

Review: Mammary development in lactating sows: the importance of suckling

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Mammary development takes place during the growing and gestation periods in swine but it also continues after farrowing. In fact, a significant proportion of mammary accretion occurs during lactation and is stimulated by suckling. After piglets are weaned, there is involution of the mammary glands and the process of mammogenesis starts again during the next parity. Suckling of a teat for the first 12 to 14 h after farrowing is not sufficient to maintain lactation, and mammary involution accompanied by alterations in gene transcription will take place. The involution process is reversible within 1 day postpartum but is not reversible if a mammary gland is unsuckled for 3 days. Mammary glands that undergo involution early in lactation do not show further involution in the post-weaning period. The action of a teat being suckled does not only affect mammary development in the ongoing lactation but it also impacts mammogenesis in the following lactation. Indeed, when a mammary gland is not suckled in first parity it has a diminished development and lower milk yield in second parity. Furthermore, it was shown that suckling of a teat for only the first 2 days postpartum in primiparous sows is sufficient to ensure optimal mammary development and milk yield from that teat in the next lactation. The behavior of nursing piglets in early lactation is also affected by whether or not a teat was previously used. Such knowledge on lactation biology is essential in order to develop the best adapted management strategies for the currently used hyperprolific sow lines and to optimize growth rate of their piglets. This review gives an update on the role of suckling for mammary development in lactating sows and on how it can affect management strategies of primiparous sows.

Keywords: involution, lactation, mammary gland, nursing intensity, piglet

Implications

Suckling of a teat is essential for mammary development in sows during lactation, as demonstrated by the irreversible involution of mammary glands after 3 days of not being suckled by piglets. Knowledge on the role of suckling for mammary development is crucial in order to develop optimal management strategies for replacement gilts and sows. We now know that a teat which is not suckled in first lactation will produce less milk in the subsequent lactation. However, if a teat is used for only the first 2 days *postpartum* in primiparous sows its milk yield will not be reduced in second parity. Producers can therefore decrease litter size of very thin primiparous sows after day 2 of lactation to increase their longevity in the herd without harmful effects on subsequent milk yield.

Introduction

In current swine production systems suckling piglets generally show suboptimal growth because their dam cannot

produce enough milk (Harrell *et al.*, 1993). Indeed, even though genetic selection led to the development of hyperprolific sow lines, it had no beneficial impact on sow milking capacity (Silalahi *et al.*, 2017) so that each piglet now consumes less milk. It is therefore imperative to understand the factors affecting sow milk yield in order to develop strategies that will increase piglet weight gain. Milk yield is related to mammary development (Head and Williams, 1991) and one factor of utmost importance for mammogenesis and milk yield is suckling of a teat by piglets (Farmer *et al.*, 2012). If a teat is not suckled for 3 days during lactation it will undergo irreversible involution (Theil *et al.*, 2006) and if a teat is not suckled at all in first lactation it will produce less milk in the second lactation (Farmer *et al.*, 2012). However, suckling for a period as short as 2 days in early lactation will ensure that milk yield in the subsequent lactation is not hampered (Farmer *et al.*, 2017). This review will cover the process of mammary involution that takes place either after weaning or during lactation when a teat is not used. Results from recent trials on the effects of teat use in first-parity sows on their mammary development, mammary gene expression and milk yield in the next lactation will be described. The impact of use

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or non-use of a teat in first parity on nursing behavior of piglets in the subsequent parity will also be discussed. Lastly, this information will be used to suggest a best-adapted management strategy for hyperprolific gilts that are overly thin.

The ongoing cycle of mammary gland development

Some mammary development takes place before puberty in gilts (Sorensen *et al.*, 2002) but more extensive mammary development occurs during the last third of pregnancy (Hacker and Hill, 1972; Kensinger *et al.*, 1982; Sorensen *et al.*, 2002) and throughout lactation (Kim *et al.*, 1999). During the last third of gestation major histological changes take place in mammary tissue, with adipose and stromal tissues being replaced by lobuloalveolar tissue in order for milk to be secreted (Hacker and Hill, 1972; Kensinger *et al.*, 1982; Ji *et al.*, 2006). There is still important development of mammary tissue in lactation. Mean mammary weight of functional glands increases linearly by 57% between days 5 and 21 of lactation (Kim *et al.*, 1999). Furthermore, there are indications that the extent of mammary development in lactation could be linked to the amount of post-ejection massage from nursing piglets (Thodberg and Sorensen, 2006). Indeed, it has been postulated in early work that each piglet could act as its own regulator of milk availability in the next suckling via the amount of post-ejection massage that it performs on the gland that it uses (Algers and Jensen, 1985). After weaning, there is a rapid and drastic involution of the mammary glands (Ford *et al.*, 2003) so that the process of mammary development undergoes a new cycle during the subsequent gestation and lactation periods. The following section will cover the events taking place during mammary involution in more details.

Mammary involution

At weaning

The process of weaning the piglets from the sow leads to an abrupt cessation of milk removal, hence involution of mammary glands. Weaning is characterized by a rapid regression of mammary tissue in the first 7 days (Ford *et al.*, 2003). During that 7-day period there is a 69% decrease in wet weight of parenchymal tissue and a 67% decrease in parenchymal DNA (Ford *et al.*, 2003). The most dramatic changes occur in the first 2 days after weaning. The cross-sectional area, gland weight and parenchymal DNA in mammary tissue decrease markedly (Ford *et al.*, 2003). In the initial phase of involution (weaning to day 2), milk is no longer removed from the glands, thereby inducing milk stasis. There is an initial engorgement of mammary glands (day 1) until milk present in the lumen starts being reabsorbed (Cross *et al.*, 1958). It was postulated that, in the absence of milk removal, an autocrine feedback inhibitor of lactation accumulates in the lumen of alveolar cells to inhibit further milk secretion (Wilde *et al.*, 1995). Marked changes in

milk composition occur during that early weaning period, namely, the dry matter, fat and protein contents increase whereas lactose content decreases. Furthermore, there is an increase in the sodium (Na)/potassium (K) ratio in milk, indicative of leakage of mammary tight junctions and concentrations of prolactin decrease while those of IGF-1 increase (Farmer *et al.*, 2007). In the second phase of involution (days 2 to 4 or 5 post-weaning) there are small changes in mammary tissue that coincide with the limited alterations observed in milk metabolites (Atwood and Hartmann, 1995). Finally, in the last phase of involution (days 4 or 5 until day 7 post-weaning), only limited mammary secretions that are very viscous can be collected (Atwood and Hartmann, 1995). At this stage, very few alveolar structures remain (Cross *et al.*, 1958) and a last decrease in mammary tissue and parenchymal DNA is observed (Ford *et al.*, 2003).

The number of days in lactation affects the process of mammary involution. Tight junctions between mammary epithelial cells become leaky as lactation progresses from days 22 to 44 (Farmer *et al.*, 2007). It was suggested that in a 44-day lactation the onset of mammary involution occurred before weaning because piglets had access to creep feed starting on day 22, which decreased their hunger and suckling intensity.

During lactation

Mammary involution does not only occur after weaning but can also take place during lactation. Mammary glands that are not suckled in the first few days of lactation will regress at a rate similar to that of mammary glands regressing after weaning (Kim *et al.*, 2001). When a gland is not suckled, there is a 67% reduction in wet weight of mammary tissue in the first 7 to 10 days of lactation and these unsuckled mammary glands show no further loss of mammary parenchyma post-weaning (Ford *et al.*, 2003). The drastic and important involution of mammary glands that are not suckled in early lactation led to the original hypothesis that the process of unsuckled glands becoming non-functional may not be reversible after a few days (Kim *et al.*, 2001). It was later shown that regression of unsuckled mammary glands during early lactation is reversible during the first 24 h but is irreversible after 3 days (Theil *et al.*, 2005). Yet, glands that were sealed for either 24 or 72 h after farrowing had lower expression levels of receptors for α -lactalbumin and prolactin, showed less proliferation of cells, and had greater messenger RNA (mRNA) abundance for *IGF-binding protein-5* (IGFBP-5) than glands that were suckled regularly. Such findings are in accordance with the fact that glands that were unsuckled for 24 h had a lower milk yield throughout lactation compared with regularly suckled glands. In a later trial, glands were as follows: (1) unsuckled, (2) suckled until 12 to 14 h *postpartum* or (3) suckled regularly (Theil *et al.*, 2006). Visual scoring indicated that unsuckled glands or glands suckled only for 12 to 14 h regressed during lactation, whereas regularly suckled glands did not. Cell proliferation was measured in biopsies of mammary glands obtained from 5 days before until 6 days after farrowing. Cell turnover was

greatest (at 13.1%) before parturition, decreased *postpartum* and then, between days 1 and 6 after farrowing, either remained low at ~5.6% (in unsuckled glands) or increased to 9.9% (in glands suckled regularly or suckled for 12 to 14 h). Nevertheless, suckling of a teat for 12 to 14 h after farrowing was not adequate for lactation to be initiated and maintained until 36 h *postpartum*. Such a finding can be explained by the fact that it is at ~34 h *postpartum* that copious milk starts to be secreted (Theil *et al.*, 2014), coinciding with the second stage of lactogenesis. The first stage of lactogenesis is characterized by the differentiation of epithelial cells into lactocytes that have the capacity to synthesize milk constituents, whereas the second stage of lactogenesis marks the onset of copious milk secretions. This last stage is hence associated with secretory activation instead of secretory differentiation (Pang and Hartmann, 2007). Theil *et al.* (2006) also looked at the mRNA abundance for specific genes. The expression level of *prolactin receptors* decreased post-farrowing and that of *IGFBP-5* increased for both unsuckled glands and glands suckled for 12 to 14 h, whereas no such changes were seen in glands that were suckled regularly. The key roles of the prolactin (positive) and IGFBP-5 (negative) receptors for the maintenance of lactation in sows is therefore evident. This also corroborates previous findings in transgenic mice whereby IGFBP-5 was demonstrated to be a determinant factor in coordinating mammary cell death (Flint *et al.*, 2005).

The importance of suckling

During lactation milk must be removed from the mammary glands in order for them to remain functional, hence, the extent of suckling by piglets is a major stimulator for the growth of mammary glands (Hurley, 2001). The size of a mammary gland (i.e. gland weight or DNA content) and the growth rate of the piglet suckling that gland are positively correlated (Kim *et al.*, 2000; Nielsen *et al.*, 2001). Yet, these two factors are obviously interrelated as heavier piglets likely have a greater ability to perform post-ejection massage of the glands, hence stimulating future milk yield. Sows producing more milk (5.25 v. 4.46 kg average piglet weight gain from days 2 to 21 of lactation) also had more parenchymal DNA and parenchymal RNA per mammary gland at the end of lactation than sows with a lower milk yield (Farmer *et al.*, 2010). Seven days after weaning, it was observed that mammary glands that had been used by piglets and remained functional until the end of lactation were larger than unsuckled glands (Ford *et al.*, 2003). Taking into account that suckled glands undergo substantial growth during lactation (approximately doubling their size), reaching a peak at the end of lactation (Kim *et al.*, 1999), it is apparent that they must be larger than unsuckled glands at the onset of the involution process taking place after weaning. This observation leads to the question of whether there could be a possible beneficial effect of a teat being used in first parity on the extent of its development (and milk yield) in second

parity. Fraser *et al.* (1992) first attempted to elucidate that question by undertaking a project where the rear teats of sows were taped in first lactation and growth rate of piglets suckling either the front or the rear teats in second lactation was determined. It is known that piglets suckling front teats are generally heavier than piglets suckling rear teats (Dyck *et al.*, 1987), and the difference in weight gain between piglets suckling the front v. the rear teats was even greater in sows that had previously taped rear teats. Differences in BW gain between the two groups were greater in the first compared with the 2nd or 3rd weeks of lactation (Fraser *et al.*, 1992). These findings suggested a beneficial effect of teats being used in first parity on their development in the next parity. However, there was a confounding effect of treatment with teat location on the udder which cannot be overlooked.

Teat use and sow mammary development

It is only in 2012 that a clear demonstration was made that an unused gland in first parity will have impaired development and lower milk yield in second lactation (Farmer *et al.*, 2012). To achieve that objective a project was carried out where either the same teats or different teats were sealed in both first and second parities. This was designed so that piglets in second lactation had access to teats that were either previously suckled or unsuckled. The growth rate of piglets in second parity differed between the two groups of sows. Suckling from a teat that was used in parity one led to a 1.12 kg greater piglet BW at 56 days of age in parity 2 compared with suckling a previously unused teat. Furthermore, growth rate of piglets between days 2 and 4 of lactation (day 1 being the day of farrowing) was already significantly different, thereby suggesting a potential beneficial effect on colostrum or early milk yield. Piglets suckling teats that were previously used gained 0.43 kg in BW, compared with 0.35 kg for piglets suckling previously unused teats, over that 2-day period.

Differences in terms of mammary development and mammary gene expression were also apparent due to treatment. On day 17 of the second lactation, mammary glands that were previously suckled had more parenchymal tissue per gland and greater parenchymal DNA and RNA contents per gland, whereas extraparenchymal tissue mass was unaffected (Table 1; Farmer *et al.*, 2012). Parenchymal tissue from previously suckled glands also showed a greater mRNA abundance for the *prolactin receptor*. Results indicated the occurrence of both increased number and increased metabolic activity of parenchymal cells from glands that were previously used, which coincides with the greater weight gain of piglets suckling those teats. Differences were seen between the first and second parity but it is not known if such would also be the case between the second and third or later parities. Taking into account the fact that mammary development during lactation is greater for primiparous than multiparous sows (Nielsen *et al.*, 2001), one may expect that differences between previously suckled and unsuckled teats

Table 1 Mammary composition in second-parity sows of four functional glands that were either previously suckled (suckled, $n = 16$) or not (not suckled, $n = 16$) in first lactation

Items	Treatment		SEM ¹
	Suckled	Not suckled	
Extraparenchymal tissue (g)	692.5	714.3	48.7
Parenchymal tissue (g)	3004.1 ^c	2608.7 ^d	141.7
Parenchymal tissue/teat (g)	800.4 ^a	641.6 ^b	24.5
DM (%)	20.4	20.6	0.3
Fat ² (%)	37.9	37.6	0.8
Fat (g)	234.9	205.7	15.1
Protein ² (%)	52.0	52.9	0.8
Protein (g)	317.0 ^c	283.3 ^d	13.9
DNA ² (mg/g)	11.1	10.6	0.3
DNA (g total)	6.77 ^c	5.73 ^d	0.37
DNA (g/teat)	1.80 ^a	1.41 ^b	0.07
RNA ² (mg/g)	24.7	25.4	0.6
RNA (g total)	14.9	13.6	0.6
RNA (g/teat)	3.99 ^a	3.34 ^b	0.10

Sows were slaughtered on day 17 of lactation. Adapted from Farmer *et al.* (2012).

^{a,b}Means within a row without a common superscript differ ($P < 0.01$).

^{c,d}Means within a row without a common superscript tend to differ ($P < 0.10$).

¹Maximum value.

²Expressed on a dry matter (DM) basis.

would be lesser between later parities. Current findings are therefore most important for the management of primiparous sows. This is of great importance due to the fact that with the current hyperprolific sow lines, the burden of feeding all the suckling piglets may overtax first-parity sows that have a poor body condition. In that context the option of removing piglets from the sow may be an avenue considered. However, the next question then arises: is there a minimum period of time that a piglet must suckle a teat in first parity to avoid hindering development of that teat in second lactation?

Duration of teat use and sow mammary development

Farmer *et al.* (2017) undertook a project where first parity sows had their piglets removed on day 2, 7 or 21 of lactation and second lactation was 21 days. In both first and second lactation, litters were standardized to 12 piglets keeping only 12 functional teats by taping any surplus teats. Weight gain of piglets in second lactation was obtained and mammary biopsies were performed on 10 sows per treatment on day 110 of gestation and day 21 of lactation. Parenchymal tissue samples were used to determine mRNA abundance for *prolactin*, *long form of the prolactin receptor*, *signal transducers and activators of transcription 5A and 5B (STAT5A and STAT5B)*, *α-lactalbumin* and *IGFBP-5* genes. Increasing the duration of lactation from 2 days to 7 or 21 days in first-parity sows did not improve growth rate of their piglets in the subsequent lactation. This suggests that suckling of a teat for

2 days in primiparous sows is sufficient to ensure optimal mammary development so that piglet growth is not hindered during the subsequent lactation. Some treatment effects on mammary gene expression were present. The most important ones being (1) greater mRNA abundance for the *prolactin* gene on day 110 of gestation in sows with a previous lactation of 21 days compared with 7 days, and (2) greater mRNA abundance for the *STAT5B* gene on day 21 of lactation for sows with a previous lactation of seven compared with 2 days. Yet, these changes were not large enough to bring about differences in milk yield, as evidenced by the similar piglet growth rates.

As stated previously, Theil *et al.* (2006) demonstrated that suckling for the first 12 to 14 h *postpartum* was not sufficient to initiate and maintain lactation in sows. Current results now indicate that a 48 h period of suckling allows enough of the lactation process to take place so that the lactation performance in the subsequent lactation is not negatively affected. Such findings are of importance for the management of first-parity sows.

Previous teat use and nursing behavior of piglets

The behavior of nursing piglets in early lactation is also affected by whether or not a teat was previously used. The development of nursing behavior in newborn piglets is an intricate process (de Passillé and Rushen, 1988 and 1989) and knowing that a previously unused teat produces less milk in parity two, it could be hypothesized that non-use of a teat in first parity could affect the behavior of suckling piglets in the next lactation. That was indeed found to be the case. On day 3 of lactation, piglets suckling a previously unused teat had more aggressive behavior, a longer duration of post-ejection massage, and a greater incidence of missed nursings compared with piglets suckling a teat that was previously used (Farmer *et al.*, 2012). The combination of those behaviors suggests that piglets were more eager to obtain milk, and therefore, hungrier. Jensen *et al.* (1998) showed that a longer period of teat massage after milk ingestion reflects a greater hunger status of piglets. Furthermore, English and Bilkei (2004) demonstrated that in large litters, low-birth-weight piglets missed more nursings and spent more time in teat disputes than their heavier littermates, thereby suggesting that a greater level of hunger leads to more aggressive encounters.

It is known that piglets show preferences for certain teats on the udder, translating into greater incidences of fighting to obtain access to these teats (de Passillé and Rushen, 1989). Teat preferences can be linked to milk yield as piglets prefer the more anterior teats (de Passillé and Rushen, 1989) that are also more productive (Kim *et al.*, 2000). Interestingly, in second lactation, neonatal piglets were able to differentiate the more productive previously used teats from the less productive teats that were not used in first lactation (Devillers *et al.*, 2016). This was demonstrated in a study where in first lactation more than half of the sow's teats were

sealed with tape and six teats remained unblocked. In second lactation none of the teats were sealed and litter size was standardized to eight piglets. There were therefore more piglets than the number of teats that had been previously used and behavior of piglets was observed on days 2 and 10 of lactation. Sealing of teats with tape affected the behavior of piglets on day 2 only, coinciding with the period where teat order is being established and piglets choose and compete for higher-producing teats (de Passillé and Rushen, 1988). In second lactation, the total number of fights was greater and the percentage of time the teat was suckled during post-massage was longer for previously used teats compared with previously unused teats. Furthermore, previously used teats had a greater occupancy rate. Piglets that suckled preferentially from previously used teats on day 2 of lactation also had a significantly greater growth rate until day 56 than piglets favoring previously unused teats (23.66 v. 21.32 ± 0.59 kg). Results therefore confirmed that teats used in first lactation produce more milk in second lactation, and also showed that piglets are able to detect this difference early on.

Conclusion

The process of mammary development is cyclic, with mammary accretion taking place during gestation and lactation, followed by involution and new development occurring in the next parity. Suckling is the main stimulus required for teats to remain functional and a gland that is not suckled will undergo involution. This can occur either at weaning or during lactation. When a teat is not suckled in first parity it will impair its development and productivity in the subsequent lactation. Furthermore, nursing behavior of piglets in second parity will be affected so that, when given a choice, piglets will fight more to have access to previously used teats. Suckling of a teat for the first 12 to 14 h *postpartum* is not sufficient to initiate and maintain lactation in sows. Yet, it is now known that a 48-h period of suckling during the first lactation is enough to avoid any negative effects on its milk yield in second lactation. This information is particularly important because hyperprolific sow lines are currently used and producers are faced with the question of what is the best litter size for first-parity sows in order to ensure their longevity and optimal reproductive performance.

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Declaration of interest

There is no conflicts of interest involved with this paper.

Ethics statement

This paper is a review of published information. No new ethical approval was required.

Software and data repository sources

No new data were generated in this paper.

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