

The appearance of lactase persistence: Between a selective genetic mutation and food and environmental adaptation

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Abstract

Approximately 70 % of the world population is lactose intolerant, whereas the rest has been able to preserve an important activity of lactase. This lactase persistence results from a genetic mutation, which the mechanism is still not clearly established. The decline of the activity of lactase depends on the ethnic and geographical origin; this disparity of lactase persistence in the various regions of the globe suggests that this mutation benefited of a very important positive natural selection. It can be influenced by the ancestral consumption of milk and dairy products which allowed them to have an adaptation to a diet rich in lactose. The lactase persistence also represents an element of survival in front of environmental conditions.

The appearance of lactase persistence remains not well clarified, other studies will be necessary to strengthen these results.

Keywords: lactase persistence, lactose, intolerance, milk

1. Introduction

Discovered approximately 10 000 years ago in the Caucasus, the lactose intolerance was only studied properly from 1960s when the exposure of lactose explicitly increased due to its important use in the food preparations ^[1, 2]. The post-war technological innovations allowed the discovery of numerous functional properties of the lactose as its fixative power of the aromas, crystallization, gelation, emulsion and coloring of products ^[3, 4]. Therefore, nowadays we do not find lactose in milk and dairy products only but also in industrialized products such as delicatessen, cake, cereal, and instant soups as well as in sauces and in the envelope of certain medicine and contraceptive pills. ^[5, 6]

Hypolactasis or lactose intolerance is a clinical syndrome marked by the appearance of the gastrointestinal symptoms due to the ingestion of lactose. This disaccharide is present in the milk of almost all the mammals ^[7]. To be digested, the intervention of the lactase is necessary. This enzyme allows the hydrolysis of the lactose in two simple carbohydrates, glucose and galactose. In the case of lactose intolerance, the production of lactase is insufficient or non-existent; therefore, the lactose is not hydrolysis and it joins the large intestine under its indigestible shape.

The decrease of the lactase is more noticed in the childhood after weaning but in certain cases the decline is later in the adolescence ^[8]. The lactose intolerance is manifested by abdominal pains, bloating, flatulence and diarrhea. It is also important to indicate that most of the people who suffer from hypolactasis can tolerate foods that contain low quantities of lactose without symptoms over 15 grams a day in small spaced intakes. Approximately 70 % of the world population is lactose intolerant, whereas the remaining minority has been able to preserve an important activity of lactase and thus they benefited

from a persistence of the lactase in their adulthood. These populations differ from others by several parameters analyzed during this article. In this review, we shall discuss the origin of the appearance of lactase persistence both genetically and from the concept of adaptation to dairy food and living conditions.

Genetic mutation at the origin of lactase persistence

The lactase activity in mammals was studied at the beginning of the 19th century. In 1903, researchers noticed that an adult dog had a very low activity of lactase, so the lactose was not hydrolysis and it caused diarrhea. The human hypolactasis was demonstrated 60 years later and its clinical symptoms became recognized. Moreover, it revealed to be more widespread than the lactase persistence in most of the regions of the world. Approximately 70 % of the world population is lactose intolerant ^[9], but their degree of tolerance is different from a person to another because of numerous nutritional and genetic factors that influence this tolerance. ^[10, 11]

In 1973, hypolactasis adult-type was described as hereditary and controlled by a unique recessive autosomal gene. The wild type of the gene of the lactase is characterized by the hypolactasis; leading to lactose intolerance. In the case of lactase persistence, two genetic polymorphisms were demonstrated responsible. Its distribution is more important in the North of Europe. ^[12]

The gene of the lactase has a size of about 50 kb and is situated on the chromosome 2 ^[13]. The non-persistence of lactase is characterized by two polymorphisms of unique nucleotide in the gene of the lactase. It's produced consequently substitutions of C / T13 910 and G / A22 018 that located between 14 and 22 kb upstream to the extremity 5' of the gene of the lactase in a region of DNA which works as an element acting in cis influencing the promoter of the gene of the lactase. This promoter has for role to improve the transcription of the gene of the lactase, and causes

it persistence in the adulthood^[14]. Studies suppose that C / T13 910 is the polymorphism dominating with the allele C bound to the decline of the expression of the ARNm of the lactase. Nevertheless, the real mechanism of this decrease after the weaning is not established yet.^[15]

For the heterozygous individuals, having an allele of wild type and mutated type, the activity of lactase is intermediate and they are more vulnerable to be lactose intolerant in case of a gastronomic-intestinal infection.^[5] Whereas the adult homozygous individuals with non-persistence of lactase (CC and GG) have an activity almost non-existent of lactase after the weaning.

The persistence of the lactase and the ethnic and geographical origin

The distribution of lactose intolerance around the globe varies significantly with an indisputable north-south gradient of 5 % to 100 % in the studied population. The decline of activity of lactase depends of the ethnic origin, in fact the African and Asian populations are more lactose intolerant than the white purebred Europeans. The physiological explanation of this difference still remains not clearly established.

The loss of lactase activity can reach almost 90 % of the Asian population and in an average of 4 years after weaning, the Jews lose 60 to 70 % several years after weaning and for the Europeans the decline of activity of lactase is noticed only after the age of 18 years and they remain nevertheless high compared to the other ethnic groups^[16].

The lactose intolerance also varies according to the geographical space: the white race North European adults, the North Americans and the Australians have the least important prevalence going up to 5 % in a British population and 17 % in Finland and the North of France^[17]. In South America, in Africa and in Asia, more than 50 % of the population is lactose intolerant and in certain Asian countries its prevalence is almost 100 %^[18].

The geneticists explain this big disparity of the lactose intolerance by two possible cases: either the expanding people who have the mutated gene are extremely favored regard to the others, or that they benefited from a very important positive natural selection^[19].

The persistence of the lactase and the consumption of the milk and the dairy products

As quoted previously, several studies highlighted that the deficiency of lactase is more often recorded in the people of Amerindian, Asian, African and Hispanic origin than in the people of European origin. The researchers consider that this deficiency is strongly bound to the ethnic groups whose ancestral food was rich in lactose.^[20]

American Academy of Pediatrics confirms in its turn that the lactose intolerance varies according to the ethnic group, and depends on the presence of milk and dairy products in the food. The incidence of the lactose intolerance is lower in the populations which frequently consume milk and dairy products in their diet. Such as noticed in the population of the Northern Europe where the prevalence of the primary hypolactasia is 2 %^[21].

The populations which domesticated the animals of breeding and which consumed their milk showed higher frequencies of mutation associated with a strong lactase activity in the adulthood^[22]. On the other hand, in the countries which have a

strong proportion of populations of lactase intolerant consume fewer dairy products^[23].

Studies based on analyses of DNA outcome of old rests, allowed the researchers to analyze a series of skeletons of the same region and to verify the known genetic markers of the lactose intolerance^[24]. The results show that there is no presence of any persistence of the lactase, so we consider that the former Europeans domesticated animals but that they did not develop genetically a tolerance to drink more important quantities of milk^[25, 26].

Recent publications on this matter consider that the European farmers of the Neolithic did not possess this mutation^[27], but at that time we often use the milk to make cheese or yoghurt and not necessarily consume it in drink^[28] and mind that yoghurt and cheese possess a rate of reduced lactose, they are easily assimilated.

The regular consumption of dairy products engenders an adaptation of the intestinal flora allowing the decrease of the elimination of hydrogen and the increase of the production of intestinal gases. We consider that the increase of the activity of β -galactosidase and the decrease of the intestinal pH due to the fermentation of the not absorbed lactose would affect the metabolism of the intestinal bacteria and would inhibit the production of hydrogen. The lactose increases the capacity of fermentation of bifidobactéries^[29] and capacity of the lactic bacteria to metabolize the lactose^[30].

The capacity of the flora of the colon to ferment the lactose varies from a subject to another, what makes the tolerance vary as well^[31].

Thus we can consider that the cattle breeding and the production of dairy products appeared at first, followed by the appearance of the mutation. What allowed the expanding people of this mutated gene to consume the milk that their cattle produced without complications. Therefore, we suppose that this genetic modification is at the origin of an adaptation to a diet rich in lactose. It's associated with the consumption of milk on the basis of the ancestral practices of breeding; especially as the consumption of dairy products can add a nutritional advantage to these populations^[32].

The lactose, the nourishing element of survival

The prevalence of the lactase persistence is more important in Northern Europe and in certain regions of Africa. Researchers studied the relation between the presence of the mutation and the living conditions of these populations. And they supposed that in Africa (with its dry conditions of climate), the drunk milk could allow the inhabitants of the desert to have an additional source of water and energy^[33]. Whereas in the North of Europe, the populations exposed to a low sunlight, which leads in a low cutaneous synthesis of the vitamin D, can have a capacity to consume more calcium by dairy products and so to compensate for their deficiency in vitamin D and to avoid the risks of rickets.^[34] Thus we consider that the persistence of the lactase benefited from an important effect of positive natural selection^[35]. This advantage was obtained by a co-evolution on the genetic and cultural aspects^[36, 37].

Conclusion

The lactase persistence allows preserving an impressive production of lactase in the adulthood; it results from a genetic mutation favored by a very important effect of a positive natural selection. It will allow a normal consumption of the milk in the

adulthood, several factors influence this mutation such as the ethnic and geographical origin as well as the environmental conditions.

The appearance of the persistence of the lactase remains however not well clarified, other studies will be necessary to strengthen these results.

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