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The Karaite Community of Iraq in Israel: A Genetic Study

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INTRODUCTION

Karaism, the acceptance of the scriptures as the sole source of religious law and the exclusion of the traditional oral law, arose as a religious movement among the Jews of Babylon during the eighth century A.D. This movement spread rapidly to communities of Babylonian and Persian Jewry and, in the course of time, to other countries in the Middle East, mainly Palestine (Jerusalem), Egypt (Cairo), and Turkey (Constantinople). Between the twelfth and fourteenth centuries Karaites also appeared in northeastern Europe, and concentrated in Lithuania and the Crimea [1].

A small group of Karaites has existed in Hit, Iraq since the tenth century A.D. [2]. This enclave is the sole remaining Iraqi Karaite community extant, but it is almost extinct. In 1869, 20 Karaite families lived in Hit; by 1951, only 13 remained [2], and most of these immigrated to a town in southern Israel in 1951. According to one immigrant, only about 14 members of the community remained in Hit. Since the Hit isolate in Israel is rapidly disintegrating due to extensive intermarriage with Egyptian Karaites, a genetic investigation of the Iraqi group was undertaken. The aim of this survey was to compare various genetic markers of the Hit isolate with other Karaite and non-Karaite Jewish groups in the hope of obtaining information relative to the influence of genetic drift and isolation on a human population.

SUBJECTS AND METHODS

In 1970, each family of the Karaite community of Hit in Israel was approached, interviewed in detail, and asked to participate in the survey. After agreement was obtained,

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TABLE 1

REAGENTS USED TO DETERMINE GM AND INV ALLOTYPES

ALLOTYPE NOMENCLATURE		ANTI-ALLOTYPE		ANTI-D	
Numeric	Alphabetic	Name	Dilution*	Name	Dilution
Gm:					
1	a	Mor	32	Bra	3
2	x	Tyl	32	Ham	3
3	b^2 or f	Aus	4	Ham	3
5	b^1	Pay	4	Cam	10/9
6	c^3	Cur	16	War	10
13	b^3	Ing	4	Cam	10/9
14	b^4	Bur	8	Cam	3
21	g	Monkey E	16	Ham	3
Inv:					
1	1	Mas	4	Roe	3

* The reciprocal of the dilution at which the reagent was used.

all family members 6-years-old and over were given a complete physical examination. Information concerning the general health status and diseases among the members of the community was furnished by the health authorities. Anthropometric measurements were performed by accepted methods using a Siber-Hegner anthropometer. Color vision was tested by Ishihara plates and HRR tables. Screening for hemoglobinopathies included the determination of hemoglobin, hematocrit, and starch gel electrophoresis of hemolysates (tris-EDTA-borate-buffer, pH 8.6). Screening for glucose-6-phosphate dehydrogenase (G6PD) deficiency was performed by the Motulsky test [3]. Blood groups were examined with the following antisera: A, A_1, B, H, M, N, S, s, C, c, D, E, e, K, Fy^a. Standard electrophoretic methods [4, 5] were used to determine haptoglobin and the following red cell isoenzyme phenotypes: acid phosphatase (ACP), phosphoglucomutase (PGM), 6-phosphogluconate dehydrogenase (6PGD), and adenylate kinase (AK).

TABLE 2

POPULATION STRUCTURE OF KARAITES OF HIT BY ORIGIN, AGE, SEX, AND BLOOD EXAMINATION

ORIGIN OF KARAITES	AGE GROUP	NO.		NO. EXAMINED		TOTAL		
		Males	Females	Males	Females	No.	No. Examined	%
Hit	0–5	7	6	...	...	13	...	...
	6–17	15	28	11	23	43	34	74
	18–65	22	27	14	19	49	33	
	66–71	4	1	4	1	5	5	
Total	0–71	48	62	29	43	110	72	...
Egypt	18–65	3	7	1	5	10	6	...
Inter-Karaite (offspring of Hit × Egypt marriages) ..	0–5	10	18	...	...	28	...	...
	6–12	18	11	11	7	29	18	62
Total	0–12	28	29	11	7	57	18	...

Gene frequencies for various systems were calculated by the gene counting method for codominant genes and the square root method for loci with two alleles showing dominance. Frequencies for the ABO system and Rh gene complexes were calculated by Bernstein's correction as described by Mourant [6] and by the method of Ceppellini et al. [7]. Inbreeding coefficients were derived by standard methods [8].

Serum samples from 60 individuals from Hit, four individuals from Egypt, and 16 offspring of matings between individuals from Hit and Egypt were available for Gm and Inv testing. These 80 samples were tested (in 1971) for Gm(1,2,3,5,6,13,14,21) and for Inv(1) with the reagents shown in table 1.

RESULTS AND DISCUSSION

Consanguinity and Inbreeding Coefficients

In 1970, the Hit community in Israel numbered 177 members among whom there were 25 couples and three widows (fig. 1 and table 2). Six of the 25 couples belonged to three bigamous marriages (III-2, 3, 4; IV-12, 18, 19; IV-4; V-19, 20), and 10 were marriages between Karaites from Hit and Egypt. Fifty members of the community were born in Iraq (Hit), 10 in Egypt (Cairo), and 117 in Israel. Among the Israel-born members, 60 are offspring of Karaites from Hit and 57 from inter-Karaite marriages.

The minimal average inbreeding coefficient of the 167 Hit Karaites (Egyptian Karaites excluded) was $\alpha = .028$. The population was not homogenous for this inbreeding coefficient. A lower coefficient of inbreeding was observed among the oldest living persons than among younger persons. This observation is probably due to incomplete information concerning mating types and consanguineous relationships among the oldest generation. In order to validate information obtained on this older generation, the date of marriage was used as a reference point. If this date was unknown, there was a good possibility that the data on consanguinity were inaccurate. Among those Karaites who married in Israel, a lower α was observed because of inter-Karaite marriages. Therefore, the population was divided into three groups (table 3): (1) Offspring of 19 couples whose approximate date

TABLE 3

MATING TYPE AND INBREEDING COEFFICIENT (F) OF THE HIT KARAITE POPULATION

	First Cousins or Multiple Consanguinity				First Cousins Once Removed	Not Related or Inter-Karaite	Unknown
Mating Type							
F	6/64	5/64	1/16	3/64	1/32	0	0
Place and date of marriage:							
Abroad, date unknown ..	...	...	4* (7)	...	1 (1)	...	14* (24)
Abroad, 1915–1950	...	1 (6)	8 (44)	...	1 (6)	2 (8)	...
Israel, 1956–1966	1 (4)	1 (4)	...	1 (2)	1 (2)	10 (57)	1 (2)

NOTE.—No. in parentheses = living offspring.
* Spouses dead or remarried.

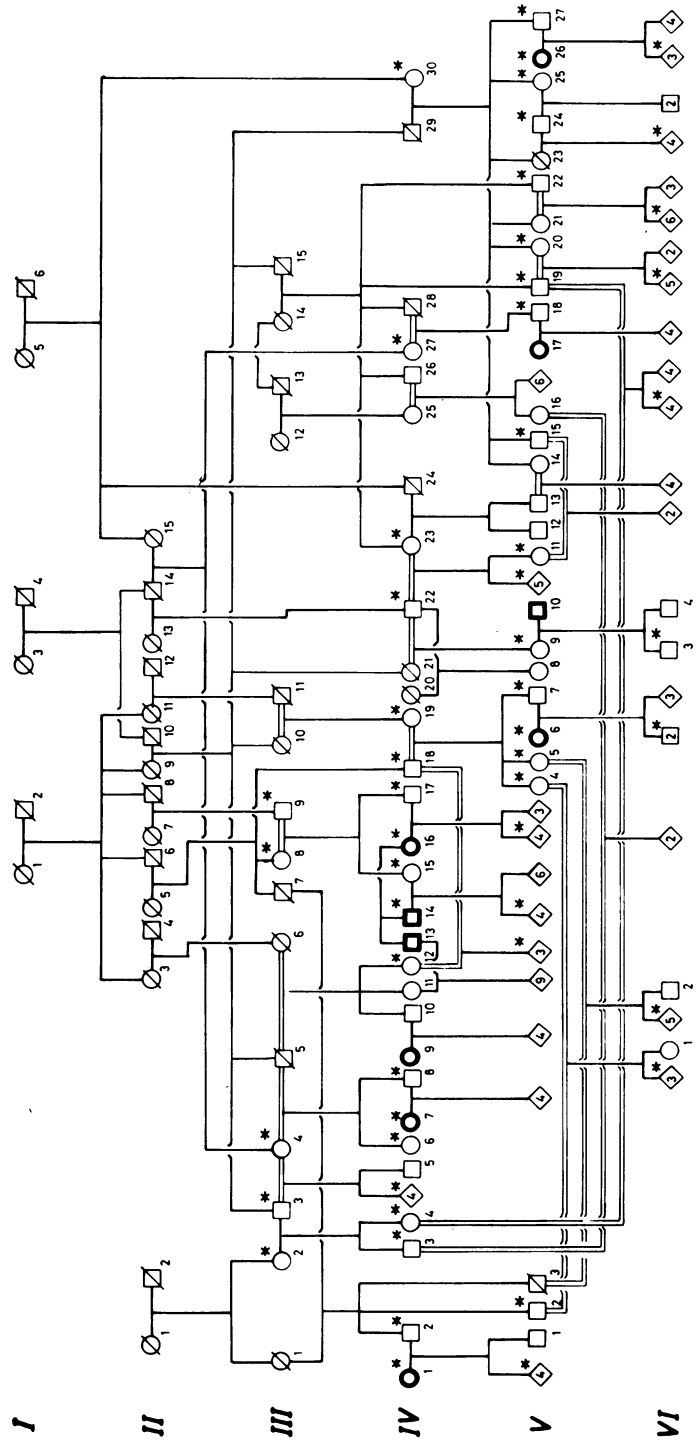

FIG. 1.—Pedigree of Karaites of Hit living in Israel

of marriage was unknown. This group contained 32 members with $\alpha = .015$. (2) Offspring of 12 couples who married abroad and whose approximate date of marriage was known. This group contained 64 members with $\alpha = .053$. (3) Offspring of 15 couples who married in Israel. This group contained 71 members with $\alpha = .012$.

Group 2 may represent a relatively accurate estimate of α for the overall Hit isolate in spite of the group's small size. Group 3 demonstrates the rapid reduction in inbreeding due to inter-Karaite marriages.

Clinical Findings and Anthropometrics

During the clinical examination, hepatomegaly was observed in eight subjects. Hospital records of three of these (IV-19; V-25, 27) and of one deceased member (V-23) revealed liver cirrhosis of unknown etiology.

Seven anthropometric measurements were performed on 120 children and adults. These included 82 Karaites of Hit (44 aged 2–17 years, 33 aged 18–65 years, and five aged 66–71 years), six Karaites from Egypt aged 26–39 years, and 32 offspring of inter-Karaite matings. Table 4 summarizes the results on 33 of 49 adults from Hit aged 18–65 years (67%). The only finding of interest is the relative short stature ($\overline{X}$ males = 160.9 cm; $\overline{X}$ females = 149.4 cm). Five females from Egypt had a mean stature of 155.0 cm.

Color vision was investigated for 93 persons 5-years-old and over; 28 males and 40 females from Hit, one male and four females from Egypt, and 12 male and eight female offspring of inter-Karaite marriages. Not one instance of color blindness was recorded.

Biochemical Markers

Electrophoresis of hemoglobin from 72 Karaites from Hit, six from Egypt, and 18 offspring of inter-Karaite marriages all revealed normal patterns of Hb A and Hb A_2.

TABLE 4

ANTHROPOMETRIC MEASUREMENTS AMONG 33 ADULT HIT KARAITES

Measurements	Males (14)			Females (19)			Female:Male Ratio
	Mean	SD	SE	Mean	SD	SE	
Weight (kg)	56.0	14.9	2.23	47.4	15.5	1.69	85
Stature (cm)	160.9	3.5	1.53	149.4	3.2	1.11	93
Sitting height (cm)	84.7*	4.2	1.00	80.0	5.2	.96	94
Knee height (cm)	45.9	7.2	.89	41.7	4.6	.44	91
Head circumference (cm)	57.1	2.9	.46	55.8	4.2	.54	98
Head breadth (cm)	14.8	2.8	.11	14.0	3.3	.10	95
Head length (cm)	19.2	2.7	.14	18.0	2.8	.11	94
Cephalic index (%)	76.9	2.3	.48	77.8	2.9	.53	101
Calf circumference (cm)	32.2	5.9	.51	30.4	7.7	.54	94

* 13 males only.

The G6PD activity of 29 males and 43 females from Hit, one male and five females from Egypt, and 11 male and seven female offspring of inter-Karaite matings was within normal limits. This result is somewhat surprising since non-Karaite Iraqi Jews have a high prevalence of G6PD deficiency; the gene frequency was approximately .25 [9]. This observation confirms the isolation of the Karaites from other Jews in Iraq. Similarly, none of the 250 Karaites from Egypt had G6PD deficiency [10].

Seventy-two of 97 (74%) Karaites from Hit, six Karaites from Egypt, and 18 offspring of inter-Karaite matings six-years-old and over (table 2) were examined for blood groups, isoenzymes, and haptoglobins. A portion of these samples was tested for Gm and Inv allotypes. Although the individuals investigated were not randomly distributed throughout the population (fig. 1), all examined members from Hit were included for gene frequency estimates (tables 5 and 6). The results demonstrate great polarity in some gene frequencies. The gene frequency for ABO

TABLE 5

PHENOTYPES OF RED CELL AND PLASMA PROTEIN MARKERS OF KARAITES OF HIT

MARKER AND PHENOTYPE	ORIGIN OF KARAITES			
	Hit (Observed)	Hit (Expected)	Hit × Egypt (Observed)	Egypt (Observed)
ABO:				
A_1	4	3.9	0	0
A_2	18	13.7	6	0
B	34	30.0	8	5
A_1B	2	2.1	0	0
A_2B	4	9.1	1	0
0	10	13.2	3	1
Total	72	...	18	6
Rhesus:				
CCDee	4	3.8	4	3
CcDee	24	24.3	8	1
ccDee	19	19.0	1	0
ccdee	20	20.0	1	0
ccDEe	4	3.7	2	1
CcDEe	1	1.4	2	1
ccDEE	0	0.1	0	0
Total	72	...	18	6
MNSs:				
MMSS	2	2.0	0	1
MMSs	22	19.3	2	0
MMss	46	46.7	13	3
MNss	2	1.6	2	1
Other	0	2.4	1 (MNSs)	1 (MNSS)
Total	72	...	18	6

TABLE 5 (*continued*)

Marker and Phenotype	Origin of Karaites			
	Hit (Observed)	Hit (Expected)	Hit × Egypt (Observed)	Egypt (Observed)
Kell:				
K+	13	...	1	1
K−	59	...	17	5
Total	72	...	18	6
Duffy:				
Fy^a+	55	...	16	5
Fy^a−	17	...	2	1
Total	72	...	18	6
PGM_1:				
1-1	36	35.0	12	4
2-1	27	29.0	5	1
2-2	7	6.0	1	0
Total	70	...	18	5
ACP:				
AA	0	0	0	1
BA	0	0	3	0
BB	67	67.1	12	5
CB	5	4.8	3	0
CC	0	0.1	0	0
Total	72	...	18	6
AK:				
1-1	71	...	15	5
2-1	0	...	3	1
Total	71	...	18	6
6PGD:				
A-A	72	...	18	6
Hp:				
1-1	3	5.5	2	0
2-1	33	28.0	7	5
2-2	33	35.5	9	1
Total	69	...	18	6
Gm+:				
3, 5, 13, 14	34	35.3	...	...
1, 3, 5, 13, 14, 21	24	21.5	...	...
1, 21	2	3.3	...	...
Total	60	...	...	...
Inv+:				
1	1	...	...	...
−1	59	...	...	...
Total	60	...	...	...

TABLE 6

GENE FREQUENCIES OF RED CELL AND PLASMA MARKERS OF KARAITES OF HIT

Marker	Gene Frequencies			
ABO	$A_1 = .043$	$A_2 = .183$	$B = .346$	$O = .429$
Rhesus	$CDe = .229$	$cDE = .035$	$cDe = .209$	$cde = .527$
MNSs	$MS = .180$	$Ms = .806$	$NS = .000$	$Ns = .014$
Kell	$K = .095$	$k = .905$	...	...
Duffy	$Fy^a+ = .514$	$Fy^a- = .436$	...	...
PGM_1	$PGM_1{}^1 = .707$	$PGM_1{}^2 = .293$	...	...
Acid phosphatase	$ACP^B = .965$	$ACP^C = .035$	...	...
Adenylate Kinase	$AK^1 = 1.0$	...	...	...
6PGD	$6PGD^A = 1.0$	...	...	...
Haptoglobin	$Hp^1 = .283$	$Hp^2 = .717$	...	...
Gm	$Gm^{3,5,13,14} = .767$	...	$Gm^{1,21} = .233$	...
Inv	$Inv^1 = .008$	...	...	...

blood group allele A_2 is extremely high (.183), while that for A_1 is low (.043). Similar results, but with higher gene frequencies for A_1 have been observed in a few non-Jewish populations such as the Flittas of Oran, Algeria ($A_1 = .115$; $A_2 = .176$) [11] and the Lapps ($A_1 = .24$; $A_2 = .19$) [12], and among Jews only in the Habbanites ($A_1 = .141$; $A_2 = .100$) [13]. The high frequency of B (.346) among the Karaites of Hit is similar to that observed in Karaites from Egypt (.345) [10], and higher than observed among Karaites from Europe (.233 and .218) [11]. The frequency of B is also higher than in the Jews of the Habbanite isolate (.213) and the Tafilalet Oasis of Morocco (.279) [13]. The very high frequency of the so called "African gene", *cDe* (.209), is notable, as is the frequency of *cde* (.527). The M allele has an extremely high frequency (.986), while only two persons, mother and son (III-2 and IV-3) carried the N allele. The frequency of the S allele is relatively low (.180) and the high frequency of K (.095) is also remarkable.

Among the isoenzyme systems examined, the most striking observation is the complete lack of the acid phosphatase allele ACP^A in the Hit isolate and a correspondingly high frequency of ACP^B (.965). It is of interest that among the 18 children of inter-Karaite marriages examined for acid phosphatase, three were of phenotype ACP AB, 12 ACP B, and three ACP BC. The ACP^A allele was introduced into the community by an Egyptian Karaite (V-26) who was phenotype A. The AK_2 allele was not present among Karaites of Hit and was similarly introduced into the community by a Karaite of Egypt (IV-14) (table 5).

The 80 samples tested for Gm(1,2,3,5,6,13,14,21) showed only three phenotypes [Gm(3,5,13,14), Gm(1,3,5,13,14,21), and Gm(1,21)] which may be explained by two common Caucasian haplotypes ($Gm^{3,5,13,14}$ and $Gm^{1,21}$). Haplotype $Gm^{1,2,21}$ was not detected. The data for the 60 samples from the Karaites from Hit are presented in tables 5 and 6. The data for these samples differ con-

siderably from those for other Jewish populations [14–16], in that there is an absence of $Gm^{1,2,21}$ and of haplotypes indicating African admixture.

The Inv data for the Karaites from Hit are presented in tables 5 and 6. Only one of the 60 samples from Hit was Inv(1) (V-22). He is a $1\frac{1}{2}$ cousin of the three siblings at the extreme right of generation VI, one of whom is Inv(1). Unfortunately neither of their parents (V-26 from Egypt, and V-27 from Hit) was tested. Hence the Inv^1 allele could have been introduced by either parent. Two of the four tested individuals at the extreme left of generation V were Inv(1). Their father (IV-2) from Hit was Inv(—1), their mother from Egypt, who was not tested, is the probable source of Inv(1). One (IV-7) of the four samples from Egypt was Inv(1). Inv polymorphism seems to be on the verge of extinction among the Karaites from Hit.

The allelic frequencies of the genetic loci investigated were in accordance with the Hardy-Weinberg equilibrium. The extraordinary diversity in gene frequencies, reaching complete allelic loss in two instances and virtual loss in a third, is most likely the result of genetic drift in a small community.

CONCLUSIONS

This small inbred Iraqi-Karaite isolate has several special features worthy of mention. Cirrhosis of the liver was diagnosed in four individuals and may be present among additional members of the community. The stature of males and females is relatively short. No abnormalities of hemoglobin, color vision, nor G6PD activity were observed. The latter finding is exceptional since among non-Karaite Jews deriving from the same geographic area G6PD deficiency is approximately .25 [9]. The allelic frequencies of several blood group systems are extreme and even the loss of the alleles ACP^A and AK_2 were observed. These results clearly indicate the strong influence of isolation and genetic drift operating in this community.

SUMMARY

Ninety-eight of 136 (72%) individuals at least 6 years of age from a small isolate of the Karaite community, known to have lived in Iraq since the tenth century, were examined. In Iraq this group maintained a highly inbred existence but married Karaites from Egypt after their immigration to Israel in 1951. Observation of several unique gene frequencies for blood group and isoenzyme markers, not described among other Jewish groups, are explicable by isolation and genetic drift in a very small community.

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REFERENCES

1. BEN-JACOB A: *A History of the Jews in Iraq (in Hebrew)*. Jerusalem, Ben-Zvi Inst., Hebrew Univ., 1956
2. BEN-ZVI Y: *Nidchei Israel (in Hebrew)*. Tel Aviv, Twersky Publ. Co., 1956
3. MOTULSKY AG, CAMPBELL-KRAUT JM: Population genetics of glucose-6-phosphate dehydrogenase deficiency of the red cell. *Proceedings of the Conference on Genetic Polymorphisms and Geographic Variations in Disease,* New York, Grune & Stratton, 1961 pp 159–191
4. GIBLETT ER: *Genetic Markers in Human Blood.* Oxford, Blackwell, 1969
5. YUNIS JJ: *Biochemical Methods in Red Cell Genetics.* New York, Academic Press, 1969
6. MOURANT AE: *The Distribution of the Human Blood Groups.* Oxford, Blackwell, 1954.
7. CEPPELLINI R, SINISCALCO M, SMITH CAB: The estimation of gene frequencies in a random mating population. *Ann Hum Gen* 20:97–115, 1955
8. CAVALLI-SFORZA LL, BODMER WF: *The Genetics of Human Populations.* San Francisco, Freeman, 1971
9. SHEBA C, SZEINBERG A, RAMOT B, ADAM A, ASHKENAZI I: Eipdemiologic surveys of deleterious genes in different population groups in Israel. *Am J Public Health* 52:1101–1106, 1962
10. FRIED K, LANDAU J, COHEN T, GOLDSCHMIDT E: Some polymorphic characters of the Karaite community (in Hebrew). *Harehuah* 75:507–509, 1968
11. MOURANT AE, KOPEC AC, DOMANIEWSKA-SOBCZAK K: *The ABO Blood Groups.* Oxford, Blackwell, 1958
12. TILIKAINEN A, ERIKSSON AW, MACQUEEN JM, AMOS DB: The HL-A system in the skolt Lapp population. In *Histocompatibility Testing* 1972, edited by DAUSSET J, COLOMBANI J, 1972 pp 85–92
13. BONNÉ B, ASHBEL S, MODAI M, GODBER MJ, MOURANT AE, TILLS D, WOODHEAD BG: The Habbanite isolate. I. Genetic markers in the blood. *Hum Hered* 20:609–622, 1970
14. ROPARTZ C, ROUSSEAU PY, RIVAT L, LENOIR J: Hypotheses sur la génétique formelle du système Gm chez les Caucasiens. *Humangenetik* 1:483–496, 1965
15. STEINBERG AG, LEVENE C, GOLDSCHMIDT E, COHEN T: The Gm and Inv allotypes in kindreds of Kurdish Jews. *Am J Hum Gen* 22:652–661, 1970
16. STEINBERG AG: The Gm and Inv allotypes of some Ashkenazic Jews living in northern U.S.A. *Am J Phys Anthropol* 39:409–412, 1973

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