example of a most unusual, important, and often deadly food resource.

The Distribution of Favism

Fava bean consumption provides a particularly interesting test case, since it involves a genetically mediated sensitivity that has been clearly associated in modern times with a potent food aversion in some populations. In the circum-Mediterranean region, individuals with a sex-linked genetic deficiency of the red blood cell (RBC) enzyme, glucose-6-phosphate dehydrogenase (G6PD) deficiency or Gd^- , are highly sensitive to RBC hemolysis after consumption of fava beans (*Vicia faba*) (Bottini et al. 1970; Katz and Schall 1986; Livingstone 1967, 1973; Motulsky 1965). Usually within several hours, but occasionally up to nine days, after consuming fava beans, hemizygous deficient males and homozygous deficient females can suffer a severe hemolytic anemia (Livingstone 1973; Mager, Razin, and Hershko 1969; Mager, Chevion, and Glaser 1980; Sartori 1971). In approximately 1 in 12 cases in modern times, this anemia can result in death (Belsey 1973; Bottini 1973; Huheey and Martin 1975; Livingstone 1964), and before modern medical treatment was instituted over the last few decades, the mortality rate was probably even greater.

Worldwide Distribution of G6PD Deficiency

Although favism occurs principally in the circum-Mediterranean region (Motulsky 1965), Gd^- is found throughout the tropical regions of the world (Bottini et al. 1970; Katz 1982; Katz and Schall 1986), throughout Europe, northern and equatorial Africa, the southern Caspian region, the entire Middle East, India and southeast Asia, southern China (Canton), Indonesia, and New Guinea. Since hemizygous males all have the full potential for developing anemia upon exposure to various foods, drugs, and viruses, it can be accurately stated that G6PD deficiency is the most common known genetic disorder in the world (Katz, Adair, and Schall; Katz and Schall 1977; Katz et al. 1978; Kirkman 1968; Motulsky 1965).

Livingstone and a number of other investigators have hypothesized on the basis of its semi-tropical and tropical distribution that G6PD deficiency is associated with resistance to malaria (Bienle et al. 1972; Livingstone 1967, 1973; Luzzato, Usango, and Reddy 1969; Siniscalco et al. 1961; Siniscalco et al.

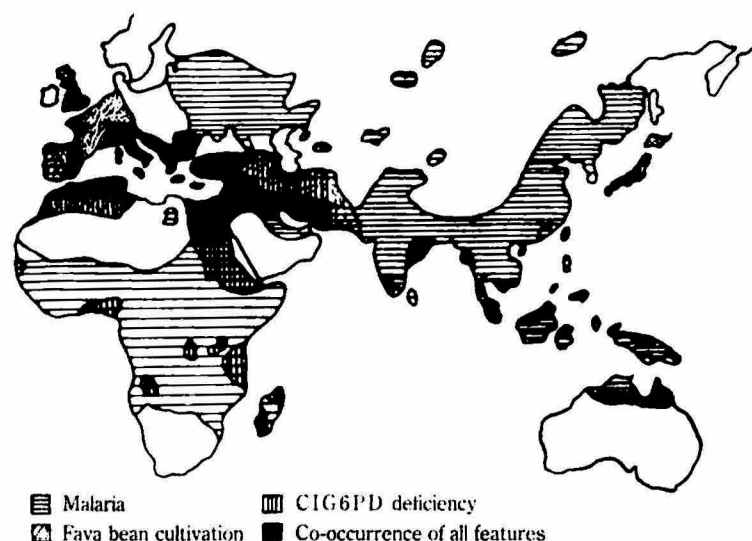
1966). However, it is important to point out that there are at least as many variants of the enzyme as there are of hemoglobin; hemoglobin variants number well over a hundred (L. Luzzato, pers. comm.; see also Belsey 1973).¹ The most common variants are GdB^- , found in the circum-Mediterranean area, which has the least enzymatic activity (0–7 percent), probably accounting for its victims' particular sensitivity to fava bean consumption; GdA^- , found in tropical African populations, with moderate activity (8–20 percent); and $GdCanton^-$, found first in China, also with moderate activity. Elsewhere I have hypothesized that forms other than GdB^- interact with naturally occurring dietary oxidants in their particular ecosystem (Katz and Schall, 1986).

Favism and Malaria

The occurrence of GdB^- gene in those populations that regularly consume fava beans is quite high, with frequencies between 5 and 30 percent regularly reported in the literature (Livingstone 1967, 1973; Luzzato, Usango, and Reddy 1969; Motulsky 1965; Siniscalco et al. 1966). With this high an occurrence of a serious illness, it is highly likely that extensive biocultural adaptations have taken place over the thousands of years since this gene first evolved in the circum-Mediterranean region. My colleagues and I initially hypothesized that regardless of the nutritional value and agricultural productivity of fava beans, the mortality rate from favism would be high enough that other crops would have evolved to take their place. Since, however, their consumption has continued essentially unabated, we reasoned that extensive knowledge would evolve about the sensitivity of susceptible individuals in order to minimize the beans' effects (Katz 1979, 1982; Katz, Adair, and Schall 1975; Katz and Schall 1977, 1979, 1986; Katz et al. 1978). Nevertheless, the evidence that favism is still a major disease throughout the region suggests that this evolved knowledge or "cultural information" was not sufficient to overcome the harmful effects of continued consumption (Katz 1979).

In a further attempt to resolve this evolutionary paradox, we generated another hypothesis that examines the benefits of the continued consumption of fava beans, particularly in view of the presence of seasonal malaria in most of the region. We were impressed by the fact that highly effective anti-malarial drugs such as primaquine also produce a hemolytic anemia in GdB^- (Mediterranean type deficient) individuals. Hence, we reasoned that the mechanism of action of these drugs might be correlated with the effects of fava beans (Huheey and Martin 1975; Katz, Adair, and Schall 1975). In other words, anti-malarial drugs that are potent oxidants may stress the GdB^- RBCs in the same way that fava beans do. Moreover, if this was the case, it was also possible that this response by GdB^- cells accounted for the mechanism by which

FIGURE 5.3. Geographic Distribution of Fava Bean Consumption, Malaria, and G6PD Deficiency



GdB⁻ cells maintained their resistance to malaria. The latter hypothesis suggested furthermore that fava beans could have anti-malarial properties for individuals not susceptible to their serious hemolytic effects. In terms of bio-cultural evolution, this hypothesis suggests that a balance exists between the selective advantages of the GdB⁻ gene in areas with high malaria and the advantages of culturally encouraged consumption of fava beans for GdB⁻ (normal) individuals in the same areas (see Figure 5.3).

We have not yet carried out a definitive field test of the *in vitro* malarial resistance of RBCs taken from individuals with normal and abnormal genotypes before and after the consumption of fava beans in circum-Mediterranean populations. There is, nevertheless, considerable evidence already available that supports the hypothesis that fava beans have anti-malarial properties. These data are presented under a series of biochemical and pharmacological, epidemiological, nutritional and agricultural, population genetic, and cultural headings.

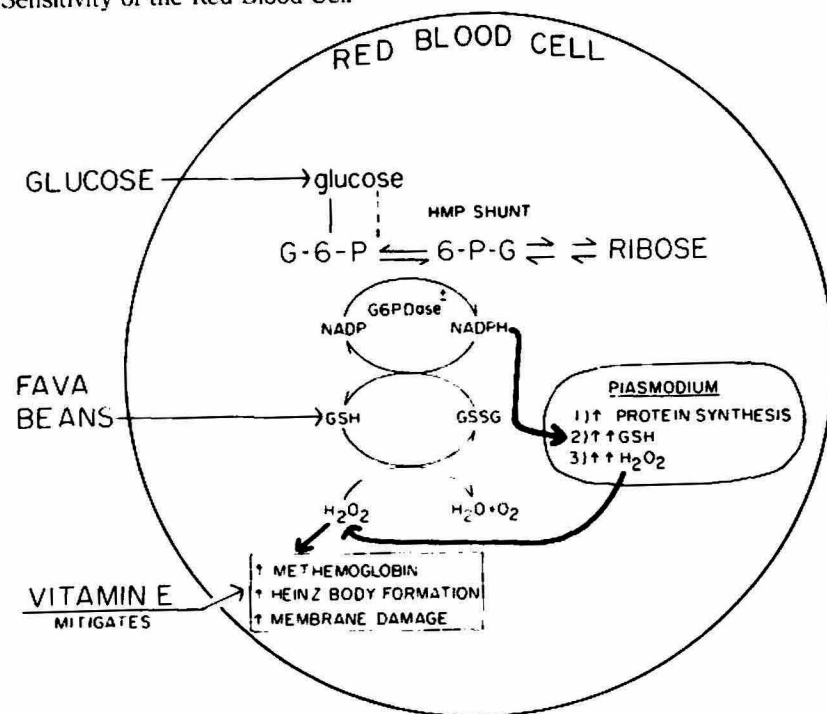
Biochemical and Pharmacological Factors

Recently developed biochemical and pharmacological evidence on the mechanism by which an RBC is resistant to malaria suggests that the intra-erythrocytic stage of the malarial parasite life cycle is particularly dependent on

erythrocytic nicotinamide-adenine dinucleotide phosphate (NADPH) as a source for maintaining high levels of reduced glutathione (GSH) (Crosby 1956; Eaton and Eckman 1977; Eaton et al. 1976; Eckman and Eaton 1977; Etkin and Eaton 1975; Friedman 1978; Sartori 1971). GSH is probably utilized for maintaining the protein synthesis necessary for this phase of the parasitic life cycle (Kosower and Kosower 1970, 1974). As protein synthesis and other intra-parasitic metabolic activities continue, they produce an abundance of hydrogen peroxide, which passes out from the parasite into the RBC. There the hydrogen peroxide is reduced to water and oxygen by a peroxidase enzyme, which requires erythrocytic stores of GSH to function (Liebowitz and Cohen 1968). In the case of the GdB⁻ RBC, the enzyme G6PD has only 1 to 10 percent of its normal activity (Eaton et al. 1976). This is critical, since the G6PD enzyme is the source of the glucose-6 phosphate metabolism necessary for NADPH formation, which is used in turn for the parasite metabolism. This condition results in a considerable decrease of available NADPH for the production of both RBCs and parasitic GSH. Without sufficient GSH to reduce the rapid build-up of hydrogen peroxide (H_2O_2) in the RBC (Liebowitz and Cohen 1968), there is a rapid increase in methemoglobin, Heinz body formation, and subsequent oxidant damage from free radicals upon the membrane of the RBC (Friedman 1978). Several investigators (e.g., Eaton et al. 1976; Friedman 1978; Sartori 1971) have postulated that the added oxidant stress provided by a malarial parasite in a G6PD-deficient erythrocyte is sufficient to result in a rapid build-up of oxidant-induced damage to the RBC membrane, so that it either prematurely ruptures or is sequestered by the spleen. (It is possible that the increased sequestration by the spleen and/or premature rupture of the infected RBCs leads to increased anti-body formation against the early forms of the parasite. This would increase host resistance to the earlier stages of parasitic infection and might provide an efficient mechanism for increased immune resistance to malarial infection; however, this hypothesis has yet to be confirmed.) The net effect is a 2- to 80-fold decrease in the level of malarial infection in individuals with G6PD deficiency (Luzzato, Usanga, and Reddy 1969).

Fava beans have a number of strong oxidant pyrimidines (vicine, divicine, isouramil) (Beutler 1970; Chevion and Novak 1983; Jamalian, Aylward, and Hudson 1977; Kosower and Kosower 1967; Lin 1963; Lin and Ling 1962a, 1962b, 1962c). In addition, they contain other, related compounds, as well as high quantities of L-DOPA (Kosower and Kosower 1967), which can be converted either in cooking or in metabolism by tyrosinase to the active oxidant L-DOPAquinone (Beutler 1970). Fava beans could, therefore, provide a series of strong oxidant stresses on the GdB⁻ RBC. Experiments in our laboratories (Katz and Schall 1977, 1979) and in others (Walker and Bowman 1960) lead to the conclusion that fava beans dramatically decrease GSH levels and, like anti-malarial drugs, produce sufficient oxidant stress to hemolyse the GdB⁻

FIGURE 5.4. Effects of Fava Beans and Malarial Parasitism on the Oxidant Sensitivity of the Red Blood Cell



NOTE: This figure appeared in S. H. Katz and J. Schall, *Favism and Malaria: A Model of Nutrition and Biocultural Evolution*. In N. Etkin, ed., *Plants Used in Indigenous Medicine and Diet: Biobehavioral Approaches*. New York: Redgrave Press, 1986. © 1986 by Redgrave Publishing Company. Reproduced here courtesy of Redgrave Press.

RBC. These findings interrelating glucose metabolism, fava bean effects, vitamin E, the significance of malarial factors, and oxidant stress in the RBC are summarized in Figure 5.4. Furthermore, it is likely that the same oxidant stress occurs in normal, G6PD-sufficient cells, except that the stress is not great enough to allow permanent damage from hydrogen peroxide. However, we hypothesize that the combination of oxidant stress provided by consumption of fava beans and infection by the malarial plasmodium is sufficient to interrupt the normal development of the parasite.

I presented this concept at the Center for Tropical Diseases in Jerusalem. Subsequent research (Golenser et al. 1983) was designed to determine in vitro the susceptibility of G6PD-deficient and normal erythrocytes incubated with and without isouramil, one of the principle pyrimidine oxidants of fava beans. The addition of isouramil decreased malarial parasite growth rates in G6PD-deficient cells, but not in normal cells. In parasitized erythrocytes, the addition of isouramil had direct anti-malarial effects in both normal and G6PD-deficient cells during the trophozoite and schizont parasite stages (Golenser et al. 1983). This evidence helps to confirm our hypothesis at the biochemical level.

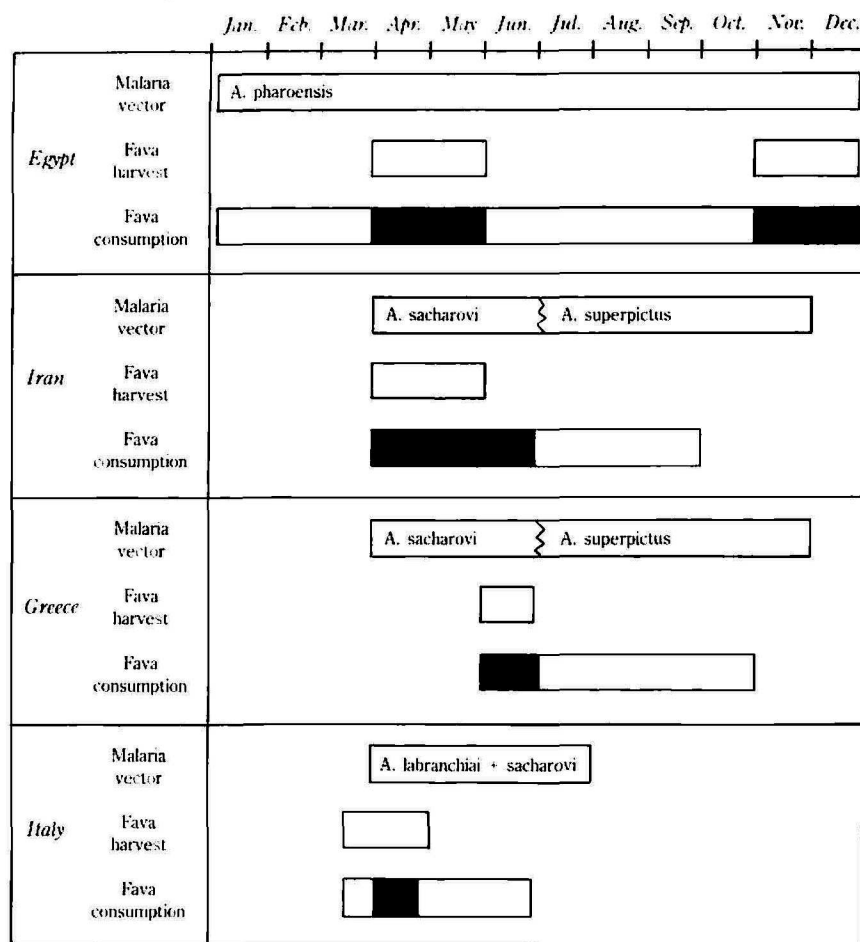
Furthermore, I propose that the anti-malarial effect of fava beans is sufficient to create the kind of equilibrium necessary to maintain a balanced presence of the genetic mechanism (GdB⁻) and a pattern of fava bean consumption in which both factors promote resistance to malarial infections. Additional evidence supporting this hypothesis is the fact that high-level depletion of vitamin E, which normally protects the RBC from the damaging effects of hydrogen peroxide, can result in protection against hemolysis in GdB⁻ individuals (Spielberg et al., 1979). Alternatively, animal studies by Eaton and Eckman (1977) and human studies by Friedman (1978) concluded that vitamin E deficiency allows for a more rapid accumulation of damage to normal cells infected by malarial parasites and a lowering of overall infection rates by intercepting the plasmodial life cycle, presumably in much the same as was in the G6PD-deficient cell. Hence, it is likely that the consumption of fava beans lowers the GSH of GdB⁺ individuals sufficiently to have a net positive protective effect on their resistance to malaria.

Epidemiological Data

We reasoned that if fava beans had some kind of anti-malarial effect on male hemizygous normals and female homo- and heterozygous individuals, then the fava bean should be widely distributed in association with the occurrence of the GdB⁻ genotype and malaria. The evidence on the distribution of all three variables shows a remarkable concurrence among them, suggesting the likelihood of a significant interaction. Moreover, the available data on the season-

ality of malaria and fava bean consumption in Egypt, Iran, Greece, and Italy (Belsey 1973; Katz, Adair, and Schall 1975) indicate a high degree of overlap between the peak season of consumption and the peak occurrence of the malarial vector (see Figure 5.5 and Katz and Schall 1979). Although these epidemiological data could reflect merely the coincidence between the climatic

FIGURE 5.5. Seasonal Variation in Malarial Vectors, Fava Bean Harvest, and Fava Consumption



NOTE: The shaded areas refer to peak consumption periods for fava beans. The ragged lines separating the species of mosquito indicate overlapping seasonal life cycles for these vectors.

TABLE 5.1. Comparative Nutritional Values for Mediterranean Region Legumes

Legumes	% Protein (dry weight)	Protein Efficiency Ratio ^a (cooked legumes)
Chick peas	17.8	2.05 ± 0.10
Lentils	24.0	1.14 ± 0.14
Kidney beans	22.5	1.51 ± 0.22
Fava beans	23.5	1.17 ± 0.17

^aGrams protein consumed, divided by grams of weight gain, in rats.
NOTE: Adapted from FAO Reports on the nutritional contents for legumes (Food and Agricultural Organization, Rome, 1959).

conditions conducive to the spread of malaria and those favoring the cultivation of fava beans, it is unlikely that such a coincidence would be distributed so widely and consistently over the region, particularly if the beans had only negative effects.

Nutritional and Agricultural Potential

Although the epidemiological data show a clear association between the seasonal occurrence of malaria and the consumption of fava beans, this evidence is not conclusive, since the extensive distribution of the fava bean could be explained, for example, by its agricultural and nutritional advantages. In this context it is clear that fava beans are highly suited to many of the environments in which they are grown. Likewise, their nutritional value is in the same range as that of other regionally grown pulses and legumes, which tend to be relatively high in lysine and low in tryptophan and the sulfur-containing amino acids. Hence, while clearly a highly productive crop, their presence is not additionally explainable on the basis of any significant nutritional advantages over other pulses and legumes found in these regions. Moreover, these other regional legumes do not contain constituents that trigger hemolytic crises in G6PD-deficient individuals (Table 5.1 and Katz and Schall 1979).

Population Genetics

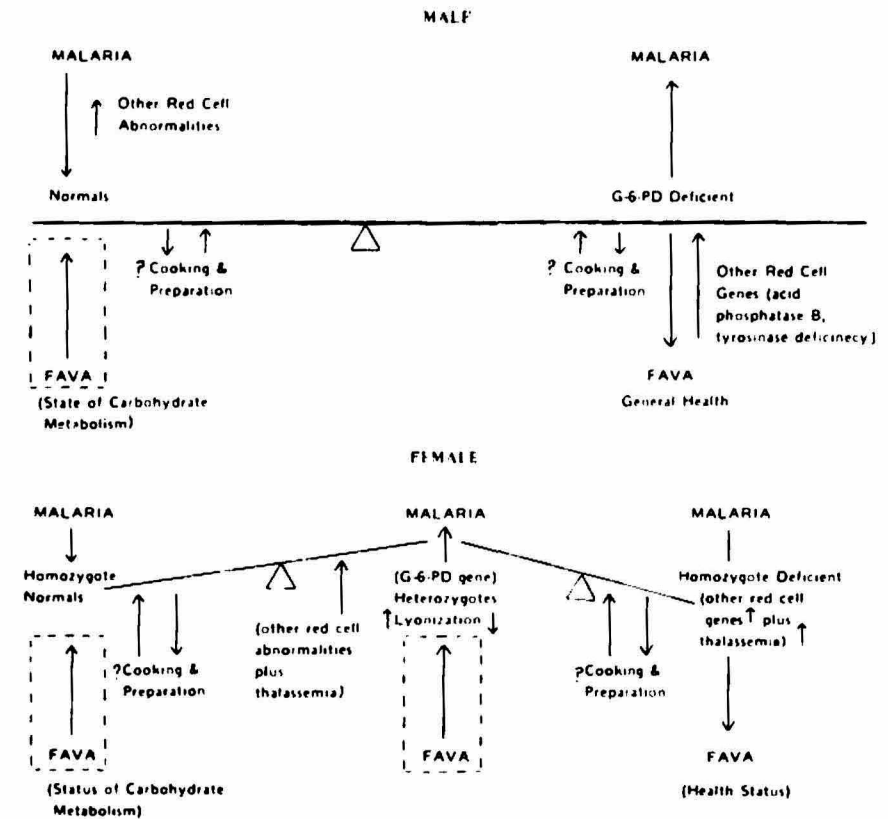
In order to test the hypothesis that fava beans provide selective advantages for the normals of both sexes and heterozygous females and disadvantages for hemizygous deficient males, I carried out analyses of the available genetic data

on population distributions of the GdB⁻ genotype. The usefulness of these rather extensive data is limited by the difficulties in classifying female heterozygotes because of the deactivation of one of the X chromosomes during embryonic development, according to the Lyon hypothesis (Motulsky 1965). The data are also complicated by the fact that other genes for acid phosphatase B (Bottini et al. 1971), thalassemia in females (Carcassi 1974; Friedman 1978), and possibly tyrosinase variation (Beutler 1970) all play roles in mitigating the hemolytic effects of fava beans. Another factor that is likely to be important in the expression of GdB⁻ in females is associated with the onset of adrenarche. Since adrenarche is associated with increased secretion of dehydroepiandrosterone (DHEA), which directly inhibits G6PD activity, it is highly likely that the unusual variation in the age at which favism is prevalent in females is closely associated with this developmental event, which occurs at age six to seven (Katz et al. 1983) and is particularly significant in children with higher body mass indexes (Katz et al. 1985). Since these interactions and other unknown factors tend to limit the data, it is more useful to compare the actual ranges of gene frequencies with various hypothetical outcomes based upon variation in consumption patterns. If we assume that fava bean consumption confers no advantage, then we should see a trend that rapidly proceeds towards a very high frequency of the G6PD-deficiency gene; conversely, if there was a high selective advantage for the consumption of fava beans by normal individuals, the GdB⁻ gene would merely disappear over time. However, if fava bean consumption was somewhat advantageous for the normals and slightly more advantageous for the heterozygotes, which would be the case if fava beans were not consistently available in areas of endemic malaria, then a balanced polymorphism could be maintained in the same range that is widely reported in the circum-Mediterranean region. Hence, the fact that the population genetic data tend to support a balanced genetic polymorphism suggests additional evidence in favor of an anti-malarial effect from fava bean consumption. A more detailed explanation of the population genetics of this phenomenon can be found in Katz and Schall (1986; see Figure 5.6).

The Evolution of Cultural Information

I postulated that if fava beans were consumed over a long enough period of time, the cultural information about them would evolve toward an optimal fit with the cumulative biological effects of the beans. The model would predict a significant growth of cultural mechanisms to prevent the continued consumption of the beans if their net effects were negative. The accumulation of knowledge would proceed to the point where they would no longer be consumed, since danger of death and illness would be correlated with their consumption. On the other hand, if in addition to their negative hemolytic effects on G6PD-

FIGURE 5.6. Selection Models: Favism, Malaria, and G6PD Deficiency, by Sex



NOTE: Males and females are separated to show the differences in selection for this sex-linked gene. The arrows refer to factors that theoretically increase (upward arrow) and decrease (downward arrow) the frequency of the G6PD Mediterranean gene.

deficient individuals, they had some benefit such as promoting "good health" (i.e., absence of disease due to malaria), we would expect to see a mixture of culturally evolved traditions, both prescriptive and proscriptive, governing the behavior surrounding their consumption.

Before the cultural and historical evidence for the pattern of consumption can be evaluated, the time frame of these biocultural evolutionary hypotheses has to be considered. Fava beans were one of the first plants to be intensively gathered by Indo-European populations. Probably coincident with or antecedent any kind of grain cultivation, they are found in association with neolithic pile

dwelling sites in Switzerland and open-air sites in northern Italy, Spain, and Hungary. Even before their human use in Europe, fava beans were established in a range that extended from Persia and the Himalayas to the East and ultimately to the Atlantic coast in the West. There is other evidence of their use in Bronze age Troy and 12th-Dynasty Egypt, and there are many references to them in classical Greek and Roman literature (Andrews 1949; Arie 1959; Cel-sus 1935; Giles 1962; Herodotus 1947; Rowlett and Mori 1970). Currently they are known to extend through China and as far as Taiwan.

Extensive archaeological and historical data allow for a more careful analysis of our hypothesis, since the period of their continuous cultivation and apparent consumption is so considerable. Given this time dimension, it seems likely that had the effects of fava beans been only negative, their use as a human food would have long since disappeared among populations with G6PD-deficiency. Yet it could be argued that no implicit or explicit knowledge ever evolved about their toxicity. This argument, as it applies to the mode of X-linked inheritance (Papavasiliou et al. 1972) of favism, has been made by Giles (1962), who hypothesized that the Indo-European kinship pattern of patrilineality and patrilocality at least tends to preclude the correlation of favism with maternal inheritance in males. That is, the females who carry this X-linked trait to their sons are continually separated out by exogamy from the lineage, which makes it difficult to correlate the illness with family lines. Thus, data about favism could also be used to test hypotheses concerning the ways in which knowledge spreads when knowledge of the disease is carried by women versus men. Presumably women would have observed that their brothers were susceptible to the disease. Therefore, if their sons had the same symptoms as their brothers, it is reasonable to suggest that the women would have drawn some conclusions about the disorder. This knowledge could have given rise to various beliefs and behaviors among women that were different from those of men. A careful investigation of historical data and the roles of women in the transmission of knowledge from one generation to the next under patrilineal, patrilocal, and a partial matrilineal cross-cousin marriage kinship system could yield fruitful tests of hypotheses concerning this aspect of the biocultural evolutionary process.

Although favism as a specifically defined disease was first described in the mid-19th century, it is not clear whether it was known by other names or clusters of symptoms at the folk level. For example, through interviews I conducted in areas of Sardinia with very high rates of favism, I uncovered—contrary to the local medical belief—a well-founded folk knowledge of favism that extended back to the childhood of the oldest members of the community, some of whom were over 70. One distinctly recalled being warned about fava beans during childhood by his grandparents. This suggests that knowledge of the beans' negative effects went back well into the 19th century. Nevertheless, it is

difficult to trace explicit knowledge before the 19th century, and this may also explain why favism was not directly correlated with fava consumption earlier. However, this does not rule out the possibility that earlier prescription or pro-scription of fava beans could evolve without any explicit knowledge of the relationship between bean consumption and favism.

More recently, studies have been conducted to determine whether traditional cooking, processing, and other dietary activities significantly alter the toxicity of the bean for individuals with G6PD deficiency (Belsey 1973; Jam-alian 1978; Jamalian, Aylward, and Hudson 1977). In other words, it is reasonable to suggest that certain appropriate processing techniques may have evolved to decrease the possibility of fatalities from favism. Since there are considerable variations in processing, only two of these pathways will be considered here. However, before considering processing per se, it is important to point out that many, but not all, populations tend to consume the beans raw without any processing. In the event of an impending fava crisis, it is reported that the folk medical treatment of Iran is a high "sweet" diet consisting of naturally occurring sweet foods. This is believed to reduce the significance of the crisis. Indeed, there may be some medical rationale for this prescription, since the increased availability of glucose to a G6PD-deficient individual may provide sufficient saturation with glucose-6-phosphate to optimize the remaining G6PD activity, which is involved in the production of NADPH and in turn maintains a necessary level of GSH (Katz and Schall 1986; Katz et al. 1978). The GSH in turn prevents the toxic build-up of cellular peroxides and thus lessens the probability of a fava-induced hemolytic crisis.

The first step in processing fava beans is soaking. Most ethnic groups studied do soak their dried beans, and it is likely that soaking is sufficient to trigger the first reactions of germination. Although significant changes in the biochemical constituents could result from this germination process, little is known about its effects upon the toxicity of the beans, except that the toxic constituents are partially water soluble and would be discarded with the soaking water. It is known that the sprouting of soybeans, another legume, rapidly eliminates the anti-trypsin protein activity that prevents insect predation. Since the principal mechanism that the fava bean has evolved to protect its seed is the production of pyrimidines, it is likely that germination would produce a significant change in its oxidant activity.

A second widely practiced step in processing consists of removing the skin of the bean. This has been studied by Jamalian and associates (Jamalian 1978; Jamalian, Aylward, and Hudson 1977), who report high toxicity for all parts of fresh mature seeds, but higher activity in the seed coats than in the fresh seed flesh, although the overall toxicity was lower in the dried beans.

Both major processing steps make a difference in the outcomes, and both are widely used. Jamalian and his associates (Jamalian 1978; Jamalian, Aylward,

and Hudson 1977) also report that the GSH levels of the processed beans were lowered by incubation, and that the level remaining was sufficient to avoid spontaneous hemolysis. This raises an important and as yet unanswered question: if the oxidant activity is lowered sufficiently to improve the survival of G6PD-deficient individuals, is it still sufficient to add any protection against malaria in the hemizygous males and homo- and heterozygous females? This question suggests that the model of the relations between fava bean consumption, favism, and the genetic factor requires a separate model for males and females, since males are hemizygous and either have or do not have the gene and the potential for the disease, whereas females have three classes of phenotypes, each with varying susceptibility. If the model also includes the potential interaction with malaria and the effects of fava bean consumption on the genetic frequency of the GdB⁺ gene, then the model begins to take on the characteristics of a more formal quantitative model of genetic change. Elsewhere Katz and Schall (1986) have developed a heuristic model of this phenomenon, which is presented here as Figure 5.6.

Folklore and Fava Bean Consumption

The fact that fava beans have had sufficient time to come to some kind of equilibrium with population groups strongly favors the accumulation of many specific beliefs about their effects. Consistent reports in the classical Greek, Roman, Egyptian, and Indian literature associate them with death (Andrews 1949). Andrews has conducted an intensive study of the ambivalence about fava beans. Although he was unable to conclude which factors besides the flatulence associated with fava bean consumption gave rise to the ambivalence of the belief that the beans were occupied by the souls of the dead, he determined that beliefs about the beans were not associated with some ancient vestige of Indo-European totemism, nor did they stem from some historical accident. The evidence he developed is extensive and relevant to the complex evolution of cultural knowledge about fava beans:

The ancients felt toward beans a mingled respect and dread, a complex of emotions suggested by the Greek term *ἱερὸς*, which apparently was generally applied to an object believed to be charged with some supernatural force, contact with which might be either beneficial or harmful. Today we generally call this mysterious power *mana* in its helpful aspect and *taboo* in its harmful aspect. Beans belonged in the category of objects possessing both *mana* and *taboo*. (Andrews 1949:277)

Such beliefs in turn led to the notion that fava beans had enormous generative power—a power to be avoided by those members of society whose social

functions required avoidance of death and sought by those whose functions were closely associated with death. Andrews has also documented that the ambivalence and controversy surrounding the consumption of fava beans are both ancient and widespread. He was able to accumulate evidence from the Greco-Roman era, ancient Egypt, India, and 19th- and 20th-century Africa. In addition, Rowlett and Mori (1970) have accumulated data for English folklore. These cultural data may be briefly summarized by area and time period.

GREECE

Despite the strong proscriptions against the beans in classical Greece, there is evidence of their continued use and consumption. The strictest avoidance of fava beans there appears to have been practiced by the Pythagoreans. Andrews relates that "the Pythagorean taboo was so stringent that it extended even to treading down the growing bean vine. According to one account . . . Pythagoras, pursued by Syracusan soldiers, could not bring himself to escape by crossing a field of beans, preferring to let himself be taken and killed. According to another . . . some Pythagoreans, fleeing from hostile soldiers, stopped when they came to a bean field in flower and defended themselves to the death" (1949:276).

Bean avoidance extended to other elements of the Greek population as well, although no one at that time seems to have known why the custom existed. Aristotle reported that the Pythagoreans, who were partisans of the oligarchical regime, detested the beans because they were used to cast a vote in elections for magistrates and were therefore a symbol of democracy. Nevertheless, Andrews notes that Aristotle supplied four more explanations for fava bean avoidance without settling on any one of them. Plutarch also offered various explanations, as did Lydus. Arie (1959) hypothesizes that at the root of the Pythagorean aversion was Pythagoras's own G6PD deficiency and possibly some knowledge about favism. What is evident is that although many ancient Greeks continued to eat fava beans, others shunned them, and those that avoided them had a plethora of reasons for doing so.

ROME

Judging from such information as Andrews provides, the prevailing rationale for fava bean avoidance among the ancient Romans was that the beans caused bad dreams. For this reason, Pliny, Diogenes Laertius, and Amphiaraus, a mythical dream interpreter, suggested abstention (1949:285). Plutarch noted that consumption of the beans was associated with increased male sexuality, restlessness, dreams, and flatulence. At the same time, others (particularly physicians) felt that fava beans were a good, healthful food. They were popular with artisans, farmers, builders, and gladiators (1949:281n).

ENGLAND

Rowlett and Mori note the presence of "unmistakable references to the magical effects of fava beans—or at least their deleterious ones"—in English folklore (1970:100). In many bean stories and superstitions, of course, it is nearly impossible to determine the identity of the bean or beans involved; but there are some stories in which the involvement of fava beans is quite beyond doubt. One of these is Ralph of Coggershall's tale of the Green Children, in which children eat beans, turn green (which is diagnostic of favism), and die. Similarly, the identification of fava beans in the Jack and the Beanstalk story is certain, as the beans in the story are very large and the stalk is tall and strong. Other folk conceptions concerning fava beans in England include the popular idea that more cases of lunacy occur when the plant is in bloom than at any other time of the year, a notion among coal miners that accidents in the pits occur more frequently when the bean plants are in bloom, and a general reluctance to have bean blossoms in the house. There is also a saying: "Sleep in a bean field all night if you want to have awful dreams or go crazy" (Rowlett and Mori 1970:101), as well as the idea that eating fava beans can harm one's senses of smell and vision and can be harmful to the blood. Rowlett and Mori suggest that "some of the most persistent English folktales" deal principally with the effects of *Vicia fava* (ibid.).

ANCIENT EGYPT

Andrews (1949:277n) notes the existence of bean avoidance in Egypt, but it is not clear how extensive or stringent the taboo was. Herodotus states that Egyptians would neither grow these beans nor eat them raw or cooked, and that they were so strongly proscribed for the priests that they could not even tolerate the sight of them; yet archaeological evidence and papyrus records at least as far back as the 12th Dynasty suggest their widespread and long-term use as a food and in funerary rites. "There is no doubt," says Andrews, "that a taboo of some kind did exist, and various implausible explanations have been advanced" (ibid.). Here again, we seem to have a situation in which fava bean taboos and widespread fava bean consumption exist side by side in the same society. Currently, fava beans are a major staple food for the vast majority of the Egyptian population.

INDIA

Other evidence for fava bean avoidance comes from Vedic India and the ethnographic present: "A bean taboo imposed on those rendering sacrifice is mentioned in the oldest Indian ritualistic text, the Yajurveda, as well as in the

Maitrayani Samhita and the Kathaka. The Bagdis of central and western Bengal are apparently of Dravidian descent. In the territory of Bankura, where the original caste structure seems to be particularly well preserved, they are divided into nine endogamous subcastes, which in turn are subdivided into exogamous clans or septs. Many of the latter are totemic, for example, the Patrischi or Bean Clan, members of which will not touch beans" (Andrews 1949:277n). Once again, it is my experience that fava beans are still widely consumed in western India today.

AFRICA

Andrews has one short but noteworthy comment on Africa: "Among the Baganda in the vicinity of Lake Victoria Nyanza, the Bean Clan will not eat or even cultivate beans. One of them is said to have eaten beans and died on the spot" (ibid.).

Other Biological Effects of Fava Beans

Fava beans have a considerable concentration of indigestible oligosaccharides, which are digested by bacteria of the lower gastrointestinal tract, the likely cause of the flatulence reported in the cultural data presented above. However, they also contain a high concentration of L-DOPA (approximately 0.25 percent by weight). L-DOPA is a potent psychoactive neurotransmitter that is known to be associated with the other symptoms Plutarch described and is consistent with English folklore. Moreover, the dose of L-DOPA obtained from one or two meals of fava beans appears to be in the range that can be effective in treating Parkinson's disease, which is the principal source of clinical data on the effects of L-DOPA (Jamalian 1978; Jamalian, Aylward, and Hudson 1977). Thus, it is conceivable that beside their agricultural efficiency and nutritional value, their possible psychoactive effects may be associated with their continued consumption. This combination of effects appears to fit well with the Greek word *hieros*, which Andrews (1949) suggested conveys the mixture of dread and respect that was applied to the harmful or beneficial supernatural force associated with the consumption of fava beans. Andrews sums up the magnitude and complexity of the "information pool" that was accumulated in ancient and historic times by concluding that "no plant or animal known to the Indo-Europeans produced a more luxuriant growth of beliefs than fava beans" (1949:290).

Conclusion

The evidence suggests that fava bean consumption throughout the circum-Mediterranean region fits a complex model of interacting biological and cultural evolution. The beans undoubtedly have highly toxic effects for many G6PD-deficient individuals, and hence there is extensive evidence for the development of taboos surrounding their use, particularly in children. In addition, many recipes for preparing the beans lower their toxic effects. However, consumption of the beans has continued since neolithic times, and it is clear that neither the taboos nor the processing techniques have mitigated this problem sufficiently to prevent a high incidence of favism. Even though their agricultural potential in the circum-Mediterranean region is high, it is still difficult to explain their continued use in light of the high morbidity and mortality rates in G6PD-deficient individuals. Hence, the evidence tends to support the addition of increased resistance to malaria as another major factor adding selective advantage to their continued consumption.

Several classes of pharmacologically active compounds in fava beans that appear to be responsible for the favism crisis in G6PD-deficient individuals produce similar increases in the oxidant sensitivity of the RBCs in normal individuals without toxic effects. Various epidemiological and biochemical evidence supports the hypothesis that an increase in RBC oxidant sensitivity as a result of fava bean consumption could lower rates of infection with malarial parasites and, therefore, be highly advantageous (Papavasiliou et al. 1972). If this hypothesis is fully substantiated, it would provide the first evidence that the biological and cultural evolution of disease resistance are linked through dietary practices.

This paper has also attempted to demonstrate the complex interactions between changes in the gene pool and changes in cultural knowledge, which accumulates over time a set of adaptive practices and information about the effects of fava bean consumption. Topics that call for further exploration in light of these cultural data include quantitative aspects of the evolution of the Mediterranean type of G6PD deficiency; folk knowledge of the sex-specific effects of the beans on males but not females, and the folk behavior and beliefs about females as carriers of the potentially lethal condition; and further research concerning the efficiency of folk medical practices for treating favism and the relations of these practices to the anti-malarial potential of the beans. The mechanism of transfer of this folk knowledge from one generation to the next and the roles of rituals and ideologies in this process could provide important clues for the assembly of a more sophisticated model. Finally, fava beans are still very widely consumed, and there is a need to integrate these findings with knowledge of contemporary social, agricultural, and food practices. The apparent net effect of these interactions is a dynamic equilibrium between biological and

sociocultural dimensions, which, I suggest, provides a test case for understanding the co-evolution of genes and culture as it relates to the human food chain.

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Note

1. This wide range of enzyme variants has given rise to several notation systems for G6PD deficiency, such as Gd⁻, which refers to the deficient variant of the enzyme.

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