

# Prevalence of primary adult lactose malabsorption and awareness of milk intolerance in Italy<sup>1-3</sup>

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**ABSTRACT** A total of 308 healthy Italian adults (192 females, 116 males; mean age 29.2 yr) were examined using a field version of the lactose tolerance test with breath hydrogen determination. Two geographical groups were formed according to the birth places of the probands' grandparents: 208 subjects from northern Italy (mainly from the regions of Piemonte, Lombardia, and Veneto) and 100 probands from Sicily. Lactose malabsorption was diagnosed in 106 subjects in group "north" (51%) and in 71 subjects in group "Sicily" (71%). Awareness of milk intolerance was more frequent in lactose malabsorbers. The incidence of diarrhea after the test dose of lactose was significantly higher in "aware" lactose malabsorbers, when compared with persons of the same group who had not experienced milk intolerance. The significant difference in lactose malabsorption frequency between northern Italy and Sicily is further evidence of a north-south gradient of lactase gene frequencies in Europe. *Am J Clin Nutr* 1984;39:100-104.

**KEY WORDS** Italy, lactose malabsorption, milk intolerance, population study

## Introduction

Primary adult lactose malabsorption, due to lactase repression in homozygotes for a recessive autosomal "hypolactasia" allele, is predominant in most human populations. Low intestinal lactase activity is normally present in adult subhuman mammals, and the high prevalence of adult lactose absorption caused by a "lactase persistence" allele in some human populations is therefore unusual and requires explanation. Current hypotheses concerning the cause of the highly variable frequencies of the two adult lactase phenotypes, lactose absorber and malabsorber, are mainly based on distributional evidence. Although data derived from lactose tolerance tests on more than 10,000 persons have already been accumulated (1, 2), lactase phenotype distribution still remains to be determined in many areas of the world. Results of lactose tolerance tests with breath hydrogen determination in more than 300 healthy Italian adults are presented herein. A higher frequency of lactose malabsorption in the south of Italy than in the north further proves the general tendency of lactase phenotype distribution in Europe.

## Materials and methods

A total of 308 apparently healthy Italian adults was examined using a field version of the lactose tolerance test with breath hydrogen determination (3, 4) at the Pediatric Clinics of the Universities of Pavia, Torino, Verona, Catania, and Palermo. Most of the subjects were staff members or students from these institutions. In order to avoid selection due to individual milk preference, prospective test subjects were asked to participate in a "disaccharide test." Immediately before the examination, probands were informed of purpose, procedure, and possible complications of the lactose tolerance test. Only three persons refused to participate after receiving full information. In order to eliminate the effects of recent internal migrations, the probands were

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classified according to their grandparents' birth places. Two main geographical groups were examined: 208 subjects from northern Italy (regions Piemonte, Lombardia, and Veneto: 131 females, 77 males, average age 28.7 yr) and 100 from Sicily (61 females, 39 males, average age 30.2 yr). The majority of the probands' grandparents originated in the areas marked in Figure 1. In the northern group, 34 of the 832 grandparents were ethnic Italians from parts of Italy, Switzerland, and France adjacent to the main area of examination and only one grandparent was not Italian (Greek). All provinces of Sicily are represented in the southern group. Only four of the 400 grandparents came from the Italian mainland, two from neighboring Calabria and two from the northern region of Emilia-Romagna.

Lactose tolerance tests were performed in the morning after a fast of at least 8 h. Test subjects received 50 g lactose monohydrate in 400 ml of boiled tap water at room temperature (20 to 22°C) and drank this solution within less than 5 min. Breath samples were collected before, and 120 and 150 min after the lactose load and stored in aerosol containers (4). Test subjects refrained from smoking for at least 20 min before breath collection. The hydrogen concentration in breath samples was determined by gas chromatography within 7 days after collection. The differences in hydrogen concentration between the zero sample and the two samples obtained after lactose were calculated, the greater of the two values ( $\Delta_{\max}H_2$ ) being the diagnostic parameter.  $\Delta_{\max}H_2$  is less than 15 vpm (volumes per million) in

lactose absorbers and usually more than 20 vpm in lactose malabsorbers (4). Before lactose ingestion, the probands answered in writing the question: "Are you aware of having experienced abdominal discomfort, eg, colicky pain, abdominal distention, flatulence, or diarrhea, after drinking whole milk?" with "yes" or "no." Three hours after lactose administration the occurrence of the aforementioned abdominal symptoms during the test period was registered.

## Results

Figure 2 shows the distribution of the  $\Delta_{\max}H_2$  values in the two main groups from northern Italy and Sicily. In both samples, the distribution is bimodal (if the scattering of high values, presumably due to small numbers, is disregarded). Five subjects with  $\Delta_{\max}H_2$  values between 16 and 20 vpm were diagnosed as lactose malabsorbers because initial breath hydrogen excretion in concentrations of 10 to 20 vpm tended to lower  $\Delta_{\max}H_2$  and a rapid fall of breath hydrogen concentration after food intake is frequent in fasting subjects (3). Four of these five probands reported symptoms of lactose intolerance during the test which included diarrhea in two subjects. Among the 208 north Italians and 100 Sicilians, 106 (51%) and 71 (71%), respectively, are lactose malabsorbers. There are no significant differences between the three regional subgroups



FIG 1. Map of Italy showing the regions where probands for lactose study were recruited. P, Piemonte; L, Lombardia; V, Veneto; S, Sicily. More than 95% of the probands' grandparents originated in the areas marked by dotted lines.

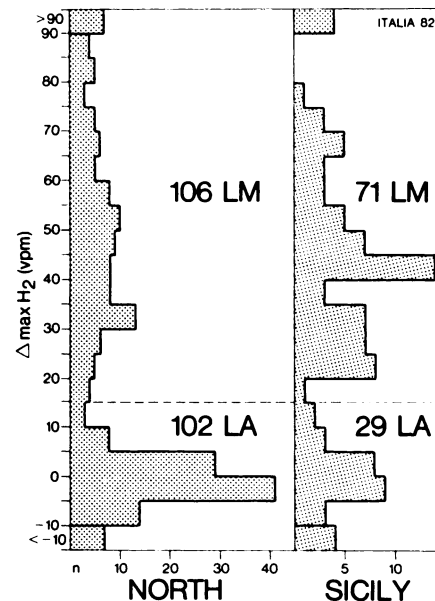


FIG 2. Distribution of  $\Delta_{\max}H_2$  values in north Italians and Sicilians.

from northern Italy ( $\chi^2 = 3.01$ , 2 df,  $p > 0.2$ ). Similarly, the difference between Sicilian subsamples from Catania and Palermo is insignificant ( $\chi^2 = 0.06$ ,  $p > 0.7$ ). However, the difference between the groups "north" and "Sicily" is highly significant ( $\chi^2 = 11.1$ ,  $p < 0.001$ ). The frequencies of the "hypolactasia allele" in groups "north" and "Sicily" are  $0.714 \pm 0.023$  and  $0.843 \pm 0.027$ , respectively.

Prevalence of milk intolerance and incidence of lactose intolerance during the test are similar in lactose absorbers and malabsorbers in the north Italian and the Sicilian groups. Both samples are therefore combined in the comparisons in **Tables 1 and 2**. As expected, awareness of milk intolerance was more frequent in lactose malabsorbers (29%), although no less than 15% of lactose absorbers claimed to be milk intolerant. The incidence of intolerance symptoms during the lactose test, however, is significantly higher in lactose malabsorbers. In Table 2, the incidence of symptoms during the lactose test is compared in milk tolerant and intolerant lactose malabsorbers. In subjects

aware of milk intolerance, diarrhea is twice as frequent as in lactose malabsorbers who had not experienced abdominal discomfort after drinking milk. Small numbers prevent a valid comparison of symptoms in lactose absorbers, and two people in this group with absent hydrogen production who experienced diarrhea repeatedly during the test may represent false-negative results due to lack of hydrogen-producing colonic bacteria (5).

## Discussion

The present study reveals that the frequency of primary adult lactose malabsorption in Italians is unusually high for a European population. Results in the north Italian group are in keeping with previous studies of lactose malabsorption on small numbers of subjects in the regions of Liguria and Lombardia (6–8). The lactose malabsorption frequency in northern Italy is likely to lie between 45 and 57% (95% confidence limits). Therefore, north Italians cannot be classified together with populations in central and northern Europe with low lactose malabsorption frequency (9). In German speaking populations inhabiting areas adjacent to Italy in the north, lactose malabsorption is significantly less frequent than in northern Italy itself [Switzerland 16% (10); Austria 14 to 23% (11)]. Evidently, the prevalence of lactose malabsorption increases abruptly at the Alpine border between German and Italian speaking people. Medical literature does not contain reports of lactose absorption studies in healthy adults in Sicily but the high frequency of lactose malabsorption there (71%, 95% confidence limits 62 to 80%) is not unexpected, being similar to that in other southern Mediterranean populations (12). Present findings are compatible with a nonlinear southerly increase in hypolactasia frequencies in Europe, as proposed by Flatz et al (3). The cline of lactase gene frequencies is characterized by increasing hypolactasia gene frequency from a minimum of 2% in southern Scandinavia (13) to Sicily, the area with the highest prevalence of lactose malabsorption so far observed in Europe. The high proportion of lactose malabsorption in French subjects of Italian ori-

**TABLE 1**  
Awareness of milk intolerance and incidence of lactose intolerance after a load of 50 g lactose in 308 Italian adults\*

Milk intolerance reported	Lactose intolerance during test	Lactose absorbers		Lactose malabsorbers	
+	+	5	3.8%	39	22.0%
+	–	15	11.5%	13	7.3%
–	+	8	6.1%	85	48.0%
–	–	103	78.6%	40	22.6%
Total		131	100.0%	177	99.9%

\* Comparison lactose absorbers/malabsorbers:  $\chi^2 = 113.7$ , 3 df,  $p < 0.001$ .

**TABLE 2**  
Symptoms of lactose intolerance and awareness of milk intolerance in 177 Italian lactose malabsorbers\*

Symptoms in lactose tolerance test	Milk intolerance reported			
	Yes		No	
Diarrhea†	21	40%	26	21%
Gas formation‡	18	35%	59	47%
No symptoms	13	25%	40	32%
Total	52	100%	125	100%

\*  $\chi^2 = 7.3$ ,  $p < 0.03$ .

† At least one loose or watery stool, usually accompanied by symptoms caused by gas formation, during the observation period of 3 h.

‡ Abdominal distention, colics, borborygmi, flatulence.



gin (14) agrees with a gradual north-south increase in lactose malabsorption frequency in Italy.

Awareness of milk intolerance in a population obviously depends on the level of milk consumption. Therefore, it is hardly surprising that in Italy where milk consumption is relatively low (15), awareness of milk intolerance is less common than in America where 55 to 72% of lactose malabsorbers and 33% of lactose absorbers give a history of abdominal discomfort after drinking milk (16). The high frequency of awareness of milk intolerance among lactose malabsorbers in the present study indicates that lactose malabsorption is a common cause of milk intolerance in this group. The relatively low level of milk consumption in Italy may explain why the incidence of symptoms is more than doubled after a large lactose dose in the tolerance test. In Table 2, the incidence of diarrhea, an objective symptom of lactose intolerance, is compared with the more subjective symptoms caused by gas formation and with asymptomatic probands in the groups of lactose malabsorbers with and without milk intolerance. Subjects aware of milk intolerance react more often with diarrhea to a lactose load than "unaware" persons. In milk-consuming societies, lactose malabsorbers with a history of milk intolerance seem to be a select group characterized by strong intestinal response to a load of unabsorbable carbohydrate, possibly caused by excessive prostaglandin production (17, 18).

The high frequency of lactose malabsorption in Italy has bearing on population and clinical studies, not only in Europe, but also in populations of mixed European origin. In the United States, for example, it is customary to classify probands in lactose studies according to race, assuming that lactose malabsorption is frequent in Blacks and rare in whites. It must be realized, however, that the prevalence of lactose malabsorption in American whites may vary from 2 to 70% depending on ancestral origin. If the ethnicity of control and patient groups is not duly considered in clinical studies of lactose absorption, erroneous conclusions are very likely.

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