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The Tammar Wallaby and Fur Seal: Models to Examine Local Control of Lactation[1]

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ABSTRACT

Mammary development and function are regulated by systemic endocrine factors and by autocrine mechanisms intrinsic to the mammary gland, both of which act concurrently. The composition of milk includes nutritional and developmental factors that are crucial to the development of the suckled young, but it is becoming increasingly apparent that milk also has a role in regulating mammary function. This review examines the option of exploiting the comparative biology of species with extreme adaptation to lactation to examine regulatory mechanisms that are present but not readily apparent in other laboratory and livestock species. The tammar wallaby has adopted a reproductive strategy that includes a short gestation (26 d), birth of an immature young, and a relatively long lactation (300 d). The composition of milk changes progressively during the lactation cycle, and this is controlled by the mother and not the sucking pattern of the young. Furthermore, the tammar can practice concurrent asynchronous lactation; the mother provides a concentrated milk high in protein and fat for an older animal that is out of the pouch and a dilute milk low in fat and protein but high in carbohydrates from an adjacent mammary gland for a newborn pouch young. This phenomenon suggests that the mammary gland is controlled locally. The second study species, the Cape fur seal, has a lactation characterized by a repeated cycle of long at-sea foraging trips (up to 28 d) alternating with short suckling periods of 2 to 3 d ashore. Lactation almost ceases while the seal is off shore, but the mammary gland does not progress to apoptosis and involution, most likely because of local control of the mammary gland. Our studies have exploited the comparative biology of these models to investigate how mammary function is regulated by endocrine factors, and particularly by milk. This review reports 3 major findings using these model animals. First, the mammary epithelial cell has an extraordinary intrinsic capacity for survival in our culture model, and the path to either function or death by apoptosis is actively driven. The second outcome is that the route to apoptosis is most likely regulated by specific milk factors. Finally, whey acidic protein, a major milk protein in some species, may play a role in normal mammary development, but that role in vivo may be limited to marsupials. Evolutionary pressure has led to changes in the structure of the protein with an accompanying change in function. Therefore, we propose that a loss of function of this protein in eutherians may relate to a reproductive strategy that is less dependent on lactation.
Key words: lactation, local control, mammary gland

INTRODUCTION

Our understanding of the endocrine regulation of lactation in most species is advanced, but it is now clear that local regulation of mammary function is equally important and acts concomitantly with endocrine stimuli. Animal models with extreme adaptation to lactation can prove useful for increasing our understanding of the latter process by revealing mechanisms that are present but not readily apparent in many eutherian animals. The lactation cycle is common to all mammals, although marsupials and some pinnipeds have evolved a reproductive strategy distinct from most eutherians. The latter have a long gestation relative to their lactation period, whereas reproduction in marsupials such as the tammar wallaby (*Macropus eugenii*) is characterized by a short gestation followed by a long lactation, and secretion of all the major milk constituents changes progressively during lactation (Nicholas, 1988; Tyndale-Biscoe and Janssens, 1988). The lactation cycle of the Cape fur seal (*Arctocephalus pusillus pusillus*) is composed of maternal foraging and infant nursing periods that are spatially and temporally separate (Boyd, 1998). Lactating mothers suckle offspring over a period of many months, and females alternate between short periods ashore suckling their young and longer periods

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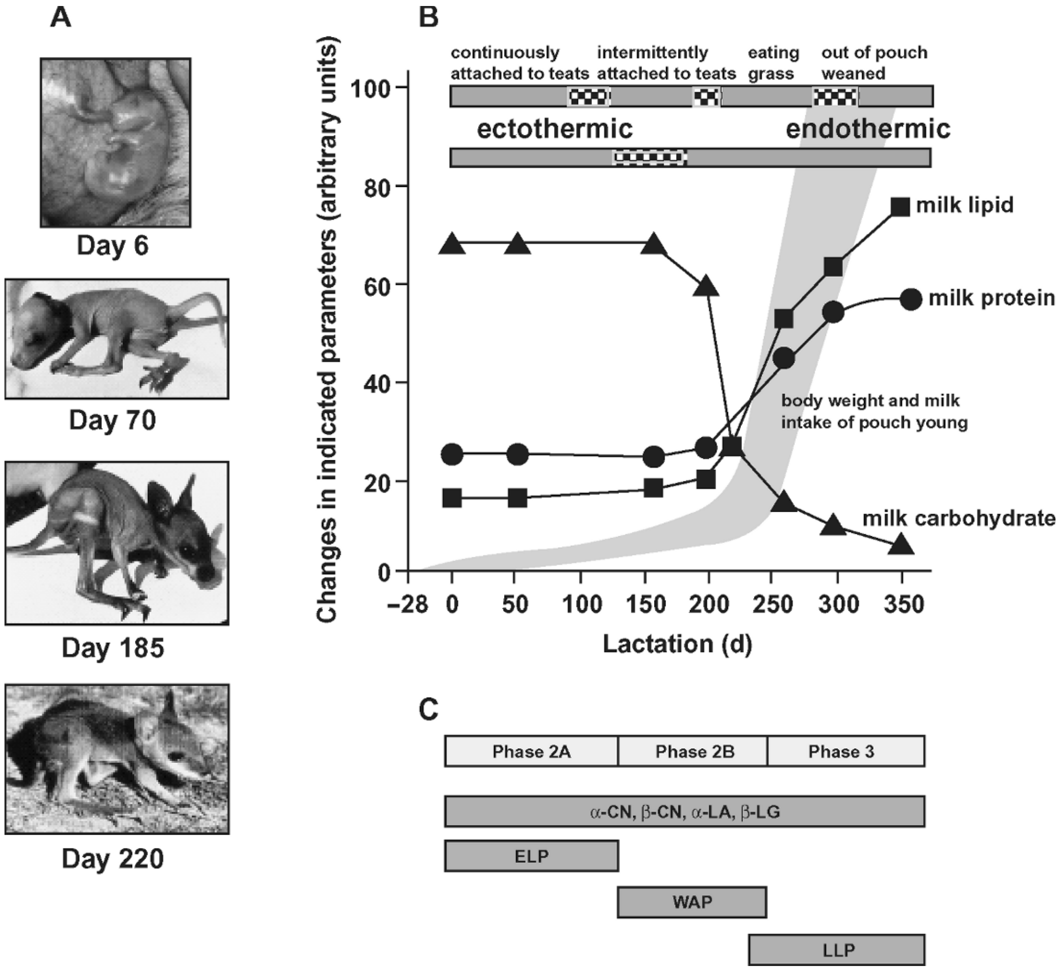

Figure 1. The lactation cycle of the tammar wallaby. (A) Development of the pouch young from d 6 to 220 of age. (B) The lactation cycle in the tammar has been divided into 4 phases, characterized by changes in milk composition and the sucking pattern of the pouch young. (C) Expression of the major milk protein genes during the lactation cycle. The α-CN, β-CN, α-LA, and β-LG genes are induced at parturition and expression remains elevated for the entire lactation. The genes for ELP (early-lactation protein), WAP (whey acidic protein), and the LLP (late-lactation proteins A and B) are expressed only for specific phases of the lactation cycle.

of up to 4 wk foraging at sea (Gentry and Holt, 1986). These animal models provide new opportunities to examine local regulation of mammary function, and particularly the potential role of milk in this process.

The Tammar Wallaby

Lactation in the tammar has been divided into phases that are defined by the composition of the milk and the apparent sucking pattern of the young (Figure 1; Nicholas et al., 1995, 1997). Phase 1 is a 26.5-d pregnancy, and the subsequent 200 d of phase 2 is characterized by lactogenesis and the secretion of small volumes of dilute milk high in carbohydrates and low in fat and protein. The pouch young remains attached to the teat for approximately the first 100 d (phase 2A), after which it relinquishes the teat, sucking less frequently while remaining permanently in the pouch (phase 2B) for an additional 100 d. Phase 3 of lactation (200 to 330 d) is characterized by a large increase in milk production, and the composition of milk changes to include elevated levels of protein and lipids and low levels of carbohydrates (Figure 1; Nicholas et al., 1995, 1997).

Two temporally different patterns of milk protein gene expression appear during the lactation cycle: One group of genes is induced to high levels around parturition and expressed throughout lactation, and a second group of genes is expressed only during specific phases of lactation (Figure 1C; Simpson and Nicholas, 2002). For example, the genes for the whey proteins β-LG and α-LA, and the α-CN and β-CN genes are induced coordinately and independently of the sucking stimulus at parturition and are expressed for the duration of lactation. In contrast, the early lactation protein gene