Patterns in the Distribution of Lactase Persistence

hhmi | BioInteractive

Activity
Student Handout

INTRODUCTION

This activity explores geographical patterns in the trait of lactase persistence (lactose tolerance), which affects whether people can digest milk as adults. Through analyzing real scientific data, you'll identify patterns in the distribution of lactase persistence around the world. You'll also discover how biological concepts and data analysis can connect to world geography and culture.

MATERIALS

- calculator
- a world map
- materials for making pie charts (may include colored pencils, scissors, and glue stick or tape)
- computer/references for geography research

PART 1: Analyzing Genetic and Phenotype Data

All mammals, including humans, are typically born with the ability to digest **lactose**, the main sugar in milk. Lactose is broken down by the enzyme **lactase**, which is produced by cells in the small intestine. As adults, most mammals stop drinking milk and no longer produce lactase. Humans who do not produce lactase as adults are called **lactase nonpersistent** and are usually **lactose intolerant**, meaning that they *cannot* digest lactose. However, some people continue producing lactase even as adults. These people are called **lactase persistent** (because expression of the lactase gene *persists* beyond childhood) and are usually **lactose tolerant**, meaning that they *can* digest lactose.

About 7,500 to 9,000 years ago, certain groups of people began domesticating cattle and drinking their milk. In populations with these **pastoralist** cultures, the lactase-persistence trait increased in frequency over time.

1. To learn more about these concepts, watch the film *Got Lactase? The Co-evolution of Genes and Culture*. Pay particular attention to the worldwide distribution of lactase persistence, shown in the map from 4:15–4:35. Summarize some of your initial observations about this distribution below.

The film mentions that in people who are lactose intolerant, the lactase gene turns "off" as they grow older. In people who are lactose tolerant, the lactase gene is permanently "on." Scientists have discovered that the lactase gene remains "on" due to mutations not in the lactase gene itself but in a nearby "switch" region.

Examine the **"Genetic Data"** table (p. 7 of this handout). The genetic data were collected by sequencing DNA near the lactase gene and looking for four specific mutations associated with the lactase-persistence trait. Each mutation has a corresponding allele, called a **lactase-persistence allele**.

Since lactase persistence is a dominant trait, a person needs only one copy of a lactase-persistence allele to be lactase persistent. In the "Genetic Data" table, the column "# people with a lactase-persistence allele" records the number of people who had at least one lactase-persistence allele (and were thus lactase persistent).

2. Using these data, calculate the frequency of lactase persistence in each population sample. Record the frequencies (rounded to two decimal places) in the column labeled **"Lactase-persistence frequency"** in the **"Genetic Data"** table. (Your instructor may ask you to work in groups or as a class.)

Examine the **"Phenotype Data"** table (p. 8 of this handout). The phenotype data were collected using tests that measured an individual's ability to digest lactose. To learn more about these tests, read the optional "Quick Guide" at the end of this handout.

3. Using these data, calculate the frequency of lactase persistence in each population sample. Record the frequencies (rounded to two decimal places) in the column labeled "**Lactase-persistence frequency"** in the **"Phenotype Data"** table. (Again, your instructor may ask you to work in groups or as a class.)
4. What are the lactase-persistence frequencies in each table based on? In other words, what was measured to collect the genetic data vs. the phenotype data?

5. In the **"Genetic Data"** table, look at the sample data for the Somali population in Ethiopia (Row A). Answer the following questions based on this sample.
   a. How many people were sampled?
   b. How many people had at least one lactase-persistence allele (out of the four considered in the studies)?
   c. How many people did *not* have any of these lactase-persistence alleles?
   d. Calculate the frequency of people in this sample who did *not* have any of these lactase-persistence alleles. Show your work.

   e. Assume this sample accurately represents the entire Somali population. In this population, which has around 10 million people, how many people would you expect to have at least one of these lactase-persistence alleles? Show your work.

6. In the **"Phenotype Data"** table, look at the sample data for the Somali population in Ethiopia (Row A). Answer the following questions based on this sample.
   a. How many people were sampled?
   b. How many people tested positive for the ability to digest lactose?
   c. How many people were unable to digest lactose?
   d. Calculate the frequency of people in this sample who tested *negative* for the lactase-persistence phenotype. Show your work.

7. Use the two data tables to find the lactase-persistence frequencies and references for the Hungarian population samples (Row X).

Population	Data Type	Lactase-persistence frequency	Reference (Author and Year)
Hungarians	Genetic		
	Phenotype		

a. Describe two differences between the genetic and phenotype data.

b. Propose two reasons why the lactase-persistence frequencies based on the genetic and phenotype data might differ.

8. One genetic study sampled 1876 people in Finland (Row U), which had a total population of 5.3 million at that time. Another genetic study sampled 58 people in France (Row V), which had a total population of 60.4 million at that time.
   a. Which sample, the one from Finland or France, do you think represents its country more accurately?

   b. Propose two questions you could ask about these samples to help determine whether they accurately represent the populations of their countries.

9. Compare the genetic data to the phenotype data for the three populations sampled in Sudan (Rows F, G, H). What patterns do you observe?

10. Compare the samples for these three populations: Wolof (Row D), Dinka (Row G), and Japanese (Row N).
    a. In the "Genetic Data" table, what do the lactase-persistence frequencies of these population samples have in common?

    b. In the "Phenotype Data" table, the lactase-persistence frequencies of these populations' samples range from 0.25 to 0.51. What might explain the difference between these frequencies and the ones in Part A?

11. Compare the three populations sampled in Uganda (Row I), China (Row P), and Papua New Guinea (Row R). Using both the genetic *and* phenotype data, develop a hypothesis about the cultural practices in these populations regarding using animals for milk.

12. The Dinka population in Sudan (Row G) traditionally has an **agropastoralist** culture, meaning that they depended on agriculture during some seasons and raising animals for food (including milk) during others. According to the study referenced in the "Genetic Data" table, the Dinka people sampled had a lactase-persistence frequency of 0, which may seem inconsistent with an agropastoralist culture. Why do you think this is? (*Hint*: What might have been a limitation of the study?)

PART 2: Mapping Lactase-Persistence Frequencies

To help visualize patterns in lactase persistence, you will now create a map of the lactase-persistence frequencies based on the **genetic data**. You will do this by drawing a pie chart for each population sample, which you'll then put on a map. (Note the exact procedure may vary from class to class. For example, your instructor may have you work on only some of the pie charts, and you could be working in small groups or as a class.)

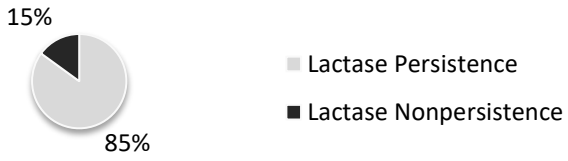
13. Choose two different color pencils or shading styles (e.g., shaded and unshaded): one for lactase persistence and the other for lactase nonpersistence. Record your choices in the table below.

Frequency	**Color or Shading Style**
Lactase persistence	
Lactase nonpersistence	

The "Pie Chart Stencils" below (p. 9 of this handout) have circles that you can use to make your pie charts. The letter in each circle corresponds to a letter for a population in the **"Genetic Data"** table.

14. For each population in the "Genetic Data" table (or whichever populations you were assigned), color/shade in the corresponding pie chart stencil to represent the lactase-persistence and lactase-nonpersistence frequencies based on the genetic data**.** An example pie chart is shown below. **Make sure to match the letter of each population to the letter on the pie chart stencil.**

Example Pie Chart



15. Cut out your pie charts. They don't need to look pretty.
16. Place the pie charts in the appropriate locations on a world map. Use a reference, such as a reliable website or textbook, to determine the locations of each population. **Don't tape or glue the pie charts yet**.
17. Once all the pie charts are placed, make sure you can see each chart clearly. You may need to slightly shift some of their positions. Once everything is finalized, neatly tape or glue the pie charts to the map.

18. Add a title and legend to the map.
19. Based on your finished map, make three general claims about the worldwide distribution of lactase persistence. Provide examples that support each claim, as well as potential counterexamples (examples that do not support the claim), if any.

Claim	**Supporting examples** and **counterexamples**

Answer the following questions based on genetic data shown in your pie charts.

20. Compare the sample lactase-persistence frequencies of the two populations from Kenya: the Maasai (B) and the Sengwer (C).
    a. How do these frequencies differ?

    b. Based on the information in the *Got Lactase?* film, what could have caused this difference? Explain your answer.

21. Compare the sample lactase-persistence frequencies of the two populations from England (S and T) and the two populations from Italy (Y and Z). What do you notice when you compare the populations within each country? What question(s) does this comparison raise for you?

22. Compare the sample lactase-persistence frequencies for Northern Europe and Asia/Australasia. In general, what differences do you observe? What reason(s) could there be for these differences?

23. The Han population (P) in China makes up 92% of mainland China's population and roughly one-fifth of the world's population. Of the 200 people sampled, what percentage would you expect to be lactose intolerant?

Figure 1 shows the consumption of milk products among China's population from 1992 to 2006.

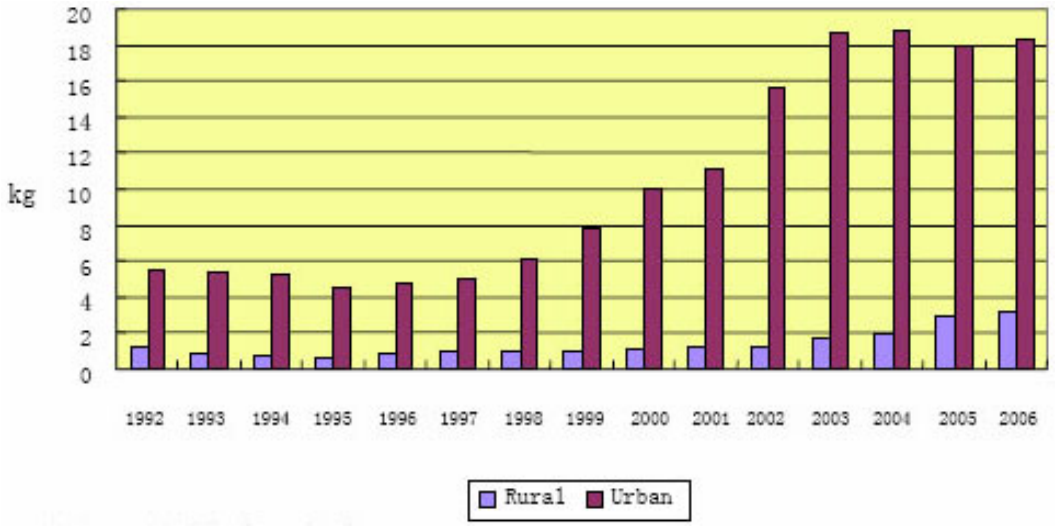


Figure 1. Per capita yearly consumption of milk (dairy) products in rural and urban households in China. Data from the Chinese Statistical Yearbook; figure provided by the FAO.

24. Based on Figure 1, predict how the lactase-persistence frequency in the Han population (P) might change after 1,000 years. Explain your prediction, noting what (if any) selective pressures might be present.

25. The traditional diet of the Bantu population (I) in Uganda has many food sources other than milk, including meat, nuts, fruits, and vegetables. Given this information, are the sample lactase-persistence frequencies for this population what you'd expect? Explain why or why not.

26. The *Got Lactase?* film claims that lactase persistence is an example of "gene-culture co-evolution." In a few sentences, explain and provide evidence for this claim. Your evidence should include one or more examples from the data you examined in this activity.

Genetic Data

Data indicate the number of people in each sample who had at least one copy of a lactase-persistence allele (out of the four considered in these studies).

Row	Continent/ Region	Country	Population	# people sampled	# people with lactase-persistence allele	Lactase-persistence frequency	Reference
A	Africa	Ethiopia	Somali	74	22		Ingram et al. (2009) *Hum. Gen.* **124**, 579.
B	Africa	Kenya	Maasai	64	54		Tishkoff et al. (2007) *Nat. Genet.* **39**, 31.
C	Africa	Kenya	Sengwer	32	4		Tishkoff et al. (2007) *Nat. Genet.* **39**, 31.
D	Africa	Senegal	Wolof	118	0		Ingram et al. (2009) *Hum. Gen.* **124**, 579.
E	Africa	South Africa	Xhosa	109	27		Torniainen et al. (2009) *BMC Genet.* **10**, 31.
F	Africa	Sudan	Beni Amer	162	73		Ingram et al. (2009) *Hum. Gen.* **124**, 579.
G	Africa	Sudan	Dinka	18	0		Tishkoff et al. (2007) *Nat. Genet.* **39**, 31.
H	Africa	Sudan	Jaali	172	46		Ingram et al. (2009) *Hum. Gen.* **124**, 579.
I	Africa	Uganda	Bantu	44	0		Mulcare et al. (2004) *Am. J. Hum. Genet.* **74**, 1102.
J	Africa	Tanzania	Burunge	36	22		Tishkoff et al. (2007) *Nat. Genet.* **39**, 31.
K	Africa	Tanzania	Maasai	38	26		Tishkoff et al. (2007) *Nat. Genet.* **39**, 31.
L	Asia	Afghanistan	Tadjik	98	19		Mulcare (2006) London: University of London PhD.
M	Asia	India	Indian	68	17		Mulcare (2006) London: University of London PhD.
N	Asia	Japan	Japanese	62	0		Bersaglieri et al. (2004) *Am. J. Hum. Genet.* **74**, 1111.
O	Asia	Russia	Udmurt	60	33		Enattah et al. (2008) *Am. J. Hum. Genet.* **82**, 57.
P	Asia	China	Han	200	0		Enattah et al. (2008) *Am. J. Hum. Genet.* **82**, 57.
Q	Asia	China	Mongol	82	8		Sun et al. (2007) *Asia Pac. J. Clin. Nutr.* **16**, 4.
R	Australasia	Papua New Guinea	Papuan	34	0		Bersaglieri et al. (2004) *Am. J. Hum. Genet.* **74**, 1111.
S	Europe	England	British, northern	1168	1098		Davey Smith et al. (2009) *Eur. J. Human Gen.*, **17**, 357-367.
T	Europe	England	British, southeastern	947	862		Davey Smith et al. (2009) *Eur. J. Human Gen.*, **17**, 357-367.
U	Europe	Finland	Finn	1876	1538		Enattah et al. (2008) *Am. J. Hum. Genet.* **82**, 57.
V	Europe	France	French	58	39		Bersaglieri et al. (2004) *Am. J. Hum. Genet.* **74**, 1111.
W	Europe	Greece	Greek	100	17		Anagnostou et al. (2009) *Am. J. Hum. Biol.* **21**, 217.
X	Europe	Hungary	Hungarian	110	95		Nagy et al. (2009) *Eur. J. Clin. Nutr.* **63**, 909.
Y	Europe	Italy	Northern Italian	28	17		Bersaglieri et al. (2004) *Am. J. Hum. Genet.* **74**, 1111.
Z	Europe	Italy	Sardinian	153	21		Anagnostou et al. (2009) *Am. J. Hum. Biol.* **21**, 217.
AA	Near/Middle East	Jordan	Jordanian	112	22		Enattah et al. (2008) *Am. J. Hum. Genet.* **82**, 57.
BB	Near/Middle East	Turkey	Anatolian Turk	98	6		Mulcare (2006) London: University of London PhD.
CC	Near/Middle East	Saudi Arabia	Bedouin	94	69		Ingram et al. (2009) *Hum. Gen.* **124**, 579.
DD	Near/Middle East	Saudi Arabia	Arab	248	206		Enattah et al. (2008) *Am. J. Hum. Genet.* **82**, 57.

Source: Global Lactase Persistence Association Database

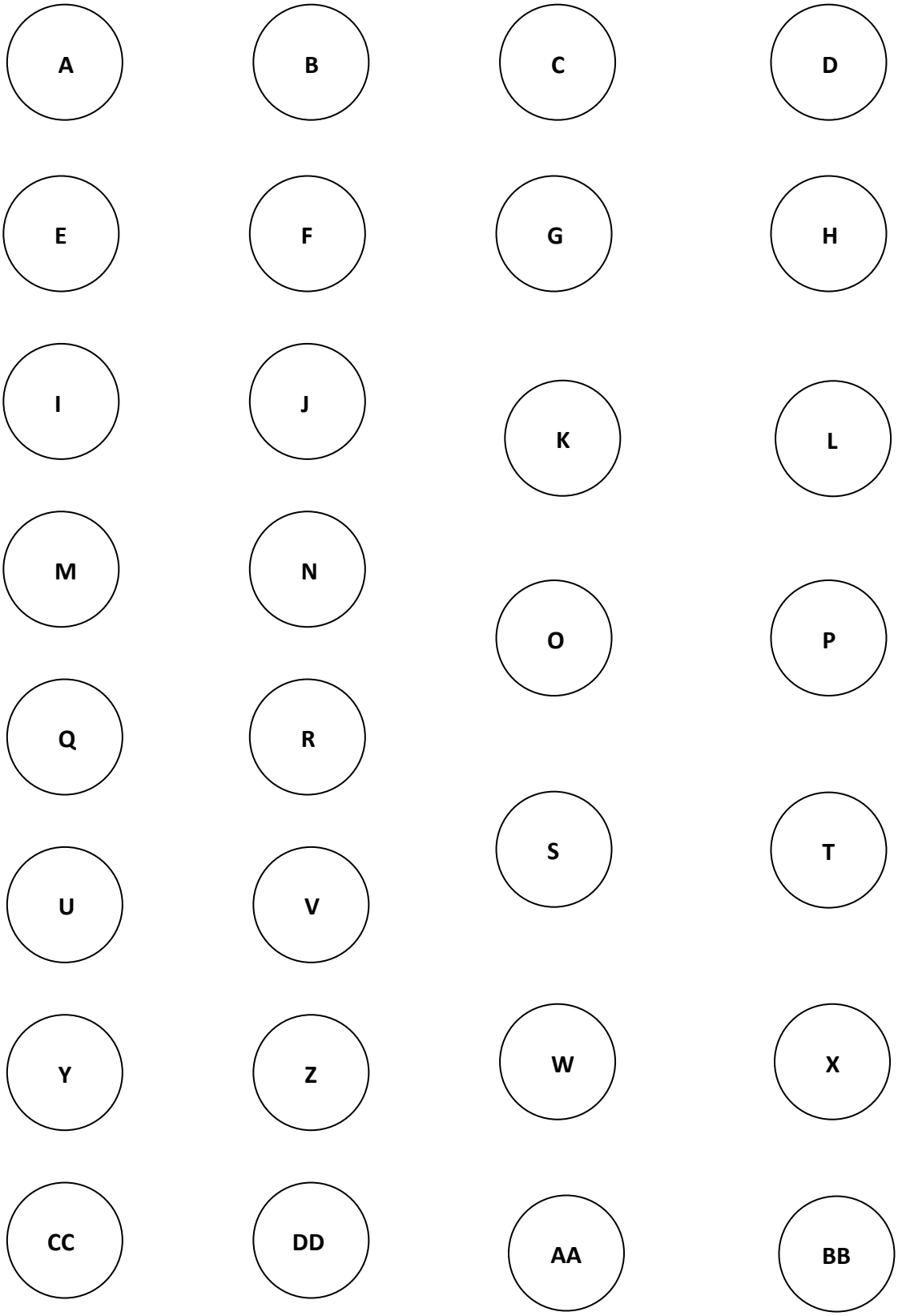
Phenotype Data

Data indicate the number of people in each sample who tested positive for the ability to digest lactose (e.g., using a blood glucose test or hydrogen breath test).

Row	Continent/ Region	Country	Population	# people sampled	# people tested positive for lactase persistence	Lactase-persistence frequency	Reference
A	Africa	Ethiopia	Somali	90	22		Ingram et al. (2009) *Hum. Gen.* ***124,*** 579.
B	Africa	Kenya	Maasai	26	23		Tishkoff et al. (2007) *Nat. Genet.* **39**, 31.
C	Africa	Kenya	Sengwer	12	2		Tishkoff et al. (2007) *Nat. Genet.* **39**, 31.
D	Africa	Senegal	Wolof	53	27		Arnold et al. (1980) *C. R. Seances Soc. Biol. Fil.* **174**, 983.
E	Africa	South Africa	Xhosa	17	3		Segal et al. (1983) *Am. J. Clin. Nutr.* **38**, 901.
F	Africa	Sudan	Beni Amer	40	35		Bayoumi et al. (1982) *Am. J. Phys. Anthropol.* **58**, 173.
G	Africa	Sudan	Dinka	208	52		Bayoumi et al. (1982) *Am. J. Phys. Anthropol.* **58**, 173.
H	Africa	Sudan	Jaali	113	60		Bayoumi et al. (1981) *Hum. Genet.* **57**, 279.
I	Africa	Uganda	Bantu	17	1		Cook et al. (1966) *Lancet* **1**, 725.
J	Africa	Tanzania	Burunge	16	6		Tishkoff et al. (2007) *Nat. Genet.* **39**, 31.
K	Africa	Tanzania	Maasai	15	10		Tishkoff et al. (2007) *Nat. Genet.* **39**, 31.
L	Asia	Afghanistan	Tadjik	79	14		Rahimi et al. (1976) *Hum. Genet.* **34**, 57.
M	Asia	India	Indian	100	36		Desai et al. (1970) *Indian J. Med. Sci.* **24**, 729.
N	Asia	Japan	Japanese	40	11		Yoshida et al. (1975) *Gastroenterol. Jpn.* **10**, 29.
O	Asia	Russia	Udmurt	30	18		Kozlov (1998) *Int. J. Circumpolar Health* **57**, 18.
P	Asia	China	Han	248	20		Yongfa et al. (1984) *Hum. Genet.* **67**, 103.
Q	Asia	China	Mongol	198	24		Yongfa et al. (1984) *Hum. Genet.* **67**, 103.
R	Australasia	Papua New Guinea	Papuan	30	3		Jenkins et al. (1981) *Ann. Hum. Biol.* **8**, 447.
*****	Europe	England	British	150	143		Ferguson et al. (1984) *Gut* **25**, 163.
U	Europe	Finland	Finn	638	530		Jussila (1969) *Ann. Clin. Res.* **1**, 199.
V	Europe	France	French	102	78		Cloarec et al. (1991) *Gastroenterol. Clin. Biol.* **15**, 588.
W	Europe	Greece	Greek	600	330		Kanaghinis et al. (1974) *Am. J. Dig. Dis.* **19**, 1021.
X	Europe	Hungary	Hungarian	535	337		Czeizel et al. (1983) *Hum. Genet.* **64**, 398.
Y	Europe	Italy	Northern Italian	208	102		Burgio et al. (1984) *Am. J. Clin. Nutr.* **39**, 100.
Z	Europe	Italy	Sardinian	53	6		Meloni et al. (1998) *Ital. J. Gastroenterol. Hepatol.* **30**, 490.
AA	Near/Middle East	Jordan	Jordanian	148	37		Hijazi et al. (1983) *Trop. Geogr. Med.* **35**, 157.
BB	Near/Middle East	Turkey	Anatolian Turk	122	32		Flatz et al. (1986) *Am. J. Hum. Genet.* **38**, 515.
CC	Near/Middle East	Saudi Arabia	Bedouin	21	17		Dissanayake et al. (1990) *Ann. Saudi Med.* **10**, 598.
DD	Near/Middle East	Saudi Arabia	Arab	109	47		Dissanayake et al. (1990) *Ann. Saudi Med.* **10**, 598.

Source: Global Lactase Persistence Association Database

Pie Chart Stencils

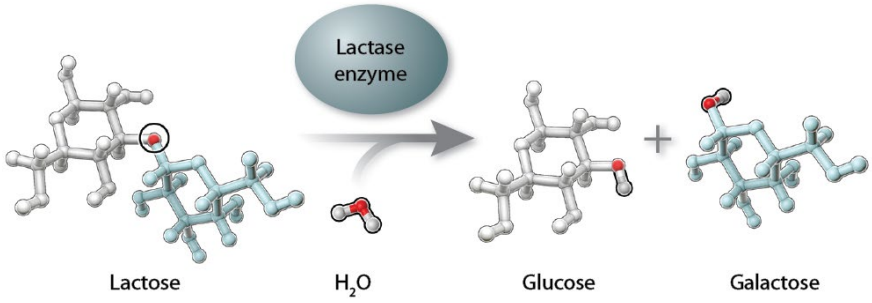


QUICK GUIDE: Measuring an Individual's Ability to Digest Lactose

Lactose Digestion

Milk is packed with proteins, fats, and carbohydrates that support the growth, development, and survival of baby mammals. The main carbohydrate in milk is a sugar called **lactose**. To digest milk, lactose must be cleaved, or broken down, by **lactase**, an enzyme produced in the small intestine. Lactase cleaves lactose into two smaller sugars, **glucose** and **galactose**, which are easily absorbed through the walls of the small intestine. Once these sugars are absorbed into the bloodstream, they can be delivered to the cells of the body and used for energy.

As baby mammals grow up and stop drinking their mother's milk, their bodies usually stop producing the lactase enzyme (presumably because it is no longer needed). Individuals that do not produce lactase as adults are called **lactase nonpersistent**. Most mammals are lactase nonpersistent and do not drink milk as adults. Humans are unusual in that some adults continue to drink milk from other mammals, such as cows.



When an individual who is lactase nonpersistent drinks milk, they cannot easily break down the lactose in the milk. The lactose passes from their small intestine to their large intestine, where it is fermented by bacteria. Fermentation produces various gases in the large intestine, which can cause abdominal pain, bloating, flatulence, and diarrhea — all symptoms of **lactose intolerance**, the inability to digest lactose. Most adults are lactase nonpersistent and thus typically lactose intolerant (although some may not know it because their symptoms are mild). However, about 35% of the global human population continues to produce lactase into adulthood. These individuals are called **lactase persistent** and are typically **lactose tolerant**, meaning that they can digest lactose easily and drink milk without problems.

Testing Methods

One way to test whether a person is lactase persistent is to use a **blood glucose test**, as shown in the *Got Lactase?* film. If the person is lactase *persistent*, their blood glucose levels will increase within 20 to 60 minutes of drinking milk.

Another way to test whether a person is lactase persistent is the **hydrogen breath test**. This test uses the amount of hydrogen in a person's breath to check for lactose fermentation. (As described above, undigested lactose is fermented by bacteria in the large intestine. Fermentation produces several gases, including hydrogen, that can exit the body through the anus. These gases can also be absorbed into the blood, circulated to the lungs, and eliminated through the breath.) If the person is lactase *nonpersistent*, the amount of hydrogen in their breath will increase after drinking milk.