Dairy Heifer Mammary Development

Kristy M. Daniels[1]
Department of Animal Sciences
The Ohio State University

Abstract

Quantity and functionality of mammary tissue affect lifetime milk production potential in dairy cows. If the tissue foundation laid down in early life is inadequate, maximum performance will never be attained and milk production efficiency will be decreased, resulting in economic losses for producers. Overnutrition of heifers is often blamed for reduced mammary development and subsequent milk yields in heifers. This article begins with a look back 100 yr in time to an early study of heifer nutrition and mammary functionality and ends with a look ahead toward the future. The main purpose of this article is to provoke thought and to demonstrate to the reader that despite over 100 yr of work in this topic area, scientists are still trying to understand the mechanisms that govern mammary growth and development in heifers.

Introduction

According to the most recent National Animal Health Monitoring System dairy survey, the average age at first calving in the U.S. dairy herd is 25.2 mo (USDA, 2007). This number is down slightly from 25.4 mo in 2002 (USDA, 2002) and 25.8 mo in 1996 (USDA, 1996) and is considerably lower than the "normal age at first calving in large dairy breeds" of 27 to 30 mo cited in Sejrsen et al. (1982) more than 25 years ago. By reducing age at first calving, dairy producers are able to shorten the period of non-productive life of their animals, and therefore, receive quicker returns on investments by putting milk in the bulk tank sooner. To achieve a reduced age at first calving, heifers must be bred at a younger age. This is not the whole story though; one must remember that breeding is not possible until puberty is attained. Given that body weight **(BW)** at puberty has not changed in the past 25 years and puberty is more closely associated with BW than chronological age, it follows that the reason for this national reduction in age at first calving results from management strategies designed to get heifers to a set-BW faster than before. Dairy farmers have attained this, in part, by feeding not only more nutrients, but more nutrient-dense diets to their prepubertal heifers. Strategies such as this hasten puberty onset in dairy heifers, with puberty observed as early as 5 to 6 mo of age and parturition at 15 mo of age in some cases. This management strategy, however, has a downside. Increased nutrient intake in prepubertal heifers has long been blamed as a cause of reduced first lactation milk yields seen in many, but not all, heifers reared on such programs. Therefore, the beneficial aspects of a decreased period of non-productive life for heifers fed increased energy diets may be outweighed by the potential loss of lifetime milk production. The march of time has not slowed research in this area, mainly because scientists are still trying to figure out the underlying biology of mammary growth and development, with hopes of making milk production as efficient as possible.

[1]Contact at: 202 Gerlaugh Hall, OARDC, Wooster, OH 44691, (330) 263-3945, FAX: (330) 263-3949, Email: daniels.412@osu.edu

A Study from 100 Years Ago

In 1906, C.H. Eckles began what was to be an 8 yr investigation at the Missouri Agricultural Experiment Station for the purpose of determining, if possible, some of the principles upon which practical methods of raising dairy cows should be based. One hundred years ago, like today, the biggest concerns with respect to rearing dairy heifers involved feed costs and the influence of management strategies upon the later value of the animal (Eckles, 1915). This paper addresses the second issue. Eckles summarized comments from a dairy farmer survey and noted that many at the time wanted to know if it were possible to follow any method of feeding and management that will make it certain that the heifers will be good milk producers. Questions they asked then are questions we still ask ourselves today; one example being: "Does a good dairy cow or an inferior one derive her special dairy characteristics by inheritance, or is it a result of her treatment from birth to maturity"? Eckles, wanting to directly aid dairy farmers, designed an experiment to collect data on 2 points of interest to help address this issue. The first item was to collect data from heifers offered either a high or light ration during the growing period (birth to first calving). The second item addressed the influence of the age at first calving in the same animals. According to Eckles, the chief objective was to learn more definitely the relation of the above factors to the value of the cow as a milk producer. Eckles planned to use 40 animals, all purebred, representing the Jersey, Holstein, and Ayshire breeds. The groups were arranged as follows: heavy fed and early calving (n=10); heavy fed and late calving (n=10); and light fed and early calving (n=10); light fed and late calving (n=10). Although included in the original experiment, insufficient numbers of full production records were obtained for the various groups of Ayshire, so they won't be discussed any further here. According to Eckles, those designated as "heavy fed" were to receive "the maximum ration that would be consumed from birth to first calving". This ration was composed largely of grain. The "light fed" group received skim milk and roughage up to first calving, with no grain. Early calvers were supposed to calve-in from 18 to 22 mo for Jersey and from 20 to 24 mo for Holstein. Late calvers were to calve-in 1 yr later, or as close as possible to that point.

Of note, the heifers in the high fed group were fed whole milk from birth to weaning, which took place at 6 mo of age; the amount fed varied with animal size and age, but averaged about 16 lb daily. The grain fed was (by weight) 2 parts corn and 1 part oats; it was offered as soon as the calves would eat it freely. Heifers also had ad libitum access to alfalfa hay (or pasture in some instances). After calving, the diet became "a normal diet" of alfalfa hay and silage, and a grain mixture of (by weight) 4 parts corn, 2 parts bran, and 1 part oilmeal; this lactation diet was "fed in proportion to the milk production of the animal".

The light-fed heifers were fed whole milk for the first 2 wk of life. This was gradually changed to skim milk, which was fed until the animals reached 6 mo of age. Alfalfa hay was offered but grain was not. After calving, animals on the light-fed diet received the same lactation diet as the heavy-fed group.

Select data from Eckles' experiment are summarized in Table 1. Major conclusions drawn 100 yr ago were that the heavy fed heifers showed more rapid skeletal growth. Later, they became fatter than the low-fed heifers. Also, the heavy-fed heifers were slightly inferior in milk production than the light-fed heifers. Eckles comment on this was, "Apparently some detrimental effect upon the milking functions followed the use of the heavy grain ration". Also, with regard to age at first calving **(AFC)**, Eckles noted that, "calving at an extremely early age is detrimental to the best development of the milking function while nothing is gained by too great delay".

The work of Eckles addressed some very practical concerns dealing with heifer rearing programs and subsequent milk production. Their work focused on monitoring feed intake and overall body growth measures and later, milk production. Eckles hinted at the possibility that diet can impair mammary function, but the udder was not itself of great experimental concern. It would take the passing of several more decades before nutritional effects on udder composition were considered as the basis for reduced milk yield in some instances.

Importance of nutrition with respect to whole body growth and organ growth

Roughly 35 yr after the report by Eckles, animal scientists E. S. Savage and C. M. McCay noted: "Growth is far more than the increase in the body weight of an animal from day to day. It involves the changes in the numerous parts of that body. These in turn are the links in the chain that determine the capacity of the body to live and to produce" (Savage and McCay, 1942). This statement calls to light the inadequacy of using overall body growth measures, like Eckles did, to characterize/assess the well-being of a given body part, such as the udder and its components.

In their comprehensive review of calf nutrition literature, Savage and McCay (1942) highlighted the findings of almost 300 reports dating back to the 1700s, but mainly from the early 20th century. They understood the importance of rearing calves with the main goal of "producing cows with bodies of a type that will permit the optimum production of milk during a long lifetime" (Savage and McCay, 1942). They recognized that optimum lifetime performance probably was not the result of maximum rate of attainment of adult body size, which was contrary to the opinion of many at the time. Savage and McCay (1942) drew attention to the important work of Brody and Kibler (1941), wherein changes in organ weights in relation to BW were discussed. The subject was correctly identified as being of great importance. They recognized "…the relation of growth of parts to the growth of the whole body may be profoundly modified by different states of nutrition. The development of these parts in turn may have great influence upon the ultimate shape of the animal's body, the productive capacity of the body and the resistance of the animal to disease".

Savage and McCay (1942), perhaps more so than Eckles, understood that the total increase in BW for an animal consuming one diet may mean different internal conditions when compared to another animal consuming a different diet, although BW increases may be identical. They were aware that "The internal structures of the body determine its productive capacity and only upon the assumption that gross BW always provides a constant internal relationship of organs and the composition of these structures would we expect to find close correlations between the increase of the whole body and of the calf and productive capacity of the cow."

Of most importance to the body of work in the remainder of this article is that in 1942, Savage and McCay said: "The greatest need today is for establishing the interrelationships between the diet of the calf, the rate of growth, the diet of the cow and the lifetime performance." The passing of nearly 70 years has not changed the relevance of that statement, despite near constant work in the area since that time.

Nutrition and Mammary Development Studies in the Past 70 Years

While discussing calf nutrition, BW growth, organ growth, and eventual milk production quite extensively, Savage and McCay (1942) did not make the obvious link between growth of the body and growth of the udder and its internal structures. Nor did they mention the impact of nutrition on udder growth. In the time since Savage and

McCay's report, researchers have been studying such links, interestingly, without much mention of the ideas of Savage and McCay. According to an online citation tracker (Web of Science, cited reference search; accessed 3-15-10), Savage and McCay's paper has been cited 2 times in recent years and Eckles' work 1 time. Silva and colleagues at Michigan State University (2002) were the group to mention the work of Eckles. They credited Eckles for his observation that rapid-growth regimens enable earlier calving and can cause reduced milk production (Silva et al., 2002). They used mention of Eckles' work much like the author of this article is - as proof that we have known of this phenomenon for nearly a century, but despite this, the physiology has eluded us. This is certainly not due to lack of investigation either!

Herman and Ragsdale (1939; 1946) were among the first to study the effects of diet on growth and lactation performance. Results of their work were apparently never presented in full manuscripts. Regardless, they concluded that heavy feeding when young results in mediocre milk production (Herman and Ragsdale, 1939; 1946). In 1945, Brownell et al. (1945) published a predictive article in the Journal of Dairy Science. The authors served as members of the American Dairy Science Association Committee on Post-War Dairy Production. They identified phases of dairy science research likely to influence the post-war dairy industry in the US. They predicted the integration of basic physiology and endocrinology with the art of milk production (Brownwell et al., 1945). As predicted by Blackwell and colleagues (1945), the 1950s and 1960s saw much work in the general area of endocrine regulation of milk synthesis (e.g., Turner et al., 1957; Williams and Turner, 1961a). Along the way, more refined ways of studying mammary growth were discovered. Likely the biggest improvement in this area was the realization that growth could be approximated by assaying DNA content of tissues; this measurement has been a staple of bovine mammary biology research since at least 1961 (Williams and Turner, 1961b; Turner et al., 1963). The DNA content in the secretory tissue is positively associated with cell numbers and ultimately milk production.

In their now classic paper, Sinha and Tucker (1969) measured mammary DNA at various timepoints and were able to demarcate for the first time, the supposed start and finish of prepubertal allometric mammary gland growth. Collectively, studies conducted in the past 40 yr have taught us that overfeeding heifers during the allometric period of mammary gland growth (roughly defined as ~2 to 11 mo of age or ~198 to 616 lb BW) can decrease mammary development and first lactation milk yields (Little and Kay, 1979; Sejrsen et al., 1982; Radcliff et al., 2000).

In the late 1990s/early 2000s, research focus shifted to pre-weaned heifers due in part to the interest of many calf milk replacer **(MR)** manufacturers. The previously neglected research area has proven to be fruitful and much effort has been placed on investigating MR formulation, and its effects on calf body growth and on mammary growth (Brown et al., 2005; Meyer et al., 2006; Daniels et al., 2009). Brown et al. (2005), using calves from 2 to 8 wk of age, demonstrated that increased energy and protein intake associated with accelerated calf growth programs *increased* growth of mammary parenchyma **(PAR)**. Mammary PAR is important because it is the glandular tissue that will eventually produce milk. However, these differences did not hold up when heifers were evaluated at 14 wk of age (after weaning). This suggests a so-called "critical period" for mammary development exists in young heifers, where PAR is sensitive and responsive to nutrient intake. Further support of this idea comes from a recent serial slaughter study by Meyer et al. (2006a). It was found that when assessed at a common BW of 220 lb, cell proliferation in PAR was 44% higher in heifers fed elevated nutrient intake, as opposed to heifers fed restricted intake. This difference was lost by

330 lb of BW. The work of Brown et al. (2005) and Meyer et al. (2006a) begs the question, what makes the mammary glands from preweaned heifers so interesting in their reaction to diet? Before that question is addressed, it is worth describing the nature of mammary tissue from heifers.

Characterization of mammary tissue from heifers

At birth (~100 lb for Holstein), PAR is present in negligible quantities, mammary fat pad (MFP) is barely palpable, and the udder is close in proximity to the body wall. The PAR and MFP are required components of all heifer mammary glands. The MFP is located more dorsally than PAR, and PAR grows into and replaces most of the MFP in due time. In young heifers, PAR and MFP are present as distinct entities and MFP predominates. In mature cows, the distinction is less clear and PAR predominates. Meyer et al. (2006b) most recently characterized mammary tissue from newborn heifers and noted: "At 46 kg (100 lb of BW), [PAR] consisted only of a threadlike mass that extended dorsally above each teat. This structure was not easily excised, so [for analysis] it was left with the MFP and assumed to have a negligible impact on MFP weight and DNA content." In contrast, by 8 wk of age (~200 lb BW), it is not uncommon to palpate a walnut-sized mass of PAR within each quarter, in addition to one grapefruit-sized mass of MFP (Akers, Virginia Polytechnic Institute, unpublished data, 2004). This claim was substantiated recently by Daniels et al. (2009). They noted only numeric differences in PAR weight and no difference in PAR composition due to diet in 65-day old preweaned heifers (with PAR averaging 9.8 g at analysis). However, marked differences in weight and composition of MFP (MFP range, 84 to 325 g at analysis) were observed. Interestingly, on average, BW of these heifers only doubled during the experiment (range, 1.7 to 2.3 x birth weight; Daniels et al., 2009). The point here is that in a period of time where BW only doubles, growth of PAR and MFP far exceeds that, despite little change in outward appearance. Also, these fractions within the udder respond differentially to diet. The PAR appears to be refractory to diet, as suggested recently (Meyer et al., 2006ab; Daniels et al., 2009), while the MFP is directly influenced by diet. This tells us that despite not being fully functional until roughly 24 mo of age, the mammary glands of heifer calves are far from inactive. These findings, coupled with the wisdom of Savage and McCay (1942) regarding growth of body parts compared to the growth of the whole body, call for further study into the role of nutrition on early-life mammary growth and development.

Nutrition and Mammary Development Studies in the Future

The PAR and MFP are two different types of tissues, which in part may explain their different reaction to diet. The PAR is, in essence, a reproductive organ; it is known to respond to certain hormones and growth factors. The MFP is composed primarily of adipose tissue and seems to be a ready depot for excess dietary energy, much like subcutaneous fat. Adipose tissue is also estrogenic. The closeness in proximity of PAR and MFP paired with their uniqueness, points to the likely importance local "crosstalk" at the cellular level between PAR and MFP. This crosstalk, in turn, is expected to be what regulates growth and development events. Deciphering this crosstalk has begun (Li and Capuco, 2008) and more thorough investigations into reciprocal signaling between MFP and PAR will become central in the future.

Future challenges

It is undesirable, from a production standpoint, to study mammary gland development and composition at select timepoints without having corresponding milk yield data. Likewise, having only milk yield data without an idea of the status of mammary development and composition is undesirable from a mammary biology standpoint. These challenges have permeated 100 yrs of study in this area. It is easy to measure such things as initial BW and final BW in experiments as measures of overall body growth. It is currently difficult, if not impossible, to measure initial PAR and MFP weights and compare them to final PAR and MFP weights as measures of mammary growth within the same animal. This is due to the mentioned scarcity of PAR at birth and because there is currently a lack of non-invasive measurement tools to aid in collection of serial measurements at desired timepoints. Other near-constant challenges in this area of research include: the sheer length of time needed to conduct birth to lactation studies (8 yr in the Eckles study), ensuring there are enough animal numbers in experiments at the outset so accurate conclusions can be drawn years later, and ensuring the absence of confounding or extraneous factors outside in designed experiments (hard to avoid in long-term studies unless numbers are large). Finding solutions to all of these challenges while addressing experimental pursuits is daunting but not impossible.

Conclusions

The ultimate goal for those in this field is to find a way to rear heifers as efficiently as possible without negative consequences for their milk yield potential as cows. Scientists and industry partners could mutually benefit from combined efforts to finally get to the bottom of diet induced changes in mammary growth and development. Over 100 yr of uncertainty is long enough!

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Table 1. Summarized data from the experiment of C. H. Eckles conducted from 1906 to 1914.[a]

Feeding program	Calving program	Lactation 1 MY[g], lb			Lactation 2 MY, lb[h]		
		Jersey	Holstein	AVG	Jersey	Holstein	AVG
Light[b]	Early[d] (AFC[f], mo; n=)	4246 (24.2; 6)	5907 (26.7; 2)	5077 (25.5; 8)	4456	6388	5422
Light	Late[e] (AFC, mo; n=)	4925 (34.3; 4)	6943 (34.5; 6)	5934 (34.4; 10)	6739	8244	7492
Heavy[c]	Early (AFC, mo; n=)	3077 (20.0; 4)	5177 (21.2; 4)	4127 (20.6; 8)	4019	6802	5411
Heavy	Late (AFC, mo; n=)	4486 (35.3; 5)	8223 (34.3; 4)	6355 (34.8; 9)	4609	7691	6150

[a]The ration and age of calving as factors influencing the growth and dairy qualities of cows;1915; Mo. Agric. Exp. Stat.; Bul. 135.
[b]A light diet, according to 1906 standards, fed from birth to first calving. A common lactation diet was fed after first calving.
[c]A heavy diet, according to 1906 standards, fed from birth to first calving. A common lactation diet was fed after first calving.
[d]Early calving, according to 1906 standards.
[e]Late calving, according to 1906 standards.
[f]Age at first calving.
[g]MY = milk yield and AVG = average of Jersey and Holstein.
[h]The same animals were studied in lactation 2; age at second calving was apparently not recorded.