The Geographic Hypothesis and Lactose Malabsorption

A Weighing of the Evidence

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Reviewed in this article is evidence bearing on the geographic hypothesis advanced eight years ago to explain the striking ethnic or racial differences in prevalence of primary adult lactose malabsorption that are found around the world. Most evidence is found to support the hypothesis and the likelihood that some human groups came to have low prevalences of such lactose malabsorption because of selective pressures over a long historical period that favored the adult lactose absorber under particular ecological conditions.

It has been a dozen years since medical researchers (1, 2) first recognized the existence in the United States of striking ethnic or racial differences in prevalence of primary adult lactose malabsorption (hereafter usually referred to as LM).* Studies completed over the next few years revealed that such differences occur in other countries as well, and they led this writer to consider the geographic distribution of high and low prevalences of LM around the world and to advance a hypothesis to explain distributional patterns in evolutionary and historical terms (3). In the eight years since that "geographic" or "cultural historical" hypothesis was first advanced, there has been an impressive accumulation of studies bearing on its validity and on that of alternative hypotheses. It seems timely, therefore, that the geographic evidence be reviewed, that problem areas be identified, and that relevant data be presented so as to facilitate further research in the matter. The focus throughout this paper, therefore, is not on practical implications of LM, but on problems of geography and evolution.

It is now clear that "primary adult lactose malabsorption" among most human groups usually comes on in the years immediately after weaning. Although onset may be delayed into the teens or even into adulthood, a more appropriate term for this form of lactose malabsorption might be "primary postweaning lactose malabsorption." There are also other forms of lactose malabsorption (4): a congenital form that occurs in infants and a secondary form that may occur in infants, children, or adults who have intestinal disorders, diseases, or surgery that reduce lactase activity to low levels. Adults who have primary adult lactose malabsorption, however, normally have experienced high intestinal lactase activity as infants. They have had no intestinal disorder, disease, or surgery that might account for the low lactase activity that develops after weaning. Yet they come to differ markedly from those individuals who experience high intestinal

*Over the years, there has been confusion over the terms "lactose malabsorption" and "lactose intolerance." Generally today a person is classified a lactose absorber or lactose malabsorber according to evidences of digestion after he consumes lactose in a test, the most common one involving measures of blood glucose levels. The lactose malabsorber may or may not develop symptoms (flatulence, intestinal cramps, diarrhea, nausea, vomiting) on consuming the test lactose. If he does, he would be classified lactose intolerant as well. Although researchers in the past often used "lactose intolerance" to refer to what today would be designated "lactose malabsorption," we have, where necessary, changed their terminology to conform with present-day usage.

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lactase activity through life, who do not undergo a postweaning decline, and who can hydrolyze lactose in quantity and continue to consume sizable amounts of milk and other lactose-rich dairy products without intestinal discomfort.

High prevalences of LM, from about 60–100% of the persons studied, are typical of the overwhelming number of ethnic groups around the world (Table 1), including all American Indians and Eskimos studied so far, some New World Mestizos, most sub-Saharan African peoples and their relatively unmixed overseas descendants, most Mediterranean and Near Eastern groups, most subjects whose origins are in India, all peoples of Southeast and East Asia, as well as the two Pacific groups, New Guineans and Fijians, who have been studied. Low prevalences of LM (from 0 to 30%), on the other hand, typify a minority of the world's peoples, primarily northern and western Europeans and their overseas descendants, but also certain peoples of the Mediterranean and Near East, three pastoral groups of Africa (Tussi, Hima, and Fulani), and several groups living in the western parts of the Indian subcontinent. There are some groups who have intermediate prevalences of LM (30–60%), but they are few, and almost all have a mixed absorber/malabsorber ancestry. Thus, the relatively unmixed ethnic groups of the world seem to fall into two population categories: lactose absorbers (0–30% prevalences of LM) and malabsorbers (60–100% prevalences). How such a striking contrast may have come about has been a matter of controversy, and we turn now to the principal explanatory hypotheses that have been advanced.

TABLE 1. PREVALENCE OF PRIMARY ADULT LACTOSE MALABSORPTION (LM) AMONG ETHNIC OR RACIAL GROUPS*

	No. of persons in study†	*Ages of persons*	*Reference*	*No. of persons with LM*	*Prevalence of LM (%)*
Category a: Hunting and gathering peoples (N = 287; with LM, 247; prevalence of LM, 86%)					
Eskimo of Greenland	81	1–>30	48	68	84
Eskimo of Greenland	25	13–75	49,50	22	88
Eskimo of Greenland	13	Adults	51	11	85
Alaskan Indians and Eskimos	36	Adults	107	34	94
Indians of Canada's west coast	30	14–24	180	19	63
Chippewa of Minnesota	15	5–73	46	14	93
Twa Pygmies of Rwanda	22	15–58	108	17	77
!Kung Bushmen of southwest Africa	40	Adults	109	39	92
‡huâ Bushmen of Botswana	25	≥10	110	23	98
Category b: Agricultural peoples from the traditional zones of nonmilking and their relatively unmixed overseas descendants (N = 1311; with LM, 1186; prevalence of LM, 90%)					
In North and South America (N = 167; with LM, 162; prevalence of LM, 97%)					
Chami Indians of Colombia	24	15–55	111	24	100
Pima	62	≥4	36	59	95
Pima	4	Adults	37	4	100
Hopi	21	Adults	37	21	100
Papago	14	Adults	37	13	93
Apache (groups varied in emphasis on farming; some had little if any)	22	Adults	37	22	100
Oklahoma Indians	20	Adults	47	19	95
In sub-Saharan Africa (N = 311; with LM, 270; prevalence of LM, 87%)					
S. Nigerians (mostly)	9	Adults	55	9	100
Yoruba	41	≥4	35	40	98
Ibo	11	13–38	55	9	82
Children in Ghana	100	2–6	112	73	73
Bantu of various tribes, Zaire	52	Adults	113	51	95
Ibo	4	Adults	113	3	75
Yoruba	48	13–70	55	40	84
Yoruba	11	≥3	42	11	100
Bush Negroes of Surinam	29	Adults	67, 68, 114	28	100
Bantu of the Cameroons	6	Adults	113	6	100

*Attempt made to include all samples of 4 or more persons tested for LM in any one study.
†In studies where a distinction was made between unmixed ("full-blooded") and mixed individuals, we included only unmixed persons where this was possible, except in category e.

TABLE 1. PREVALENCE OF PRIMARY ADULT LACTOSE MALABSORPTION (LM) AMONG ETHNIC OR RACIAL GROUPS* (CONT'D)

	No. of persons in study†	*Ages of persons*	*Reference*	*No. of persons with LM*	*Prevalence of LM (%)*
In Southeast and East Asia (N = 829; with LM, 750; prevalence of LM, 90%)					
Thai	9	10–45	29	9	100
Thai	75	Adults	115	75	99
Thai	24	4–12	115	24	100
Thai	100	Adults	116	96	96
Thai	140	Adults	117	136	97
Thai	39	13–72	118	39	100
Thai	16	2–4	39	16	100
Chinese, Malays, Indians in Singapore	22	15–42	16	22	100
Chinese in Singapore	10	5–10	32	9	90
Chinese in Taiwan	71	Adults	119	71	100
Chinese in Australia	34	13–34	11	19	56
Chinese in Australia	20	≥17	120	16	80
Chinese in Australia	30	Adults	10	27	90
Chinese in U.S.	6	Adults	121	6	100
Vietnamese in U.S.	31	Adults	122	31	100
Orientals in U.S. (Japanese, Koreans, and Chinese)	11	Adults	123	11	100
Orientals in U.S. (Chinese, Filipinos)	20	Adults	124	13	65
Japanese	40	Adults	125	29	73
Japanese	8	Adults	126	8	100
Filipinos	20	2–14	127	9	45
Indonesians on Java	50	1–6	128	36	72
Indonesians on Java	53	Adults	129	48	91
In the Pacific Region (N = 20; with LM, 20; prevalence of LM, 100%)					
New Guineans	8	14–30	10, 14	8	100
Fijians	12	Adults	130	12	100
Category c: Agricultural peoples whose ancestry lies in the traditional zones of nonmilking but who migrated into an adjacent zone, to become milk-users at a relatively recent date (N = 226; with LM, 199; prevalence of LM, 88%)					
Kenyans (mainly Kikuyu, Kamba, and other Bantu agricultural tribes)	71	5–15	131	52	73
Bantu of Zambia	26	17–59	132	26	100
Bantu of South Africa	31	Adults?	133	28	90
Shi, Bantu of Lake Kivu area	28	Adults	108	27	96
Ganda and other agricultural Bantu of Uganda	52	11–70	53	50	96
Ganda and other Uganda Bantu	12	13–43	54	12	100
Ganda	6	5–12	134	4	67
Category d: Peoples, including some of pastoral tradition, who have consumed amounts of milk and lactose-rich dairy products for a long historical period and have lived under conditions of dietary stress (also their relatively unmixed overseas descendants) (N = 3489; with LM, 376; prevalence of LM, 11%)					
In Africa and the Near East (N = 101; with LM, 10; prevalence of LM, 10%)					
Nomadic Fulani	9	≥4	35	2	22
Bedouin Arabs	14	Adults	52	2	14
Urban Saudi Arabs	8	17–65	52	1	13
Hima pastoralists	11	6–53	53	1	9
Tussi pastoralists in Uganda	12	10–50	53	2	17
Tussi, in Congo	15	Adults	113	0	0
Tussi, in Rwanda	27	Adults	108	2	8
Tussi	5	12–33	54	0	0
Europeans and their overseas descendants (N = 3269; with LM, 344; prevalence of LM, 11%)					
Danes	670	Adults	135	16	2
Danes	91	Adults	136	3	3
Swedes in Finland	91	Adults	85	7	8
Swedes in Sweden	400	Adults	137	4?	1
Finns	159	Adults	92	27	17
Finns	156	Adults	28,138	27	17
Finns	134	Adults	139	24	18
Finns	129	7–15	93, 140–142	8	6
"Europeans" tested in Nigeria	9	≥3	42	2	22
Northwest Europeans (British, Irish, Scandinavian, German)	90	Adults	143	11	12
"Anglo-Saxons" (Canadians, Americans, and Britons tested in Nigeria)	8	Adults	35	1	13
"Anglo-American" whites	142	Adults	81	21	15
American whites	20	Adults	2,65,124	2	10

TABLE 1. PREVALENCE OF PRIMARY ADULT LACTOSE MALABSORPTION (LM) AMONG ETHNIC OR RACIAL GROUPS* (CONT'D)

	No. of persons in study†	*Ages of persons*	*Reference*	*No. of persons with LM*	*Prevalence of LM (%)*
American whites	145	3–80	63	28	19
American whites	93	Adults	144	18	19
American whites	8	Adults	61	1	13
American whites	12	Adults	121	1	8
American whites	16	Adults	107	4	25
"Caucasian" control group in Congo	10	Adults	113	2	20
American whites	65	>5	78	16	25
American whites	19	14–78	1	3	16
Non-Jewish American whites	53	Adults	145	21	11
American whites (northwest European ancestry)	59	Adults	83	7	12
American whites	17	10–14	62	15	9
American whites	100	Adults	146	6	6
American whites	18	Adults	147	3	17
Canadian whites	16	15–26	108	1	6
Australian whites	100	Adults	17	6	6
Australian whites	10	Adults	120	0	0
Australian whites	23	Adults	8,10,14	0	0
French	14	Adults	148	1	7
Germans from Central Europe	55	Adults	149	8	15
Dutch in Surinam	14	Adults	67,68,114	2?	14?
Poles in Canada	21	17–65	150	6	29
Czechs in Canada	17	17–65	150	3	18
Czechs from Bohemia and Moravia	20	Adults	182	0	0
Spaniards	265	Adults	151,152	39	15
In India and Pakistan (N = 119; with LM, 22; prevalence of LM, 18%)					
Punjabis	9	Adults	87	3	33
Indians of New Delhi region	70	17–74	153,154	19	27
Punjabis	9	Adults	155	0	0
Sindhis	12	Adults	155	0	0
Baloochis	4	Adults	155	0	0
Pathans	15	Adults	155	0	0
Category e: Mixed groups of milking/nonmilking ancestry (category d × a, b, or c)					
In Africa					
Iru (mixed Bantu/"Hamitic")	13	7–60	53,54	5	39
Hutu (mixed Bantu/"Hamitic")	15	8–60	53,54	5	33
Hutu	36	Adults	108	21	58
Hutu/Tussi mixed persons	11	Adults	108	6	55
Town Fulani (mixed Fulani/Hausa)	24	≥4	35	17	71
Hausa/Fulani	15	17–60	55	9	60
Yoruba/European mixed	43	≥3	42	19	44
Nama Hottentots (Bushman/"Hamitic"?)	18	Adults	156	9	50
In the Near East					
"Khadiry" (mixed Arab/African people)	9	14–60	52	7	78
"Mohajirs" (mixtures of Pakistani native groups with Dravidians)	15	Adults	155	3	20
In the Americas					
Surinam creole adults	31	Adults	67,68,114	22?	71?
American blacks	31	*ca.* ≥5	86	14	45
American blacks	20	Adults	2,65	15	75
American blacks	22	3–80	63	17	77
American blacks	24	Adults	64	18	75
American blacks	41	14–78	1	30	73
American blacks	25	4–5	157	6	24
American blacks	98	Adults	83	79	81
American blacks	32	11–18	79	19	59
American blacks	89	6–14	80	48	54
American blacks	8	19–43	147	6	75
American Indian/"Anglo" mixed persons	6	Adults	91	3	50
American Indians of mixed ancestry	16	Adults	47	10	63
American Indian/"Anglo" mixed persons	41	≥4	36	25	61
Chippewa/northwest European mixed persons with 84% or less Indian blood	39	5–73	46	14	36
Greenland Eskimo/northwest European mixed persons	97	1–≥30	148	38	39
Greenland Eskimo/northwest European mixed persons	7	13–75	49,50	1	14

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	No. of persons in study†	*Ages of persons*	*Reference*	*No. of persons with LM*	*Prevalence of LM (%)*
Greenland Eskimo/northwest European mixed persons	4	Adults	51	2	50
Colombian Mestizos	16	Adults	56	4	25
Colombian Antioqueños (Spanish, Indian, Negro mixture)	29	Adults	56	11	38
Mexican Americans	17	Adults	43	8	47
Mexican Americans	11	Adults	60,61	6	55
Mexican Americans	75	10–14	62	42	56
Mexican Americans	277	Adults	81	144	53
Mexican Mestizos	100	Adults	59	74	74
Peruvian Mestizos	50	16–54	57	40	80
Peruvian university students (many Mestizo?)	44	Adults	158	28	63
Southeast Asia					
Thai/northwest European persons	6	11–59	29	3	50
Category f: Peoples who have used milk since antiquity but who do not meet conditions of strong selective pressures against LM (N = 716; with LM, 514; prevalence of LM, 72%)					
Jews in Britain	10	Adults	143,159	8	80
American Jews	41	Adults	145	29	71
Canadian and American Jews	32	Adults	160	22	69
Jews in Israel	50	8–16	91	27	54
Jews in Israel	93	Adults	161	57	61
Jews in Israel	58	Adults	41	35	60
Jews in Israel (overall summary of below)	215	17–70	90	153	71
Ashkenazi	53	Adults	90	42	79
N. African Sephardi	32	Adults	90	20	63
other Sephardi (from Turkey, Bulgaria, Greece)	36	17–69	90	26	72
Yemen Jews	36	Adults	90	16	44
Iraqi Jews	38	17–65	90	32	84
Other Oriental Jews (mainly Persian)	20	Adults	90	17	85
Arab villagers in Israel	67	Adults	162	54	81
Syrian Arabs	40	Adults	163	38	95
Jordanian Arabs	56	17–48	164	43	77
Arabs from Jordan, Syria, and Morocco	14	Adults	181	14	100
Arabs from Jordan, Syria, Saudi Arabia, Egypt, Iraq, Tunisia	26	Adults	165	21	81
Egyptian fellahin	14	13–65	166	13	93
Category g: Problems					
Italians and Greeks					
North Italians (Ligurians)	40	Adults	144	12	30
Italians in Naples area	9	15–45	167,168	9	100
mainland Greeks	600	15–78	102	268	45
mainland Greeks	16	Adults	169	6	38
Greeks (not identified further)	82	1–13	170	55	67
Greeks (not identified further)	24	7–13	171	13	54
Greeks in Britain (not identified further)	8	Adults	143,159	8	100
Greek Cretans	50	Adults	102	28	56
Greek Cypriots in Britain	17	Children and adults	172	15	88
Greek Cypriots	50	Adults	102	33	67
Peoples of India					
Indians in Canada (from outside the Punjab)	15	Adults	87	14	93
Indians in U.S.	18	Adults	173	15	83
Indians in Surinam	27	7–12	67,68	?	66?
Indians in Hyderabad (Deccan)	18	Adults	174	11	61
Indians in Bombay	100	Adults	175	64	64
Indians in Bombay	17	Adults	176	4	24
Indians in Fiji	8	Adults	130	5	63
Indians in Australia	5	Adults	8,10,14	4	80
Indians and Pakistanis	16	Adults	143,159	15	93
Indians in Singapore	5	5–8	32	4	80
Indians from Trinidad	5	Adults	87	1	20
Indians from Trinidad	25	Adults	177	15	60
Ceylonese	200	Adults	178	145	73

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	No. of persons in study†	*Ages of persons*	*Reference*	*No. of persons with LM*	*Prevalence of LM (%)*
Finnish Lapps					
Skolt Lapps in Finland	176	≥ 15	138	[106]	60
Mountain Lapps in Finland	75	≥ 15	138	[28]	37
Fisher Lapps in Finland	110	≥ 15	138	[28]	25
Mountain Lapps some with Fisher Lapp ancestry	160	≥ 15	138	[54]	34
Semites of Ethiopia and Yemen; Hausa of Nigeria					
Ethiopians/Eritreans (mainly Amhara and Tigre)	58	7–13	179	52	90
Yemen Arabs	8	16–40	52	2	25
Hausa	17	≥4	35	13	76
Nilotes and Rehoboth Basters					
Nilotes or Nilo-Hamites in Uganda	9	16–35	53	4	44
Dinka	5	Adults	113	5	100
Rehoboth Basters (50% Caucasoid, 50% Hottentot?)	20	Adults?	156	13	65

TWO EARLY HYPOTHESES: DISEASE AND DIETARY INHIBITION

The disease hypothesis and the hypothesis of dietary inhibition were based on the observations that decrease in lactase activity can result from intestinal disorders, diseases, or from ingestion of some foods or drugs, for example neomycin (5), cochicine (6), or certain sugars (7). May it be, a few researchers have queried, that group differences in prevalence of LM merely reflect contrasts in disease or intake of food or drugs that inhibit lactase, which would make the group differences secondary rather than primary? With respect to the disease hypothesis, it should be noted that in the studies cited herein medical researchers have usually tried to include only normal persons without recent histories of intestinal surgery, disease, or diarrhea. Although peoples around the world differ notably in prevalence of subclinical intestinal problems and malabsorption, the disease hypothesis does not fit with the occurrence of significant differences in prevalence of LM among groups living in the same environment who have been exposed to similar risks of disease and intestinal damage, for example blacks, Orientals, and whites living in America; or "Hamitic" pastoralists and Bantu farmers in east Africa. As for the dietary inhibition hypothesis, no evidence has ever been put forward to support it, and it remains highly speculative. Because of this, these hypotheses have few adherents today, and it seems that one must look elsewhere for an explanation of group differences in prevalence of adult lactose malabsorption.

THE INDUCTION HYPOTHESIS

The induction hypothesis, whose leading early advocates were the Australian medical researchers T.D. Bolin, A.E. Davis, and their colleagues (8–19), differs from that of dietary inhibition in holding that ingestion of certain foodstuffs, those containing lactose, induces (rather than inhibits) intestinal lactase activity. Thus, it was suggested, observed group differences in prevalence of adult lactase deficiency and lactose malabsorption reflect contrasts in patterns of milk consumption. Those peoples who consume little or no milk after weaning have high prevalences of LM, whereas low prevalences are typical of those who consume milk in quantity through life. The evidence advanced by Bolin and Davis in support of the induction hypothesis was of two types. First was that derived from studies of humans, especially prevalence and age of onset of LM as these relate to milk consumption by Australian whites and peoples of South and East Asian origin. Second was evidence obtained from studies of rats, which involved prolonged lactose feeding. Their animal results, however, differed with those of several animal studies done previously (20–24), although not with all of them (25–27).

In addition, their results were subject to conflicting interpretations. Thus, most other researchers remained unconvinced.

There has since developed overwhelming evidence against the induction hypothesis. For one thing, all efforts at inducing lactase activity in humans through lactose or milk feeding have failed (28). Most such efforts have been continued for just a short while, but there are cases of lactose malabsorbers consuming lactose or milk for periods of a year or more without significant increases in intestinal lactase activity (29–32). Relevant, too, is the observation that nine of ten patients (ages 7–17 years) with galactosemia, who had consumed no milk or lactose-containing foods since infancy, were nevertheless able to absorb lactose (33). There have also been studies of institutionalized children in Thailand (34), and southern Nigeria (35), both areas of high prevalences of adult LM. Even though the children in question had consumed milk since birth and apparently in quantities similar to those of Europeans, virtually all proved to be lactose malabsorbers by four years of age. Furthermore, there have been studies, as of the Pima and other Indians of the American Southwest (36, 37), that found very high prevalences of LM among adults who had consumed sizable amounts of milk and lactose-rich dairy products throughout life. An animal study bearing on the induction hypothesis is that by Lebenthal, Sunshine, and Kretchmer (38). These researchers attempted to determine the effect of prolonged nursing on intestinal lactase activity in rats. One group of rats was denied all foods except milk. These rats experienced a significant delay, as compared with a control group, in decline of lactase activity, and their lactase activity remained significantly higher at 24–30 days of age. Overall, however, the decline in activity paralleled that of the control group and did not, as expected if the induction hypothesis were valid, remain at the high levels of early infancy. In a somewhat similar longitudinal study (39), 69 normal Thai infants were divided into groups. One group received animal milk (to supplement their traditional nondairy diet) regularly throughout the study period, and the other, the control group, were given traditional foods but no milk after weaning. All children who were followed to age 4, whether or not they received milk supplements, developed lactose malabsorption by that age.

THE GENETIC HYPOTHESIS

From the first awareness of ethnic or racial differences in prevalence of primary adult lactose malabsorption, many researchers suspected a genetic etiology, in part because several studies had found adult LM to have a family basis. In recent years, moreover, many additional family studies have become available, and these clearly support the view that adult lactose absorption is an inherited trait (28–29, 40–45). Of special significance in this regard is John Johnson's recent summary (36) of the results of all family studies completed, to the date of writing, in various parts of the world. Included were 146 families. In ten of them, both parents were lactose absorbers; in 60, one parent was a lactose absorber and the other a lactose malabsorber; and in 76, both parents were lactose malabsorbers. In considering the matter, Johnson first made the assumption that adult lactose absorption is inherited as a completely penetrant dominant trait. He also assumed that all absorber parents were heterozygous for the gene of adult lactose absorption. Then he determined the theoretical mendelian proportions of lactose malabsorption that would be expected for each type of mating, and compared these with observed proportions in the 447 offspring in the families involved. As will be seen on Table 2, there were only slight deviations from expected proportions, and these are within the range of testing error

TABLE 2. SUMMARY OF FAMILY STUDIES OF INHERITANCE OF PRIMARY LACTOSE MALABSORPTION (LM)*

Matings	*No. of families*	*No. of progeny*	*Progeny with LM*	*Observed proportion LM*	*Expected proportion LM*
la × la	10	31	8	0.26	0.25
la × lm	60	196	101	0.515	0.50
lm × lm	76	220	208	0.945	1.00

*The data represent families reported in various works and assembled by Johnson et al (36). la = lactose absorber; lm = lactose malabsorber. Expected proportions of LM are the theoretical mendelian proportions assuming lactose absorption is inherited as a completely penetrant dominant trait with all lactose absorbers in these studies assumed to be heterozygotes.

or may have been possible cases of nonpaternity, secondary lactose malabsorption, or delay in age of onset. In conclusion, Johnson noted that the results in general are consistent with the hypothesis that adult lactose absorption is an autosomal dominant characteristic (and primary adult lactose malabsorption, an autosomal recessive one).

Additional support for the genetic hypothesis is found in several studies of native groups in North America, Africa, and southeast Asia who are characterized by high prevalences of lactose malabsorption, but who to some degree have interbred with persons of northwest European origin, most of whom are absorbers. In those studies, subjects were questioned in an effort to determine whether they were unmixed or of mixed European ancestry. In some cases, researchers also attempted to establish degree of intermixture. In every study, lower prevalences of lactose malabsorption were found in mixed persons than unmixed ones. Moreover, where such information was obtained, it was found that as percentage of European ancestry increased, prevalences of lactose malabsorption dropped. Thus Johnson et al (36) in a study of the Pima Indians of Arizona found 95% (59 of 62) of unmixed persons age 4 or over to be lactose malabsorbers, compared to 76% (16 of 21) of those who were 1/8 Anglo, and 39% (7 of 18) of those who were 1/4 or 1/2 Anglo. In another study of Indians from various tribes of the Great Basin and Southwest, Johnson et al (37) found a 92% prevalence of LM (92 of 100 subjects) among unmixed Indians, but only 50% (3 of 6 persons) among Indians with known grandparents or great-grandparents of European origin. Newcomer et al (46) found that Chippewa Indians who were 84% or more Indian had a prevalence of LM of 93% (14 of 15 subjects); 50–84% Indian, 52% LM (13 of 25); and those less than 50% Indian, 7% LM (1 of 14). Similar results were obtained by Bose and Welsh (47) with Oklahoma Indians. In one study Gudmand-Høyer et al (48) found unmixed Eskimos in Greenland (ages 1–>30) to have an 84% prevalence (68 of 81 subjects) of LM; those whose latest intermixing with Danes was four generations ago, 47% (27 of 58); three generations, 31% (9 of 29); two generations, 25% (1 of 4); one generation, 17% (1 of 6). Danes, it might be noted, have among the lowest prevalences of adult LM (2–3%) of any peoples of the world. In another study, Gudmand-Høyer and Jarnum (49, 50) found an 88% prevalence (22 of 25 subjects) of LM in unmixed Greenland Eskimos, but only 14% (1 of 7) in Eskimos with a known Danish ancestor. Similar results were obtained with another group of Greenland Eskimos by Asp et al (51): unmixed adult Eskimo, 85% prevalence of LM; Eskimo of mixed ancestry, 50% (2 of 4). In Africa, Ransome-Kuti et al (42) found 100% prevalence (11 of 11) among a group of "proper" (unmixed) Yoruba (ages 3 and over) but only 44% (19 of 43) among persons of mixed Yoruba/European background. And in Thailand, where prevalences of adult LM range from 96 to 100%, only 50% (3 of 6) of a group of Thai/northwest European mixed persons had LM (29).

Also bearing on the genetic hypothesis are various studies of social classes or ethnic groups known to be of mixed absorber/malabsorber ancestry (2, 35, 43, 52–68). Unlike the studies considered in the previous paragraph, these contain no information on the ancestry of individuals, but one would nevertheless expect the classes or ethnic groups in question to have prevalences of LM intermediate between those of the unmixed parental groups. Those prevalences have indeed proved to be intermediate.* Moreover, in the case of the American blacks, the amount by which prevalences of LM are lower than those of their African ancestors fits with information on degree of black/white mixture as revealed by a study of the *Gm* genotype in American whites and blacks (42). Overall the evidence for the genetic hypothesis is overwhelming, and the main question remaining seems to be how the observed group differences in LM may have evolved.

THE GEOGRAPHIC VARIANT OF THE GENETIC HYPOTHESIS

In a review several years ago, Theodore Bayless (70) suggested that, historically, genetic selection for lactose absorption may have preceded milk use. The implication is that through random genetic drift or some other process of selection independent of dairying, certain human groups developed high prevalences of lactose absorption and that this led them to take up dairying and the use of milk as food. As I have noted in detail elsewhere (71), however, the adoption of dairying and milk use by human groups derives not from a single determinant, but from a range of interrelated influences, from human culture and ecology more than biology. High preva-

*One possible exception: the Rehoboth Basters, believed to be a Hottentot/Caucasian mixture, but who were found to have a 65% (13 of 20 subjects) prevalence of LM (69).

lences of LM have not prevented human groups around the world from consuming dairy products, for malabsorbers of lactose can reduce their consumption of lactose-rich products to amounts they can take without symptoms; they can process milk into forms, such as fermented milks and aged cheeses, in which the lactose content is greatly reduced; or, in many cases, malabsorbers in time can develop a tolerance of milk, can consume it in quantity without symptoms. Therefore, if merit exists in the Bayless view of that time, one would expect to find somewhere on the earth a human group characterized by high intestinal lactase activity throughout life which, because of an absence of animals suitable for milking or other factors, was unable to take up dairying and milk use. That no such group has been found, despite more than a dozen years of research in various parts of the world, suggests that one must look elsewhere for an explanation, and we turn now to the "geographic" or "culture historical" hypothesis.

The starting points of the geographic hypothesis were three. One was the belief that present-day group differences in prevalence of LM are genetic in origin. Second was the observation that for most of mankind, as for almost all land mammals, adult lactose malabsorption is the normal state. In approaching the question of group differences in prevalence of LM, therefore, it seemed reasonable to focus primarily on absorber groups and to question how they may have come to depart from the usual mammalian pattern, to experience high lactase activity throughout life. Third was the conviction that group differences in prevalence of LM relate somehow to patterns of milk consumption over a long historical period.

In the Paleolithic, according to the geographic hypothesis (3), humans, like other land mammals, underwent a normal decline in intestinal lactase activity after weaning. As hunters and gatherers, they had no animals suitable for milking and their diet included no animal milk. If an individual did depart from the normal pattern and experienced a lifelong high level of intestinal lactase, he would have enjoyed no selective advantage over his fellows. With the origins of dairying, however, the situation changed. Such an aberrant person would then, under particular conditions, enjoy a significant selective advantage. That advantage would occur within groups, especially pastoral or semipastoral ones, who lived under marginal nutritional conditions and who consumed substantial amounts of dairy products in lactose-rich forms. The conditions would not be met if a group, as is typical in large parts of the Old World, processed the bulk of its milk into fermented products or aged cheeses in which the lactose was largely hydrolyzed by bacterial lactase. This is because the malabsorber could consume such products without symptoms and as readily as could the absorber. Under the hypothesized conditions, however, the aberrant lactose absorber who would experience no adverse symptoms on consuming lactose-rich dairy products, would use more of them than did malabsorber comrades. He or she would therefore grow taller, stronger, and healthier. He or she would better be able to care for and protect the family. And in time adult lactose absorption would become characteristic of his group, whereas human groups not subject to such selective pressures would continue to have high prevalences of LM.

HAS THE TIME SINCE THE BEGINNING OF DAIRYING BEEN SUFFICIENT TO BRING ABOUT PRESENT-DAY GROUP DIFFERENCES IN PREVALENCE OF LM?

In initial question that may be raised about the geographic hypothesis is whether observed group differences in prevalence of LM can have developed in the limited time period since humans first began to milk domesticated animals and consume their milk. The question has been considered in only two studies. In one L.L. Heston and I.I. Gottesman (72) of the University of Minnesota first assumed that selection for adult lactose absorption began 10,000–8,000 BC, with domestication of sheep and goats. Accepting present-day prevalences of adult lactase deficiency as high as 90% in some populations and as low as 10% in others, Heston and Gottesman note that gene frequencies for adult lactase sufficiency are, respectively, 0.05 in malabsorber groups and 0.60 in absorbers. They estimate further that in the 400 generations since that domestication, it would take a selection intensity against homozygote lactose malabsorbers of about 0.01 to bring about such a change in gene frequency. This means that if lactose absorbers averaged 1% more children per generation than did lactose malabsorbers, present-day differences in LM could have developed in the time available. They note that a selection intensity of 0.01 is a common one, not unreasonable in size.

A second study, by L.L. Cavalli-Sforza (73), a Stanford human geneticist, starts with the assumption that the trait of adult lactose absorption began increasing with the domestication of cattle, leaving at most 10,000 years for the genetic changes to have occurred. He estimates that a selection intensity of 0.02 or 0.03 was necessary to bring about the observed group differences in prevalence of LM in the time available.

One might object to the above researchers' use of dates of 10,000–8,000 BC. Convincing evidence for dairying goes back only to 4000–3000 BC or so (74). At the same time, various scholars (75–77) have suggested dates for dairying of from about 6700–5000 BC, and one expects future archeologic discoveries to confirm such early dates. Moreover, as Heston and Gottesman observed (72), selective pressures must have been more intense at some periods than at others. One might add that some groups at certain times must have been subjected to more intense pressures. This would certainly have been true of the peoples singled out by the geographic hypothesis, for they lived under conditions of nutritional stress, and lactose-rich dairy products were major and essential dietary items. Despite the uncertainties remaining, the conclusion of Heston and Gottesman seems reasonable, that "there has been plenty of time for plausible selection pressures to bring about the results that have been observed in human populations."

OTHER QUESTIONS ABOUT THE GEOGRAPHIC HYPOTHESIS

Even if one acknowledges that the time since earliest dairying was indeed sufficient for the development of observed differences in prevalence of LM among the world's peoples, further questions remain about the process of selection. For one thing, what evidence is there that lactose malabsorbers are more likely than absorbers to develop symptoms on consuming lactose? What evidence is there that symptomatic malabsorbers associate symptoms with milk consumption, and that some, as a result, reduce such consumption? And, finally, can one demonstrate a significant difference, under conditions as stated in the geographic hypothesis, in average amount of milk consumed by groups of absorbers and malabsorbers?

With regard to the first question, it has been clearly established that individuals with low lactase activity are more likely to develop symptoms when they consume lactose or milk (36, 43, 46, 47, 57, 78–81). It has also been demonstrated that some lactose malabsorbers recognize that milk consumption would bring on distress (2, 36, 37, 46, 47, 57, 79, 81–83), and that such recognition is more common in malabsorber adults than in malabsorber children (36, 46), presumably because malabsorber adults' lactase activity is normally lower and symptoms on ingestion of milk are more severe. Although most investigators seem not to have queried such aware intolerants on the matter, there are some reports of individual malabsorbers deliberately decreasing their milk consumption as a result of symptoms (1, 37, 44, 79, 81, 84, 85).

Two studies, moreover, have been carried out under controlled conditions to determine relative amounts of milk normally consumed by lactose absorbers as compared to malabsorbers. In one study (82), of 166 black and white hospital patients in Baltimore, researchers found a significant positive correlation between lactose malabsorption and milk rejection [31% of 89 malabsorbers were "nondrinkers" of milk (persons who, in two or three lunch or dinner sittings, drank less than a fourth of the 240 ml of milk provided), compared to 13% of 77 absorbers]. Questioning revealed, moreover, that 64 of the 89 malabsorbers (72%) recognized before the study began that they would experience symptoms if they consumed milk. Most indicated that their threshhold was one glass of milk or less. A second controlled study (84, 86), involving 533 black and white elementary school children, found a similar positive relationship between lactose malabsorption and failure to consume milk provided at a school lunch.

Although the above evidence is clearly in line with what one would expect if the geographic hypothesis were valid, certain other evidence is equivocal. This evidence derived from efforts to determine, by questioning subjects about their milk consumption, whether there are significant differences in amounts used between groups of lactose absorbers and malabsorbers. In some such efforts, everyday milk consumption by lactose absorber groups has indeed been found to be significantly higher than for lactose malabsorber groups (1, 11, 12, 53, 58, 78, 87–89). In others, however, significant differences have not been found (28, 47, 53, 59, 62, 81, 85, 90–94). Unfortunately none of these group studies was carried out specifically to test the geographic hypothesis under the conditions set down. They contrasted notably in method of determining

amount of milk consumed, ages of malabsorbers studied, subjects' economic system and income level, availability and dietary importance of milk, and other factors of relevance. Needed now are carefully designed prospective studies of malabsorbers and absorbers in pastoral groups living under the conditions hypothesized. In such studies, it would be necessary, as well, to pay attention to differences in milk consumption by age group. As Norman Kretchmer has observed (95), critical differences in milk consumption between absorbers and malabsorbers may occur only at a single developmental stage, and yet be of great importance to individual survival and well-being.

The possibility must remain open, however, that selective advantages different from those hypothesized may also have been enjoyed by the lactose absorber. May it be, for example, that it was not the larger amount of milk consumed by a lactose absorber that alone was important, but his greater ability at utilizing its nutrients? It is widely recognized, for example, that even in the absence of frank diarrhea, milk consumption does bring on greater intestinal motility in lactose malabsorbers than in absorbers. May it be that such increased motility reduces the malabsorber's ability to absorb certain nutrients? It seems, from studies completed to date, that the major significant loss to the malabsorber is in calories from the maldigesting of lactose (96). Subsequent studies may yet identify other such losses, but in any case, as Johnson has noted (96), while loss of calories may be insignificant to most Americans, it could be nutritionally significant for persons with marginal caloric intakes.

Another possibility is that the selective advantage was not a generalized one, but a specific one. Two groups of researchers, Flatz and Rotthauwe (97) and Cook and Al-Torki (52), have identified specific selective advantages that may have been enjoyed by lactose absorbers. Flatz and Rotthauwe base their views on the well-known fact that calcium absorption is facilitated by the presence of vitamin D, and on animal studies indicating that calcium absorption is also enhanced by lactose hydrolysis. Under conditions of heavy prevailing cloud cover and low ultraviolet radiation, as in northwestern Europe, they observe, poor adults in the past commonly suffered a dietary deficiency of vitamin D and, because of a general lack of sunshine, their biological ability to produce vitamin D was also low. Such persons thus frequently developed late rickets and osteomalacia. They not only suffered greater morbidity, but women among them were more subject to pelvic deformation and reduced ability to bear young. Under such conditions, the lactose absorber, through greater ability at hydrolyzing the lactose in the milk consumed, could absorb more calcium and better survive and produce offspring. This selective advantage, in the minds of Flatz and Rotthauwe (97), likely accounts for the low prevalences of adult lactose malabsorption among northern Europeans.

As it applies to northern Europe, the Flatz and Rotthauwe hypothesis offers an interesting alternative to a generalized selective advantage. It is difficult to see, however, how the hypothesis could apply to groups of lactose absorbers outside of Europe. Saudi Arabia, Pakistan, and tropical Africa—areas where absorber groups are also found—are places of quite abundant solar radiation. Moreover, one might question whether Indo-European peoples have been in cloudy northern Europe for a sufficiently long historical period to account fully for their low prevalences of LM. The ancient Indo-European homeland is believed by many to have been in the Pontic and Caucasian steppes and, when the Indo-Europeans first gained prominence, they were pastoralists. From there, Indo-European peoples are believed to have pushed outward, with some reaching northern Europe about 2300 BC (98) and others entering what is now Pakistan about 1500 BC. That Indo-Europeans in regions as far apart as Pakistan, Scandinavia, and Spain should have low prevalences of LM, leads to the question whether selection against LM may have begun in their ancient homeland, which likely was a sunny, subhumid region. One suspects that whatever the selection pressures against LM may have been in cloudy northern Europe, they simply added to selective pressures that had long operated in the ancient Indo-European homeland.

Cook and Al-Torki dismiss as untenable the Flatz and Rotthauwe hypothesis and, following a study of the Bedouin of Arabia, they advance an alternative specific selective advantage. Their view (52) is based on knowledge that absorption of monosaccharides is linked with water absorption, and that water absorption provides a clear survival advantage, at times of cholera and other epidemics, to groups such as the Bedouin who derive the bulk of their fluid from milk.

One is forced to conclude that however attractive the above selective hypotheses may be for certain groups and under particular ecological conditions,

they are unlikely to have prevailed everywhere or to have been solely responsible for the genetic selection involved. It seems more likely that there was a generalized selective advantage and that this was enhanced by specific advantages, both the ones considered above and others, which operated at one time and place or another.

THE DISTRIBUTIONAL EVIDENCE

Remaining to be weighed is the distributional evidence bearing on the geographic hypothesis. That evidence has been treated on a case-by-case basis elsewhere (3, 99), and here our main concern is with how overall distributional patterns of high and low prevalence of lactose malabsorption fit the hypothesis. One would, if the geographic hypothesis were valid, expect: (a) all groups who traditionally were hunters and gatherers to have high prevalences of LM, for they had no animals suitable for dairying, consumed no animal milk, and would have remained true to the ancient land mammalian pattern of low lactase activity in adulthood; (b) all agricultural groups who lived in the traditional zones of nonmilking in America, Africa, Asia, and the Pacific to have similar high prevalences of LM, along with those of their overseas descendants who remain relatively unmixed or who have interbred only with malabsorber populations; (c) agricultural groups whose ancestry lies within the traditional zones of nonmilking but who migrated into an adjacent zone of milking to become milk users at a relatively recent date to have high prevalences of LM.

Low prevalences of LM, on the other hand, would typify (d) groups, especially those of pastoral tradition, who are characterized by high consumption of milk and lactose-rich dairy products for a long historical period and who have lived under conditions of dietary stress. Such prevalences would also occur among their relatively unmixed overseas descendants. Where (e) pastoral and other groups from category d have interbred with peoples from categories a, b, or c, one would expect, in the mixed population, prevalences intermediate between those of the parental groups, and to have them reflect degree of intermixtures. And (f) where there are peoples, especially unmixed agricultural ones for whom dairy products, although long used, were not used in large quantities, were not critical in diet, and/or who processed their milk into low lactose forms, the hypothesized selective pressures would have been slight; such peoples, as a result, would be characterized by high prevalences of LM, although possibly lower than those of nonmilking groups.

There are, of course, serious problems about fitting human groups neatly or certainly into the categories above, for data is often quite incomplete on diet, form of dairy products used, antiquity of dairying and milk use, and nature and degree of intermixture with other groups. With respect to category a, however, one is on reasonably firm ground in the knowledge that among peoples who remained hunters and gatherers until recent times, milk use is, at best, a relatively new practice. Although the hunters and gatherers studied so far derive from widely scattered regions, all have high prevalences of LM, from 63 to 98%, if one eliminates persons reported as having ancestors of European origin (Table 1a). Included are Twa pygmies of Rwanda, ǂhuâ Bushmen of Botswana; !Kung Bushmen of Southwest Africa; Greenland Eskimos; Alaskan Indians and Eskimos; Indians of Canada's west coast; and Chippewa Indians of Minnesota (a few bands of whom cultivated maize).*

Turning to category b, agricultural peoples from the traditional zones of nonmilking and their relatively unmixed overseas descendants are seen to have high prevalences of LM, from 65 to 100% among all adult groups. This evidence, too, fits the hypothesis. Those results, moreover, involve an impressive number of peoples from the zones of nonmilking in the Americas, Africa, Southeast and East Asia, and the Pacific (Table 1b).

The only peoples who seem to fit category c are the Bantu of East and South Africa. The consensus among scholars is that the Bantu homeland was somewhere in the tropical African zone of nonmilking. The Bantu seem to have migrated beyond that zone into eastern and southern Africa in relatively recent historical times, perhaps mainly from the middle to the end of the first millennium AD (3). Bantu agricultural peoples of Kenya, Uganda, Zambia, and South Africa, all presumably recent in adopting dairying and milk use, fit the hypothesis by having high prevalences of LM, from 67 to 100% in groups studied (Table 1c).

Category d includes peoples who seem best to

*Because of deficiencies in the data, we have not included on Table 1a three groups of Australian aboriginal children (ages 0–15 years) who were tested for lactose malabsorption (100, 101). That they had prevalences of 70–90% suggests that most Australian aboriginal adults, like other hunters and gatherers, are also lactose malabsorbers.

meet conditions for intensive selection, over a long historical period, for high, lifelong lactose absorption. As will be seen on Table 1d, peoples included in this category, whether in Africa and the Near East, northern and western Europe, or India and Pakistan, have quite low prevalences of LM, from 0 to 30% in all ethnic groups. These results also fit the geographic hypothesis.

In category e are included mixed peoples believed descended from groups in category d—dairying peoples *par excellence*—who have mixed with groups from categories a, b, or c—who were nonmilking until recent or relatively recent times. Category e, therefore, would be expected to have quite variable prevalences of LM because of widely differing degrees of intermixture. Each group, nevertheless, would have a prevalence intermediate between those of their parental groups. Table 1 reveals a variability in prevalence of LM among groups in category e greater by far than in categories a–d. Moreover, in all cases except that of the Rehoboth Basters, to be considered in a "Problems" section, prevalences are indeed intermediate, thus fitting the hypothesis in that regard as well.

Category f includes groups with a long dairy tradition, but who seem to have consumed animal milk in small quantities or who processed most of it into low lactose forms. They would be expected, by the hypothesis, to have high prevalences of LM, and all those listed here, mainly settled Arabs and Jews, do.

There remain to be considered several problem cases, although some can be fit into one or another of the categories above. First is that of Greeks and Italians (Table 1g), who are included here because prevalences of LM have been quite variable in the groups tested: from 38 to 100% among Greeks and 30 to 100% among Italians. The number of Italian individuals tested, it is true, is quite small, altogether 49, but the Greek sample is large, more than 800 persons. In both Italy and Greece there seems to be a notable north–south difference, with lower prevalences of LM in the north and higher ones in the south. We may be dealing here both with a greater Indo-European genetic contribution in the northern areas as well as contrasting patterns of milk consumption. Kanaghinis et al (102), in commenting on the significantly higher prevalences of LM on Cyprus and Crete than on the mainland, observe that peoples of those islands drink virtually no milk, but largely process what sheep and goat milk is available into cheese or other dairy products. They note that a similar pattern is found in the rural sections of southern and central Greece, but that in northern Greece and Thessaly cow's milk is used more extensively. Even there, however, adults usually do not drink milk. Indeed, the northwest European pattern of high milk consumption is a recent phenomenon in Greece and is mainly found in large towns and cities. Thus Greece fits the expectations of the geographic hypothesis, with persons on the Aegean islands belonging with the malabsorber groups of North Africa and the Near East, and northern Greeks perhaps more akin to the absorber groups of northern Europe. Perhaps the same will prove true in Italy.

A second problem is that of the Indian subcontinent. Most studies of LM in India have not separated subjects as to ethnic or regional origins, although the geographic hypothesis leads to the expectation of significantly lower prevalences in the northwest than in the south and east. This is because the milk-using Indo-European Aryans invaded India from the northwest, about 1500 BC, and their genetic impact is greatest there. They are, moreover, the earliest people known to have practiced dairying in the Indian subcontinent (103). In addition, consumption of milk is greater in the northwest than in other parts of the subcontinent. We have seen, in category d, Table 1, that all groups tested in the western margins of the subcontinent do have low prevalences of LM, but it is unclear what the pattern is elsewhere in the region. To this writer, it seems likely that there is considerable variability in prevalences of LM in India, but with generally lower prevalences to the east and south (99). It is my expectation that India, like Greece, will prove to be a zone of transition. This, however, must be confirmed by subsequent studies.

The only Lapp groups studied so far are those from Finland, which we include on our problem list. These reindeer-herding, milk-using people of the Arctic tundra and forest are a problem because of the great differences in prevalence of LM that occur among subgroups. Whereas the Skolt Lapps have a 60% prevalence of LM, the Mountain Lapps and Fisher Lapps have much lower ones, of 25–37%. It should be noted, however, that greater interbreeding of other Lapp groups with Finns and other Scandinavians is believed to have made them taller than the Skolts and that the Skolts seem also to differ from other Finnish Lapps in distribution of blood groups (104). That the Skolts differ in preva-

lence in LM as well thus may be a reflection of their genetic distinctiveness and lesser degree of intermixture with other Scandinavian peoples. A 60% prevalence of LM among the Skolts fits, moreover, with the belief that the Lapps were hunting and fishing folk who first took up the practice of milking from other Scandinavian groups (104, 105).

The Amhara and Tigre of Ethiopia and Arabs of Yemen are problems because there are Semitic peoples living in neighboring areas, yet striking differences of LM seem to exist between them. It must be admitted that there have been long historical links between Yemen and Ethiopia, with the ancestors of the Semitic Ethiopians invading from Yemen about 1100–400 BC (106). One explanation of the differences in question might be that, despite historical and linguistic links, the genetic contribution of the early invaders from Yemen to the present-day Amhara and Tigre is small, that these groups remain genetically more akin to those agricultural Cushites of highland Ethiopia whom they conquered and absorbed. This view would fit with the striking differences in skin color that are found today between the Amhara and Tigre on one hand, and Yemen Arabs on the other. It also would fit with the remarkable similarity in physical appearance of the Semites and Cushites of highland Ethiopia. In any case, the Amhara and Tigre, in terms of prevalence of LM, seem to be grouped not with the Yemen and Saudi Arabs, but with the agricultural peoples of their language family, including, in Africa, the Egyptian fellahin, Arabs of North Africa, and the Hausa of Nigeria.

The most troublesome problems are those of the Rehoboth Basters of southern Africa and the Dinka of the southern Sudan. The Rehoboth are believed to be half Boer/half Hottentot in ancestry. Boers have not yet been studied, but, as persons of northwest European background, likely they have low prevalences of LM, 0–30%, whereas the Hottentots, judging from the one study done among the Nama, have a 50% prevalence of LM. It seems reasonable to expect the Rehoboth to be intermediate in prevalence between those figures, yet they are not. In a similar vein, one might expect the Dinka, those cattle-complex, milk-using Nilotic peoples of the southern Sudan, to have low prevalences of LM. Yet five Dinka tested in the Congo were all malabsorbers. That this is not typical of Nilotes in general is suggested by the 44% prevalence of LM found among Nilotes or Nilo-Hamites in Uganda.

The above problem cases are minor ones, and most call attention to gaps in general knowledge rather than to deficiencies in the geographic hypothesis. Indeed that hypothesis fits quite well with the available data. If subsequent research further confirms its validity, we would be dealing with an unusual situation involving significant genetic changes in human populations brought on by consumption of a food under particular ecological conditions over a long historical period. The question would then arise whether, if there is one case of this sort, there might be others as well. If so, the research on lactose malabsorption would have pointed the way to an exciting new area of research on the links between food use, human evolution, and matters of nutrition, health, and disease.

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