

# The problematic evolution of mammary glands: milking the ‘soured’ evidence for all it’s worth

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The evidence for the evolution of the human mammary gland was reviewed. While many theories have been proposed, all have been either refuted or are very problematic. The main difficulty with any evolutionary theory of the mammary gland system is that it requires a large set of complex structures to function, for which no evidence of viable evolutionary precursors exists. It has even been very difficult to propose ‘just-so’ stories to explain how it could have evolved. As admitted by the leading researcher in the field, “the origin of the mammary gland is one of several unresolved issues that hamper attempts to reconstruct the evolution of lactation.”<sup>1</sup>

All female mammals, by definition, possess mammary glands in order to feed their young. In most cases, their young are born alive, and require breast milk to survive. The term *mammal* is Latin from *mamma*, meaning breast. Other major mammalian characteristics include a neocortex (a complex region of the brain), fur or hair, being warm-blooded, having a four-chambered heart, and possessing three middle-ear bones. Mammals live in nearly every habitat on Earth, from the deep seas, to tropical rainforests, and in sandy or icy deserts. They range in size from one-ounce shrews to 200-tonne whales. Mammals are also some of the most familiar animals, including dogs, sheep, horses, squirrels, and mice.

## The highly complex mammary gland design

The mammary gland is a sophisticated and complex system used in all mammals, but in no other vertebrates. The focus in this discussion is on the human mammary gland or breast (figure 1). The breast in other primates, the udder in ruminants (cows, goats, and deer), and the dugs (nipples, teats) of other animals (e.g. dogs and cats) are not covered.

## Milk-secreting cells produce the milk

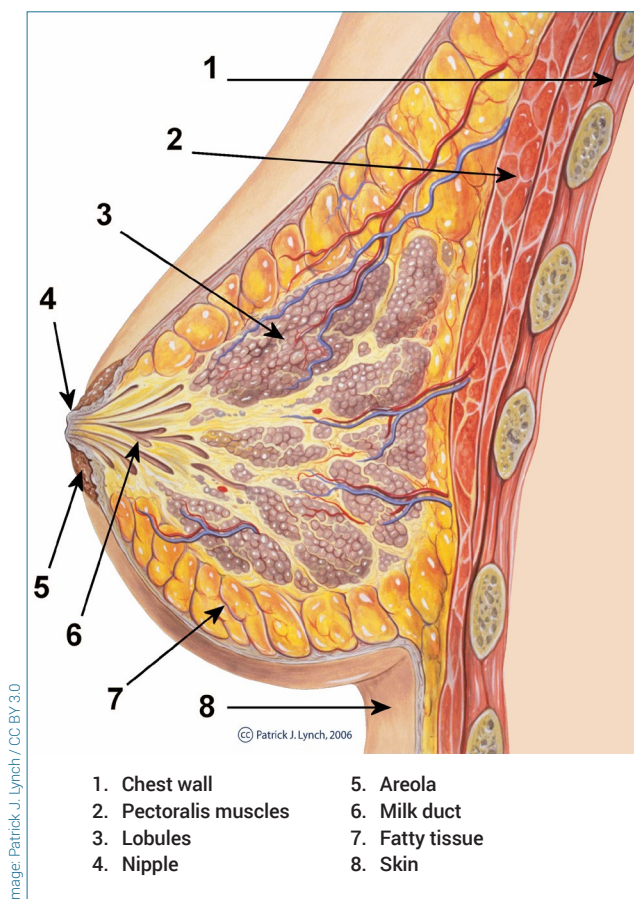
The milk-secreting cells (*lactocytes*) are the heart of the mammary gland, within small sacs a few millimetres in size, called *alveoli*, which are themselves clustered into *lobules* (figures 2 and 3). The hormone *prolactin* stimulates the lactocytes to produce milk. These lactocytes are surrounded by *myoepithelial* (smooth muscle) cells which contract when stimulated by the hormone *oxytocin*, squeezing the milk into small *ductules*, which lead into a larger lactiferous

duct within each lobule. This drains towards the nipple. As the infant begins to suck, the oxytocin-mediated ‘let down reflex’ ensures that the mother’s milk does not require the infant to suck from the gland, but rather it is secreted into the baby’s mouth.

Milk-secreting tissue leading to a single lactiferous duct is called a ‘simple mammary gland’. Humans employ a ‘complex mammary gland’ system. In this design every simple mammary gland leads via the lactiferous duct system into one nipple. Humans have two complex mammary glands, one in each breast, and each complex mammary gland is composed of up to 20 simple glands. The myoepithelial cells are in turn surrounded by a *basement membrane*, which is in contact with the mammary *stroma*. This consists of an extracellular matrix (ECM), together with adipocytes (fat cells), fibroblasts, endothelial cells and various immune and other cells.<sup>2</sup> The basement membrane of these myoepithelial cells (figure 3) not only helps to support the mammary structure, but also serves as a communicating bridge between mammary epithelia and their environment throughout this organ’s development. In addition, the system is served by a complex network of nerves, veins, arteries, capillaries, various ligaments plus a system of muscle and connective tissues.

## The central role of the hormone system

Breast development and function requires the presence of a complex system of hormones. These hormones include those that cause or support mammogenesis (breast development that begins during puberty). Without the required hormone levels, the breasts would never develop and, therefore, this must be included when considering the evolution of these glands. Increased breast maturation and size during



**Figure 1.** Cross-section of the human mammary gland

pregnancy is due primarily to estrogen, while the required lobuloalveolar development is facilitated predominantly by progesterone. The support of these and other hormones, including prolactin and placental lactogen, is required to cause breast glandular tissue to further differentiate. In addition, hormonal support causes the alveolar epithelium to proliferate and become secretory.<sup>3</sup> The complex interplay between breastfeeding and hormone production (via positive feedback) must be functional and in place to produce and secrete milk of the required composition. Only when all of these systems are in place can the mother breastfeed her child.

### The complexity of milk

The milk-secreting lactocytes are the heart of the system because it is they that manufacture the milk to exacting conditions.<sup>4</sup> Specifically, they formulate the contents of human breast milk which is (by volume) about 0.9% protein, 4.5% fat, 7.1% sugar and carbohydrates (mostly lactose), and 0.2% minerals.<sup>5</sup>

Research since the 1970s has documented that human breast milk is far more complex than naively thought before that time.<sup>6</sup> As will be discussed, these findings have created major problems for all breast-related evolutionary theories. It has been shown experimentally that human breast milk is by far best for human infants because it is *designed* for the specific needs of human health.

For example, the proteins in human breast milk (which include casein, albumin, and alpha-lactalbumin) contain all 20 amino acids found in proteins. That includes the 9 essential amino acids, that cannot be manufactured and are needed in the diet. These essential amino acids are present in human breast milk in a pattern which “closely resembles that found to be *optimal* for human infants [emphasis added]”.<sup>7</sup> The protein lactoferrin in breast milk has an important role in iron-binding and absorption, and also the regulation of the infant’s developing gut flora (the ‘good bacteria’ in the large bowel). Breast milk also contains lysozyme, produced by macrophage cells. This enzyme, also produced in tears, has significant antibacterial properties.

The most common sugar in human milk is lactose, but 30 or more other oligosaccharide sugars are also found. The principal mineral constituents in human milk are sodium, potassium, calcium, magnesium, chlorine, and phosphorus.<sup>7</sup> Besides these essential components, every required vitamin is in human breast milk in nutritionally significant concentrations—except for vitamin K, which is only in very low concentrations.<sup>8</sup> Vitamin K is central for blood clotting, and may cause problems in newborns, thus it is not produced by the infant but rather by the bacteria that progressively colonize the large bowel at maximum clotting levels until eight days after birth. Probably for this reason, God instructed the Jewish people to circumcize males only on, and not before, the eighth day (Leviticus 12:3; Luke 1:59; 2:21; Philipians 3:5).

Lastly, human breast milk is made up of close to 5% fat, including phosphatidyl ethanolamine, phosphatidyl choline, phosphatidyl serine, phosphatidyl inositol, and sphingomyelin.<sup>8</sup> These complex milk requirements are problematic for evolution because survival was seriously compromised, if not impossible, until the complex mix that enabled the newborn to live existed. This required virtually all of the components listed above to be within the required tolerances.

### Breast milk strengthens the immune system

Human breast milk also strengthens the newborn child’s immune system by several mechanisms. One important protein is critical to confer protection from pathogens, namely immunoglobulin A (IgA). IgA protects the large, vulnerable outer surface of the gastrointestinal, respiratory and genitourinary tracts.<sup>9</sup> These areas are the major sites of attack by invading pathogenic microorganisms. IgA, the principal

antibody class in the secretions that bathe these mucosal surfaces, is a critical first line of immune defence.

IgA is also an important serum (blood) immunoglobulin, mediating a variety of protective functions. It acts through interaction with specific receptors, such as the pIgR receptor located on mucosal cells. IgA also protects the immune mediators supporting the body's intestinal flora,<sup>10</sup> the important bacteria and other microorganisms that live inside of the intestines.<sup>10</sup> One reason for this protection is that intestinal microflora manufacture certain vitamins, including biotin and vitamin K.

The specific details of how the microflora and their molecular support systems are maintained have largely remained elusive until recently. Part of the answer is a class of proteins called *alarmins* that prevent intestinal colonization disorders that can lead to blood poisoning and intestinal inflammation.<sup>11</sup> A Hannover Medical School (Germany) research team has concluded *alarmins* are important in maturing postnatal intestinal flora and mucosa through interactions with bacteria in the environment. They give rise to optimal bacterial diversity, and protection against many diseases.

This adaptation process is controlled by peptides and proteins derived from breast milk that arise in the child's intestinal tract.<sup>12</sup> Specifically, they determine that S100 calcium binding proteins (S100A8 and S100A9, and their extracellular complex form, S100A8–A9) are present in high levels in human breast milk. The Hannover team also observed that only a single dose of alarmins in mice conferred some protection against poor bacterial colonization and associated diseases.<sup>13</sup>

To properly nourish the infant, the milk-secreting cells must ensure these components are in the milk within the required narrow tolerances. Too high or too low amounts of each component can be lethal for the infant. To help ensure this balance, the mother's body puts the child's needs above her requirements, and dietary recommendations for the mother reflect this. Of note is the fact that race, age, or even healthy diet variations do not usually significantly affect milk composition. Furthermore, milk from each breast is compositionally equivalent to ensure that the infant consistently receives essential nutrients regardless of which breast is used for feeding.<sup>8</sup>

### Theories of the gland's evolution

Many theories exist on how mammary glands could have evolved.<sup>13</sup> The main problem for evolution, then and now, is

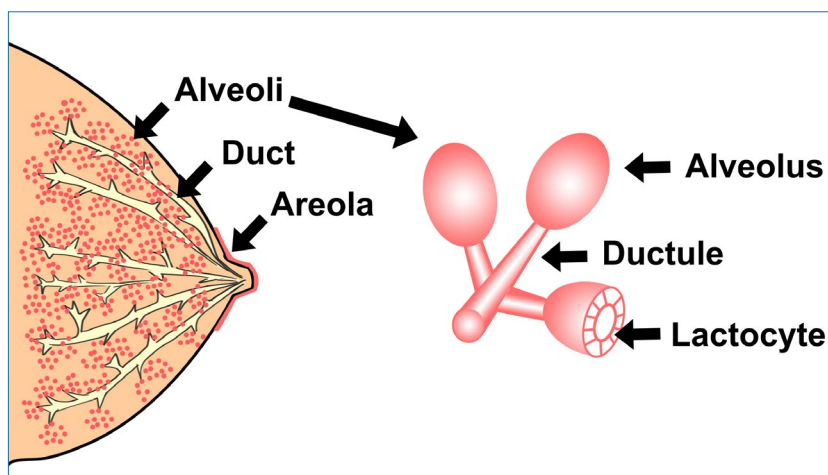


Figure 2. The alveoli clustered within lobules

that, as described above, the system is horrendously complex. It will not operate properly until all of the many required components are in place and functioning:

“The presence and secretory capacity of the mammary gland provided the basis for the taxonomic grouping of species into the class Mammalia more than two centuries ago; and Darwin’s explanation of how lactation may have evolved satisfied an early challenge to his theory of evolution by natural selection. The challenge was that evolution of lactation was not feasible, because a neonate could not obtain a survival benefit from consuming the chance secretion of a rudimentary cutaneous gland.”<sup>14</sup>

To respond to this challenge,

“Darwin hypothesized that mammary glands evolved from cutaneous glands that were contained within the brood pouches in which some fish and other marine species keep their eggs, and provided nourishment and thus a survival advantage to eggs of ancestral species. Two hundred years after Darwin’s birth, ... it is now clear that the mammary gland did not evolve from a brood pouch.”<sup>14</sup>

The innate problems of Darwin’s conjectures have forced evolutionary theorists to move on to other hypotheses. The most common evolutionary speculation today postulates that the mammalian breasts evolved from some type of sweat glands: “Lactation appears to be an ancient reproductive feature that predates the origin of mammals. ... the mammary gland is hypothesized to have evolved from apocrine-like glands associated with hair follicles.”<sup>14</sup> Note the words ‘appears’ and ‘hypothesized’ used in this explanation. This claim is rank speculation.

Another claim is that the mammary gland is a highly evolved skin gland, but which one has not been

demonstrated.<sup>3</sup> After reviewing a dozen theories, Professor Blackburn concluded that “Of the numerous structures that have been hypothesized to have given rise to the mammary gland, only three remain as plausible progenitors: sebaceous glands, eccrine glands and apocrine glands.”<sup>16</sup> (The latter two are categories of sweat glands.)

Because mammary glands are constructed from soft tissue, they rarely fossilize. Consequently, current theories are based on comparisons between living mammals—specifically monotremes (egg-laying mammals), marsupials (pouched mammals), and eutherians (placental mammals). The leading researcher in this field, Professor Olav T. Oftedal, asked the still unanswered queries regarding breast-gland evolutionary origin:

“Many scenarios disregard the fossil record, but those that do address mammalian ancestry argue that lactation had evolved in the earliest mammals but without specifying when lactation first appeared. Did lactation suddenly blossom on the evolutionary tree as an evolutionary novelty, or did it evolve gradually and incrementally, as Darwin thought? It is easy to be confused by the plethora of hypotheses, many of which sound attractive but have little predictive value, and cannot be falsified.”<sup>17</sup>

Nonetheless, despite these problems evolutionary theories abound. One popular theory proposes that mammary glands evolved from glands used to keep the eggs of early mammals moist.<sup>16,18</sup> Of course, an enormous gap exists between glands supposedly used to keep the eggs of early mammals moist and any that would be capable of generating even very simple milk formulas. JBS Haldane (1892–1964) suggested that the ancestors of mammals moistened their fur by bathing. Thirsty hatchlings benefited from sucking on the wet fur, including fur moistened by sweat. And from this sweating, mammary secretions evolved.<sup>19</sup>

Other theories suggest that early secretions were used directly for nutrients by hatched young and only later the gland evolved.<sup>20</sup> Other researchers suggested that secretions were used by young to help them orient to their mothers.<sup>21</sup> These secretion theories only move the origin of milk glands further back in time. They still have to explain the origin of the lactation secretion system cells described above which must exist before they can evolve into functional mammary glands.<sup>22</sup> One theory even speculated that the mammary gland evolved *de novo* from the embryonic ectoderm and mesenchyme.<sup>23</sup>

Another proposal is that the mammary gland evolved from components of the innate immune system. As explained by Professor Vorbach:

“The purpose of the mammary gland is to provide the newborn with copious amounts of milk, a unique body fluid that has a dual role of nutrition and

immunological protection. Interestingly, antimicrobial enzymes, such as xanthine oxidoreductase or lysozyme, are directly involved in the evolution of the nutritional aspect of milk. We outline that xanthine oxidoreductase evolved a dual role in the mammary gland and hence provide new evidence supporting the hypothesis that the nutritional function of the milk evolved subsequent to its protective function.”<sup>24</sup>

The logic of this assumption is that the mutation(s) that changed the sweat composition to enhance its innate immune functions facilitated health and survival, and thus were selected by natural selection.<sup>25</sup>

### Immunoprotective gland theory

American biologist Professor Paul Z. Myers supports the theory that the mammary gland originated from an immunoprotective gland which helped keep the animal free from infection.<sup>26</sup> Myers ignores the problems of the origin of the immunoprotective gland system, which must be assumed to exist before its evolution into functional mammary glands can occur. He admits:

“It’s a speculative story at this point, but the weight of the evidence marshaled in support of the premise is impressive: the mammalian breast first evolved as an immunoprotective gland that produced bactericidal secretions to protect the skin and secondarily eggs and infants, and that lactation is a highly derived kind of inflammation response.”<sup>26</sup>

No evidence supports the conclusion that immunoprotective glands could produce anything even close to nutritionally supporting complex animal offspring. It also begs the major question: how did the young survive until the immunoprotective glands evolved? All of these possibilities are mere speculation, “Because the mammary gland has no known homologue among the extant reptiles, [and thus] attempts to reconstruct its evolution must focus on evidence from living mammals.”<sup>17</sup>

Therefore, some evolutionists propose that *viviparity* (the development of the embryo inside the body of the mother followed by live birth) evolved *first* and was succeeded by *oviparity* (production of young by means of eggs that are hatched *after* they have been laid by the mother). This theory is the reverse of the standard evolutionary theory. The required hormones must have first evolved, then the milk ducts and nipples, followed by the other accessory organs.<sup>26</sup> Nevertheless, we see once again that the problem is that many systems must have evolved separately, yet somehow managed to operate together as a functional unit.

The problem with all of these theories is that they ignore the other very effective methods of feeding infants. The two main alternatives include: eggs which supply the nutrients

until the young hatch, and infants born at the point of development where they can fend on their own. Some mothers feed their young with food taken from the environment, such as robins feeding their young until they are mature enough to leave the nest. Given how common and successful these methods were (allegedly going far back in history), what factors would favour mammals to evolve breastfeeding, given that the feeding methods noted above are very successful?

1. Transitions from these infant feeding systems to the mammal system are recognized as so difficult that even ‘just-so’ stories are rare, and are generally admitted to be very speculative. The big problem for evolutionary theory is that the key breast structures are largely useless until they exist as a functional unit that can nutritionally support the infant.
2. Finally, another theory would have us believe that mammary gland secretion originally evolved as a means of supplying water to parchment-shelled eggs, theorizing that “... mammary gland secretions first evolved in synapsids that laid parchment-shelled eggs. Unlike the rigid-shelled eggs of birds and some other sauropsids, parchment-shelled eggs lose water very rapidly when exposed to ambient air of lower vapor pressure, whether due to differences in relative humidity or to

differences in temperature. ... mammary secretion may be an ancient trait of egg-laying synapsids, having had an important role long before milk became obligatory for suckling young.”<sup>13</sup>

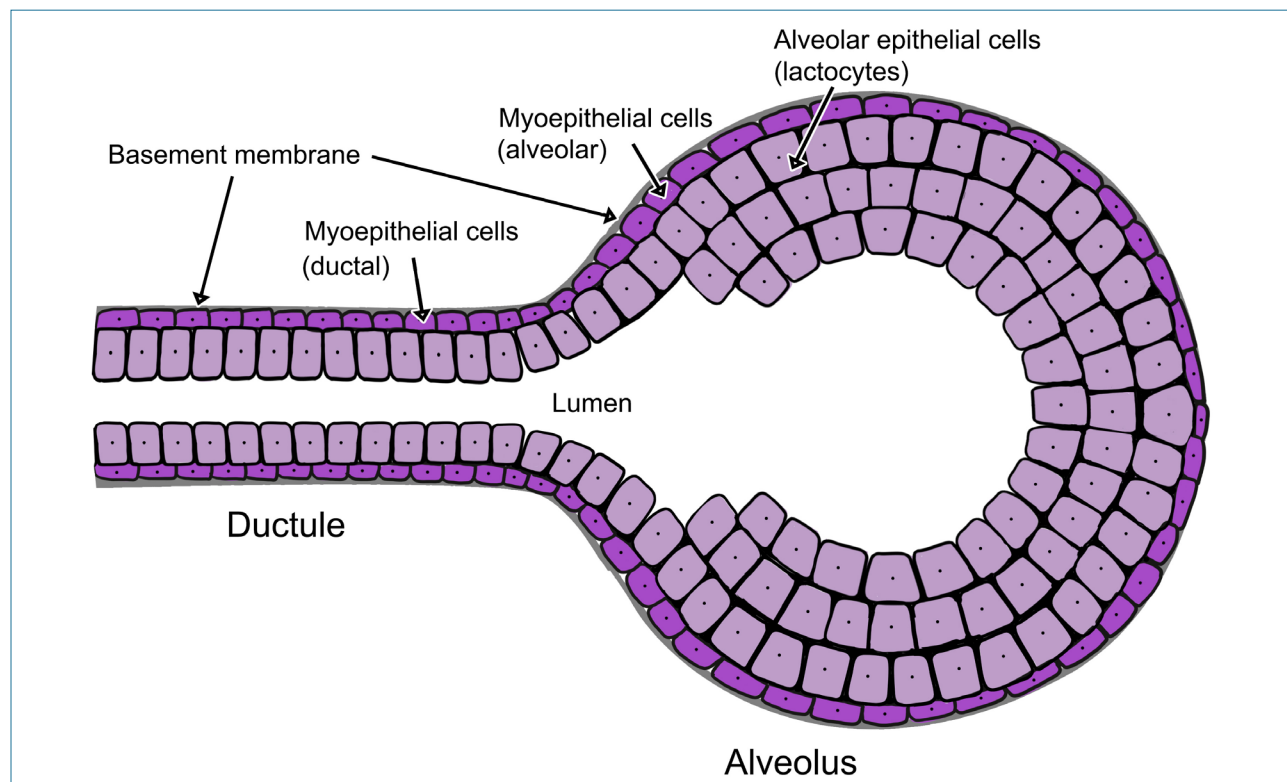
In response to some of the early theories of breast evolution, specifically evolution from some cutaneous secretory gland, the eminent St. George Mivart correctly observed:

“Let us consider the mammary gland, or breast. Is it conceivable that the young of any animal was ever saved from destruction by accidentally sucking a drop of scarcely nutritious fluid from an accidentally hypertrophied cutaneous gland of its mother?”<sup>27</sup>

### Conclusion

All attempts to support a theory of human breast evolution are either problematic or have been rejected. Most are fanciful imaginary ideas totally lacking in empirical support. This was recognized a century ago by Professor Ernst Bresslau who wrote:

“None of the many attempts to explain the phylogeny of the mammary apparatus, or parts of it, has been able to withstand searching criticism. They have all failed because of the discrepancies between theory



**Figure 3.** A simple illustration of the relationships of the fundamental layers in the alveoli and ductules. The (myoepithelial) basement membrane surrounding all is in contact with the surrounding stroma.

and facts which come to light when one follows these speculations to their logical conclusion.”<sup>28</sup>

The same generalization is still very valid today. As research has progressed, the breastmilk feeding system has proven to be more and more complex, increasing the contrast between other biological systems used to provide nutrients to newborns. Many newborns are fed by the mother, such as is true of many birds (e.g. robins feed their brood worms). Others must fend for themselves, such as newborn turtles.

Aside from logical guesses, no evidence exists to explain the evolution of the highly complex mammalian milk-feeding assemblage, and therefore trying to explain its evolution will continue to remain elusive. As Blackburn summarizes: The “literature on the evolution of lactation presents the history of valiant but unsuccessful attempts to link the mammary apparatus to a single extant population of integumentary glands.”<sup>29</sup> Blackburn, as an evolutionist, concluded that we should give up on searching for a glandular precursor to explain the origin of the mammary gland. Recognizing that complex structures arise through the modification of genes controlling developmental pathways, he concluded we should focus on genetic analysis.<sup>30</sup> This approach also will likely fail as it has in all other attempts to determine the evolution of new organs by the analysis of evolutionary relationships using genetic comparisons.

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