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A 100-Year Review: Historical development of female reproductive physiology in dairy cattle[1]

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ABSTRACT

The objective of this historical review in female reproductive physiology is to encapsulate major advancements since the founding of the American Dairy Science Association in 1906. The emphasis is on landmark publications in the *Journal of Dairy Science* since its first volume in 1917. A historical perspective and inferences are made in forecasting evolution of female reproduction and links between physiology of reproduction and the mammary gland. Subsequent sections are focused into main physiological categories and the temporal advancements within these physiological windows. Time points of understanding vary considerably within categories due to various advancements in technology, biological techniques, experimental design, data collection, statistical analyses, and computational forecasting. The physiological windows examined are hypothalamic and pituitary control of the ovary related to estrous behavior and cycle; differential control of the corpus luteum and uterus as influenced by cycling and pregnancy statuses; peripartum and postpartum programing of reproduction; and scientific foundation for the next century. The importance of interdisciplinary programs and integration of reproduction, nutrition/metabolism, genetics, health, and management are emphasized. The modern dairy cow of 2017 exemplifies excellence in both reproductive and lactational performance and is the foundation biological model for the next century.
Key words: reproductive physiology, pregnancy, estrous behavior, 100-year review

INTRODUCTION

It is quite appropriate to reflect on the landmark contributions over the last 100 years of the *Journal of Dairy Science* related to female reproductive physiology in dairy cattle. The modern dairy cow has been selected and managed for high production and efficiency. Indeed, it is a particular challenge to optimize the fertility of the lactating dairy cow, but major advancements have been made that are operational and based on our understanding of the underlying processes of reproductive physiology. These advancements provide the basic technology that has been transferred to the modern day dairy producer (Appendix Table A1). This historical review of female reproduction sets the stage for current and future advancements in female reproduction.

Of course, not all original advancements were published in the *Journal of Dairy Science*, and the dairy cow animal model is not necessarily the all-encompassing original animal model for initial advancements in female reproductive physiology. However, there is indeed a legacy of advancements, based on the scientific method, that have been published in the *Journal of Dairy Science*. The foundation of knowledge in the bovine provides unique insights that benefit not only the health and well-being of cattle species but other species as well, including humans. It is indeed insightful as to how accurate early sequential descriptions of female reproduction (Willett, 1956) predicted our current in-depth understanding of reproductive function utilizing the temporal advancements in the array of scientific tools and methodology developed to date. The classical areas of reproductive physiology focused on disciplines of anatomy and physiology and expanded with advancements in development of knowledge and technology such as branches of microscopy (i.e., optical, electron, and scanning probe microscopy), chemistry, biochemistry, endocrinology, hormonal measurements, tissue/cell culture, quantitation of DNA/RNA, in vitro maturation, fertilization, and development of embryos, experimental models, ultrasonography, statistics combined with computer technology, sequencing of the bovine genome, functional quantitation of the transcriptome (i.e., RNA microarrays and deep RNA sequencing), genomic selection, and gene editing. These historical and temporal advancements are instrumental to understanding the fundamental makeup and complexity of reproductive processes subsequently described.

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HISTORICAL INSIGHTS FORECASTING STRATEGIES AND WINDOWS OF INVESTIGATION IN FEMALE REPRODUCTION

Gaines (1927) hypothesized that the service period (between date of calving and date of successful conception; comparable to days open) would be related to high milk production during the first calendar month of lactation. He pointed out that lactation is known to affect the reproductive cycle in humans and some of the lower animals such as the rabbit, whereby lactation proceeding at a high level inhibited pregnancy. Nevertheless, the coefficient of variation for service period was high and not associated with yield during the first calendar month of lactation. He noted that these 2 responses appeared to be independent of each other. The mean estimate for service period was 170 d in 1927 (Gaines, 1927). The mean estimate published in 2010 (2.1 million observations between 2001 and 2007) was 146.5 d and the 50th percentile was 119 d (Pinedo and De Vries, 2010). The processes of lactation, homeorhetic metabolic changes, postpartum diseases, and so on may contribute to timing of first estrus, ovulation, and pregnancy at first service. Indeed, the specific level of production early in lactation may not be the sole source associated with fertility.

At the time of these early scientific investigations, it is useful to reference the earlier publications of Halban (1905), an obstetrician/gynecologist in Vienna who linked and described in women the dynamics of mammary gland and uterine development throughout their lifespan (i.e., embryonic to postmenopausal senescence) and conducted early experimental investigations in animal models. This is a vivid example of the past that retrospectively provided the framework for reproduction and lactational physiology for dairy cattle during the subsequent 112 years captured in the publications of the *Journal of Dairy Science*. "Embryonal impulse" represented rapid growth of the fetal mammary gland and uterus in the 8th and 9th months of pregnancy. Neonatal swelling and regression of the mammary gland and uterus were due to active substances from the placenta and their withdrawal. There was a "puberty impulse" on the mammary gland and uterus due to activity of the ovaries, and this was further characterized by ovariectomy and re-transplantation experiments. After puberty, periodic swelling of the mammary gland and uterus occurs with re-occurring estrous cycles (i.e., in humans, the "menstrual impulse"). There is the "pregnancy impulse" of rapid proliferation, with hyperplasia of the glandular tissue but at a much greater rate than postpubertal changes, leading to the inference that the placenta produces more regulatory substances than does the ovary. Pregnancy changes were not due to the fetus but to the placenta because mammary growth proceeded after death of the fetus and subsided with loss of placenta. Secretions produced by epithelium of the placenta (i.e., trophoblast and chorionic epithelium) and not stromal tissue were inferred. The corpus luteum (**CL**) persisted during pregnancy under influence of the placenta. Changes in the maternal and fetal uterus were correlated because both regress in the postpartum or puerperium period. Puerperal involution of the maternal uterus occurred only after delivery of the placenta and was considered a true atrophy. Emptying of the uterus was considered critical to onset of milk secretion (i.e., 3 to 4 d after birth). Secretion from the mammary gland before placental delivery was characterized as colostrum, not milk. Suckling did not induce milk secretion and only maintained secretion after the uterus was emptied, and suckling was associated with quiescence of the ovary. Distinct differences or uncoupling were observed between uterus and mammary gland following pregnancies in the nonsuckled and suckled states. Nonsuckled or nonlactating state resulted in a coupled decrease in both the uterus and mammary gland and an earlier recrudescence of ovarian cycles. In contrast, the suckled or lactating state resulted in a greater rate of uterine regression and a marked delay in recrudescence of ovarian cycles.

Willett (1956) noted, "A pygmy sitting on the shoulders of a giant can see farther than the giant." Due to the background of fundamental research during the half-century preceding 1906, physiologists thereafter have been pygmies or giants able to see and understand phenomena that were beyond the view of the giants of yesteryear and were able to broaden ever further the horizons of our knowledge. When Asdell (1949a,b) reviewed the studies dealing with hormonal and nutritional treatments of sterility in dairy cattle, he emphasized the need to develop more sensitive tools of investigation and specified the need for adequate controls to account for spontaneous recovery of experimental animals and the need for the biochemist or nutritionist to work closely with the physiologist. These basic principles have been emphasized extensively within the *Journal of Dairy Science* with publication of strategies for design and statistical analyses of sensitive experiments across a wide array of experimental variables (discrete and continuous) with chosen confidence (α) and power (β) to detect treatment differences (Tempelman, 2009; Lean et al., 2016).

A classical experiment begun in 1947 and completed over a 7-yr period (Reid et al., 1957, 1964; Sorenson et al., 1959) examined the influence of 3 planes of nutrition fed to heifers from birth until first calving. The dietary treatments provided approximately 65% (low), 100% (medium), and 140% (high) of Morrison's TDN