This is to certify that the

thesis entitled

FAVISM AND G6PD DEFICIENCY IN RHODES, GREECE.
THE INTERACTION OF ENVIRONMENT,
INHERITANCE AND CULTURE

presented by

Deanna J. Trakas

has been accepted towards fulfillment
of the requirements for

Doctorate degree in Anthropology

Major professor

Date 2/21/91

O-7639

# FAVISM AND G6PD DEFICIENCY IN RHODES, GREECE. THE INTERACTION OF ENVIRONMENT, INHERITANCE AND CULTURE

By

Deanna J. Trakas

A DISSERTATION

Submitted to
Michigan State University
in partial fulfillment of the requirements
for the degree of

DOCTOR OF PHILOSOPHY

Department of Anthropology

1981

# ABSTRACT

## FAVISM AND G6PD DEFICIENCY IN RHODES, GREECE. THE INTERACTION OF ENVIRONMENT, INHERITANCE AND CULTURE

By

Deanna J. Trakas

Fava beans are cultivated in most areas of rural Greece even though their consumption is associated with the acute hemolytic crisis diagnosed as favism. This reaction occurs in some, but not all, individuals with a reduced activity level of the red blood cell enzyme, glucose-6-phosphate dehydrogenase. The interaction between this genetic trait ($Gd^-$) and culturally influenced behavior makes favism an interesting problem in epidemiology and preventive medicine. The findings of this study, conducted on the island of Rhodes, Greece, illuminate the epidemiological characteristics of favism and address the interests of preventive medicine.

Screening results for the $Gd^-$ trait in boys, aged seven to twelve, from seven villages revealed an average frequency (26%) compatible with earlier studies on the island. Even though this average is very high, and fava beans are grown and consumed on the island, the annual average frequency of favism (1966-1978) is only 0.16 per thousand. Differences in micro-regional $Gd^-$ frequency and consumption of fava beans, as well as other socio-economic and behavioral factors suspected to contribute to the low favism

frequency were examined during ethnographic field work conducted in two villages. Both villages were similar in size; one was a mountain location, the other coastal. They differed in $Gd^-$ (43% and 27%) and favism frequencies (nine and two cases).

The distribution of land-holdings, necessitating daily and seasonal movement through a variety of eco-niches, and patterns of village endogamy and residence preferences after marriage, promote differences in the distribution of the $Gd^-$ trait in Rhodes which is not necessarily related to the physical environment; the inverse relationship between altitude and trait frequency, reported in the literature, was not observed in Rhodes. Health and fertility histories comparing $Gd^-$ individuals with their non-trait counterparts indicate that the trait may be selectively neutral.

The regional and seasonal distribution of the 123 favism episodes reported in Rhodes during 1966 to 1978 is in agreement with earlier studies. Yearly fluctuations in favism frequencies appear to be associated with the interaction between the timing of Easter and the harvest of fava beans. Village locations at the highest altitudes reported the greatest number of total favism cases, with coastal villages reporting a longer favism season each spring and an earlier period of peak cases. For every adult case of favism, nearly two (1.7) pediatric ones were reported, with the female to male ratio (1:1.4) more nearly equal than reported elsewhere.

According to eighteen case histories (10 boys : 8 girls), children under six did not report hemolytic signs any earlier than their older counterparts, and 80% of the episodes in the 0-5 age cohort presented additional symptoms other than the hemolytic signs alone. The majority of these cases were associated with fresh fava beans which had been consumed outside of the household.

In popular usage, the word favism is replaced by the phrase, "poisoning from fava beans." This neatly implicates only the fava beans, associates favism with other types of food poisoning and ignores the stigmatizing effect of having a familial disease or a blood deficiency. The emphasis on the genetic trait involved in the biomedical etiology of favism requires that the individual, and even the entire family line, share in the blame for the hemolytic crisis. Food sharing cements social relationships in Greek society, while the presence of fava beans in the home during the Lenten period show that the family is observing the fast. Avoiding the beans, in the name of preventive medicine, may affect the family's or individual's social relationships and community position.

Dedicated to

Woodaki

## ACKNOWLEDGEMENTS

The field research for this study was made possible through funds from a Michigan State University Biophysical Research Grant, the National Science Foundation, and the Wenner-Gren Foundation for Anthropological Research. At the Institute of Child Health in Athens, Greece, Dr. Spiros Doxiadis, President, and Dr. Stephanos Pantelakis, Director, were instrumental in obtaining permission for the research project and appropriate assistance for the hematological screenings. The hematological tests were conducted under the auspices of Dr. Aris Karaklis, Director of the Hematology Laboratory at Aghia Sophia Children's Hospital, Athens, Greece. The blood samples in the villages of Rhodes were collected with the help of the agrarian physicians serving their internship requirements and assigned to the different localities by the Ministry of Social Services, Dodecanese Islands, Greece. Mary Basilakis, registered midwife, was among the several medical professionals who assisted in the rural areas of Rhodes by providing advice and a sympathetic ear during the many phases of the field work.

Dr. Joseph Spielberg, Professor of Anthropology and Chairman of my Dissertation Committee, never seemed to tire as he provided continual challenges during the review and analysis of field data. Throughout the writing of this dissertation, he refused to allow me to lose sight of the goals of anthropological inquiry. Dr. John Hunter, Professor of Geography and Co-Chairman of my Dissertation

Committee, helped me to develop the methodology (and courage) to investigate a subject which heretofore had been reserved for medical scientists, and, was ever-constant in his clear and constructive criticism. Dr. Arthur Ruble, Professor of Anthropology and Member of my Dissertation Committee, gave me insights into the merits of social epidemiology and ethnographic information, helping me to place this study in larger context. Dr. Cheryl Ritenbaugh, Assistant Professor of Anthropology, helped with the technical parts of the dissertation devoted to population genetics. Dr. Anne Millard, Assistant Professor of Anthropology, graciously reviewed these parts in the final draft. Dr. Bernard Gallin, Professor and Chairman of the Department of Anthropology, provided me with his steady and foresighted knowledge of the discipline of Anthropology. It has been a pleasure knowing and working with these people.

The manuscript was prepared by Merrilyn Wenner, and David Brown attended to the graphics. They both added their expertise to the format of the completed work.

My parents, John C. Trakas and Virginia Niendorf Trakas, supported me throughout all the stages of this study. They were all and more that a daughter and student could desire. If it had not been for their value of education and knowledge, I would not have completed this dissertation. My brother and sister, Charles and Victoria Trakas, allowed me the privilege of sharing my ideas with them, even though I am sure that they preferred to talk about their own interests. Finally, my son, Woodaki White, is most certainly unaware of how much he contributed. Through the trials,

tribulations and travel involved in this project, he kept me going by giving me his child's-eye-view of another culture.

To all these people, and the people of Rhodes, Greece . . . Thank you.

TABLE OF CONTENTS

Chapter IV (Con't)

Chapter V (Con't)

LIST OF TABLES

## LIST OF FIGURES

# INTRODUCTION

Seeking to purify their bodies and psyches, the Ancient Greek Pythagoreans developed a list of taboo foods. Among these were the large unusual-looking fava beans (*Vicia faba*) which have since become identified in the biomedical and biochemical etiology of acute hemolytic crises. This reaction to the fava beans, named *il favismo* by Italian physicians in the late 1800s (e.g., Mina la Grua 1856 cited by Sansone et al. 1958; Gasbarrini 1915) is characterized by Rene Dubos in the following quote:

> Favism, an anemia that occurs in some persons when they eat fava beans, can be regarded as a symbol of the manner in which environment and genetic endowment constantly interplay in all manifestations of life. As far as is known, the only persons who suffer from favism are those who genetically have erythrocytes susceptible to the constituent of the fava bean which brings out the anemia. In this case, the culprit is a recessive gene that causes a reduced activity of glucose-6-phosphate dehydrogenase. The affected persons are essentially normal unless they consume fava beans. (DuBos 1965:1947-8)

The mother of a young boy from Rhodes who had been stricken with the hemolytic crisis presents another picture:

> Several years ago, when my son was younger, he went to stay in the other village down the mountain. We have relatives there. Someone gave him fava beans to eat, and soon after, he started vomiting. Then he became yellow and his urine turned black. We took him to the hospital where he was given blood transfusions. We don't have anything inherited in our family that would make him become sick like that. You won't learn anything from writing down our family tree -- he simply ate bad beans. Maybe some people get sick from fava beans because they have something -- some deficiency in their blood, but not our family.

> The beans were spoiled, that's all there is to it.

In these two statements, all the elements for a multifaceted investigation are present. This thesis is the result of field research in rural Rhodes, Greece, about favism. Why the subject of this hemolytic crisis which affects primarily Mediterranean populations would appeal to an ethnographer should be apparent in the contrasting statements, one by a medical physician, and the other from a mother of a favism victim. More than the interaction of inheritance and environment, as DuBos suggests, there are several contrasts represented in the hemolytic phenomena of favism:

TABLE 0.1

CONTRASTS IN NATIVE VERSUS BIOMEDICAL EXPLANATIONS OF ILLNESS AND DISEASE

| | |
|---|---|
| fear, superstition | scientific knowledge |
| popular etiology | biomedical etiology |
| illness, a socio-cultural concept | disease, a biomedical concept |
| preventive behaviors | preventive medicine |

It might be noted that the column on the left in Table 0.1 lists topics of interest to anthropology (e.g., superstition, behavior) and on the right, topics of concern to medical science (e.g., scientific knowledge, biomedical etiology). It is no mistake that they are listed in opposing columns. These contrasts are deliberately set forth here as a heuristic device to generate a polemic which will become increasingly apparent during the following chapters of the thesis. Many have commented on the shared interests of the medical and social sciences, and on the possibility for collaborative efforts between the two disciplines (e.g., Cassel 1964; Engle 1960; Kleinman 1973; Polgar 1962). In basic assumptions and goals of research, the social and medical sciences do not simply represent two disciplines, but two different paradigms and sets of goals. Medical science attempts to explain disease: social science, to explain behavior. These differences are not limited to the theoretical level alone; they permeate the operational levels in the development of research strategy and methodology. These differences become increasingly played out in medical anthropological studies, of which this present thesis is one.

The biomedical paradigm includes at least the following parts: (1) a reliance on the scientific method, (2) a concern with the identification of pathogenic, genetic and/or possibly adaptive factors which contribute to the pathway of disease causation, and (3) the identification, control and eventual eradication of disease as the motivating force behind research. Preventive medicine as well as therapy grounded in scientific knowledge and disease etiology is included in the third dimension of the paradigm. All the points of contrast mentioned in Table 0.1 are present in this description: i.e., scientific knowledge, biomedical etiology, emphasis on disease as a deviation in the somatic norm, preventive and therapeutic medicine. Preventive medicine is distinguished from preventive behaviors; the latter may or may not be grounded in biomedical principles. In the search for causes, ecological and/or epidemiological approaches may be used. This has helped support the suggestion that social and medical sciences can and should collaborate.

Describing illness behavior requires the use of a separate paradigm, one which stresses subjective experience and cultural influences on behavior (e.g., ideology, social sanctions, ecological and economic pressures). The ethnomedical paradigm developed out of these behavioral and cultural concerns, and is usually classified as a branch of ethnoscience and cognitive anthropology. In its strictest application, (e.g., Frake 1961), biomedical concepts are ignored and the native etiology, explanations, categories and descriptions of symptoms are analyzed. The analysis may stop once a single illness has been explained on these terms, or it may continue by using the illness categories, illness behaviors, and so forth, as ways of illuminating the culture. This is analogous to other anthropological analyses which may use, for example, the kinship system to explain the way people calculate kinship relationships and responsibilities, or to explain something else more basic to the entire culture. The early studies of health and disease conducted by anthropologists (before "medical anthropology" became a separate sub-discipline), approached this goal more than some of the more recent studies. For example, the studies of witchcraft, the evil eye, spirit possession, and body concepts, which reflected the social structural and ideological reality of a cultural system, were more clearly anthropological studies than they were medical. For lack of a better or more precise term, I refer to these types of studies as ethnomedical, as well as those which embrace the more narrowly defined methodological parameters of ethnoscience. In this definition, the ethnomedical approach involves two facies: (1) the use of ethnographic information to illuminate illness behavior; and (2) the use of illness behavior to illuminate ethnographic (cultural, social, economic, ideological) data.

In this discussion of ethnomedicine, the word "illness" has been preferred over "disease." Medical scientists have often interchanged the two terms, but social scientists interested in socio-medical studies have preferred to differentiate between them. Disease is a category created by biomedical diagnostic procedures; it is a product, and in fact, a necessary part of the biomedical model. Illness is a creation of the socio-cultural system; it may have meaning which is limited entirely to that sphere, or it may resemble the disease category used in the medical system. The latter is the case in Western, industrialized societies. When speaking of the biomedical model, it is more appropriate to use the term, disease. The term illness is reserved for use with ethnomedical, sociological and/or culturological studies which focus on behavior.

Returning to the Table 0.1, the next question is whether or not it is possible to bridge the two columns with yet a third model which would allow medical sciences to collaborate on an inter-disciplinary basis. DuBos suggests that since both the medical and the social sciences are essentially human sciences, collaboration should be easy to achieve. During the time of Hippocrates, the interaction of the environment and the psycho-social dimensions of the human experience played an important role in the theory of good health and in the diagnosis and treatment of illness and disease.

With the evolution of cosmopolitan medicine and the development of increasingly sophisticated technologies for the identification and treatment of disease, these other dimensions became overlooked if not neglected altogether. The need for the reintegration of the earlier holistic type of disease theory has been emphasized by contemporary medical and social scientists (Engle 1977). They stresss the ecological, open-model approach to disease and health (Gordon 1966; May 1960). In such a model, the interaction of environment and adaptation through both genetic inheritance (e.g., Alland 1968 and 1970; Harris 1970) and culture (e.g., Fenner 1970; Hughes and Hunter 1970) would be included. Others suggest that social epidemiology as a methodological perspective can speak to the interests of both disciplines. Social epidemiology, an outgrowth of descriptive rather than analytical epidemiology, was introduced to the social sciences through the work of Cassels (1964) as a potential bridge between the two disciplines. Here, various social structural and social demographic variables such as occupation, education, family size, etc., were taken into the model of disease causation. Later, Kleinman (1973) stressed that at least two dimensions, the biophysical and the socio-psychological, were involved in disease phenomena, and therefore, the model needed expanding to include the socio-psychological. Although using behavioral and socio-cultural variables, all of these approaches focus on explaining disease. As such, they fall within the biomedical, not the ethnomedical, paradigm.

An outstanding demonstration that ethnographic details could help explain disease resulted from the series of research efforts about the neurological dysfunction of the disease called Kuru in New Guinea (e.g., Fisher and Fischer 1961; Alpers and Gadjusek 1965; Zigas 1970). This success gave impetus to other anthropologists hoping to show that ethnographic data was invaluable in medical studies. This also played a role in initiating the present study about favism, and it was hoped that such a study would bridge the two paradigms. In retrospect, this is considered to be a premature and perhaps naive expectation. Even though this research is not a medical study, it is fully within the biomedical paradigm. This is, of course, not the first time that this has happened in medical anthropology, and, in fact, may be a major dilemma which faces the sub-discipline.

Fabrega (1974) writes that the inability of most socio-cultural research about disease and health to leave the parameters of the biomedical paradigm is not unique to only a few studies. Even though the terms "ecological" or "socio-epidemiology" may be substituted for the term biomedical, the framework for these studies is still biomedical. He states that (1974:46) "....the ecological framework or approach has always been an inherent feature of medical epidemiology and that distinguishing between the two is somewhat arbitrary." In this model, the individual is not considered as an active agent in the epidemiological variables, but merely as a passive recipient of particular ecological forces. "... the way disease may affect the quality of social life is not explored, nor are the people's ways of responding socially to the disease considered relevant." (ibid.) The fact that epidemiological and/or ecological approaches to behavior and disease result in serving the interests of biomedical science in their goal to explain disease rather than behavior, is dramatized by Fabrega (1974:47):

> Particularly important is the fact that medical studies of this genre (that is, what I have termed epidemiological and ecological) tend to disregard the perspective of the actor, the rules and the values of the people, the meaning that illness has, and the way subjects orient and respond to illness or disease occurrences. The principal questions tend to be causal, and consequently the disease itself (that is, its occurrence, prevalence and incidence) is seen in the context of the (correctionistic) goals of Western medical science which are to control disease.

These are the contradictions which repeat themselves throughout this thesis, particularly in the last two chapters. From what has been said of the two disciplines, the medical and the social, it does not appear that collaboration is a possibility. The two approaches, the biomedical and the ethnomedical, have been discussed here to clarify that this thesis is not an attempt to bridge the two paradigms: it uses ethnographic and ethnomedical data in the service of the biomedical model. I believe it clearly shows the strengths and weaknesses of using this type of approach, and illustrates how culturally influenced behaviors and beliefs contribute to the epidemiology of favism. It does not attempt to show how favism can be used to understand Greek rural culture and society, even though in the course of studying favism, certain cultural traits were emphasized. From its original conception, the research was designed to supplement and expand the biomedical and clinical findings about favism. Some of the questions posed in the early stages of the study remained in the forefront throughout all phases of the research project.

For example, these questions were asked:

1. Is the G6PD deficiency ($Gd^-$ trait) adaptive, or does it appear to have neutral selection?

2. How many individuals with the $Gd^-$ trait actually report episodes of favism?

3. What are the general patterns of fava bean cultivation and use?

4. How do the standard epidemiological variables referred to in the literature (e.g., age, sex, season, region) relate to the Rhodian samples?

5. Are there any preventive behaviors, folk lore, and so forth, which relate to fava beans?

Through the review of the scientific and biomedical literature about favism in Chapter One, the lack of ethnographic data from situations outside the clinical setting is exposed. Chapter Two discusses the concerns involved in developing a research strategy which can facilitate the collection of ethnographic information and which is able to meet scientific standards. The physical, historical and contemporary social setting of the field work site, which is standard for all ethnographic research studies, is described in Chapter Three. Chapters Four, Five and Six present the data collected during the field work, showing the continual interaction between behavior and the epidemiological characteristics of favism. Chapter Four presents the results of the screenings for the G6PD deficiency ($Gd^-$) in Rhodes and discusses the applicability of various hypotheses to account for the distribution of the trait. Chapter Five takes the major epidemiological variables used in the literature, compares them with the distribution of favism in Rhodes, and shows where ethnographic data can be used in refining these variables.

In the last chapter, the question of fava bean consumption and preventive behavior is discussed. This has implications beyond the scope of the thesis, emphasizing the need for behavior oriented explanations when seeking answers to questions related to prevention. The organization of the chapters in this way enables the reader to move from the level of scientific knowledge and biomedical etiology (in Chapters One and Three) to popular etiology and preventive behaviors in Chapter Six. In this way, the bridge between the ethnomedical and the biomedical approaches is not fully constructed, but merely suggested.

## CHAPTER I

## OTHER STUDIES ABOUT FAVISM:
## MEDICAL ETIOLOGY

This chapter reviews the scientific and medical research which has been published about favism and the models which were used in analyzing the data gathered during the present study. The existing studies about favism generally fall into two categories; (1) the etiological and (2) the epidemiological. These are not necessarily mutually exclusive, but represent an arbitrary division which serves as a heuristic device in examining the state of research about favism. In etiological studies, favism is examined in order to describe its pathology and/or its biochemical etiology. The early studies of this type attributed the disease to a principle of contagion, which also fit with the seasonal epidemics of favism which occurred during the spring. Later the disease was explained as an allergic reaction of some unknown cause. During this time, research was directd by concerns for diagnosing, prescribing therapy, giving a prognosis and identifying the "causes" of favism.

With the identification of the red blood-cell enzyme, G6PD, in a deficient or partially deficient form as an etiological factor, research mushroomed with respect to the biochemical and genetic nature of the enzyme. Simultaneously, research focusing on the hemolytic action of fava bean extracts also accumulated. These identified the fava bean as a hemolytic agent, although the specific hemolytic chemical in the bean could not be isolated. Both approaches represent examples of the etiological model where causation is discussed in terms of principles of biochemistry of either the bean or the affected blood. Epidemiological studies have generally focused on the distribution of etiological factors, particularly the $Gd^-$ trait (the G6PD enzyme deficiency), rather than on the distribution of the disease itself. For example, the distribution of the disease is often described by using age and sex variables which are related, in turn, to the distribution of the $Gd^-$ trait. These are not examined as to how they might be related to fava bean consumption, or to other aspects of the disease such as the presentation of symptoms of ways of reporting episodes.

## Etiological Models and Favism Research

Studies of favism which are guided by etiological concerns can be divided into three groups: (1) those which were conducted before the enzyme deficiency was identified as an important factor in the etiology of favism; (2) studies which analyze hematological characteristics of the enzyme deficiency; and (3) research which aims to identify hemolytic properties of the fava bean. The early studies about favism succeeded in standardizing the diagnosis of favism. Since jaundice can result from a variety of diseases and conditions (i.e., it is not a disease in and of itself), it was important to separate the jaundice which occurred in favism, from jaundice which was associated with any number of other diseases. The emphasis was on developing an understanding of the pathology of favism in order to define a syndrome of hemolytic anemia were caused by exposure to a deleterious agent. Hematological studies of the enzyme deficiency, and biochemical research concerned with the hemolytic agents of the fava beans, accumulated after the G6PD enzyme had been definitely linked with fava bean extracts under laboratory conditions.

## Early Ideas about the Etiology of Favism

It is not clear from the research whether or not favism, as a biomedical disease, actually existed in the ancient populations of the Mediterranean where it is now so prevalent. As stated in the Introduction, many different Mediterranean peoples had taboos, or at least exercised caution, regarding their consumption. It is not clear if these resulted from the recognition of the hemolytic properties of the beans, or from other, possibly symbolic, reasons. For example, it is not clear if the Pythagorean warnings about eating fava beans were based on the symbolic properties of the beans, a philosophy of good nutrition, or due to observed hemolytic reactions to the beans. In ancient Egypt and Rome, the beans were considered to be unfit for consumption by the upper classes. Perhaps this had to do with the association of the beans "... with a certain coarseness of habits, presumably because of their proverbial flatulence-inducing properties" (Donoso et al. 1969:513). It is also said that Egyptian priests were not allowed to eat the fava beans. The reason for the taboo might have been symbolic as well as practical. These early cautions about the beans do not include reference to jaundice as a result of eating the beans; therefore, it is possible that these taboos represent symbolic and/or social meanings rather than scientific observations. Only in an old Portugese proverb is the reason for avoiding the beans at all similar to the biomedical one. In the proverb, people with a weak liver were warned to avoid passing through a fava field (Flatz and Duren 1967).

Early references to favism and/or the fava bean are difficult to isolate from a general bulk of writings which discuss several illnesses associated with beans, legumes and pulses. Hippocrates wrote about an illness, since labeled "Lathyrism," which affects the lower limbs with paralysis after the ingestion of the legume *Lathyrus sativus* and possibly *Vicia sativa* (the latter in the same genus as fava beans). In the 1850s, the "vegetable disease" was said to affect Italians after the consumption of certain beans, legumes, and possibly other greens (Mina la Grua 1856, cited by Bottini 1973). Whether or not some of these diagnoses included instances of favism is not clear, although certainly possible.

References to favism as a distinct disease are first noted in Italian sources. Montano (1895) postulated that some hereditary factor operated in cases of *il favismo* which were found in the Italian population. Later, Gasbarrini (1915) published a relatively complete description of favism, considering the time during which he wrote. Fava beans were implicated in the cases of hemolytic anemia and hemoglobinuria reported by Gasbarrini, and he also suggested that certain drugs might bring about similar reactions. He divided the progression of the illness into five different states; individuals may suffer from one or all of the states. The most grave form resulted in death, while the light hemolytic reactions eventually stabilized themselves without therapeutic intervention. The grave form of favism was described by Gasbarrini to involve signs of recovery from the hemolytic crisis followed by a sudden relapse; this is a major danger of the disease today.

Several years later, the term "Lederer's anemia" was applied to conditions of unexpected, spontaneous hemolytic crisis, suspected to be both contagious and associated with the diet. Some (e.g. Belsey 1973) have speculated that this condition was actually favism, but went undetected because no one inquired about the consumption of fava beans. Fear of the fava beans was still considered to be little more than a peasant superstition.

In the 1940s, the disease began to be characterized as related to some unidentified blood condition, similar to that which would cause allergic reactions to fava beans (Luisada 1941; Carcassi 1958; Kantor and Hoch 1961; Kantor, Pinkhas and Djaletti 1962). An allergic pathology, it is noted, was given credit for the disease for approximately twenty years.

By the 1950s, it was noted that the "sensitivity to fava beans" (Sansone and Segni 1957) and the hemolytic anemia which followed their consumption was strikingly similar to that occurring in American Blacks after exposure to or ingestion of certain antimalarial drugs (Beutler 1954a and b; Browne 1957; Carson et al. 1958). Those suffering hemolytic anemia after exposure to these drugs were known to be affected by the G6PD enzyme deficiency (or the Gd-trait). The hemolytic conditions so closely resembled each other that the enzyme deficiency was suggested as the blood trait for which scientists had been searching. Subsequent studies of the effect of fava bean extracts on G6PD-deficient blood cells clearly established this association (Mela and Perona 1959). Following this discovery, earlier theories about favism as an allergic reaction were abandoned, and research emphasis became directed toward diagnosing the disease on the basis of the deficiency and fava bean consumption.

Since the identification of the enzyme deficiency as the major predisposing factor in favism, research about the $Gd^{-}$ trait has accumulated much more rapidly than studies which suggest that other factors potentially involved in favism should be investigated. An Italian scientist, Sartori (1971) advocates a multicausal etiology of favism which gives less emphasis to the deficiency as a primary cause. He contends that the deficiency contributes only to the "... hemolytic course of the disease among individuals bearing the autosomal favic predisposition or its phenocopy" (1971:462). That is, favism has two diatheses, one hemolytic, the other not hemolytic. Individuals with a favic predisposition and the deficiency suffer from clinical hemolytic favism. Those who have only the favic predisposition also suffer from reactions to the fava bean, but do not present hemolytic symptoms. The diagnosis of favism which requires both the deficiency and hemolytic anemia to be present is considered to be clinically severe and *a priori*. This diagnosis promotes the false assumption that favism must always involve the dramatic hemolytic symptomology.

Sartori proposes that a milder form of favism exists which does not entail the hemolytic crisis. In Sardinia, he found that in nineteen cases of favism among male subjects, only one showed a positive identification of the enzyme deficiency; the other eighteen did not "have" the enzyme deficiency on the basis of scientific testing. On the basis of this study, Sartori claims that it is possible for favism to occur in the absence of the enzyme deficiency, but that severe hemolytic favism is never encountered without the deficiency. It is the latter type of favism which reaches hospitalization; the milder forms do not, and go unnoticed in the scientific studies of the disease.

> The erroneous opinion which identified G6-PD deficiency with a predisposition to favism arises from this indirect connexion between the enzyme deficiency and the number of patients admitted to hospitals. In reality, strong G6-PD deficiency only causes the hemolytic course of the disease among individuals bearing the autosomal favic predisposition of its phenocopy. (Sartori 1971:465)

## The G6PD Enzyme Deficiency
## ($Gd^-$ Trait)

The G6PD enzyme (glucose-6-phosphate dehydrogenase) is normally active in the red blood cells of the circulatory system. A reduction or deficiency in the level of the enzyme activity is not considered pathological in itself (i.e., it is not classified as a hemoglobinopathy), but it places the individual at risk of developing hemolytic anemia following the ingestion or contact with certain hemolytic agents. These agents include aspirin, many anti-malarial drugs, napthelene, vitamin K, sulfa derivatives, and *Vicia faba*. The deficiency is controlled by a sex-lined genetic trait. Males are always genotypically hemizygous; they carry the trait on their one X chromosome. Females may have the trait on both chromosomes (homozygous) or on only one (heterozygous). When only one X-chromosome is affected, phenotypic expression of the deficiency vary from definitely deficient to nearly normal in terms of enzyme activity levels. Research has explained this by demonstrating that heterozygous females have two populations of red blood cells, one normal and one deficient (Kattanis 1967; Beutler et al. 1962). Blood mosaics from heterozygous females show different ratios of normal to deficient red blood cells. Hypothetically, they can show the enzyme deficiency in a screening test, but it may not be sufficient to interact with the fava beans. According to probability figures for the distribution of hemi-, homo- and heterozygotes in a given population, more females than males would be expected to suffer from severe favism. This discrepancy is accounted for by heterozygous females whose deficient red blood cell population is nearly equal to those who are genotypically fully affected by the enzyme deficiency[1] (Russo et al. 1972; Sartori 1963). Males have also been noted to show differences in the phenotypic expression of the deficiency, even though they are fully affected genotypically (Stamatoyannopoulos et al. 1964).

These problems related to the x-linked character of the enzyme deficiency, and to the variation in its phenotypic expression, have been referred to in order to explain why all individuals with the eznyme deficiency do not suffer from favism. Another explanation calls upon the variations in the enzyme itself, either with respect of its chemical composition or to levels of its activity.

When favism was first associated with the enzyme deficiency, two types of the deficiency had been identified: (1) the A- variant, found in American Blacks suffering hemolytic anemia from anti-malarial drugs (Beutler et al. 1954a, b; Beutler et al. 1955a, b; Gross et al. 1958); and (2) the Mediterranean variant, so-named because those suffering from the fava bean induced hemolytic anemia were first identified in Mediterranean populations. The Mediterranean variant is the most severe form of the enzyme deficiency, with activitiy levels of the enzyme below 1/20 of normal (Sartori 1971). Compared with the A-variant, with activity levels of up to 25% of normal, the Mediterranean variant may show only 5% of normal enzyme activity. Degradation of these activity levels during red blood cell aging is much accelerated with the young erythrocytes being almost as deficient as the older ones (Motulsky and Stamatoyannopoulos 1966; Stamatoyannopoulos et al. 1964). As a consequence, hemolysis in subjects with the Mediterranean variant is more acute and severe, with almost all erythrocytes being subject to destruction.[2]

Those with the Mediterranean variant are susceptable to a wider range of drugs than those with the A- variant, and have a greater tendency to show neonatal jaundice (Kirkman et al. 1964a). Those with the Mediterranean variant are not subject to chronic hemolytic disease which is observed in other Caucasians with more rare types of the deficiency. The Mediterranean variant is associated with hemolytic crisis following consumption of Vicia faba, sulfa derivatives, aspirin, and contact with napthelene. It has not been associated in the literature with anti-malarial drugs as has been the A-variant.[3]

Since the early research about the A- and the Mediterranean variants of the enzyme deficiency, at least seventy-five other variations have been identified (Beutler 1970; Yoshida et al. 1971; Kirkman et al. 1964a and b, Marks and Gross 1959, Rattazzi et al. 1969). These studies are briefly reviewed in Appendix A. While it is possible that one of the reasons that not all individuals with the enzyme deficiency suffer from favism is because they do not have the variant which interacts with the fava beans, this hypothesis has not been tested in medical research. When people are hospitalized and treated for favism, it is assumed that they have the Mediterranean variant. They are tested for the presence of the deficiency, but not for which type of the deficiency.

For the purposes of this present study, it was assumed that individuals suffering from favism have the Mediterranean variant of the deficiency. Since it is the Mediterranean variant which is predominant in Greek populations, individuals identified with the deficiency (with or without reporting favism) are also assumed to have this variant. Even though variants have been discovered in the Greek population, their interaction with fava beans and other hemolytic agents has not been investigated.

## The Hemolytic Agent in Vicia Faba

Studies which focus on the hemolytic agent in the fava beans are expected to clarify the etiology of favism by identifying which type of fava beans which cause the disease. In these studies, the appearance of favism in some enzyme deficient individuals and not others is explained by the activity and/or toxicity of some unidentified hemolytic agent in the beans. Different beans, grown under different conditions perhaps, are hypothesized to possess different levels of activity of the hemolytic agent. The crucial variable is not whether one has the $Gd^-$ trait, but whether or not beans with critical levels of the hemolytic agent, have been consumed.

A wide body of laboratory research using _in vitro_ fava bean extracts, has been generated to support this position (e.g., Mela and Perona 1959; Bowman and Walker 1960 and 1961; Zacchello and Panizon 1964; Lin and Ling cited in Patwardham and White 1973; Kosower and Kosower 1967; Braham and Sarova-Pinhas 1971). Some of the chemicals suggested to be hemolytic agents are found in other vegetables which are not associated with hemolytic episodes. In general, these studies have yielded unconclusive results.

Some studies suggest that environmental factors affect the toxicity of the fava beans, hypothesizing that growing and ripening conditions are more closely associated with the toxicity of the beans (Sartori 1971; Marcolongo 1941). Information gathered by Sartori from hemolytic cases produced by fava beans suggests that climatic differences are definitely involved. Favism is more prevalent during a sunny, dry spring, than during a wet, rainy one. It is expected that areas where arid springs are the norm would have higher favism frquencies.

## Research on Synergistic Etiology

The phrase, synergistic etiology, is used in three ways: (1) synergistic activity between the deficiency and some other blood or genetic variable; (2) synergistic activity between the chemical compounds in the fava bean; and (3) synergistic activity between the chemical compounds in the fava bean; and (3) synergistic activity between both the deficiency and the bean. The details of these proposals are too numerous to be dealt with here. Other blood factors or genetic traits which may interact with the deficiency have been suggested to include non-corpuscular factors (e.g., Panizon and Vullo 1961), the thalassemia allele (Carcassi 1974; Siniscalco et al. 1961; Bottini 1973), an autosomal gene (Stamatoyannopoulos et al. 1966) or "favic sera" (Nathan et al., 1974) which favor hemolytic episodes, and the functioning of other red blood cell enzymes (Bottini 1973; Beutler 1970; Palmurino et al. 1978).

The deficiency and the fava beans are also suggested to interact with the general status of individual health and immunity. Favism does not confer immunity against future episodes. It may occur in individuals who had consumed fava beans on earlier occasions without hemolytic crisis, or it may follow the first time the beans are consumed (Kattamis et al. 1969b; Belsey 1973). Sartori (1971) has repeatedly suggested that immunity to the beans may be accumulated through exposure in small, non-dangerous doses. More recent information indicates that cases of favism following the first consumption of the beans do not actually occur and that some sort of cumulative effect of the beans must be involved. This is in contradiction to Sartori's hypothesis. Those with a history of favism during infancy and subsequently exposed to the beans may not develop the disease a second time (Motulsky and

Stamatoyannopoulos 1966); however, one episode of favism does not provide immunity against a second or even a third. Of 120 patients with favism in Greece ten had already experienced at least one previous episode; four had it two previous times and one had reported several attacks (Kattamis et al. 1969b).

It has also been suggested that favism in enzyme deficient individuals is often precipitated by infection (Beutler 1970), particularly of viral origin, which may in itself produce acute hemolysis in these individuals without the intervention of fava beans (Kattamis and Tjortjatou 1970). This has not been followed up in the collection of case histories in the literature, but provides a provocative epidemiological suggestion.

These studies which focus on the etiological factors in favism are concerned with describing and analyzing differences in either the enzyme deficiency or the fava bean, or both, which can then be associated with the disease. The questions of why there are differences in the toxicity of the bean, or why there are variants in the deficiency, or why the deficiency is distributed the way that it is, are not central to these studies. These questions are taken up in studies which are structured by ecological paradigms.

## Epidemiological Studies of Favism

Medical ecology, like all ecological paradigms, accepts that adaptation is a basic concept in explaining the distribution of disease. Adaptive processes may act directly on disease, or indirectly by selecting for or against certain disease "causes" or risk factors. With infectious or parasitic diseases, the adaptation of invading organisms is considered in competition with human adaptation. In diseases which are related to diet, adaptive processes are considered with respect to the use of various animal and vegetable materials in a population. Medical ecology therefore invites the interest of many sub-disciplines of both the biomedical and social sciences. The concept of an open-systems model, expanding the links of disease causation, becomes a provocative subject for the various research interests of these human sciences.

Using an ecological model, epidemiological studies may examine how causes and risk factors of disease are distributed in populations and how these are influenced by the physical environment, society, psychological characteristics, and so forth. This type of model has been most often used in studies of favism and is summarized in Table 1.1. Epidemiological studies also examine certain of these environmental, societal, psychological, cultural factors in direct association with the distribution of a disease. That is, these factors will be considered independently, not as they contribute to the distribution of risk factors, but as they contribute to the disease itself. Previous epidemiological studies of favism examine primarily the environmental factors which contribute to the distribution of the enzyme deficiency. Social and/or behavioral factors which may contribute to the risk factors or to the disease itself, but have not systematically described or analyzed them.

## Epidemiology of the $Gd^-$ Trait

Since the enzyme deficiency was first associated with favism, a large body of research has been conducted to locate the predominant

TABLE 1.1

EPIDEMIOLOGY OF KNOWN FAVISM RISK FACTORS

| Risk Factors | Environment | Influencing Variables: Age | Sex | Familial Tendency | Socio-Cultural |
|---|---|---|---|---|---|
| $Gd^-$ Trait | Natural Selection | Unknown | x-linked nature of allele | interaction of genetic factors with the deficiency | unknown, but suggested that marriage patterns influence distribution of the deficiency |
| | Altitude | | | factors are not identified | |
| Fava Beans | Influence of latitude and altitude on growing | Unknown<br>Suggested that age and sex might influence fava bean consumption; not explored in existing literature. | Unknown | Unknown | Unknown<br>Suggested that protective behaviors exist, but not explored |

geographic areas where the trait is found, suggesting that environmental factors select for the deficiency. Genetically, the heterozygous state is given credit for helping to perpetuate the allele for the deficiency, perhaps independent of selective pressures. Heterozygotes, as noted in the previous section, are often just as severely affected by favism as are hemi- and heterozygotes; therefore, this theory needs reconsideration.

Some believe that the allele for the deficiency provides raw material for natural selection (e.g., Allison 1964; Blumberg et al. 1964). The phenotypic expressions and variants of the enzyme deficiency are polymorphisms which do not necessarily involve pathological states. Motulsky (1960 et al.; 1962) gives a comprehensive overview of this subject.

Others have concerned themselves primarily with the geographic distribution of the deficiency, often in connection with hemoglobinopathies such as thalassemia and sickle-cell anemia (e.g., Choremis, et al. 1963a; Pellicer and Casado 1970; Arends 1966; Carcassi 1974). Still others assume that the allele serves an adaptive purpose or that it is genetically tied to one which does (e.g., Stamatoyannopoulos and Fessas 1964; Bienzle et al. 1972; Choremis et al. 1962). The most popular hypothesis associates the deficiency with malaria, stating that the allele may offer protection against malaria in the same way that the sickle-cell trait in the heterozygous state does (Livingstone 1971; Siniscalco et al. 1961; Siniscalco et al. 1966).

Often the geographic distribution of the enzyme deficiency does little to explain frequencies of favism, and therefore, may have limited value. Belsey (1973:4) found that in areas of Iran "... where the genetic defect is prevalent and the fava bean is a major food staple, only 10-20% of the population at risk ever appear to develop the disease" Siniscalco et al.(1961) found that only 20% of enzyme deficient Italian males reported episodies of favism, while Kattamis et al. (1969a) found that only 10.3% of Greek males did.

Epidemiology of Fava Bean Consumption

In several agricultural areas of Greece, a fifth or greater proportion of the male population shows the enzyme deficiency. Cultivation and consumption of *Vicia faba* in these areas is very extensive with virtually all individuals frequently exposed to the beans. Favism is comparatively rare in spite of these frequent opportunities for exposure to the bean (Stamatoyannopoulos et al. 1966). Further, in the Karditsa area of Greece where the deficiency is 25%, favism is relatively rare, while in Corfu, where the rate of the deficiency is only 5%, favism is more common. In fact, favism and hemolytic crisis after exposure to the beans and hemolytic drugs are surprisingly rare when considering the number of individuals at risk and the frequency of exposure. The relatively low numbers of favism episodes could be attributed to a variety of causes, such as the "... limited occurance of the noxious agent and differences in *Vicia faba* consumption in individuals at risk" (Stamatoyannopoulos et al. 1966:253).

Actual fava bean exposure, in terms of form of the beans consumed or type of preparation in which they used, prior to the hemolytic episode is usually not considered, even though many studies suggest that this might be an important factor.

Favism is most often associated with the fresh bean and with the months during which the beans are ripe and harvested. It is not only the fresh bean which is toxic; both fresh and dry forms of fava beans are implicated in episodes. Most studies show that the fresh form is involved more than the dry one. In Greece, Kattamis et al. (1969a) showed that 83 of 120 patients with favism had eaten fresh beans (68%) while 31 of the 120 had eaten dry beans. Two people in the sample had eaten both fresh and dry beans immediately prior to the onset of the disease. In the Caspian region of Iran, fresh beans account for nearly all reported cases of favism. Raw, fresh beans accounted for 26-70% of all cases, while fresh, cooked beans accounted for 5-27% of all cases, depending on the year. Nearly all cases of favism in Egypt associated with the dry, stewed bean, but this is the major form in which the beans are consumed.

## Descriptive and Social Epidemiology of Favism

In the epidemiological surveys of favism, five variables are included: (1) the seasonality of favism; (2) the geographical distribution of the episodes; (3) the tendency for pediatric episodes to outnumber adult ones; (4) the sex distribution of cases; and (5) the familial tendency to have multiple episodes. These are shown in Table 1.2 along with the few social factors which are suggested in the literature to influence the epidemiology of favism.

TABLE 1.2

EPIDEMIOLOGICAL VARIABLES AND FAVISM
(A GENERAL MODEL FOR THE EPIDEMIOLOGY OF FAVISM)

| | Influencing Factors | | | |
|---|---|---|---|---|
| Distribution | G6PDd | Bean Exposure | Environ-mental | Socio-Cultural |
| Seasonal | Unrelated | Strongly implicated | Unknown | Unknown |
| Region | Related | Related | Unknown | Unknown |
| Age | Unrelated or not clear | Unknown | Unknown | Unknown |
| Sex | Related | Unknown | Unknown | Unknown |
| Familial Tendency | Related | Unknown | Unknown | Unknown |

Seasonal distribution of favism

Seasonal peaks in favism are related to the availability of the fresh bean. These seasonal fluctuations tend to support the interpretation that it is only the fresh bean which is dangerous. Latitude and altitude affect the time at which the beans are ready for fresh consumption, and this is reflected in the figures for favism episodes (Patwardham and White 1973). In Iran, favism is referred to as "Bahgdad spring fever" (Amin-Zaki et al. 1972) suggesting that the local inhabitants recognize this seasonal aspect of the disease. In Greece, 42% of all cases occur in May (Kattamis et al. 1969a); in Bulgaria, 90% of all cases occur in June (Angelov and Andrev 1959). This shows the effect of latitude on seasonality: Bulgaria at a higher latitude than Greece, reports the seasonal peak a month later than does Greece. In Egypt, there are two peaks of favism, the first coinciding with the harvest of fresh beans, and the second with the marketing of dried beans which have been stored underground in anaerobic conditions for six months since the harvest. The beans stored in this manner closely resemble the fresh beans (Belsey 1973).

The accumulation of favism episodes each year during the time when the beans are fresh tends to not support the theory that the inhalation of pollen provokes the disease. Both early and contemporary studies about favism (e.g., Gasbarrini 1915; Wharton and Duesselman 1947; Keller 1971) have suggested that for some individuals the fava plant is so toxic that by simply coming into contact with it, individuals have been known to suffer from favism. Kattamis et al. (1969b; 1971) conclude that the pollen hypothesis needs further investigation. In their data, no cases of favism were precipitated by exposure to pollen:

> Furthermore, the low incidence of the disease which was noted during February and March when the plants are in blossom stands as further indirect evidence that inhaled pollen does not commonly (if at all) precipitate hemolysis at least in Greece. (Kattanis 1971:741)

Geographic distribution of favism

Favism is noted to occur primarily in the circum-Mediterranean, but cases have been reported in France, the northern Balkan peninsula, and north-central Africa. These occurred among indigenous people (or it is assumed so, since the investigators did not always specify in their reports) therefore, the Mediterranean variant of the deficiency or other variants which interact with the beans circulate outside the major circum-Mediterranean area. Favism has also been reported by individuals living in North America, but who had their origins in circum-Mediterranean countries. Favism has been reported in almost all of these countries: In Spain (Caforio 1973; Flatz and Duren 1967; Pellicer and Casado 1970), in Italy (Sartori 1971; Crosby 1956; Cutillo 1972; Carcassi and Pinzus 1957; Gasbarrini 1915; Russo et al. 1972), in Sardinia (Sinisalco et al. 1961) and in Greece (Kattamis 1969a; Stamatoyannopoulos and Fessas 1964; Stamatoyannopoulos et al. 1966; Allison 1963). Crosby (1959) reports a frequency of 6.39 and 2.23 per 10,000 for two regions in Iran. The disease has also been reported in Bulgaria (Angelov and Andrev 1959), and Egypt (Belsey 1973). It has also been noted to a lesser degree to occur in France (Collombel et al. 1970; Gaudier et al. 1972), Tunisia

(Belsey 1973), and Sudan (Hassan 1971). These cases were not associated with hemolytic drugs, but with the fava bean. Favism is, therefore, not a strange or localized disease, and fava beans are a relatively wide-spread food staple in these areas.

### Age and sex distribution of favism episodes

Although the distribution of favism according to age and sex often noted in the literature, most researchers agree this is an unclear aspect in the epidemiology of the disease (Kattamis 1971; Kattamis et al. 1969b; Donoso et al. 1969; Stamatoyannopoulos et al. 1966; Sartori 1971; Kattamis 1969; Kattamis et al. 1971; Lapeysonnie and Keyhan 1966). Favism affects more males than females and tends to be a pediatric disease, disappearing gradually after the age of six, and dropping drastically after age ten. The x-linked character of the deficiency helps to explain the sex distribution, however, the age-ratios have not been fully investigated for their medical and cultural significance.

Kattamis (e.g., 1969b) argues that incidences of favism decline with increasing age simply because affected children tend to avoid consuming fava beans after their first hemolytic episode. If these were true, one would expect all patients to have a hemolytic crisis on their first and all subsequent contacts with the beans. Only 25% of the affected individuals in Kattamis' study reported that the episode occurred after their first ingestion of the beans, and some had repeated attacks. Sixty-five percent of the cases in the study belonged to the 2-5 year old age group, with only 5.2% of the cases occurring from age 10 to 15. Adult cases were reported to be difficult to find. In Iran, Donoso et al. (1969) found that favism shows up most often in children under four years of age. During 1958 to 1962, 663 cases of favism were reported in Iran. Only 36 occurred in children over ten years of age, with the most frequent cases occurring in children from ages two to four. This is less than 1% of favism episodes reported in people over the age of four and represents a dramatic difference from the Greek data. Even though in both areas favism peaks during the ages of approximately two to four or five, the drop in cases to only 1% is not reported. Even in the 10 to 15 age group, a higher percentage is reported.

The use of fava beans during infancy and childhood has not been described for different regions in the Mediterranean, except to note that in some countries they are used as a weaning food. This would help to account for the sudden rise in cases during the 2-5 age group. Infant cases of hemolytic crisis have been noted in Gd-trait babies and even new borns, in the absence of fava bean consumption. Some studies indicate that the milk of breast feeding mothers may be affected by the hemolytic factor in the fava beans. It is then highly likely that breast-feeding mothers who consume fava beans might affect their infants with favism. Kattamis (1971) found that among twenty-eight infants under twelve months who were affected with a hemolytic crisis, eighteen had been breast-fed by mothers who had consumed fava beans during the same period of time. They had eaten the beans two to six days prior to the onset of the hemolytic crisis in their infants. Cases of favism among breast-fed infants in Iran have also been recorded (Donoso et al. 1969) which is consistent with reports from other geographic areas (e.g., Chung 1965; Angelov and Andrev 1959).

While both males and females report favism, it is always more common in males. The male to female ratios range from 21:1 in Cyprus (Joannidis 1952), 6:1 in Greece (Kattamis et al. 1969b); 5:1 in Italy (Sartori 1973) and 3:1 in Iran (Lapeyssonie and Keyhan 1966). These figures do not resemble the ratio for male to female $Gd^-$ trait distribution which is calculated to be 100:201. The distribution of these ratios according to country, is in itself, interesting. No explanations for this have been offered in the literature, but it is possible that bean exposure by sex may differ in these areas, or that favism among females may be underreported in some areas.

### Familial predisposition and multiple cases of favism

The fact that favism has a genetic etiological factor promotes the repeated appearance of the disease in families. This is to be expected on the basis of the enzyme deficiency, but is unexpected on behavioral grounds. Families which have had one episode of favism would logically avoid the beans, and would have more reason to avoid them than families which have not shown episodes. One major study examined the familial predisposition to show repeated episodes (Stamatoyannopoulos et al. 1966), illustrating that certain families with the deficiency among their members never show episodes of favism. Other families with both the deficiency and favism have the tendency to have multiple cases. The study is used to support the hypothsis that a second genetic factor interacts with the deficiency in the multiple-episode families. Families share many characteristics than genetic inheritance, particularly with respect to the fava beans, which can be investigated using an epidemiological approach.

## Ethnographic Data and Epidemiology

Previous studies of favism are weak in their use of ethnographic data, and usually limited to a very general description of the way in which fava beans are consumed and/or to an investigation of what people believe about favism. The present study was designed to use ethnographic information to a greater degree than any previous research about favism. The paucity of ethnographic data from existing studies about favism can be illustrated by (1) describing what has appeared in the literature, and (2) presenting the general epidemiological framework which was used in my own research in rural Rhodes, Greece.

### Fava Bean Consumption as Described in the Literature

There is little ethnographic information about fava beans, how they are used, cultivated and prepared by human populations and essentially nothing which demonstrates an association between these practices and specific favism episodes. In considering why different villages in Iran might have different rates of favism, Belsey (1973: 9) states that a possible explanation "... may lie in different folk attitudes and the manner in which the bean is prepared and consumed in the two areas, particularly since the attack rates based on raw bean ingestion are similar (assuming equal risk of exposure)." These attitudes and modes of preparation are not investigated in spite of this suggestion that they might be important.

An investigator living outside the Mediterranean has very little idea of the varieties of bean preparations which use the fava beans. The fresh bean is recorded to have a variety of preparations. In Ethiopia, the fresh fava bean is used in a fried cake, where it is soaked first, formed into a small cake with the hands and fried in oil (Dr. Patel, Food Science, Michigan State University, verbal communication). In Iran, where the bean is extensively cultivated and consumed, the majority of the population consumes it several times a year. People of the working class buy the bean from street vendors, in a preparation where the dry bean is soaked in water making it soft. It is served on disks of oriental bread which are also soaked in the bean water (Amin-Zaki 1972). The fresh bean is also consumed in Iran, with or without the pod, however, it is not considered appropriate food for children (Belsey 1973). In some areas of Iran, the raw bean is consumed much more often than in others, most often eaten after peeling off the pod and cuticle and salting the bean (Donoso et al. 1969). In Tunisia, too, it is usually the large fresh bean which is eaten without the cuticle. In Egypt, the fresh cooked beans are not commonly consumed (Belsey 1973).

Dry beans are used in Iran when fresh beans are unavailable. The dried form can be bought in two varieties, one with the bean slit and peeled of its cuticle, and the other still in the cuticle (Donoso et al. 1969). Presumably, the former type is used for cooking into a puree. Dried stewed beans form a major stapel in the Egyptian diet and are often fed to infants. The skins are not removed. Most cases of favism in Egypt are associated with the form, while in Greece it is usually the fresh raw bean which is involved. Another preparation in Egypt involves soaking the dry beans over-night in water. In this case, the skins are removed once the beans have reached a soft state. Boiled dry beans are sold by street vendors in both Iran and Tunisia. They are cooked in their cuticles which might be removed at the time that the bean is eaten. In Iran, these vendors "... carry a pot of boiling water and serve a portion of hot fava beans for the price of 3-5 rials (3-6 U.S. cents)" (Donoso et al. 1969:514).

Descriptive information of this sort is exceedingly rare in the literature. Pursuit of similar data for other countries, regions, ethnic groups, age cohorts, and so forth, would help test hypotheses which state that favism is related to differences in consumption patterns.

Cultivation and storage practices related to the beans are entirely absent in the literature, with one exception. When it was noted that two peaks of favism episodes occur each year in Egypt, it was explained by the practice of storing the beans in anaerobic conditions. Many of the epidemiological studies of favism include seasonality of favism, but do not take the opportunity to discuss cultivation and storage practices. Reports of favism occurring from passing through fava patches or from pollen inhalation are not followed with respect to participation in agriculture which places individuals in contact with the growing beans.

## Attitudes about Favism Reported in the Literature

Fava beans are often reported to be dangerous for children in Iran and Egypt (Belsey 1973). The consumption of the beans in Iran carries socio-economic connotations:

> In Rasht, where all classes consume the fava bean, the lower class peasants look upon the disease as being imposed on them because they are too poor to afford the sweets and meats of the upper-class diet. (Belsey 1973:10)

This observation leads to the consideration that not only is the disease viewed as a socio-economic stigma, but that the people believe that the consumption of sweets and meats protects them against favism. In this connection, protection against favism may include general taboos in these countries, aside from being considered not fit for children to consume.

Local names or expressions for favism may illustrate how the people categorize the disease. Translations may or may not coincide with what is recognized in favism in biomedical diagnosis. Gasbarrini (1915) reported that favism was called zafara in Sicily and straiu in Cagliari. In Iran, favism is recognized as baghalazaleh and juice from the wild persimmon or concentrated grape juice (Donoso et al. 1969) and large amounts of sweets such as honey, dates, sugar-water (Belsey 1973) are consumed in order to prevent such attacks.

Kattamis (1969a) mentioned that some of the differences in cases of favism which reach the point of hospitalization may have to do with the understandings and perceptions of the disease by those affected. This is not further explored in his work or in other studies.

In Iraq (Amin-Zaki 1972) the symptoms of favism are associated with the consumption of a type of bull-rush as well as with fava beans. The peasants in the part of the country where the illness is noted

> ... appear to know the condition, which they call khsaissa, however, they do not associate it with the fava bean, but with the bull-rush (*Typha angustata*) which they consume in a special form with sugar; children are warned against eating it as they are warned against fava beans. Khsaissa occurs only in children who have eaten the bull-rush preparation.

This syndrome sounds similar to favism, however, the symptoms which were reported show that jaundice is either a relatively minor sign, or that it is not given much emphasis in reporting. Among ten adults questioned about khasaissa, all reported sudden onset and pallor. Seven reported dark red urine and six reported feeling chilled. Vomiting was reported by three, and abdominal pain by three. All of these symptoms are reported in episodes of favism, but jaundice, the biomedical indicator of favism, was reported in only four of the ten cases. Further, "only two people said to be suffering from khasaissa showed the classical clinical symptoms of favism were proven to have the G6PD deficiency" (Amin-Zaki 1972:4).

Both from a medical and an anthropological perspective, these reports are extremely provocative, even though limited in their reporting. They illustrate the ways in which the people themselves view favism, having their own protective behaviors and illness terminology, perceptions of symptoms and emphases in reporting them. In these instances ethnographic information is an asset in treating the areas of grey which seem to stand outside the biomedical conceptions of favism. At the same time, they are valuable in indicating other aspects of illness beliefs, health behaviors, and of culture in general.

## Models Used in the Present Research

The previous sections show that research attempts have elected to generate hypotheses about favism which have become increasingly specialized and most often focussed on the enzyme deficiency. What is needed is perhaps the opposite: Instead of a specialized model, a general one is needed. A descriptive epidemiology of favism is needed, which, rather than condensing the model, expands it to examine behaviorally and culturally influenced factors. Such factors would include the growing and consumption patterns of fava beans, and socioeconomic characteristics of those areas using the beans. The present research uses two epidemiological models: The first uses ethnographic information to examine the distribution of one of the etiological factors, and the second, to examine the distribution of favism itself. Earlier it was discussed that it is perfectly legitimate to construct epidemiological models to examine risk factors as well as disease.

Table 1.1 presents a model for the epidemiology of the risk factors in favism, the deficiency and bean consumption, and indicates where data needs to be collected. This model was used directly in the examination of the distribution of the enzyme deficiency on Rhodes, but it was not used to examine bean consumption patterns. It influenced the construction of a second model, which introduces the consideration of bean exposure along with other factors, as shown in Table 1.2. In this table, it is clear that the epidemiology of the favism risk factors requires additional work to begin to hypothesize and fill-in the "unknown" squares. It should be noted that these risk factors are not shown on this table in terms of etiology. Studies which have dealt with the variants of the enzyme deficiency, the hemolytic agent in the fava bean, the interaction of the biochemistry of the blood and the bean, are not included in this model. Each of the factors in the first column (seasonal, region, age, sex, familial tendency) were discussed in the preceding section and are shown here again with respect to factors which may influence the distribution of favism. The enzyme deficiency and fava bean exposure are, of course, the factors for which the greatest amount of information is available. The influence of environment, socio-economic variables and ideological constructs have not been researched according to their influence on season, region, age, and so forth.

A third model is used in this research which promotes the collection and analysis of ethnomedical data. Disease or illness involves at least two levels of reality, the one biophysical, which is treated in epidemiological studies, and the other cultural, which must be handled through an ethnomedical approach. This is shown in Table 1.3 in a general ethnomedical framework of the central variables none of which have been investigated in the literature.

These tables will be referred to in the following chapter which describes the methodology and research strategy used in the

TABLE 1.3

GENERAL MODEL FOR THE ETHNOMEDICAL INVESTIGATION OF FAVISM

FAVISM AS AN ILLNESS

Perception of symptoms

Social meaning of the illness

Relationship to other illnesses

Relationship to preventive behavior

Relationship to other aspects of culture

study. They are introduced here to illustrate the aspects of favism which have not been investigated in previous research. Following the presentation of methodology, a short chapter will describe the setting in which the research took place. Chapter Four focuses on the distribution of the enzyme deficiency on the island of Rhodes. This is consistent with the model in Table 1.1, where the factors affecting the distribution of the deficiency are shown. Chapter Five uses the model shown in Table 1.2, where the "unknown" squares in the table are filled-in through the use of data collected during the field work. Finally, Chapter Six presents the ethnomedical information about favism as it is understood in rural Rhodes.

## Footnotes

### Chapter One

1. If the frequency of hemizygotes (p) is 1 for every 100 males, the frequency of homozygotes ($p^2$) is expected to be 1 for every 100,000 females, and the frequency of heterozygotes (2p) is calculated to be 1.98 for every 100 females. "Homozygotes are therefore 100 times less numerous than hemizygotes; and heterozygotes are almost double in number of hemizygotes" (Russo et al. 1972:856). For every 100 males with the deficiency, it is predicted that there will be 1 homozygous female and 200 heterozygous females. According to these calculations, if only hemi- and homozygous individuals suffered from favism, the male to female ratio would be 100:1. This does not conform to the numbers affected by favism in any area of the world which it has been reported. Obviously, a good number of female heterozygotes suffer from favism in order to account for the male to female ratios which range from approximately 2:1 to 22:1.

2. In the A- variant, the younger red blood cells in enzyme deficient individuals show normal enzyme activity levels. This has implications for the process of hemolysis. Upon the ingestion of hemolytic agents, hemolysis affects only the older red blood cells while the younger ones act to stabilize the condition. For this reason, individuals with the A- variant are often noted to show a remission of hyperbilirubinemia without the need for blood transfusions. In the Mediterranean variant, the age of red blood cells does not seem to have an effect on the enzyme's level of activity in deficient cells (Motulsky and Stamatoyannopoulos 1966; Beutler et al. 1954a and b; Beutler et al. 1955 a and b; Marks and Gross 1959).

3. It is possible that those with the Mediterranean variant have not been experimentally exposed to anti-malarials as were the American Blacks in the studies conducted in the early 1960s. In this connection, it might be added that American Blacks were fed _Vicia faba_ under experimental conditions and did not suffer hemolytic anemia.

## CHAPTER TWO

## RESEARCH METHODOLOGY AND STRATEGY

In eleven months in 1975 to 1976, and four months in the spring of 1977, I lived on the island of Rhodes in order to carry out this research on favism. It was a major goal of this field research to collect ethnographic and medical data which were not attended to or not emphasized in the earlier studies. The techniques and strategies used gathered from both medicine and anthropology are reviewed in this chapter. The models which were outlined in Chapter One served to guide the collection of information from the rural areas of Rhodes. In addition, a comparative framework was continually referred to in designing and carrying out the research. Two populations eventually became the focus for the collection of ethnographic data: Both were exposed to the risk factors, but only one reported frequent favism. These populations, in addition, were selected from two villages which contrasted in environmental and socio-structural ways.

### Review of Models and Types of Data Collected

In the previous chapter, three models were presented which illustrated the state of etiological and epidemiological studies of favism. These are referred to again with some of the vacant spaces filled in with topics which were investigated during the field work. This approach helps to delineate the hypotheses which were investigated, and to show what information was necessary to collect. Table 2.1 expands upon the epidemiological model for the Gd$^-$ trait, a major or risk factor for favism, by suggesting that environmental and social structural factors are involved in the distribution of the trait. This also shows the types of information which were collected with respect to these variables and the Gd$^-$ trait. This information included geographic and historical information about Rhodes, marriage patterns in the two villages studied, and fertility and health histories from families in these locations.

Information about fava bean exposure, the second major etiological factor in favism was collected according to the hypothetical statements in Table 2.2. These potentially important aspects of exposure were not used to simply describe the use of fava beans, but were then placed in the context of the more general model for the epidemiology of favism. The general epidemiological model was shown in Chapter One, in Table 1.1. It appears again in Table 2.3 in an expanded form to indicate factors investigated and hypotheses suggested to help account for the distribution of favism by season, region, age, sex and family. Ethnographic information about the production, consumption, preparation of fava beans was collected with attention to age, sex, and practices within individual families. Environmental and economic data were collected about the villages, their settlement patterns, their association with the urban center, their economic base, and their demographic structure. Socio-economic information about families included the family size and structure, living accommodations, participation in agriculture, and

TABLE 2.1

FACTORS FROM EPIDEMIOLOGICAL MODEL OF
GD- TRAIT

| Environmental Factors | Necessary data |
|---|---|
| The enzyme deficiency frequency is inversely related to altitude. | Altitudes of locations in Rhodes. |
| | Exploitation of altitudinal ranges in Rhodes. |
| The deficiency is adaptive advantage in areas of malarial endemicity. | Historical information about malaria on Rhodes. |
| The deficiency is neutrally selective. | Fertility patterns, growth figures, health history of those with the deficiency compared with normal population. |
| **Social Structural Factors** | |
| Marriage patterns affect the distribution of the enzyme deficiency. | |
| Sizes of breeding populations affect the distribution of the deficiency. | Marital unions, endogamy, and residence patterns. |

TABLE 2.2

EPIDEMIOLOGICAL MODEL FOR FAVA BEAN CONSUMPTION

| Exposure Factors | Environmental | Socio-Structural | Ideological |
|---|---|---|---|
| Exposure in growing and cultivation | Different rural locations have growing schedules which promote fava beans as a staple. | | |
| Exposure in preparation activities | -- | Divison of labor by sex is expected to place women in greater contact with fava beans which they are being prepared for consumption. | |
| Exposure in consumption | -- | Different types of preparations are promoted or avoided on the basis of age, sex, familiar roles and statuses. | Certain beliefs promote or prohibit fava bean consumption and/or its consumption in particular forms. |

TABLE 2.3

EPIDEMIOLOGICAL VARIABLES AND FAVISM:
A MODEL TO DIRECT RESEARCH STRATEGY
(EXPANSION OF TABLE 1.2)

| | Gd- Trait | Bean Exposure | Environment | Socio-Cultural |
|---|---|---|---|---|
| Seasonal | Not known to be related | Suggested that seasonal differences in production and consumption play a role in seasonality. | Altitude known to affect ripening of fava beans. | Fasting cycle interacts with agricultural cycle. |
| Regional | Potentially adaptive allele in malarious areas. | Suggested that regional differences in production and consumption need to be investigated. | Settlement pattern and location of fields interacts with exposure. | Suggested that economic productive differences region interact with exposure and settlement pattern. |
| Age | Not known to be to be related. | Consumption and other exposure may differ by age. | Not investigated. | Age and sex roles, particularly those which involve production and use of beans are expected to be important. |
| Sex | X-linked allele influences the expression of the trait. | Consumption and exposure suggested to differ by sex, but not investigated in literature. | Not investigated | |
| Familial Tendency | $Gd^-$ known to be inherited; may be accompanied by other inherited traits. | Similarities in familial use of fava beans may interact with the genetic basis of the hemolytic reactions. | Not investigated. | Familial taboos and avoidance of fava beans; beliefs about the beans may differ from one family to the other. |

presence of out-migration. Fasting practices associated with religious events, expected behavior by age, sex roles, and ideas about favism and the fava bean were included under the variable of ideology.

This last topic, ideology, was particularly important in developing the ethnomedical model for favism. From restrospective case histories, native etiological explanations were extracted and analyzed without respect to the biomedical model. Near the end of the field work period, families known to be at high risk of developing favism (i.e., they had the $Gd^-$ trait in one or more child) were visited and presented with the biomedical explanation of favism. Their reactions and subsequent behavior and/or plans to change behavior were collected. This was then analyzed from two perspectives: First from the goals of preventive medicine and second from the perspective of the goals of the rest of the rural Greek culture. Ultimately this analysis was used to further illuminate the epidemiology of favism, rather than in the pursuit of the essence of Greek culture. In this same sense, the study leans toward the biomedical rather than the anthropological model.

## Selection of the Research Sites

Since the G6PD deficiency is so strongly implicated in episodes of favism, it was essential that the research take place in an area of the world already noted for the presence of the deficiency as well as the disease.[1] This narrowed possible research sites to the cirum-Mediterranean.[2] Aside from the Kurdish Jews which were found to have as high as 58% of the males tested identified with the $Gd^-$ trait

(Szeinberg and Sheba 1958; Szeinberg et al. 1961), Sicily (Russo 1967) and Sardinia (Carcassi and Pitzus 1957), and Greece (Choremis et al. 1963a; Kirmlides et al. 1965) were also reported with very high frequencies of the trait (i.e., 25-35% of those tested showed the trait). Two major pices of research (Kattamis et al. 1969; Allison et al. 1963) documented that the Greek island of Rhodes showed "... remarkably high frequencies of the enzyme deficiency" (Allison et al. 1963:239). The research which had been conducted on the island provided a data base of seven village locations, and the City of Rhodes, which had been screened for the deficiency in the early 1960s. In the present research, two of these villages were rescreened for the deficiency and five other locations added. Cases of favism which had been reported to the only hospital on the island were collected for the years 1966 to 1978.[3] The results of the screening for the $Gd^-$ trait, and the distribution of favism cases, aided in the selection of the two villages which were used for the collection of ethnographic data. The two villages which were ultimately selected presented contrasts in the frequency of favism and the $Gd^-$ trait frequency. They occupied two different types of econiches, one coastal and the other mountainous, which was expected to have certain effects on the social organization of each. The coastal-mountain dichotomy was used to help select the villages because altitude is involved in both the distribution of the enzyme deficiency and in the production of fava beans. Both of the villages had similar demographic features; they had approximately the same number of children screened for the deficiency, and the approximately the same percentage of the population was represented in the screening.

<u>Identification of Favism Episodes</u>

Episodes of favism which occurred during the years 1966 to 1976, and which were clinically diagnosed, were identified and collected from the hospital records of the Queen Olga Hospital in the City of Rhodes. These figures were used in the statistical survey of the frequency of favism, and were useful in delimiting areas to be screened for the enzyme deficiency. In latter stages of the research, the hospital cases of favism were used in follow-up studies in the village locations. In the course of the field work, other episodes were reported from the local inhabitants. These had occurred before 1966 and did not appear in the survey of the number of favism cases. Many of these episodes could not be verified in hospital records since they were either not hospitalized or they occurred before favism was the type of disease to be reported to medical professionals. While these cases reported by word-of-mouth were not used in the survey of favism on the island, they were used in the collection of ethnographic information. Since the diagnosis of a disease/illness can represent a cultural as well as a medical phenomena, several non-clinical cases of favism were recorded. These cases, and the individuals reporting them, were subjected to the same research protocol, questionnaires and interviews, as were those who had been identified from hospital records. This has two rationales: (1) This study was designed to uncover sub-clinical cases of favism as well as medically diagnosed ones, and (2) reactions to fava beans in some individuals may not include the presentation of all the symptoms necessary to diagnose hemolytic favism. These latter cases may represent valid claims which are culturally relevant, even though they do not meet medical diagnostic criteria.

## Identification of the $Gd^-$ Trait

The $Gd^-$ trait can be identified through the use of a variety of laboratory tests, but the constraints of the field situation, transportation difficulties, and time, indicated that methods used in other screening studies would be most appropriate. Since the deficiency is a sex-linked trait, it is most easily identified in males when rapid and simple screen procedures are called for. Most of these methods do not detect female heterozygotes in sufficient numbers to justify their use among female members of the population. It was desirable that as many members of the designated age group of males be screened, therefore, elementary school boys of the selected villages were chosen as the most easily accessible participants. These boys were from 7 to 12 years of age. This approach is compatible with other screenings for the enzyme deficiency which, to date, have taken place under similar circumstances and constraints.[4]

In all the samples, none of the boys were known to be enzyme deficient prior to being selected for screening. They were chosen by their age, without prior knowledge of having suffered from favism. The goal of 100% participation from each village for the designated age cohort was nearly met in all but one of the locales screened.

The high proportion of participation, and therefore the reliability of projections based on the samples, is shown in Table 2.4. The samples taken from the school boys represented from 4.5 to 14% of the male population in each locale. This is compatible with other studies where similar screening rationale was used.

Actual numbers of subjects screened for the deficiency in Rhodes are lower than those from other screenings,[5] but this is a function of the low population densities found in these locations rather than from the omission of a large number of children in each age cohort. The present study was designed to be an in-depth examination of favism rather than a statistical survey of the $Gd^-$ trait.

Figure 2.1 shows the type of representation which was achieved on a familial basis in the two villages selected for in-depth study. All families with at least one elementary school child are contrasted with those who provided at least one child for screening. In Massari, 33 of 51 families (65%) with elementary school children were represented by at least one child in the screening. In Kritinea, the representation was even better with all but nine of 38 families (76%) having at least one child screened.

Laboratory facilities and services for the analysis of blood samples for the enzyme deficiency were obtained through affiliation with the Institute of Child Health, Aghia Sophia Children's Hospital in Athens, Greece. The hospital hematological laboratory and the Institute have been involved in research efforts related not only to the enzyme deficiency[6] but to other blood problems which are represented in the Greek population.[7] The physicians[8] at the hospital

TABLE 2.4

POPULATIONS REPRESENTED IN SCREENING FOR $GD^-$ TRAIT

| Village | Tested / Age Cohort | | Tested/Males in Population | |
|---|---|---|---|---|
| | Number | % | Number | % |
| Lardos | 14/14 | 100.0 | 14/237 | 5.9 |
| Lindos | 32/35 | 91.4 | 32.354 | 9.0 |
| Massari | 37/38 | 97.5 | 37/266* | 13.9 |
| Malona | 28/30 | 93.3 | 28/460 | 6.0 |
| Pylona | 11/11 | 100.0 | 11/88 | 12.5 |
| Kritinea | 37/38 | 97.5 | 37/293* | 12.6 |
| Embona | 29/58 | 50.0 | 29/636* | 4.5 |

Sources for Population Figures: Asterisk (*) indicates author census. All other figures are estimated on the basis of population given in the National Statistics Yearbook, 1971.

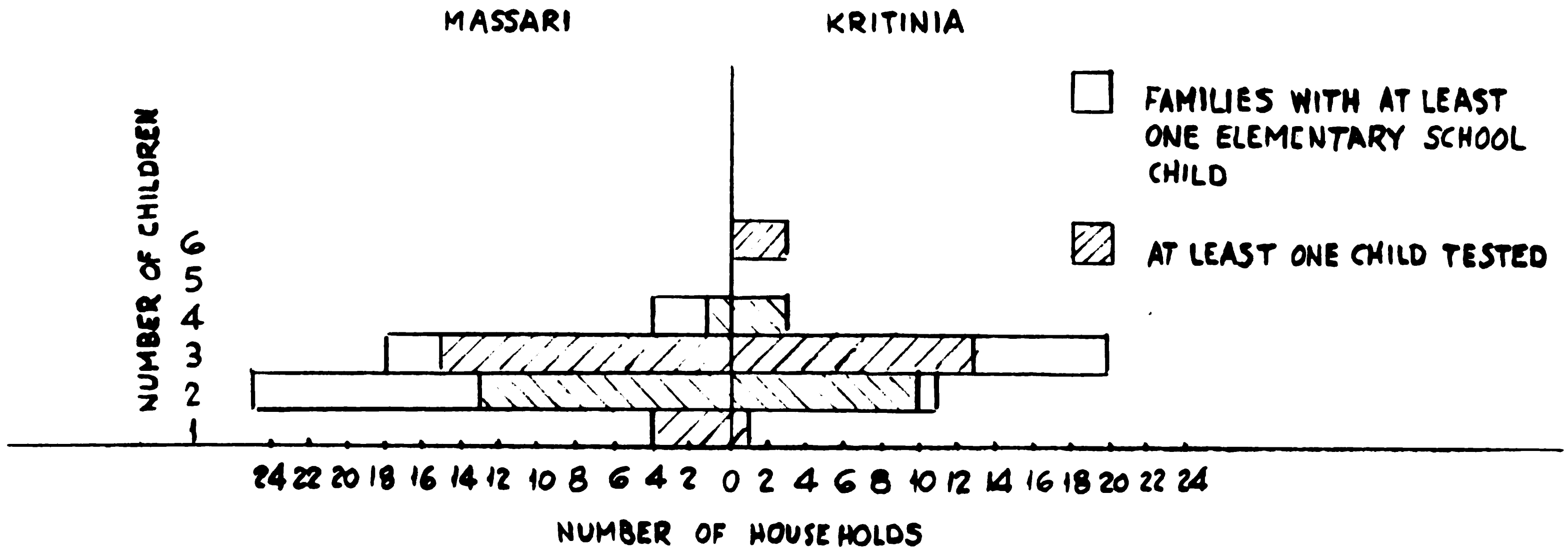



Fig. 2.1 Households with Elementary School Children in Massari and Kritinia Showing Proportions Represented in Screening

and at the Institute discussed with me the various aspects of drawing, handling and transporting the specimens to insure that they would meet the requirements of the laboratory personnel and standard procedures. The samples were drawn from the finger and stored in hematocrit tubes (Heparinized). These were kept under refrigeration until they were transported by air to the hospital in ice-filled, insulated containers. Air times between Rhodes and Athens is approximately one hour. To guard against any possible problems with time or equipment, the thermoses were placed under refrigeration when they arrived at the Athens airport until they were received by a representative from the hematology laboratory. Testing for the deficiency began the day after the specimens had been received in the laboratory.

The local agrarian physician serving in regions of Rhodes through the Ministry of Social Services, assisted in drawing blood samples.[9] Samples were taken during four-day periods, stored under refrigeration, and on the fifth day they were packed in an ice-containing thermos and transported to Athens. A total of 189 specimens were collected from elementary school boys (ages 7-12) in seven villages of Rhodes. It was intended that all the samples be subject to the same analysis for the deficiency and that all results be read by the same laboratory technician. Neither of these was possible. Five villages were screened during 1975-76 and all five were subjected to the discolorization brilliant cresyl blue (BSB) method of analysis, using procedures outlined by Motulsky and Campbell-Kraut (1962).[10]

Two villages were screened at a later time, in 1977, and a different laboratory technician conducted the analysis and the reading of the results.[11] Further, the reagent necessary for the BCB method of analysis was not longer available in 1977. The Beutler fluorescence test was used. Both the BCB and the Beutler test have the same reliability, according to the standards of the laboratory personnel, and both can be used for capillary blood from hematocrit tubes.

## Identification of Fava Beans in Local Environments

The distribution of favism episodes in the different locations on the island of Rhodes, and the results of the analysis of the blood samples, were important in selecting specific village sites for in-depth investigation. Equally important, was the second risk factor in favism, the fava bean. While villages were screened for the enzyme deficiency, it was possible to survey the local setting for the presence of the fava beans in the environment. In some villages, they were not observed except in local groceries in the dry form. It was important that the villages where the field research would take place had the beans grown in the agricultural cycle. This did not turn out to be the most crucial variable in the selection of village localities for the field work because the beans were grown throughout the island, with the exception of only a few areas. There were no areas which were visited which appeared to have large tracts of land devoted to the cultivation, however, some villages had plots of fava beans within the village, while others had them mainly outside the village, mixed with other plots of land. This was a difference which was noted, and which contributed to the selection of the two villages in the study. One village showed the garden-lot growing pattern of the beans, and the other did not.

The actual exposure to the beans, and their consumption in these localities, could not be surveyed. It was assumed that the presence and location of plots of land devoted to fava bean cultivation would be reflected in general consumption patterns.

### Other Considerations in Site Selection

The villages screened for the enzyme deficiency were selected because other villages in their regions had been screened in earlier surveys, they were accessible to the major transportation lines which would facilitate the handling of the blood samples, and they represented a variety of econiches, some being mountainous and others coastal. The selection of the two villages which participated in the ethnographic field work was based on the survey of general environmental features and settlement patterns. These variables were considered along with the results of the screening, the distribution of favism episodes, and the appearance of fava beans in the natural environment. Agricultural production was particularly noted in the environmental survey, and as it turned out, the villages which were selected for the ethnographic research showed distinctly different patterns of agriculture. This was a difference which was selected for in making decisions about which villages would be involved in the ethnographic study.

## Field Techniques

Social institutions which most directly affect genetic inheritance and food habits were most closely examined during the field work. These included marriage patterns, food sharing, feasting and fasting observations, and food preparations related to fava bean consumption. Informal interviews, open-ended questionnaires, and participant observation were the basic techniques used in the research protocol. While techniques which involved my active participation in eliciting data provided a standard base of information, this base was further explored through observations where I was not directing the exchange of information.

### Ethnographic Field Methods: Participant Observation and Interviewing

The classical anthropological works begin with solid ethnographic description. This, in turn, relies on the use of participant observation and ethnographic interviewing (as described by Spradley 1979). These are utilized on a daily basis by those able to live among the people in the area where they are carrying out research. Cultivated as methodical tools of field investigation, participant observation and ethnographic interviewing allow the anthropologist to supplement and clarify the information which was gained through laboratory tests, questionnaires, demographic figures, and so forth.

While there are many formal tools of recording and gauging human behavior, most of which must bear up under statistical analysis, there are many aspects of human behavior which do not easily allow such analysis. Information gained through methodical observation may become extremely valuable when statistical measures fail to describe, explain, analyze or predict human behavior. The anthropological method which emphasizes the development of skills of observation and which strives to describe human behavior before analysis is pursued contributes to the methods used in other social and human sciences. Instruments such as structured and standardized questionnaires, interview protocals, and health histories are important because they give an indication of what people think they are doing, and what they believe they have experienced. Actually observing behavior, participating in daily life, shows how the people carry out these ideas and beliefs.

Participant observation cannot verify, for example, the results of the clinical analysis for the enzyme deficiency. On the other hand, rumors that an individual has suffered from favism without clinical evidence that anyone in the family has the deficiency can challenge both the medical scientist and the anthropologist. While the former would order more tests, the latter might search for social and cultural explanations. It might be asked, what does the rumor mean in terms of the individual's relationships with others in the society. A decision to treat the rumor in biomedical terms alone may result in ignoring other important dimensions of the society.

Ethnographic interviewing as the second major tool of the anthropological field experience is grounded in two assumptions: (1) that people hold an ideal model of what their behavior should be like, vis-a-vis their culture, and (2) that a member of a culture cannot give direct answers as to why they do the things they do, or why their culture works the way it does. Ideal, rather than real behavior, is often stated as responses to standardized questionnaires and even open-ended questionnaires tend to provide empty categories for the participant to fill-up, whether or not they reflect cultural reality. Through participant observation, coupled if one wishes with questionnaires, some of the ideal vs. real behavior can be clarified. Through ethnographic interviewing, the problem of forcing the informant to respond or provide meaning for terms, ideals, models, etc., which run contrary to his/her notion of reality, is avoided. Ideally, ethnographic interviewing elicits categories from the informant rather than providing them on behalf of the interviewer. One can see that this approach is most suitable for collecting the informant's view of favism, outside the strictures of the biomedical model. In this approach, even the disease category should be avoided in initial interviewing sessions.

It is notable that the word informant is used here rather than other similar terms used in other branches of the social sciences; e.g., "subject," "participant," "respondent." The difference is more than semantic even though the word, informant, conveys an active component while the terms, subject and respondent, do not. The informant gives the information, he does not simply respond to questions or participate in tests. Unfortunately, the structure of the ethnographic interview and the fact that not every participant in a study is a good informant, does not lend itself to all aspects of an epidemiological study. Therefore, ethnographic interviewing was not used intensively with all in the study; it was used selectively with certain participants who also happened to be good informants.

## Selection of Participant Families

Families which had reported episodes of favism in their members, or which showed children with the enzyme deficiency from the screening, were encouraged to participate in the research by allowing themselves to be observed and interviewed in their homes. Other families which did not show the $Gd^-$ trait and did not report episodes of favism were asked to participate. Thirty-nine families formed the core of the research. Twenty-four families were from one village and fourteen from the second. The twenty-four families from the first village were divided into two groups, ten having at least one child affected by the $Gd^-$ trait and fourteen not showing the trait. Ideally, the samples might have been balanced, but not enough children with the $Gd^-$ trait and/or favism could be identified. In the second village, all fourteen were identified by the trait and/or favism episodes. From this village, several families were identified which did not have the $Gd^-$ trait or any known cases of favism. Time did not permit their inclusion in the study.

The term, family unit, refers to units of residence and biological kinship, which contain only the nuclear family. This conforms with the ethnographic reality for Rhodes. Those familiar with the ethnography of the Aegean and Dodecanese Islands (Rhodes being a member of the latter group of islands) know that there is an emphasis on the ability to establish a family which is separate from the family of birth (Dubish 1976; Hoffman 1976). Unlike other areas of mainland Greece where the extended family, in some form or another prevails, the islands show the nuclear family residential pattern. A house as the major item in a dowry is almost always provided for daughters, and tends to reinforce the idea of separate households between generations. It is almost unheard of for newlyweds to occupy the home of one or the other set of parents. If parents are unable to provide a daughter with a home of her own, they will move out of their own home, giving it to the newlyweds, and move into other quarters, rather than share a home with the new couple.

Even though there is an emphasis on the nuclear family, child care is not restricted to its boundaries. This is an important consideration when calculating the possibilities for children to be exposed to fava beans. Even though certain nuclear units may not grow or consume the beans, a child may have plenty of other opportunities to come into contact with the beans while in the care of other family members. It is reasonable to assume that in villages which grow fava beans, all members of the community are at risk of fava bean exposure, whether or not they are cultivated and consumed within the nuclear family unit.

## Ethnographic Questionnaires

Ethnographic questionnaires is used here to refer to standard and open-ended questionnaires which elicited ethnographic data, but did not follow the protocol of ethnographic interviewing techniques as described above. Certain data of a quantifiable nature was desired, and this required some form of standardized system of questioning. Aside from the identification of the enzyme deficiency and/or favism cases in a family, familial information was collected through three other devices: (1) Recording of ethnographic food habits and culinary behaviors; (2) Collection of genealogical information; and (3) Description of family health and fertility patterns. These are discussed below.

## Food habits

A short questionnaire regarding food habits and observation of food preparation activities and consumption, elicited information about the general and individual patterns of food behaviors. This necessitated gaining access to cooking areas in the households, participating in food preparation activities, sharing recipes and eating with families. Having been persuaded on many occasions prior to the field work to join families during meal times and to discuss foods and recipes, I considered that this information would be relatively impersonal (e.g., compared to asking about fertility patterns). This promoted the scheduling of this part of the field work early, during the first months of my residence in the village. Additional information specifically related to fava beans was collected through interviewing. All participating families were questioned as to whether or not they grew fava beans, where they grew them, if they ate fava beans, in what form, and which preparations of fava beans predominated in the household. These data were checked by observations. These families were also questioned about their understandings about the beans, for example, if they understood that the beans might have deleterious effects on certain people, which people were affected, what happens to people when they are affected by the beans, and how these effects might be avoided. Other food-related questions involved asking about attitudes toward nutrition, ideas about foods considered to be good for the health or the blood, foods which some members of the family refused to eat, food allergies in the family, and preferred diet of different family members.

Genealogical information

Genealogies of four generations in depth (when possible to recall) were collected for all individuals identified with at least one $Gd^-$ trait child and from those having reported cases of favism. At least half of each of the two villages was represented in these genealogies. These genealogies were used to supplement other demographic data on full-time village residents, out-migration and marriage patterns.

Genealogical materials such as these have the advantage of serving both medical as well as anthropological interests. While the geneticist may be primarily interested in examining the distribution of a trait through the generations, or to examine the phenotypic expression of the trait in different members of the pedigree, the anthropologists are more interested to see the trait in familial settings which are influenced by society and culture. Through gaining genealogical information, the anthropologist collects data which can emphasize the cultural environment surrounding those individuals who have a genetic trait, or a disease associated with a genetic trait. Genealogies are also useful for collecting chronological information such as when deaths and births occurred, intermarriages between villages and families, migration out of the village.

Health and fertility histories

From each of the thirty-nine families in the study, information about the family's general health, the children's health history, and the mother's pregnancy history was collected. In the health history, participants were questioned about childhood illnesses, jaundice, hepatitis, allergies, the last visit to the physician and the use of vitamins and pharmaceuticals. This series of questions included those which related specifically to favism and other blood conditions; e.g., knowledge of one's blood group, recognition of jaundice, understandings about anemia, and the association of fava beans with jaundice.

Fertility and pregnancy histories included questions regarding the number of children conceived and the results of each pregnancy, birth order of the children and their spacing. Information about the attitudes of the women toward health care during pregnancy, precautions taken to promote safe delivery of the infants, methods of birth control, and diet during pregnancy was also elicited. This information was often difficult to bring out since many did not remember or recognize spontaneous abortions which happened early in a pregnancy. Others did not want to admit that they had consumed fava beans while pregnant or lactating, stating that they did not eat the beans during these periods, and then later changing their answers. While there is no particular prohibition about eating fava beans at this time, some remembered having been cautioned about them. Others showed they had strong feelings about abortions, making it difficult for women to admit having sought them. Still others had difficulty explaining why they had not sought medical advice during pregnancies.

## Collection of Case Histories of Favism Episodes

Eighteen case histories of favism episodes were collected. With the exception of two which occurred before medical diagnosis and treatment of the disease was used, all were verified through standard medical diagnosis and hospital records. Aside from providing standard information such as, how old the person was at the time of the episode, and the form of the bean eaten, informants were requested to recount the episode in their own words (without being provided with biomedical categories). Following this, each was asked if anyone else in the family had ever experienced any "problem" from eating the beans, and, how the individual came to recognize the episode as associated with the fava bean. They were asked if they had recognized the episode because it had occurred in another family member, or if the attending medical professional had explained the relationship of the bean to the hemolytic crisis.

Several possible cases of favism (i.e., showing sub-clinical symptoms, those which never reached hospitalization, and/or where $Gd^-$ trait was not tested for) were reported during the field work, sometimes in the course of taking family genealogies or in recording a clinical episode. These were not used in the case histories since the individual involved in the episode was not available; some had moved away from the island, while others had died. These cases were indicated as "probable" in family genealogies, and used in analyzing familial tendencies to show favism.

The goals of the present research project directed a protocol which could be of use to medical as well as social scientists. The actual feasibility of this goal was not thoroughly considered before going into the field. The problems of one person, trained as an ethnographer, to attend to all the medical and technical aspects of the identification of risk and favism episodes were not overwhelming, but time consuming. As a solo attempt, the project represents a divergence from other research which examines favism, and was successful in gaining considerable information which had not been treated in earlier studies about the disease.

## Footnotes

## Chapter Two

1. Motulsky (1960; 1962; 1965) and Livingstone (1967) have compiled figures which show that the Gd- trait is nearly absent in Northern and Western European populations, in northern Asia, and in North America. Individuals affected with the deficiency and/or favism in these regions are usually from an ancestry which was initially located in these areas of the world where the deficiency is present. Some have reported unusual varients in non-Mediterranean populations; (e.g. Vuopio et al. 1975) their varients may go unnoticed since they are not often involved in severe hemolytic crises. Populations located in various regions of Africa, Indian, southeast and south Asia, and the circum-Mediterranean have a tendency to be affected with the deficiency. As indicated in the review of the literature, the deficiency is not uniformly distributed in these areas.

2. In Spain, a screening of 2520 males (Flatz and Duran 1967) showed the G6PD deficiency to be limited to the coastal areas of Valencia and the Balearic Islands. A later screening (Pellicer and Casado 1970) found the trait to be fairly evenly distributed although low in frequency, throughout five provinces in Spain.

   The deficiency is also found on the Italian mainland (Livingstone 1967) but its most significant populations affected are found in Sardinia, with frequencies of up to 35% of those tested (Siniscalco et al. 1961) with overall average of 12.5% (Carcassi 1958).

   Iran (Belsey 1973; Donoso et al. 1969; Daneshbod 1975) , Bulgaria, Cyprus (Joannides 1952), have been noted to have high rates of the deficiency and favism, along with being noted in Yugoslavia (Fraser et al. 1966).

   African populations have also been noted to show the deficiency, but these are not known to be the same varient of the enzyme deficiency trait as the Mediterranean, e.g., in Nigeria (Gilles and Taylor 1961) and Sudan (Hassan 1971).

3. Statistics for favism were originally collected for the years 1966-76; these figures were updated during subsequent visits to Rhodes during 1977 and 1979, the latter visit not related to further field work.

4. Particularly when working with time and geographic limitations, previous screenings for the enzyme deficiency involved school aged boys from elementary and secondary schools (e.g., Choremis et al. 1963a; Stamatoyannopoulos and Fessas 1964; Siniscalco et al. 1961).

5. When Rhodes is contrasted with other regions of Greece and the Mediterranean where screening for the deficiency has taken place, it is clear that we are dealing with a much smaller population in Rhodes. Choremis et al. (1962 and 1963a and b) screened the population of Arta, Greece, by sampling 532 males in a population of 82,630. This represented less than 0.6% of the total population of the region. It should also be noted that the entire population of Rhodes is less than 70,000 inhabitants.

   Pellicer and Casado (1970) screened five areas of Spain, resulting in the collection of 320 blood samples from 48 villages, and 6,610 samples from the city of Madrid.

   Five provinces in represented in the screening of Spain conducted by Flatz and Duran (1967). Samples from these provinces range from 93 to 504.

   All of these areas are larger than the regions screened in Rhodes, on the basis of overall population, and consequently the size of the samples are larger.

6. The G6PD deficiency and favism have been investigated at Aghia Sophia Children's Hospital by numerous pediatricians, including, but not limited to, the following:

   In 1961 by Zannos-Mariolea and Kattamis;
   In 1963 by Valaes et al.
   In 1964 by Stamatoyannopoulos and Fessas; and Stamatoyannopoulos et al.
   In 1965 by Kirkman et al.; Kirmlides S. et al.
   In 1966 by Stamatoyannopoulos et al.;
   In 1967 by Kattamis; and Pantelakis and Doxiades
   In 1969 by Kattamis et al.;
   In 1970 by Kattamis and Tjortjatou;
   In 1971 by Kattamis et al.; and Pantelakis and Doxiadis.

7. Neonatal jaundice has been investigated at the Children's Hospital by Doxiadis et al. (1961, 1962, 1964) and Valaes et al. (1964).

   Sickle-cell anemia has been researched by Choremis et al. 1963, and Stamatoyannopoulos and Fessas 1964.

   Thalassemia studied by Kattamis and Lehmann (1970); Kattamis et al. (1972), and Matsoniotis and Kattamis (1969).

8. The two physicians which were instrumental in helping me select the research site, design the strategy for testing for the deficiency, and assuring me that the blood samples would be correctly handled in the laboratory were Dr. Stephanos Pantelakis, Director of the Institute of Child Health, and Dr. Aris Karaklis, Director of the Hematological Laboratory at Aghia Sophia Children's Hospital.

9. Agrarian physicians stationed in the rural areas of Greece immediately after finishing medical school participated in the screening. Dr. T. Latifis and Dr. Stelios Valsamakis helped in taking blood samples from school children in five villages in 1975 and 1976. Dr. Georgios Sisamatos helping in drawing blood samples from children in two villages in 1977.

10. This method utilizes a dye indicator, brilliant cresyl blue, which is mixed with the blood sample. If the blood sample is normal (non-Gd$^-$ trait) it is reduced to a colorless state within an hour. Readings of the reaction are made every five to ten minutes, starting at forty minutes after the indicator has been introduced into the sample. Samples that are normal usually discolor within the first 65 minutes, while those which take over 100 to 150 minutes are considered to be deficient and those which take over 100 to 150 minutes are considered to be deficient and those over 180 minutes are believed to be the Mediterranean variant. Only the USA National Aniline preparation of BCB can be used in this test. This reagent was not available after the first five villages had been screened.

11. For these two villages a fluorescence test described by Beutler was used to indicate the presence of the deficiency. Prepared blood is spotted onto a paper every five minutes for 25 minutes (five drops, that is). The spots are allowed to dry, then read by the use of a fluorescent lamp. Those with the deficiency appear different under these conditions. This test can be used effectively with blood samples which have been stored under refrigeration, for up to 2½ weeks after the blood was collected.

# CHAPTER THREE

## RHODES: THE ISLAND AND ITS VILLAGES

According to Greek myth and the poetry of Pindar (writing in 464 B.C.), it is told that...

> When Zeus was dividing the islands of the Mediterranean and Aegean Seas among the gods and goddesses of Mt. Olympus, he forgot to allot one to the sun god, Helios. Suddenly, a new island arose off the coast of Anatolia in the Aegean. Zeus gave this island to Helios who named it for his wife, Rhoda. The children of Rhoda and Helios, the Heliades, populated the island, and the generations that followed became referred to as the "descendants of the Heliades." (Paraphrased from Rhodes, 1977)

Although Rhodes has been covered by water at different times in its geological history, it is unlikely that it arose suddenly from the sea. The appearance of Rhodes just off the western coast of Turkey had nothing to do with either catastrophic or volcanic events, although it averages about two major earth quakes every century with minor tremors each year. Periodic oscillations in the sea level have given the island a dissected rather than truly mountainous character.

Rhodes is not a particularly large island and one might assume that its population and history must be homogeneous. This is not the case. While it has experienced certain historical events in common throughout the island, these events have not affected all of the regions in the same way. These historical events are listed in Table 3.1, and since they can be found in almost any tourist guide

TABLE 3.1

MAJOR HISTORICAL EVENTS IN RHODES

| | |
|---|---|
| 2500 B.C. | Charian and Phonecian trade contacts |
| 1550 | Minoean settlement of west coast of Rhodes |
| 1450 | Occupation of the west coast (Ialyssos) by Mycenaeans |
| 1200-1000 | Arrival of the Dorians: establishment of three city-states (Ialyssos, Lindos and Kamieros) |
| 700 - 500 | Extension of Rhodian naval influence to the Balearic Islands, Sicily and Asia Minor |
| 480 | Joins the Athenian League |
| 305 | The Great Siege of Rhodes (after which Rhodes becomes independent for limited time) |
| 316 | Part of population of Rhodes City lost in flood |
| 227 | Rhodes City partially destroyed by major earthquake with part of population lost. |
| 332 | Rhodes sends troups to take part in the siege of Tyros (Tyre) on behalf of Alexander the Great |
| 42 A.D. | Resieged by Rome |
| 70 | Incorporated in the Roman Empire |
| 155 | Major earthquake drives out most foreigners from Rhodes |
| 263 | Raided by Goths |
| 344 | Major earthquake |
| 515 | Major earthquake partially destroys the City of Rhodes |
| 620 | Sieged and occupied by Persians |
| 653 | Arab Saracens sack Rhodes City |
| 807 | Seljuk Turks siege the City |
| 1082 | Trade contacts established with Venice |
| 1097 | Rhodian harbors used during the Crusades |
| 1248 | Temporary occupation by the Genoans |
| 1309 | Rhodes ruled by the Knights of St. John |
| 1444 | Siege by the Sultan of Egypt (Marmeluks) |
| 1453 | First siege by the Turks |
| 1480 | Second siege by the Turks (Mohamed II) |
| 1522 | Third Siege by the Turks (Suleiman the Magnificent) |
| 1912 | Italians take Rhodes from Turkey |
| 1947 | Rhodes is annexed to mainland Greece |

Sources: Compiled from Dicks 1974; Nixon 1968; Taylour 1964; Rhodes (Clio Edition) 1977.

to the island, it is not necessary to describe each one. Certain events in history which influenced population size and composition are extremely important to questions which will be raised in Chapter Four regarding the dynamics of the $Gd^-$ trait distribution. These events and population movements are described in this present chapter, along with others which have a bearing on regional divisions in contemporary Rhodes. For example, the two villages which formed the comparative base of the study represent two different historical and geographical aspects of the island. Kritinea on the western part of the island, located in the mountains, claims to trace the ancestry of its inhabitants to the earliest settlements. Massari, on the coastal, alluvial eastern part of the island has no similar claims to an uncontinued line of habitation. These divisions will be referred to again in subsequent chapters, related to the distribution of the $Gd^-$ trait and favism episodes. Finally, certain historical (or mythological) events are included which give color to the present-day socio-cultural life in Rhodes.

## Population Movements in Historical Rhodes

At some point in time, mythical or real, the descendents of the Heliades became the modern Rhodians who now populate the island. Those who inhabit the western part of the island trace their origins to the nearby island of Crete, the center of the Minoean culture in ancient history. Their foundation myth states that at one time the Cretan prince Althaemenes (grandson of Minos, the legendary king of Crete) was warned by a seer that he would someday kill his own father, Katreas. To avoid this, he fled from Crete and settled in the mountainous western part of Rhodes. By standing on the highest mountain, he could see his home island.[1] The archaeological record confirms that the west coast of Rhodes was in fact inhabited first by the Minoeans from Crete. With the exception of earlier trading outposts, established by the Carians, Phonecians and other Asia Minor groups, the Minoeans were the first to establish actual settlements on Rhodes with a neolithic site dating to about 1550 B.C. This same region was eventually occupied by another group of people, this time, from the mainland, the Mycenaeans.[2] They eventually replaced Minoean influence in Rhodes by 1450[3] (Dicks 1974; Rhodes-Clio Edition 1977).

The Dorians, another group from mainland Greece,[4] arrived on the island and established city-states as they had done in the other areas of the Mediterranean which they conquered.[5] Two were founded on the northwest and west side of the island: Ialyssos, nearly on the same site as the original Minoean settlement, and Kaimeros, near the present-day mountain villages of Embona and Kritinea which were screened in the present research. A third city-state of Lindos was established on the east side of the island. The present-day village of Lindos occupies this ancient site, and was screened in this research, as well as the surrounding coastal areas which were probably encompassed by the power of this city state. Lindos, from its geographic position and natural harbor was able to extend maritime power over areas outside of Rhodes and contrasts with the other side of the island which remained agricultural.

Early Invasions of Rhodes

In spite of repeated invasions by the Romans, the Egyptians, the Turks, the Persians and even the Goths, the Rhodians always tried to maintain their island as a politically independent unit. From the 12th to the 5th century B.C., Rhodes exercised independence and fostered overseas communities which reached Sardinia, Sicily and the Balearic Islands. In 480 B.C., Rhodes became officially a subject of Athens by joining the Athenian League, which further solidified its ties with mainland Greece. Turkey beseiged the island three times after the 5th century B.C., and took control of the island by 42 B.C. for the following 110 years. The Turkish control of the island ended when Rhodes was incorporated into the Roman Empire. Throughout this period, the island had maintained its Greek (Doric) culture, and the population which numbered about 500,000 at the time was still regarded as Dorian and not Turkish.

Following the subdivision of the Roman Empire (395 A.D.) Rhodes was again subject to repeated attacks and sackings by populations from the Anatolian mainland. The Persians attacked in 620 A.D., the Arab Saracens in 653 A.D., followed by the Seljuk Turks, who besieged the island and disrupted trade relations between Rhodes and other ports, for a major historical period. The Knights of St. John, a military order created during the crusades, besieged Rhodes, taking it by force, and slaughtering the majority of the Turkish population. They formally gained control of Rhodes in 1309, and under their control, the island reestablished its important trade links. In spite of the relative peace and economic prosperity, the population of the island was half of what it had been when it belonged to the Roman Empire. The drop from 500,000 to 250,000 may have resulted from the mass slaughter which preceded the take-over by the Knights.

## Turkish Occupation of Rhodes

In 1522, Suleiman the Magnificent laid siege to Rhodes, took the island from the Knights, and 390 years of Turkish domination began. Initially the Turkish policy towards Rhodes was one of autonomy. The only intrusion of the Turks on the island seems to have been in the City of Rhodes where taxes were collected from the countryside once a year. After 1826, the autonomous policy towards Rhodes gave way to one directed by harsh assimilation measures. This was apparently precipitated by a series of rebellions against the Turks through the Aegean. Following this change in policy, wholesale emigration from the islands in the Aegean occurred, Rhodes taking part along with the other islands. From a total population of 250,000 during the era of the Knights, the population of Rhodes fell to 35,000 (Myres 1953) in the mid-1800s. The Turkish population was located primarily in the urban area (as was their usual practice in conquered lands) and in villages especially created for them. These are shown in Figure 3.1.

## Italian Occupation 1912-1947

Immediately following the Turkish occupation of Rhodes, the Italians took the island. During the years of the Italian occupation, the Turks gradually moved out of the countryside into the City of Rhodes, and away from the villages which had been created by them.

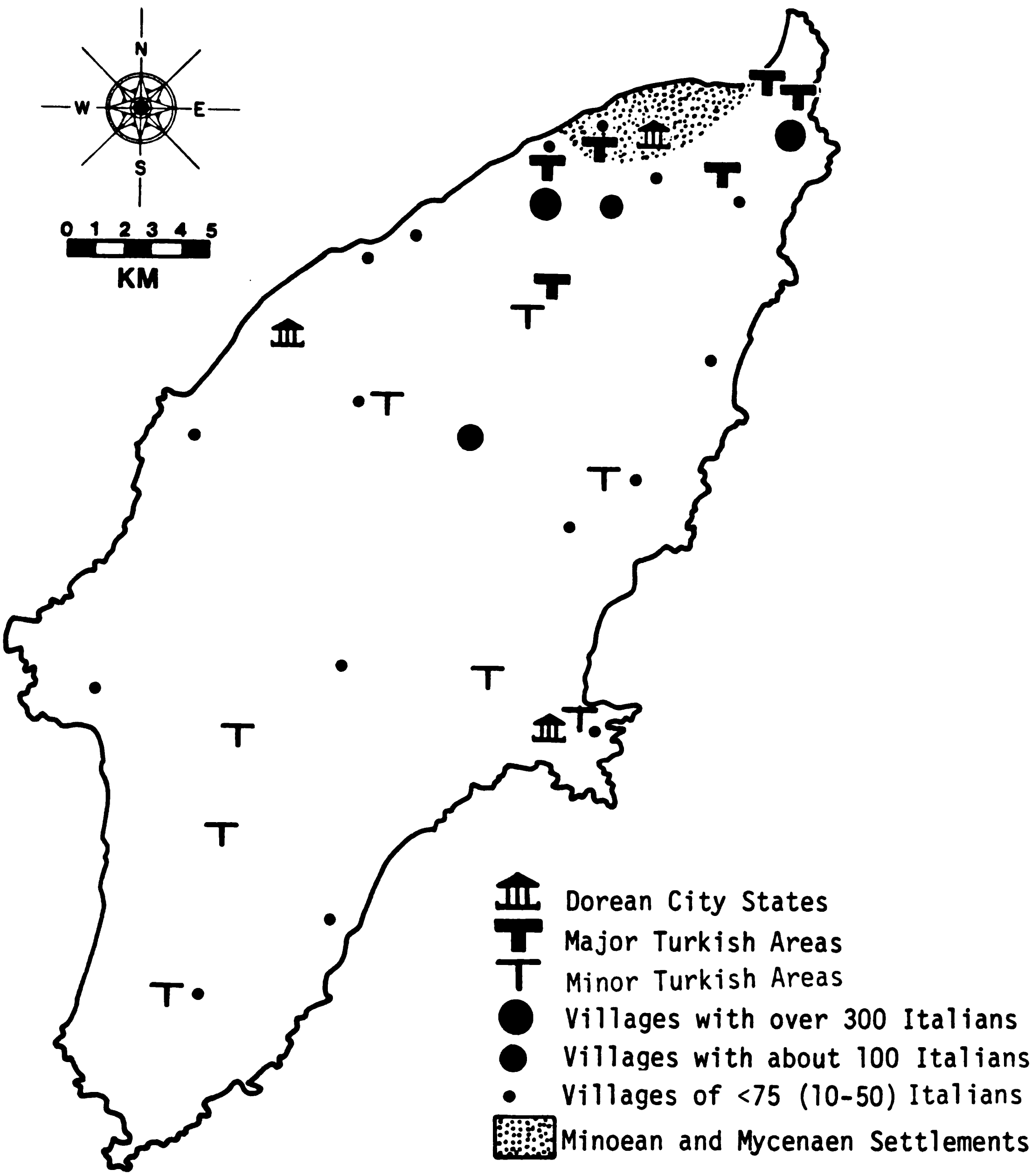



Fig. 3.1 Location of Historical Populations in Rhodes

Population figures during this period reflect a drop in the Turkish population and a rise in the overall population. Meanwhile, the Italians moved into the countryside, imposing new rules and regulations on the rural inhabitants. They required the registration of surnames (until this time, village registers were not kept by local inhabitants), and made Italian the official language, and Roman Catholicism the official religion of the island. During this period, intermarriages between Italians and Greeks occurred, but the contemporary villagers contend that none of these unions or the results of them can be found in the countryside. Couples where one spouse was Italian, left the island, and went to Italy after 1947. Areas where the Italians settled during 1912-1947 are shown on Figure 3.1. Administrative duties and attempts to assimilate the island into an Italian colony devoted primarily to tourism required that at least a handful of Italians were present in every major village, or, more often, on the outskirts of the village on separate farm compounds.

In 1947, Rhodes became part of Greece politically. Residents of Rhodes still consider themselves as distinct from mainland Greece, even though they maintained the Greek language, religion, and customs in the face of so many repeated foreign invasions. They still refer to a trip to Athens as ".... going to Greece."

## Contemporary Rhodes

The climate and certain geographic features contribute to the agricultural potential of Rhodes, and aid in attracting tourism to the island, an economic venture which was initiated by the Italians.

Often called the "Island of Sun," the maritime climate of the island is marked by periodically high winds and humidity. Although it rarely rains after May and before October each year, it has an ever-present humidity, particularly along the coastal lines. The mountain areas on the west side of the island receive the major portion of the rainfall, with the eastern areas taking advantage of the watershed. Among these mountains are the two highest elevations on the island, Mt. Attavyros (1356 meters) and Prophet Elias ($\simeq$900 meters).

The massive core of hard rocks, particularly limestone beds which are poor both in marble and ore, retain moisture and help to make Rhodes more agriculturally productive and greener than other islands of the Aegean Sea. It possesses a significant degree of ground cover, with irrigation being possible in selected coastal areas in the northern half of the island and along the alluvial west coast.

## Rural Rhodes

All the villages are economically linked to the City of Rhodes, located at the northern-most point of the island, through their agricultural production for the main wholesale market in the city. This applies more to the northern villages than to the ones located in the southern most regions of the island. Vegetables and fruits are taken daily from the villages. They are trucked to the wholesale market where they are sold to middlemen who in turn sell the produce to grocers, restaurant owners, and to the retailers who open the other open-air city markets. In the northern part of the island, there are no rotating markets which operate in one village during one day of the week and another village on the following day. These open air markets (laikí agorá) which operate on a rotating basis and help link villages on a regional basis on other parts of Greece, do not operate in Rhodes. Small trucks or carts may travel from village to village with produce, however, this occurs under individual direction. Villages of Rhodes, therefore, are not economically interdependent on each other through regional distribution of agricultural produce. While certain villages specialize in their productive efforts, it is in the service of the city market, not regional ones.

The agricultural cycle on the island is divided into two periods; the summer, dry season, and the winter, rainy one. There are climatic indications of transitional periods which might be called spring and autumn, but they are short in duration and subsumed by the major seasons. The summer, dry period from May to October represents the time of the most intensive agricultural activity, beginning with the clearing of fields in preparation for sowing. Villages cultivating a variety of crops must schedule their exploitation of the land according to the growing requirements of the cultigens which include tomatoes, cucumbers, zuccini squash, black-eyed peas, peppers, egg plants, green onions, melons, non-citrus and citrus fruits, and grapes. All villages have olive trees, which produce enough olive oil to last throughout the year. For villages which rely on irrigation, such as those on the north-west and east coast, April marks the time during which irrigation ditches must be cleared in order to receive the stored water from under- and above-ground wells and cisterns. Irrigating the fields particularly the orchards, consumes a good deal of time in the summer dry months. Grapes, melons, and fig and olive trees do not require irrigation, in fact, it is said that the sun, not water, makes their fruit sweet, but citrus crops cannot be produced without lots of water.

The end of the summer (August, September), is marked by the grape harvest, an extremely intensive period for all areas which cultivate grapes as a major product. Grapes are trucked to the city wine factories, but some keep at least half of the produce in order to make their own local wine. Even though Rhodes is not known for its olives and olive oil, as are other areas of Greece where they are produced as cash crops, but each village has its own trees.

It is highly likely that the fava bean was among the cultigens during the neolithic period in Rhodes, where it may have been cultivated for both human and animal consumption. In contemporary Rhodes, fava beans are cultivated primarily for human consumption. While some of the villages have stopped or cut back on its production since the end of the Second World War, the fresh bean is still seasonally available throughout all regions of the island. The beans are planted during the rainy winter, and become ripe and fit for consumption from March to May. The dry form is sold in groceries during the winter months, at which time the dry fava beans are used in a variety of preparations, as are other dry beans and pulses.

Major Regions of Rhodes

Contemporary Rhodes is so influenced by the presence of tourism that it is sometimes difficult to comprehend at first glance that a rural, agricultural life exists side-by-side with a cosmopolitan, fast-paced, international tourist economy. Once the tourist centers are left behind, one of the most striking features of the island which emerges is its regionality. Traveling through the countryside, different settlement patterns and house styles are noted in the different villages; it is possible to hear a variety of expressions and words not used in standard Greek conversation, and which differ by village; some areas display traditional dress even in everyday life; and some villages show that they have slowly abandoned agricultural production in order to attract tourism which small shops and locally produced handicrafts.

Geographically, the island is divided into four regions as shown in Figure 3.2. These divisions are complemented by historical, demographic and economic characteristics which are further accentuated by differences in cultural content (e.g., dialect, dress, celebrations, social ties between villages). It is important to have an appreciation of these differences as they will again be referred to in subsequent chapters. The mountainous spine culminating in the central peaks forms a natural division separating the east and west coasts of Rhodes. This divide is cross-cut by the northern tip of the island and the southern half. The northern tip of the island, which includes the contemporary City of Rhodes, shows the longest period of human occupation for the island. Reviewing

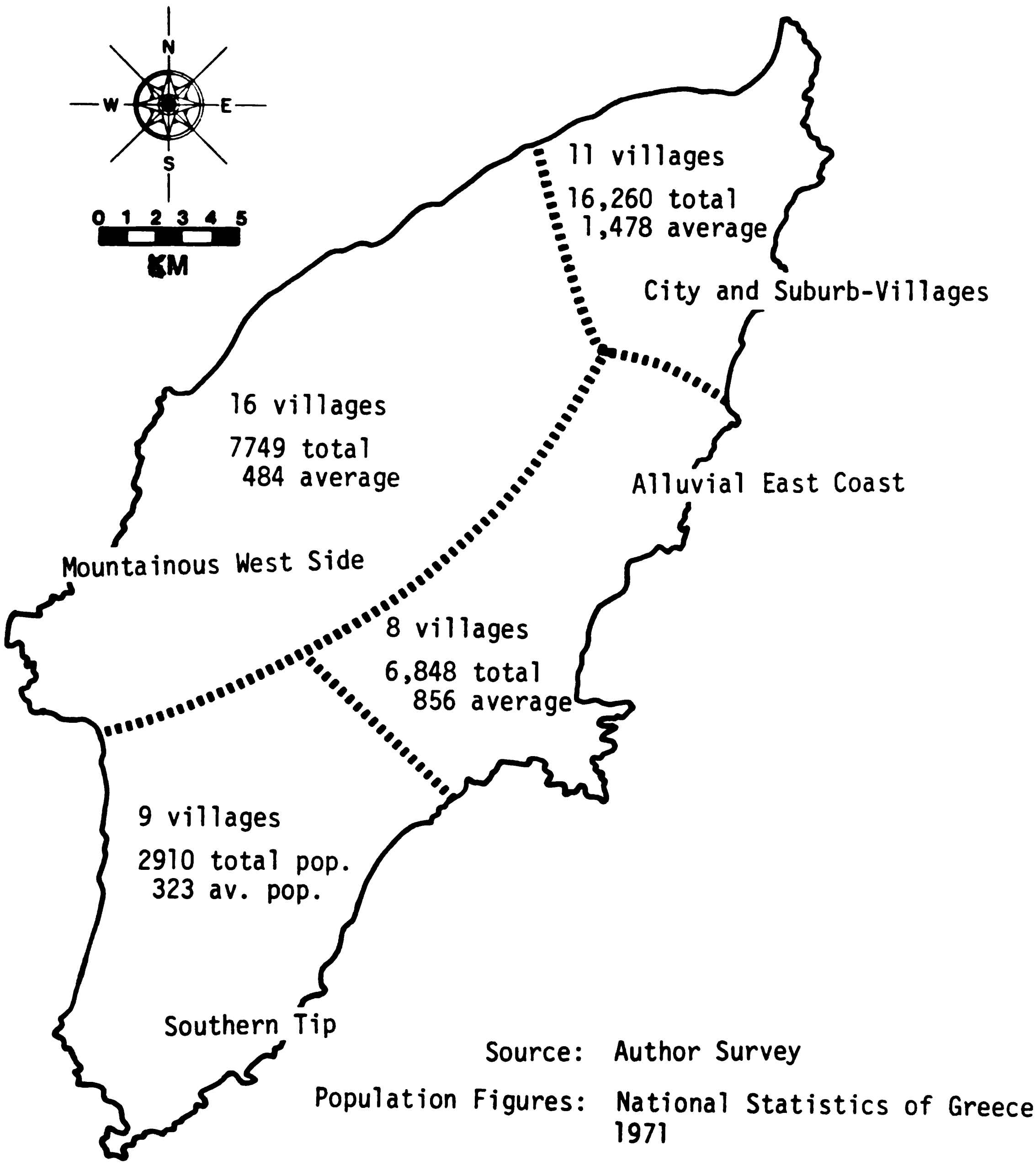



Fig. 3.2 Major Regions of Rhodes

Figure 3.1, it is clear that this area has been most subject to various populations, beginning with the Minoean, the Mycenean, the Dorean civilizations, and later with large numbers of Turkish and Italian settlements. The southern tip has the least record of intruding populations and today consists of very small settlements. These are not easily brought into the rest of the island's influence nor do they participate in the major economic pursuit of the island's tourism. The east and west coastal areas and the inland locations influenced by them are so different in physical environment that their resulting and economic differences are expected. These points of differences are discussed according to the four regional divisions: (1) The City of Rhodes and its suburb-villages; (2) the southern tip; (3) the eastern alluvial plain; and (4) the mountainous Western flank.

### The City of Rhodes and its suburb-villages

The eleven villages immediately surrounding the City of Rhodes have come to serve as suburbs to the city as well as maintain their rural character. Tourists pass regularly through them on their way to the beaches and/or hotels which have been built on the outskirts of these villages within the last few years. Agriculture is irrigated in these areas, with the cultivation of a variety of crops. The villages here have retained much of their agricultural origins and it is possible to see villagers on their way to the fields side-by-side with tourists in open-topped cars on their way to the beaches. Year by year, even since the time of the beginning of this research, an increasing number of fields are being left fallow, and windmills left unused. Ironically, the windmills which were built during the Italian occupation of the island for irrigation agriculture, have become a symbol associated with the island of Rhodes. One of the first things noted upon arriving at the airport in Rhodes is the row of windmills lining the runway, and a most characteristic spot in the city is a pier lined with three windmills which were once used to grind grain.

Because these villages are close enough to the city for its inhabitants to choose from a variety of occupations ranging from full-time agriculture to full-time tourist related economic pursuits, they have been successful in holding on to their populations. This is the area of densest population with these villages being the largest on the island. With their total population of 16,260 inhabitants, they average 1478 to a locale. Some range to over 2500 inhabitants.

The southern tip of the island

The southern, triangular portion of the island is characterized by nine small villages of around 325 inhabitants each (total population is only 2910). Transportation links are not regular, which may relate to their being left-out of the mainstream of tourism. Bus service does not connect the villages with the city on a daily basis which would facilitate commuting to the city to work during the tourist season. Even if it did, the condition of the roads and the distance involved would make the connection take over two and a half hours.

Some of the settlements in the area were established during the Italian occupation when an air strip was constructed to aid in the war effort. In ancient history, this part of the island was of little interest to those traveling the Aegean trade route to Anatolia, no city-states were established here, no evidence of early settlement has yet been uncovered, and it is generally treated as an area of marginal interest on the island.

None of the villages were screened for the $Gd^-$ trait primarily due to transportation difficulties which would have impeded correct handling of the samples. Few of the villages reported cases of favism to the hopital. It would be worthwhile to look at this area at some time in the future simply because it has been so neglected in previous studies of the island, as well as in the present one.

The alluvial east coast

Although strongly pulled into the tourists interests of the city and to those of Lindos to the south, the alluvial expanse on the east coast of Rhodes has been able to enjoy a fruitful economic base through the extensive cultivation of citrus and vine products. The villages in this area are easily accessible to each other and to the city. Settlement patterns are not restricted by sharp altitudinal increases, with village centers occupying flat areas which radiate out from a central square. Agriculture is heavily dependent on the cash cropping of citrus and vine, with some production of varieties of vegetables. Olives are produced only for village consumption and for their oil.

Historically, these areas were under the domination of the ancient city-state of Lindos, which has become the second most important tourist attraction on the island (in fact one of the highest ranking tourist attractions for all of Greece), drawing heavily upon these villages for personnel to provide the necessary commodities and services to maintain the tourist trade. Many fields have been abandoned in favor of the seemingly more lucrative and easy life of tourist related work. Economic alternatives and access to the cash market is considerable.

Next to the northern tip of the island, this area is the most densely populated. A total of 6848 inhabitants occupy its eight villages, for an average of 856 per village.

The mountainous west side

As described in the history of the island, this area of the island was probably associated with Kamieros, the ancient city state. Today it is not densely populated. A total of 7749 inhabitants are scattered among sixteen villages (about 484 per village). The coastal villages of this side of the island have a strong connection to the city, while the village slightly to the south in the mountains have maintained a more traditional agricultural and herding economy. Five villages on the island can be considered as truly mountain villages, in geographic location, settlement pattern, and ecological situation. These five, plus adjacent villages in the foothills of these mountains form what is referred to here as the mountainous western flank of Rhodes.

Agriculture and herding dominate these villages. The valleys are expoited for fruit trees and vegetables, middle levels for grape and olive production, and the higher altitudes for grazing flocks. The small strip of arable land on the coast of the west side is used for the cultivation of the earliest spring crops. The use of "hot-houses" constructed from vinyl plastic and wooden frames, and set next to the sea to take full advantage of the sun's reflection, produce early tomatoes and other vegetables which are not usually available until later in the summer. Instead of abandoning plots of land in this area, new fields are continually being prepared and cleared. Some of these will be given to sons and daughters when they marry, and one has the sense of agricultural continuity which does not exist either in the suburban-villages around the city, or in the alluvial east coast villages.

Participation in the high-paced tourist trade is lacking with the exception of the village of Embona, which imports tourists on a daily basis to tour the village, eat at the local tavernas where cutlets of goat and sheep are the local specialty along with the locally produced wine, and learn folk dances from the villagers. Land is heavily exploited by intensive labor, and the land is terraced to accomodate the vineyards located on the sloped of the mountains. Settlement patterns in these villages conform to topographic contours of the mountains.

## The Villages of Massari and Kritinea

Based primarily on the results of testing for the enzyme deficiency, the survey of favism cases reported in different areas of Rhodes, survey of fava beans in the rural locations, and knowledge of the regional characteristics of the island, two villages were selected for the collection of ethnographic data. One of these villages, Massari, is located in the eastern alluvial coastal region, the second, Kritinea, is in the mountainous western flank of the island. Both villages showed high frequencies of the enzyme deficiency, with Massari being closer to the average for the island with Kritinea being considerably higher (27 and 40% respectively). A substantial number of favism cases were reported in Kritinea, while Massari had very few. Possible reasons for differences in the frequencies of the deficiency and favism will be discussed in subsequent chapters. For the present these villages will be described and placed in their regional context.

Massari and Kritinea are located at two opposite ends of the widest part of the island of Rhodes. Since the island is twenty-two miles across at its widest portion, they represent the two villages located at the most extreme part of the island's width. The spine of mountains which runs the length of Rhodes separates these two villages, with travel between them almost impossible. If one wants to go from Kritinea to Massari, the mountains must be circumvented. Travel by bus requires a trip all the way into the City, one and a half hours away, where a connection is made to go to the opposite side of the island, again one and a half hours outside the City.

## Massari: Environment and Economic Setting

A little over two kilometers from the sea, Massari occupies the alluvial coastal plain on the east side of the island. Access to the sea is direct by foot a thirty minute walk along a dirt road that slopes gradually to the sea. The village itself is barely twenty-five meters above sea level, and the intermediate plain which is full of olive trees, fig trees, and grape vineyards shows signs of underexploitation. This area of the island, it is presumed, has not been subject to the invading populations which characterize the history of the other half of the island. Evidence of early occupation of the area between contemporary Massari and the sea is found in the remnants of house foundations which are scattered among the vineyards. Since an old fortress (Kástro) perches on a nearby hill, it is thought that the inhabitants of these old structures used the fortress for storage of agricultural produce and protection.

The inhabitants of Massari say that the old village of Massari was leveled by an earthquake some 160 years before (around 1810), during the last stage of the Turkish occupation of the island. The survivors were forced to go to nearby villages, to Malona in particular, for refuge. Slowly the village of Massari was rebuilt, closer to Malona and farther from the sea. Even though traditional enemies, the people of Massari consider themselves linked to Malona by biological ties, marriage and ritual kin.

Settlement pattern

The flat plain of Massari allows for the settlement pattern of the village to show a simple grid pattern. The village has one major plateía (square) onto which all the major public institutions open. The center of the plateía was once dominated by an open well surrounded by benches and trees, but this has been rebuilt and is now little more than a ceramic structure with several spigots which are used only occasionally. Three cafeneía (coffee houses or cafes), three small grocery shops, the school, the church, and the equipment shed for the local football team surround the plateía. Almost all inhabitants pass by or through the plateía at least once a day, on the way to shop, on the way to the fields, to collect mail from the passing mailman who arrives on motorcycle, or to meet the children at school. The plateía also makes a convenient stopping off point for tourists on their way to visit Lindos, twenty minutes away by automobile, who are out of earshot of the comments being passed around about them at the cafeneía which enjoy a clear vantage of all events transpiring around the plateía.

The houses in Massari are connected to each other in block form, sharing courtyards which are separated by walls and gates. In most cases, the wall seems to be purely a matter of style, as one can easily see directly into the neighbor's courtyard by simply peering over the low wall. Even so, the courtyard is defined as part of the house, not the outside or the street. Rarely does anyone pass through the gate of the courtyard without first shouting to ask permission to enter.

The oldest homes in Massari date to 1870, the first ones rebuilt after the earthquake. These were one-room structures built in a row, attached and not separated at that time by a courtyard. Some had a small shed attached perpendicular to the main one-roomed house. Because they were attached on either side, the only place for a window was on the side of the door. Inside, the ceiling was made of cane and held up by major wooden strips transcrossing the cane. The large room was superficially divided and supported by an archway. Space in these one-room homes is used economically. The "first room" the one before the arch, is usually left open, but the second room is again subdivided with the use of a raised platform or loft at about 5 feet above the ground. Underneath, the area is used for sleeping. This style is noted throughout the islands. Even in homes built in the 1940s, the loft was retained, or modified for sleeping areas. Sanitary facilities (e.g., running water, toilet and bath facilities) in the oldest homes were non-existent as people used the fields and carted water from central wells. The oldest members of Massari's population still live quietly in these homes, all of which have at least one electric fixture, although many do not have running water either inside or in the court-yard.

Sometime between 1870 and 1950, houses were enclosed with courtyards, a second room added (or even a third) perpendicular to the main room, and some outdoor plumbing installed in the way of a _cabinét_, that is a small outhouse with a hole in the ground and/or a sink in the courtyard with running water. This likely happened to most homes during the Italian occupation. The houses then assumed and L-shaped enclosed court with all rooms opening onto the court, the _cabinét_ being unattached. Some even had a special cooking hut, set next to the _cabinét_ where water was supplied to both. These houses still stand; in fact, I occupied one such house during field work.

Until the last ten years, this form dominated, being elaborated upon with improved sanitation facilities, a kitchen or cooking shed or extra room. Lately, entirely new homes are being built, all enclosed, surrounded by a courtyard. These are made with all the rooms opening onto the hall, each being able to be shut off. Many, although enclosed, have an additional room which is roofless and has a storage closet in it for all the things which were at one time stored under the loft in the traditional house.

Friedl (1967) has argued that due to the agonistic character of the Greeks, households are placed so that windows and doors do not face each other so that no one can look directly into another's home. This does not hold true for Massari: houses are laid out quite symmetrically, and it is not uncommon to be able to see into a neighbor's home from one's own courtyard. The flat environment surrounding Massari, plus the fact that all the structures were built within the same period following the earthquake, promote a predictable regularity in the placement of the hoses. Gates to the courtyards, more often than not, open directly across from each other. In Kritinea, where the houses are built on terraces cut into the mountain, it is difficult to have rows of structures which face each other at the same level. Entrances to houses are made according to the convenience allowed by the immediate surroundings. If houses happen to have doors which face each other, it is by chance just as is the reverse.

## Links with the outside

The presence of tourism on the island, and particularly the link necessary to transport tourists from the City for one or two day visits to the Acropolis of Lindos puts Massari in greater contact with the outside world than is possible in Kritinea. Transportation is direct, with several daily bus lines running through the village. These are increased in number during the tourist season to accommodate not only tourists, but those from Massari and surrounding villages to travel to their tourist-related jobs.

Although Massari is on a much traveled bus line, it has limited facilities for communication with the City and neighboring villages. There is only one telephone in the village, located in a small grocery store where everything said becomes public knowledge. Telephone connections are often not reliable, and if one wants to send a telegram and/or make a reliable phone connection, travel to another better equipped village is advised. Mail arrives usually on a daily basis in both villages, brought by a postman on motorcycle to Massari where all converge on the central square to hear if they have received anything. In Kritinea, the central post office for the village and surrounding areas receives and sorts all incoming mail.

## Agricultural activity

Agricultural efforts in Massari are directed toward the production of citrus fruits for the wholesale city market and of grapes which are processed into wine in the city wine factories.

Most of the inhabitants of Massari who have been born into the village hold plots of land exploited for vine production. Others with more extensive holdings have citrus orchards in addition to their vineyards. None of the land around Massari is intensively exploited; in fact, it is common to see large vineyards left untended. The orchards, located immediately surrounding the village center, are very well tended.

During the summer, beginning in late April, most of the agricultural activity is centered around grape production: e.g., weeding, cutting back the vines, dusting the leaves with pesticides. The vines are not staked up and therefore require careful attention that they do not become too heavy and spread out before they reach their peak of production. Because as many as eight varieties of grapes may be cultivated, the harvest is separated into distinct periods. Scheduling for their harvest and sale must be arranged so that virtually everyone in the village is concentrating on the harvest of a particular variety at the same time. Each variety is scheduled to be weighed during specific time periods lasting about two weeks each. This is handled by the agricultural union with duplicate records kept by both the individual producer and the village secretary. Grapes are brought to the central weighing station where they are weighed, recorded, and taken to trucks for their transport into the City of Rhodes. It may take up to three months after the final harvest for the producers to receive their cash from the union, which means that from the beginning of the time when the vineyards are first attended to in November, to the time when cash is received for the harvest, more than ten months may have passed. During this time, pesticides and fertilizer may be purchased from the agricultural bank on credit. While it is forbidden to harvest certain varieties of grapes during the period of time other than those specified by the wine factory, additional harvesting may take place in order to send grapes to the open market in the City of Rhodes, or for personal family consumption. Many families with large vine holdings have a difficult time harvesting all their grapes in order to meet the wine factory deadlines, and may employ others in the village to help.

Members of the village who do not have large vineyards may supplement their income and family diet by fishing. Access to the sea is direct from Massari, and as such promotes fishing as an economic activity, although few inhabitants state their occupation as fishermen. During the summer months, the sea on this side of the island is tranquil enough so that small boats can be used for fishing. The larger boats, adapted to the requirements of open-sea fishing are not required. Portions of the catch may or may not be sold within the village.

Although tourists often pass through Massari, stop and take snapshots, or have a drink at one of the cafes, the village does not have any small business enterprises which cater specifically to tourists (e.g., handicraft shops, small restaurants). In spite of the lack of visible tourist enterprise, Massari's participation in the tourist business is essential to its economy. A substantial number of the village's men, particularly those under thirty years of age, leave the village for the entire summer to work as hotel night clerks, servitores, janitors in hotels and restaurants, and so forth, in the City of Rhodes and in Lindos. Others confine their supplemental economic activities where they are able to commute on a daily basis. Many of the women sew, crochet or embroider items for the tourist shops in Lindos (at the rate of 25 drachma a dress, which will sell for 350 drachma in some Lindian tourist shop: 1975 figure). Within the last generation, many of the younger women of Massari have been traveling on a daily basis to the City of Rhodes to offer their services as chambermaids at hotels; others prepare food or wash dishes at the seaside restaurants in Lindos.

### Kritinea: Environment and Economic Setting

Although the west side of the island has exhibited the longest continual habitation, it is probable that Kritinea developed somewhat later than the original settlements slightly to the north (e.g., Embona, Aghios Isideros). Located in the mountains, 350 meters above sea level, Kritinea probably arose in response to the needs of the ancient city-state of Kamieros, located to the northeast of the present day village. Descending to the sea, the ancient ruins of Kamieros Scala (steps of Kamieros) can be found, which indicates that original habitation in the area included all the area from the acropolis of the city-state, Kamieros, to the sea. Kamieros Scala was at one time the harbor for the west coast of the island. This is evidenced by the still-standing custom's house for which there is no longer enough business flowing in from the outside to warrant a staff.

It might be assumed by the remains of an ancient period, that this harbor also serviced ancient Kaimeros.

The inhabitants of Kritinea trace their ancestry to the Cretans, maintaining Cretan surnames which all end with "-akis". Local inhabitants say they descended more recently from a pair of shepherds and their wives who came to inhabit the region. They eventually quarreled, with one of the two families moving higher up the mountain to found the present-day village of Embona. Even though they trace common ancestry with Embona, little attempt is made to maintain transportation and communication links between the two villages, nor are intermarriages common between them. Close to Kritinea, slightly north along the sea coast from Kamieros Scala, is a small village which is a direct offshoot from Embona. Although Kritinea is closer to Mandriko geographically, ties between Embona and Mandriko usually exclude Kritinea.

Settlement pattern

Kritinea is a nucleated mountain village, not unlike the majority of Mediterranean villages in similar environments. The mountainous topography promotes the placement of structures on terraces which were cut into the mountainside. The village has only two major roads running through it, although it is connected together by a series of winding small roads and pathways, from level to another. These are laid such that from the road or path, one is able to step onto the roof of the houses at the immediately lower level. Assent to the road behind a row of houses requires that one climb at an angle of approximately 45 degrees. The important public institutions such as the coffee houses, the central square, the church, the school, the village hall and the post office are all located at different levels throughout the village. There is virtually no central plateia, such as is found in Massari, where the majority of the members of the village converge at some time during the day. With the school located at the edge of the village, even mothers taking children to and from school do not pass at all through the central parts of the village.

Houses are laid out according to the contours of the land, which does not allow them to be connected in a block pattern. Only at the lower levels of Kritinea are the houses likely to be connected in groups of three or four households. Traditional homes have one or two rooms, the second room servicing as a store room where food preparation may also take place, such as sifting flour for bread, sorting dried beans, cleaning vegetables. These homes have outside plumbing in the form of one spigot emptying into an outdoor sink fixture. Here, dishes are washed throughout the year, even in the winter when it is likely to be raining, and chilly. Water for personal hygiene is drawn from this central faucet as well as the water for flushing the toilet facility in the outdoor cabinet, and water for the small gardens which often surround the house. In the summer, water shortages result in a lack of piped-in water to the homes. During these periods, water is drawn from the central village well, on the lower level of the village. This well was renovated by the Italians.

Unlike Massari, the houses of Kritinea do not have an enclosed courtyard. Houses are usually rectangle and composed of two rooms, or L-shaped with three rooms. The majority have plumbing located outside these two or three rooms; toilet facilities are enclosed in a cabinet, and the sink for washing dishes may or may not be enclosed in a cooking hut. Often steps may go up to the house or down to the house area. Some houses have courtyards, not enclosed by walls or fences. As with Massari, the newer houses are all enclosed, with all facilities inside, but again, rarely having courtyard space. Instead of a courtyard, however, many homes have small gardens in their immediate environment, some of these include fava beans. Newer houses are often built on two levels, the upper for living, the lower for parking machinery, storing foods and holding animals. Even though there is the tendency to make newer style homes, therefore, the necessity exists to have an area set aside for storage. In the older houses this was handled by a second or third room of the house where animals and fodder and stored commodities were all housed.

## Transportation and communication

Transportation facilities to and from Kritinea are less accessible than to any of the neighboring villages at the same elevation. There is one bus which leaves the village early in the morning and returns the same day in the mid-afternoon. The bus is primarily to service young people going to the public high school a half an hour away from the village. The roads to neighboring villages are not being well-kept, and often the road through Kritinea is avoided when descending from villages higher up the mountain. Individuals from these other villages do not pass through Kritinea on their way to the City of Rhodes. Kritinea is actually no farther from the City of Rhodes than is Massari on the opposite side of the island, yet Kritinea manages to be more isolated. What Kritinea lacks in roads and transportation, it makes up for in communication facilities. It houses the regional post office, telephone and telegraph office, as well as the regional police station. The major pieces of information then are usually funneled through Kritinea. The postman from Kritinea services five other villages in the region; telegram messages from other villages are sent out and received in Kritinea; telephoning to areas of Greece outside of Rhodes may often require a trip to Kritinea.

Economic activity

Kritinea is primarily an agricultural village, with a few families engaging in fishing activities at nearby Kaimeros Scala. This handful of families, who are winter residents in the village of Kritinea, take up summer residence at the small hamlet of Kameros Scala. These families do not have extensive land holdings, if any at all, and their sole livelihood during the summer is based on fishing. Their catch goes to one of the restaurants in Kameiros Scala. The sea on this side of the island is more exposed than on the east side. There are fewer protective harbors here, with the consequence that fishing requires larger boats and more elaborate equipment. There is no possibility that agriculturalists can supplement their income with daily fishing excursions since they cannot afford the capital investment which would be necessary to support both economic activities.

Aside from these few families involved in fishing, the rest of the population in Kritinea relies on agricultural production, the major crops being grapes, olives, and a variety of fruits and vegetables. The more successful farmers produce a variety of crops which are regularly taken to the city market. Although the village has several cafeneia, small groceries and one restaurant, these establishments are run by individuals who also engage in agricultural activities.

Kritinea is not among the several villages of Rhodes which participate in the tourist economy. Except as producer of certain vegetables for the City which may eventually be consumed by tourists, Kritinea does not participate in the tourist trade. This was not always the case. During the Italian occupation of the island, Kritinea and its neighboring village of Embona, would stage folk dancing competitions for the benefit of visiting tourists (and for the benefit of the local economy). Embona has continued this tradition to the present day, and expanded it to the point that tourists arrive daily by bus to watch folk dancing, dine at the local restaurants and buy traditional Rhodian commodities from small tourist shops. Since the departure of the Italians, Kritinea has not continued with this practice. Many felt that it was doing more harm than good to the village. Kritinea does not, today, draw tourists into the village, and it does not export personnel or products out of the village to directly serve tourist interests.

## Demographic Comparison of Massari and Kritinea

In terms of settlement patterns, general environment, economic pursuits, Massari and Kritinea represent two different types of villages found in contemporary Rhodes. Kritinea, in the mountains, shows the typical nuclear settlement pattern, an economy based on agriculture and herding which take place in a variety of altitudinal ranges. Massari, in the alluvial west coast region, shows a different settlement pattern, agriculture centered on the production of two crops, and with economic alternatives such as fishing and services related to the tourist trade.

Both have frequent transportation links with the City of Rhodes. What Massari lacks in communication facilities is compensated for by transportation links with the city. Kritinea, better equipped in communication networks, lacks transportation facilities which are as good as those surrounding Massari. In spite of the reasonable transportation and communication links between the villages and the City of Rhodes, neither village has its own resident physician, mid-wife or nurse, its own pharmacy or clinic. Villagers must rely on the agrarian physician who visits the village on a weekly basis, bringing with him (or her) an assortment of pharmaceuticals, limited diagnostic equipment, and therapeutic advice. Emergencies must be treated on the spot by local people, or taken to the nearest village with a full-time physician, or taken into the City of Rhodes.

The demographic features of Massari and Kritinea are more similar than are their respective ecological settings and economic adaptations. Fifty-two percent (52%) of Kritinea's 516 inhabitants are male, forty-eight percent (48%) are female. This compares favorably with Massari's population of 540, with fifty-four percent (54%) males and forty-six percent (46%) females. Table 3.2 shows these figures.

TABLE 3.2

POPULATION IN MASSARI AND KRITINEA

| | Massari | Kritinea |
|---|---|---|
| Males | 292 (54%) | 266 (51.5%) |
| Females | 248 (46%) | 244 (48%) |
| Total | 540 | 516 |

Age pyramids for each village are presented in Figures 3.3 (Massari) and 3.4 (Kritinea). Each step in the pyramids represents a ten year period. Table 3.3 distributes the population in each village by twenty-year age cohorts, showing that even though the pyramids have some major dissimilarities, the populations compared by twenty-year cohorts are quite similar. Massari's population distribution (Figure 3.3) more clearly approximates the classical pyramid form than does Kritinea's. No explanation can be given for the lack of females born between 1916 to 1925 in Kritinea, shown by the obvious space during that time period in Figure 3.4. Women who were 52 to 61 years of age at the time of the present study would be included in this age cohort. No similar drop in Massari's population is noted at that time period.

The composition of the actual samples used in the study were described in Chapter Two. The number of households with young

Source: Village of Massari Records

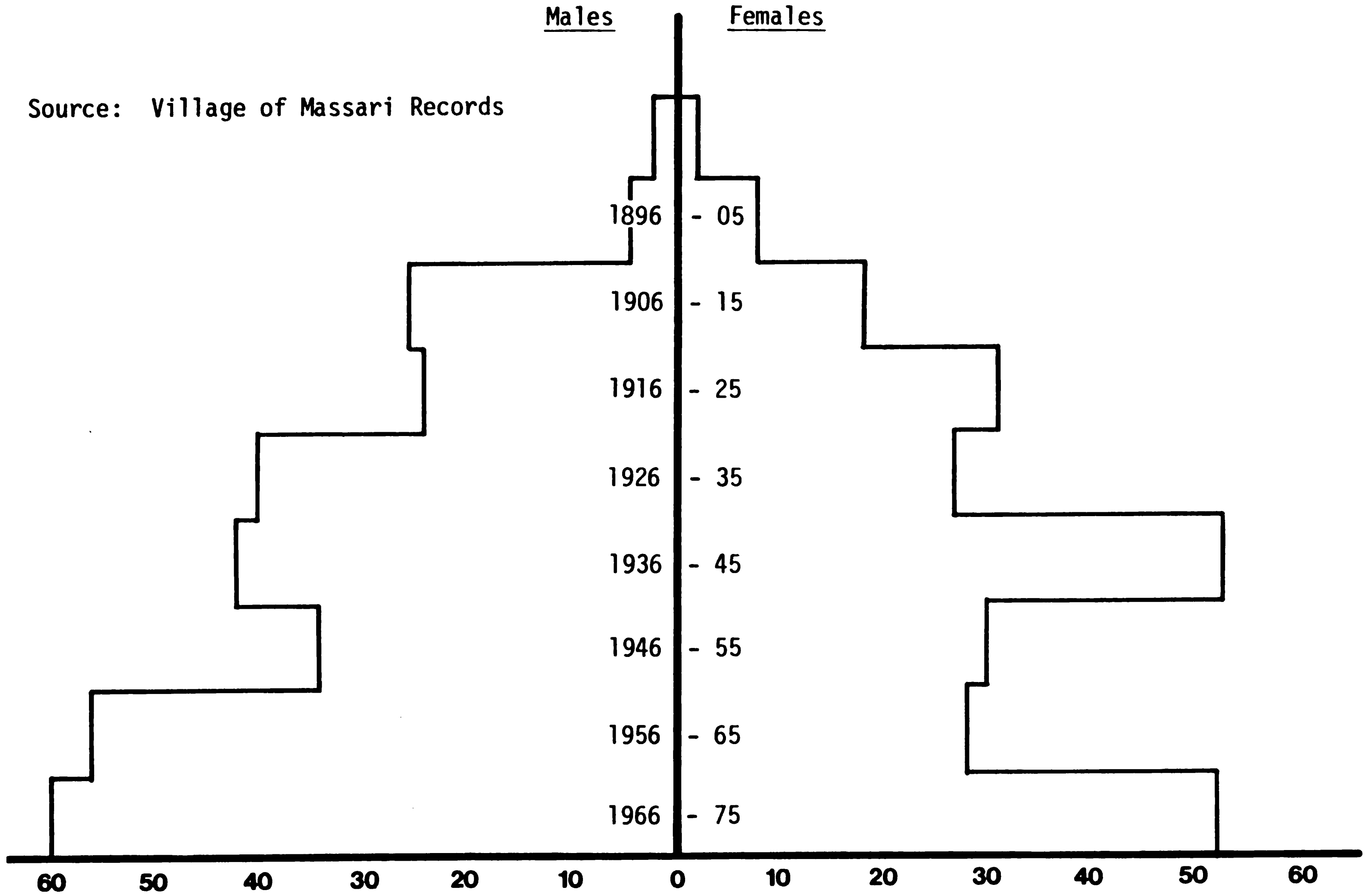



Fig. 3.3 Age Pyramid of Massari

Source: Village of Kritinea Records

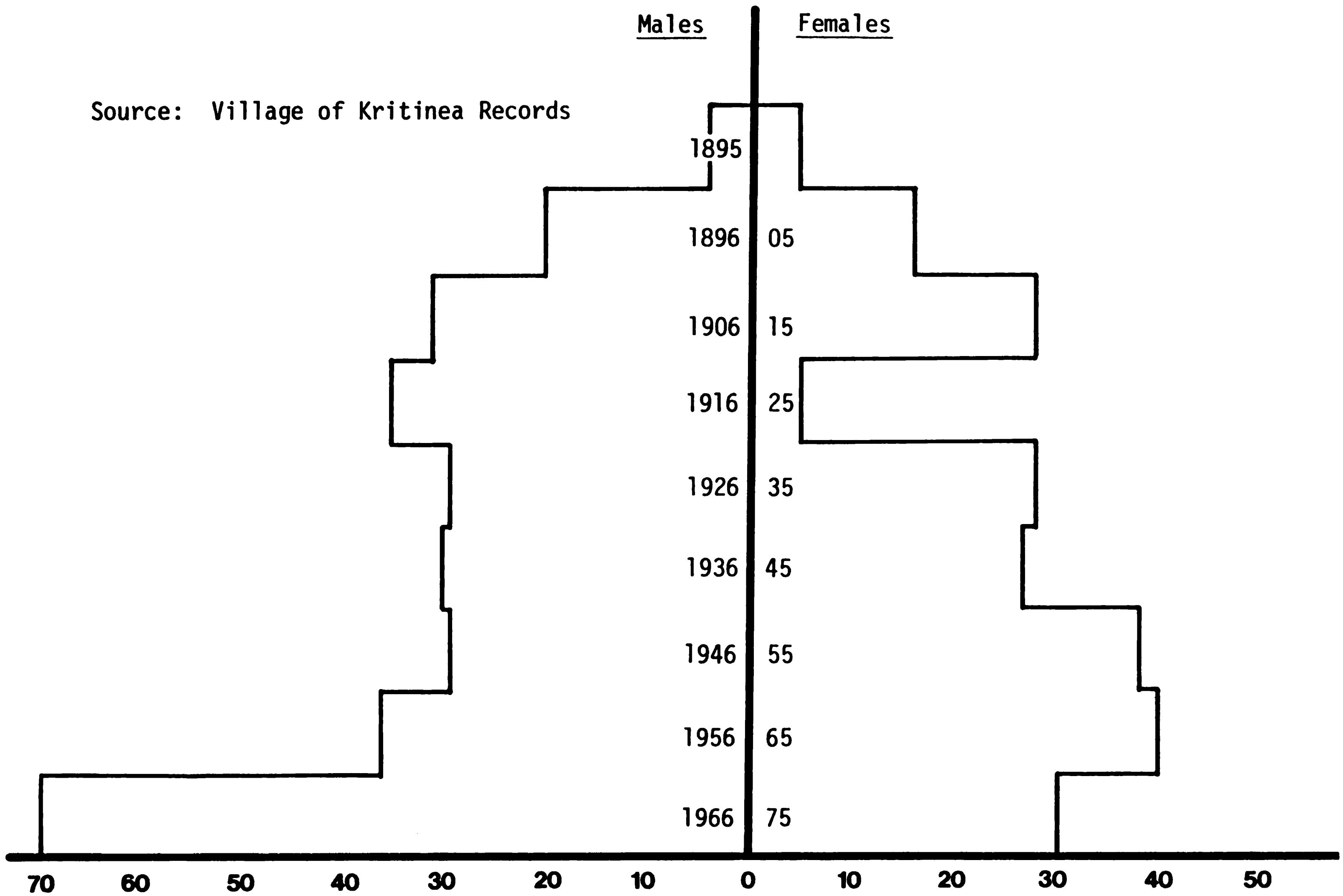



Fig. 3.4 Age Pyramid of Kritinea

TABLE 3.3

DISTRIBUTION OF AGE GROUPS IN
MASSARI AND KRITINEA

| | Massari | Kritinea |
|---|---|---|
| Under age 21 | 34.5% | 38.1% |
| 21 to 40 | 28.3 | 25.2 |
| 41 to 60 | 22.5 | 18.0 |
| 61 to 80 | 13.7 | 17.2 |
| 81 and over | 0.9 | 1.4 |

children (aged 7-12) in Massari comprised 37% of the total number of households, and in Kritinea 23% of the total number of households. While Massari and Kritinea had nearly the same total number of households, Kritinea had fewer with school aged children. The number of children per household was slightly more in Kritinea which helps to account for the difference in the number with school-aged children. Table 3.4 summarizes these differences.

TABLE 3.4

FAMILIES WITH ELEMENTARY SCHOOL CHILDREN
(AGES 7-12) IN MASSARI AND KRITINEA

| | Massari | Kritinea |
|---|---|---|
| Total households | 163 | 159 |
| One or more elementary aged child | 52(37%) | 37(25%) |

## Summary

The selection of Massari and Kritinea for ethnographic investigation in this study was related to the factors outlined in the methodology. I wanted to find two areas which were representative of two different types of physical environment, and which showed differences in both the rates of the enzyme deficiency and in the numbers of favism cases reported. The earlier studies of Kattamis et al. (1969a) and Allison et al. (1963) gave an idea of where these villages were most likely to be found. The screening for the deficiency and the identification of the numbers of favism episodes from different areas on the island supported the selection of Massari and Kritinea on the basis of their environmental differences and other impressionistic observations.

## FOOTNOTES

### CHAPTER THREE

1. Local legend in Kritinea says that one of the sons of a Minoan noble came to the area of Kritinea selected in order to avoid an oracle's prediction that he would kill his own father. The son settled in Kritinea with his family and entourage. Years later, a ship arrived from Crete (Kriti), and the son mistook his own father's ship for that of an invader. He fired on the ship and killed his father. The remainder of the crew then stayed on in Kritinea. Another local legend says that two brothers came to Kritinea with their wives and families. They quarrelled, and separated, with the one brother staying in Kritinea and the other settling higher up the mountain.

   Surnames in Crete are noted to end in -akis, which, in Greek usually indicates a diminuative form of the noun. Some scholars follow the theory that the ending was imposed during Turkish rule in Crete (and in Greece) to indicate the subjugated position of the Greeks with respect to their Turkish rulers. Others, however, believe that the -akis indicates the equivalent of the English "son of" in surnames. Villagers in Kritinea, with very few exceptions, use the ending, akis, in their surnames. This ending is found in other surnames throughout the island of Rhodes, but only in limited number. Certainly no other village which was visited during the course of the field work in Rhodes exhibits surnames with this ending to the extent that Kritinea does. Massari surnames do not have this ending.

2. Evidence of the Mycenaen settlement in Rhodes comes from two sources: (1) the presence of Linear B writing, and (2) the distribution of pottery styles. The Mycenaen Linear B was distinctly different from the Minoan system of notation: Linear B "... was in fact an early form of Greek virtually identical with the Achaen (or Arcado-Cyprian) dialect which survived in Cyprus and Arcadia into historical times." (Nixon 1968:3) The Minoan system, in contrast, was written in hieroglyphics similar to that which the Egyptians used.

3. The change from Cretan to Mycenaean activity in Mediterranean commerce is signaled by the nature of pottery finds at Trianda, in the northern part of the island. At first, only Minoan wares were brought to Rhodes, but as time went on, Minoan and Mycenaean pottery was intermixed, with Mycenaean styles eventually dominating. (Samuel 1966:111)

4. Nixon (1968:102) contends that the Mycenaeans and Dorians held the same ancestry; the Mycenaeans representing the southern branch, the Dorians, the northern branch. The link between the two groups is considered to be the Minyans, which had appeared in Macedonia about 2500 B.C., spreading to Chalkidiki and Thessaly (all regions in northern mainland Greece). He states, "It appears, therefore that we can regard the Minyans as the cement which held the Greek peoples together. They must have played much the same role in the Aegean as the Normans did in forming the English people. The Greeks, whether Mycenaean, Dorian or the later classicial Greeks, must in just the same way be looked upon as a blend of the various people who came into the land at various periods. Thus the Greeks ultimately became an ethnical composite of at least the early Neolithic settlers, who probably came from Asia Minor or Syria, with the Early and Middle Bronze Age (or Minyan) peoples from the north, together with other intrusive elements." The Minyans, Nixon contends, intermingled with the people already in the Mediterranean area of contemporary Greece. Skulls from graves of the period (2500 BC) show a blending of broad-headed and long-headed peoples, indicating that the "Nordic" invaders and their "Mediterranean" forerunners had settled down side by side.

5. Archaeological evidence from the mainland shows that at the time of the Dorian invasion, "... the culture of the greater part of the areas from which they came (Thessaly and Macedonia) was primarily Mycenaean. It is therefore not surprising that the culture of the areas overrun by the Dorians should remain Mycenaean." (Nixon 1968:59) Nixon reiterates this point: "The Dorians from the north and the Mycenaeans from the south therefore must have had a common nationality varying only in the predominance of one ethnic group or the other. We can therefore describe the Dorians as being Mycenaeans, or at least "fringe" Mycenaeans, because by this we understand primarily the culture corresponding to the people known as "Mycenaeans," and the archaeological evidence makes it clear that by the time of the Dorian migrations, the Mycenaean culture had spread over Thessaly and into parts of Macedonia." (102)

# CHAPTER FOUR

## THE GD$^-$ TRAIT ON RHODES

In the medical diagnosis of favism and scientific research about the disease, the G6PD enzyme deficiency (Gd$^-$) is always given prime importance. It is listed as a critical but not sufficient factor in the etiology of favism; as such, it assumes the role of risk factor in the epidemiology of favism. The distribution of this risk factor in a given population is not always directly related to the frequency of favism, therefore it has limited predictive value; however, it is convenient to begin with the distribution of this central risk factor in our discussion. The dynamics of the genetic inheritance of the Gd$^-$ trait are not necessary in order to gain understanding of its distribution in a population. Rather, it is more important to appreciate that certain environmental and socio-cultural factors, as well as random events, may influence the distribution of the trait.

The screening in the present and previous studies in Rhodes show that the Gd$^-$ trait fluctuates in its distribution. Although the average figure for Rhodes is one of the highest in the world, the fluctuations may be from 18.8% to 46.6% of the males in the village sample showing the trait.

The trait has been shown to be inversely related to altitude, where different altitudinal locations have been screened and compared (e.g., Siniscalco et al. 1966; Stamatoyannopoulos and Fessas 1964). The results from Rhodes show that while this is the general rule, some locations fall outside the predictable range if altitude alone is considered, with some of the highest elevations on the island showing the highest frequencies. Malarial endemicity, known to be a function of altitude and known to be related to the sickle cell trait, has been suggested as a selective factor in the environment which helps regulate the $Gd^-$ trait/altitude relationship. Possible selective and/or neutral features of the $Gd^-$ allele are discussed in this chapter with respect to the data for Rhodes.

Among certain endogamous, ethnically closed groups, the frequency of the allele is higher than in surrounding populations. For example the Kurdish Jews have a very high frequency, while the adjacent Arab populations have much lower frequencies (Allison et al. 1963; Szeinberg and Sheba 1958). This leads to speculation that the factor of isolation, either by geography (e.g., island community) or by social sanction (e.g., marriage customs) may exacerbate the extreme-end frequencies found in areas where surrounding populations have much different, more uniform average frequencies. This hypothesis will be discussed with respect to the Rhodian data.

Finally, the chance factors from history and others operating in present populations are suggested to have contributed to the higher average frequency of the trait in Rhodes and to the unexpected fluctuations from specific locations. Based on historical events in Rhodes, the principle of genetic drift explains the high average frequency of the $Gd^-$ trait on the island. This same principle, emphasizing the breeding population size as a factor influencing randomness in gene frequency, aids in explaining the $Gd^-$ trait distribution by altitudinal location.

Five hypotheses are offered to explain the distribution of the $Gd^-$ trait in Rhodes:

1. Altitude is expected to be inversely related to the $Gd^-$ trait frequency;
2. Malarial endemicity, past or present, is expected to promote higher frequencies of the trait through the process of natural selection;
3. The trait appears randomly as a result of neutral selectivity;
4. Marriage customs promote village-endogamous unions, thereby exacerbating extreme-end differences in $Gd^-$ trait frequencies;
5. Chance events in history as well as in present-day differences in size of breeding populations have acted to promote both the high average and the fluctuations in village-by-village frequencies.

The first hypothesis is discussed in the first major section of this chapter which gives the results of the screenings. Points two and three are treated in the section on national selection and points four and five are included in the last section about genetic drift.

## Results of Screenings for the $Gd^-$ Trait

The results of the screening among 189 male school children, ages 7-12, showed a high average frequency (26.5%) for the $Gd^-$ trait on Rhodes. This is in keeping with the earlier literature for the island which reported an average of 25% (Kattamis et al. 1969a) to 31.8% (Allison et al. 1963) for locations screened. The results of the present screening are compared with these earlier studies in Table 4.1 which shows all the locations in Rhodes which have been screened to date. In the Allison study, three villages were screened: Aghios Isideros, Laerma, and Massari. Four other villages were screened by Kattamis: Kremasti, Siana, Pylona, and Archangelos. The present study screened for the trait in a total of seven villages, five of which had not been previously screened. Embona, Kritinea, Lindos, Lardos, and Malona. Two villages were re-screened from earlier studies: Pylona and Massari. For these latter two villages, frequencies for the $Gd^-$ trait will be given as they were calculated in the present study unless otherwise indicated.

### Distribution of the $Gd^-$ Trait

The results of the present screening along with earlier studies showed that the range of the $Gd^-$ trait among those tested is from 18.7% in Lindos (present study) to 46.6% in Laerma (Allison et al. 1963). This latter figure may be high, but even in the present study similarly high figures were found; for example, 43.2% in Kritinea. These findings are shown in Figure 4.1 and Table 4.1.

As discussed in Chapter Two (Research Strategy), the numbers

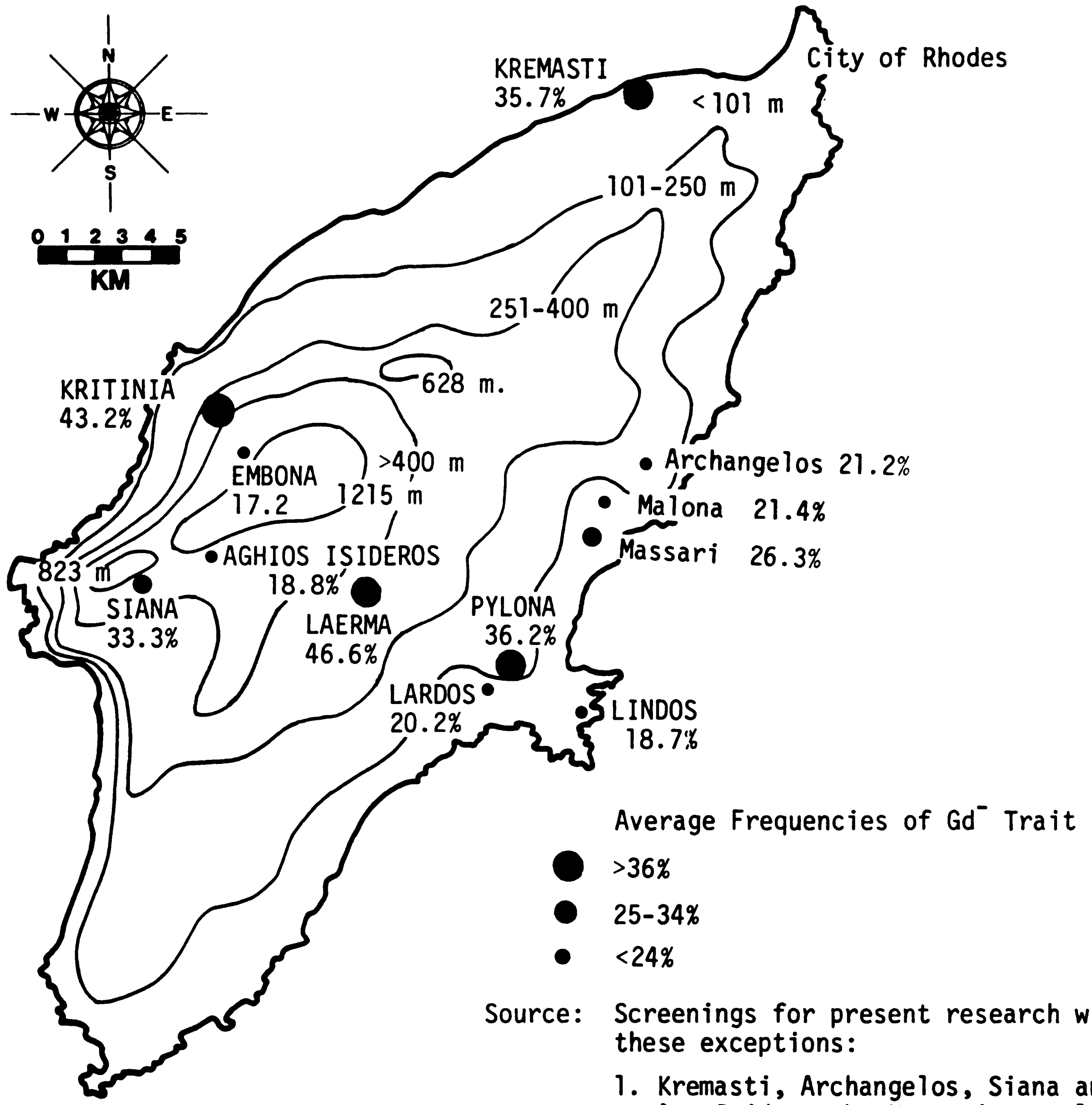
TABLE 4.1

DISTRIBUTION OF G6PD DEFICIENCY IN RHODES

| Village | N Tested/ N Age Cohort | % Age Cohort Represented | N $Gd^-$ Trait/ N Tested | % $Gd^-$ Trait | Source |
|---|---|---|---|---|---|
| Lardos | 14/14 | 100% | 3/14 | 21.4 | Trakas 1976 |
| Lindos | 32/35 | 91.4 | 6/32 | 18.7 | Trakas 1976 |
| Kremasti | unknown | -- | 17/49 | 35.7 | Kattamis 1969a |
| Massari | 37/38 | 97.5 | 10/37 | 27.0 | Trakas 1976** |
| Malona | 28/30 | 93.3 | 6/28 | 21.4 | Trakas 1976 |
| Pylona | 11/11 | 100.0 | 4/11 | 36.3 | Trakas 1976* |
| Archangelos | unknown | -- | 28/132 | 21.2 | Kattamis et al. 1969a |
| Kritinea | 37/38 | 97.5 | 16/37 | 43.2 | Trakas 1977 |
| Laerma | unknown | -- | 19/40 | 46.6 | Allison et al. 1963 |
| Siana | unknown | -- | 8/24 | 33.3 | Kattamis et al. 1969a |
| Embona | 29/58 | 50.0 | 5/29 | 17.2 | Trakas 1977 |
| Ag. Isideros | unknown | -- | 10/53 | 18.8 | Kattamis et al. 1969a |

*Also screened by Kattamis et al. 1969 with frequency of 25.0% tested with the $Gd^-$ Trait.

**Also screened by Allison et al. 1963 with frequency of 25.0% tested with the $Gd^-$ Trait.




Source: Screenings for present research with these exceptions:

1. Kremasti, Archangelos, Siana and Ag. Isideros by Kattamis et al. 1969
2. Laerma by Allison et al. 1963

Fig. 4.1 $Gd^-$ Trait Distribution in Rhodes screened for the $Gd^-$ trait in each location are to be considered representative. The size of the samples used from each village are in keeping with other screenings which have been conducted at the village level in terms of the proportion of the entire male population represented by the sample. These figures are expected to give at least as good an indication of the $Gd^-$ frequency for the generation involved in the present study as for earlier studies. Representation in the seven to twelve year old cohort was 91.5 to 100% in all the villages screened in the present study, with the exception of Embona.

In both Massari and Kritinea, 37 school boys, aged 7-12 were screened. This represents 97.5% of all the boys in the cohort for each location, with 12.6% and 14.2% of all the males in these village poulations represented. Twenty-eight nuclear families are represented from Kritinea, and thirty nuclear families represented from Massari. Kritinea had five additional families with children from 7 to 12 years of age at the time of the screening, but none were males, and therefore were not represented in the screening. Massari had 22 families with young children not appearing in the screening for the same reason. That is, there was no male representative of the family in the age cohort.

## $Gd^-$ Trait and Altitude

Studies of the relationship between altitude and frequencies of the enzyme deficiency in Greece and Sardinia show that there is an inverse relationship between elevation above sea level and the frequency of the enzyme deficiency, that is, the $Gd^-$ allele (Siniscalco et al. 1961; Carcassi 1957; Allison et al. 1963; Stamatoyannopoulos and Fessas 1964). In fifteen Sardinian villages, Carcassi reported a general drop in the enzyme deficiency frequency as altitude increased. At altitudes of under 100 meters the frequency was given at 17.5% while at over 501 meters the frequency dropped to 4.9%. The work of Siniscalco et al. (1961 and 1966) supports this material by adding 37 more Sardinian villages to the ones which Carcassi had screened. From these 52 total villages, those under 100 meters show an average of 19.3% affected with the $Gd^-$ trait. In the intermediate altitudes (101-400 meters) the average remains nearly the same at 19.8%, while in the higher altitudes of over 401 meters, the average drops dramatically to 7.3%.

These data were compared with those from Rhodes, excluding eight Sardinian villages at elevations of over 525 meters above sea level. Rhodian villages are not located at higher altitudes than 525 meters, and for this reason the eight Sardinian villages were excluded. The comparison is shown in Table 4.2. All the Rhodian villages show higher frequencies in comparison with the Sardinian ones. In each altitudinal grouping the average and range are higher than those for Sardinia. No inverse relationship between altitude and $Gd^-$ trait frequency can be observed in the Rhodian locations, and, in fact, no real systematic distribution of the trait is shown. Possible reasons for the lack of agreement with previous altitude/trait relationship involve the nature of the samples in Rhodes as compared to those in Sardinia. The Sardinian samples involved much

TABLE 4.2

ELEVATION AND DISTRIBUTION OF THE GD$^-$ TRAIT IN RHODES AND SARDINIA

FREQUENCIES OF GD$^-$ TRAIT

| Elevation | Average | | Range | | Rhodian Villages | | |
|---|---|---|---|---|---|---|---|
| | Sardinia | Rhodes | Sardinia | Rhodes | By Name | | |
| Under 101 m | 19.3 | 24.5 | 5.0 - 32.0 | 18.7 - 35.7 | 20.2 | Lardos | 15 m |
| | | | | | 18.7 | Lindos | 15 m |
| | | | | | 35.7 | Kremasti | 25 m |
| | | | | | 26.3 | Massari | 25 m |
| | | | | | 21.4 | Malona | 70 m |
| 101 - 400 m | 19.8 | 36.8 | 6.1 - 35.7 | 21.2 - 46.4 | 36.2 | Pylona | 120 m |
| | | | | | 21.2 | Archang. | 160 m |
| | | | | | 43.2 | Kritinea | 270 m |
| | | | | | 46.6 | Laerma | 280 m |
| 401 - 525 m | 7.3 | 23.1 | | 17.2 - 33.3 | 17.2 | Embona | 430 m |
| | 8.9 | | 7.0 - 11.8 | | 33.3 | Siana | 450 m |
| | | | | | 18.8 | Ag. Isid. | 520 m |

Sources: for Sardinia: Siniscalco et al. (1966)
for Rhodes Elevations: National Statistics Services of Greece, 1971.
for Rhodes Gd$^-$ Trait: See Table 4.1.

greater representation of locations at each altitude, both in number of villages and in population. While the eight Sardinian villages found at altitudes of over 525 meters were excluded, the sample still included 22 villages at locations of under 100 meters, 17 villages from 101 to 400 meters, and 5 at the highest locations. For these three altitudinal groups, the number of villages from Rhodes were five, four and three, respectively, as Table 4.2 shows. In addition, the frequency of the $Gd^-$ trait in Rhodes is so much higher on the average than for Sardinia, that it may not be subject to the same type of processes as it is in Sardinia in general, let alone at the different altitudinal locations.

The range of 18.7 to 35.7% of the $Gd^-$ trait frequencies for most of the locations screened in Rhodes is included in each of the three altitudinal ranges. While this range is expected in the lower elevations, the high frequencies found at the higher elevations is not. When unexpectedly high frequencies of a genetic trait are found in populations, two different hypotheses can be offered to explain them: (1) natural selection, and (2) genetic drift. On the basis of research in other geographic areas, the high frequency of the trait in the high Rhodian elevations provides an example of what is meant by "unexpected", and offers a challenge to utilize environmental and ethnographic information in checking these hypotheses.

## Natural Selection and the $Gd^-$ Trait

Natural selection favoring a genetic trait results from the trait's adaptive advantage. This is demonstrated in populations where that portion of the population with the adaptive trait has the advantage and is able to survive in order to reproduce the following generation, where in many more of whom will have the trait. Some alleles are selectively neutral, while other potentially lethal ones manage to continue to circulate in the gene pool from one generation to the next by mechanisms associated with (1) inherent characteristics of the allele (e.g., attached to another adaptive trait, recessiveness, sex linkage), (2) through the interruption of natural selection by human intervention (e.g., treating congenital inherited defects, sexual selection), or (3) as a balanced polymorphism. According to the theory of natural selection, the $Gd^-$ trait has been maintained in certain populations because it aids in the adaptive process in favor of humans in a particular environment. Even though selection may be working against the trait in the homozygous and hemizygous condition by provoking hemolytic crises, the trait is perpetuated by the heterozygous female and this state, may have some advantage (e.g., Doxiadis et al. 1961; Allison et al. 1963). In order for traits to be perpetuated they do not need to always be adaptive: some are perpetuated because they are not strongly maladaptive or they form a balanced polymorphism. A 1967 report by a World Health Organization research team assigned to investigate the distribution of the enzyme deficiency summarizes the need for further research on the topic of the selective aspects of the deficiency:

> Further information is required regarding the positive and negative effects that G6PD (variants) may exert upon the biological fitness of affected individuals. In particular, the possible contribution of G6PD deficiency to mortality and its interaction with

> malaria and possible other disorders require study. (p. 26)

The arguments generated by the theory of natural selection have at least three subparts:

1. The $Gd^-$ allele and/or fully expressed has adaptive advantage.
2. The $Gd^-$ trait has negative features (e.g., hemolytic crisis), which are overshadowed by its Selective advantage;
3. The factors which led to the perpetuation of the allele have ceased to exist in the environment but the negative effects are still limited or even neutral and the trait persists by virtue of its genetic composition.

The first and the third points are treated in the following sections.

## Selective Advantage of the $Gd^-$ Trait

The demonstration that the allele for sickle-cell anemia in the heterozygous state offers protection against malaria (Livingstone 1971; Wiesenfeld 1967) has led to the hypothesis that the allele for other hemoglobinopathies (e.g., thalassemia) and abnormal hemoglobins (e.g., G6PD deficiency) may also confer some protection against the disease. Considering that altitude often delineated malarial regions, and that the Rhodian data show little association between the deficiency and altitude, it might be projected at the start that the malaria hypothesis will not aid significantly in clarifying the problem of the distribution of the deficiency in different altitudes. The argument must be considered on the basis of established knowledge about red blood cell chemistry and malaria. Malarial organisms depend on the integrity of red blood cells; they need some of the enzymes and metabolites of the erythrocyte, therefore, one would expect "...suboptimal growth of malarial parasites in red blood cells which deviate from the norm" (Motulsky 1960:44).

Theoretically the trait or allele is suspected of offering some protection against malaria, and even in the presence of selective forces against it (e.g. favism), the G6PD deficiency continues to appear as a balanced polymorphism. The evidence which has been reported in the Mediterranean areas more clearly than not supports the malarial hypothesis. Siniscalco et al. (1961) find that variations in the gene frequency for the deficiency in nineteen Sardinian villages where malaria has been endemic until about 1950 are directly related to variations in the prevalence of malaria in these locations. The study did find, however, some areas of very high incidence of the enzyme deficiency without malaria having been significantly present in the population. Flatz and Duran (1967) also found the same association in Spain between the deficiency and malarial endemicity. Malarial areas tended to be associated with those where the enzyme deficiency was present, although the deficiency is reported in much lower frequencies in Spain than in either Greece or Sardinia. Further, from their data in five Spanish provinces, Pellicer and Casado (1970) were unable to support the hypothesis that high malarial endemicity is associated with high frequencies of the enzyme deficiency.

In Greece, five areas examined by Stamatoyannopoulos and Fessas (1964) showed a good degree of correlation between areas of high enzyme deficiencies and those areas which had been endemic with malaria prior to 1945. The deficiency in highly malarious areas was six times more frequent than in non-malarious ones. Choremis et al. (1963) also found the same association between malaria and enzyme deficiency frequencies.

Archival research in the City of Rhodes, Public Health Department (which holds records for the entire twelve-island group of which Rhodes is the administrative center) indicated that malarial records before 1954 are not available for specific village locations on the island. Cases before then were reported by island in the twelve-island group (Dodecanese). Cases occurring after 1954 are minimal. Village records are in greater disarray due to the various administrative upheavals which occurred in recent history. A careful search of statistics for the island, through the collaboration with officials of the Department of Public Health both in Athens and in the City of Rhodes revealed that since 1955, the majority of malaria cases reported were from two sources: (1) relapses of old cases which cannot show endemicity; and (2) new cases which first appeared outside of Greece and were returned to Rhodes for medical care and recuperation. These often occurred in people who had migrated to Africa, or in sailors who were exposed to malarial conditions in other countries and then had to be returned to Greece for treatment.

Actual figures, by village or micro-region, then, are not available to trace areas of malarial endemicity on the island. By interviewing health officials located on the island for the last thirty years, information was gained on the regional distribution of malaria within Rhodes. This information which cannot be statistically verified, is presented descriptively below.

Coastal examples: Mandriko,
Massari, and Lindos

Malarial breeding grounds are not necessarily associated with coastal areas since it is standing and stagnant fresh water as opposed to salty sea water which facilitates the propagation of the anopheles mosquito. In some areas of Rhodes, particularly on the eastern alluvial flank, water tends to collect more than it does in the raised elevations along the central mountain spine. Further the human settlements in these areas have shifted around during at least the last 400 years such that the actual malarial conditions in these areas must be reconstructed.

Mandriko and Massari, both coastal villages, were noted for their continued persistence of malaria even after the advent of DDT. Both of these villages fell within the epidemiological and ethnographic focus of the present research. Massari, as discussed in Chapter Three, participated in this present study and Mandriko is the coastal village closest to Kritinea. Both Massari and Kritinea were researched for factors other than the enzyme deficiency, therefore both these environments are quite familiar in the study.

In both cases, the ecological situation is not grossly different from any number of coastal villages in Rhodes; they are located two kilometers from the sea shore, on land that slopes toward the sea. In both areas it is likely that the sea level was at one time lower, judging from remains of old structures in the strata along the coast.

It is interesting that, while screening did not take place in Mandriko, the closest village to it is Kritinea. Kritinea is located about 350 meters above Mandriko but shows unexpectedly high frequencies for the deficiency. Plots of land belonging to villagers in both Mandriko and Kritinea extend to the sea, even though Kritinea is at a higher elevation than Mandriko. Therefore, in order to work their land, individuals form Kritinea must travel regularly to the area of Mandriko, and are assumed to have been subject to the same malarial exposure as those in Mandriko, and consequently subject to the same selective pressures. Perhaps this is a plausible hypothesis which explains the unexpectedly high frequency of the deficiency in Kritinea. It is not only where villages are located in terms of altitude and malarial endemicity, but where villagers work and which altitudes and areas they exploit in agriculture which may be important. High altitudes which are not intermixed or close to malarial areas may be expected to show the expected enzyme deficiency frequency. Areas which are close to malarial centers, even though these areas may be high in altitude, are expected to share essentially the same environmental factors as those in the malarial areas.

Lindos represents a different case. Traditionally it has not been involved to a great degree in agricultural pursuits. Historically it is the site of the ancient city-state of Lindos, taking in the surrounding agricultural territory as well as the natural harbor. Its inhabitants are not expected to have devoted time to agricultural emphasis since Lindos had become a powerful maritime center. It is unusual in the contemporary village of Lindos to find the occupation of field worker or farmer given (children in Lindos were questioned about father's profession during screening). It is more common to find those who are descendents and wives of sailors and merchants, or who are involved in tourist related activities. Present-day inhabitants of Lindos are almost always involved in tourist related occupations: photographers, keepers of donkeys to take tourists around the village and the Acropolis of Lindos; waiters, bartenders, bus drivers, tour guides. Wives may tend tourist shops and wash dishes in small restaurants and taverns. Grandmothers often cook at restaurants, or crochet and embroider fabrics for table cloths and dresses for sale to tourists. The area around Lindos is not noted as a region of past malaria endemicity. Among the villages screened, Lindos has the lowest $Gd^-$ frequency.

Inland examples: Pylona
and Lardos

There are many examples which illustrate the exchange of populations or the movement of populations, in altitudinal locations on a seasonal or daily basis. Villages located in middle range altitudes are most likely to exhibit population changes. Pylona and Lardos, both middle-altitude villages, show 36.3 and 21.4% for the $Gd^-$ trait. Lardos is noted to have been among the first villages on Rhodes where malaria was reported according to the information of the Public Health officials in Rhodes. It is located at a slightly lower elevation than is Pylona, however, plots of land belonging to the inhabitants of the two villages overlap. Even though the two villages occupy different altitudes, the populations in both should be considered as participants in the same interdependent econiche. Both villages then should have similar frequencies of the trait since they exploit the same range of altitudes and environments. The more than 15% difference does not follow this hypothesis. It might be explained by reasons: (1) The size of the samples influenced the results of the screening, both being too small to give an adequate picture of the frequency of the trait; and (2) Differences may have been smaller, even fifteen years ago. With respect to the last point, Pylona was reported to have a frequency of 25% in the Allison study which took place fifteen years before the present one.

Mountain example: Embona

The village of Embona represents another situation. The frequency of the deficiency is lower here than in the seaside areas on the west coast of the island surrounding the village of Embona. This is consistent with what would be predicted according to the altitudinal location of the village. Embona has been traditionally a herding and agricultural village. Plots of land and grazing areas take the inhabitants of Embona down to the lower elevations less frequently than in villages of the intermediate altitudinal range. In spite of the high altitude of the village itself, one can see the plots of land and the pasture areas for goats and sheep even higher up the mountain.

These examples from the different altitudinal and historically different areas of Rhodes illustrate that more than statistical correlations between malaria and the $Gd^-$ trait are necessary in order to unravel the nature of their relationship to each other. Some preliminary conclusions may be drawn from the present data:

1. The intermixture of land holdings at different altitudes such that exploitation of land at these altitudes at different times of the year places people in varying degrees of exposure to malaria. This tends to even out the malarial factor at the intermediate altitudes of under 400 meters.

2. In altitudes of over 400 or 500 meters, the limits of the physical environment or the adaptation to higher altitudes in economic exploitation, promote less exchange of populations with lower altitudes. This does not seem to be the case for any of the villages in Rhodes, but may hold true for Sardinia where many villages of over 500 meters above sea level were screened in earlier studies.

Certainly, the problem of ascertaining the relationship of the $Gd^-$ frequencies to altitude and malaria has so far given inconclusive results. The trait may in fact have been a protective feature against malaria, but to map out the areas which were endemic without taking into consideration the economic and physical adaptations in the different altitudes results in the inconclusive data. According to the most recent research on the subject:

> The hypothesis that G6PD deficiency protects in some way against malaria derives solely from the association between the high frequency of G6PD deficiency and endemic malaria and should be considered unproven until other evidence becomes available. (Martin et al. 1979: 562)

## Selective Neutrality and the $Gd^-$ Trait

The interaction of the enzyme deficiency with hemolytic agents is known: acute hemolytic anemia, hyperbilirubinemia, and urine discolorization. The effects of the $Gd^-$ trait in the absence of these agents are not known. It is possible that there are none that can be attributed to the allele or to the fully expressed G6PD deficient phenotype. That is, the deficiency in and of itself is not a pathological hemoglobin type. It is possible that the enzyme deficiency allele or fully expressed phenotype is selectively neutral. Evidence supporting the malarial hypothesis is not conclusive, especially when dealing with small village populations where agricultural practices and land tenure patterns require mobility between several areas, often quite distant and occupying different altitudes and econiches. Malarial conditions which existed for Rhodes in general may have promoted the deficiency in the gene pool, but in contemporary Rhodes, malaria is not an important selective factor. The allele may be neutral.

During the research, information was gathered which may aid in assessing the possible natural effect of the $Gd^-$ trait. These data are discussed in the four following sections: (1) fertility patterns of $Gd^-$ trait mothers; (2) neonatal jaundice in $Gd^-$ trait infants and their siblings, (3) childhood episodes of blood-related conditions (such as jaundice and hepititis) in $Gd^-$ trait children and their siblings, and (4) height, weight and relative weight (Quetelet Index) distribution of children with the $Gd^-$ trait compared to those without the trait.

### Fertility Patterns of $Gd^-$ Trait Mothers

Biological adaptation is often assessed by measuring fertility. With human populations, where a variety of choices about number of children in a family may be exercised, indicators related to fertility may have limited use. (For example, the figures may be unreliable due to family planning, induced abortions, neglect of perinatal health care, etc.) By using small samples some of the choice related problems may be compensated for since, among the families of the small samples in this study, methods of family planning and birth control were nearly identical. In the course of gathering information related to other topics, many of the women themselves broached the subject of birth control. Their questions, as opposed to those which I constructed for fertility patterns, are considered as a much more accurate gauge of childbearing and perinatal concerns. Women in the villages often try to hide the number of spontaneous abortions which they have experienced since women who have difficulty bearing children are not thought to be fully fulfilling their sexual role. The use of solicited abortion as a form of birth control is an even more seriously guarded secret. While morally objectionable it is nevertheless practiced. The major methods of limiting families are not particularly reliable. They include periodic abstinence (modified rhythm method), interrupted sexual coitus, and prophylactic use among men.

Abortion is the major form of controlling births in Rhodes as well as in all of Greece. It is not performed in rural Rhodes at present, although at one time, the practical midwife was credited for knowing the appropriate measures to end an unwanted pregnancy. The procedure is usually handled by going into the City of Rhodes to a private gynecologist's office where the abortion is performed and the woman is able to leave the office in a matter of two to three hours. Hospitalization is not required, and if desperate enough the woman might go by herself to the physician in order to maintain her secret. Women do not go to physicians alone as a rule, but this situation may prompt them to go without a relative in order to avoid gossip. In spite of precautions, women usually fear that their abortion will be learned of in the village, or that they will become sterile from the abortion. This relates to the question of barrenness, again, since women who are unable to conceive after marriage may be the object of gossip which claims they became barren from having an abortion. Thus, seeking and going through with abortion may not affect the decision of a woman who has already had as many children as she desires, but is a consideration for a young woman who has not yet married and started her family.

From Massari, seven mothers affected with the $Gd^-$ allele were compared to fourteen non-trait mothers for differences in their fertility patterns, e.g., number of children, number of pregnancies, childbearing histories, spacking of offspring, etc. These mothers were selected through their sons who had been identified with the trait. Three additional mothers had daughters with the trait (identified by favism episodes). They were not included in the fertility history analysis since they were either not tested or they showed normal enzyme activity (which is not necessarily an indication that they do not possess at least one $Gd^-$ allele). The fourteen other mothers from Massari had sons who had been screened and did not show the trait and did not have any genealogical links to anyone with either the trait or favism. Fourteen mothers from Kritinea were identified by having at least one son affected with the trait, or by having had a clinical episode of favism herself. These fourteen $Gd^-$ trait mothers were compared to the seven mothers with the allele from Massari.

### Ages at first and last pregnancies

In Massari, the average for the first pregnancy of $Gd^-$ trait mothers was 22.6 years; for non-trait mothers, 22.2 years. Among $Gd^-$ trait mothers in Kritinea, the average first pregnancy was at 23.7 years, slightly older than either of the averages for Massari. The range of last pregnancies for $Gd^-$ trait Massari mothers were given at 23 to 36 years. Non-affected mothers in Massari reported last pregnancy at 35-40 years. Affected mothers from Kritinea reported last pregnancy at 35-40 years. Affected mothers from Kritinea reported last pregnancy at 24-43 years. These figures are shown on Table 4.3 Mothers in Kritinea begin child-bearing a year later than both Gd$^-$ trait and non-trait mothers from Massari (for this sample). These same mothers from Kritinea reported their last pregnancy at least three years later than the mothers from Massari, independent of the enzyme deficiency. Child-bearing years cover a longer period of time for Kritinean mothers than in Massariani mothers. Half of the mothers in the sample from Kritinea had pregnancies after thirty years of age, while in Massari, only five of twenty-three mothers had pregnancies after this age.

TABLE 4.3

RANGE AND AVERAGE OF CHILDBEARING AGES
IN GD$^-$ TRAIT AND NON-TRAIT MOTHERS

| | Massari | Kritinea |
|---|---|---|
| Gd$^-$ Trait | | |
| Average | 22.6 | 23.7 |
| Range | 15 - 32 | 18 - 27 |
| Non-Trait | | |
| Average | 20.7 | unknown |
| Range | 19 - 31 | |

Number of children
and spacing

Seven Gd$^-$ trait mothers from Massari reported a total of eighteen live births, an average of 2.6 births per mother. The fourteen non-trait mothers from Kritinea had forty live births, for an average of 2.8 live births/mother. These figures are shown in Table 4.4. They are consistent with what might be expected on the basis of the demographic characteristics of the two villages, rather than from differences in fertility related to the enzyme deficiency. Kritinea has larger families than does Massari, independent of the $Gd^-$ trait. It may be that cultural pressures have more influence on the number of pregnancies a woman will experience than does the enzyme deficiency.

TABLE 4.4

NUMBER OF CHILDREN PER MOTHER IN MASSARI

| Mother's Status | Number of Children 2 | 3 | 4+ |
|---|---|---|---|
| $Gd^-$ Trait | 5 | 3 | 0 |
| Non-trait | 10 | 4 | 0 |

Even though Kritinea mothers have more children, they begin reproduction a year later than those in Massari, on the average. Mothers from both villages tend to go through full-term pregnancies at about the same rate, i.e., they have approximately the same number of live births in the same period of time. Mothers in Kritinea continue reproduction into later years, while mothers in Massari usually stop after two children. Table 4.5 shows that there is little difference between the three groups of mothers according to the number of live births compared to the number of years in which they occurred. For example, women with three live births showed a range approximately four to seventeen years during which they occurred regardless of village or the $Gd^-$ trait. More mothers in Kritinea had three live births than did those in Massari.

TABLE 4.5

NUMBER OF PREGNANCIES BY NUMBER OF CHILDBEARING YEARS IN MASSARI AND KRITINEA - RANGES IN

| | Number of Childbearing Years | | |
|---|---|---|---|
| Number of Children | Massari Non-Trait | Massari $Gd^-$ Trait | Kritinea $Gd^-$ Trait |
| 2 | 2 - 11 | 3 - 11 | 2 - 5 |
| 3 | 4 - 9 | 4 - 17 | 3 - 17 |
| 4 | --- | 4 --- | 7 - 17 |

Fetal loss and perinatal deaths

Pregnancy results for twenty-one $Gd^-$ trait and fourteen non-trait mothers are summarized in Table 4.6. The figures are given in raw numbers and in % (rather than o/oo). The 21 $Gd^-$ trait mothers shared a total of 58 live births from 65 pregnancies; 89.2% of their pregnancies resulted in live births, with the rate being only slightly more successful in Massari than in Kritinea. Non-trait mothers had 89.1% of their pregnancies end in successful births. The category of abortions and miscarriages includes only abortions which were non-solicited (i.e., spontaneous), miscarriages up to the 5th month of pregnancy, and still births in the last trimester. These figures were slightly higher for the $Gd^-$ trait mothers (10.7%) than for the non-trait ones (8.1%). The sample is too small to conclude that the $Gd^-$ trait in mothers contributes to lower fertility (and hence suggests less adaptability).

TABLE 4.6

PREGNANCY RESULTS IN $GD^-$ TRAIT AND NON-TRAIT MOTHERS
(MASSARI AND KRITINEA)

| | Live Births per Pregnancies | | Fetal Losses* | | Perinatal Deaths | |
|---|---|---|---|---|---|---|
| | n | % | n | % | n | % |
| $Gd^-$ Trait Mothers | | | | | | |
| Massari (7) | 18/20 | 90.0 | 2 } 7/65 | 10.7 | 2 } 2/65 | 3.0 |
| Kritinea (14) | 40/45 | 88.8 | 5 | | 0 | |
| Non-Trait Mothers | | | | | | |
| Massari (14) | 33/37 | 39.1 | 3/37 | 8.1 | 1/37 | 2.7 |

*Fetal loss = Abortion (spontaneous) miscarriage, still birth.

Source: Fertility Histories from present study.

Infant deaths include those which occurred before the infant reached twelve months, the standard cut-off point for infant mortality figures. In this case, all infant deaths occurred before six months; one within the first week from a "difficult birth", one within the first month from an infected umbilicus, and one in the first five months from meningitis. The phrase, "difficult birth," was provided by the mother and usually implies that the physician was at fault (according to the mother). It is therefore, difficult to ascertain exactly what the cause of the infant or perinatal death was without reference directly to the death certificate. Difficult birth is not used often to refer to many hours of labor, but to the manipulations of the physician during the birth; e.g., the use of forceps, a breech presentation, which are believed to cause perinatal deaths and/or retardation. This category provides a safe zone for mothers when commenting on their infant's death or consequent mental and/or physical problems. The situation does not have to be one which acknowledges an inherited dimension to the problem. Rather, the delivery or the doctor, not the mother, is at fault.

Tables 4.7 and 4.8 show the details of the fertility histories. Ages of mothers are given as reported for the time of conception rather than delivery, while the number of years (column 3) were calculated by the difference from the first to the last conception (not completed birth). In general, the fertility histories do not reveal that mothers with the $Gd^-$ allele or fully expressed trait have less chances of successfully completed pregnancies than do their non-trait counterparts. The offspring of $Gd^-$ trait mothers appear to have as favorable

TABLE 4.7

CHILDBEARING PROFILE OF NON-TRAIT MOTHERS (MASSARI)

| | PREGNANCIES | | PREGNANCY RESULTS | | | |
|---|---|---|---|---|---|---|
| Age with First | Age with Last | Number /Years | Age of Last Child | Live Births | Ab/Misc* | Infant Deaths |
| 19 | 25 | 3/5 | 7 | 3 | 0 | 0 |
| 19 | 28 | 4/8 | 3 | 3 | 1 | 0 |
| 19 | 31 | 3/9 | 3 | 3 | 0 | 0 |
| 21 | 24 | 2/3 | 5 | 2 | 0 | 0 |
| 21 | 24 | 2/2 | 2 | 2 | 0 | 0 |
| 21 | 25 | 2/5 | 7 | 2 | 0 | 0 |
| 21 | 25 | 2/3 | 2 | 2 | 0 | 0 |
| 21 | 29 | 4/6 | 4 | 3 | 1 | 0 |
| 23 | 26 | 2/4 | 11 | 2 | 0 | 0 |
| 23 | 27 | 4/4 | 8 | 3 | 0 | 1(infected umbilicus) |
| 24 | 28 | 3/5 | 7 | 2 | 1 | 0 |
| 24 | 28 | 2/6 | 19 | 2 | 0 | 0 |
| 24 | 35 | 2/11 | 11 | 2 | 0 | 0 |
| 31 | 40 | 2/7 | 1 | 2 | 0 | 0 |

*Abortions/miscarriages

TABLE 4.8

CHILDBEARING PROFILES OF GD$^-$ TRAIT MOTHERS (MASSARI AND KRITINIA)

| | PREGNANCIES | | RESULTS OF PREGNANCIES | | | |
|---|---|---|---|---|---|---|
| Age with First | Age with Last | Number /Years | Age of Last Child | Live Births | Ab/Misc* | Infant Deaths |
| Massari | | | | | | |
| 15 | 26 | 3/11 | 12 | 2 | 1 | 0 |
| 20 | 36 | 3/17 | 1 | 3 | 0 | 0 |
| 21 | 23 | 2/3 | 9 | 2 | 0 | 0 |
| 23 | 29 | 2/7 | 7 | 2 | 0 | 0 |
| 25 | 29 | 3/4 | 2 | 2 | 1 | 0 |
| 25 | 29 | 3/4 | 5 | 3 | 0 | 0 |
| 32 | 36 | 4/4 | 11 | 4 | 0 | 2 |
| Kritinea | | | | | | |
| 18 | 23 | 4/4 | 1 | 2 | 2 | 0 |
| 20 | 36 | 7/17 | 3 | 4 | 3 | 0 |
| 21 | 23 | 2/4 | 5 | 2 | 0 | 0 |
| 21 | 24 | 2/4 | 11 | 2 | 0 | 0 |
| 21 | 25 | 2/5 | 5 | 2 | 0 | 0 |
| 22 | 28 | 3/7 | 6 | 3 | 0 | 0 |
| 22 | 28 | 4/7 | 7 | 4 | 0 | 0 |
| 23 | 31 | 4/9 | 4 | 4 | 0 | 0 |
| 25 | 29 | 3/5 | 8 | 3 | 0 | 0 |
| 25 | 30 | 3/6 | 10 | 3 | 0 | 0 |
| 25 | 32 | 3/8 | 6 | 3 | 0 | 0 |
| 26 | 35 | 3/11 | 8 | 3 | 0 | 0 |
| 27 | 31 | 2/5 | 20 | 2 | 0 | 0 |
| 27 | 43 | 3/17 | 10 | 3 | 0 | 0 |

chances of survival through the first year as do their counterparts from non-trait mothers, not withstanding exposure to hemolytic agents should the former have the $Gd^-$ trait.

## Neonatal Jaundice in $Gd^-$ Infants and Their Siblings

Unexplained, spontaneous neonatal jaundice in the absence of any known hemolytic agent has been noted to occur in infants with the enzyme deficiency (Cutillo 1972; Doxiadis et al. 1961; Flatz and Duren 1967). If it is, in fact, the enzyme deficiency which is responsible in these cases, it may be considered to be maladaptive along with its sequalae of kernicterus, mental retardation, and death. Studies of Greek infants with neonatal jaundice indicate that when neonatal jaundice occurs in enzyme deficient infants, its "cause" is not clearly linked to any identifiable factor. Comparing two groups of infants having jaundice, the one group with known etiology and the other group with unknown etiology, it was found that the presence of the enzyme deficiency was twenty times more prevalent in the latter group (Doxiadis et al. 1961, 1964 and 1969; Fessas et al. 1962).

Whether it is the enzyme deficiency alone, some variant of the deficiency or some other unrelated hereditary or environmental factor which is responsible for these cases of spontaneous jaundice is not established. For example, Black enzyme deficient infants do not develop jaundice in the absence of hemolytic agents, while Greek and Sardinian infants do (Kirkman et al. 1964a). In Israeli communities high in the deficiency, the presence of the enzyme deficiency does not correlate with neonatal jaundice at all. Infants born in these Israeli communities with the $Gd^-$ trait are not at any higher risk than those without the trait (Sansone et al. 1975). Further, infants with the deficiency and having one or more sibling affected by jaundice are considered to be in a higher risk group for neonatal jaundice than those with the deficiency and without one or more sibling previously affected by neonatal jaundice (Doxiadis et al. 1960 and 1964).

It is possible that an additional hereditary factor may be acting in conjunction with the deficiency to promote neonatal jaundice in children born to mothers which carry at least one allele for the deficiency may be subject to developing neonatal jaundice at a higher frequency than from mothers without the allele. Others suggest that some unidentified hemolytic agent is acting on the enzyme deficiency to produce the jaundice, and that cases of neonatal jaundice in enzyme deficient infants are in fact a result of hemolytic agents, not spontaneous or unexplained (Weatherall 1960).

Unidentified environmental factors may also be at work. Valaes (1969) compared three areas of Greece for jaundice and found that the rates are not uniform throughout. Among non-trait infants alone, the ratio for neonatal jaundice to all births in Greece varied from 1:400 for Athens, 1:100 for Rhodes, and 1:15 for the island of Lesvos. These ratios indicate that additional factors are responsible for neonatal jaundice particularly on Rhodes and even more so on Lesvos.

Using the data collected from participating families in Massari and Kritinea, the question of whether or not the $Gd^-$ allele increases the risk of neonatal jaundice is considered here in three parts:

(1) ratios of neonatal jaundice in $Gd^-$ trait vs. non-trait children; (2) ratio of neonatal jaundice in children born to affected mothers vs. non-affected mothers; (3) neonatal jaundice in sibling pairs.

### Neonatal jaundice in $Gd^-$ trait and non-trait infants

Fifteen enzyme deficient children (10 males, 5 females) from Massari were compared with their ten, non-sibling males from the same village. Two of fifteen $Gd^-$ trait infants, and none of ten non-trait infants were affected by neonatal jaundice (Table 4.9). The two cases of neonatal jaundice were found in $Gd^-$ trait females who had a history of at least one other blood-related condition (e.g., anemia, hepatitis, unexplained jaundice) occurring in childhood. This supports the suggestion that some factor other than the $Gd^-$ trait alone is involved in provoking cases of neonatal jaundice.

TABLE 4.9

NEONATAL JAUNDICE IN $GD^-$ TRAIT AND NON-TRAIT INFANTS

| | Infants | |
|---|---|---|
| | $Gd^-$ | non-trait |
| Total | 15 | 10 |
| Neonatal Jaundice | 2 | 0 |

### Neonatal jaundice in infants of $Gd^-$ and non-trait mothers

Regardless of their own G6PD enzyme activity status, the children of $Gd^-$ trait and non-trait mothers from Massari were compared for a history of neonatal jaundice. Of eighteen children from eight

$Gd^-$ trait mothers, only one reported an episode of neonatal jaundice. Of the thirty two children of fourteen non-trait mothers, four reported neonatal jaundice. According to Table 4.10, only 12.5% of $Gd^-$ trait mothers compared to 28.5% of non-trait mothers, potentially have a chance of delivering an infant with neonatal jaundice. This is the opposite of the results which would be expected if the $Gd^-$ trait alone was involved in cases of neonatal jaundice.

TABLE 4.10

NEONATAL JAUNDICE IN INFANTS FROM
$GD^-$ TRAIT AND NON-TRAIT MOTHERS

| | Mothers | |
|---|---|---|
| | $Gd^-$ | non-trait |
| Total | 8 | 14 |
| Infants with neonatal jaundice | 1 | 4 |
| | (12.5%) | (28.5%) |

Comparing children of $Gd^-$ trait from Kritinea with those from Massari, a total of thirty-seven children of fourteen $Gd^-$ trait mothers were studied. Four cases of neonatal jaundice were found in these thirty-seven children, which is not significantly higher than the figures for Massari, from either the trait or non-trait mothers. One of these cases appeared in an enzyme deficient male child, two in females with unknown enzyme activity status, and one in an unknown male. These latter three children had at least one male sib affected by the enzyme deficiency. The ratios of children with neonatal jaundice compared to their mothers are listed in Table 4.11.

TABLE 4.11

INFANTS WITH NEONATAL JAUNDICE ACCORDING TO GD$^-$ TRAIT STATUS OF MOTHER

| | Infants with Neonatal Jaundice/Mothers | |
|---|---|---|
| | Gd$^-$ Trait Mothers | Non-trait Mothers |
| Massari | 1 / 16 | 4 / 14 |
| Kritinea | 4 / 14 | --- |

Neonatal jaundice in Gd$^-$ trait and non-trait siblings

In both Massari and Kritinea, Gd$^-$ trait children were compared to their non-trait siblings for the presence of neonatal jaundice. Five enzyme deficient males from Massari and ten enzyme deficient boys from Kritinea were compared with their respective siblings who were known to be normal in enzyme activity. Sibling sets which consisted of two children, both known to have the enzyme deficiency were excluded from comparisons since the object was to reveal if there is a tendency for neonatal jaundice to appear more often in families showing the Gd$^-$ trait in one or more member, independent of the Gd$^-$ trait in any particular child of the family. Children in families with one or more sibling identified with the deficiency do not appear to be at any greater risk of developing neonatal jaundice than the children in the general population. Table 4.12 shows that 20-30% of the sib-sets (one Gd$^-$ trait, one non-trait) reported neonatal jaundice in the non-trait sib of the pair. Reviewing the data from Massari again, children of non-trait mothers reported a greater number of neonatal jaundice cases than did children of trait mothers.

This suggests that cases of neonatal jaundice may have as much to do with some maternal or environmental factor as they do with the enzyme deficiency in either the children or their mothers.

TABLE 4.12

NEONATAL JAUNDICE IN $GD^-$ CHILDREN AND THEIR NON-TRAIT SIBLINGS

| | Massari | Kritinea | (Total) |
|---|---|---|---|
| Number of Sibling Pairs ($Gd^-$/non-trait) | 5 | 10 | (15) |
| Non-trait sibs with Neonatal Jaundice | 1 (20%) | 3 (30%) | ( 4) |

Comparing the enzyme deficiency affected individuals alone, in this present study, does not have a striking effect on the number of cases of neonatal jaundice in any of the above comparisons. Children with the deficiency and those from affected mothers do not appear to be at any greater risk of developing neonatal jaundice than do their normal counterparts, at least in the areas under investigation. The data suggest that there is a greater tendency for children in Kritinea, rather than in Massari, to develop neonatal jaundice whether or not they are affected with the enzyme deficiency, indicating that environment or health status of the women during pregnancy might be investigated.

## Blood-Related Conditions in $Gd^-$ Trait Children and Their Non-Trait Siblings

It has been suggested in the literature that individuals with the enzyme deficiency have a predisposition to develop hemolytic anemia, jaundice and possibly hepatitis under conditions of physiological stress, e.g., when viral infection is present. To test these suggestions with the data from the present study, two questions were raised: (1) Do children with the $Gd^-$ trait report more blood related conditions than their non-trait counterparts?, and (2) Do children with $Gd^-$ trait mothers (with or without the trait themselves) report more blood-related conditions when compared to children of non-trait mothers? The phrase, "blood-related conditions" refers to any condition, snydrome, or disease that results in the presentation of anemia or jaundice, aside from the presence of the enzyme deficiency itself. The first question relates to the effect of the trait itself on the child, while the second relates to the testing for a maternal effect where, by virtue of having the $Gd^-$ trait in the mother, the child, regardless of his own $Gd^-$ status, is more vulnerable to hemolytic conditions.

Sixteen children of eight $Gd^-$ trait mothers were compared to thirty-two children from non-trait mothers in Massari for the presence of blood related problems other than neonatal jaundice. Four children of the eight $Gd^-$ trait mothers reported some type of blood related condition: two of them reported anemia, one unexplained jaundice and one favism. Four children of the fourteen non-trait mothers reported anemia, jaundice, or hepatitis. For this sample, more children of affected mothers developed blood-related problems than did children from non-trait mothers. As Table 4.13 shows, twice as many children from trait mothers tend to develop hemolytic conditions, than do children from non-trait mothers.

TABLE 4.13

BLOOD-RELATED CONDITIONS IN CHILDREN OF GD- TRAIT AND NON-TRAIT MOTHERS

| | Gd⁻ Status of Mothers | |
|---|---|---|
| | $Gd^-$ (8) | Non-Trait (14) |
| Total mothers | 16 | 32 |
| With Blood-Related Conditions in Their Children | 4 (25%) | 4 (12.5%) |

Children of the eight $Gd^-$ trait mothers were compared to the children of non-trait mothers in Massari. Of the eight mothers, five had one or more child affected with a blood-related condition (other than, of course, the $Gd^-$ trait itself). Of fourteen non-trait mothers, only four reported some blood-related condition in one or more off-spring. Table 4.14 shows that $Gd^-$ mothers have more than double the chance of having children who at some time develop blood related conditions.

TABLE 4.14

$GD^-$ TRAIT AND NON-TRAIT MOTHERS COMPARED ACCORDING TO REPRINTED EPISODES OF BLOOD-RELATED CONDITIONS IN THEIR CHILDREN

| | $Gd^-$ Status of Mothers | |
|---|---|---|
| | $Gd^-$ | Non-trait |
| Mothers | 8 | 14 |
| With child(ren) affected with blood-related condition | 5 (62.5%) | 4 (28.5%) |

Thirty-seven children from fourteen $Gd^-$ mothers in Kritinea were compared with those in the same category from Massari. Nine cases of some sort of hemolytic condition or blood-related disease were reported among the thirty-seven children from Kritinea: five of these were identified with favism. Deleting the cases of favism from the total, the children of the trait mothers are compared to those from Massari in Table 4.15. Here it shows that Massari has relatively more children affected with blood related conditions than does Kritinea.

TABLE 4.15

CHILDREN FROM MASSARI AND KRITINEA COMPARED ACCORDING TO REPORTED EPISODES OF OF BLOOD-RELATED CONDITIONS

| | Total Children | Children with Blood-related Conditions | |
|---|---|---|---|
| Massari | 18 | 4 | (22.2%) |
| Kritinea | 32 | 4 | (12.5%) |

Working with sample sizes of small numbers makes the conclusions of these comparisons tenuous. Nevertheless, they provide a basis for future investigation. The data from Massari and Kritinea indicate that, aside from episodes of favism, individuals with the $Gd^-$ trait do not suffer higher incidences of neonatal jaundice and other blood-related conditions, than does the population at large. Further, the cases of blood-related conditions which are reported suggest that factors other than the trait itself may be implicated.

## Comparisons of Height, Weight, and Relative Weight

Height, weight and relative weight serves as rough indicators of the general nutritional status and viability of children in different age groups. If the enzyme deficiency represents a maladaptive trait, one might expect to find height and weight differences between $Gd^-$ and non-trait children. Heights and weights, along with other anthropometric measurements, were recorded for all children from ages 7 to 12 in Massari and Kritinea. Relative weight was calculated for these children by using the Quetelet Index ($ht/wt^2$ in kilograms and centimeters).

In terms of height, the $Gd^-$ trait boys in the study are well within the ranges and averages exhibited by others in their age cohort from the two villages. Comparing the averages for the two groups, $Gd^-$ vs non-trait, all averages with the exception of the eleven year olds, the averages from the trait children are higher than those without the trait. The eleven year olds with the trait showed a figure of two centimeters under the average for the rest of the non-trait children. These comparisons are shown in Figure 4.2.

A comparison of weights reveals this same conclusion, that is, trait children do not differ from their non-trait counterparts with respect to weight. The trait eleven year olds, again, were under the average weight for their non-trait counterparts. These comparisons are shown in Figure 4.3.

The Quetelet Index shows relative weight with the values

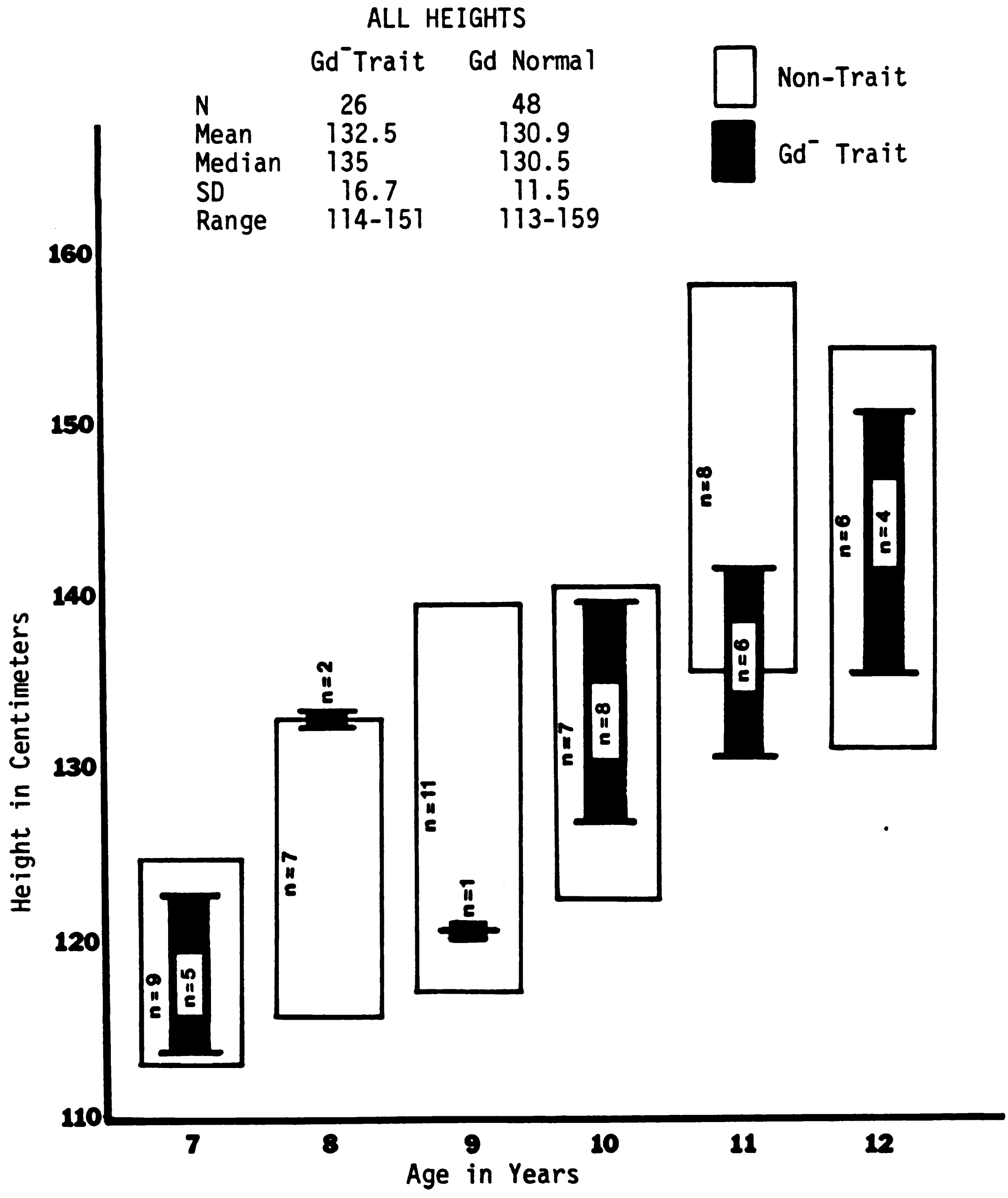



Fig. 4.2 Heights of All Boys in the Massari and Kritinea Samples

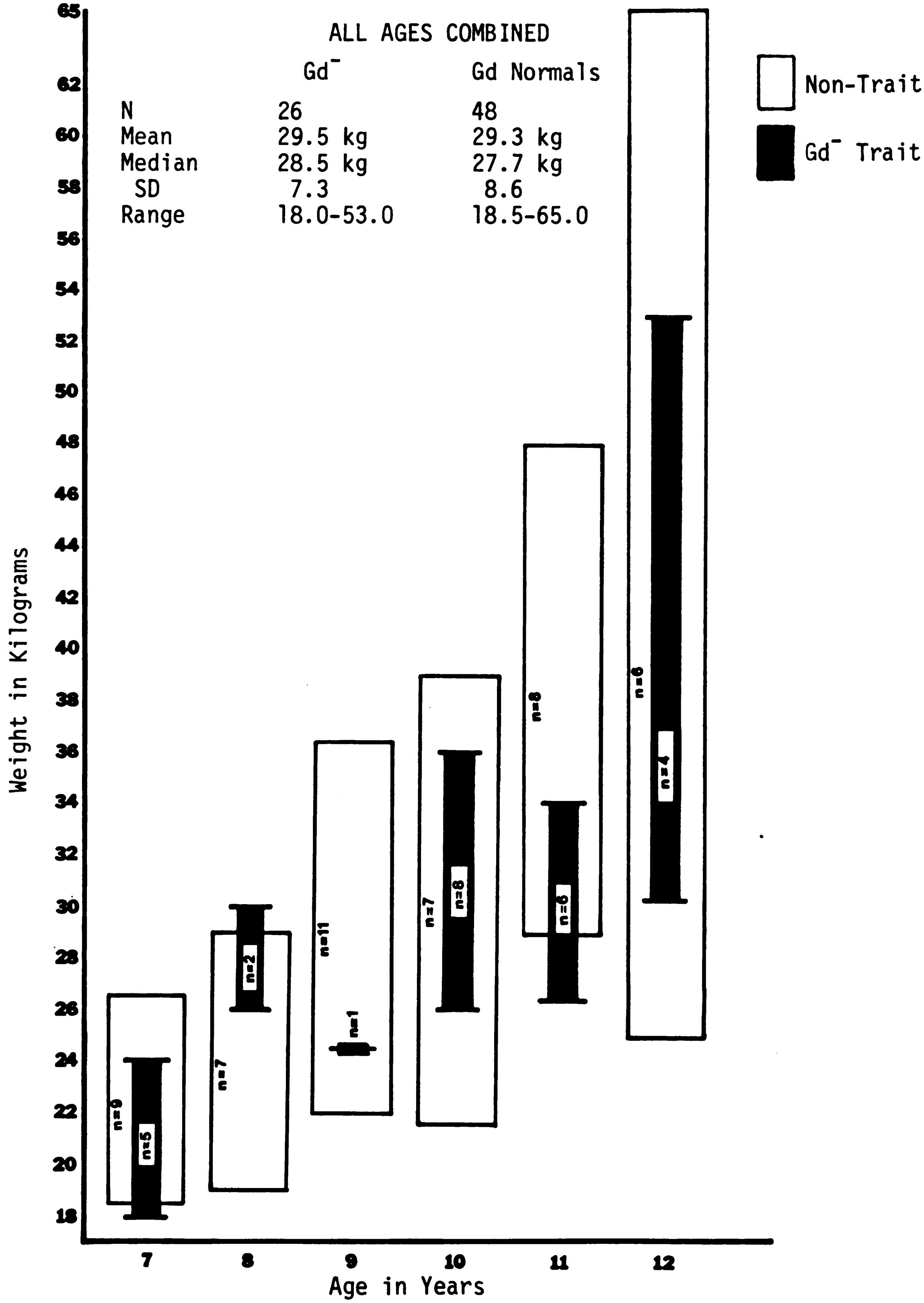



Fig. 4.3 Weights of All Boys in the Massari and Kritinea Samples

not necessarily related to age. Values are given by numbers which usually begin around 12, and, for normal, non-obese statures, end at 20. Values of over 20 are considered to be in the slightly overweight to obese ranges. The Index is especially useful for the present study where small samples were used in each age group. The Index allows for the combination of all ages and gives a relative ranking regardless of age. Figure 4.4 shows the indices rounded to the nearest 1.0., and clearly indicates that the 26 $Gd^-$ trait boys have higher indices than the 48 non-trait boys. That is, the trait boys have more body weight than their non-trait counterparts. Table 4.16 compares the average values for the boys from the two villages, showing that the boys from Kritinea tend to have slightly more relative body weight than do those from Massari.

TABLE 4.16

COMPARISON OF RELATIVE BODY WEIGHT IN BOYS FROM KRITINEA AND MASSARI (QUETELET INDEX)

| | Kritinea | | Massari | |
|---|---|---|---|---|
| | $Gd^-$ | non-trait | $Gd^-$ | non-trait |
| Number | 16 | 21 | 10 | 27 |
| Mean | 16.9 | 16.9 | 16.8 | 16.6 |
| Median | 16.8 | 16.5 | 15.7 | 15.5 |
| Stan. dev. | 1.21 | 1.46 | 3.46 | 1.34 |
| Range | 15.2-20.8 | 15.1-20.8 | 13.2-25.5 | 12.4-28.5 |

On the basis of the comparisons which have been made between trait and non-trait children, sib pairs, and between $Gd^-$ trait

| | All Boys | |
|---|---|---|
| | Gd$^{-}$ | Non Gd$^{-}$ |
| n | 26 | 48 |
| Mean | 16.9 | 16.8 |
| Median | 16.6 | 16.2 |
| Standard deviation | 2.3 | 2.6 |
| Range | 13.2-25.5 | 12.4-28.5 |

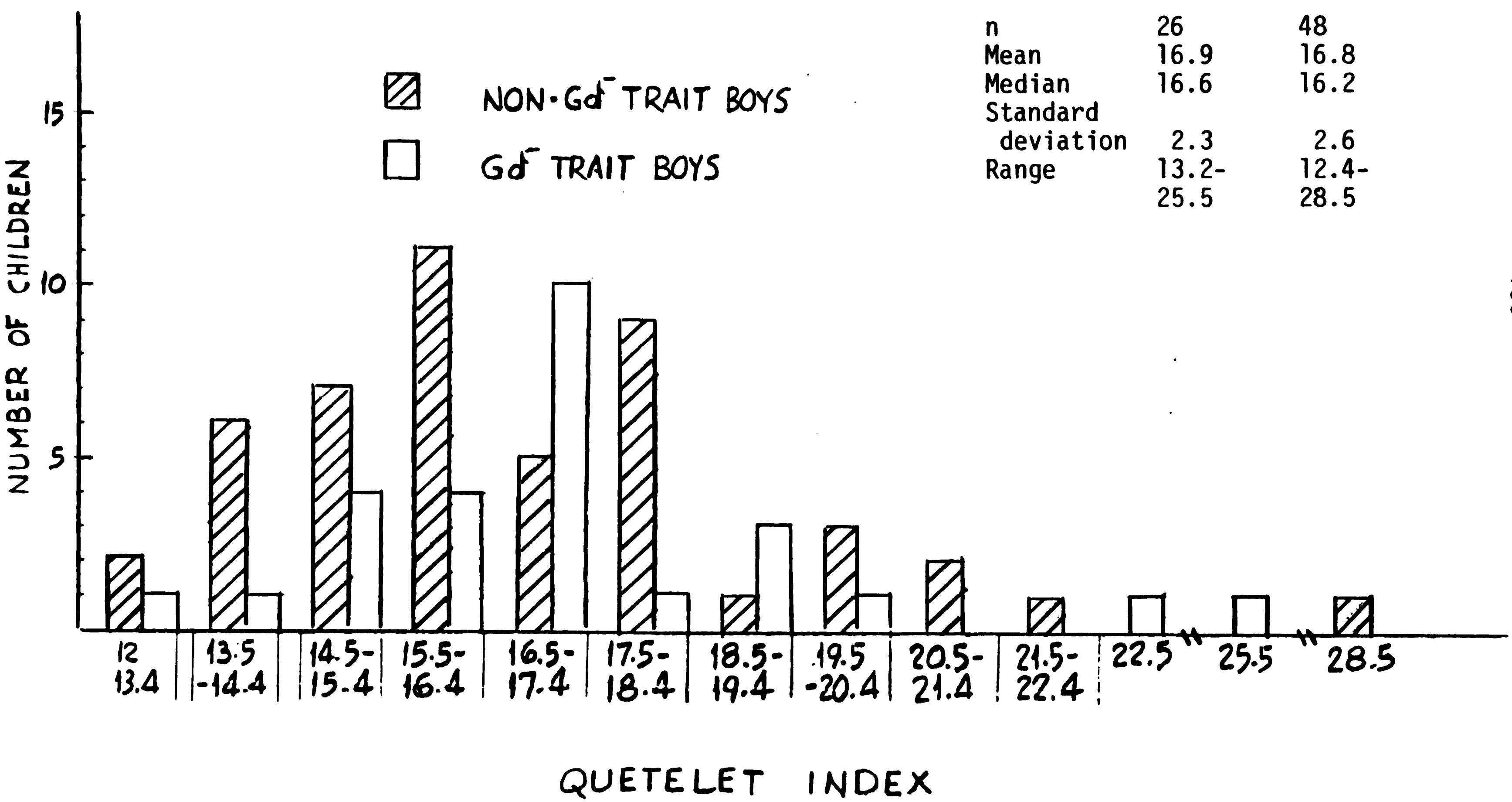



Fig. 4.4 Quetelet Index: Boys from Massari and Kritinea

and non-trait mothers of these children, no substantial differences could be found to indicate that the $Gd^-$ trait is maladaptive. While malarial conditions may have played a role in selecting for the trait at one time, in the absence of contemporary malarial conditions, the trait may be perpetuated because it does not carry particularly strongly maladaptive aspects. Even considering that favism may occur in individuals with the trait, frequencies of the illness are always significantly lower than would be expected on the basis of $Gd^-$ trait frequencies, while mortality figures for favism are even lower.

## Genetic Drift and the $Gd^-$ Trait

From the information for contemporary Rhodes, selection does not appear to have an influence on the distribution of the $Gd^-$ trait frequency or geographical range. In the introductory section of this chapter, five hypotheses were advanced to account for the trait distribution. Three have been discussed (relationship to altitude, selection for the trait by protection from malaria, and neutral selectivity). Two hypotheses remain: (1) Endogamous marriage customs contribute to the perpetuation of the trait in high frequencies in some isolated areas, and (2) Random factors contribute to the high frequency and fluctuations in $Gd^-$ trait distribution. These latter two are taken up in this section.

Given the situation in the micro-regions of Rhodes, there is a reasonable indication that genetic drift contributes to the rather significant differences in $Gd^-$ frequencies which are found in the different localities on the island. Genetic drift acts independently of natural selection, and can promote a predominance of alleles that actually oppose adaptation. Genetic drift is a random fluctuation in the gene frequency from one generation to the next (Cavalle-Sforza 1969). As an example, two villages which had been screened in earlier studies of the Rhodian population showed differences from one period to the next which might be explained by genetic drift. In one of these villages (Massari), Allison et al. (1963) found 34.4% of the males tested to be enzyme deficient. Approximately fifteen years later, the screening for this study shows 27% of those tested with the trait. In another village (Pylona), Kattamis et al. (1969a) found 25% of those tested with the $Gd^-$ trait. Nearly ten years later, the present study found 36.3% of those tested with the trait. In one area, the percentage was lower and in the other, it was higher, than those reported by the earlier studies. These differences are probably not related to environmental factors but are most likely random.

Genetic drift is influenced by a variety of non-genetic factors, particularly those related to demographic dynamics (population size, breeding population size and random out-migration). Random historical events and natural or man-made catastrophes which severely reduce population size without preference for any particular genetically determined trait, play an important role in promoting genetic drift. When considering genetic drift, population size does not refer to the actual number of individuals residing in a locale, but to the possible parameters of the breeding population. Therefore, cultural practices which relate to the selection of marriage partners must also be taken into account. Genetic drift has a strong influence in small populations where a slight change in the actual number of people with a trait causes a large change in the proportion of the population affected by it. For example, Cavalli-Sforze (1969) found in a study of Italian villages, that genetic variation between villages declined as population size increased, but that,

> under the influence of drift, village populations will tend to become more different, even if at the beginning they were homogeneous in the composition of hereditary types. (p. 334)

In this section it is suggested that random historical events which occurred in Rhodes aided in promoting high over-all frequencies of the $Gd^-$ trait. Contemporary marriage and residence patterns in certain villages act to make genetic drift a more important variable in explaining $Gd^-$ distribution (than other environmental causes).

## Genetic Drift and Historical Events

Temptations are strong to search for historical causes to explain the high average frequency and range of frequencies of the deficiency on Rhodes. Given the island's tumultous history (invasions, sieges, sackings and rapes) and lack about the origins and interrelationships between the early peoples on the island, these temptations may only result in interesting but unscientific speculations.[1] Siniscalco (1966:372) had to come to the same conclusions for the questions of the deficiency and its presence on the island of Sardinia, where, in spite of being an island and historically "intact," it must be accepted that "... a few sets of 'external' genes must have entered the genetic pool from time to time."

The history of Rhodes is replete with events both man-made and natural which contributed to the random and fairly rapid population declines. During the Dorian period in Rhodes, the population of the island grew to 500,000 inhabitants, a figure which has not since been equalled. Following this population zenith, the island suffered two distinct periods of drastic and rapid decline (Kolodny 1974).

When Rhodes began its alliance with the Roman Empire in 395 A.D., the population was nearly 500,000, the same that it had been during the Dorian period. Six hundred fourteen years later, when the Knights of St. John began their occupation of the island in 1309, the population had halved to 250,000. There are no indications that the drop in the number of inhabitants was related to selective features promoting or inhibiting the perpetuation of particular genotypes. No epidemics are recorded during this historical period of the isalnd which would have tended to wipe out certain sectors of the population which may have shared a genetic weakness toward the disease. Rather, the population decline is attributed to random factors, such as those which resulted from repeated sackings and seiges of the island, and natural catastrophes such as earthquakes.

Again, the population fell to the figure of 35,000 recorded after the Turkish occupation began harsh assimilation tactics in 1826. It is not clear if the depopulation from 250,000 (in 1309) to 35,000 occurred during the entire 517 years of the Turkish occupation of Rhodes, or if it happened suddenly around 1826. During a period of no more than 517 years, the population declined by 214,000 inhabitants. This drop is attributed to extremely high rates of out-migration and mass slaughter. Both of these factors are random with respect to particular genetic characteristics shared by those eliminated in the drastic reduction of the population.

These two significant periods of depopulation, each occurring within about a 600 year time span, give plausibility to the theory that genetic drift may have been at work in the Rhodian population. It is possible that the random forces of history and geology, the enzyme deficiency became predominant throughout the island, at higher frequencies than would have been promoted by natural selection. Further, these frequencies then became associated with particular localities by chance, and cultural factors reinforced them. In particular, cultural practices related to the selection of marriage partners acted on these distributions.

## Genetic Drift and Endogamous Marriage Practices

Certain groups with very high $Gd^-$ trait distribution are noted to be ethnically endogamous, possibly perpetuating the trait in spite of pressures of natural selection. The Greek Islanders have been noted to stress the practices of insular endogamy, if not village endogamy. As with the falacious idea that island communities can be treated as genetic isolates, the same applies for villages.

The cultural ideal of village endogamy, while promoted by economic constraints as well as ideological sanctions, does not hold true throughout the island of Rhodes. It is not only marriage, but residence after marriage which must be considered. The latter gives an estimate of possible breeding population which is importance in calculating the potential for genetic drift to be an active factor in influencing trait frequencies. Some villages may allow fully exogamous marriages, both on and off the island. In this case the potential breeding population is larger than the population of the village, and genetic drift less likely to be a factor in affecting frequency fluctuations. Other villages enforce only endogamous marriages and/or expell the couple who have married outside the village. In this case the breeding population is limited to the size of the village, and drift is expected to be a more significant factor in explaining fluctuations in gene frequency.

### A description of marriage and residence practices in Rhodes

The practice of provisioning marriageable young Greek women with a dowry (príka) has been noted in the ethnographic literature (e.g., Friedl 1963; Dubish 1975; Hoffman 1975), however the form and content of the dowry differ by region. While the intent of the dowry is to provide the new couple with an economic basis with which to begin their life together, it also promotes female premarital chastity and emphasizes the arrangement of an honorable and economically profitable union. Even though the dowry is now illegal in Greece, it is no secret that young men and women consider more than romantic attraction when selecting their marriage partner. In Athens, Salonika and other large towns of the Greek mainland, the dowry may consist of money or a promised position in the father of the bride's business. In the rural areas of the mainland, the dowry may involve little more than a trousseau, household linens, and other household items, and land. In the Greek islands, in general, the dowry reaches its most elaborated form where it included not only all the aforementioned goods and promises, but a house as well. This tends to promtoe the selection of marriage partners from one's own island if not village. It is not uncommon to find a mother who will completely ostracise a son or daughter (more often a son) who has married someone from another island. Even if the entire family has migrated to an urban center on the mainland, it may be expected that their children will marry someone from their native island. Some young men have purposely concealed a financee for several years simply because she is not from the island of their birth.

In Rhodes, the dowry consists of a house, its furnishings, and land holdings. Men also have an inheritance in the form of land, if they marry outside the region, they must leave their share of the family inheritance behind. If they make a marriage with a woman from their own region, they can maintain their own landholdings, and combine them with those in the wife's dowry. Since these are basically unmovable holdings, it is economically wise for both sexes to marry within one's own village or region.

Pressure is exerted for village endogamy, not only from the economic position, but from the moral one as well. Ideally, young men and women should behave so as not to damage the honor of the family, and thus lessen their marriagability. Informants during the research expressed the opinion that the selection of marriage partners within the village was the ideal situation. This insured that the family knew where the intended spouse came from in terms of family background, honorability, honesty, and potential. In both Kritinea and Massari, there was the explicitly stated preference that the young people in one's family select to marry another person from the same village. Mothers would say that if the daughter was good and proper, that she need not look elsewhere for a husband. If the young man is honorable, then he does not need to go to another village to search for a good wife. Although arranged marriages are uncommon, the fact that the spouse is from the same village helps to insure the family position is clearly known, and behavior patterns of the intended are known from childhood.

The pressure to marry and the emphasis on family honor result in the situation where there is virtually no institution for social relationships between unrelated young men and women, except through the institution of engagement and eventual marriage. Engagement, although no longer marked by a large public ceremony in Rhodian villages, represents a serious and singular step toward marriage. It is, at the same time, the only way in which a young man and woman may keep company together away from the other members of the family.

Being engaged means that arm-in-arm walks together may be taken, that the young man may take some of his meals at the home of the intended bride, that the couple may attend summer festivals together, and spend extended periods of time in each other's home. The act of engagement breaks all the barriers formerly standing between the young man and woman, and, in the eyes of the community, they are as good as married.

There are exceptions to this rule. Engagements may follow family pressure when continual company kept between a young man and woman becomes noticed by others in the community and family honor is threatened. This may result in a marriage which was not really the choice of the couple involved. Pregnancy may suddenly become evident and an engagement forced to be announced before actually intended. In this way, the pregnancy is considered as legitimate as one which occurs within the marriage, since, they rationalize, the couple had publically announced the engagement. The actual wedding ceremony is not as important as the fact that it followed an engagement which was formally recognized.

Often, illegitimate births are excused by this as well. An unmarried mother will say that her fiance was killed before they could marry; or is involved with the army and will come shortly to marry her. These women, if the fiance does not show up, are usually barred from ever marrying.

The seriousness with which engagement is considered helps to explain why the breaking of one causes public shame. Engagements are, nevertheless, broken, with the result that the young woman becomes morally marked, and may find it difficult to contract a marriage within the village. This is another reason why marriages with outsiders are often thought to be only for young women whose virtue is flawed.

The engagement is marked by two objects: the wearing of a gold band on the left ring finger (later changed to the right ring finger upon marriage), and the beginning of the construction of the dowry house by the bride's family (if construction had not already begun). If, during the time of the engagement, a pregnancy does occur, but the house is not ready for occupancy, it is considered that the marriage ceremony is bound to take place sooner or later, and the young couple simply miscalculated the time at which the house would be ready. The families of the bride and groom begin to call each other by the appropriate kinship terms following the engagement. The young woman refers to her finace as "my husband" (o ándras mou), and her family calls him "our son-in-law" (o gambrós mas). Equivalent terms are used for the bride to be, (y gynaíka mou; y nífi mas) "my wife", and "our daughter-in-law". In-laws also call each other by appropriate terms (sympetherós - masculine; sympetherá - feminine), and the young couple address the in-law relations by correct terminology. Even the best-man (koumbáros - masculine) will also be addressed by his ritual kinship term even before the wedding has taken place.

The accumulation of household goods begins long before the house construction is under way. Young girls begin to learn to sew, crochet, embroider and weave during their elementary school years. By the time they have finished the elementary school, they begin these chores on a more regular basis, as many still do not attend school after the age of twelve. Often, they are engaged by the age of fourteen, and married by seventeen.

Women who marry outside of their village usually bring their husband into their dowry home, but when the woman leaves her own village to go to that of her husband, she is at a disadvantage. Not only does she leave her dowry land behind, but also her dowry home. Even though the plots of land may be near to the village which she has married into, her husband must provide a home for them. Men who do this are often thought to be a little stupid by others in his village; even worse, is the husband who is willing to contribute the building of their home. Sometimes it is virtually impossible for the bride's family to provide her with a house, and she and her husband may build their own. Even though the resulting home and its furnishings might be more luxurious and modern than either would have been able to afford separately, the husband is referred to as stupid (vlácas) when he undertakes such a venture.

The importance of the dowry house, both practically and symbolically is most in evidence immediately preceding the wedding ceremony. During the week prior to the ceremony, the house and all its furnishings is open to the public eye, with the bride and groom receiving guests in the home. Gámos, the word for both the wedding ceremony and the marriage itself, is also used to refer to the actual house where the new couple will live. People will often use the expression, "... go to see the gámos..." when they mean to visit the house of the bride and groom. They may say in passing the new house, "There is the place of the *gámos*." The bride and her best girl friends will stay in the house the night before the wedding ceremony takes place. The day of the ceremony, as well as earlier, relatives of the bride gather at the house to cook, to prepare the bride for the ceremony and to dance local folk dances.

If a family cannot provide a new home for the daughter, she is given the home of her parents who then move into another, older and smaller dwelling, which is usually from a grandparent of the male side of the family. It is uncommon for parents to share a dwelling with a married offspring of either sex. The occupation of a parental home by a married daughter happens when the family is unable to provide a full dowry, or when the daughter is the last in the family to marry. There is no particular social stigma attached to this; the important thing is the daughter has her own place which has been given to her by her parents, and will not be shared as a dwelling unit by her parents.

When land holdings as part of the dowry tend to promote regional marriages, the house as part of the dowry promotes a pattern of residence in the bride's village. This encourages the selection of marriage partners within one's own village. In villages with a population of little more than 600, such as in Massari and Kritinea, it is difficult to find anyone not distantly related. Marriages with first cousins are said to be avoided, but do in fact happen. Second cousin marriages are not necessarily avoided, occur sporadically, along with marriages between affinal relatives. Since there are no mechanisms for courtship outside of engagement, certain courtship behaviors are played out within the context of the family. Small flirtations and gift bringing takes place between cousins and affinal relatives of the opposite sex, with the result that some of these lead to rather inescapable commitments for marriage between second and third cousins. Further, it often happens that two sisters will marry two brothers, or two men who are related to each other as cousins. Again, once a daughter has married, the groom's entire family becomes included in family gatherings, and contact the unmarried brothers and sisters of the bride and groom become regular.

In general, Kritinea and Massari follow the same patterns for marriage, with the majority of unions taking place between individuals from the same village. One major difference is observed which will be considered here with respect to genetic drift.

### Regional endogamy and the selection of marriage partners

Neither Massari nor Kritinea follow the ideal marriage behavior for selecting mates from within the same village. Both have nearly the same rates of out-marriage from the village. In Massari, a total of 222 marital unions were counted from village records and genealogies. Of these, 31.9% were village exogamous. In Kritinea, 251 unions were counted, with 32.2% of them being village exgamous. Considering the place of residence after marriage, over half of the village exogamous unions in Massari continue to live in the same village (52%) while only 8.6% of the village-exogamous unons from Kritinea continue to live in the same village. This is a significant factor in terms of the implicatons for genetic drift. All but a few of the individuals who marry outsiders to the village of Kritinea continue to live in the village.

Residence after marriage effects the representation of genetic factors in small local units such as Massari and Kritinea. The breeding population represented in Kritinea is smaller than that shown in Massari; in Kritinea, the pattern of residence after exogamous marriages tends to limit the introduction of outside genetic material into the village. In Massari, where there is an equal tendency for those marrying out of the village to either remain in the village or to leave, it can be expected that there are more opportunities for genetic mixture from outside the village. In reviewing the localities from which new alleles and genetic material might come, in the case of Massari, it is evident that the introduction of new genetic material is not random but comes regularly from the region immediately surrounding the village. These locations are shown in Tables 4.17, 4.18, and 4.19, and summarized in Figure 4.5.

As Table 4.17 shows, the greatest number of marriage partners from outside the village of Massari were chosen from the region on the east coast. This region to which Massari belongs, shares many of the economic and geographic as well as cultural patterns which are found in Massari itself. Considering the nature of Massari's dependence on the City of Rhodes (as described in Chapter Three), the daily interchange of people on their way to the city would make relationships outside the village a likely outcome.

TABLE 4.17

VILLAGE-EXOGAMOUS MARRIAGES IN MASSARI AND KRITINEA ACCORDING TO RESIDENCE OF SPOUSE

| Birth-Place of In-Marrying Spouse | Number of Exogamous Marriages: Massari | Kritinea |
|---|---|---|
| Island of Rhodes (total) | (45) | (25) |
| City | 6 | 5 |
| East coast | 28 | 0 |
| West coast | 3 | 16 |
| Southern | 1 | 1 |
| Unknown village | 7 | 3 |
| Other Islands | 4 | 18 |
| Mainland and Other | 23 | 37 |
| Total | 72 | 80 |

Table 4.18 illustrates the overwhelming difference between Massari and Kritinea when the number of village-exogamous, but in-resident marriages are totaled. In-resident marriages are those where one or both spouses and their unmarried chidren claim residence in the village and were in fact in residence during the time of the study. Exceptions to this might include children who were momentarily in the army or attending a higher education institution outside of the village.

Of the seventy-two exogamous marriages from Massari (see Table 4.17), thirty-seven still reside in the village, while only six of the eighty village-exogamous unions from Kritinea still reside in the village. There is a much greater tendency for villagers of Massari to remain in the village after they have married an outside than was observed in Kritinea.

TABLE 4.18

EXOGAMOUS MARRIAGES STILL RESIDING IN THE VILLAGE

| In-Marrying Spouse's Birthplace | Massari | Kritinea |
|---|---|---|
| Rural Rhodes, 1-6 km radius | 11 | 0 |
| Rural Rhodes, 6+ km radius | 13 | 0 |
| Rhodes City | 2 | 1 |
| Other Islands | 3 | 5 |
| Mainland Greece | 3 | 0 |
| Unknown | 5 | 0 |
| Totals | 37 | 6 |

Of the thirty-seven unions between villagers from Massari and spouse from elsewhere in Rhodes, twenty-six remained in Massari. Of the twenty-four in Kritinea (with spouse from elsewhere in Rhodes), only one stayed in the village after marriage. The unions from Massari in this category are shown in Table 4.19.

TABLE 4.19

VILLAGE-EXOGAMOUS MARITAL UNIONS FROM MASSARI COMPARING RESIDENCE AFTER MARRIAGE

| Birthplace of Spouse, km Distance | Total Unions | In-Resident Unions |
|---|---|---|
| 1 - 6 | 20* | 11 |
| 6 - 20 | 19 | 13 |
| 20+ | 6 | 2 |

*Fourteen of these twenty were exchanges between Massari and Malona

Massari acts not only as a donor population to other areas of Rhodes, it is also a recipient of new genetic material. Kritinea is primarily a donor population, receiving little new genetic material from the rest of the island.

Compared to the 45 marital unions in Massari where one of the spouses came from outside of the village, Kritinea had only six such unions. All of the other village-exogamous marriages from Kritinea are now found outside of the village. Figure 4.5 illustrates these differences between village-exogamous marriages and subsequent residence in Massari and Kritinea. Only one of the six village-exogamous unions which was residing in Kritinea at the time of the study involved a spouse from Rhodes. The other five village-exogamous unions consisted of one member from Kritinea and the other from another island of the Aegean. That is, when and if the people of Kritinea marry outside of the village they do not usually continue to live in Kritinea. Those who did maintain residence in Kritinea, had spouses from areas of Greece other than Rhodes. This has ramifications for the size of the breeding population in each village. In Kritinea, the breeding population is nearly equal to the number of inhabitants. In Massari, with the exogamous parameters extending to a radius of more than twenty kilometers, with the greatest concentration within a six kilometer radius. The most modest estimate of the increased breeding population would include at least the population of the adjacent village to Massari, Malona. This more than doubles the breeding population of Massari when compared to that of Kritinea.

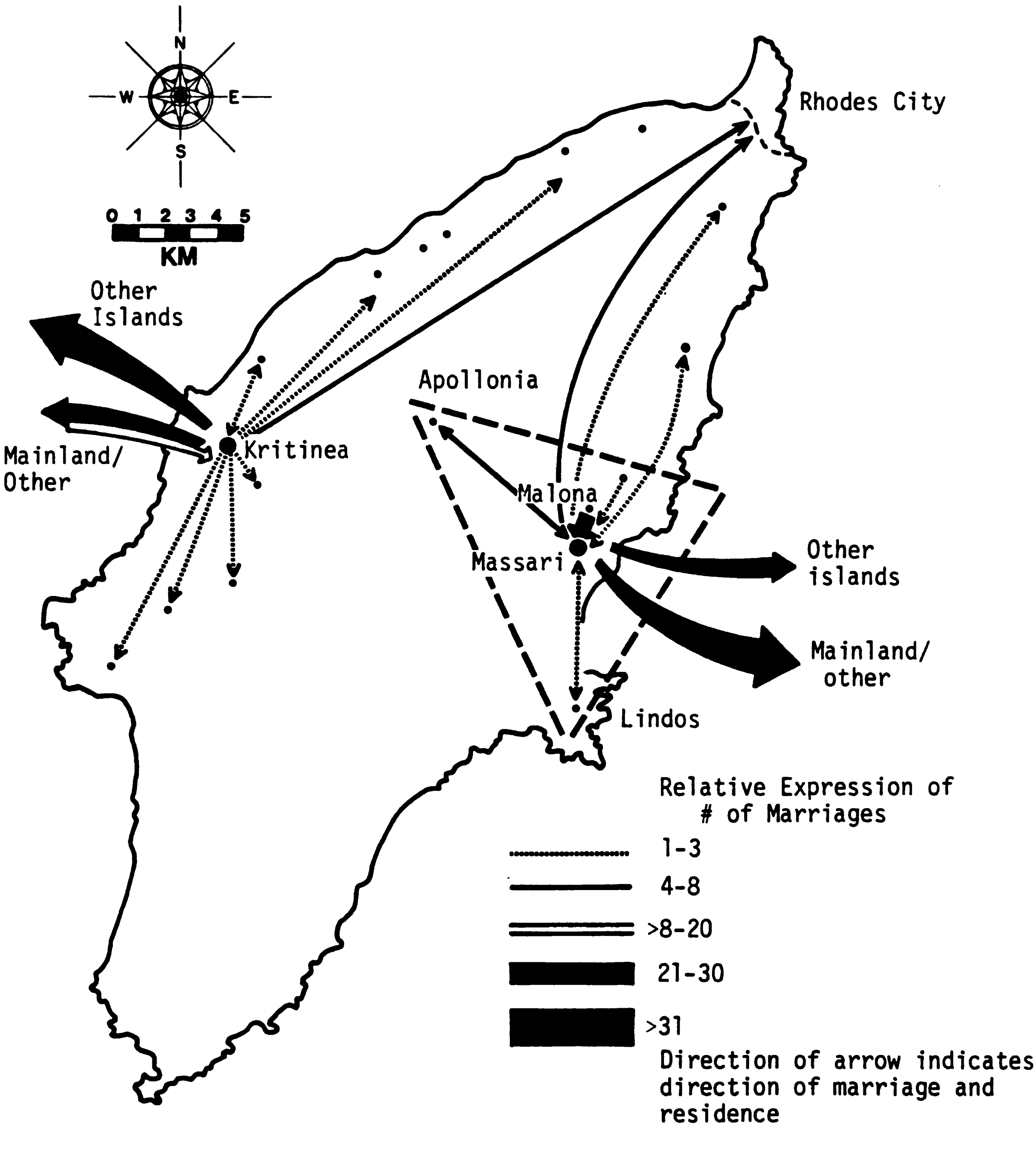



Fig. 4.5 Village-Exogamous Marriages in Massari and Kritinea

While the populations of Massari and Kritinea are nearly equal, Massari has many more genes entering its gene pool on a continuous basis from areas outside of the village boundaries. Kritinea's gene pool, in contrast, remains closed. Its smaller breeding population means that less genetic material enters from the outside, and therefore, is more likely (than Massari) to be subject to genetic drift. If an equivalent number of elementary school boys were to be tested in another ten to fifteen years, one would expect to find that the frequency of the trait fluctuating more than it would in Massari, on the basis of genetic drift alone.

The unusually high frequency of the $Gd^-$ trait in Kritinea, located 300 meters higher than Massari, and probably not as subject to malarial endemicity as Massari, is explained by two factors. First, the altitudinal location of Kritinea is not sufficiently high enough to inhibit its livestock herders and agriculturalists from moving through intermediate and even sea level eco-niches, some of these potentially malarious. The location of agricultural lands and the arrangement of these holdings necessitates travel to these different eco-niches on a daily, weekly and seasonal basis. Calculating the possibility for malarial infection by taking into consideration only the altitudinal location of the villages does not consider the pattern of movement through these other regions. Secondly, populations of villages which tend to maintain endogamous marriage and rather exclusive residence patterns after marriage, have a smaller breeding population than can be calculated for populations which follow more open marriage and particularly residence patterns.

## Summary

In the scientific literature, conclusions about the nature of the relationship between altitude, malarial endemicity and the possible protective advantage of the $Gd^-$ allele are not yet unequivocably established. Statistically, the direct correlations between malarial endemicity and $Gd^-$ trait frequencies are supported in the literature. The problem arises when the exceptions to the standard correlation of high malarial endemicity and high $Gd^-$ frequency are noted. Considering the types of land holding patterns, modes of agricultural and horticultural exploitation, and population movements (either related to land holdings or to livestock patterns) on a daily to seasonal basis through different eco-niches, may help to explain some of the exceptions.

The inverse relationship between altitude and the frequency of the $Gd^-$ trait, most clearly supported by the literature from Sardinia, does not hold true for Rhodes. The inverse relationship may not be observed in Rhodes because the $Gd^-$ trait frequencies are uniformly higher and altitudinal ranges less diverse than those represented in Sardinia. From a historical perspective, the principle of genetic drift may help to explain the high frequencies for the entire island, Rhodes having suffered severe and random depopulation at various periods of time. This principle may also be at work on a regional or village-level where differences in marriage and residence practices encourage great differences in the size of breeding populations and allow genetic drift to operate to a greater degree in some areas (e.g., Kritinea) than in others (e.g., Massari). This, in turn, gives at least one indication of why the frequency of the $Gd^{-}$ trait is higher than would be expected, both on the basis of past malarial exposure and altitude.

## FOOTNOTES

### CHAPTER FOUR

1. Hypothetically, one might insist that the Dorians brought the G6PD deficiency allele with them and spread it throughout the island of Rhodes. It was the Dorians who were responsible for populating the island, although other settlements had been on the island, they were confined to the sea coasts. The Dorians were responsible for constructing the three city-states of Kamieros, Ialysos and Lindos. The latter became a powerful maritime center with trade outposts established in Sardinia and the Balaeric Islands. Both of these have much higher frequencies of the deficiency than do their respective mainland areas (Italy and Spain). The areas on mainland Greece from which the Dorians originated (Macedonia, Thessaly and Thrace) also happen to show higher frequencies of the enzyme deficiency than any other areas of the mainland thus far screened. Some of these regions, in fact, show even higher frequencies than the average found in Rhodes.

# CHAPTER FIVE

## THE SOCIAL EPIDEMIOLOGY OF FAVISM

The results of the survey of reported favism episodes in Rhodes for 1966-78 show that the distribution is in general agreement with that which is described in the literature. The epidemiological pattern of favism includes these five characteristics:

1. Seasonality: It is a seasonal disease, usually occurring in the spring.
2. Regionality: Certain geographic areas often show high frequencies of favism, with these frequencies not always related to the distribution of the major risk factors (the $Gd^-$ frequency and/or the level of fava bean exposure).
3. Age-Related: Favism is most often reported in children under the age of ten.
4. Sex-Related: More males than females report episodes of favism.
5. Familial: Certain families with the $Gd^-$ trait will more often report episodes than other families, equally affected with the trait.

At least four major types of variables, other than the $Gd^-$ trait itself, are suggested to relate to the distributional patterns of favism: (1) fava bean exposure, (2) environment, (3) socio-economic factors, and (4) ideological influences. These are shown in Table 5.1 which reintroduces the epidemiological model shown in Chapter One. Using the categories shown in this Table, a set of hypotheses was formed for each of the known distributional traits of favism (seasonality, regionality, etc.). The investigation of these

TABLE 5.1

EPIDEMIOLOGICAL MODEL FOR FAVISM

| | $Gd^-$ Trait | Bean Exposure | Environment | Socio-cultural |
|---|---|---|---|---|
| Seasonal | Not known to be related. | Bean production schedule related to seasonality of favism episodes; making more cases in peak productive season. | Altitudinal differences alter patterns of fava bean production and harvest. | Fasting periods promote fava bean consumption, contributing to peaks in favism. |
| Regional | Known to be related (Chapter Four). | Fava beans are expected to be used more often in rural areas; may differ also by village. | Altitudinal and rural-urban differences are expected to be found in favism frequencies. | Ruralites are expected to follow fasting more rigorously and use the beans more often. |
| Age | Not known to be related. | Fava bean exposure is expected to differ by age. | Age differences according to village location and urban-rural gradient are expected to be found in frequencies of favism. | Age roles will allow fava consumption -- or will allow freedom at later ages to consume the beans. |
| Sex | X-linked nature of $Gd^-$ trait makes more males than females at risk; more males are expected to report favism. | Fava bean exposure expected to be lower among male children who are protected from the beans. | Sex differences in the division of agricultural labór will allow greater exposure among males. | Sex roles will promote differential protection of members of the population vis-a-vis age. |
| Familial Tendency | $Gd^-$ known to be inherited; may be accompanied by other traits. | Families will be differently ranked according to quantity and type of fava bean preparations used. Families using more of the beans will be at greater risk. | Families which have their own gardens with fava beans or own fields with the beans will be at greater risk. | Familial taboos, as selected from the cultural food taboos, will promote different treatment of favism, and different attitudes toward risk. |

hypotheses is presented in this chapter.

Factors which were suspected to influence the seasonality of favism were:

1. The schedule of fava bean production;
2. Micro-environmental differences such as altitude which might affect availability of fava beans;
3. Seasonal dietary differences regulated by the agricultural and ritual calendar.

The fluctuation of the $Gd^-$ trait by season was not believed to play a role in the seasonal differences in the number of reported episodes of favism. While the scientific literature indicates that the trait does not change according to season, it was not possible to check for this during the present research.

In the literature, regional differences in favism frequencies are usually related to the distribution of the $Gd^-$ trait, even though some areas do not fit the pattern expected if only the $Gd^-$ trait is considered to be involved. Differences in fava bean exposure by region is suggested to influence the distribution of favism, but is not usually investigated in the research. Hypothetically, villages in different kinds of physical and social settings are expected to exhibit variations in the cultivation and quantitative use of the beans. This is aside from the influences that environment might have on the $Gd^-$ trait. In the present study, the following aspects of region were explored:

1. Regional and village variations in the cultivation and use of fava beans;

2. Comparison of features of the physical environment; such as altitude, settlement patterns, distance from urban centers;
3. Economic pursuits of village members which might tend to influence the level of bean exposure;
4. Regional economic integration (or lack of it) and interdependence of villages in a given region.

As Table 5.1 shows, age is not known to be related to fluctuations in the $Gd^-$ trait, which would then help to explain why favism is not reported in older members of populations with the trait. A variety of other factors might operate to influence the age distribution, some of these related to fava bean exposure, others to organic characteristics of the individuals involved. In addition to organic and environmental factors, it is suggested that fava bean exposure and age might be regulated by:

1. Use of fava beans within the household, e.g., as a weaning food;
2. Protection from fava bean exposure, of certain age groups, e.g., very young children; following an episode;
3. Settlement in areas where fresh, ripe fava beans are available and where certain age groups participate in agricultural activities which bring them into close contact with the beans.

Potentially, organic factors might be involved in the age distribution of favism, with the older children and adults having acquired some form of resistence. Roles prescribed by age may also intervene to influence the reporting of symptoms and episodes to health authorities.

These same factors were looked at regarding the sex-distribution of favism. The x-linked nature of the $Gd^-$ trait is expected to influence the ratio of males to females suffering from favism. Beyond the trait, additional environmental, social and ideological factors are expected to influence fava bean exposure, reporting of episodes, and perhaps organic resistence. The study checked to see if there were any variations in:

1. Expression of symptoms by sex, such that reporting of episodes might be affected;
2. Distribution of cases by rural-urban and altitudinal locations according to sex;
3. Exposure to fava beans by sex, either through sexual division of agricultural labor or sex role differences.

The familial tendency to report multiple favism episodes (in different members of the same familial pedigree), is related to the $Gd^-$ trait being an inherited characteristic. More than genetic inheritance is shared by families. Of interest to the present study were familial differences in fava bean use, in economic activities and the interrelationships of the nuclear units of the $Gd^-$ pedigrees to each other.

This chapter has three major parts. The first deals with the seasonal and regional distribution of favism cases, these being most closely tied to the physical environment. Part II presents the age and sex distributions and investigates different hypotheses which might help explain them. Part III presents the familial data on favism, comparing pedigree materials with other characteristics of the family.

## PART I

### Seasonal and Regional Distribution of Favism

The seasonal and regional distribution of favism episodes are closely related to the agricultural practices and cycles in Rhodes; for this reason they are treated together in this part. Ideologically influenced behaviors also have an effect on the seasonal distribution of the disease.

#### Seasonal Distribution of Favism on Rhodes

Consistent with the reports from the literature, the figures for favism from Rhodes show it to be a spring disease, with 111 of 123 total cases reported during the months of March, April and May each year. A second period of increase in the number of favism episodes occurs in late November and December as shown in Figure 5.1. This has not been noted in the favism literature for Greece. In fact, there may be many more unreported or undiagnosed cases of favism during these months since both the public and the physicians tend to be more alert in recording fava consumption during the spring "epidemics" of hemolytic anemia. Cases of hemolytic anemia happening in the winter may not be diagnosed as favism because during the collection of case information the patient is not asked about fava

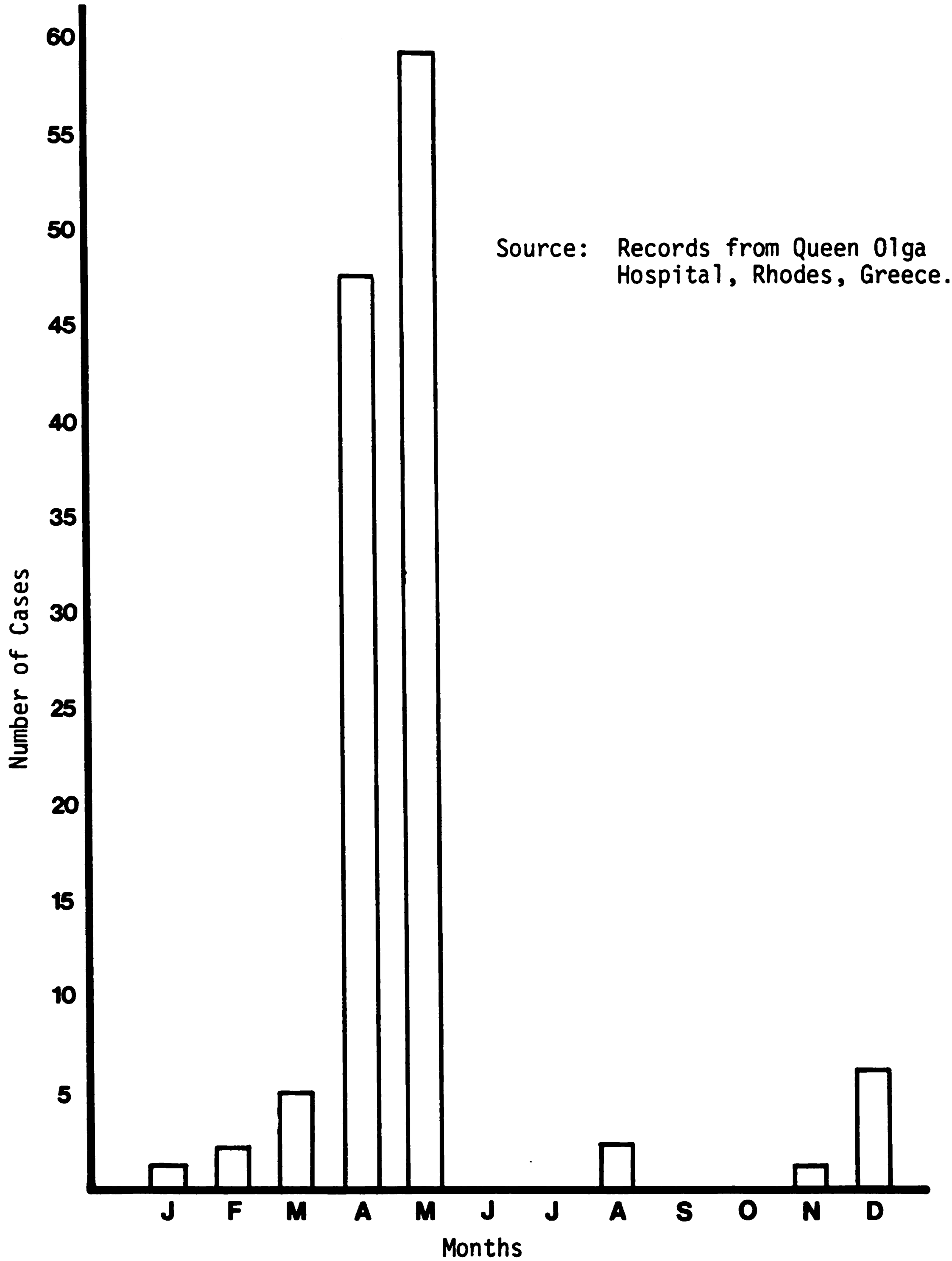



Fig. 5.1 Monthly Distribution of Reported Favism Episodes in Rhodes: 1966-78

consumption prior to the attack.

The spring months in Rhodes coincide with the period during which fava beans are ripe as well as with the pre-Easter fasting period of Lent. The December cases also happen to coincide with another period of ritual fasting which precedes the Christmas feast. These periods of fasting as coincident with at least one major season of favism have not been referred to in the literature. The fact that fasting periods coincide with peaks in favism episodes is a new finding, and represents an additional approach to studying the seasonality of favism.

### Hemolytic agents in the environment

Hemolytic anemia and jaundice in enzyme deficient individuals is known to occur from a variety of substances; the most common of these which circulate widely in Greek rural society are aspirin and napthelene. Episodes of hemolytic crisis associated with aspirin and napthelene have been diagnosed only recently and sporadically. The records from Rhodes in 1966-78 show only three cases from aspirin and two from napthelene. The vast majority of hemolytic episodes in enzyme deficient people are associated with the fava beans. It is the cases of favism associated with the beans which are the major concern here; however, the use of other hemolytic agents, or the circulation of these agents in the environment, may be involved in episodes of favism because these agents interact with the hemolytic agent in fava beans. The overwhelming peak of favism episodes in the spring coincides with not only the ripe fava bean season, but also with the widespread use of napthelene at this same time. The slight rise of episodes in the winter, again, coincides with the use of napthelene.

In village homes, all clothing and bedding, regardless of fabric, are stored in napthelene moth balls when they are not in use. Items which are included in the bride's trousseau, dowry, and wedding gifts are often too numerous to be displayed in the house at all times. Pillow cases which were embroidered for the marriage, table covers, crocheted items, and so forth, are usually reserved for display during particular times of the year, especially during the spring celebration of Easter, the summer feast of the Virgin Mary on August 15th, and the winter Christmas celebration. The celebration of these holidays is preceded by intensive household cleaning, the opening of closets and trunks which contain the specially stored linens and other items and bringing them out for display in the central room of the house.

In April and May, as the weather becomes warm, the family's wardrobe is changed from the heavy woolen clothes of the winter to the summer cotton clothes. Again, closets and trunks containing the summer clothes are opened, summer items taken out and aired to remove the smell of the moth balls, while winter clothes are washed and stored in the trunks with moth balls. This same wardrobe change takes place again in late October when the weather change requires the use of woolen attire and heavy bedclothes. Individuals come into direct contact with napthelene when they wear these items for the first time.

This variable was not examined as systematically as it could have been. It is mentioned here to draw attention to the fact that the fava beans are not the only hemolytic agents circulating in the villages during the spring months when favism is so prevalent.

### The production and use of fava beans

The cultivation of fava beans and their harvest covers a period of approximately six months, with the greatest period of exposure to the fresh bean occurring in the three months when it is ripe and becomes fit for consumption. In Rhodes, the summer months are devoted to the daily harvest of a variety of vegetables such as tomatoes, cucumbers, zucchini squash, eggplants, and to the tending of citrus orchards and vineyards. It is a period marked by several different kinds of agricultural activities in all areas of the island without involving daily, and intensive labor. The participation in agricultural labor is not characterized, for example, by the family leaving before sun-up and returning after sun-down as it is during the grape or the olive harvest. In August, September, and October, a period of intense activity is noted in areas which produce grapes as cash crops. Most of the villages on the island have some of their own grapes, but not all are intensively involved in their cultivation. Beginning in November, the citrus crops and olives are harvested, along with a variety of greens, both wild and cultivated. This is a period of intense agricultural activity, but due to the rain, not all days are suitable for harvesting activities. Spring brings the continuation of the citrus harvest, the continuation of using available greens, and introduces early garden vegetables such as artichokes. The fava bean is the first bean available in the spring months; other beans do not become available until late summer.

Cultivation of fava beans. Fava beans are planted during the rainy winter months of November and December, using the dry beans which had been saved from the previous year's harvest. The beans themselves are large, flattened rather than rounded, and with a distinct black mark at the one end of the bean. They are found in well-padded pods which are five to seven inches in length. Families which plant the beans save a few dozen each year which will be used to start the new crop. Those which are said to be best suited for planting have an extra mark which distinguishes them from those for consumption. This extra mark results from the way in which the beans are aligned in the pod. Beans for planting and beans for consumption are not grown on separate stalks. Those for planting are referred to as paligári; those for eating, thilikó. The former term is the same as the word used to refer to a young, tough and courageous boy; the latter is a gender term for female.

The beans are put in small plots of land, or in the corners of citrus orchards, olive tree fields, or vineyards. They are not intercropped with other vegetables within a plot, but may be placed among olive trees which have been long-standing on the plot of land. Their placement among citrus trees is more difficult since the orchards are covered with clover around each tree; however, they may appear at the edges of these citrus orchards. Those which are put in vineyards are again placed in the corners or edges of these plots, so as not to interfere with the expanding root system of the vine.

The bean plants are not staked up, even though they will reach a height of over a meter at maturity. The stalks are quite sturdy, and the plant does not tend to branch out or develop large leaves which would require tying them to stakes. Once the plants blossom in early February (depending on altitude), the bean pods appear and mature rapidly, leaving the beans available for consumption in some areas by March.

Fava beans are most often grown for household use and very limited market exchange; the latter are sent to the City of Rhodes, but they are not exported from the island. They are usually found in small plots and household gardens, rather than in large fields which would be associated with their production as a cash crop. Villages close to the city supply its inhabitants with a limited amount of fresh beans every spring.

Harvest and storage of fava beans. Because the beans are not a basic cash crop, large-scale harvesting of both the fresh and the dry form of the bean does not occur. In many areas of Greece where beans are grown as cash crops, the entire stalk of the bean will be cut or uprooted, and the beans sorted out within the confines of the villages. At the end of their growing cycle, beans will be left on their stalks, and harvested in that form. Such activities require that the stalks, pods and beans, are all loaded onto carts (or trucks, depending on the area), taken back into the village, laid out in the street where the individual beans are separated from the rest of the plant bulk, and again separated by desirability for consumption. Such gross exposure to both the fresh and dry plant does not occur in Rhodes. Rather, the fresh beans are gathered by handfuls from their stalks while the plant is still green. Many times, a handful of pods will be gathered as people pass by on their way to work in an adjacent field. The pod will be cleaned away, and the raw beans eaten during a work break. Those which are gathered for home use are picked by the pod, and put into sacks to be taken back to households in the village. Often they may be picked while other fresh greens are gathered, and placed in the same sack or basket.

By the time the plant begins to dry out, most of the beans have already been picked. At this time, the remaining pods are picked and taken to the households where they are left to dry out completely in the courtyard or outside work area. Beans which will be used to plant the following years crop are separated from the others which may be used during the winter. These are stored in separate sacks in the household storage area. These usually do not fill very large sacks.

General consumption patterns: how and when fava beans are eaten. The fava beans and their pods become fit for consumption when the plant is nearly a meter high. At this time, the pod is about three to four inches in length (early March). Only the beans and occasionally their pods are consumed; no other parts are consumed. The plant greens may be fed to other livestock, such as the goats and sheep. The period during which the beans begin to be available starts in March, representing one of the early spring cultigens and coinciding with the last months of the citrus harvest and the gathering of wild, edible greens. These early fresh beans are often eaten raw or cooked with the pod along with other wild greens. The combination is served as a luke-warm or cold salad, with chopped onions or garlic sauce, or with olive oil and lemon juice. By middle April, depending on the location in Rhodes, the pod becomes too tough to be consumed; therefore, the beans are shelled and eaten either raw or in the boiled salad form. Others are simply boiled in water without the addition of other ingredients and served plain or with a small amount of oil and lemon juice.

As the beans grow larger, on stalks of over a meter and with the pods reaching seven inches in length, they continue to be available through the month of April. They are stripped of their cuticle which has become fibrous and not very tasty (or easy to swallow), eaten raw, boiled in salads, or boiled and mashed into a puree called fava. This is served with chopped fresh onions and olive oil spread over the top of the puree.

By May, the stalks begin to droop downward from their weight, the pods begin to dry and open, dropping some of the beans onto the soil. This easy self-seeding means that not all fava bean patches are cultivated, and some may perpetuate themselves from year to year without human intervention. Usually by late May, fava bean consumption has dropped off and the diet replaced by other vegetables which have become available. The people still find them in the fields while working and may eat them raw, stripping them of both the pod and the cuticle. Care is exercised in eating the raw beans at this time since they may contain small larva or worms. The same care is exercised in sorting out dry beans for cooking. These are carefully inspected for the presence of worms before being stored or cooked, while beans which rise to the top of boiling water are often picked out of the water and discarded as they are believed to be spoiled.

The fava bean, therefore, represents a crop which is seasonally available in the fresh form, consumed raw or with other greens which are ripe at this time. The greatest levels of fresh fava bean consumption occur during the months of March, April and May. The beans are consumed during other times of the year after the ripe period has passed, particularly during the winter when other dry bean preparations are widely used. As shown in Figure 5.1, the majority of favism episodes coincide with the spring months when the bean is widely consumed and handled, and abundant opportunities exist for its raw consumption even though it may not be brought into certain households.

### Fava bean consumption and the ritual calendar

With a few exceptions, the villagers on the island of Rhodes are Greek Orthodox in religion, and as such, they observe days of fasting and days of feasting as designated in the ritual calendar. These complement the agricultural cycle in terms of available foods which are reserved for fasting and others which are used in feasting.

Aside from one-day fast periods, there are three major and lengthy fasting periods in the ritual calendar: (1) the pre-Easter Lenten season which spans more than forty days in the spring; (2) the pre-Christmas Advent period which also spans forty days; and (3) the fifteen-day period from August 1st to the 15th before the Feast of the Virgin Mary (Panaghía) which falls on August 15th. Aside from breaking the year into special periods of time related to a variety of agricultural, household, and social activities, these fasting and feasting days promote the consumption of certain foods which are considered appropriate during these days.

Many of the feast days emphasize the consumption of special foods, such as lamb at Easter, egg-lemon soup following the midnight church services on the Saturday night preceding Easter Sunday, pork on Christmas and freshly slaughtered lamb on August 15th. Fasting involves the avoidance of animal products such as meats of all types, fish, cheese, eggs, yoghurt and butter. Olive oil, a non-animal product is also included on the list of forbidden foods during fasting, but it is avoided only for a limited period of time. The reason for this is unclear, except that the oil is so central to the diet that its denial represents austerity in the diet. It is not only the foods which are avoided, but the use of other foods which may be conspicuously present in the household, often more for social than religious reasons. The use of these foods in the home attest to the fact that the family is observing the fast. The importance of these additional fasting-foods in the diet is emphasized by the use of a semantic category for these foods (nistísima). Such foods include boiled potatoes, pickled vegetables such as cauliflower and peppers, octopus and squid (not classified as fish), fresh fruits and vegetables, nutmeats, and halvás (sesame and honey past cake), and boiled beans.

All individuals claiming the Orthodox faith do not maintain strict fasting rules, especially when the period is a long one such as the three mentioned above. Generally, the elderly women of the villages observe the strictest rules of fasting. Men do not consciously adhere to fasting rules except as they are promoted by their mothers and wives within the context of household cooking. Children and pregnant women are exempt from fasting. Many women presently of child bearing age claim that they do tend to observe fasting because they are ashamed to go to the market to buy meat, or to slaughter their own household chickens and rabbits. The village, as a body, promotes the abstinence of meat by not slaughtering the large animals such as lamb, goat and pig. Social pressure therefore tends to reduce the consumption of the various foods forbidden during fasting periods.

More than any other part of the fasting cycle, Lent is set apart from the normal diet. Even though strict fasting may not be observed throughout, the period introduces a different set of food into the diet. It is not only the foods which are avoided during this time period which are important to note, but those which are considered as appropriate and are therefore conspicuous in the households. The nistísima foods which are consumed during this time, are not symbolic or ritual foods in and of themselves, but their consumption exaggerates that the Lenten period is symbolically set apart from the rest of the year. During this time, whether or not the entire family is fasting, the women attend to the display of particular Lenten foods in the home. When visitors come to the house during Lent, the usual sweet, cooking and liqueurs are not usually offered to them. Since hospitality dictates something be offered, no matter how simple, the _nistísima_ foods may be used.

While Christmas and the August 15th Feast of the Virgin Mary do not change from year to year, the celebration of Easter does. Consequently, the former two fasting periods are fixed from one year to the next, while the fasting period preceding Easter is not set to cover the same days every year. Easter may occur anytime from the first week in April to the first week in May. Lent begins with "Clean Monday" _(Kathará Deftéra)_ forty-eight days before the Easter celebration. Lenten fasting may begin very early in February and end very late in April, or it may begin late February early March, and end in the first week of May, depending upon the year.

_Fasting periods and the distribution of favism episodes._ Of the 123 favism episodes which occurred in Rhodes during 1966-68, 111 occurred in the spring months of March, April, and May, which are potentially covered by the Lenten fasting period. Of the twelve remaining cases, eight occurred during the pre-Christmas fasting period, and one occurred during the August fasting period. Only three episodes were reported during periods other than these periods. All the spring cases of favism cannot automatically be considered as ones which followed the consumption of fava beans from the Lenten fasting period, because Lent changes each year.

Lent and spring episodes of favism. In order to determine the spring cases which have potentially followed beans consumed during Lent, the dates that the episodes were reported to the hospital were considered to be a week later than the dates at which fava beans had been consumed. Seven days were subtracted from each date that favism was reported to the hospital and, according to the year, each episode was then determined to have occurred from beans which had been potentially consumed during Lent. This is actually a large figure which was used to calculate on which day the "faulty" beans might have been consumed. Most cases of favism show signs of hemolytic anemia within 24 hours after eating the beans, according to both the medical opinion and to the reports of informants in this present study. Some, however, have been noted (e.g., Kattamis) to show hemolysis at a later time. Even if hemolysis is noticed to occur within 24 hours following bean consumption, it may take another three to four days before the affected individual reaches hospitalization. Therefore, a period of time from four to seven days before the episode reaches the hospital should be calculated to show the earliest time at which the fava beans were eaten. I selected to use the figure of seven days. Using the larger figure has the advantage of covering the possible cases which resulted from Lenten fava beans; on the other hand, during a period of seven days, the beans may have been eaten two or three times, and the actual date of the beans which "caused" the onset of hemolysis is obscured. Some feel that the disease actually occurs after the beans have been eaten several times during a period of a few days, and that the effects are cumulative; therefore, the actual date is not as important as are the dates. This type of information was not available for the 111 spring episodes of favism, and for this reason, the potential consumption of the beans was calculated as a rough estimate of whether or not they had been consumed during the Lenten period.

Figure 5.2 shows the distribution of spring episodes of favism in Rhodes for 1966-78. The shaded portion indicates the episodes which are calculated to have occurred following beans consumed during Lent. Lenten fasting (expected to promote fava bean use) and the easy availability of the ripe, fresh beans are believed to act in conjunction with each other to promote a greater number of episodes during this time of the year. This is demonstrated by the yearly fluctuations in episodes of favism, and in the time of Easter.

Spring favism and yearly differences in Easter. While it might be suggested that the yearly fluctuations in the number of favism episodes is related to differences in climatic condition which affect the ripening and toxicity of the beans, the present study shows that the episodes in Rhodes tend to fluctuate in accord with the time of Easter. During 1966 to 1978, the date of Easter ranged from April 9 to May 4, which means the period of Lent differed by as much as 26 days. Because the beans ripen quickly and are most desirable for fresh consumption for approximately a month, these 26 days can make a difference in the coincidence of the ripe

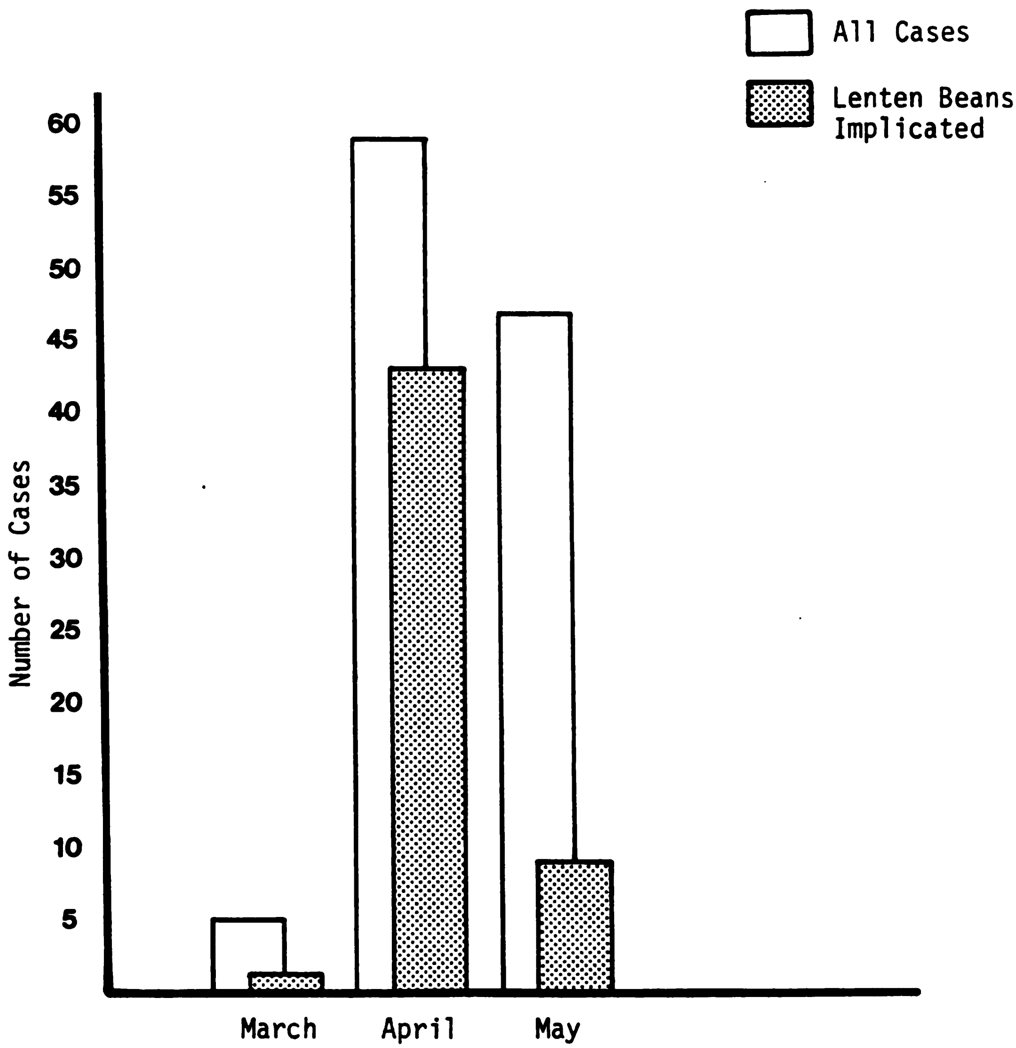



Fig. 5.2 Distribution of Spring Episodes Showing Cases Where Lenten Beans Are Implicated

period and the use of the beans in fasting.

As Figure 5.3 shows, more than half (65) of the 111 cases of spring favism occurred during a 14-day span from April 25th to May 9th. No spring cases were reported before March 7th or after May 23rd. When Easter falls late, for example on May 4th as it did in 1975, almost all of Lent has spanned the time of the ripe beans, offering sufficient opportunities for their consumption. When Easter falls as early as April 9th, as it did in 1972, the fresh beans have been available for only half of the Lenten fasting period.

Hypothetically, it might be expected that the timing of Easter would have an effect on the number of Lenten cases of favism, and perhaps on the total number of annual cases, with the more numerous cases reported when Easter occurs late. A "late" Easter is defined as one which falls after April 25th, the date shown to be the latest one at which spring cases peak. In the thirteen years included in the present survey, Easter fell after April 25th in six years: 1967, 1970, 1973, 1975, 1976 and 1978. Figure 5.4 shows that in these years, there is a definite tendency for spring favism to be higher than in the other years when Easter fell early.

This tendency is further supported by totalling all the spring episodes for these six years when Easter fell late, and comparing this sum to that for the seven years where Easter was early. The difference of nearly 20 episodes, not striking perhaps, but the late Easter years include one less year than the early ones.

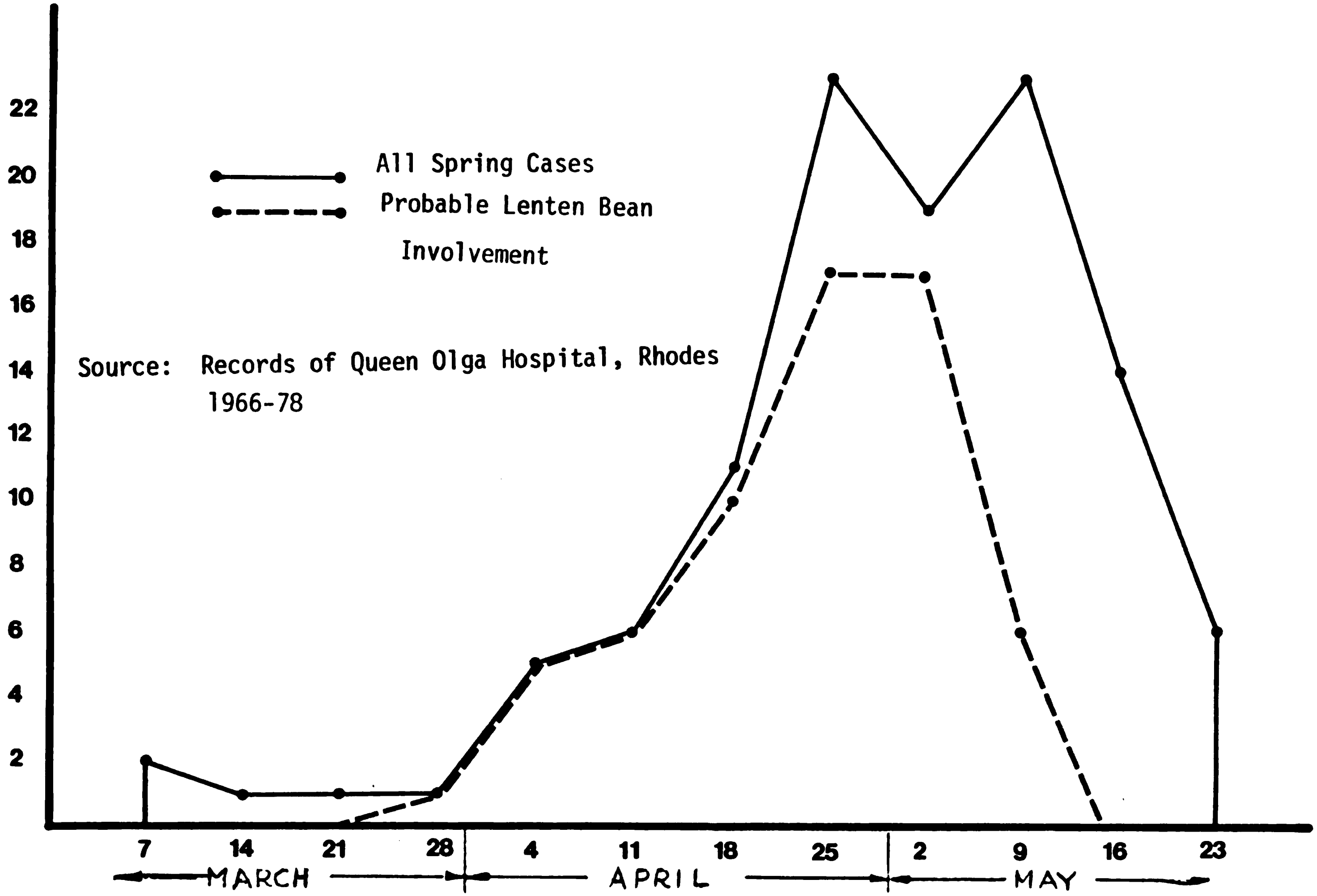



Fig. 5.3 Spring Episodes of Favism by Seven-Day Periods

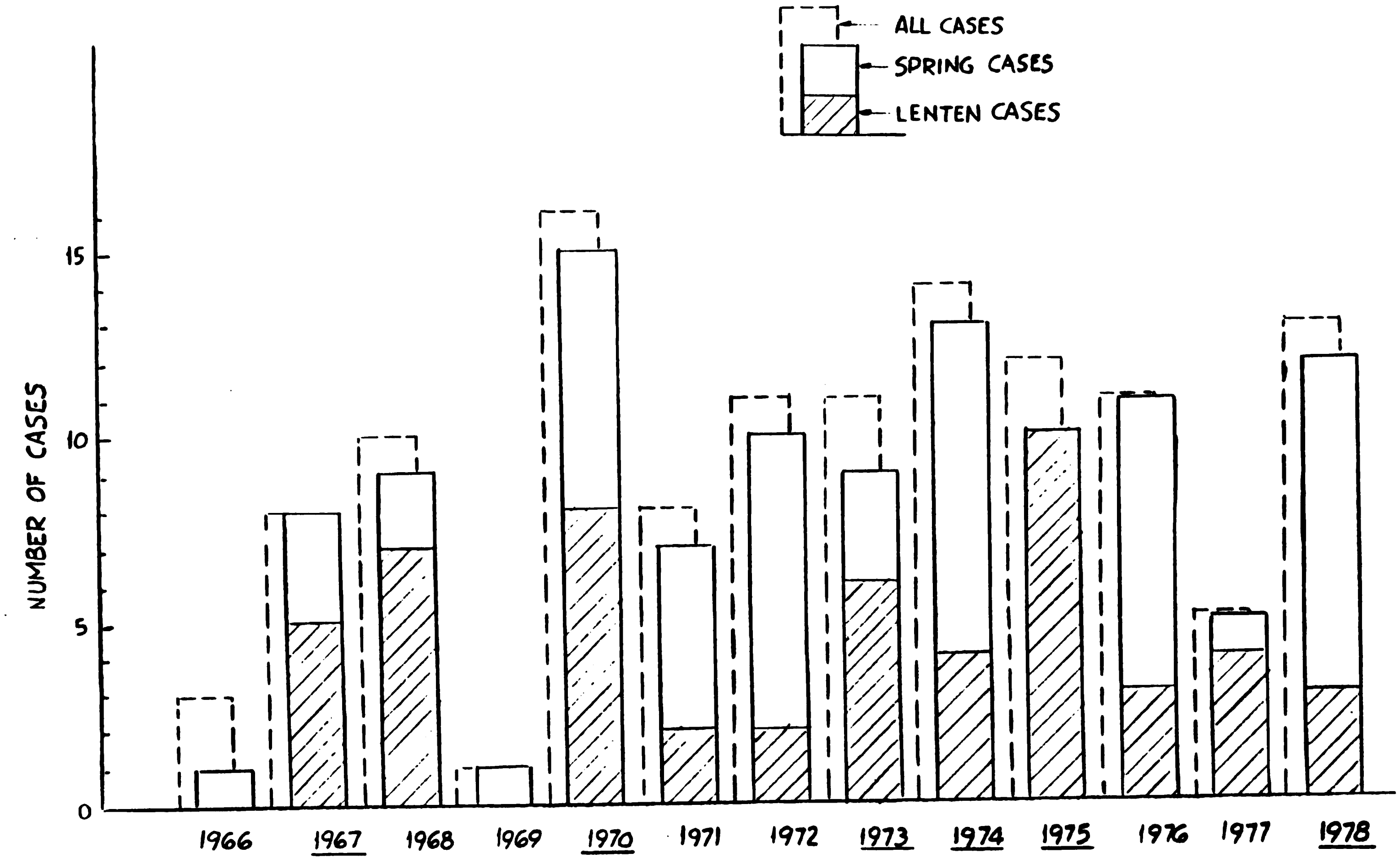



Fig. 5.4 Distribution of Favism Episodes by Year

Calculating an average for each group gives a figure of 10.8 cases in years where Easter was late, and only 6.6 cases in years where Easter was early.

TABLE 5.2

SPRING EPISODES IN LATE AND EARLY-EASTER YEARS

| | Number of Years | Number of Spring Episodes | Average Episodes per Year |
|---|---|---|---|
| Late Easter | 6 | 65 | 10.8 |
| Early Easter | 7 | 46 | 6.6 |

To summarize, while only 54 of the 111 spring episodes of favism could be accounted for by beans consumed during Lent, the yearly totals indicate the Lenten period plays a role in promoting higher numbers of favism cases in the years when it ends late in the fresh fava bean season. This is supported by the individual yearly fluctuations as well as combined totals for those years where Lent ends late compared to years where it ends early.

## Regionality and the Distribution of Favism Episodes

Ten regions of Rhodes were designated according to their geographical characteristics, agricultural similarities, and social interrelationships within the region such as dialect and sharing the celebration of religious events. These divisions were not made on the basis of either the known distribution of the $Gd^-$ trait or the frequency of favism. The regions are depicted in Figure 5.4 and in Table 5.3.

TABLE 5.3

GD$^-$ TRAIT AND FAVISM FREQUENCIES IN TWELVE VILLAGES, LISTED BY REGION

| Village | Gd$^-$ Frequency (%) | Favism Frequency (0/00) By Village | By Region |
|---|---|---|---|
| Kremasti | 35.7* | 1.3 | 1.6 (A) |
| Archangelos | 20.2* | 1.3 | 1.7 (F) |
| Malona | 21.4 | 4.4 | 1.7 (F) |
| Massari | 27.0 | 4.7 | 1.7 (F) |
| Kritinea | 43.2 | 13.5 | 7.0 (D) |
| Embona | 17.2 | 5.5 | 7.0 (D) |
| Isidoros | 18.8* | 11.4 | 11.5 (G) |
| Siana | 33.3* | 19.0 | 11.5 (G) |
| Pylona | 36.3 | 11.4 | 3.5 (H) |
| Lindos | 18.7 | 4.2 | 3.5 (H) |
| Lardos | 21.4 | 3.6 | 3.5 (H) |
| Laerma | 46.6** | 1.3 | 3.5 (H) |

Source for Favism Frequency:
Records, Queen Olga Hospital, Rhodes 1966-1978.

Source for Gd$^-$ Trait:
Screening by Kattamis et al. 1969(*); by Allison et al. 1963(**) and present study.

Population totals for each of the ten regions were calculated on the basis of the latest census from the National Statistics Services of Greece. These totals were used in estimating the (1) frequency quency of favism, and (2) the actual number of males expected to be at risk, projected on the basis of the results of the $Gd^-$ screenings in previous studies as well as the present one.

As suggested earlier in this chapter, factors other than the general growing and consumption patterns of fava beans must be considered in explaining the regional distribution of favism episodes. Figure 5.4 shows the regional distribution of favism on Rhodes, indicating that the frequencies range from 0.8 to 8.2 per thousand inhabitants in any given region. These frequencies are also listed in Table 5.3. The projected number of males expected to be at risk, on the basis of the $Gd^-$ trait frequencies, and male population size are shown in Table 5.4. The actual number of males projected to be at risk is then standardized on the basis of 1000 in order to compare with the favism frequencies in each location.

At least three categories of information are suggested to be useful in examining the distribution of favism in Rhodes:

1. Distribution of the enzyme deficiency;
2. Altitude and frequency of favism episodes;
3. Regional differences in exposure to fava beans.

According to epidemiological principles, certain correlations are expected on the basis of the distribution of risk factors and the appearance of the actual disease. In Rhodes, the average

TABLE 5.4

DISTRIBUTION OF $GD^-$ TRAIT IN TWELVE VILLAGES PROJECTED $GD^-$ TRAIT MALES BASED ON FREQUENCY IN 7-12 YEAR OLD BOYS

| Village | % $Gd^-$ | Male Population | Expected Number | $Gd^-$ Males Rate/1000 | Source for Population |
|---|---|---|---|---|---|
| Lardos | 21.4 | 137 | 29 | 212 | National Statistics Services of Greece (1971) |
| Lindos | 18.7 | 350 | 65 | 186 | National Statistics Services of Greece (1971) |
| Kremasti | 35.7 | 986 | 252 | 256 | Kattamis et al. 1969 |
| Massari | 27.0 | 266 | 72 | 271 | Author Conducted Village Census |
| Malona | 21.4 | 255 | 55 | 216 | National Statistics Services of Greece (1971) |
| Pylona | 36.3 | 88 | 32 | 364 | National Statistics Services of Greece (1971) |
| Archangelos | 21.2 | 650 | 138 | 212 | Kattamis et al. 1969 |
| Kritinea | 43.2 | 293 | 127 | 433 | Author Conducted Village Census |
| Laerma | 46.6 | 318 | 148 | 465 | Allison et al. 1963 |
| Siana | 33.3 | 176 | 59 | 355 | Kattamis et al. 1969 |
| Embona | 17.2 | 636 | 109 | 171 | Author Conducted Village Census |
| Ag. Isidoros | 18.8 | 496 | 93 | 188 | Kattamis et al. 1969 |

proportion of $Gd^-$ hemizygote males in 25%; one-fourth of the male population is expected to develop favism on the basis of the enzyme deficiency alone. Because of the x-linked nature of the trait, it can be assumed that the gene frequency of the $Gd^-$ trait should approximate 25% in any population of the island. The annual frequency of favism for the island as a whole is calculated to be 0.16 per thousand (or 1.6%). Only 15.7% of those with the $Gd^-$ trait become affected by favism. As Table 5.4 and Figure 5.5 show, the frequency of the $Gd^-$ trait ranges from 0.8 in the City of Rhodes to 11.5 in Region G. In five regions of Rhodes outside the city, (A, D, F, G, and H), where both favism and $Gd^-$ frequencies were available for comparison, no concrete relationship between the two could be recognized. Table 5.5 shows that neither a direct nor an inverse relationship can be established between the $Gd^-$ trait and favism frequencies on Rhodes. The Table lists the five rural regions in ascending order according to favism frequencies.

TABLE 5.5

FIVE RURAL REGIONS OF RHODES COMPARING $GD^-$ AND FAVISM FREQUENCIES

| | Frequencies | |
|---|---|---|
| | Favism (0/00) | $Gd^-$ Trait (%) |
| Region | | |
| A | 1.6 | 35.7 |
| F | 1.7 | 22.8 |
| H | 3.5 | 30.6 |
| D | 7.0 | 22.6 |
| G | 11.5 | 26.0 |

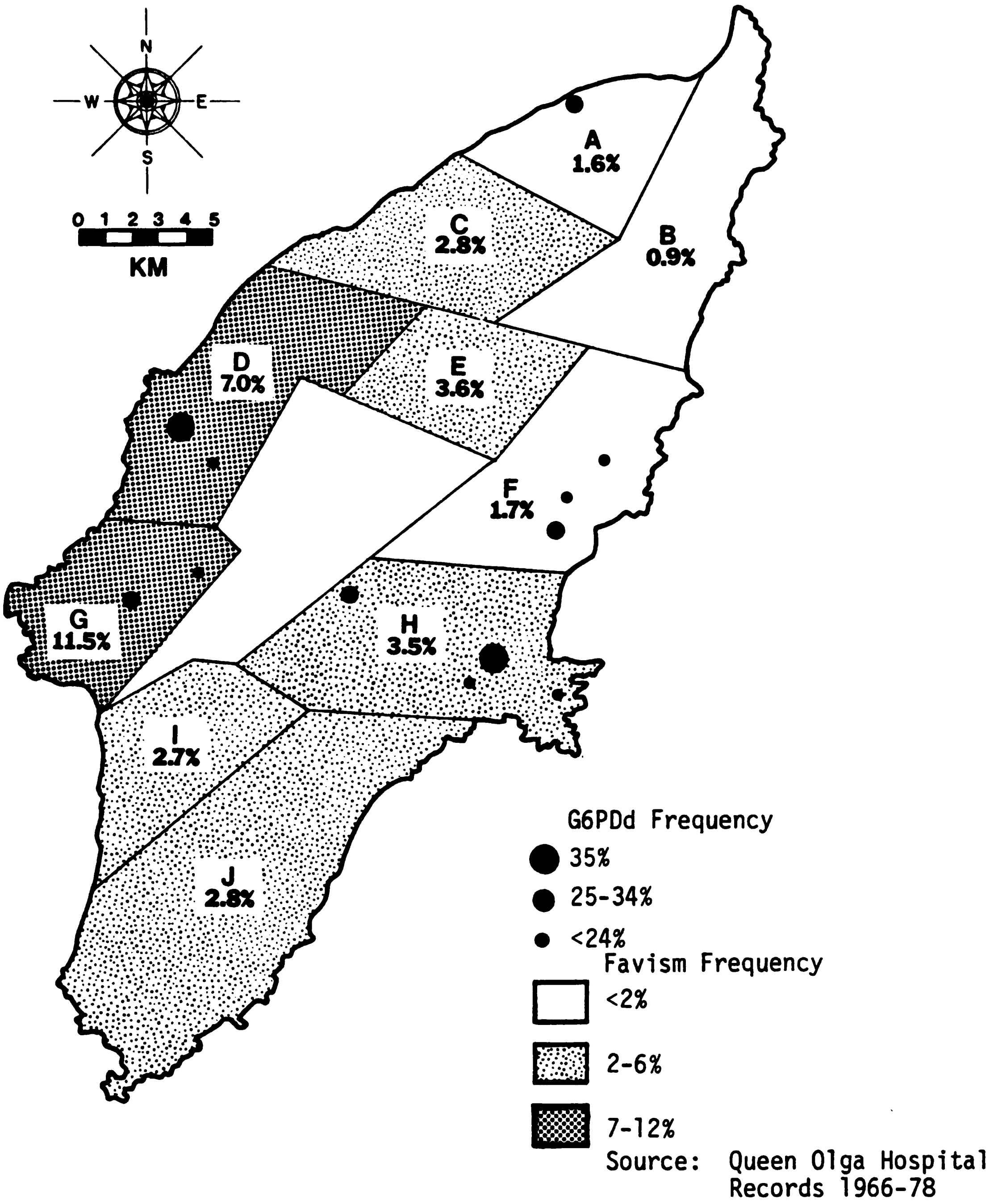



Fig. 5.5 Regional Distribution of Favism

Only Region F approximates what might be expected on the basis of the $Gd^-$ trait frequency. Both the $Gd^-$ frequency and the favism frequency are below the average for the island. Region F consists of three villages, all which have been screened (either in the present study or in earlier ones) for the $Gd^-$ trait. If this relationship between the trait and the disease is considered as parity, then we can say that where the gene frequency of the $Gd^-$ trait is at about 23%, we should expect to find approximately 2/1000 affected with favism.

Region A shows the highest trait frequency but the lower rate of favism. This is the inverse of what one might expect if only the $Gd^-$ trait was involved in cases of favism. The figure of 1.6 (favism) was calculated for the entire area, while the figure of 35.7% $Gd^-$ frequency was taken from one village. In this village, the rate of favism was nearly the same as for the region in general. The average favism frequency for the region is nearly the same as the frequency for one village.

Region G shows the highest rates of favism, but an average $Gd^-$ frequency very nearly the same as for the island in general. This, again, is the inverse of what would be expected if only the enzyme deficiency was involved in the cases of favism. By comparing Regions A and G, one might hypothesize that fava beans are eaten in much greater amounts in Region G than in Region A. In the latter, nearly no fava beans would have to be consumed to account for the great discrepancy between the high $Gd^-$ trait frequency and the extremely low favism frequency.

Altitude: Its relationship
to favism frequencies

The thirty-five rural locations which had reported favism episodes during 1966-78 were divided into three groups according to their altitudinal characteristics: (1) mountainous, (2) inland foothills, and (3) coastal elevations. These are shown on Figure 5.6 which, when compared with the earlier regional map (Figure 5.5) shows that some of the regional lines have been interrupted by altitudinal ones. These figures ae given in Table 5.6.

TABLE 5.6

ALTITUDE AND FAVISM FREQUENCIES
IN RURAL RHODES

| | Population Represented | Number of Episodes | Frequency |
|---|---|---|---|
| Mountain | 4556 | 35 | 7.7 |
| Inland/foothills | 10981 | 22 | 2.0 |
| Coastal | 18324 | 38 | 2.1 |

The data show the definite trend for episodes of favism to increase as does altitude. This is in keeping with the direct relationship between altitude and the $Gd^-$ trait (contrary to all other literature as stated in Chapter Four). What is of interest here is not how altitude interacts with the $Gd^-$ trait, but how it interacts with the growing and consumption of fava beans.

Altitude and fava bean production. As would be expected, altitude affects the time at which fava bean plants reach their peak in ripeness. The annual rainfall, which is in turn associated with altitude, also affects the ripening of the beans.

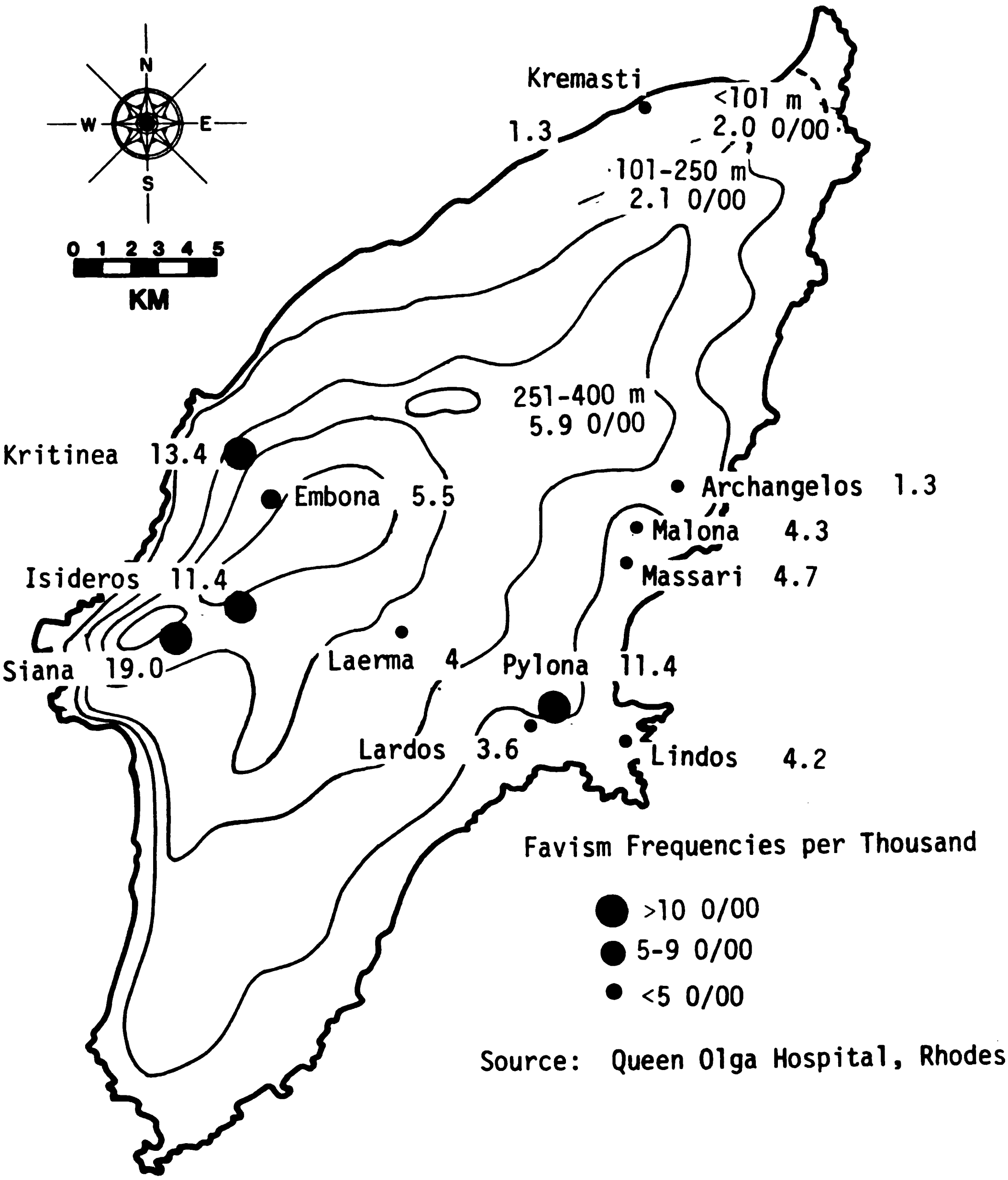



Fig. 5.6 Favism Frequencies and Altitude

In Rhodes, the village in the mountainous chain on the west side of the island received the greatest amount of rainfall during the winter months. The rainy season coincides with the time that the beans are planted and reach maximum growth.

The higher the altitude at which the beans are planted, the later in the spring months during which they are ready for consumption. The distribution of spring favism episodes, considered by seven-day intervals reflects these altitudinal variations. Figure 5.7 shows that mountain cases peak from the 9th to the 16th of May, while coastal ones peaked by April 25th. The fluctuation in inland and foothill episodes which peak twice, once before April 25th and again by May 16th, may result from the variety of eco-niches which the intermediate level villages occupy. The inhabitants of the intermediate-range villages exploit a variety of levels which inhabitants of coastal villages do not.

Spring favism, altitude and Lent. Fifty-four of 111 spring episodes could be attributed to beans eaten during Lent. This is the figure for the entire island (48.6% of all the cases in the spring were associated with Lenten beans). Taking the cases reported only from the rural areas, forty-one of eighty-five rural cases were attributed to beans eaten during Lent (48.2%). The distribution of these Lenten and spring cases according to altitude is shown in Table 5.7. From these data, altitude is shown to have an inverse relationship to the proportion of spring-Lenten cases, even though the higher elevations have a higher favism frequency (Refer to Table 5.6). Given the previous discussion about altitude, this is

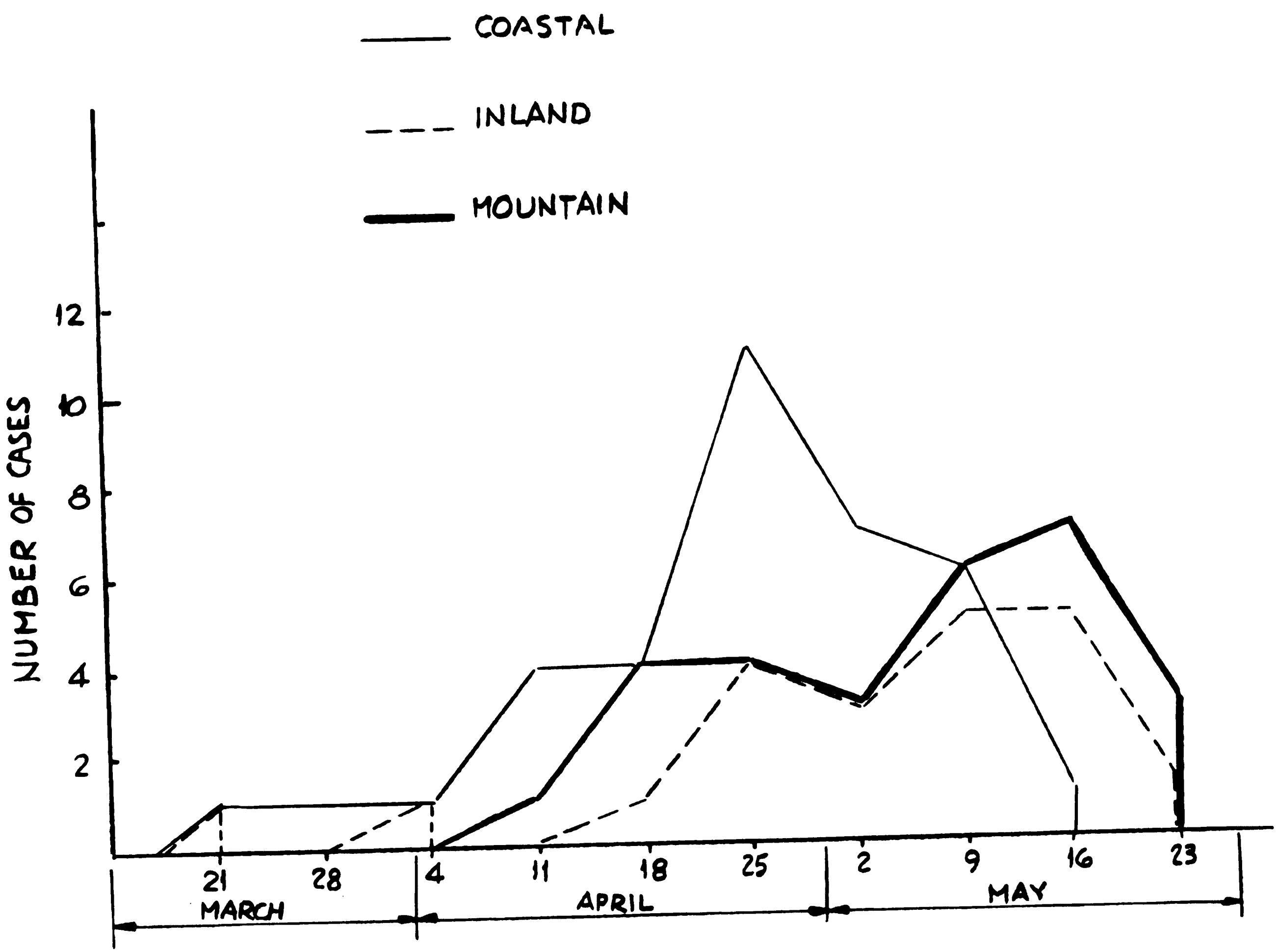



Fig. 5.7 Altitude and Timing of Reported Spring Favism Episodes in Rural Rhodes

TABLE 5.7

LENTEN AND SPRING EPISODES OF ALTITUDE

| | Lenten Beans* | Spring Beans | Lenten/Spring Cases (%) |
|---|---|---|---|
| Mountain | 11 | 28 | 39.3 |
| Inland | 8 | 21 | 38.0 |
| Coast | 22 | 36 | 61.1 |

*Beans which are calculated to have been consumed during Lent.

to be expected, as the beans ripen slightly later in the higher altitudes than they do in the lower ones. As shown, greater numbers of spring cases tend to occur slightly later in the higher altitudes than the lower ones. Aside from these factors, three other explanations might be offered:

1. In the coastal areas, fava bean consumption stops with the end of Lent; therefore, fewer cases of favism are observed in this area following Easter;
2. In the mountains, fava bean consumption continues after Lent has passed;
3. The availability of the fresh beans cases earlier in the lower elevations and are therefore not consumed after this time.

With the available data, it is not possible to determine which of these might be the more accurate suggestion.

## Bean use and distribution of favism

The potential for exposure to fava beans differs by region, altitude, and particular practices in different villages. These factors of exposure can be expected to relate to the distribution of favism episodes.

Urban-rural differences. It has been suggested in other studies on the distribution of favism episodes in Greece that only a fraction of the rural episodes are reported due to problems in understanding the need for hospitalization or in transportation difficulties from remote areas. Further, those in rural areas are known to tend to many of their health and medical needs without the intervention of health professionals. Based on these factors, one might expect that statistics for favism would show more urban than rural cases. This is not the situation for Rhodes. From a total of 123 cases, 95 were from villages and only 28 from the City of Rhodes.

Kattamis et al. (1969) found that 8% of the males tested in the City of Rhodes had the enzyme deficiency. The present study and earlier ones find that the enzyme deficiency was over 10% in each of the rural locations screened. While these figures make it difficult to deny that the deficiency is implicated in the urban-rural distribution of favism, it must be stressed that those in the urban areas have little access to the fava plant. While they have many opportunities to buy the fresh bean from local markets, those in the urban center are not likely to have opportunities to eat the fresh, raw fava beans while working in agricultural fields, or to handle the bean as it is picked from the field, or to gather the fresh beans from the fields. To emphasize this, regions immediately outside the City of Rhodes show relatively more favism episodes reported. In the City, the frequency is only 0.8/1000 while in the regions surrounding the City (the village-suburbs), it ranges from 1.18 to 2.42. Certainly the greater participation in the production of fava beans in these village-suburbs effects possible exposure to the beans. Depending on location, the rural consumption of fava beans is spread throughout the entire year and not confined only to the spring. Nonspring episodes of favism were more predominant in the rural locations than in the urban ones. From twelve off-season (non-spring) cases, ten were from villages. Considering that half of the island's inhabitants are located in the City of Rhodes, the figure of 2/32,517 is lower than 10/33,861. Table 5.8 shows this rural to urban distributional pattern.

TABLE 5.8

RURAL/URBAN OFF-SEASON FAVISM CASES

| | Off-Season Episodes | All Episodes | % Off-Season to All Episodes | Total Population |
|---|---|---|---|---|
| Villages | 10 | 95 | 10.5 | 10/33,861 |
| City | 2 | 28 | 7.1 | 2/32,517 |

In the villages, 10.5% of all episodes were accounted for by off-season favism, while in the City, only 5.2% of all the urban episodes were accounted for by the off-season ones.

Differences in village production of fava beans. Using data from Massari and Kritinea demonstrates that all the villages in Rhodes do not produce relatively the same amount of fava beans. Massari and Kritinea serve as representative villages of the two regions described earlier in this section (regions F and D). They also represent two altitudinal differences, Massari being a coastal village, and Kritinea a mountain location. In the Massari region the frequency of favism was calculated to be 1.7 with the frequency for Massari itself at 4.7/1000. As a member-village of a mountainous region where the average favism frequency was calculated at 7.0/1000 the frequency for Kritinea was 13.4/1000 Again, it is tempting to attribute these differences to the enzyme deficiency frequencies which are 27.0% in Massari and 43.0% in Kritinea; however, the concern here is with the differences in fava bean production and consumption. The two villages are compared in Table 5.9.

TABLE 5.9

GD$^-$ TRAIT AND FAVISM FREQUENCIES IN THE REGIONS OF MASSARI AND KRITINEA

| | Gd$^-$ Trait Frequency | Favism Frequency | Favism Frequency in the Region Represented |
|---|---|---|---|
| Massari | 27.0% | 4.7/1000 | 1.7/1000 (Region F) |
| Kritinea | 43.2% | 13.4/1000 | 7.0/1000 (Region D) |

In these two villages, 36 families were questioned about their production of fava beans. Twenty families were from Massari, and sixteen from Kritinea. In Massari, only three of the twenty families grow their own beans. In Kritinea, fourteen of the sixteen families interviewed produce their own beans. The fewer families from Massari who produce their own fava beans tend to lower the population at risk. In Kritinea, the greater number of families producing their own beans complements the high $Gd^-$ frequency. In both locations, the fava bean exposure risk factor at the $Gd^-$ frequency are directly related.

Two annual periods of fava bean consumption patterns were designated in the analysis of regional variations in fava bean exposure: the first coincides with the fresh beans season in the spring, and the second covers the remainder of the year. While the majority of cases occur in the spring, it should not be assumed that all of these resulted from fresh beans, or that it is only the fresh bean which is associated with episodes. Fava bean consumption tends to be higher in the spring; if the same level of fava consumption continued throughout the year, it is likely that more episodes would be reported.

Nutritional information from thirty-nine families in Massari and Kritinea shows that the families from Kritinea tend to eat fava beans more often throughout the year and in greater variety. This information was collected from families which all had school-aged children so that the differences between them with respect to using the beans cannot be attributed to having only infants of pre-schoolers in the family (a factor which might tend to influence their use). In Massari, six families did not consume the beans at all, thirteen ate them only in the fresh form, and one family ate the beans in both fresh and dry forms. In Kritinea, two families did not eat the beans at all, seven ate them only fresh, and ten ate them in a variety of fresh and dry preparations. These characteristics are summarized in Table 5.10

TABLE 5.10

FRESH AND DRY FAVA BEAN CONSUMPTION
IN MASSARI AND KRITINEA

| | Massari | Kritinea |
|---|---|---|
| Don't eat | 6 | 2 |
| Fresh only | 13 | 7 |
| Both Fr/Dr | 1 | 10 |

In Massari fourteen families used the fava beans. While in Kritinea seventeen families used them, the majority of these latter used them in both fresh and dry preparations. It is possible that using the beans throughout the year in a variety of preparations is related to growing them in greater abundance. Earlier, it was shown that sample families in Massari usually do not grow their own beans. Considering only those families involved in agricultural pursuits from both villages, those from Kritinea eat the bean more often than those from Massari. Table 5.11 summarizes these data.

TABLE 5.11

FAVA BEAN CONSUMPTION IN AGRICULTURAL AND
NON-AGRICULTURAL FAMILIES IN
MASSARI AND KRITINEA

| | Massari | | Kritinea | |
|---|---|---|---|---|
| | Agriculture | Other | Agriculture | Other |
| Don't eat | 5 | 1 | 1 | 1 |
| Only fresh | 5 | 8 | 7 | 0 |
| Both forms | 0 | 1 | 9 | 1 |

Those in Kritinea not only grow more of the beans, but eat them more often throughout the year in a variety of forms. Consumption of the beans may be related to features of the environment (such as altitude) or other cultural traditions which are not investigated here.

## Conclusion to Part I: Seasonality and Regionality of Favism

In Rhodes, the rural locations which have the highest altitude happen to be those with the highest frequencies of the enzyme deficiency and the greatest amount of exposure to the fava beans. In these areas, the beans become ripe later in the spring than they do in the coastal areas, and show more cases of favism occurring later in the spring when compared to coastal villages. Almost all the coastal cases in the spring are accounted for by fava beans consumed during ritual fasting associated with Lent. Following this period, the use of the fava beans drops considerably in the coastal areas, while their use continues in the higher elevations.

Even though the $Gd^-$ frequencies are high for certain villages at high altitudes (e.g., 33.3% in Siana, and 42.3% in Kritinea) the average for the mountainous regions is not any higher than it is in the coastal areas around Massari (See Table 5.3 for review). Although the other villages around Kritinea were not examined for bean consumption patterns in families, it can be assumed that they follow similar patterns to those found in Kritinea. Therefore, high risk for favism in Rhodes is associated with living in high altitudes, regardless of particular enzyme deficiency frequencies.

## PART II

### Age and Sex Distribution of Favism

Favism is primarily a pediatric disease most often affecting male children under the age of ten. The epidemiological attributes of favism, known in scientific research, are reflected in popular belief as well. The statistics gathered in this study show the age distribution to be in conformity with the literature. The females to males ratios in Rhodes for 1966-78 are more nearly equal than has been reported in the literature (from 1:2 to 1:22 female to male). Reasons for the age and sex distribution of favism are suggested to relate to organic and/or exposure (to the fava bean) factors. Organic factors may directly affect the level of the G6PD enzyme activity or indirectly related to the general resistence of the individual when exposed to hemolytic agents. Behavioral and cultural variables are suggested to affect these distributions of favism. The present study was able to elicit some of this information which is used to discuss the age and sex distribution of favism on Rhodes.

### Age Distribution

As reported in the literature, favism occurs most often in children under the age of ten, at which point, the numbers of episodes drop drastically. In at least one major series of studies in Greece (Kattamis et al. 1969, 1971) the research team had difficulty in finding adult cases, however, as Figure 5.8 shows, adult cases do indeed occur in Rhodes. From 123 cases of favism, 79 occurred among children (64.2%) under the age of fifteen. For every one adult case of favism, 1.7 cases of pediatric favism were reported. Reasons for this age distribution are often examined in terms of organic factors. Other variables related to environment, exposure to fava beans, and socially influenced practices such as changes in consumption patterns by age which may be implicated are not explored in the literature one considered in this section.

Organic factors

It is usually suggested that children have a greater "vulnerability" than do adults, to the effects of the fava beans. This lack of resistence may result from at least two organic factors: (1) changes in the levels of the enzyme deficiency in terms of the number of red blood cells affected with the deficiency; and (2) some unknown factors related to acquired immunity or autoimmunization which act either on the red blood cell itself or in other features of blood biochemistry. Childhood illnesses, bacterial or viral infections, may also interact with the $Gd^-$ trait so that children show more hemolytic episodes than do adults with the trait. These episodes are attributed to the beans in the diagnoses rather than the viral infection.

It is generally accepted that the enzyme deficiency genotype does not alter with time; individuals carrying the trait on one or more x-chromosome are recognized as bearing the trait and capable

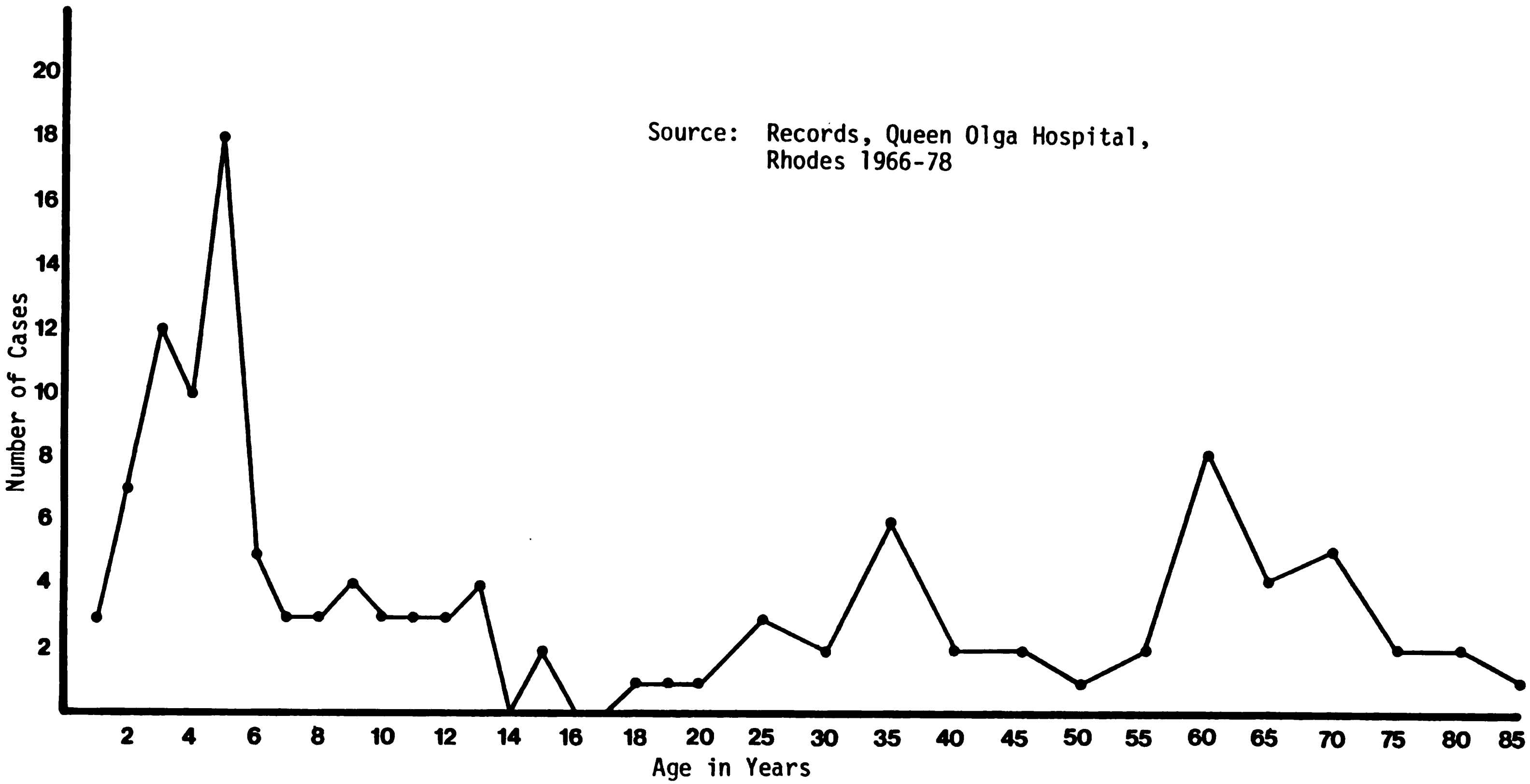



Fig. 5.8 Age Distribution of All Reported Favism Episodes in Rhodes

of passing it on to the next generation. It is not clear if the population of enzyme deficient red blood cells changes through time, as a consequence of age, or acquired immunity through low levels of fava bean exposure. It is also possible that the ratio of affected to unaffected blood cells may be altered by unspecified dietary and environmental factors. Virtually no research has examined if, or how, populations of enzyme deficient red blood cells change. Since screening has usually taken place using school-aged populations, no comparison can be made with individuals of ages over, say, twenty to sixty with respect to the level of enzyme activity. Recently, regular screening of newborns has been instituted in various areas of Greece (Institute of Child Health, Athens, Greece). This will provide a basis for rescreening at later dates if research can be promoted in this area. Therefore, at the present, potential changes in either the blood or immunological factors present must be examined indirectly.

If changes involving the blood chemistry of deficient cells actually take place through aging, either in the population of the red blood cells or in the acquisition of immunity, it should be expected that children in the younger age groups will have more serious episodes of favism. Further, if autoimmunization is involved, which is predicted to occur by low and long-range exposure to fava beans, those families which consume the beans throughout the year in a variety of preparations, would be expected to report fewer children showing episodes of favism.

Presentation and Severity of Symptoms. Sixteen episodes of favism were reviewed according to their case histories collected through interviews and the severity of symptoms. All the cases which occurred when the affected individual was from 0-13 years of age, were divided into two groups: 0-5 (ten cases) and 6-13 (six cases). The method of calculating the severity of the episodes involved the following: (1) the onset of signs of hemolysis in number of hours after fava bean consumption (jaundice and discolored urine), and (2) the manifestation of other symptoms such as dizzyness, headache, and temperature, along with the hemolytic signs.

As Table 5.12 shows, the children in the 0-5 year old cohort did not show any tendency to present hemolytic signs earlier than their older counterparts. Four of the children in the young age cohort presented hemolytic signs within 24 hours after eating the suspected fava beans, and six showed these signs after 24 hours. Among the eight older children, five showed hemolytic signs within 24 hours, and three showed them after 24 hours.

TABLE 5.12

PRESENTATION OF HEMOLYTIC SIGNS IN
PEDIATRIC FAVISM: TWO AGE
COHORTS COMPARED

| | Hemolytic Signs | |
|---|---|---|
| | w/in 24 hrs. | after 24 hrs. |
| Age | | |
| 0 - 5 | 4 | 6 |
| 6 - 13 | 5 | 3 |

Of seven cases where only the hemolytic signs were reported, two were in the 0-5 year old cohort, and five in the 6-13 cohort.

Regardless of age, the majority of these seven cases which showed only the hemolytic signs, were reported to have occurred within 24 hours after the beans were eaten.

Table 5.13 shows a comparison of the manifestation of only the hemolytic signs with cases where other symptoms were also present (such as dizzyness, palor, fever, vomiting). In all cases these symptoms preceded or occurred simultaneously the hemolytic signs of jaundice and/or discolored urine. Of the ten episodes in the younger age cohort, eight involved additional symptoms. The distribution of the hemolytic compared to additional symptoms in the older age cohort was evenly distributed.

TABLE 5.13

CASES WITH ONLY HEMOLYTIC SIGNS V.S. THOSE WITH OTHER SYMPTOMS: TWO AGE COHORTS COMPARED

| Age | Only Hemolytic Signs | Additional Symptoms |
|---|---|---|
| 0 - 5 | 2 | 8 |
| 6 - 13 | 3 | 5 |

Episodes which involved only the hemolytic signs usually showed these signs within 24 hours of eating the suspected fava beans, as Table 5.14 shows.

In eleven cases, additional symptoms as well as the hemolytic signs were reported. Eight of these were in the 0 - 5 cohort, and only three in the 6 - 13 cohort. All but two of these eleven cases were associated with hemolytic symptoms which appeared within 24 hours, and both were in the younger cohort. Regardless of age, when additional symptoms are reported the hemolytic signs appeared after 24 hours. All additional symptoms preceded the hemolytic signs. It appears that when the hemolytic crisis became evident within 24 hours after consuming fava beans, additional symptoms were not experienced (or, in any case, reported).

TABLE 5.14

CASES WHERE ONLY HEMOLYTIC SIGNS WERE REPORTED

| | Hemolytic Signs Presented | |
|---|---|---|
| | Within 24 hours | After 24 hours |
| Age | | |
| 0 - 5 | 2 | 0 |
| 6 - 13 | 3 | 2 |

TABLE 5.15

ONSET OF HEMOLYSIS IN CASES WHERE OTHER SYMPTOMS ARE REPORTED

| | Hemolytic Signs Reported | |
|---|---|---|
| Age | Within 24 hours | After 24 hours |
| 0 - 5 | 2 | 6 |
| 6 - 13 | 0 | 3 |

In summary, the children in the younger age cohort did not report hemolytic signs any faster than did their older counterparts, however, they did show a variety of accompanying symptoms which preceded the manifestation of jaundice and anemia. Therefore, it is not possible to say that hemolysis occurs more rapidly in younger children. From the data, younger children suffer a complex of symptoms more often than do their older counterparts. The greater number of symptoms in younger children may be related to a number of factors not dependent on the $Gd^-$ trait. Some of these might include the closer observation of symptoms by adults or the lack of reporting early symptoms by the older children.

Autoimmunization. If acquired immunity is a factor not only in the age distribution of favism, but in the etiology of the disease as well, at least two variables would be expected to play a role: (1) the ability of one episode to confer immunity, and (2) immunity acquire by the low grade, continuous exposure to fava beans. It is well documented that same person recorded. Indeed, one of the dangers of favism is that after remission of hemolytic signs, a relapse may occur without subsequent consumption of fava beans. Nutritional information collected from the families in Massari and Kritinea indicates that favism is suffered more often in families consuming the beans throughout the year and in a variety of forms. In many instances, the episode followed the consumption of fresh beans, even though the family consumed the beans in a variety of preparations, both dry and fresh, at other times of the year.

Other organic weaknesses in children. Individuals with the enzyme deficiency have been known to exhibit hemolytic episodes unassociated with any known hemolytic agent. These episodes are generally attributed to organic stress, particularly viral infections. Children between the ages of two to twelve are subject to a variety of viruses and microbes for the first time, passing through a number of infectious diseases to which they are rendered immune. This is more the case for the children of Greece than for the children of the United States because many children are not routinely immunized for the diseases that U.S. children are, in particular, mumps and rubeola. Immunization for rubella and polio is a relatively new feature of the public health program. These childhood diseases may possibly play a role in provoking favism episodes, which are in diagnosis attributed to fava beans, but which in reality have multiple causes associated with childhood diseases and infections. Of the eighteen cases for which histories were taken, two had been preceded by infectious diseases. The one followed a prolonged episode of tonsilitis, where the symptoms of favism were at first mistaken for a continuation of the tonsilitis. The other occurred following measles.

In many childhood diseases and common colds, various drugs are administered, some of which are known hemolytic agents for the enzyme deficient individual. Therefore, it is not certain if hemolytic episodes following infections and infectious diseases might not be attributed to the use of aspirin, Novalgin (a popular pain reliever), and sulfa derived antibiotics. In Greece, many of the drugs which are regulated through prescriptions in northern Europe and Canada and the U.S., are available without signed prescriptions. This allows the circulation and use of drugs for infections and diseases for which they might not be prescribed by a physician. For viral infections, many people use antibiotics, which in turn might affect the appearance of a hemolytic episode. One of the eighteen cases in the present study followed the use of aspirin (for a toothache) as well as the consumption of fava beans. Therefore, it is not clear which of these hemolytic agents was the "cause" of the hemolytic crisis. These cases which were attributed to the fava bean, but which might have involved viral infection and/or the use of hemolytic drugs indicate that more information is needed on this subject. This type of information could be routinely collected during the admittance and treatment of favism episodes, which has not been the practice in the past. This should aid in gaining a clearer picture of the association of favism, childhood diseases, and the use of antibiotics and other hemolytic drugs.

Other than the episodes of favism which followed viral or bacterial infections, and the use of hemolytic agents, other hemolytic episodes were noted in children with the deficiency, some of whom suffered also from favism. If some unknown organic factor promoted hemolytic episodes from fava beans in the young children, it might be expected that cases of such episodes would also be more prominent in these children. To explore this hypothesis, two groups of enzyme deficient children were examined: (1) those <u>with</u> favism plus at least one previous case of hemolytic crises suffered under other conditions, and (2) those <u>without</u> favism, but which reported one case of hemolytic crisis not associated with fava beans.

Of thirty-four children identified with the deficiency, and for which case histories of diseases and conditions related to health were available, seven had experienced hemolysis or jaundice for reasons other than those associated with the fava bean as the hemolytic agent:

(1) Three were jaundiced shortly after birth;

(2) One had unexplained, severe anemia at age two;

(3) One had hepatitis at age four;

(4) Two had spontaneous, unexplained jaundice at the ages of eight and ten.

These episodes of non-fava bean episodes of hemolytic crisis are shown in Table 5.16.

TABLE 5.16

HEMOLYTIC EPISODES IN GD$^-$ TRAIT CHILDREN
(OTHER THAN FAVISM)

| | Total | Hemolytic Episodes Not Related to Favism | |
|---|---|---|---|
| Favism | 12 | 3 | (25%) |
| No Favism | 22 | 4 | (18%) |
| Total | 34 | 7 | (20.6%) |

Three of twelve Gd$^-$ trait children who suffered from favism also reported earlier episodes of hemolytic anemia (25%), while four of twenty-two children not reporting favism had suffered previous episodes of hemolytic anemia (18%). Children with favism had a higher percentage of earlier hemolytic episodes than did those with the deficiency but without favism. From the sample, those having had hemolytic anemia from non-fava bean related agents at earlier ages were more likely to report favism later in life. This does not mean that children with the deficiency have a greater tendency toward favism at earlier ages, but have a tendency toward hemolytic episodes in general. Of the thirty-four children, sixteen suffered from at least one hemolytic episode from fava beans or from some other cause (twelve cases of favism and four cases of hemolytic not related to favism).

Analyzing the age distribution of favism episodes from health histories has not been considered in the literature. The cases in the present study which had other physical factors preceding the onset of favism episodes are too few to make any conclusions about the relationship between the health status at the time of the episode and the favism case itself. This needs further investigation, along with the role which previous hemolytic episodes play in individual cases of favism.

Environmental factors

The distribution of favism episodes among the different age groups is now shown to vary according to either urban-rural or altitudinal locations. Figure 5.9 shows the age distribution by urban-rural cases. The upper line, showing the total cases, is nearly parallel to the line showing the urban and the line showing the rural cases by age. That is, there is no appreciable difference by age in these distributions.

Figure 5.10 shows the age distribution of rural cases by altitude. In the children under six years of age, the mountain cases account for 44% of all the rural episodes. In the coastal areas, the 6-10 year old cohort accounts for 57% of all rural cases

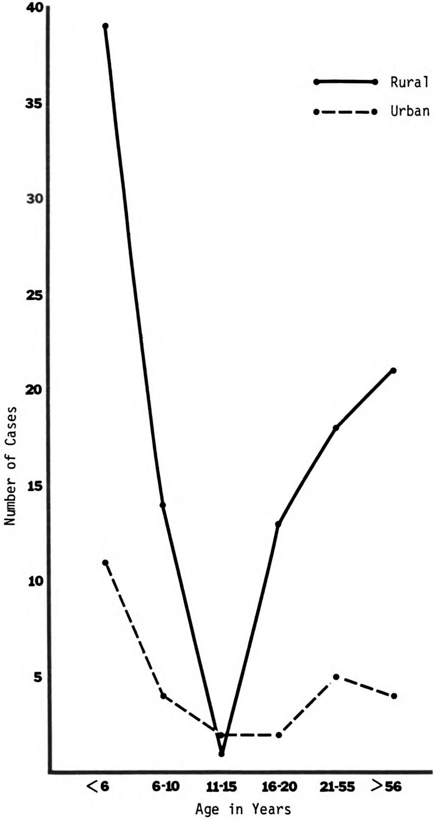



Fig. 5.9 Age Distribution by Rural and Urban Episodes

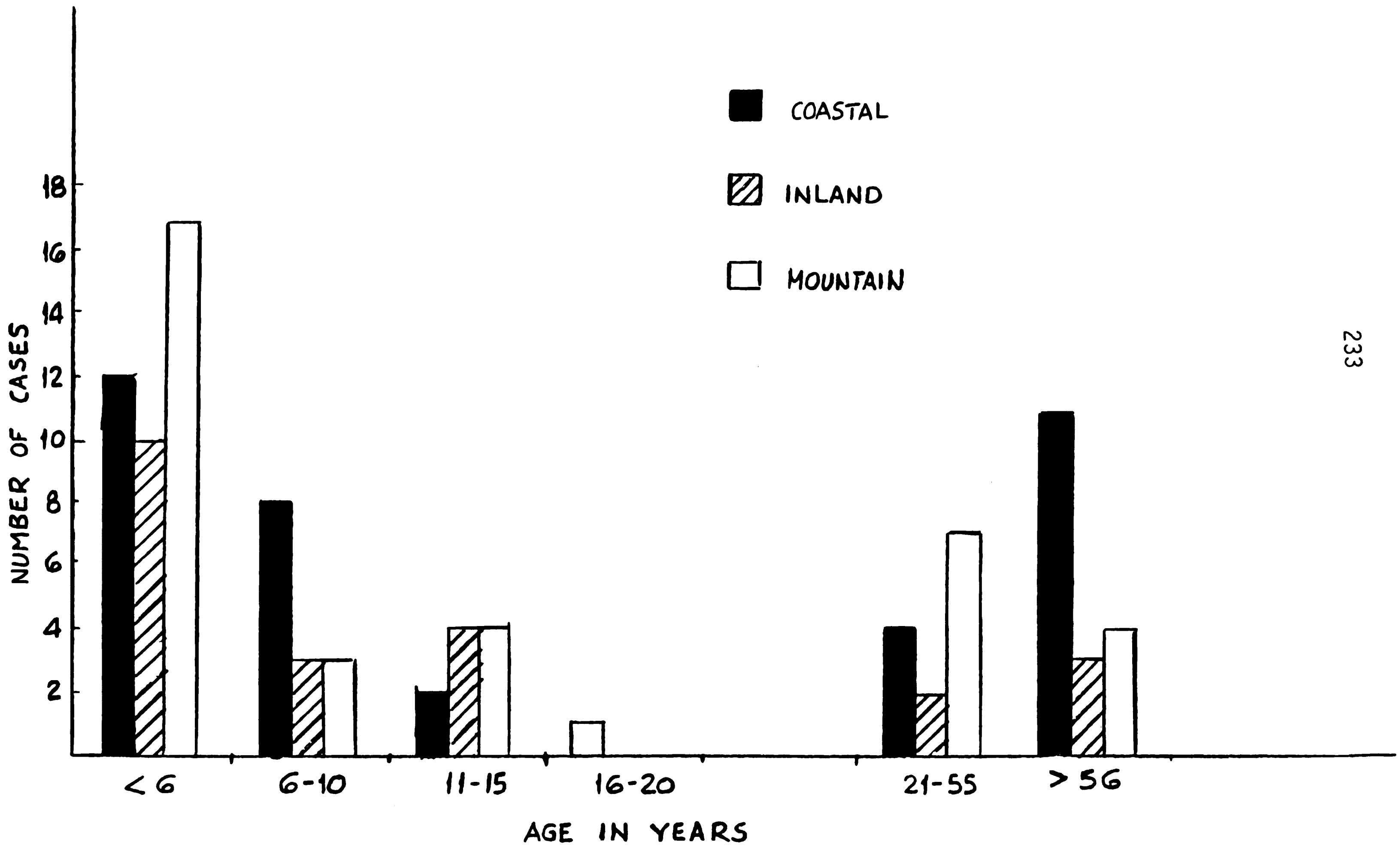



Fig. 5.10 Age Distribution of Rural Cases by Altitutde

in this cohort. For this sample, the youngest children in the mountain regions and the six to ten year olds in the coastal regions show the greatest number of episodes.

TABLE 5.17

AGE DISTRIBUTION AND ALTITUDE

| Age | Coast | Inland | Mountain | Total |
|---|---|---|---|---|
| 0-5 | 12 | 10 | 17 | 39 |
| 6-10 | 8 | 3 | 3 | 14 |
| 11-15 | 2 | 4 | 4 | 10 |
| 16-20 | 1 | 0 | 0 | 1 |
| 21-55 | 4 | 2 | 7 | 13 |
| $56^+$ | 11 | 3 | 4 | 18 |
| Total | 38 | 22 | 35 | 95 |

While all cases drop after age five to six, according to the Rhodes figures, the drop in cases in the mountain areas is larger than would be expected based on (1) the previous representation in the 0-5 age cohort, and (2) the fact that the greatest frequencies are from the mountain areas, and these would be expected to influence the characteristic pattern for all total episodes. More information is needed about the age composition in the localities in order to account for this drop by demographic factors. (The distribution of the population among the different age groups in Massari and Kritinea is nearly the same.) While changes in consumption patterns are expected to vary by age and by region, separately, they are not expected to vary by age <u>between</u> regions. That is, it is not expected that 6-10 year olds in the mountains would abruptly stop eating fava beans, while their inland and coastal counterparts would continue. This requires further investigation to rule out that purposeful changes take place in fava consumption from ages six to ten; it is more likely that the drop in mountain cases in this age group is a chance event.

Exposure to fava beans and age

Exposure to fava beans is expected to include that which takes place both in and outside of the household unit. These were listed in the introduction to be (1) use in home, (2) protection of young children; (3) protection after 1st episode; and (4) participation in agriculture. While families may not use the beans or offer them to children, other potential exposure to the beans may exist outside of the home.

Use in the home. Fava beans are often used as a weaning food for infants in many parts of the Mediterranean because they can be mashed up easily into a puree, and perhaps because they have been long-recognized for their nutritious value. This is not the case for Rhodes where they are not usually given to children under the age of two. The age distribution shows very few cases occurring before the age of two, which is probably a reflection of this practice. Italian observers, in the early history of the medical recording of favism episodes, wrote that Italian mothers have been known to feed their children small amounts of fava puree or soup to protect them from the effects of larger doses. This behavior was not observed in Rhodes. Depending on the particular caution exercised in different families, fava beans may or may not be given to young children under the age of six. Some of the episodes in this age group occurred from fava beans given to the child by neighbors, relatives, or from beans which were taken from a plate of beans left unguarded during their preparation.

Protection of children from eating fava beans. Throughout Rhodes, the idea is expressed that fava beans should not be given to children; however, the conviction that children must eat, and eat a lot, in order to grow interferes with this idea of protection. When families are asked what foods are good for children, they almost always respond, "all foods". If asked specifically about fava beans, they will, on the other hand, say that they should not be given to younger children. Therefore, if a child who is viewed as a difficult eater, which most infants and toddlers are considered to be, any food that they show interest in will be given to them. One dramatic episode of favism occurred in a two-year old child who had seen the family eating cooked fava beans in a tomato soup mixture. The infant cried and carried on so, insisting that he wanted a portion of the beans, that he was finally given a piece of bread soaked in the soup by his resigned mother to stop his crying. Shortly thereafter, hemolytic signs appeared, the child was taken belatedly to the hospital, but the hemolytic crisis was sufficiencly severe to result in death. This was the only death recorded among the children in Rhodes during the twelve year survey. It was well known to the inhabitants of the region, who supplied the details of the episode.

The emphasis on food consumption among young children involves the idea that chubby and even obese children and infants are most healthy. The most common complaint from parents in interviews and in the local agrarian physician's office is that one or more of their children "refuse to eat". This phrase must be considered in relation to the proportion of food which children are given on a plate and expected to consume entirely. The portion is usually adult-size, and when they do not consume all of it during the meal-time, it may be left out for several hours, during which time the mother, grandmother, or older sister will try to give the young child a spoonful of the serving every so often. Many children before the age of eight become passive eaters; that is, they never sit down to eat a meal, but circulate while the family is eating, and are given portions of food off the table by different family members. While fava bean preparations may not be cooked with the idea of serving the child a portion, it is common to find a child being given a spoonful or even taking a few beans from the table.

This holds true when children visit other homes in the village. If they happen to visit a neighbor's home with other family members or children, they will be offered whatever happens to be on the family table, or whatever the housewife has cooked for her family. Again, fava bean may be among these preparations, and children may be given a serving, perhaps on the assumption that well-cooked beans cannot harm them. As an example from the present study, one favism episode occurred following fava beans which were offered to the child from the neighbor's kitchen. The child wandered into the kitchen while playing with the neighbor's children, and was given the beans. The bean had not reached the family's meal table.

Even though many adults and parents adamantly claim that fava beans should not be given to children to the point of arguing with grocers who have left the beans outside of the store, the emphasis on food consumption for children overrides this concern for fava beans to be avoided by them. Further, the majority of the eighteen children who suffered from favism stopped eating the beans thereafter but the rest of their families continued to consume them.

Fasting behavior and age

Lenten fasting coincides with the ripe fava bean season, but not all spring cases are associated with beans consumed during Lent. Figure 5.10 shows the distribution of all the favism episodes by age compared to both the spring and the Lenten episodes. It would be expected that all age groups would show relatively fewer cases from beans consumed during Lent, however, the marked difference in the total cases compared with Lenten cases in the 0-5 age group indicates that children may be protected from fava bean consumption most strictly during this period.

Of all the seasons during the year, the fava beans (fresh or dry) are most likely to be in the households during the Lenten fasting period. Due to the coincidence of Lent with the ripe period, the majority of these beans are likely to be ripe which means that they can be easily picked up and eaten by the children while left laying around in the home or the outside area adjacent to the home. From the case histories of eighteen favism episodes, none of the Lenten cases followed the consumption of beans which were given to the child within the home. Some followed the consumption of beans which had been taken from the kitchen, unknown to the family; others were given to the child by friends or neighbors, and others were taken from the field.

While the use of case history information from a small sample of cases cannot verify that fava beans used during Lent are even more cautiously not served to children than during the rest of the year, they indicate that the interplay of general food habits in children, protection from fava beans and Lent might be looked at closer in other epidemiological studies. For the present data, the protection of children from fava beans operates to lower the number of expected episodes. Even though entire families, aside from the children under five, may consume the beans during Lenten fasting, the children appear to be quite protected from exposure. As soon as Lent ends each year, a drop in the cases is observed, suggesting that the self-will of the children overrides protective precautions.

### Participation in agricultural and age

Children after the age of six begin to be more mobile outside the household. Often they will be taken into the fields surrounding the village. At this time, they have come into greater contact with the growing beans and those which are seasonally present outside of grocery stores. Because the bean pods are easily visible on the plant, they may be picked by the children, and held in the hand or saved in a pocket. Their large size makes them a likely target to be picked up by young children, whether or not they are actually given to the children by older adults.

By the age of twelve, young people are left to go into the fields and participate in harvesting activities. They may be sent to gather grape leaves for other food preparations (especially young girls),to gather greens, to check olive trees, and so forth. Again, they come into direct contact with the beans as they are growing, and abundant opportunities exist for picking and eating the beans while other agricultural activities are pursued.

By the time young people reach the age of fifteen, they are participating in most of the agricultural chores that adults do, and have equal opportunity to eat the fresh beans at will, as do the adults. By this time, however, the number of reported cases of favism has dropped drastically from the earlier years. Adults over the age of fifty eat the beans by habit, since they grew up with the beans being a much more conspicuous feature of the annual diet. These are those adults who were born before the Second World War, when the beans were widely eaten, and meat was rarely available.

Summary of age distribution

By the age distribution of the 1966-78 reported episodes of favism in Rhodes, the highest risk group was found in children from one to five years of age living in mountain villages. The ratio of pediatric to adult cases was 1.7:1, more nearly equal than has been noted in the literature. The sample of eighteen favism cases showed that hemolysis did not appear earlier in the youngest children (0-5) than in older cohorts, but that additionally symptoms occurred more often in the former group. Data is inconclusive on whether or not viral and bacterial infections and/or exposure to other known hemolytic agents immediately prior to the episode is an important variable. $Gd^-$ trait children who suffered previous hemolytic anemia had slightly greater tendency to develop a second hemolytic crisis (favism) later. Children under 5 in the mountains are almost two times more likely to have favism than inland and coastal children in the same cohort. After this, their risk drops. Coastal children are at their greatest risk until ten years of age. Families with beans in the home have more episodes, even though most occur from unsupervised bean consumption outside of the home. This suggests that autoimmunity is not a factor in protecting against favism, and a complex interplay between familial habits and physical environment.

In Rhodes, the individual most likely to suffer from favism would be expected to be under age six, regardless of altitude. Those in the coastal areas over fifty-five years old are also at a higher risk of favism than other age groups. A previous hemolytic crisis was not a particularly reliable indicator of whether or not an individual would later suffer from favism. In children, eating fava beans after Lent and/or in an unsupervised manner was more often associated with favism than not. The consideration of the age distribution of favism is complimented by looking at factors which interact with the sex distribution. Some of these have already been mentioned; for example, the participation in bean production activities by age also relates to the sexual division of agricultural labor where women are more often involved in gathering and food preparation activities than men.

Sex Distribution of Episodes

Medical investigators who have noted the sex distribution of favism, which shows more males than females represented, have often remarked that it is yet another enigmatic aspect of the disease. As with the explanations offered to examine the age distribution, the focus in previous research has been on characteristics of the enzyme deficiency or other organic factors which might interact with the deficiency. Environmental factors, differences in fava bean exposure and other social or ideological variables have not been investigated. In Rhodes, the male to female ratio of favism episodes is more nearly equal than in any of the reports from other areas. Of 123 total cases, 52 were reported in females, 71 in males for a ratio of 1:1.36. Figure 5.11 shows that age does not appear to act on this nearly balanced ratio. In all age cohorts, more than as many females as males report favism. Aside from the x-linked nature of the $Gd^-$ trait, three other factors listed in the introduction will be discussed in this section. (1) differences in expression of symptoms; (2) environmental differences; (3)

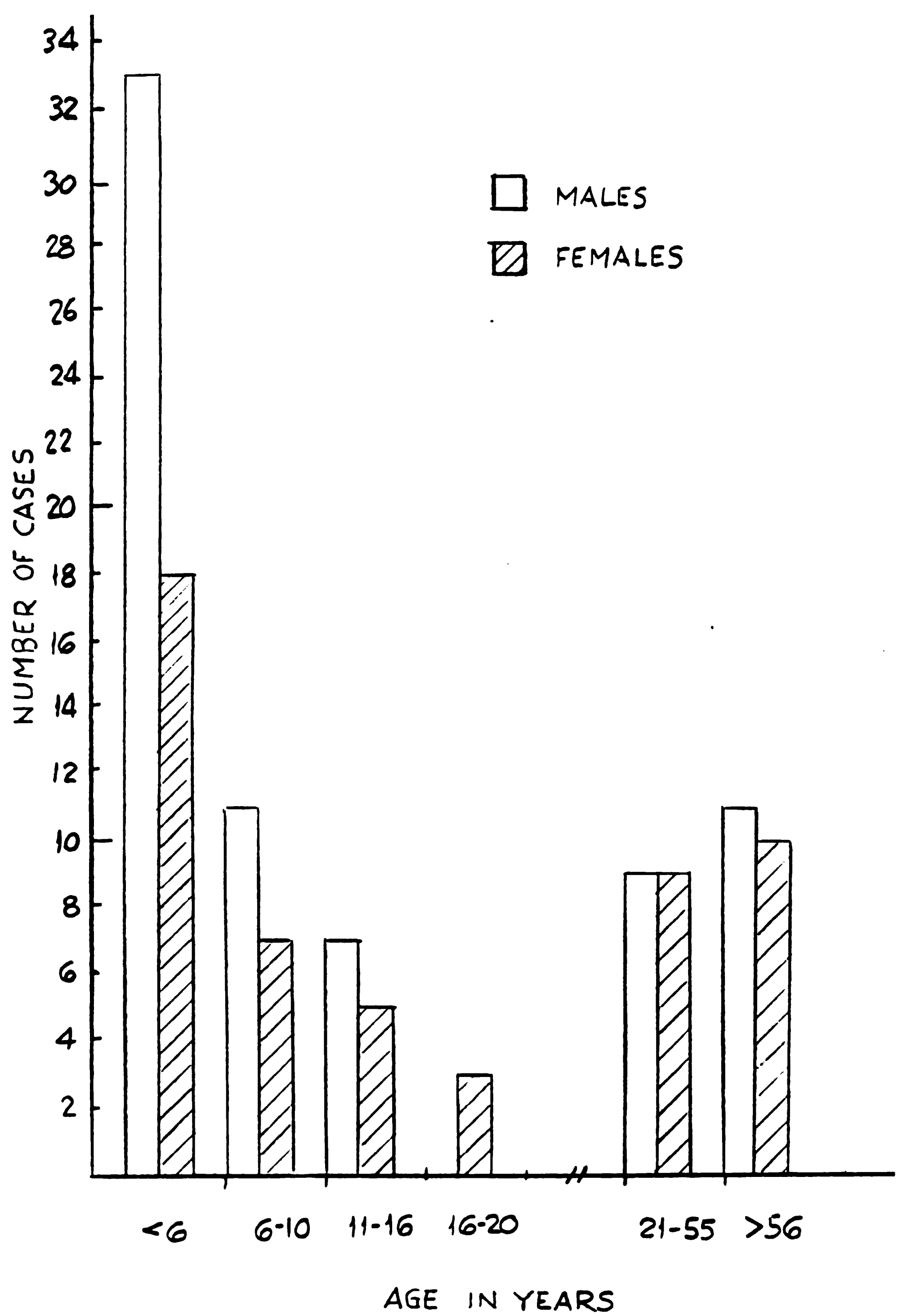



Fig. 5.11 Age and Sex Distribution of Favism Episodes

exposure factors.

G6PD deficiency and sex
distribution of favism

Because the enzyme deficiency is an x-linked trait, it is tempting to explain the sex distribution of favism episodes on this basis, but this temptation is best avoided. As discussed in Chapter One, genotypes and phenotypic expression may have little to do with each other. Males who are expected to be fully enzyme-deficient according to their genotype show a wide range of enzyme activity on the basis of phenotypes. Female heterozygotes complicate the picture even further as their phenotypic expression may show cases as nearly deficient as male hemizygotes while others are nearly normal. Episodes of favism which are used in the present study were not tested as to quantifiable levels of enzyme activity preceding the hemolytic crisis. Further, while such information would have been valuable, it is not the object of this present study to make these distinctions.

It is possible that the differences noted in the sex ratios of favism are due to differences in the symptoms and progress of the disease as experienced by males on the one hand and females on the other. These differences may be due to organic and/or socio-psychological factors. It is not the object here to establish one or the other: certainly social constraints on sex-role behaviors have an impact on the presentation of symptoms just as much as purely physiological sex-related differences. Using the case histories from 18 cases from Massari and Kritinea, this possibility is discussed in two parts: (1) the timing of hemolytic signs; and (2) the manifestation of accompanying symptoms or conditions.

<u>Hemolytic signs.</u> Table 5.18 shows that females tend to manifest hemolytic signs sooner than do males among the 18 cases. Hemolytic signs of jaundice and/or discolored urine usually appeared more often after 24 hours following bean ingestion (10 of 18 cases) with the largest number of these showing hemolytic signs after 24 hours being males (7 of 10 cases). Those assumed to hemolyze slower were, in the majority males.

TABLE 5.18

PRESENTATION OF HEMOLYTIC SIGNS BY SEX

| | Presentation of Hemolytic Signs | | |
|---|---|---|---|
| | w/in 24 hours | after 24 hours | (total) |
| males | 3 | 7 | (10) |
| females | 5 | 3 | ( 8) |
| (total) | (8) | (10) | |

From eight female cases of favism, three showed hemolysis after 24 hours (37.5%), while seven of ten males (70%) showed hemolytic signs after this same time. Females did not tend to show hemolytic signs any sooner than did their male counterparts, and in fact, the opposite trend was observed. The idea that males hemolyze faster following bean consumption, perhaps due to some characteristics of the level of enzyme activity, is not supported by this data. It is not possible to state if this is applicable to all the 123 cases which were reported in Rhodes during 1966-78.

<u>Accompanying conditions.</u> In both sexes, the majority of

all cases showed other accompanying conditions such as dizzyness, palor, vomiting and elevated temperature. Where one or more of these accompanying symptoms were noted, they first appeared before or in conjunction with the hemolytic signs, never after. Six of ten males showed additional conditions, while seven of the eight females were in this group. These results are shown in Table 5.19.

TABLE 5.19

PRESENTATION OF ADDITIONAL SYMPTOMS BY SEX

| | Additional Symptoms | Only Hemolytic Signs | (Total) |
|---|---|---|---|
| Males | 6 | 4 | (10) |
| Females | 7 | 1 | ( 8) |

Considering both hemolytic signs and additional conditions together, all males which reported hemolytic signs within 24 hours did not have any other signs, while all males which hemolyzed after 24 hours had other accompanying conditions. Among males in this sample, early hemolytic signs did not carry other conditions with them, while later hemolysis did. Females in contrast, showed accompanying conditions even when the hemolytic signs were reported early. It might be concluded that female episodes of favism are perceived to be more severe in that they present hemolytic signs sooner as well as involve accompanying conditions.

Environmental factors

As with age distribution, urban and rural ratios of the sex distribution in Rhodes show little difference. The rural female to male ratio was 1:1.3 and the urban female to male ratio was 1:1.5, as shown in Table 5.20.

TABLE 5.20

MALE TO FEMALE EPISODES SHOWN BY URBAN AND RURAL LOCALITIES

| | Female to Male Episodes | |
|---|---|---|
| | Number of Episodes | Ratio |
| Urban | 11 : 17 | 1:1.5 |
| Rural | 41 : 54 | 1:1.3 |
| Total | 52 : 71 | 1:1.4 |

Both female and male rural episodes were higher than female and male episodes when compared within the same sex. For all male episodes, the rural to urban ratio was 1:3.2, while for all female episodes, the rural to urban ratio was 1:3.7. These figures are given in Table 5.21. Since the urban and rural population in Rhodes is nearly equal, these ratios are not a result of demographic factors (such as the largest proportion of the population being located in the rural areas).

TABLE 5.21

URBAN TO RURAL RATIOS BY SEX DISTRIBUTION

| | Urban: Rural Episodes | |
|---|---|---|
| | Raw | Ratio |
| Males | 17 : 54 | 1 : 3.2 |
| Females | 11 : 41 | 1 : 3.7 |
| Total | 28 : 95 | 1 : 3.4 |

In the 95 rural cases of favism, the 41:54 female to male ratio (1:1.4) is distributed according to the altitude in which the village cases are found. Using the mountain, inland and coastal divisions introduced earlier, slight differences in each altitudinal group appear. These are shown in Table 5.21. The most striking point is that the female to male ratio is equal in the coastal areas. This is the first time that as many female as male cases of favism have been reported. In fact, the average ratio of 1:1.4 for Rhodes is the most equally balanced ratio for a population.

TABLE 5.22

FEMALE TO MALE EPISODES BY ALTITUDE

| | Female to Male Episodes | |
|---|---|---|
| | Raw Number | Ratio |
| Mountain | 13/22 | 1:1.7 |
| Inland | 8/14 | 1:1.8 |
| Coast | 19/19 | 1:1.0 |

Reasons for this distribution may have to do with the way in which the altitudinal groups were subdivided, however, it should be emphasized that the population in the coastal area includes the major centers of population on the island, which gives greater importance to the equal female to male ratio.

### Differences in fava bean exposure by sex

From the 18 cases of favism, 11 were found to have been associated with fresh raw fava beans. Seven of these (eleven) episodes from raw beans occurred in female children aged five to fifteen. None of these involved beans which were given to these young girls, but were from beans eaten during food preparation or gathering activities. Only one episode in female children followed the consumption of dry beans. These figures are shown in Table 5.23.

TABLE 5.23

FORM OF BEANS ASSOCIATED WITH FAVISM EPISODES IN MALES AND FEMALES

| | Form of Bean | | Cases caused by | | |
|---|---|---|---|---|---|
| | Fresh : | Dry | Fresh | : | Dry |
| Male | 6 | 4 | 1.3 | : | 1 |
| Female | 7 | 1 | 7.0 | : | 1 |

This table also shows that six of ten males had eaten the fresh bean before the episodes, while four of ten had eaten it in the dry form. Male cases from fresh beans compared to dry were 1.3 cases from fresh for every case from dry beans. Female cases were 7 to 1, fresh to dry. That is, females suffering from favism from the fresh form were 5.4 times more numerous than the male form (7.0/1.3). Even though males are allowed greater access to the fields, their cases of favism do not occur following beans consumed from this location as often as they do among the young girls. Male cases occur often from beans consumed in the home or from prepared beans given to them by other relatives or neighbors.

Agriculture and exposure

As mentioned earlier, age differences in fava bean exposure are also influenced by age. Young children of both sexes usually have contact with the bean only in the household or neighborhood setting, however, as the children become older, different amounts of freedom are influenced by being male or female. Boys at a younger age than girls have greater chances of going to the close-in fields (vis-a-vis the village center) to play. Here they are likely to come into contact with the fresh, ripe bean as it grows. Girls, on the other hand, begin to take part in duties related to food gathering and preparation, beginning around age eight. They too, have opportunities to eat the bean in the process of preparing them for a family meal. Males after the age of eighteen begin to frequent the local cafeneia (coffee houses) on a daily basis. Here they drink coffee in the early morning before going to the fields, and again, sit there in the afternoon to play cards and drink coffee or a whiskey or ouzo. In the evenings, they may drink beer, ouzo or wine together. Alcoholic beverages are never served alone in Greece (outside of tourist restaurants or bars), but are always accompanied by meze or mezedakia. These are small food items such as bread, a small portion of fried potatoes, sliced cucumber or tomatoes, and often, fava beans. This places males after the age of twenty at greater risk of coming into contact with fava beans, however, they have already passed the age at which the majority of cases occur.

### Social factors affecting exposure by sex

The ethnographic studies of Greece and the Mediterranean area almost always include an examination of sex roles, and in particular, the place of female and male children in the Mediterranean family. Female children are depicted as a burden, both economically and morally, on their families. Fathers are perpetually concerned about the loss of a young daughter's virginity as well as the accumulation of her dowry; however, in observing the treatment of young female children under the age of six in rural Rhodes, it is no less affectionate than the treatment extended to male children of equivalent age. It is only at puberty or pre-puberty that the parental affection changes from open display to concern for the future for the young girl. Her circulation on the village is suddenly restricted; she is allowed out of the household area or neighborhood only for agricultural duties or errands which can take place before early afternoon. It is worth noting that only two of the total eighteen cases occurred in female children from the age of 0-5, while six more were reported after that age. That is, the majority of the 18 cases were reported in male children in this age group. This does not support the thought that female children are neglected and male ones protected. These figures are presented in Table 5.24.

TABLE 5.24

SEX DISTRIBUTION OF FAVISM EPISODES BY AGE COHORTS (0-5 AND 6-15)

| | Ages | |
|---|---|---|
| | 0 - 5 | 6 - 15 |
| Males | 8 | 2 |
| Females | 2 | 6 |

The fact that more cases among males in the present sample followed beans which were consumed in a cooked form (either dry or fresh), indicates that they may have been given these bean preparations by a relative or neighbor. This is consistent with what has been observed in the villages. While young girls are not "neglected" in their disease and presentation of symptoms, they are not pressured to eat the amount of food that young boys are.

In order to explore the idea that male children are protected more than females, the reporting of episodes to medical personnel was examined. The results show that male episodes reach medical personnel before female ones do on the bases of the time of hemolytic signs. Only hemolytic signs were used as indicators that the disease represented a condition more serious than usual colds and influenza, since many of the preceding and accompanying symptoms could be contributed to "non-serious" disease. For example, vomiting might not be immediately reported to a physician, while jaundice and discolored urine were expected to be more rapidly reported following their manifestation.

Using case history material from 18 cases it was found that all ten males represented were reported to the hospital within 24 hours after hemolytic signs were first noted, while only three of the eight female cases were reported in this time. Three additional female episodes were not reported at all, but two of these occurred in the late 1940s when favism was not generally recognized as treatable in hospitals and, in all fairness, they should not be considered in the figures. Even discarding these two female cases, it is still evident that female cases in this sample reached the notice of medical personnel later than did the male ones. This must also be considered with respect to the severity of symptoms. Female episodes tended to show more additional symptoms and to present hemolytic signs earlier than did male cases.

Based on this data, there appears that some preferential treatment of males may influence the sex ratios of favism. Males may not be protected from fava bean consumption any more than females, in fact, many of the male cases resulted from beans which had been offered to them rather than taken from fields. This is consistent with the emphasis on children's eating patterns where they are continually being offered something to eat during and after meal times. Further, this is more likely to be the case with male children as males are believed to need more food than females. The cases of favism among young boys reach hospitalization sooner than do female ones, which may be a result of greater precaution taken about the signs of illness in males, or a result of the role model for young boys which promotes greater activity levels. If the young boys are not as active as expected to be by the model, they are considered to be affected by illness much more often than young girls. The latter may sit quietly for longer periods of time, and go unnoticed. These are suggested because the severeity of symptoms did not relate to the time of hospitalization in the sample.

Age and sex role expectations may interact with the presentation of non-hemolytic symptoms such that the reporting of episodes is affected even if equal protection of both sexes is exercised. For example, six of eight children affected by favism and reporting vomiting as a symptom were females. Two of these reported dizzyness as an accompanying symptom, while none of the male children mentioned this consistent with illness behavior in the villages of

Massari and Kritinea. Women almost daily complained of dizzyness (zaláda), while men rarely complained of feeling off balance or dizzy. Women are more likely to mention vomiting either in relation to a specific disease, or alone, while men conceal it or ignore it as important.

## Summary, Part II: Age and Sex Distribution of Favism

The cases of favism reported in Rhodes show a more nearly equal distribution by sex than any earlier studies. It cannot be stated conclusively if the distribution is a result of preferential treatment of male children of the nature of the disease which allows more females to be reported than they are in other areas. Both males and females in rural areas are more likely to suffer from favism than their urban counterparts.

The greatest number of rural favism episodes are accounted for by the 0-5 age cohort, with almost half of these being reported from mountain locales. This suggests that either high elevation in and of itself (as physical environment ) or some aspect of it adaptative process demanded by the higher elevations, may be a factor in promoting more cases in this youngest age cohort. After six years of age, the number of episodes in all areas drops, except for the coastal area where 58% of the cases in this cohort are accounted for by the coastal. Further, in the 0-5 mountain cohort, four of the seventeen cases were male (23.5%), while in the 6-10 coastal cohort, six of eight (75%) were male. Table 5.25 shows this inverse relationship of sex ratios in the two age cohorts in the two altitude groups. The reasons for this distribution are not known but may relate to agricultural participation of women. In Massari, a coastal village fewer women participate in agricultural activities to the extent that they do in Kritinea, a mountain village.

TABLE 5.25

MOST FREQUENT FAVISM BY AGE COHORTS IN MOUNTAIN AND COASTAL VILLAGES

| | Mountain | Coast |
|---|---|---|
| Age cohort | under 6 | 6 - 10 |
| Female: male | (4:14) | (6:2) |
| Ratio | 1:35 | 3:1 |

Males who suffered from favism were more often from the inland and mountain locations, under the age of six, and had not eaten fava beans from the fields prior to favism. Female children were most often from the coast, over the age of six, and had eaten beans from the fields prior to their episodes. This is the opposite of what would be projected on the basis of sex roles. Obviously, a more complex process is going on. This may have something to do with the role of the young boy who is conditioned to having more freedom in the home and allowed to break rules more often than the young girls. The latter, trained to uphold the household rules, have a chance to be on their own more often when they are with other young girls, outside in the fields and away from the home.

# PART III

## Familial Favism

Many medical investigators contend that one episode of favism should be expected to promote changes in familial habits with respect to fava bean production and consumption. The tendency for cases of favism to be reported along familial lines shows that this is probably not the case. The familial tendency for favism cases to repeatedly appear was noted before the enzyme deficiency and its genetic pattern of inheritance could be used as a reason for these familial episodes. This tendency was initially explained by the theory of contagion; that family members spread the disease among themselves. Later, an inherited allergic weakness was suspected which led some families to show the disease. Members of families known to have reported favism who did not themselves develop favism were suspected of having developed an immunity to the beans. Since the deficiency was discovered, this factor was thought to explain the familial distribution of favism; however, it was soon found that not all individuals and familial lines with the deficiency in many members all reacted in the same way to the fava beans. This led to the hypotheses that some unidentified characteristic, also genetically inherited, was involved. This trait was hypothesized to act separately from the enzyme deficiency but to interact with it in certain families. Families might have only the enzyme deficiency and not the other, unidentified, genetic trait, and therefore did not report favism in any members. Families having both the deficiency and the genetic factor, were expected to show multiple episodes of favism. This hypothesis was studied by Stamatoyannopoulos and Motulsky (1969), whose work shows that favism does indeed have a tendency to appear in familial lines and that certain familial lines show multiple episodes of favism. The fact that a multitude of other variables which are not inherited genetically, but shared by virtue of location, tradition, fava bean consumption, etc., was not considered in their study.

## Familial Favism and Genealogical Data

The Stamatoyannopoulos and Motulsky study is one of the few existing works on the subject of favism which utilized genealogical information (and extrapolating pedigrees). This research showed that certain family lines with the $Gd^-$ trait tended to report favism more often among their members than did other pedigrees also affected with the trait. These data were taken from the Greek islands of Lemnos and Corfu, and the north-western mainland area of Karditsa. The Rhodian pedigrees collected during the present study showed the same type of familial tendency that Stamatoyannopoulos found for his data. The comparison of these pedigrees appears in Appendix B.

Aside from comparing pedigrees where multiple favism cases had been noted, the Stamatoyannopoulos study did not compare families with the $Gd^-$ trait who did not ever report favism to those who reported one or multiple cases. It does not include any information about the consumption of or exposure to fava beans in these different pedigrees. Even though they are from three different regions of

Greece, the basic assumption was that all families are likely to be exposed to the beans in nearly the same manner and amounts. The present study did not begin from this assumption, and while collecting genealogical information, other data regarding familial differences in fava bean use and exposure were also elicited.

Thirty nuclear family units with the $Gd^-$ trait and/or favism in one or more number from Massari and Kritinea were used for the analysis familial favism. While twenty of these did not report favism in the nuclear unit, eight of them reported favism in a consanguineal relative. Ten others reported favism in the nuclear unit with sex of these ten also reporting the disease in other consanguineal kin (either sibling or cousin-related). Two units reported single cases of favism in both the nuclear unit and in consanguineal kin, and three reported favism in a parent but not in $Gd^-$ son. Genalogical information was taken from all thirty nuclear families, even though some were included in the genealogical information from other nuclear representatives. The information was then worked into simplified pedigreed based on the circulation of the $Gd^-$ trait in a pedigree and in the presentation of favism episodes.

Pedigrees differ from genealogies in that the latter is an ego-centered reporting of biological kinship as perceived by the person giving the genealogy. It has social and cultural meaning as well as biologically related kin for reasons known or unknown to the individual reporting the genealogy (e.g., family feuds, absent members, unrecognized marriages). Pedigrees are schematic representations of actual biological descent which are gathered through reported genealogies, village records, double-checking information given in the ego-centered reckoning of kinship. In the pedigree, certain individuals are identified with particular genetic traits or diseases; in this case, they were identified with the $Gd^-$ trait and/or reported favism episodes. The term proband is used in pedigrees instead of the term, ego, which is reserved for genealogies, to refer to the focal point of the schematic representation of biological kinship.

In addition to the thirty families in the study, two others were added from a nearby village of Kritinea. These were included because they added to the analysis of sibling pairs, and were used only for this portion of the study. The probands were first analyzed by biological relationships, describing the different types of pairs which were found. These were considered in three categories: (1) Sibling pairs: (2) Parent-offspring pairs: and (3) Cousin pairs. In each set of pairs, the status of each member was known, either through screening or through the identification of a favism episode.

### Sibling pairs and the distribution of favism

Nine sibling pairs where the status of both was known, appeared in the data from Rhodes. Seven of these were from Massari and Kritinea, and two more were added from a village adjacent to Kritinea. In three of these, both siblings showed favism; in five, neither sibling showed favism; and in one pair, only one of the siblings was affected by the disease. In this case, both boys had eaten the fava beans on the same day, in the same form, and the one was affected by favism, while the other was not. Table 5.26 shows the comparison of these sibling pairs.

TABLE 5.26

SIBLING PAIRS DIVIDED ACCORDING TO FAVISM IN PROBAND AND SIBLING

| | Status of Sibling | |
|---|---|---|
| | Favism | No Favism |
| Status of Proband | | |
| Favism | 3 | 1 |
| No Favism | 0 | 5 |

Eight pairs had the same reaction to the fava beans; that is, they either reacted with hemolytic crisis or they did not. Only one pair showed different reactions to the fava beans, the one suffering from hemolysis and the other not. In four no-favism pairs, three pairs included one sibling who was still under seven years of age at the time of the study (i.e., the sibling was still within the high risk category by age alone). Two of these pairs with one sibling still under the age of seven were both males, the other pair was composed of a male and female child (the female child considered to be at less risk than her brother). The three sibling pairs with favism in both members involved cases where both were over seven years of age at the time of the study. Because the sibling sets where neither child suffered from favism are composed of younger children, it is possible that the distribution of these pairs will change within five years after the study (i.e., that some of these children will suffer from favism during that time).

Parent-proband sets

All but six probands were identified by the $Gd^-$ trait and/or clinical favism in a male child. Therefore, the $Gd^-$ trait status of the mother in all but six cases was automatically known to be at least heterozygous. This section is divided into the consideration of all parent-child pairs, and only the mother-son pairs (where the status of the son is known, and the status of the mother is extrapolated from that of the son).

Children with the $Gd^-$ trait and/or favism were compared with their parents of both sexes. The $Gd^-$ trait/favism status of the child or children was considered as one variable in the set, and the status of both of the parents as another variable. None of the nuclear units showed favism in both parents, although in all cases where a child had the trait, at least one of the parents was considered to have at least one allele for the trait. In the cases where two siblings were both $Gd^-$ trait, they were considered as a unit of one in the set. Favism in one of the two is treated as the presence of favism in the set of siblings (i.e., whether it occurs in one of the two or in both is not relevant in this comparison).

As Table 5.27 shows, except for the instance of favism in both generations, favism in the parent is the least reliable indicator in potential favism in the child(ren). Only three cases of parental favism were found, and in all instances, favism has not yet been reported among the child(ren). Favism was more likely to occur in the child(ren) than either parent. Eight of thirty pairs shown favism in the child(ren) and not the parent; i.e., a quarter of the cases were found here. Over 63% of the cases showed favism in none of the $Gd^-$ trait children or their parents. No cases of favism in both parent and child(ren) were reported from Massari or Kritinea, but one case from another Rhodian village, found during field research, is worth mentioning. A mother had suffered from favism two times during her childhood and adolescence. She continued to use the beans in food preparations for her family after she married, and only when her son suffered from favism did she stop using the beans. This was the only triple instance of favism in one nuclear family unit found during the research.

TABLE 5.27

PARENT-PROBAND PAIRS AND FAVISM

| | Status of Parent | |
|---|---|---|
| | Favism | No Favism |
| Status of Proband | | |
| Favism | 0 | 8 |
| No Favism | 3 | 19 |

Twenty-three males were identified with favism or the $Gd^-$ trait, which automatically makes their mothers at least heterozygous for the trait. These pairs were compared with the results that none of them showed favism in both mother and son (with the exception of the above case). One pair showed favism in the mother and not the son, four showed the disease in the son and not the mother, and the remaining eighteen showed favism in neither. These are shown in Table 5.28.

TABLE 5.28

MOTHER-SON PAIRS AND FAVISM

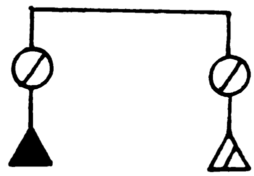
| | Status of Mother | |
|---|---|---|
| | Favism | No Favism |
| Status of Son | | |
| Favism | 0 | 4 |
| No Favism | 1 | 18 |

These data from all parent-child pairs (both mother-son and mother daughter pairs show that favism in a parent cannot be used as a reliable indicator of expected favism in an offspring, regardless of the sex of the child.

### Cousin pairs and the manifestation of favism

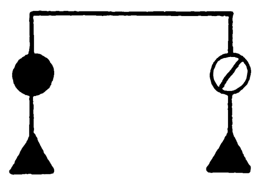
Six first-cousin pairs, both affected by the enzyme deficiency and/or favism were found in the present study. These are represented by four types as are summarized in Figure 5.12. Two of these four types were parallel cousins related through their mothers, the other two were cross-cousins. One cousin pair both suffered from favism, in fact, this pair was composed of four members rather than two, all suffering from favism. Four pairs showed one favic member and the other non-favic, while the last pair showed neither member with favism. Table 5.29 shows this information.

Out of curiosity and in the interest of preserving certain data for further comparisons in later studies, second cousin pairs were extracted from the Rhodes data. From a total of eight pairs, three showed the same reaction to fava beans, and in five pairs, Parallel Cousin Pairs

1) 

This configuration shows at least one favic male and a male first parallel cousin who was deficient but non-favic.

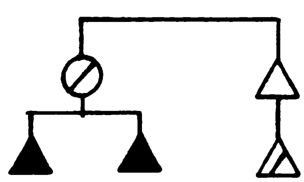
Three cases were found with the type of configuration.

2) 

A second configuration of two male first parallel cousins shows both members to be favic.

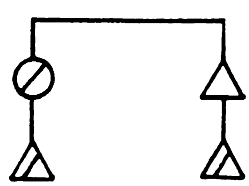
One case was found in this type of configuration.

Cross Cousin Pairs

3) 

This shows two favic sibs with their first cross-cousin with the deficiency but without favism.

One case was found with the type of configuration.

4) 

A final configuration was found with two cross-cousin males both deficient but neither affected with favism.

This configuration included one pair.

---

Non-Gd$^-$ trait male
Non-Gd$^-$ trait female
Male with 1 allele for the Gd$^-$ trait (hemizygote)
Female with at least 1 allele for the Gd- trait (either hetero- or homozygote)
Male with the Gd- trait and favism
Female with the Gd$^-$ trait and favism

Figure 5.12: Types of First Cousin Pairs with the Gd$^-$ Trait and/or Favism.

one showed favism, the other did not. These data are shown in Appendix B.

TABLE 5.29

COUSIN PAIRS AND FAVISM

| | Status of Cousin | |
|---|---|---|
| Status of Proband | Favism | No Favism |
| Favism | 1 | 4 |
| No Favism | 0 | 1 |

The analysis of data by pairs of sibs, parent-proband, and cousins, shows that while favism may occur along familial lines, the lack of favism cases also follows familial lines. Further, the closer in relation to each other two enzyme deficient individuals are, the more likely they will experience the same reaction to the beans. Eight of nine sibling pairs showed the same reaction to the beans, eighteen of twenty nine parents-probands showed the same reaction, and two of six cousin pairs showed the same reaction (88%, 62% and 33% respectively).

## Fava Bean Consumption in Gd- Trait Families

While the study of Stamatoyannopulous and Motulsky represents the first use of genealogical data to study favism, the examination of fava bean consumption patterns was largely neglected. It was assumed that in all areas, the exposure to the beans was relatively the same; that means that all individuals with the $Gd^-$ trait were considered equally at risk of developing favism. The present study in Rhodes shows that not all individuals at risk consume the beans in the same quantity or type of preparation. Families with the enzyme deficiency identified in one or more child were questioned about their use of fava beans in the family diet. Some claimed that they did not use them at all, and observations from other members of their neighborhoods proved these claims to be correct. Others used the beans in different forms, ranging from fresh and raw, fresh and cooked and dry boiled or soaked beans.

Use and preparation of
fava beans in the diet

While fava beans can be eaten both raw (only the fresh beans) and cooked (both fresh and dry beans), several families claimed that they ate them only in the raw form. Some of these had originally stated that they did not eat the beans at all, but later revealed that they might eat them from the growing plant while they were in the fields, or along with a glass of ouzo. Others may bring a small amount of the fresh raw beans into their home, but not use them in any specific food preparation. Instead, they are cleaned of their pod and outside covering, as they are in the fields, and eaten this way. If the beans are young, newly ripe, they may not be cleaned of the outer cuticle before being eaten. This is primarily a matter of taste. Where the beans are grown, it is probably safe to say that "all" individuals have eaten at least one raw fava bean.

The fresh beans may be boiled separately or with other greens, with or without the pod, depending upon how young the beans are.

When the fresh beans are used in their pods, they are treated as any other green fresh bean (e.g., string beans). They are cleaned, the ends of the pod cut away, stringy portions of the pod removed, and then they are boiled until tender. When the individual fresh beans are boiled, the first batch of water in which they are boiled may be discarded, the beans rinsed, and fresh water used to replace the other for boiling to continue.

The fresh beans are rarely boiled alone, they are usually combined with fresh greens (wild or cultivated), served with olive oil and lemon or with garlic or onions. A garlic sauce skordaliá is usually made to top the fresh boiled beans and their pods (as with other green beans and pods). Skordaliá is made from crushing garlic, adding moistened bread and mashing it with the garlic, and adding oil and lemon. The dry beans are used in a variety of preparations, perhaps even more than the fresh ones. The fresh, raw beans are edible alone, while the dry ones require soaking and boiling and usually additional ingredients. The dry beans may be boiled or soaked over night to provide meze mentioned earlier, as an addition to alcoholic beverages. They may be boiled with other winter greens, served with oil, lemon, fresh onions, or skordaliá sauce. They may also be boiled with other ingredients such as a combination of tomatoes, onions, and olive oil, or they may be boiled with lentils. One of the most tasty preparations for dry beans if in fava, where the beans are parboiled, stripped of their cuticle, and reboiled until they form a puree. Olive oil and freshly chopped onions are poured over the top of the puree. The term fava is taken from the

Greek word for the preparation, which refers to both this mixture made from fava beans and another puree made from small dry yellow lentils.

Another popular preparation from the dry beans uses tomatoes, onions and olive oil which are boiled along with the beans in a preparation called yioknié. This is a term used for tomato sauce preparations using other types of dried beans as well.

### Fava bean preparations and favism episodes

Earlier, fava bean consumption patterns in Massari and Kritinea were compared to see how village levels of exposure differ in order to help account for the more numerous in Kritinea than Massari. Here, these patterns are re-examined with respect to only families with the deficiency, comparing those who report favism to those who do not. Table 5.30 reviews this distribution for Massari and Kritinea. The total column shows that favism affects more often families which eat a variety of fava beans than those who eat them only in one type of preparation (or only fresh and raw). Eight of the eleven families eating both fresh and dry fava beans reported favism in one or more member. Two of these families had reported favism in more than one child such that eight cases of favism are accounted for by those eleven families eating fava beans in both forms. Two other cases were accounted for by families eating only the fresh fava beans.

This shows that the greater the exposure to fava beans, the more likely favism will be experienced, which is exactly as

TABLE 5.30

FORM (DRY, FRESH) AND PREPARATION (RAW, COOKED) OF FAVA BEANS IN THIRTY FAMILIES

| Forms that the Beans are Used | Massari: Number of Families with Favism/Total | | Kritinea: Number of Families with Favism/Total | | Both Villages: Number of Families with Favism/Total | |
|---|---|---|---|---|---|---|
| Don't use | 0 | 2 | 0 | 2 | 0 | 4 |
| Fresh, Raw ONLY | 0 | 2 | 1 | 4 | 1 | 6 |
| Fresh, Raw and Cooked | 1 | 6 | 0 | 3 | 1 | 9 |
| Both Forms | 1 | 1 | 7* | 10 | 8 | 11 |

*Nine episodes of favism came from these 7 families would be expected. Further those who eat <u>both</u> forms of fava beans, fresh and dry, usually suffer from favism following fresh beans rather than from dry. Four of the ten cases of favism occuring in families consuming both fresh and dry beans, were from dry beans. The other six cases were from fresh ones.

Families which consume larger amounts of fava beans tend to use them in cooked preparations as well as raw. These include the families shown in Table 5.30 listed in the categories of (1) fresh raw and cooked, and (2) both forms. These twenty total families consumed the beans in some preparation which requires cooking them, whether they are dry or fresh. Nine of these families reported favism. The total number of favism cases in these nine families was eleven. Of these eleven cases, seven were from beans which had been cooked, four from fresh, raw beans. This indicates that (1) something might happen to the beans as they are cooked, or (2) the raw beans do not appear to be as deleterious as others have suggested. The distribution of cases does not conform to what the people themselves believe about the beans, suggesting that empirical knowledge is not always correct. They believe that the raw, fresh beans are the most dangerous. Table 5.31 shows that distribution of favism episodes according to the reported form of the bean eaten (raw or cooked). These are crossed with whether they were fresh or dry. Table 5.32 adds six episodes of favism which were collected from a village adjacent to Kritinea where information about the form of beans consumed immediately prior to the episode. This shows that the distribution is approximately the same, even in adding other cases. Eleven of the eighteen episodes followed the consumption of cooked beans, and seven from fresh, raw.

TABLE 5.31

TWELVE CASES OF FAVISM LISTED BY FORM AND PREPARATION OF BEANS IMPLICATED

| Form of Bean | Type of Preparation: Cooked | Raw | |
|---|---|---|---|
| Fresh | 3 | 5 | (8) |
| Dry | 4 | 0 | (4) |
| Total | (7) | (5) | (12) |

TABLE 5.32

EIGHTEEN CASES OF FAVISM LISTED BY FORM AND PREPARATION OF BEANS IMPLICATED

| Form of Bean | Type of Preparation: Cooked | Raw | |
|---|---|---|---|
| Fresh | 6 | 7 | (13) |
| Dry | 5 | 0 | ( 5) |
| Total | (11) | (7) | (18) |

From the seven episodes following cooked beans, three were from fresh and four were from dry beans. These were analyzed according to the use of water in the preparation of the beans (see Table 5.33). Three of the four dry-cases, involved beans which had been soaked in water. This water was generally retained as the beans were processed into the final mixture or preparation in which they were served. In one of these cases it was not clear if the beans had been rinsed after they had been soaked; they were used for roasting after they had been soaked overnight. The fourth case involved dry beans which had been boiled with lentils. The water was not discarded after the mixture was boiled. Although many dry bean preparations include the discarding of the first water, when lentils are used, the water is retained.

TABLE 5.33

USE OF WATER IN COOKED FAVA BEAN PREPARATIONS
BY FAMILIES REPORTING FAVISM

| | |
|---|---|
| Fresh Beans, Water Retained | 3 Families |
| Fresh Beans, Water Discarded | 3 Families |
| Dry Beans, Water Discarded AND Fresh Beans, Water Retained | 2 Families |
| Fresh and Dry Beans, Water Retained | 2 Families |

Three cases involved fresh cooked beans and in all cases the first water was retained. Fresh beans are not usually rinsed free of the water used in the first boiling.

Of the seven cases following the consumption of cooked beans, all but one involved the retention of the water in which the beans had been either soaked or boiled. The one case where the water was probably discarded involved beans which had been soaked overnight then roasted. This suggests that the retention of water in which the beans are boiled or soaked, and not washing the beans before continuing with their preparation or mixture with other ingredients, play a significant role in provoking favism. This suggests that the retention of water in which the beans are boiled or soaked, and not washing the beans before continuing with their preparation or mixture with other ingredients, play a significant role in provoking favism.

These seven families were compared to ten $Gd^-$ trait families which also consumed cooked fava beans but have not reported any cases of favism. In this group of ten families, no clear pattern is observed regarding either the disposal of the first water, and/or the form (fresh or dry) in which they are cooked. Six of these ten non-favism families consume only the fresh beans, and four consume both fresh and dry. An almost equal number in each retained the first water in which the beans were boiled. All four families using both forms of fava beans retained the first water when using fresh beans; two of them also retained the first water during the preparation of dry beans.

It would have been convenient to find that in all the ten families not suffering from favism, and cooking the fava beans, all threw out the "first water" in preparing the beans. This would have complemented the data on the families which suffered from favism, but it also assumes that all members of a family are in equal contact with the beans, which is probably not the case.

### Genealogical Information and Fava Bean Consumption

Using thirty nuclear family units from Massari and Kritinea, single and multiple episodes of favism in family pedigrees were examined according to the consumption of fava beans. Fourteen of these thirty nuclear units did not report favism in any members either of the nuclear family or in the genealogy. Seven pedigrees showed only one case of favism. In three of these pedigrees, two nuclear families were represented, only one of which reported favism. Three pedigrees showed multiple cases of favism, representing nine nuclear units in various configurations.

### Fava bean consumption in families without favism

Fourteen families from Massari and Kritinea had not reported favism in any of the nuclear family members or in any of the consanguineal relatives. Three of these nuclear families did not eat fava beans at all, eight ate them only in the fresh form (either raw or fresh), and three ate them in both dry and fresh forms. Compared to the overall distribution of fava consumption in the thirty enzyme deficient families, the level of consumption can be said to be lower in these non-favic families, which is as would be expected. These figures are compared in Table 5.34.

TABLE 5.34

FAVA BEAN USE IN PEDIGREES WITHOUT FAVISM (NO FAVISM IN EITHER THE NUCLEAR UNIT OR IN ANY CONSANGUINEAL KIN)

| | Non-favic Families | Total Families |
|---|---|---|
| Don't Eat | 3 | 4 |
| Fresh Raw Only | 4 | 6 |
| Fresh Raw and Cooked | 4 | 9 |
| Both Forms | 3 | 11 |

Fava bean use in pedigrees
reporting one favism episode

Seven pedigrees showed favism in only one member. Three of these were simple pedigrees in that no one else was identified with either the $Gd^-$ trait or favism. All three of the simple pedigrees involved young girls who suffered from favism. None of their consanguineal kin showed any evidence of the enzyme deficiency or favism. In all three cases, favism was associated with fresh, raw beans. In two of the families (from two different pedigrees), only the fresh beans were used. In the third, both the fresh and dry forms were used.

Four pedigrees were recorded where from two to eight members were known to have the $Gd^-$ trait and/or reported a favism episode. These are distinguished as complex pedigrees, in contrast to the three simple ones above. In one pedigree, the mother of an enzyme deficient boy had been affected by fava beans. No one else among the consanguineal kin had suffered from favism. Since the mother's episode, she forbid the son to eat fava beans in any form, and she herself does not use them in any food preparation.

Three of the complex pedigrees involved other nuclear units where one or more individuals were also identified with the deficiency in these nuclear families. Figure 5.13 shows the first of these pedigrees. Five male consanguineal kin, all between the ages of seven and twelve, were identified with the enzyme deficiency during the screening of their school. They are distributed among three nuclear families, with each of their mothers also being heterozygous for the enzyme deficiency. Only one of these boys (F) has suffered from favism thus far, his case resulting from beans which had been used in the dry form and soaked over night. He had eaten them during the week immediately preceding Easter. His brother (G) also has the trait, but has not suffered from them even though it is likely that he consumed them at the same time and in the same form as did his brother. Up until the time of the episode, the family consumed a variety of the beans, in both fresh and dry forms.

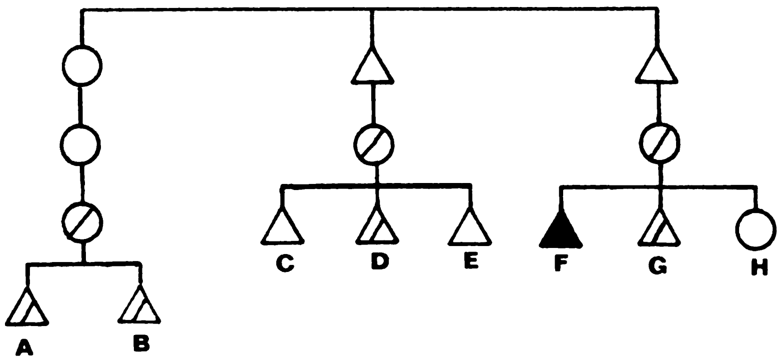



Figure 5.13 Pedigree #1: $Gd^-$ Trait and Favism in Distant Cousins

Child D of the same pedigree has the $Gd^-$ trait, identified upon birth during a routine screening at the hospital, and was re-identified in the present study. His brothers, C and E, were not screened for the trait. The entire family eats fava beans in the fresh form, both raw and cooked, with the exception of Child D. His mother says she cannot allow him to eat the fava beans because of what the doctor told her about the deficiency, however, having the beans in the home places them within his immediate environment. The mother herself also eats the beans, unaware that she is also at risk of favism. She said that the doctor had told her it was her "fault" that her son had "weak blood", but did not realize that she probably should avoid hemolytic agents as well.

In the same pedigree, two brothers (A and B) were identified with the $Gd^-$ trait during the present study, neither of whom has suffered from favism. The family uses fresh fava beans, both cooked and raw. The mother claims she does not give them to the children, but, again, using them in the home puts them within the young boys' environment. The cooked beans are prepared by throwing out the first water, to "take away the poison," as the mother says.

Figure 5.14 shows a second pedigree where only one member was affected by favism, but with two other male relatives identified with the $Gd^-$ trait. The pedigree is joined by marriages to two other pedigrees which will be discussed in the next section. This pedigree was separated from a genealogy with several cases of favism. (Figure 5.16 shows this separation.) In this pedigree (Figure 5.14) all the boys were identified with the $Gd^-$ trait in the present screening. The three nuclear families, represented by the children A, B, and C, all use fava beans in their diet, primarily in the fresh form. The family represented by C uses them in only the raw, fresh form. They claim very limited usage of the beans. In the family represented by A, the fresh beans are used both raw and cooked, with the water discarded. Both of these nuclear families are from the same village, while segment B of the pedigree lives in another village. The child B, who suffered an episode of favism, is not considered as a member of Massari or Kritinea. The family was visited and interviewed about fava bean consumption and the favism episode. They use the beans in the fresh form, even after the episode had occurred. The water is usually retained when the fresh beans are cooked. The particular episode followed the consumption of beans which had been given to the child by a neighbor, unknown to the mother. They had been cooked with lentils and presumably the water had been retained (as it usually is when the beans are cooked with lentils).

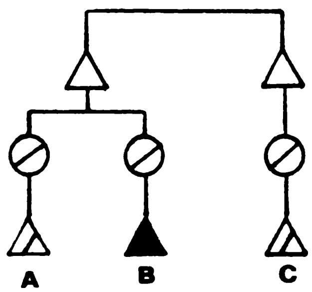



Figure 5.14 Pedigree #2 $Gd^-$ Trait and Favism in First and Second Counsins

The pedigree shown in Figure 5.15 appears in the same genealogy as does the pedigree from Figure 5.14. Their relationship is shown in Figure 5.16. The lack of favism in the line of child B of this pedigree showing two second cousin males, is easier to explain than in the other situations. The nuclear family represented in segment B does not consume the fava beans at all. The father was suspected of having suffered from favism as a child and has forbidden the use of the beans in the home. The episode in Child A was associated with dry fava beans which had been cooked with lentils, the water having been retained. The family continues to consume the beans, with the exception of the one child who suffered from favism.

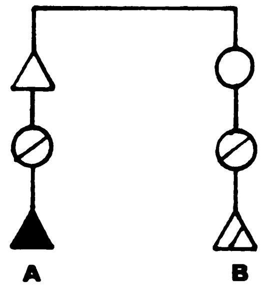



Figure 5.15 Pedigree #3: $Gd^-$ Trait and Favism in Two Second Cousins

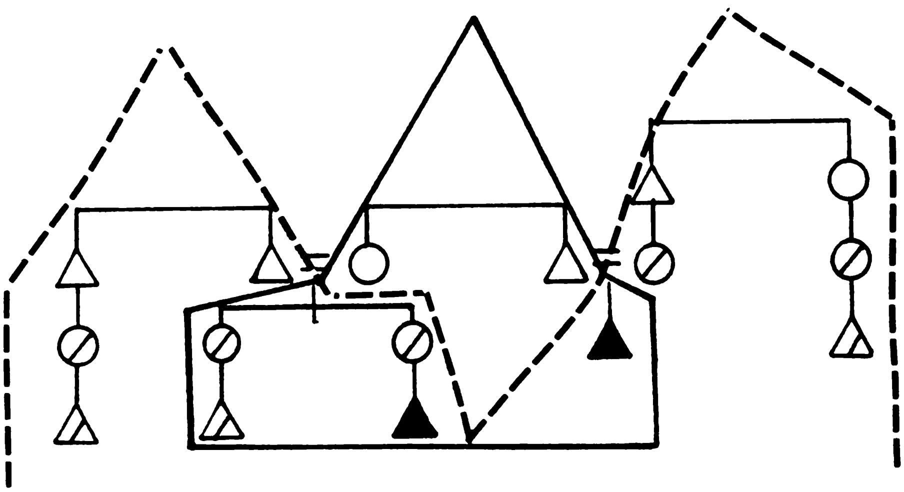


Figure 5.16 Genealogical Links between Pedigrees #2, #3 and #4

### Fava bean use in pedigrees with multiple cases of favism

Three pedigrees were identified which showed multiple cases of favism. The first of these is included in Figure 5.17. The two young boys, A and B of this pedigree, were discussed with respect to Pedigree Two (Figure 5.14) and labeled as A and B in that pedigree also. Child C was discussed in respect to Pedigree Three (Figure 5.15) as child A which was presented from his mother's side. In this Pedigree Four, he appears from his father's side; i.e., both sides of his family have association with the $Gd^-$ trait and favism.

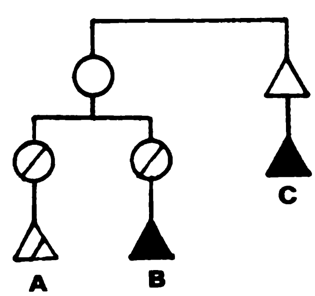



Figure 5.17 Pedigree #4: $Gd^-$ Trait and Favism in Two First Cousins and Their Cousin Once Removed

To recapitulate, child A belongs to a nuclear family which uses the fava beans in a limited amount in only the raw form. Child B suffered from favism following the consumption of dry beans which had been mixed with lentils, as did child C. These two episodes from the same type of fava preparation did not occur simultaneously, but interestingly, they resulted from serving the preparation to the child by a neighbor. Both cases occurred without the mother knowing that the beans had been eaten at all, and in both families, the beans are still eaten by the other members.

Figure 5.18 shows the second pedigree with multiple episodes of favism. Two distant cousins, both females are both affected by favism. These two young women were identified from hospital records not in the screening. This is the only example of two related females showing favism. Both cases followed the consumption of raw fava beans. Fava bean consumption continues in their respective families, although they themselves avoid the beans.

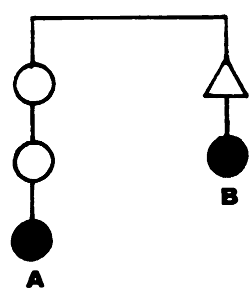



Figure 5.18 Pedigree #5: Favism in Two Female Distant Cousins

Figure 5.19 shows the last pedigree extrapolated from the genealogical data. Here, of five young boys with the enzyme deficiency, four of them suffered from favism, with both brother pairs reporting favism (A and B, C and D). Two brothers, A and B, suffered from favism simultaneously at the ages of three and five. Fava beans which had been frozen (fresh) in the refrigerator were boiled for use during the pre-Christmas season. The water in which they were cooked was not discarded. Brothers C and D suffered favism at different times, the one at four years of age, the other at twelve. Both cases followed the consumption of cooked beans, the

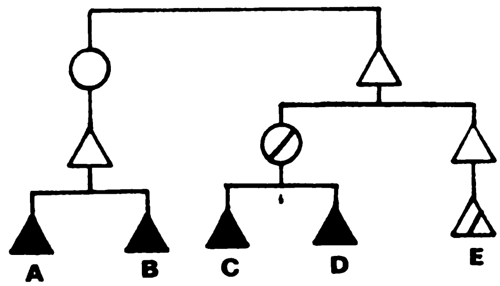



Figure 5.19 Pedigree #6: Consanguineal Relationship of Two Sets of Brother-Pairs with Favism

one from dry and the other from fresh. In both cases, the cooked water had been retained. The twelve-year old boy, E, a consanguineal relative to the two brother pairs was also identified with the $Gd^-$ trait. He has not yet suffered from favism. His mother uses the fresh beans, both in the raw and cooked form, and does not discard the water when they are boiled. Why the family still uses the beans with so many cases of favism in the relatives, and why this child has not suffered from favism even though the beans are used in the family, cannot be answered with the present data. Among other things which might be investigated are the personal habits of the child and children in other similar pedigrees.

Summary, Part III: Familial Favism

The data from pedigrees and $Gd^-$ trait pairs (siblings, cousins, parent-child) support the tendency for favism to occur in certain family lines and not in others, even though the trait circulates in the selected families. In only one of nine sibling pairs, both $Gd^-$ trait, did one child report favism while the other $Gd^-$ sibling did not. Seven of these pairs were from families who consume(d) the fava beans. Three of these reported favism in two siblings; one in only one of the pairs; and three in neither of the $Gd^-$ trait pairs. The three cases of no favism in either sibling of families consuming the beans indicates that fava bean consumption, alone, cannot explain the absence of familial favism.

None of the parents of children with favism in Massari and Kritinea were themselves positively identified as having suffered from favism. Twenty of the thirty parent-child pairs did not show favism in either member of the pair. Sixteen of these pairs were from nuclear families who consume(d) the fava beans. Fava bean consumption patterns between parent and child do not explain the greater number of episodes among the children of a $Gd^-$ parent. In most of these cases, the parent was the mother, potentially showing a greater range of deficient red blood cells than her hemizygous son (see Chapter Two). The reason for the lack of favism cases in the majority of mother-son pairs, many of whom eat the beans, cannot be answered from the present data.

Cousin pairs offered little opportunity to generalize about the relationship between fava bean exposure and genetic inheritance at this degree of consanguinity. Perhaps with larger samples, these comparisons can be made more conclusive.

## Discussion: Directions for Further Research

The research about the distribution of favism in Rhodes has presented some tentative conclusions about the social epidemiology of the disease. In order to investigate these in further research it is suggested that the methodology in this chapter be used to analyze other cases of favism and its distribution. Throughout the analysis, the major difficulty came in the size of the sample, not in the questions asked. Generating a more secure model of risk must involve a larger sample collecting the same sorts of information as gathered in the present study. This would require a follow-up on all the cases of favism in the major mountain and coastal village of Rhodes, with adequate screening of the population in these villages. The comparison of two villages, each representing a different "type" of ecological setting and showing slight variations in social phenomena has provided a base for future research using this same approach.

The differences found in the seasonal and regional distribution of favism episodes are only partially explained by the $Gd^-$ trait frequency and the fava bean production cycle. To follow the model of this study, future research should identify cases of favism which are associated with fava beans consumed during periods of ritual fasting, check yearly incidences of spring favism in relationship to the timing of Lent, and investigate individual and familial fasting behaviors.

While the higher altitudes in Rhodes tend to have higher frequencies of the $Gd^-$ trait (contrary to the literature on this subject), fava bean consumption is also greater in the mountains than in the coastal area. Whether or not this higher level of fava consumption is characteristic of mountain locations, or is unique to Rhodes, should be explored for other Mediterranean areas.

Age appears to interact with season and region with the greatest number of under-five year-old episodes coming from the mountain areas. The majority of pediatric (i.e., under eighteen years of age) episodes occurred after the Lenten fasting period, indicating that the beans are being consumed outside of the home and without adult sanction. Case histories support this. Again, whether or not this is true for other areas of Greece or the Mediterranean is not known, but deserves further investigation.

Distribution by sex was found to be almost equal from the Rhodian data, although more boys under six and more girls and women over six report favism. Possible sex role differences may help account for this distribution. Future research should explore these roles, not only as general models, but by different strata of the society.

Familial tendencies toward repeated or multiple episodes were not supported with the Rhodian data. None of the participants in the study reported repeated episodes in the same person, and only a limited number of instances of multiple favism were reported. Most of these came from sibling pairs, and a few were found in the extended family genealogy. Data collected from families with the $Gd^-$ trait and/or favism episodes, indicates that fava bean consumption in and of itself is not as important as the form (dry or fresh) and preparation (raw or cooked) of the bean which is eaten, and possibly the handling of the water in which the beans are boiled. This aspect of the epidemiology of favism deserves much greater emphasis, as well as the beliefs and attitudes about protective measures. These will be discussed in the next chapter.

One factor which was not investigated in the present study involves relating favism episodes to the socio-demographic factors in families: e.g., the number of children, the spacing, the birth order of the children. Also, other socio-cultural factors could be added to the analysis, such as the presence or lack of help from other villagers and/or relatives in child rearing in the family, and the distance of the family from the members and the extended family. These should be expected to clarify aspects of role behavior in the family, protection of children, work habits, and other similar factors which potentially relate to exposure to fava beans.

# CHAPTER SIX

## AN ETHNOMEDICAL DESCRIPTION OF FAVISM AND ILLNESS PREVENTION

Favism presents not only etiological and epidemiological challenges, but preventive ones as well. The biomedical model, including its extensions of medical ecology and social epidemiology, cannot fully address this challenge without assessing the impact of culture as it affects variables other than those which are defined by medical science. An ethnomedical approach which examines native etiological explanations of illness/disease as well as culturally shared behaviors and ideology which relate or interact with these explanations is well suited for the challenge of prevention. Preventive medicine utilizes both the biomedical etiology and the epidemiological knowledge about a disease in prevention strategies. These are often determined by the creation of laboratory conditions which aid in the identification of etiological factors but which neglect the behavioral dimension which occurs outside the laboratory. Preventive medicine then takes this artificially created model and, ideally, tries to control for as many epidemiological variables as possible, in order to duplicate the laboratory conditions. For example, with favism, at least two etiological factors are identified with others which await discovery and identification as to their etiological impact. In the absence of one or the other, or both, of these factors (the deficiency and fava bean consumption), favism does not occur. Epidemiological variables which are associated with the disease include age, sex, and seasonal patterns of fava-bean consumption. Medical investigators have not often commented on favism as a problem in preventive medicine. If asked, they might state the disease could be prevented if people did not use fava beans, or at least those who were informed of their enzyme deficiency and instructed not to eat the beans. In this way, they would remove one or both of the known etiological factors and would aid in the eradication of the disease.

This characterization of biomedicine and preventive medicine serves to dramatize that the "causes" of a disease are those which the biomedical model defines, and that a strategy of preventive medicine should be expected to follow the same course as implicit in the biomedical etiology. Preventive behaviors have at least two sources. Some result from the dissemination of biomedical knowledge among the lay public, but the majority of them have symbolic content and are usually related to other aspects of culture. For this reason, an ethnomedical approach is of importance. Native etiology of favism rarely coincides with biomedical etiology. It is no wonder that the preventive behaviors are different than those suggested by preventive medicine. This is discussed in the following four sections:

1. Native conceptions and explanations of favism
2. Reasons for continued consumption of fava beans
3. Preventive behaviors and fava beans
4. Preventive medicine and favism.

Popular Conceptions and Explanations of Favism

When villagers in Rhodes were casually questioned about favism (kiamismós), they invariably responded with raised eyebrows or the tilting of the head, gestures which indicate either a negative response or a desire for more information, depending upon the context of the question. They were then asked about "jaundice which often happens in children after they have eaten fava beans (koukiá)." This prompted them to ask what was meant by "jaundice" or to ask, "Do you mean when they become yellow after eating koukiá?" or, "Do you mean when they become poisoned by koukiá?" These initial responses, which usually led to an abandonment of carefully prepared questions in the research protocal, indicated that favism as a biomedical disease was not the same as "poisoning from fava beans" as an illness. Disease is an operational concept central to the biomedical model. While disease may or may not have meaning for the individual affected by it, it has a standardized meaning for physicians and other medical personnel (e.g., diagnosis, treatment, prognosis, etc.). Illness is a cultural, and consequently symbolic category, which carries with it certain attitudes, behaviors, methods of treatment, which are not always considered by medical personnel.

The initial reactions to my questions about favism stimulated at least two further questions:

1. How does the description of favism as a medical disease compare with the Rhodian conceptions of favism (and/or poisoning from fava beans)?

2. What part does the popular conception of favism play in the over-all scheme of health and illness?

## Two Etiologies of Favism: Biomedical and Popular

As has been repeatedly mentioned, biomedical diagnosis of clinical favism relies on two etiological factors: the enzyme deficiency and the consumption of fava beans. Popular etiology relies on only one of these, the consumption of the beans. Following statements such as those reported above, where it was clear that favism was expressed as a reaction to poisoned beans, other questions probed for additional "causes." Most said that there was something wrong with the particular beans which had been eaten preceding an attack; that not all beans were at fault, just some of them. Other responses included, "My neighbor shouldn't have given my child the beans," or, "The children ate the beans when I wasn't watching," and "People who have a weak constitution shouldn't eat the beans." Aside from the richness of these explanations from the cultural point of view, they indicated that the major etiological factor in favism was the fava bean itself.

When asked about the factors which might make the beans "toxic" or "spoiled" (halasména), the informants suggested that it was either the growing or the storage conditions which might play a role. Some stated that beans grown in a field where iron was rusting in the ground were sure to be poisoned. Others said that certain beans may become affected by mildew under damp storage conditions which in turn affects people. They said that for this reason, the beans should be inspected individually before cooking, to make sure that they do not contain any unusual marks such as spots which indicate that they had been infected by a small worm or larve, or show signs of mildew. Some stated that the toxicity of the beans can be reduced by cooking procedures or cutting off portions of the bean. If a name for the toxic factor in the beans was used, it was always given as cyanide; that is, those who were <u>able</u> to give a label to the poison in the beans (not many) unanimously agreed on cyanide. This, they said, was present in all the fava beans, but some had a greater amount than others, and this is why people became "poisoned by fava beans." These ideas are not limited only to the rural populations of Greece. They also circulate in urban areas, in fact an article in a recent woman's (1978) periodical wrote that fava beans contain potentially dangerous dosages of hydrocyanide (<u>hydrokíanos</u>, sometimes translated as hydroprussic acid) which may seriously poison people. Aside from attributing the dangerous chemical in the beans to one which has not been mentioned by medical science, the description of the ways in which the poisoning might take place, or the symptoms which would be expected, were not described.

Even though the bean is the central factor in the popular etiology of favism, villagers often hesitate to state to medical authorities that the beans were consumed. The following cases illustrate this point, although they are not the only ones which involved hesitance to report fava bean consumption.

Case One: Favism was diagnosed in one of the four male children in this nuclear family of six in December 1970 when the child was four years old. At the time of the interview, he was eleven but did not remember any explicit details of the episode. The child was also identified with the $Gd^-$ trait during routine screening of his village in the present study. Two of his older brothers were also tested for the trait and reported to be normal.

The episode in this child followed the consumption of dry fava beans which had been cooked together with lentils. He began vomiting within thirty-six hours after eating the beans and within forty-eight hours he had become jaundiced. Shortly, thereafter, he presented hemoglobinurea, and was taken to the hospital where he was given blood transfusions.

The father reported the episode in this way: "Once my son was poisoned by fava beans, but I didn't recognize it at the time. All I knew was that he was very sick, with vomiting and the color of yellow. His urine also turned black and this is when I took him to the hospital. His mother was also in the hospital at the time for an operation. My neighbors and relatives had been taking care of the boys and this is why I didn't know he had eaten fava beans. I only found it out later from my neighbor women who had given him the beans. At the hospital they didn't ask me about the beans and even if it might have crossed my mind, I didn't say anything about the possibility that someone might have given them to him. I guess I thought if they didn't ask me, why should I tell them?"

Case Two: Favism was diagnosed in a young girl of eleven who participated in recalling the episode for the study. She had eaten fresh fava beans from the fields and remembered that she also had eaten a very large quantity of the beans. The following day, she began vomiting and developed a high fever. The local physician attributed these symptoms to tonsilitis, which she had had prior to eating the beans and developing the hemolytic crisis. The vomiting continued, the young girl was unable to eat anything, and the following day, she became jaundiced showing hemoglobinurea. She remained in this condition for another full day, still believing she had tonsilitis. On the following day, she was taken to the hospital where she was transfused. She was tested for the deficiency at the same time, and upon positive results, she was finally asked about fava bean consumption.

The young girl herself added these comments: "It seemed like I did nothing but vomit for three days. I couldn't do anything. I thought at first that it was because I ate lots and lots of fava beans, but the doctor kept saying it was from my tonsils, so I didn't tell about the beans. I was really surprised when they asked me about eating the beans at the hospital and even more surprised when they said I was sick from the beans."

Case Three: Favism was diagnosed in a five year old boy on the Wednesday preceding Easter Sunday following the consumption of dry beans which had been boiled. He was initially taken to a children's clinic in the City of Rhodes where hepatitis was diagnosed, however, the attending pediatrician requested blood analysis for the deficiency, directing the famiy to the main hospital. Here the deficiency was identified. Only at this time was the family asked about fava bean consumption preceding the hemolysis.

The mother tells the story that, "I knew I had fava beans in the kitchen -- we were eating them for Holy Week. When I saw my son turn yellow, I had a thought he might have taken some beans without my knowing. I never gave them to him, but he might have taken them behind my back. Well, when we took him to the doctor he said it was probably hepatitis. I didn't want to tell about the beans since I wasn't sure. After his blood was tested and they had given him transfusions, they asked my son about the beans. He said that he had eaten them."

Symptoms and Their Meaning

Native conceptions of the symptoms of "being poisoned by fava beans" (dilitiríasi ápo koukiá) are also different from those of clinical hemolytic favism. While fava beans are considered in the native etiology of favism as they are in biomedical etiology, the hemolytic crisis which marks medically diagnosed cases is not always a major concern to the lay-public. Dizzyness, inability to get out of bed, possible and actual coma, and prolonged vomiting were also considered very important in the cases which involved reactions to the fava beans. While these are associated with the effects of the hemolytic crisis in biomedical etiology of favism, these are symptoms which are also associated with other disease and with food poisoning as a more general category.

While jaundice is among the most important symptoms of favism in the biomedical model, it is not so in the epidemiological one. Reactions to the fava bean are not always associated with the presence of jaundice, according to the statements from the people of Rhodes. Anemia and jaundice are often confused with each other, jaundice and hepatitis are also often interchanged, and poisoning from fava beans are seen no more serious than food poisoning from other causes. These illness conceptions are shown in Table 6.1.

As the Table shows, these illness categories which appear in the conceptual framework of the rural medical system, have points of convergence. For example, all five illness conditions may involve palor, most involve dizzyness, and all but anemia involve yellowing in color. Even anemia is sometimes confused with the terms used for jaundice, and it is said that both anemia and jaundice are "when the blood becomes like water," and the person has a terrible color. Anemia, poisoning from fava beans, and general food poisoning, are all associated with consequences from food.

### Yióktéros and Krísi (jaundice)

In the ethnographic literature for Greece (e.g., Blum and Blum 1965; 1970; Mills 1948), jaundice is usually listed among the "folk illnesses." It is classified as such by using the criteria that the people themselves do not believe that it can be effectively

TABLE 6.1

NATIVE TERMINOLOGY FOR CONDITIONS RELATED TO FAVISM

| Illness | Symptoms | Cause | Therapy |
|---|---|---|---|
| Anamía (Anemia) | "blood like water" dizzyness, palor | Not eating the right foods | Vitamins with iron Eating a "better diet" |
| 'Ikteros (Jaundice) krisi Yiokteros | palor, yellowed skin yellowed eyes | Something is wrong with the liver Fear (trómos or phóvos) | "cutting the jaundice" |
| (ipatítida) (hepatitis) | yellow skin, yellow eyes | caught from others playing in an unclean area | bedrest or hospitalization a diet of tea and boiled greens |
| dilitiriasi apo koukiá (poisoning from fava beans) | dizzyness, gastric distress vomiting, fever, palor, coma yellowed skin and eyes, red to black urine | spoiled fava beans too much fresh fava eating fava beans with a high level of poison | for mild case, bed rest for severe case, hospitalization |
| dilitiriasi apo fagitó (food poisoning) | dizzyness, gastric distress vomiting, diarrhea fever, coma, palor, yellowing | spoiled foods eating too much of one type of food eating heavy food late in the evening | for mild case, bed rest for severe case, hospitalization |

treated by a physician. While this idea still circulates in Rhodes, people also accept that jaundice can also be treated by a physician. The separation of diseases into biomedical and folk does not have much utility because diseases always have multiple etiologies, mixing the cultural (e.g., folk, popular, traditional) with biomedical explanations. The idea that some diseases cannot be treated by physicians indicates that an etiology outside the realm of cosmopolitan medicine should be uncovered. This has not been explored in either the Greek or the Mediterranean literature with respect to jaundice, yet it perpetually appears in the list of "folk diseases."

Villagers in Rhodes state that jaundice can be associated with poor health and hepatitis. Most mothers and women of child-bearing age find it a rather normal consequence in the newborn. In this way, their etiological concepts approximate those of cosmopolitan medicine, but at the same time another factor is not only associated with jaundice but is believed to cause it: the factor of fear. This may be extended to anxiety and other severe psychological stress but not extended to include anger or rage. Most often, the fear is the result of a sudden, abrupt movement which results in acute fear. The event is not described to be as a swift one (e.g., a surprise in the dark), but one which is accompanied by a sense of pressure.

In spite of additions to the etiology of jaundice from cosmopolitan medicine, some still believe the most important and effective cure for it is the traditional "cutting the jaundice". This procedure was described by Blum and Blum (1970: 135 and 143) and the current practice remains the same. It involves making a small cut in the labial frenum (the flap of skin joining the upper lip to the upper gum line of the mouth), followed by making a cross over various parts of the head, such as over the ears, forehead, and behind the head. Only certain people know how to cut the jaundice and others who attempt the same cure will not be successful. People claim that even though a physician can help with curing jaundice, the most sure way is to have it "cut" by the local practitioner.

Not all types of jaundice must or should be treated by "cutting the jaundice", according to the people in Rhodes. Jaundice which occurs in newborns is now treated in the hospital because nearly all the births on the island take place either in the maternity clinic or the general hospital in the City of Rhodes. No one advocates bringing in a local practitioner to cut the jaundice of a newborn; if the jaundice is severe enough, the child will be flown to Athens for treatment. Jaundice in newborns is so common in Rhodes that the people accept it as part of the first days of life. Some even say that if the infant passes through jaundice as a newborn, he will not suffer from it as an adult.

Jaundice, and different degrees of "palor" and yellowing, in children is always taken as a sign that the child is not well. There is a fine line between "palor" and jaundice in terms of assessing the hue of the complexion, and seeking the help of a physician has to do with the accompanying symptoms as well as the extreme end of the color change. Parents will complain continually about the color of their children's complexion, associating it with "lack of appetite," and often stating that the child must surely have anemia or be on the verge of jaundice. Jaundice in the absence of other noticeable signs is usually not immediately taken to the physician; it is often viewed as a condition which will cure itself, like a fever. If there are other symptoms, such as extreme lethargy, vomiting, or coma, a physician will be sought. Some of the cases of favism in the present study were not immediately taken to the physician even though jaundice was clearly present.

Adult jaundice and hepatitis are used interchangeably by many, and it can be said that jaundice is considered as an illness condition (and a disease) in and of itself, as well as a sign of something being amiss as indicated above in the discussion about jaundice in children. Jaundice is recognized to occur in the population in conjunction with other illnesses. Perhaps for this reason, the jaundice which accompanies clinical favism is not considered to be the crucial marker of favism, but rather a consequence of the general debilitation which results from eating poison fava beans. This same sort of reaction is believed to be possible from consuming other foods which have spoiled or have poisons in them. Appearing jaundiced (_kitriníso_) is accepted as a consequence of different illnesses, as fever is considered a symptom of infection in biomedicine. One can become jaundiced, yellowed, or paled from eating bad food, from excessive vomiting, from a weakened condition of the blood which has resulted from (e.g.,) being over-tired, and from not eating enough. In short, reactions to fava beans are not always linked with jaundice in the popular ideology. When they are, jaundice is not considered the crucial symptom in determining whether or not one has been poisoned by the fava beans.

Delitiríasi ápo Fagitó
(food poisoning)

In many respects, poisoning from fava beans does not differ from other forms of food poisoning. Foods often blamed in poisoning include mushrooms, watermelon, and a variety of fruits. Poisoning may result from eating either a "bad" mushroom or fruit, or eating too much of one type of food. The same scheme applies to fava beans. In cases of poisoning, whether from fava beans or other foods, mild and severe poisoning are differentiated from each other. Mild forms include dizzyness, gastric distress, mild vomiting, and such cases usually do not come to the attention of the physician. Severe cases are reported to the local doctor or the hospital, and these involve severe vomiting, coma, possible palor and yellowing, and in the case of reactions to fava beans, jaundice and discolored urine.

In addition to food poisoning, certain foods are considered to be heavy and should not be eaten by those with gastro-intestinal problems, those who are not in good general health, and should not be consumed late in the evening. Beans, particularly dried beans of all sorts, fall into the category of heavy foods. At times, people will complain that their stomach has been "spoiled" or "ruined" by beans (hálase to stomáhi mou), and the beans are specifically blamed for this, even though clinical favism is not involved. These cases do not receive attention as episodes of favism, however, adults with the enzyme deficiency have reported such reactions to fava beans, but have not reported them to a doctor.

Judging from the number of hospital cases of favism, and the clustering of these cases within a two-month span each year has made it easy for native population to recognize favism as a seasonal illness. For centuries, the local inhabitants have accepted the possibility of fava bean poisoning as part of the yearly cycle. Because it tends to occur most often among children, it is conceptually placed along with other childhood diseases, and while it is a cause for concern, it is not taken any more seriously than are measles or mumps. These other childhood diseases are almost always taken to the general hospital in the City of Rhodes, which has a special section in the Pediatric Clinic for the infectious childhood diseases. Parents do not usually want to treat these childhood diseases in their home, and their decisions to hospitalize their children during the disease are usually related to the type of home they live in. Their reasons to hospitalize the child may include, (1) lack of water in the home, (2) no heat in the house, while the hospital is warm, (3) too many other children (either the siblings or cousins) in the home area where the sick child needs to be cared for. When a child is in hemolytic crisis, favism is dramatic; however, the seasonal and chronological configuration of favism episodes allows its acceptance as part of the natural yearly and life cycle, rather than as a disease which causes great alarm. Some even claim that, as with other childhood diseases, it is better to pass it in the younger years of life than to wait until an adult. As a childhood illness, then, it is not something which must be hidden and it does not carry any social stigma with it. Further, since these cases are believed to have resulted from something wrong with the beans, not the individual, there is not personal threat if the illness is reported.

From the ethnomedical point of view, the illness of fava bean poisoning is not equivalent to the medical diagnostic category of favism as a disease. Most notably, jaundice is not always present in cases of bean poisoning; more often than not, the bean rather than some inherent trait of the individual is blamed for the reaction. The acceptance of the illness in this light, along with some conceptions of protection through precautions in handling and cooking the beans, partially explain the continued consumption of the beans.

## Reasons for Continued Consumption of Fava Beans

Since the fava beans play such an important role in the popular etiology of "fava bean poisoning," the logical question follows: "Why are the beans still eaten?" The previous discussion showed that, with respect to other illness and instances of food poisoning, the fava beans are no more or no less dangerous than other foods commonly associated with food poisoning. Other hypotheses which may account for the continued consumption of the beans are reviewed here. They can be organized into three categories: ecological arguments, socio-psychological ones, and cultural explanations.

## Ecological Arguments for Fava Bean Consumption

Ecological explanations for behavior rely on the concept of adaptation, analyzing what goes on in the man-nature interchange with culture as a mediator which either promotes or eradicates a particular practice or trait. Assuming that the "real" reason for a practice has been lost in symbolic behavior, the cultural reasons for particular behaviors are not recognized or given credit by those carrying out the practice. It is possible that at some point in time, a rational decision was made from epirical observation, but that through time, the cultural content has obscured this reason for the actors. The ecological position gives rationality to cultural phenomena by examining behavior from history and adaptation. Using this argument, two suggestions can be generated with respect to the use of fava beans: (1) The bean has nutritional advantages which promote its consumption; and (2) An economic necessity exists for its production and consumption.

### Nutritional advantage argument

Since fava beans are rich in essential nutrients, particularly protein, it is suggested that in a situation of otherwise low protein diets, the beans were selected and perpetuated in usage. Those who ate the beans and were able to tolerate them outnumbered those who had hemolytic reactions to them, and were thus conferred adaptive advantage in the course of history. Noting that the beans were probably a very early cultigen in the Mediterranean in general, and that a mixture of lentils and fava beans was used to fortify athletes in Ancient Greece, this argument is credible. Consciously or not, the bean was then retained in the diet and as a central crop.

It has been more recently suggested (Katz, unpublished abstract) that since both the fava bean and certain anti-malarial drugs can cause hemolytic crisis in enzyme deficient individuals, both may contain some similar pharmaceutical agent which has antimalarial qualities. The fava bean was possibly eaten to prevent malaria. While those eating the bean were protected from malaria, those with the enzyme deficiency suffered reactions to the beans which at some times included death. Subject to hemolysis, their numbers are hypothesized to not have comprised a sufficient percentage of the population to promote abandoning the bean as a natural anti-malarial drug; neither was their loss significant in terms of the beneficial effects of the bean in combating malaria. As recognized in ancient writings, malaria was a source of concern which may have prompted seeking natural and fabricated cures and preventive substances. No where is the bean mentioned as one of these substances in folk lore or ancient medical writings which have been reviewed to date. This is not crucial to the ecological argument, because adaptive traits, both biological and behavioral are not personally or knowingly selected for in adaptation models.

## Economic necessity argument

Regardless of the reasons for the presence of the beans in the ancient populations, they were retained in the diet to the present day. Due to their biological characteristics which include easy mutations, and cross pollination, and forms of the beans which can be used for animal and human consumption, the fava plant fitted well with neolithic ecology. Being easy to grow and harvest, requiring little care, and maturing rapidly at a time when other garden crops are not available, the fava beans have economic advantages. It has traditionally been a cheap crop when sold on the market in comparison to other pulses and legumes. For this reason, perhaps, it is associated with the urban poor as well as rural inhabitants in some parts of the Mediterranean.

The beans also grow from one year to the next without human intervention. As the stalks and pods dry out, the beans drop to the ground, lie dormant during the dry summer and begin to grow during the rainy winter months. In this way, they are ripe again in the early spring, along with the other beans which were purposefully cultivated. The population could not logically abandon either the cultivation and use of the fava beans.

The economic importance of fava beans in present day Rhodes is minimal, even though they were extremely important before 1950. The older people in the villages remember a time when they had little else to eat but potatoes and different types of beans; this diet has changed drastically since the end of the Second World War. Other cultigens now have greater importance in both the household and cash economy of the villages. The climate, and the promotion of irrigation agriculture during the Italian occupation of Rhodes (until 1947), allow for the production of a wide variety of garden and cash crops. The beans are not grown in Rhodes as a cash crop as they are in other areas of Greece where they are marketed not only fresh, but dried and packaged. In Rhodes, fava beans are grown entirely for individual household use. They were never grown for export and their production has been drastically cut back since the end of the Second World War. Finally, wealthy families consume the beans, as the following case history shows, just as much as "poorer" families.

> Case Four: Favism was reported in a girl, five years old, from one of the predominant, non-agricultural families in the village. Her father has finished a university education, has a non-agrarian position, and has land holdings in the village which are worked by others since his own work takes him out of the village for most of the year. His family accompanies him, which means that he holds not only the house in the village, but another as well. His oldest child was entering medical school at the time of the study, and the others were pursuing education beyond the usual 6th grade level which is the norm for the rural areas.
>
> The little girl had eaten the fava beans during the week preceding Easter, and within 24 hours she began presenting the classical signs of favism. The following day she was taken to a nearby town where the physician examining her concluded that she had been "poisoned by fava beans" and prescribed a diet of tea, suggesting that the crisis might pass by itself. The following day, she was hospitalized for blood transfusions, even though the hemoglobinurea showed signs of remission.
>
> The family still consumes the fava beans, only when fresh. They are usually prepared by boiling the beans with wild greens, and served in a salad form with lemon, olive oil, and garlic sauce. The family members all eat the beans, except for the young girl who had been affected by favism. They do not express any any concern that they, too, will be "poisoned by the beans."

## Socio-Psychological Reasons for Continued Bean Consumption

Two socio-psychological suggestions are made with respect to the continuation of fava bean consumption. The first relies on a general "national character" type of explanation, that of "Mediterranean fatalism" which is often discussed in the ethnographic literature of the areas. The second, the model of risk taking, is drawn from social psychology.

### Mediterranean fatalism

Mediterranean peoples are often depicted as fatalistic, a characteristic which is called upon to explain a variety of behaviors, which seem to be calculated on the basis of luck. Given the attention which Mediterranean fatalism attracts in the ethnology of Greece (e.g., Blum & Blum 1970), one might hypothesize that it has a central role in the continued consumption of fava beans. Some have suggested that fatalism play a role in the lack of preventive medicine, works against a "preventive mentality", and promotes the acceptance of illness as "part of life." Further, fatalism makes preventive medicine difficult to implement because people operate on a principle of chance.

Whle it is true that phrases such as "Thus is life," and "What can we do" (étsi ein' y zoí and ti na kánoume), accompanied by a helpless hand gesture or shrug of the shoulders, are heard on a daily basis in Rhodes, they are not necessarily reflections of fatalism and futility. It must be argued that the pervasiveness of these expressions of futility are not carried out in actual behavior. The widespread use of them does not reflect the reality when it comes to taking an active part in one's fate or destiny, when humanly possible, and even at times when it appears impossible. Fatalism sets in only when the situations are, in perception or reality, out of the hands of the person, and this point is not easily reached for the Rhodian. Until this point is reached, a wide battery of behaviors which are directly manipulative and culturally encouraged are employed in order to reach individual, familial and/or social goals. Bargaining, threatening, making secret deals, and even outright lying are all used to manipulate social relations. As often as one hears fatalistic expressions in the village, one sees the opposite behavior. Contrary to the picture that these expressions of fatalism provoke, the reality is that Rhodians (and Greeks in general) do not sit passively awaiting any situation.

With respect to illness, even after it has passed a considerable course, wide varieties of therapy are still sought. The same people who vocalize the phrases suggesting futility are the very same ones found waiting for the agrarian physician on the weekly visit to the village. Whether or not they follow all his advice, they eagerly await modern pharmaceuticals which he delivers to them (preferably in injection form).

The continued consumption of fava beans should not be construed as a manifestation of a fatalistic mentality, if, in fact, one exists. Rather, the erratic nature of favism, well-documented in scientific literature, plays a decided significant role in the "fatalistic" consumption of the beans. Moreover, it should be emphasized that cultural traditions resist change: Why should one change a long-held behavior simply because scientists and physicians have an etiological model which is still baffling?

### Risk taking and consumption of fava beans

It has been suggested that individuals and families which continue to consume fava beans, even after episodes have occurred in the village, might present a certain social profile. For example, they might represent a sector of the population which is described by the use of socio-cultural variables such as occupation of the household head, exposure to non-Mediterranean society through out-migration, educational level of parents, and so forth. Included in these variables, one might add from medical histories, number of childhood illness, number of accidents, and use of pharmaceuticals. This approach would resemble that used to identify suicide prone individuals, potential alcoholics and/or substance abusers as they are in other studies where certain indicators such as economic status, number of life traumas, out-migration, mobility, etc., are used. There are some weaknesses in applying the model to the present study.

First, the application of the model requires an adequate sample which is socially heterogeneous, but where knowledge of the interaction between the enzyme deficiency and fava beans is homogeneous (or at least the interaction of an inherited tendency and fava beans). The present study used small samples from each village, which in themselves were small and relatively homogeneous, but with individuals who displayed a heterogeneity in understandings about favism. For example, families which continued to eat and grow the beans were primarily agriculturalists, however, the majority of all the families in the study were agriculturalists. Bean eating is more a factor of exposure than of risk taking that can be associated with a particular occupational category. Further, whether or not the beans are grown by particular agricultural famlies, they are likely to have members which come into contact with the bean in their daily routine than families who do not work in the fields.

The model also carries the assumption that all individuals have the same level of knowledge about the bean and its effects regardless of how heterogeneous they might be in other socio-cultural characteristics. From the field work and interviews in the present study, this is not the case. The people with more years of formal education showed greater interest in the enzyme deficiency and its relationship to inheritance and even blood chemistry (some of the people in the study had sons and daughters who were hoping to go to medical school). Others had no interest in any of the medical explanations about favism, but, one thing was clear: these different people had different levels of knowledge about the reactions to fava beans to begin with. That is, one might be vaguely aware that fava beans can be related to jaundice, while others say that they are a heavy food and might only upset the stomach. Others remember a distant relative who was poisoned by the beans, and others neglect to recount that a first cousin was affected within the last five years. With the variety of understandings about the beans, and the familial tendency to show favism, the members of the adult population cannot be considered equivalent to each other with respect to their understanding about favism. Continued consumption of fava beans cannot be attributed to risk-taking in those cases where the level of knowledge does not approximate a reasonable standard. The measure of the tendency to take risks therefore becomes confused with lack of knowledge.

Families were divided into those which had migrated out of Rhodes and had returned to their village, and those which had not left the village. It was hypothesized that those which had left would have stopped eating the beans, not willing to take a risk in developing favism. This did not reflect itself in the data. Some of the families had continued to eat the beans even outside the country, finding them in a canned form or growing them in their own household garden in Australia, Germany and other countries. Others had stopped eating the beans during their absence, but recontinued upon their return. Only one returning family did not eat the beans, but they had abandoned the use of other beans in the diet as well, due to intestinal problems in the head of the household. No thread of commonality could be found among the migrants which would explain their variety of consumption patterns.

Using other variables became tautological, for example, more agriculturalists ate the beans, but agriculturalists have more opportunities to come into contact with the beans simply by virtue of their economic activity. Those with higher educational levels tended not to eat the beans, but they were not usually agriculturalists, and they also used a greater variety of other preventive behaviors. It is difficult to conclude that their avoidance of the beans is due to low level of risk-taking, or if it is an outgrowth of a preventive attitude which coincides more with the medical models of prevention.

On the basis of the available data, the application of the risk taking model further was abandoned, not only because it became increasingly tautological but because it classifies continued bean consumption into a behavioral mode which is "irrational." It assumes that it is more rational and less risky to not eat the beans than to eat them, and avoids considering other more important social and cultural realities.

## Using a Cultural Argument

From the present study, neither the ecological nor the psychosocial arguments to explain continued fava bean consumption could be supported. A fuller, more integrated, cultural examination of why fava beans are still grown and consumed looks at the matrix of production and consumption patterns for other foods as well, and as the activities are influenced by: (1) Time in terms of seasons and traditional celebrations; (2) Patterns of taking and offering foods; and (3) Food use in familial settings.

Time: Seasons and celebrations

In Chapter Five, the inter-scheduling of the agricultural cycle with the religious calendar was discussed. This is reintroduced here to emphasize how the "appropriate" time for the use of certain foods is important in Greek society. In all rural areas, food consumption patterns are influenced by the seasonal availability of cultivated crops and domesticated livestock. This seasonal distribution is supplemented by hunting and gathering activities which most often take place in the winter months. Other foods are preserved for consumption at later times in the agricultural cycle.

Gathering and preserving activities are carried out by women and young girls. In the winter they are occupied with gathering wild greens, in the summer, with gathering for teas and spices (e.g., camomile and oregano). In the summer, they work together to clean and preserve foods which will be used later in the winter. At this time, many jars of sweets, and preserved fruits are processed in the households which include orange rinds, grapes, and small eggplants. Tomatoes which are abundant and very ripe by the end of July are preserved whole or made into tomato paste. This paste is left to dry in the sun. The sun is also used to dry a number of other fruits and herbs, including raisins, wild oregano, garden mint leaves, grape leaves and assorted beans. A mixture of goat's milk and wheat is spread out to dry in the sun. The small pieces of this mixture (<u>trahana</u>) will be used later in the winter by mixing them with hot water to form a warm cereal-type meal. These foods which are preserved during the summer are not usually used at this time, even though they are available. They are not considered to be appropriate foods for the summer, and there are other types of agricultural produce available.

The summer diet is composed of other foods, particularly a wide range of vegetables and fruits. The vegetables are often boiled separately or together and served with olive oil and lemon. A common dish at this time uses egg plants, potatoes, garlic and tomatoes, which are all boiled together in water after they have been fried first (partially) in olive oil. Vegetables may be completely fried in oil, for example zuccini squash, egg plant, potatoes and green peppers which may form an entire meal. Meat and egg consumption is generally lower during the summer months, than it is during other times of the year, with fish consumption higher in the coastal villages. The people believe that meat is more appropriate food for the winter months than the hottest months of the summer. Eggs in particular are avoided during the summer, as they may cause pimples and skin rashes. Summer salads of tomatoes and cucumbers are eaten every day. They are served with olive oil; vinegar is not mixed with the salads containing tomatoes since the two are not considered a healthy mixture. Various vegetables may be prepared by stuffing them with a rice and meat mixture; these are rarely consumed during the winter months.

The winter diet consists mainly of greens, soups, and a larger quantity of meat than in the summer diet. The greens and the meat are both homegrown/domesticated or wild, and are often cooked in soups or with a heavy red-tomato and olive oil sauce. Both of these preparations are absent in the summer diet. Various dried beans and pulses which were left from the summer harvest or bought in the local grocery, are consumed from one to three times a week in most families during these winter months. These include fava beans, lentils, white beans of several sizes, and are rarely, if ever, consumed in the dry form during the summer. <u>Pátsa</u>, a traditional soup made from the parts of either the goat or pig head, is served during the late autumn (October) and winter months, which, again, is not part of the summer diet. Salads in the winter are made from thinly sliced cabbage, or from boiled cauliflower, beets, greens, all which are served cold or lukewarm, with olive oil and lemon.

One of the year-round items consumed in Greece and Rhodes is olive oil. It is used every day for fresh vegetables, soups, meat dishes, fish, and even may be swallowed in the spoonful once a day in the morning by some of the people. (Some swear by this as the best way to insure good health, particularly with respect to the gastro-intestinal tract.) Only during certain fasting periods are preparations using olive oil avoided. The oil is very special when it is freshly pressed in November and December. At this time it is used in a special preparation called <u>alévria</u>, where the oil is combined with onions (both are fried together), sugar is added with flour to make the mixture into a cream which is poured over bread. The heaviest oil which is pressed from the olives is used to keep the light before the ikons burning in the church and in the family devotional corner or the home. The oil is used as a flamable substance, where a small amount of it is floated on the top of water, and a wick in a cork floated on top of the oil.

Social custom requires that certain foods be consumed or offered during special holidays and celebrations of birth and marriage, and rememberances of death. Easter is celebrated by the slaughter of lambs for feasting (and on August 14th and 15th). Christmas is marked by the slaughter of pigs for the period of feasting which lasts until January 7th. During this same period of time, the intestines of the hogs are stuffed with spices and meat pieces to make frankfurter-type loukánika. The predominant sweet at this time is the cookie covered with powdered sugar, kourabiédes, which is also served at other times of the year, but most prominant at Christmastime. Name day celebrations involve the feasting on foods which are seasonal, but involve sweets which have been preserved all year or baked especially for the occasion. To refuse food which is offered during these celebrations is considered an affront to the one being honored at the celebration. Formalized engagements involve the distribution of sugar coated almonds; baptisms and weddings also distribute these almonds. People are invited to weddings by the sharing of sesame and honey cake confections; deaths are remembered by the distribution of a mixture of raisins, wheat, pomegranate seeds and mint (kolíva). This preparation is often involved in epidemics of food poisoning, which occur following a memorial service, yet it is always used at the memorial service and no one expresses the thought that the practice might be abandoned to avoid these health problems. As another contrasting example, many cases of poisoning from mushrooms occur each year. These are from mushrooms which have been gathered from the mountains during the winter and are of a poisonous variety. People have a fear of eating _all_ mushrooms fresh, canned or cooked, or in prepared dishes. Some have expressed awe that tourists are so willing to eat mushrooms on pizza (a fairly new business in Greece), or that I myself wanted to use them in my own cooking. In the supermarkets they are available, specially grown in hot houses, but the public avoids them, believing they might be of the poisonous type (in spite of the reassurances of the shopkeeping that they are grown under controlled conditions). The fact that koliva is continually used in ritual without fear, while mushrooms are purposely avoided, is an example of the paradoxes in the ways that food is used or refused.

### Hospitality: Taking and offering food

During celebrations and visits to households, it is not only the specific preparations which are important, but the way in which they are served which is critical in maintaining proper social relationships. Guests visiting a home for the first time are always welcomed by the offering of a sweet, confection, liqueur, or whatever else is on hand. A stranger to a home remains a stranger until food or drink is offered to and taken by him. To refuse the offering means that the hospitality is refused, or the holiday being celebrated is ignored. If one is unable to eat what is offered, a small piece must be taken, placed in a napkin and taken from the home of the family which has offered the gesture of hospitality. (Since cooked preparations of fava beans cannot be wrapped up in paper napkins, this almost forces the person to take at least a small portion and eat it on the spot.) Excuses for not partaking in an offered food may be expressed, but cannot be acted upon without evoking offense. One may claim dieting, or problems with teeth which make eating sweets painful, or claim that food does not sit well on the stomach, but these protestations are overridden and the person is urged to take "just one." In this context, it is not easy to forcefully admit a weakness about fava beans (if one is known) or to refuse them on these grounds.

Informal rules of hospitality also apply between neighbors. These call for the sharing of food when another woman neighbor is unable to cook for her family. She may be sick herself, or be out of the village attending to a sick child in the city hospital. When children wander into neighboring houses or courtyards, they are usually offered food, particularly if the family is sitting down to a meal. In the latter case, the child may be invited to share the meal with the family. The same holds true for hospitality extended to adults when they visit neighboring villages.

Husband-wife roles: fava
bean use in households

Fava bean consumption in families is related to what the homemaker chooses to prepare. Even though she is the guardian of the family diet, her choices of foods and recipes rest strongly on what the head of the household wants. If he has a desire for fava beans in different preparations, his wife will, of course, cook them for him, even if she herself had a former episode of favism. If the husband does not want to eat the beans in any preparations, whether for reasons of intestinal difficulties or a prior episode of favism, his wife will completely delete them from the family's diet, and will most likely not have them in the house. She may be given the beans in a preparation from a relative or neighbor, or take the ripe beans from the field and eat them while away from her husband, but she will not eat them or use them while in the home. At least three families in the present study showed this type of situation. One of the three was among the families which did not eat the beans at all because the father or the children (one with the enzyme deficiency) forbid the consumption of the beans in the house. In another family, only the raw beans were eaten because the father cannot tolerate the beans while cooking. In yet another, the father had also forbidden the use of the beans in the house, not only because he found the smell offensive, but he had suffered from favism as a child.

From this, it may well be that fava beans are used or not used in families under the direction of the male head of the household. Even in families which had reported favism in a child usually continued to eat the beans unless the father specifically forbid their use. This role of the male head of the household is played out in other health-related matters. Women were often eager to participate in interviews and informal conversations during the field work for this study, but were sometimes "protected" from doing so by their husband. A handful of families did not participate in the study because the husband refused to have an outsider investigating the health status of his family members. Other husbands expressed a desire to be present during interviews, and/or their wives were reluctant to answer questions without the husband being present. Health interests of the family are taken care of by the woman within the household context, however, when these interests involve an outsider (e.g., a practitioner, medical personnel, interviewer), the husband/father steps in to oversee the situation.

## Illness Causation and Preventive Behavior

In the etiology of favism, the illness is likened to food poisoning where the bean, not the individual, is at fault. Nevertheless, the fava beans are still consumed, promoted by a matrix of cultural practices associated with other food behaviors and protective behaviors which are, in turn, related to the preparation and consumption of the beans. These behaviors are described in this section in relation to both the general ideology of illness causation and its prevention. In Greek society, the individual plays a passive role in illness causation; the blame for becoming sick is not on the shoulders of the afflicted person, but placed elsewhere. This is true for both biomedical categories of disease and popular categories for illness. Given this, it is easy to understand that diseases which are explained by medical science to involve an inherited deficiency of the blood do not fit with the scheme.

Placing the blame elsewhere should not be regarded as simply another expression of Mediterranean fatalism, rather, it is a way of explaining a disease or illness which exonerates the afflicted individual during a time of stress. When villagers were asked about the idea of blame or fault and how it figures into illness and disease, they said that it was not logical to blame the sick person for his own illness; this places additional burden on him when he should be relieved from such concerns.

The fact that the illness ideology leaves little room for personal blame in illness and disease does not mean that individuals do not participate in preventive behaviors. One of the most popular explanations for illness involves the evil eye where the blame for the affliction is placed entirely on another person, not on the afflicted one. Even this illness calls upon the use of some forms of preventive behavior. As used in popular explanations, the evil eye is not only an illness category but a cause of not feeling well. Sickness from "the eye" is described using active verb phrases, rather than as a diagnostic label alone. In fact, the verb, matiáso, is used much more often than the word for evil eye (kakó máti). People do not say, "I have the eye," they say, "Someone has given me the evil eye; some one has evil-eyed me." Therefore, it is more in keeping with the semantic and cultural meaning to use the phrase "affected by the evil eye" rather than "having the evil eye."

The Evil Eye: Prevention and Cure

Symptoms of having been affected by the eye include headache, dizzyness, and lethary. (Somewhat similar to those of favism.) Some individuals claim that they experience a personal sign which marks him as having been afflicted by the eye. For example, one complained that his eye always had pain in it when he was affected by the eye. More important than actual symptoms is the way in which they occur: suddenly, unnanounced, and unassociated with any specific thing or event from the environment, diet, behavior, and so forth.

Various techniques of diagnosing and treating one affected by the evil eye are documented in the literature (e.g., Blum and Blum 1965, 1970; Mills 1948) and the data from Rhodes do not deviate from these. Diagnosing the eye involves dropping oil into a glass of water; if the oil forms a circle on the top of the water, the evil eye is involved. If the oil separates into smaller droplets on the top of the water, then the evil eye is not involved. This process may be performed several times during the period when the individual presents symptoms, either to verify the diagnosis, or to gauge when the affliction is likely to pass.

Certain individuals, usually older women, have the power to rid one of the effects of the evil eye. They have retained certain special prayers or chants or poems, and say these as they are incensing ("smoking") the afflicted person and the area around him. Used with the incense are the flowers from the Good Friday church services which had been used to decorate the epitaph in the recreation of the death of Christ. Others will take a scarf or other small clothing item worn by the person affected by the evil eye. This is used in private consultation where the curer will knot the cloth in a special way, making the appropriate incantations. This should be done three times.

While jealousy and envy are often given credit for the evil eye in the literature, the rural inhabitants of the Rhodian villages claim this is not so. They say that admiration rather than jealousy is at fault in provoking the evil eye. Therefore, one cannot purposely "put the eye" on another through malice. Admiration is a positive emotion, while jealous a negative one which may cause the jealous person to suffer from all types of afflictions. For this reason, it is important to retrace where one has moved during the day preceding an attack of the evil eye. Often admiration from a stranger is at fault. Either an entirely unknown person has looked at another and unwittingly afflicted him with the eye, or a known person has noticed the other, and for some reason, afflicted him with the eye. Perhaps the afflicted person invited admiration by wearing something new for the first time, changed hairstyle, showing wealth, and so forth. In this way, admiration from a long-standing friend was evoked, and the person became affected by the evil eye.

Protective devices against the eye include spitting three times when one compliments another, pinning a variety of amulets on one's apparal which may include a small blue-eye bead, a cross, a beaded case with special prayers inside, an eye of a sea shell, and the wearing of certain items of clothing upside-down or inside-out, or wearing clothing which obviously does not match (e.g., mismatched shoes or stockings; mismatched set of earrings).

Theories of Contagion

Very few illnesses are accounted for by a germ theory of contagion. As a consequence, many of the hyper-sterile measures for the prevention of disease which are found in the United States do not exist in the Rhodian setting. Colds (kriόma) and influenza (gríppe) explain many symptoms from headaches to stomachaches, leg pains, etc. Krioma refers not only to the "common cold" but to the exposure to the cold on the affected part of the body. People adamantly argue that microbes are not involved in many diseases that biomedicine explains by bacteria and viruses; they argue instead that only a "cold" is involved.

Childhood diseases such as measles, mumps, whooping cough, are appreciated to be contagious, however, extreme caution is not exercised when these diseases occur in order to avoid contageon between children. One of the worst circumstances that can befall anyone is to be ill with no one around, not only for help, but to keep company with the one who is ill. Even though the sick person may be sleeping or not in need of extra help, someone from the family or neighborhood will always be near at the bedside. This applies even when the person has diseases recognized to be highly contagious in medical explanations. This is in direct contrast to middle-class western society where preventive behaviors involve taking vitamins to fortify one's self after coming into contact with "cold germs", gargling to prevent sore throat, and generally avoiding the person who is sick with the common cold or influenza.

One way in which microbial contagion is ignored in the daily life is in the handling of food, dishes, glasses and cooking utensils. Dishes are never submerged all together for washing in one pan, even in soapy detergent water. This is not considered the clean or appropriate way to wash them. It is better to wash each plate or glass, one-by-one. Sometimes, soap is not used, and the glass is merely rinsed and set to drain. This is preferable to letting all the dishes sit in the same dishwater. Families often eat from the same plate, particularly if the food is a type of salad, if it is a group of fried vegetables, and cheese. They dip their bread into the same olive oil which is poured over and surrounds these foods. Glasses are interchanged, even with people who are outside of the central family group. One might rinse out the inside of a glass with clear water, swish the water around and toss it on the ground (if eating outside) or throw it out the open door, not particularly cleaning the rim of the glass, in order to offer a glass of wine or ouzo to a guest at the family table.

## Smells, Odors and Preventive Behavior

Smells and the use of various natural substances to enhance or mask them, are often thought to bring on illness, and therefore, they must be carefully managed. In the spring months, when many plants and flowers are in bloom simultaneously, many say that the air becomes heavy with their perfume, and one might become dizzy from the odor. On the other hand, the smell of incense, usually a mixture of a basic burning substance and a herb, which can also become extremely heavy is used to cleanse the home every evening before sunset. When visitors are present, particularly those visiting for the first time, the house may be incensed, and each person invited to "smoke" (i.e., sniff of the incense) the incense as the woman of the house passes by them with the smoking container of incense. It is said that this practice wards off strange "spirits" and cleanses the home of whatever has passed during the day. Smells from cooking in an indoor kitchen are often thought to be unfit and offensive to circulate throughout the house. Traditional style homes have cooking facilities which are separated from the main rooms of the household structure. The modern, self-contained houses separate the kitchen from the rest of the house, and it may in fact be the room farthest from the public room (<u>salóni</u>), even though it is more practical to be close to the saloni because holidays and feasts are celebrated here.

Colognes and natural leaves of plants may be carried around to be used by a person when other odors become offensive; usually these are not body-related or even animal related odors. They are usually related to human-made substances (like cooking, as described above) which may include gasoline fumes and smoke (other than incense). At times, people may take a swig of basil or a few lemon tree leaves, crushing the leaves between the fingers and smelling of them. This often happens when people are in an unusual situation, when one feels dizzy, or needs to be refreshed. Visitors to a home may be given a small branch of basil or other pungent herb upon their departure. The people say this is for remembrance, but the offering of "something -- anything" is so deeply ingrained in social interactions which involve visiting, that it is difficult to fully analyze this activity here. (The visit to the church also includes taking something, in this case, a piece of bread from the priest. This is for the people who do not participate in the communion ritual, and it is often explained by the idea that "no one leave without something.")

### Food Consumption and Preventive Behavior

Moderation in food, drink and activity is an important concept in the prevention of illness. Often, these moderations in activities involve the concept of balance, rather than abstinance, and even more often, they rely on concepts of hot and cold, heavy and light. The hot and cold balance was not found to be as symbolic as it is in areas of Mexico, Guatemala, and Latin America (e.g., see Currier 1966). The balance of heavy and light is more often grounded in empirical observation and the actual measure of hot and cold by thermal indications. Foods are often classified as heavy or light, based upon intrinsic rather than symbolic qualities. It is believed best to maintain a balance between these foods within meals, and/or throughout the day, and to avoid heavy foods at particular times of the day or year.

Foods which are considered heavy and light are given in

Table 6.2. These are used at different times of the day and year. The combination of certain foods can result in a doubly heavy meal, if two heavy foods are consumed at the same meal. Heavy foods are to be avoided in the evening, in the summer hot months and when one is ill. They can be "double-dosed" by, for example, adding garlic to fried foods; using dried beans in a tomato sauce and having a side dish of fried eggs. Earlier, it was mentioned that many attribute their distress following fava bean consumption to the fact that they are a heavy food, not that they interact with anything inherent in the individual. At the same time, it might be expected that people with a weakened health condition would also suffer from the beans.

TABLE 6.2

HEAVY AND LIGHT FOODS

| Heavy Foods | Intermediate, depending on preparation | Light foods |
|---|---|---|
| Dried beans | Eggs | Milk |
| Lentils | Fresh beans | Boiled foods |
| Fried foods | | Lemon-oil on salad |
| Red-sauce foods | | Rice |
| Fried in oil and then boiled foods | | Soups |
| | | Cheese, yoghurt |
| Beef, pig | Other meats | Fish, chicken |
| "Fava" from lentils | | |

## Protective Behaviors and Fava Bean Consumption

Given the level of the enzyme deficiency and the presence of fava beans in the Rhodian diet, it is fortunate that more cases of favism do not happen. Even though the beans comprise an important part in the spring and Lenten diet, considerably fewer cases of favism occur during Lent when the bean is present in homes, than would be expected. Ideas about protection from the effects of fava beans must circulate to some degree and might involve the following:

1. The beans are avoided by those considered sensitive to them, e.g., children and families which have had favism episodes in the past.
2. Certain forms of the bean are selectively avoided by all people.
3. The beans are treated and prepared in ways which the people believe confers protection.

### Avoidance of the Beans

Families in Rhodes are aware that fava beans potentially affect more children than adults. When families are interviewed about fava bean habits, they often state that they do not allow the children in the family to consume the beans. Children are often warned not to eat the beans in the general population. This is counteracted by two other factors. First children are urged to eat continuously, whenever they are around food or a meal. Sometimes they will continually take food from the table or be urged to eat a spoonful of food offered to them. At the same time, children are often told to "watch out," to "be careful" and "don't run, don't get overheated," and so forth. There are so many negative verbal contacts between children and adults that admonisions not to eat a certain food are not well heeded. Other families, however, allow the children of all ages to eat the beans, and do not try to conceal this practice. While adults may not purposely give the beans, they still have enough opportunities to eat them in the fields, from the family kitchen, and from neighbors, unknown to the family. There is no systematic way of protecting the children from not eating the beans.

It has been suggested that families having problems with fava beans are self-identified; they know who they are, accept that they cannot eat the beans, and do not use them. The study in Rhodes could not verify this. While it makes sense that individuals and/or families should alter their bean habits once a case of favism has been experienced, this is not in reality the case. Even though one child in the family is protected from the beans following an episode, familial patterns usually do not change. This means that the bean is equally available to the child as it was in the past, to say nothing of the opportunity for consumption of the fresh, raw beans in the fields. In cases where the child was sufficiently old to have remembered the trauma of the illness, the hospitalization and the blood transfusions (s)he obtains from the beans by volition, even though the mother of the family continues to have them in the home.

In eighteen cases from fourteen families, all but two favic children abstained from the beans following the episode. In these two, one suffered from favism a second time, and continued eating and cooking the beans. She now has a son, to whom she also gave the beans, who subsequently suffered from favism. Now no one in the family eats the beans. In the second cases, the boy who suffered favism as a young child still eats the beans. His mother was convinced that there was something wrong with the particular beans which were eaten preceding the episode, and she refused to accept that there was any connection between the episode and anything, inherited or not, to do with the blood.

Among the fourteen remaining cases, representing twelve families, the beans have not been consumed by the children who suffered from favism. The majority of the families, however, still use the beans. Of these twelve families from which the favic children come, four have stopped using the bean altogether. Among these four families which had stopped eating the bean, one reported two episodes of favism within the same nuclear family. In this case it was two brothers who both suffered from favism, and the family stopped using the beans as a result.

These data from families support the suggestion that favic children will avoid the beans following their own episode. It does not support the hypothesis that favic families identify themselves as such, and henceforth change their habits vis-a-vis the beans.

It was also suggested that certain forms of fava beans are avoided by all families. Rural inhabitants associate possible disease reactions to the bean with the fresh, raw form, however, their behaviors are in direct contradiction of this belief. Of twenty six families in the study known to regularly consume fava beans, seventeen consume only the fresh beans. Seven of these consume them only in the fresh, raw form; the other ten use them both raw and cooked, but only in the fresh form. The seven families insisting that they eat only the fresh, raw form may be assumed to fall into the lowest-consuming group, even though popular conceptions of favism attribute the disease only to the fresh bean. They often claim that the raw bean is safe to eat if the cuticle is removed, while others say that a small white portion must be removed as well.

## Conceptions of Protection

It is possible that the fava beans are treated and/or prepared in ways which the people believe confer protection, either by their combination with other foods, or in some other aspect of their cleaning and cooking. It is often the case with different legumes and pulses that certain potentially deleterious chemicals are leached out in preparation. Some have suggested that this may be the case with fava beans. Earlier, it was shown that the majority of cases in the small sample of those following cooked beans, involved preparations where the first water had not been discarded.

Throughout Greece one hears the popular belief expressed that fava beans consumed with either milk or yoghurt can cause gastric distress and vomiting. The beans are therefore avoided in such combinations. The belief may have survived from the time of Hippocrates who warned about eating different beans and pulses in combination with cheese or beef as they "... pass through some people's bowels very readily...in others not accustomed to them, they endanger what is called dry cholera" (Adams and Kelly 1939:94). In none of the episodes reported from Massari and Kritinea was it stated that the beans had been consumed with milk or cheese or yoghurt preceding the episode.

Although certain ideas circulate which attribute the poison in the fava beans to growing conditions or to particular parts of the beans, precautions which follow these beliefs are not systematically followed. Earlier it was mentioned that some say that certain parts of the beans contain poison, often identified as cyanide. Among these parts are the cuticle, the black end of the bean, and the small white spur on the inside of the bean. These, all or one, should be removed before eating, according to some, but they usually are not removed. Boiling the beans two times, as was described earlier, is sometimes claimed to remove the poison from the beans. Since this is a process used for other dry beans, people were asked whether or not they reserved the process only for fava beans, or for all beans. Those who discard the first water from fava beans, also do so with other beans, and the opposite. Therefore, this "protective" behavior against favism is one which is used for other beans as well. Many who follow it say that they do so because all beans are potentially harsh on the stomach, and that discarding the water, and rinsing the beans helps to avoid stomach distress and flatulence. They also say that removing the cuticle for all dry beans after the first boiling also helps with the same problem.

It is interesting that the word, cyanide, comes up often in explanations about fava beans and their possible poisonous effects. It is even more notable that the Ancient Greek word for fava beans is kiámos, from which the Greek name for favism, kiamismós (or kiámosis) is derived. The Greek words for cyanide and cyanosis are kianioúhon and kiánosis, the latter which so closely resembles the word, kiamosis or kiamismos, for favism that this confusion is quite understandable. In actuality, the fava beans do not contain cyanide, and it is probably the linguistic similarity between these words which has resulted in fava beans being associated with cyanide.

## Preventive Medicine and Favism

Preventive behaviors with respect to favism and the beans exist, just as they do for other diseases and illnesses, even though these behaviors are often not those which would be suggested by preventive medicine. Factors which promote the consumption of the bean, such as the matrix- of food-related behaviors, and popular ideas of prevention, interfere with the establishment of preventive behaviors based on biomedical principles. Continued fava bean consumption may not be logical in terms of preventive medicine, but it is logical in terms of native beliefs about the etiology of favism, food behaviors in general, and native suggestions about prevention. It could be argued that the rigor of preventive medicine which would promote abandoning the beans altogether, and educating the public about the enzyme deficiency, would act in discord with ideas about food, inheritance, and blood.

At the present, a program directed by the goals of preventive medicine is underway in several provinces of Greece. This program identifies those at risk of developing favism by screening newborns for the presence of the enzyme deficiency. The parents of infants identified with the deficiency are instructed about its relationship to fava beans and other hemolytic agents. While my own research on Rhodes was not directed by the goals of preventive medicine, there were abundant opportunities to observe the reactions of the people when the problem of the enzyme deficiency and the fava beans was presented to them. Analysis of prevention from an anthropological perspective and the use of these observations from rural Rhodes can clarify the possible effects (and perhaps results) of the screening programs. (Rhodes is one of the areas included in the screening).

## Prevention from an Anthropological Perspective

As emphasized in the introduction to this chapter, preventive behaviors and preventive medicine are two separate categories. Preventive behaviors are generated not only through biomedicine but through cultural practice as well. Medical scientists who became involved in the early programs of hygiene and preventive medicine in non-western cultures found that a "preventive mentality" which was congruent with the goals of preventive medicine did not exist. Many assumed that preventive medicine was difficult to implement because of the lack of a preventive mentality, and further, assumed that preventive behaviors did not exist. They pondered about the difficulties in promoting preventive medicine in these cultures, and, with the help of anthropologists, decided that preventive behaviors are generated from a foundation which is different from the scientific premises of biomedicine; and as such, they are tied to superstition, religion, peasant mentality, fatalistic attitudes, and symbolic categories. These were analyzed to interfere with the acceptance of modern biomedical medicine.

This view was challenged by others (e.g., Erasmus 1952) who claimed that the basis for preventive behaviors in all cultures was empirical, just as it is in the scientific model, but that observations made without the sophistication of laboratory techniques and technology could not be expected to produce behaviors which were similar to those which were produced with the aid of these devices. Cause-effect observations were suggested to be made by all peoples, and behavior adjusted accordingly to what they "saw." Biomedical science, with a radically different level of technology with which to make these observations, explained cause-effect relationships differently, and, thus made suggestions about different preventive behaviors.

Therefore, both medical science and non-western cultures were seen as making empirical cause-effect judgments. The difficulty in accepting biomedical ideas about prevention was attributed by the inability of non-western peoples to see the cause-effect relationships in the way that biomedical scientists did. And, somewhere along the way, the biomedical explanations of disease took precedence over popular explanations of illness.

In reality, both the symbolic and the empirical foundations operate to formulate preventive behavior. In public health programs which focus on preventive behavior, the complaint is often heard that cause-effect is difficult to demonstrate in disease prevention. This is blamed by public health officials for the rejection of prescribed behavior changes. Cause-effect difficulties are only part of the problem; equally important is the symbolic content of the behavior and its "fit" with the rest of the culture and/or other health beliefs and practices. A classical example for this comes from the study of Wellin (1955) and water boiling in Peru. While the effect of boiling water is difficult to demonstrate with respect to the eradication of certain health problems, this alone was not the cause of the people's rejection of the prescribed practice. Aside from difficulties in the daily scheduling of work and cooking activities by the women, the utilization of the household fire, and the division in labor, the symbolic meaning of water which had been boiled and then left to cool was vitally important. Water which had been boiled and left to cool overnight placed it in a dangerous category, symbolically, and therefore the practice was abandoned by many.

Empirical observations, visible proof of new, health-related practices, may be used in trying to establish a preventive medicine program. Often, these empirical observations are doubted, or rejected, and the people are consequently described as ignorant or superstitious. However, the fact that certain empirical observations or scientific "facts" may clash with the established wellness-illness ideology, or with certain symbolic meanings which circulate in the culture, is not examined. Further, behaviors themselves play symbolic roles in the society and to change them may mean that other facets of the culture must be changed as well.

Examples from western society are abundant. For example, young people begin smoking in spite of the attempts to show them the empirical results of smoking, because the act carries symbolic meaning (e.g., adulthood, masculinity, availability as a young woman, freedom, rebellion against society). The symbolic meanings are more urgent; the need to express the symbolic meaning is a pressure which overrides the empirical evidence. Obesity or even plumpness, while not an ideal in American society, remains one for the rest of the world. Beauty and plumpness are often synonymous--or at least, beauty cannot exist without a little plumpness. Plumpness in women is a sign associated with motherhood; fatness in men shows that they are well-cared for by their wives. Only with the distribution of magazines showing thin models has this characteristic begun to change, but, the symbolic meanings are still ever present.

Preventive behavior, then, may be carried out in a symbolic manner or it may serve symbolic purposes. Knocking on wood, spitting three times, making the sign of a cross over an infant's open mouth, are only a few of the symbolic acts which people make which are associated with preventive behavior. More than any other reason, when preventive medicine does not take hold, it may mean that the symbols which it manipulates are not powerful enough to influence behavior, or that the symbols which it attempts to manipulate are contrary to long-standing practices and ideology which carry their own symbolic power.

Returning to the question of why fava beans are still consumed, it is not sufficient to evaluate it in light of the goals of modern preventive medicine, but in light of (1) what not eating the beans means, and (2) what symbols are associated with blood and inherited conditions. This information helps to explain why the goals of preventive medicine might not be met, in spite of dissemination of information and the use of modern technology. At least two questions can be asked about fava bean consumption, and favism:

1. What are the symbolic meanings associated with blood and, particularly, a "deficiency of the blood?"

2. What are the beliefs about inherited conditions which are associated with disease?

Blood symbolism

For rural Greeks, and to some extent, all Greeks, blood carries powerful symbolic connotations. One may become ill because the same blood is shared with another who has also become affected by the same sickness. This idea transcends both genetic inheritance and the germ theory of contagion. Blood can both contaminate and cleanse, depending upon where it is found and under what circumstances.

Clean blood is essential to good health. Some diseases are said to occur in order to cleanse the blood. Certain foods are prescribed to strengthen the blood, others to clean the blood. People pride themselves in having good, strong, clean blood. Women are believed to have more blood than men, children less than adults.

The thought that one is going to give blood in order to have it sent away and examined often prompts parents of children to avoid the drawing of blood samples. Many believe that taking blood from children would weaken them, stating that children did not have as much blood as adults, and that taking even a small sample might cause the child to become physically weakened. Adults also may reject giving blood because they have much work to do and do not want to be weakened. When blood was taken from women, or young women, comments were often made by husbands or fathers, about the redness or the quantity of the blood. When it was easy to take the blood sample because of the abundance of blood, the comment was overheard, "Look at what a bad girl she is, she has so much blood."

Practical fears also exist regarding blood samples. Some believe that unusual diseases will be uncovered in the analysis, others that they will become infected by unclean needles. Needles in and of themselves are fearsome, however, they appear to have less symbolic meaning than when blood is drawn from the finger. When needle-syringes are used, the blood does not flow onto the skin, something which is particularly repulsive to the people. The needle-syringe combination does not permit this, and is in keeping with the people's expectations of scientific procedures. Children actually show more fear when they see their own blood on the tip of their finger than when it is collected into the syringe.

The enzyme deficiency was interpreted as a deficiency of the blood, which would be expected given the idea that blood does not regenerate or regenerates slowly. Children with the deficiency were thus seen to be at a double disadvantage; not only did they have less blood volume by virtue of being children, but they also had the deficiency. Parents feared that these children would be inferior both personally and socially. Upon hearing about the deficiency in their child, parents feared that (s)he would be tired more than other children and not able to live a normal life. Socially, some feared that the deficiency would put their children at a disadvantage when they reached adolescence and approached marriageable age.

Familial diseases

Added to these fears and suspicions about blood, the drawing and examination of blood, is the idea that one might have an inherited condition of "family disease" (<u>oikogeniakí aróstia</u>). Family diseases and inherited diseases are the same in the thinking of the rural inhabitant of Rhodes (and indeed, in most rural Greek inhabitants). These include diseases which are apparent at birth, as well as others which appear later such as "craziness" (<u>tréla</u>) which includes epilepsy and personality disorders) and those which repeatedly occur in families (either environmentally induced or genetic).

Inherited diseases are among those most feared. An identified predisposition to a disease which is inherited is nearly the same as having the disease, in social terms. The cause for this concern centers around marriage. Every parent wants each child to make a marriage which will produce healthy grandchildren. Regardless of which occupation may be pursued, how much money may be accumulated, parents want to see that their children will participate in at least the perpetuation of standard family expectations. Children suspected of having some inherited disorder are not considered for marriage; it is difficult to find mates for them. Nearly all diseases are hidden, for fear that they will reveal some familial weakness.

Mothers of deficient sons, who know they are enzyme deficient, may continue to eat the beans simply to show that the sensitivity to the beans is not a family trait. For this same reason, children may be allowed to eat the beans. Others deny that genetic inheritance has anything to do with favism, rather, it is a result of something in the bean, not a failure in the individual.

## Conflicts between Preventive Medicine and Cultural Norms

According to the informants from Rhodes, favism is explained as either a childhood disease or a type of food poisoning which results from beans. The characterization of favism as a childhood disease resembles the biomedical description, but the idea that it is a part of the pediatric collection of diseases (mumps, measles, chickenpox) which are viewed as a rather inevitable part of childhood, much better suffered in childhood than later, and which are necessary as part of the accumulation of immunities, is not congruent with the biomedical epidemiology of favism. This helps to explain why the beans are not religiously excluded from familial diets, and even though children are cautioned about eating them, they are cautioned about a good number of other activities as well. A risk-taking model cannot be applied to behavior which is considered as a potentially necessary aspect of life, any more than mothers who do not protect their youngsters from chicken pox are subject to risk taking models. By like token, Mediterranean fatalism does not work as an explanation of why the beans still appear as a cultigen and in the diet.

In addition to being viewed as a childhood disease, other cases of favism occurring after early childhood, are explained as food poisoning, and, indeed, the symptoms can be easily construed as such. This explanation does not involve personal value risk in admitting that one has suffered from favism.

Recalling the story of the woman told in the Introduction, one or both explanations might be called upon. These explanations avoid the acceptance that one or one's family is afflicted with a weakness which appears in the blood, which is inherited, and which implicates the family line. Other stigmatizing blood traits, such as the B-thalasemia trait, may go unnoticed until a child with thalassemia is born to a couple, each carrying one B-thalassemia allele. Engaged couples are encouraged to be tested for the allele, however, when one or both of the individuals are identified with the allele the results may be quite drastic. When both are identified with the trait, i.e., with 25% probability of producing a child with thalassemia, the resulting stress may end in a broken engagement. This has particularly serious consequences for women, as described in Chapter Four. Even when one of the two people is identified with the allele, the result may be so stigmatizing that the engagement is broken and either one or both individuals remain unmarried, or are forced to offer more in the way of material goods in order to contract a second marriage.

In the last analysis, not eating the beans means that one must acknowledge a weakness; one which appears in the blood and which implicates the family line. While some foods are accepted as not always good for the health, particularly heavy foods, they are still consumed. Food, food sharing, food exchange, is so central to the family and public life. It is emphasized during periods of feasting, family holidays, and fasting. If fasting is viewed not only as the denial of certain foods but the reinforcement favoring the consumption of others, the place of fava beans during the Lenten period of fasting is illuminated.

Food sharing, and offering food to strangers, and visitors, is a means of securing a social bond of hospitality and indebtedness. It is quite impossible to refuse food on the pretext that one is dieting, or that one's teeth hurt when eating sweets. The pressure is still exerted to take at least one small bite, one small piece of cake, or one small drink. Children are taught to always refuse candies, sweets and other foods offered to them; they should wait until they are offered them for the second time, and most people, young and old, wait to be coaxed. Pressuring is a way of life; children initially say no with the desire of saying yes when offered the second time, and they are always offered a second time. Adults do the same, in fact, one villager characterized himself and other Greeks by saying "Whatever we do, it has to be done by nearly forcing us." "Me to zóri," the phrase used by the man, refers to forcing another person to comply with one's wishes which might even involve physical pressure.

While it was shown earlier that favism, or poisoning from fava beans, does not occupy a serious position in the series of illnesses and diseases which can happen, this is only a partial explanation of why the beans are still eaten. One might say that, considering the symbolic meanings of blood, genetic inheritance and food habits, denying the fava beans when offered is more dangerous socially than physically, both to the individual and his family. Avoiding fava beans as a preventive technique, rigorously carried out in public, would disrupt social relationships which are cemented through food sharing, and affect the family's position in the community. By accepting the medical etiology of favism which implicates the inherited genetic trait, individuals and families might be compelled to alter their status in the village and their relationships with other families.

The way in which biomedical information is disseminated, received and acted upon by the members of a culture, is an aspect of the social epidemiological model which is not usually explored.

In the present study, it was seen that cultural factors (e.g., food sharing, avoidance of admitting "familial" disease) potentially contribute to the continued occurence of favism. The more the genetic dimension of favism risk is emphasized through screening and health education programs, the more the public might resist changing their fava bean consumption patterns. Aside from favism, the effects of the $Gd^-$ allele (partially or fully expressed) are apparently unnoticed, making it easy to deny that it exists as a risk factor (as was found in some cases in Rhodes). Screening for the trait at birth now takes place in most maternity hospitals of Greece, with the parents informed about the list of foods and drugs which must be avoided in the infant's diet, a practice which must be continued throughout its life. How families actually follow-up on the information is not known. The research in Rhodes gives an example of the possible range in reactions and reasons for lack of behavior change observed in the families.

While the medical consequences of screening are clear, the social ones are not so self-evident. This is a theme which repeats itself continuously in preventive medicine. Monitoring individuals and families which have been identified with risk factors is an important dimension of preventive medicine. In some cases, the social costs may be more than the medical benefit gained. The effects of knowledge about the $Gd^-$ trait with respect to behavioral change and marriageability in Rhodes deserve future investigation.

# APPENDICES

# APPENDIX A

## Variants of the Enzyme Deficiency

Originally it was assumed that only the heterozygous female showed variations in the phenotypic expression of the Mediterranean variant. Stamatoyannopoulos et al. (1964) drew attention to a number of intermediate male cases of the deficiency from Greek populations. This was unexpected given the early theories about the nature of this variant. These males showed variations in the phenotypic expression of enzyme activity levels, just as did heterozygous females. In these intermediate males, levels of activity ranged from 5 to 75% normal. Given this spread, it was hypothesized that certainly there should be variants in the enzyme deficiency within the Mediterranean population. On the basis of electrophoretic analysis, in all cases, the Mediterranean variant was identified, not another variant. The investigators concluded that while the activity level of the Mediterranean variant may cover a wide range, it is of only limited value in discriminating between the various types of the deficiency. It was suggested in the study that it is more important to consider whether or not other factors, such as anemia and thalassemia might be affecting the activity of the enzyme in these intermediate cases.

Meanwhile, in other populations, the investigation of the variants accelerated, prompted by the differences which had been observed in activity levels in the Greek populations with the

Mediterranean variant. The number of variants increase each year. In 1970, Beutler reported 49 variants. Later, Yoshida et al. (1971) reported 75 in their review of the literature on the subject. These variants were classified not only according to the measured activity level of the G6PD enzyme, but also through at least one or more other biochemical tests. The most widely used test for differentiating between variants has been through electrophoresis where the enzyme forms bands in test tube according to its specific properties. Variants which appear to be similar on the basis of activity levels, such as the Seattle I and the Barbieri (Marks et al. 1969) are shown to be electrophoretically different, and are accordingly given different names. Still other variants can be differentiated from each other only on the basis of a full battery of laboratory tests which include heat lability, inhibition of NADPH and the comparison of $k_m$ values for G6PD and NADPH.

While variants have been noted in many geographic areas, what is of concern here is the Mediterranean variant and how many other variants have been reported in Greek populations. Rattazzini et al. (1969) found in a series of screenings that four unrelated Greek families showed four different variants of the deficiency. The size of the sample in which these four families were found is not stated. In the same study, school boys were screened from Cephalonia, an island in the Ionian Sea. Here three boys showed slightly different variants of the deficiency. Several other variants have been found in Greek population, some have not been published, among these, (1) the Corinth variant, thought to be fairly common, but not noted to be associated with favism, is reported by Yoshida in unpublished observations; and (2) the Orchomenos variant, another severe form is noted by Stamatoyannopoulos, also in unpublished observations.

Three moderate to mild variants have been noted in Greek populations: (1) the Melissa variant (Stamatoyannopoulos, unpublished observations); (2) the Athens variant (Stamatoyannopoulos et al. 1967); and (3) the Attica variant (Rattazzini et al. 1969). These areas from which the variants take their names, are all in the central mainland area of Greece. Four very mild forms of the deficiency have been also identified in Greece: (1) in Levadia, an area in central mainland Greece; (2) in Thessaly in northern Greece; (3) in Karditsa, northern central mainland Greece; and (4) in the western coastal area of mainland Greece. For the most part these variants were identified in only one person each.

## APPENDIX B

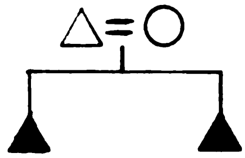
## Familial Favism

It has been suggested that some inherited predisposition acts in conjunction with the enzyme deficiency to promote hemolysis in certain individuals following exposure to fava beans. Part of the basis for this hypothesis lies in the fact that favism has been noted to occur in certain families with the enzyme deficiency, while it is not noted in other families also with the enzyme deficiency. The one major work which investigated this hypothesis using familial data is that of Stamatoyannopoulos, Motulsky et al. 1969; they used family pedigrees from three regions in Greece: Corfu, Karditsa and Lemnos. Using the prototype for presentation used by their research, the Rhodes data is presented. In the earlier research, fourteen pedigrees were used, the present study adds four more. (These are pedigrees where more than one person was affected by favism, without considering fava bean consumption patterns, and other familial information.) These data are presented in three figures:

1. Sib pairs, both affected by favism;
2. Proband -- parent pairs, with or without others affected with favism;
3. Proband and at least one other ascending consanguineal relative other than the parent affected by favism.

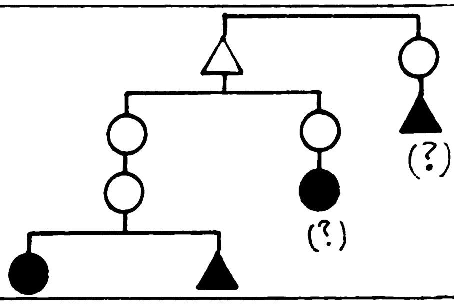
Sib Pairs:

A total of ten sib pairs are represented here:



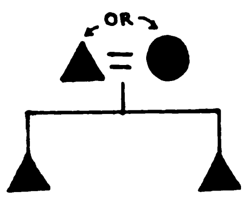
Configuration from Stamatoyannopoulos and Motulsky; The Rhodes study did not show any singular sib pairs, both with favism, but without other relatives affected.

Five pairs.



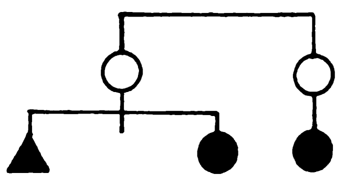

Configuration from Rhodes where the two sibs were affected with favism, and possible other relatives.

One pair.



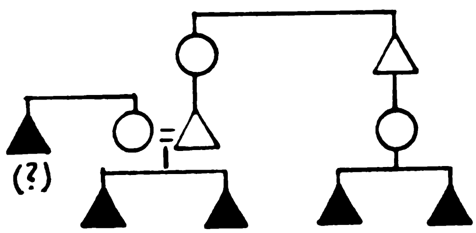

Configuration from earlier study, showing sib pair plus one of the parents affected with favism. The sex of the parent was not given.

One pair.



Configuration from earlier study, showing sib pair plus a parallel cousin, all with favism.

One pair.

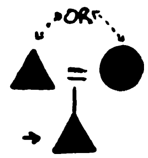



Configuration from Rhodes study, showing sib pair and assorted other consanguineal relatives affected by favism.

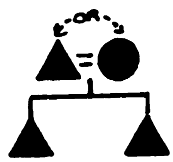
Two examples.

Proband and Parent Configurations

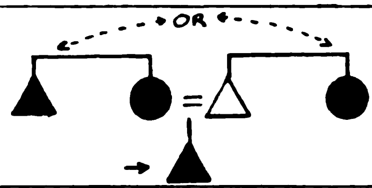
Four different configurations where a proband and a parent suffered from favism are shown here; three of these are from the earlier study, and one from the Rhodes data.



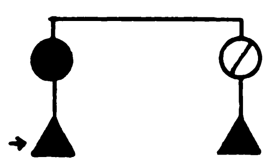

The simplest configuration where only the proband and a parent were both favic. (earlier study)




Two sibs and one or the other parent, all favic. (earlier study)

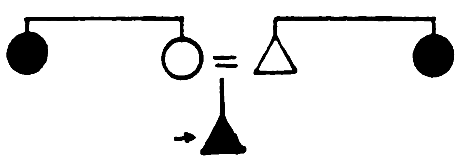



Proband, parent, and parental sib all affected with favism. (earlier study)



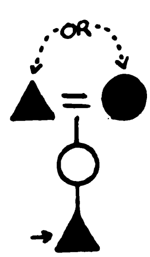
Proband, parent, and parallel cousin to proband all affected by favism. Rhodes.

Proband and Ascending Generation, other than Parent



Proband plus a sibling of one or the other parent.

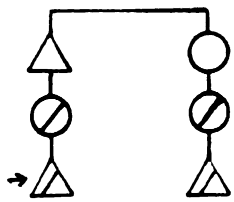
(Two cases, earlier study)




Proband, and one or the other grandparent, sex not given.

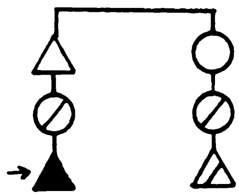
(Earlier study, two cases)

Second Cousin Pair Configurations



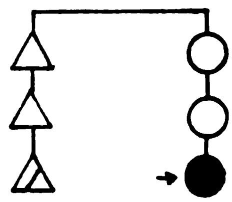
Two 2nd male cousins
Neither with favism

One pair



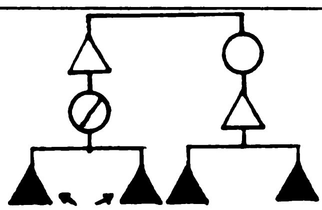
Two 2nd male cousins
One with favism, the other not

One pair



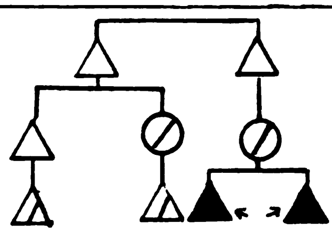
Two 2nd cousins, one male, one female
One with favism, the other not

One pair



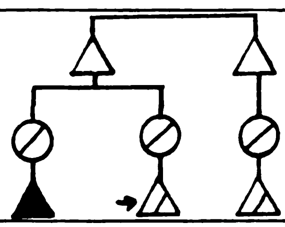
Two pairs of male cousins
Each pair of sibs is treated as a unit in comparison

One pair



Two pairs of male cousins
The two brothers, each with favism, are treated as a unit in comparison to each non-favic second cousin.

One pair



In this configuration, the non-favic proband was compared to each of his male second cousins.

Two pairs

BIBLIOGRAPHY


Adams, F. and Kelly, E. C.
1939 The Genuine Works of Hippocrates Translated from the Greek by Francis Adams. Introduction by Emerson Crosby Kelly. Baltimore: The Williams and Wilkins Company.

Alland, A. Jr.
1968 Medical anthropology and the study of biological and cultural adaptation. Amer Anthro 48:40-51.

Alland, A. Jr.
1970 Adaptation in Cultural Evolution: An Approach to Medical Anthropology. New York: Columbia University Press.

Allison, A. D.
1961 Genetic factors in resistence to malaria. Ann NY Acad Sci 91:710-729.

Allison, A. C.
1964 Polymorphism and natural selection in human populations. In: Cold Spring Harbor Symp Quant Biol 29:137-149.

Allison, A. C.; Askonas, B. A.; Barnicott, N. A.; Blumberg, B. S. and Krimbas, C.
1963 Deficiency of erythrocyte glucose-t-phosphate dehydrogenase in Greek populations. Am Hum Gen 26:237-242.

Alpers, M. and Gajdusek, D. C.
1965 Changing patterns of Kuru: Epidemiological changes in the period of increasing contact of the Fore people with Western civilization. Am J Trop Med and Hyg 14:852-879.

Amin-Zaki, L.; Taj el-Din, S. and Kubba, K.
1972 Glucose-6-phosphate dehydrogenase deficiency among ethnic groups in Iraq. Bull WHO 47:1-5.

Angelov, A. and Andrev, I.
1959 Vop Pediat Akas i Ginek 2:7.

Arends, T.
1966 Haemoglobinopathies, thalassemia and g6pd deficiency in Latin America and the West Indies. New Zealand Med J 65:412:831-844.

Belsey, M. A.
1973 The epidemiology of favism. Bull WHO 38 (1):1-13.

Beutler, E.
1970 (Annotation) Glucose-6-phosphate dehydrogenase deficiency. Brit J Haemat 18:117-121.

Beutler, E.
1974 Screening for glucose-6-phosphate dehydrogenase deficiency. In: Genetic Polymorphisms and Diseases in Man, B. Ramot, ed. New York: Academic Press. pp. 224-226.

Beutler, E.; Dern, R. J. and Alving, A. S.
1954a The hemolytic effect of primaquine: III: a study of primaquine sensitive erythrocytes. J Lab Clin Med 44:177-184.

Beutler, E.; Dern, R. J. and Alving, A. S.
1954b The hemolytic effect of primaquine: IV: the relationship of cell age to hemolysis. J. Lab Clin Med 44:439-442.

Beutler, E.; Dern, R. J. and Alving, A. S.
1955a The hemolytic effect of primaquine: VI: an in-vitro-test for sensitivity of erythrocytes to primaquine. J Lab Clin Med 45:40-50.

Beutler, E.; Dern, R. J.; Flanagan C. L. and Alving, A. S.
1955b The hemolytic effect of primaquine: VII: biochemical studies of drug sensitive erythrocytes. J Lab Clin Med 45:286-295.

Beutler, E.; Yeh, M. and Fairbanks, V. R.
1962 The normal human female as a mosaic of X-chromosome activity: studies using the gene for g6-pd deficiency as a marker. Proc Nat Acad Sci U.S.. 48:9.

Biddau, I.
1930 Considerazioni sulla patogenesi e sulla terapie del favismo. Terapia 20:106-118.

Bienzle, U.; Lucas, A. O.; Ayeni, O. and Luzzatto, L.
1972 Glucose-6-phosphate dehydrogenase and malaria. Lancet 1(January):197-110.

Blum, R. and Blum E.
1965 Health and Healing in Rural Greece. Stanford, California: Stanford University Press.

Blum, R. and Blum E.
1970 The Dangerous Hour: The Lore of Crisis and Mystery in Rural Greece. London: Chatto and Windus.

Blumberg, B. S.; Murray, R. F.; Allison, A. C.; Barnicott, N.A.; Herschfeld, J. and Krimbas, C.
1964 Serum protein polymorphisms in Greek populations. Ann Hum Genet 28:189-194.

Cassel, J.
1964 Social science theory as a source of hypotheses in epidemiological research. Am J Pub Health 54:1482-88.

Cavalli-Sforza, L.
1962 Genetic drift in an Italian population. Sci Am 221: 30-37. Reprinted in Human Populations, Genetic Variation and Evolution. L. N. Morris, Ed. San Francisco: Chandler (1971).

Choremis, C.; Zannos-Mariolea, L. and Kattamis C.
1962 Frequency of glucose-6-phosphate dehydrogenase deficiency in certain highly malarious areas of Greece. Lancet i (1962):17-18.

Choremis, C.; Fessas, P.; Kattamis, C.; Stamatoyannopoulos, G.; Zannos-Mariolea, L.; Karaklis, A. and Belios, G.
1963a Three red-cell abnormalities in a district of Greece: thassemia, sickling and glucose-6-phosphate dehydrogenase deficiency. Lancet i (1963):907-909.

Choremis, C.; Ikin, E. W.; Lehmann, H.; Mourant, A. E. and Zannos, L.
1963b Sickle-cell trait and blood groups in Greece. Lancet ii(1963):909-911.

Chung, S. F.
1965 Paediat indones 5, supplement 880.

Collombel C.; Kissin, C. and Cotte, J.
1970 Four cases of hemolytic anemia following ingestion of beans. (in French: A propos de quatre cas d'anamie hemolytique apres ingestion de feves) Eur J Toxicol 3 (1):36-41.

Crosby, W. H.
1956 Newsletter -- Favism in Sardinia. Blood 11:91-92.

Currier, R. L.
1966 The hot-cold syndrome and symbolic balance in Mexican and Spanish American folk medicine. Ethnology 5:251-263.

Cutillo, S.
1972 Favism, hemolytic attacks caused by drugs, and grave neonatal jaundice in populations with high incidence of G6PD deficiency. Pediatria (Napoli) 80:(2):6.

Dicks, B.
1974 Rhodes. Harrisburg: Stackpole Books.

Donoso, G.; Hedayat, H. and Khayatian, H.
1969 Favism, with special reference to Iran. Bull WHO 40:513-519.

Doxiadia, S. A.; Fessas, P.; Valaes, T. and Mastrokalos, N.
1961 Glucose-6-phosphate dehydrogenase deficiency: A new aetiological factor of severe neonatal jaundice. Lancet i (1961):297.

Doxiadis, S. A.; Fessas, P. and Valaes, T.
1962 Neonatal jaundice in glucose-6-phosphate dehydrogenase deficient infants. Brit Med J 2:1359-62.

Doxiadis, S. A.; Karaklis, A.; Valaes, T. and Stavrakis, D.
1964 Risk of severe jaundice in glucose-6-phosphate dehydrogenase deficiency in the newborn: differences in population groups. Lancet ii:1210-12.

Dubish, J.
1975 Ethnography of the islands: Tinos. In Regional Variation in Greece and Cyprus. E. Friedl and M. Schien, eds. NY Acad Sci.

DuBos, R.
1965 Man Adapting. New Haven: Yale University Press.

Engle, G.
1960 A unified concept of health and disease. Per Biol and Med 3:459-485.

Engle, G.
1977 The need for a new medical model: a challenge for biomedicine. Science 8(4286):129-136.

Erasmus, C. J.
1952 Changing folk beliefs and the relativity of empirical knowledge. Southwest J. Anthro 8:411-428.

Fabrega, H.
1974 Disease and Social Behavior: An Interdisciplinary Perspective. Cambridge: MIT Press.

Fenner, F.
1970 The effects of changing social organization on the infectious diseases in man. In: The Impact of Civilization of the Biology of Man. S. V. Boyden, Ed. Toronto, Canada: University of Toronto Press.

Fisher, A. and Fisher, J. L.
1961 Culture and epidemiology: a theoretical investigation of Kuru. J Health and Hum Beh 2:16-25.

Flatz, G. and Duren, R.
1967 Glucose-6-phosphate dehydrogenase deficiency and neonatal jaundice. Arch Dis Child 38:566-570.

Frake, C. O.
1961 The diagnosis of disease among the Subanum of Mindanao. Amer Anthro 63:113-132.

Fraser, G. R.; Grunwald and Stamatoyannopoulos, G.
1966 Glucose-6-phosphate dehydrogenase deficiency, abnormal hemoglobins, and thalassemia in Yugoslavia. J Med Genet 3:35-41.

Friedl, E.
1963 Some aspects of dowry and inheritance in Beotia. In: Mediterranean Countrymen, J. Pitt-Rivers, ed.

Friedl, E.
1967 Vasilika. New York: Holt, Rinehart and Winston, Inc.

Gasbarrini, A.
1915 Il favismo. Policlino (sez. prat.) 22:1505-37.

Gaudier, B.; Ryckewaert, P.; Carrier, J.; Giard, P. and Foulard, M.
1972 Hemolytic anemia due to G6PD deficiency apropos of 3 cases. Lille Med 17(3):487-493.

Gilles, H. M. and Taylor, G. H.
1951 The existence of the glucose-t-phospahte dehydrogenase trait in Nigeria and its clinical implications. Ann Trop Med Parasit 55:64-69(April).

Gordon, J. E.
1966 Ecologic interplay of man, environment, and health. Am J Med Sci 121/341-136/356.

Gross, R. T.; Hurwitz, R. E. and Marks, P. A..
1958 An hereditary enzymatic defect in erythrocyte metabolism: glucose-6-phosphate dehydrogenase deficiency. J Clin Inves 37:1176-84.

Harris, H.
1970 Heredity and environment as causes of disease. CIBA Foundation Study Group 35:60-72.

Hassan, M. M.
1971 Glucose-6-phosphate dehydrogenase deficiency in the Sudan. Hygiene and Trop Med(1971):187-188.

Hoffman, S.
1975 The ethnography of the Islands: Thera. In: Regional Variation in Greece and Cyprus. E. Friedl and M. Schien, eds. NY Acad Sci.

Hughes, C. A. and Hunter, J. M.
1970 Disease and "development" in Africa. Soc. Sci Med 3:443-494.

Joannides, C.
1952 Cyprus Med J 5:795.

Kantor, S. Z. and Hock, D.
1961 Studies on the pathogensis of favism. Bull Res Counc Israel. Sec A Chem 10a:142.

Kantor, S. Z.; Pinkhas, J. and Djaletti, M.
1962 Immunologic studies in a case of favism. J Allergy 33:390.

Kattamis, C.
1967 Glucose-6-phosphate dehydrogenase deficiency in female heterozygotes and the X-inactivation hypothesis. Acta Pediatr Scand 172(Supple):102.

Kattamis, C.
1971 Favism in breast-fed infants. Arch Dis Chil 46(249): 741.

Kattamis, C.; Chaidas, A. and Chaidas, S.
1969a G6PD deficiency and favism on the Island of Rhodes. J Med Gen 6(3):286-291.

Kattamis, C.; Kyriazakous, M. and Chaidas, S.
1969b Favism, clinical and biochemical data. J Med Gen 6:34-41.

Kattamis, C. and Tjortjatou, F.
1970 The hemolytic process of viral hepatitis in children with normal or deficient glucose-6-phosphate dehydrogenase activity. J of Pediatrics 77(3):422-430.

Kattamis, C.; Karambula, K.; Metaxotou-Mavromati, A. and Matsoniotis, N.
1971 Hematologic data in children from Rhodes. Iatriki 21:206.

Kenny, M.
1962 Social values and health in Spain. Human Organization 21(4).

Kidson, C. and Gorman, J. G.
1962 A challenge to the concept of selection by malaria in glucose-6-phosphate dehydrogenase deficiency. Nature 196:49-51.

Kirkman, H. M.; Schettini, R. and Pickard, B. M.
1964a Mediterranean variant of G6PD. J Lab Clin Med 63:726.

Kirkman, H. M.; Rosenthal, I. M.; Simon, E. R.; Carson, P. E. and Brinson, A.
1964b "Chicago 1" variant of glucose-6-phosphate dehydrogenase in congenital hemolytic disease. J Lab Clin Med 63:715-725.

Kirkman, H. M.; Doxiadis, S. C.; Valaes, T.; Tassopoulos, N. and Brinson, A.
1965 Diverse characteristics of glucose-6-phosphate dehydrogenase from Greek children. J Lab Clin Med 65:212-221.

Kirmlides, S. et al.
1965 G-6-PD deficiency in Greece. Hel Paediatricia Acta 20:490-496.

Kleinman, A. M.
1973 Toward a comparative study of medical systems: an integrated approach to the study of the relationship of medicine and culture. Science, Medicine and Man 1:55-65.

Kolodny, E. Y.
1974 La population des iles de la Grece: essai geographie insulaire en Mediterranee orientale, public avec le concours du Centre Nationale de al Recherche Scientifique Aux-en-Provence Edisud.

Kosower, N. S. and Kosower, E. M.
1967 Does 3, 4-dihydrophenylalanine play a part in favism? Nature (London) 215:285.

Lapeyssonnie, L. and Keyhan, R.
1966 Proceedings of the First Seminar of Favism in Iran. Tehran: Food and Nutrition Institute of Iran. (p. 36).

Liener, I. E.
1962 Toxic factors in edible legumes and their elimination. Am J Clin Nutr 11:281-298.

Livingstone, F. B.
1967 Abnormal Hemoglobins in Human Populations: A Summary and Interpretation. Chicago: Aldine.

Livingstone, F. B.
1971 Malaria and human polymorphisms. In: Annual Review of Genetics 5:33-64.

Luisada, A.
1941 Favism. A singular disease chiefly affecting the red blood cells. Medicine, Baltimore 20:229-250.

MacMahon, B. and Pugh, T. F.
1970 The place of epidemiology in the investigation of disease. In: Epidemiology: Principles and Methods. Boston: Little-Brown. (pp. 3-22).

MacMahon, B.
1970 The strategy of epidemiology, ibid: pp. 32-50.

Marcolongo, F.; Carcassi, U. and Cugudda, U.
1950 Ictero-hemoglobinuric favism: a new interpretation of the hemolytic mechanism. Sc med ital. 1:625.

Marcolongo, F.
1951 Favism. Fattori geografici e razziali nella patogenesi della malattia con particolare riguardo al favismo in Sardegna. Rassegna Medica Sarda 53:89-131.

Marden, P. S.
1908 Greece and the Aegean Islands. New York and Boston: Houghton Mifflin and Co.

Marks, P. A.; Johnson, A. B. and Hirschberg, E.
1958 Effect of age on the enzyme activity of human erythrocytes. Proc Nat Acad Sci 44:529-536.

Marks, P. A. and Gross, R. T.
1959 Erythrocyte glucose-6-phosphate dehydrogenase deficiency: evidence of differences between Negroes and Caucasians with respect to this genetically determined trait. J Clin Inves 38:2253.

Matsoniotis, N. and Kattamis, C.
1969 Thalassemias, a social problem in Greece. Ann Soc belge Med Trop 40:223-239

Martin, S. K.; Miller, L. H.; Alling, D.; Okoye, V. C.; Esan, G. J. F.; Osunkoya, B. O. and Deane, M.
1979 Severe malaria and glucose-6-phosphate dehyrogenase deficiency: A reappraisal of the malaria/G6PD hypothesis. Lancet(March 10):425-526.

May, J.
1960 The ecology of human disease. Ann NY Acad Sci 84: 789-794.

Mela, C. and Perona, G. P.
1959 Sulla resistenze in vitro del glutatione ridotto eritrocitario al succo di fave fresche. Boll della Soc Ital di Biologia Sperimentale 35:146-148.

Miller, A. R.
1948 Peasant remedies from the Greek islands. Bull History of Medicine 22:441-450.

Montano, G.
1894 Del favismo o intossicazione fabacca. In: Biddau, I., Considerazioni sulla patogenesi e sulla terapie del favismo. Terapia 20:106-118. 91930)

Motulsky, A. G.
1960 Population genetics of glucose-6-phosphate dehydrogenase deficiency of the red cell. Proc Conf on Genetic Polymorphisms and Geographic Variations in Disease. B. A. Blumberg, ed. Washington D.C.: Public Health Service.

Motulsky, A. G.
1964 Theoretical and clinical problems of glucose-6-phosphate dehydrogenase deficiency. In: Abnormal Hemoglobins in Africa. J. H. P. Jonxis ed. Oxford: Blackwell. (pp. 143-197).

Motulsky, A. G.
1972 Hemolysis in G6PD deficiency. Fed Proc 31 (4):1286-92.

Motulsky, A. G. and Campbell-Kraut, J. M.
1962 Population genetics of glucose-6-phosphate dehydrogenase deficiency of the red cell. In: Proc Conf on Genetic Polymorphisms and Geographic Variations in Disease. New York: Grune and Stratton: pp. 159-180.

Motulsky, A. G. and Stamatoyannopoulos, G.
1966 Clinical implications of glucose-6-phosphate dehydrogenase deficiency. Ann Intern Med 65:1329-34.

Myres, J. L.
1953 Geographic History in Greek Lands. Oxford: Clarendon Press.

Nathan, R. D.; Pachtman, E. A.; Fiorelli, G. and Frumin, A.
1974 A serum defect in favism. Am J Clin Pathology 61(4): 462-464.

National Statistics Service of Greece
1971 Directory of Towns and Villages. Athens: National Statistics Services.

Nixon, I. G.
1968 The Rise of the Dorians. Puckeridge Herts: The Chancery Press.

Palmarino, R.; Agostino, R.; Gloria, F.; Lucarelli, F.; Businco, C.; Antognoni, G.; Maggioni, P.; Workman, H. and Bottini, E.
1978 Red cell acid phosphatase: another polymorphism correlated with malaria? Am J Phys Anthro 43:177-186.

Paniker, N. Vasudeva
1975 Red cell enzymes. Critical Rev Clin Lab Sci 5:469-502.

Panizon, F. and Vullo, C.
1961 The mechanisms of haemolysis in favism: researchers on the role of non-corpuscular factors. Acta Haemat (Basel) 26:337-343.

Pantelakis, S. N. and Doxiadis, S. A.
1967 Serum lipoproteins in school boys in relation to G6PD deficiency and thalassemia trait. Arch Dis Child 42:328-331.

Patrick, A.
1967 Disease in antiquity: Ancient Greece and Rome. In: Disease in Antiquity. Brothwell and Sandison, eds. Springfield, Illinois: Charles C. Thomas. (pp. 238-246).

Patwardham and White
1969 Favism. In: Toxic Constituents in Plant Foodstuffs. Irvin E. Liener, ed. New York: Academic Press.

Pellicer, A. and Casado, A.
1970 Frequency of thalassemia and G6PD deficiency in five provinces of Spain. Am J. Hum Gen 22(3):298-303.

Polgar, S.
1962 Health and human behavior: areas of interest common to the social sciences. Current Anthro 3(2):159-205.

Rattazzi, M. C.; Lenzerini, L.; Meera Khan, P. and Luzzatoo, L.
1969 Characterization of glucose-6-phosphate dehydrogenase variants. II: G6PD Kephalonia, G6PD Attica, and G6PD "Seattle-like" found in Greece. Paed Act: 154-167.

Rhodes
1977 Clio Edition

Russo, G.
1967 Il favismo in Sicilia. Rev Pediat. Sicil 22:317.

Russo, G.; Mollica, F.; Pavone, L. and Schilliro
1972 Hemolytic crisis of favism in Sicilian females heterozygous for G6PD deficiency. Pediatrics 49(6): 854-859

Samuel, A. E.
1966 The Mycenaeans in History. Englewood Cliffs, New Jersey: Prentice Hall, Inc.

Sansone, G. and Segni, G.
1957 Sensitivity to broad beans, letter to the editor. Lancet ii (August 10):295.

Sansone, G.; Piga, A. M. and Segni, G.
1958 Il Favismo. Ed Minerva Medica, Torino.

Sartori, E.
1971 On the pathogensis of favism. J Med Genet 8(4): 462-467.

Siegle, B.
1968 Medical practitioners and social structure in Brazil and Portugal. Sociologia 20(4):463-476.

Siniscalco, M.; Bernini, L.; Latte, B. and Motulsky, A. G.
1961 Favism aned thalassemia in Sardina and their relationship to malaria. Nature (London) 190:1179-80.

Siniscalco, M.; Bernini, L.; Filippi, G.; Latte, B.; Meera, Kahn P.; Piomelli, S. and Rattazzi, M.
1966 Population genetics of haemoglobin variants. Thalassemia and glucose-6-phosphate dehydrogenase deficiency with particular reference to the malaria hypothesis. Bull WHO 34:379-393.

Stamatoyannopoulos, G. and Fessas, P.
1964 Thalassemia, glucose-6-phosphate dehydrogenase deficiency, sickling and malarial endemicity in Greece: a study of five areas. Brit Med J i: 875-879.

Stamatoyannopoulos, G.; Panayotopoulos, A. and Panayannopoulou, T.
1964 Mild glucose-6-phosphate dehydrogenase deficiency in Greek males. Lancet ii:932-935.

Stamatoyannopoulos, G.; Motulsky, A. G. and Fraser, G. R.
1966 On the familial predisposition to favism. Am J Hum Gen 18(3):253-263.

Szeinberg, A. and Sheba, C.
1958 Hemolytic trait in Oriental Jews connected with an hereditary enzymatic abnormality of erythrocytes. Israel Med J 17:85.

Szeinberg, A.; Sheba, C.; Adam, A.; Ramot, B.; Ashkenaze, I. and Oliver, M.
1961 Glucose-6-phosphate dehydrogenase among Jews. Genetic and anthropological considerations. Proc Conf on Human Population Genetics in Israel. Jerusalem.

Taylor, W.
1964 The Mycenaeans. New York: Frederick A. Praeger.

Tolmas, H.²C.
1957 Favism: case report showing heredofamilial tendency. J Pediat 51:445.

Valaes, T.; Doxiadis, S.A. and Fessas, P.
1963 Acute hemolysis due to napthalene inhalation. J. Pediat 63:904.

Vuopio, P.; Harkonen, M.; Heiske, T. and Naveri, H.
1975 Red-cell glucose-6-phosphate dehydrogenase deficiency in Finland: characterization of a new variant with severe enzyme deficiency. Scand J Haematol 15:145-152.

Weatherall, D. J.
1960 Enzyme deficiency in haemolytic disease of the new born. Lancet ii:835-836.

Wellin, E.
1955 Water-Boiling in a Peruvian Village. In: Health, Culture and Community, B. Paul, ed. New York: Russell Sage Foundation.

Wharton, H. J. and Dusselman, W.
1947 Favism -- A short review and report of a case. New England J Med 236:974.

WHO Scientific Group
1967 Standardization of procedures for the study of glucose-6-phosphate dehydrogenase. WHO Techn Rep Ser 366:30-53.

Wiesenfeld, S. L.
1967 Sickle-cell trait in human biological and cultural evolution. Science 147:1134-40.

Yoshida, A.; Beutler, E. and Motulsky, A. G.
1971 Human glucose-6-phosphate dehydrogenase variants. Bull WHO 45:243-253.

Zacchello, F.; Panizon, F. and Zanesco, L.
1964 Primachina e fave. II. Effetti in vitro sul glutatione enritrocitario et sulla metemoglobina. Acta Paed Latina 17:173-181.

Zannos-Mariolea, L. and Kattamis, C.
1961 Glucose-6-phosphate dehydrogenase activity in erythrocytes of Greek patients with favism. Blood 18:34-47.

Zigas, V.
1970 Kuru in New Guinea: discovery and epidemiology. Am J Trop Med and Hyg 19:130-132.