MILK COMPOSITION AND LACTATION STRATEGIES ACROSS MAMMALIAN TAXA: IMPLICATIONS FOR HAND-REARING NEONATES

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Introduction

The two major features of mammalian reproduction are viviparity and lactation (milk production); of these, only lactation is both unique to mammals and occurs in all living species of mammals. Milk is the complex lacteal secretion of the mammary gland responsible for the provision of nutrients and energy to the growing neonate. Once adopted during the course of mammalian evolution, milk secretion was universally retained. Some birds, including pigeons and doves, the greater flamingo, and the emperor penguin also produce nutritive fluids for the young, but their secretions are of crop or esophogeal origin, and are not the exclusive food of the young.

In mammals, milk is synthesized in the mammary gland from substrates derived directly from maternal diet or from physiological reserves stored elsewhere in the body. The evolution of milk was likely tied to the transformation of well-developed reptilian hatchlings to the more altricial mammalian young. With the development of milk secretion, the mammals or their reptilian forebears were able to store energy, minerals, and other nutrients for mobilization as needed, suggesting that lactation may have been one of the major adaptations which enabled mammals to prosper in impoverished or rapidly changing or ecologically homogeneous environments.

All mammals produce milk as the primary source of nutrients for their young, and all mammalian young are completely dependent on their mother's milk until they begin to feed on their own or are weaned. Thus milk is essential for the normal growth and development of mammalian offspring. However among diverse mammalian species, there are vast differences in the composition of milk, as well as in the developmental stage at with young are born, milk output, frequency of nursing, and length of lactation. These patterns and differences likely evolved from the interaction of various selection pressures such as environment and physiological constraints on the mother, as well as body size and nutrient requirements of the offspring.[8,11] However, because all mammals so far studied possess mammary glands that are similar in morphology, ultrastructure and secretory processes, most biochemical constituents of milk are generally shared across taxa.[9] Additionally, the proximate composition of a species' milk is largely a function of phylogeny and genetic regulation, with little influence from environmental variability such as maternal diet (only milk output is substantially influenced by maternal plane of nutrition).[7,11] Thus, given appropriate data collection, the characteristic milk composition of a species can be accurately summarized, from which artificial formulas and feeding regimes may be developed for the rearing of abandoned, orphaned or injured neonates. Clearly, neonates must be highly adapted to their species-specific milk composition and thus it is critical to mimic natural feeding as much as possible when neonates cannot be fed by their mothers.

The Composition of Milk

Milk is a complex secretory fluid containing primarily water, lipids in emulsion, proteins in colloidal dispersion and carbohydrates (when present), with minor amounts of various organic and inorganic constituents such as vitamins and minerals.[1,8,10,11] The major components besides water are described below.

Milk lipids. Lipid content is the most variable constituent of milk among species, ranging from 0.2% in the black rhinoceros to 60.0% in the milks of some phocid seals,[5,6] although in all species studied milk lipid is composed primarily (97-99 mass%) of triacylglycerols (TAG; three fatty acids (FA) esterified to a glycerol backbone). Minor lipids include mono- and diacylglycerols, free FA and sterols. The FA composition differs markedly among species, largely as a function of the relative contribution from de novo synthesis (or modification) of FA in the mammary gland versus direct uptake of circulating FA, the latter of which can originate to a large degree directly from diet.[5] The relative contribution from these two sources is largely species-specific. For instance, the mammary glands of ruminants, rodents, lagomorphs and primates synthesize significant quantities of short- (4:0-6:0) and/or medium-chain (8:0-12:0) FA,[5] which are generally exclusive to mammalian milks and not typically found in other foods. In contrast, in carnivores, pinnipeds and cetaceans, most milk FA are derived directly from diet via the circulation.[4,7] In marine and aquatic carnivores (including marine mammals) this results in milks containing very large quantities of the nutritionally significant and essential n-3 and n-6 long-chain polyunsaturated FA (PUFA, most well-known as the ω-3 and ω-6 FA). The significance of mimicking these FA compositions in formula feeding should be considered. For instance, short- and medium-chain FA are more readily hydrolyzed, transported, and metabolized during digestion, which may be an important feature to the more altricially born neonates of those species which synthesize these FA, especially those species who's neonates possess specific lingual and gastric lipases.[2] Developing neonates of all species will require the essential FA 18:2n-6, 18:3n-3 and 20:4n-6, which can only arise from maternal diet and must be present in any artificial formula. Whether the more abundant longer-chain n-3 and n-6 PUFA are really "essential" FA to neonatal marine mammals is unclear. However, given that their natural milks contain very high levels of these FA (from their mothers' marine-based diets), it is prudent to increase levels of these FAs in formulas by incorporation of fish oils.

Milk proteins. The principle proteins found in all milks are the caseins (α-, β-, and κ-) and the whey proteins α-lactalbumin and β-lactoglobulin, all of which are found in nature only in milk.[8,11] Other important whey proteins include immunoglobulins, lactoferrin and enzymes. Besides supplying essential and non-essential amino acids to the neonate, caseins are central to the entire process of milk digestion, as their interaction with stomach enzymes is the basis for gastric curd formation, which then allows retention of fat and protein in the stomach and continued and gradual delivery of milk nutrients to the intestines, preventing rapid overload which could otherwise lead to intestinal distress. This feature of gradual milk nutrient delivery is especially important in species which suckle infrequently, such as the rabbit that suckles only once per day. Finally, the immunoglobulins secreted in milks play an important role in transfer of passive immunity to the newborn. In the first few days postpartum, there is generally a high and very selective rate of secretion of immunoglobulins into colostrum (early milk), which is critically important in ruminants and some non-ruminant species (e.g., artiodactyls and perrisodacyls), where there is no immunity acquired by the fetus in utero. Additionally, in most of these species, there is only a short period after birth (~24 hours), when these immunoglobulins can be absorbed intact across the intestine, after which "gut closure" occurs and further absorption of intact proteins becomes negligible. Thus, it is critical that neonates of these species receive typical colostrum immediately after birth. Even in other species that transfer passive immunity across the placenta and do not secrete typical colostrum, the milk secreted in the first day or two after birth tends to contain elevated protein and immunoglobulin levels.

Milk carbohydrates. Lactose is by far the most common carbohydrate found in milk, synthesized only in the mammary gland, and in fact is often referred to as "milk sugar". Synthesis of lactose appears to be central to secretion of the aqueous phase of milk (due to osmotic regulation within the mammary gland). Since lactose is a disaccharide, it confers twice as much energy per osmotic increment as would a monosaccharide.[8] Lactose also promotes calcium absorption from the neonatal gut. However, the digestion of lactose requires a specific enzyme (lactase) in the gut to break the distinctive β-galactosidase linkage, without which can result in severe intestinal upset. Feeding a formula containing lactose to a neonate not adapted to digesting this sugar can lead to severe diarrhea and thus water and electrolyte loss and potentially death. Some species produce milks containing primarily other kinds of sugar, such as very large oligosaccharides (e.g., marsupials), while milks of other species (e.g., pinnipeds) contain no or only trace levels of carbohydrate. Thus, a successful practice in hand-rearing is to pre-digest formula carbohydrates using commercial enzyme treatments and/or to substantially reduce carbohydrate levels.

Variation in Milk Composition and Output within and across Mammalian Taxa

There are over 4,200 species of mammals comprising three subclasses: the Prototheria, containing the single order Monotremata (e.g., duck-billed platypus and echidna), the Metatheria, containing the single order Marsupialia, and the Eutheria, containing all placental mammals (over 95% of all mammalian species). In general, the most dilute milks and with the highest sugar levels are produced by species that nurse frequently and on demand - the perissodactyls (horses, rhinos), the primates, and in some artiodactyls (the domestic cow and goat). These species suckle their young very frequently (e.g., every half-hour in the horse). In contrast, the most concentrated milks are secreted by species that nurse infrequently and on a scheduled basis - these include lagomorphs (the rabbits and hares), some rodents and carnivores, with marine mammals being the extreme. These milks are high in both fat and protein and low in sugar. While species such as the domestic dog suckle their young about 8 times a day, many others exhibit prolonged intersuckling intervals, such as the tree shrew, which suckles only once every 48 hours. Some of these suckling and milk composition patterns may have evolved as means to allow the mother longer foraging forays between nursing when maternal food sources are spatially and temporally separated from the nursing area. Marine and dessert mammals have the additional constraint of needing to conserve maternal water and thus may have also evolved concentrated milks as a consequence; alternatively or in addition, marine mammal young may have greater energy requirements for thermoregulation. Relatively concentrated milks may also have evolved in bats, given the issue of wing-load in addition to having to leave young in a cave, and in smaller mammals in general, which have higher metabolic requirements but smaller gut capacities, in contrast to neonates of large animals, which have greater gut capacity for consuming large amounts of dilute milk.

In addition to the variation in milk composition across species, there can also be substantial variation in composition across lactation stages.[5,11] In many species, early milk often rapidly changes and may be more dilute than later stages, perhaps reflecting the needs of the developing gut of the neonate. During mid-lactation, milk composition is generally stable and often more concentrated; this is generally considered the period of peak milk yield. Late lactation is generally characterized by even greater concentration but declining yields and more intermittent suckling, as the young are gradually or abruptly weaned. However, changes that occur vary with individual species, both in magnitude and direction, and some do not follow the above patterns – all of which may require consideration in hand-rearing. Clearly, patterns of milk composition, changes over neonatal development, and rates of milk delivery differ dramatically among diverse species. However, while attempts to mimic natural patterns in hand-rearing are important to consider, it would likely not be possible to successfully duplicate certain aspects such as especially concentrated milks and long intersuckling intervals with artificial formulas. Prudence suggests that in any neonate, it is safer to start slowly with a more dilute formula to allow acclimation of the neonatal gut to a new and non-natural diet. Additionally, feeding lesser amounts more frequently further avoids potential intestinal upset with artificial formulas and feeding.

A summary of some characteristics of the major orders follows, which should provide a framework for formula development. Nevertheless, it is important to note that reliable data are not available for many species and some families and orders.

Montremata (egg-laying mammals). Data available suggest that relatively dilute milks are secreted shortly after hatching, followed by milks quite high in dry matter (49% in the echidna and 39% in the platypus), and comprised of 20-30% fat, 8-12% protein and 2-4% carbohydrate (primarily fucosyllactose in the echidna and sialyllactose in the platypus, with very minor amounts of free lactose).[5,11] During mid-lactation the echidna suckles only once every few days; suckling frequency of the platypus is unclear.

Marsupialia. Milk composition changes dramatically over lactation in the marsupials, comprised of only 8-15% dry matter at birth and rising to about 23-27% at mid-lactation.[5,11] In general, at this latter time, milk is comprised of 3-7% fat, 6-11% protein and 11-14% carbohydrate. These are the highest milk carbohydrate concentrations produced by any mammal and these levels are only possible because they are comprised primarily of oligosaccharides, which contribute less osmotic effect in the mammary gland than do mono- or disaccharides. The very high levels of carbohydrate and very low fat in milk at birth may relate to the almost fetal-like state of the newborn marsupial; that is, the mammalian fetus relies on glucose for metabolism and is not able to use fat as an energy source until after birth. Thus, initial lactation in the marsupial pouch may to some extent relate to this constraint. Late lactation milk in marsupials contains much higher fat and very low levels (and different kinds) of carbohydrate.

Insectivora. The insectivores represent a diverse group of mammals that includes very small species with high metabolic rates (e.g., shrews) and large species that undergo periodic torpor (e.g., tenrecs). But in general, insectivores appear to secrete milks relatively high in dry matter (~50%). For example, the milk of the white-toothed shrew contains 30% fat, 9% protein and 3%

carbohydrate.[5,11]

Chiroptera. Bats also represent a large and diverse group with relatively few species analyzed. However, insectivorous bats (*Myotis sp.*) secrete a milk at mid-lactation comprised of 25-27% dry matter, 13-16% fat, 6-7% protein and 3% carbohydrate.[5,11] Old world fruit bats (*Pteropodidae*) appear to secrete milks lower in dry matter (13-20%), with 6-10% fat, 2-3% proteins and 6% carbohydrate.[11]

Primates. In general, milks of the *Lemuridae* (lemurs), *Cebidae* (howler monkeys), and *Cercopithidae* (baboons and macaques) are relatively dilute at 10-14% dry matter during mid-lactation.[5,11] They are also low in fat (1-4%) and protein (1-4%) and high in carbohydrate (7-8%). However, the milks of the *Lorisidae* (bushbabies) and *Callitrichidae* (tamarins) appear to be more concentrated at 16-19% dry matter, 7-10% fat, 3-5% protein and 6-7% carbohydrate.

Carnivora. Carnivore milks tend to be relatively concentrated at mid-lactation. Milks of foxes, domestic dogs and the raccoon dog contain 18-23% dry matter, 3-9% fat, 3-5% protein and 4-5% carbohydrate; the milk of the Arctic fox is even more concentrated at 29% dry matter, 13% fat, 11% protein and 3% carbohydrate.[2,8] The milks of the *Mustelidae* and *Felidae* contain 22-30% dry matter, 8-14% fat, 7-12% protein and 3-4% carbohydrate. The milks of the *Ursidae* are most concentrated (32-38% dry matter) and highest in fat (17-25%). However, almost like the marsupials, neonatal bears are born after only a short period of development in utero and are thus extremely altricial at birth. Hence large changes in milk composition occur from early to mid- and late-lactation, as fat and protein contents increase and carbohydrate levels decrease.

Pinnipedia. Pinnipeds are characterized by the secretion of very concentrated, high-fat milks, which contain no or trace levels (0.1-0.8%) of carbohydrate. Milks of the otariids (fur seals and sea lions) are generally somewhat less concentrated (41-63% dry matter), containing 32-50% fat and 8-10% protein, while milks of the phocids (true seals) contain 66-71% dry matter, 47-61% fat, and 5-10% protein.[5,11] Large changes occur from early to mid-lactation in many species, especially in fat content. For instance in the grey seal, milk increases rapidly from about 39% fat at birth to ~60% fat within 7 days.[6] Vast differences occur in the lactation length and suckling intervals of these species as well, with otariids lactating for 4-12 months and exhibiting intersuckling intervals of 2-3 days and up to 7-12 days in some species. In contrast, phocids lactate for only a few days or weeks, secreting massive daily amounts of milk energy (22,000 kcal/d in the grey seal and ~60,000 kcal/d in the hooded seals) and rapidly wean very fat offspring.[6,7,10]

Cetacea. More limited data are available for the whales and dolphins, however, like the pinnipeds, milks are generally concentrated (30-60% dry matter), with high fat (22-41%) and protein (11-15%) levels.[5,11] Lactation lengths may be 6-7 months in baleen whales and 12-24 months in many odontocetes (toothed whales).

Proboscidea. Milks of Asian and African elephants are similar to those of many ruminants, containing moderate dry matter (17-18%), 5-7% fat, 4-5% protein and 5% carbohydrate and lactation may last 2 or more years.[5,11]

Perissodactyla. All studied species of horses, zebras and asses produce very dilute milks (10-11% dry matter), containing 1-2% fat, 1-2% protein and 6-7% carbohydrate.[5,11] Tapir milk is somewhat more concentrated (13-15% dry matter), containing 2-4% fat, 4-5% protein and 5% carbohydrate, while milk of the black rhinoceros is the most dilute (9% dry matter), containing 0.2% fat, 1% protein and 7% carbohydrate. All species suckle frequently.

Artiodacyla. Most non-domestic ruminants and related species produce milks that are relatively similar in composition, containing 18-24% dry matter, 5-10% fat, 5-8% protein and 3-5% carbohydrate.[5,11] Thus, the more dilute milks of dairy cattle and goats are not typical of their wild counterparts. Milks of reindeer and musk ox tend to be the most concentrated at 26-28% dry matter.

Rodentia and Lagomorpha. Even though neonates of these species are born at quite different stages of development, most rodents, rabbits and hares produce moderately concentrated milks (22-35% dry matter) at mid-lactation, containing 11-22% fat, 6-15% protein and 2-5% carbohydrate.[5,11] More concentrated milks (41% dry matter) are produced by the house mouse. The least concentrated milk (17% dry matter) is produced by the guinea pig, which may be related to the highly precocial state of the newborn, which already has substantial body fat stores.

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