Association of Maternal Obesity Before Conception with Poor Lactation Performance

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Abstract

The objective of this review is to evaluate the evidence for a link
between maternal obesity and poor lactation performance. In non-
human species, excess maternal fatness is deleterious for lactation
and also for maternal health and survival. These effects occur dur-
ing pregnancy and as milk production is beginning. They may re-
sult in poor growth and survival of the young. In women, there
is a negative association between maternal obesity and the initia-
tion as well as the continuation of breastfeeding. This appears to be
derived from biological as well as sociocultural factors that are still
poorly understood. Excessive gestational weight gain, complications
of pregnancy and delivery, and the condition of the infant at birth
may also contribute to this association. Given the increasingly high
rates of obesity among women of reproductive age worldwide and
the importance of breastfeeding for infant health, further study of
this association is essential.

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INTRODUCTION

Although it has been understood for some time that excess fatness contributes to poor health outcomes as well as to reduced milk production in dairy cows, it has only recently become evident that excess fatness may also be disadvantageous for lactation in women. The objective of this review is to evaluate the evidence for a link between maternal obesity and poor lactation performance. Much new information is available since this subject was last reviewed (81, 82). Data from production and experimental species are used to provide biological plausibility and information about potential mechanisms for this association. Data from women, which are primarily from observational epidemiologic studies, are used to establish that this association exists in women and to generate hypotheses about the additional factors that might also contribute to it.

The underlying conceptual model is complex (**Figure 1**). Excess maternal adiposity may interfere with successful lactation by several different routes. Excess maternal adiposity may interfere with the development of the mammary glands at various times (before conception, during pregnancy, and during

lactation, depending on the species). Along with hormonal and metabolic abnormalities associated with excess maternal adiposity, these developmental problems contribute to a delay in the onset of copious milk secretion (secretory activation or lactogenesis II) and, thus, to early cessation of lactation (**Figure 1A**). Excess maternal adiposity may also lead to complications of pregnancy (such as preterm birth or cesarean section that themselves are associated with reduced success in lactation), the birth of a large baby who may be treated in ways that are not optimal for successful breastfeeding, and physical conditions (such as large breasts) that make proper breastfeeding more difficult (**Figure 1B**). Several of these factors themselves lead to a delay in lactogenesis II and to early cessation of breastfeeding. Finally, excess maternal adiposity is negatively associated with the choice to breastfeed at all. This choice is modified by a variety of sociodemographic and psychosocial factors. These factors also modify the duration of breastfeeding among women who have chosen to breastfeed as do the physiological and mechanical factors previously associated with difficulties in establishing breastfeeding (**Figure 1C**). In this review, these various possibilities are explored in turn.

BIOLOGICAL BASIS FOR AN ASSOCIATION BETWEEN MATERNAL OVERFATNESS AND MILK PRODUCTION

Production Species

In dairy cows, "high body condition" or excess fatness is associated with the development of "fat cow syndrome," which is characterized by "depression, anorexia, ketonuria, marked decrease in [milk] production . . . " as well as other problems (66). These "overconditioned" cows experience an excessive depression of appetite after calving and, as a result, an even more negative energy balance than that of normally conditioned animals. Metabolic changes at this time include a

reduction in Krebs cycle capacity as well as the inhibition of fatty acid synthesis and oxidation (68). This leads to an excess of nonesterified fatty acids in the blood, an amount that is more than the liver can process. This produces a build-up of triacylglycerols in the liver and, eventually, fatty liver (97). Animals may die from this condition (63, 66).

Although the negative energy balance that begins after delivery may precipitate the death of overconditioned dairy cows, poor milk production may have additional, earlier origins. It has long been known that "mammary development [is] incomplete in cows raised on a high feeding level" (102). "High feeding" (usually a high energy intake, but other dietary components may also be fed in excess) affects development of the mammary gland differently at various stages in the life of the dairy cow. Increased growth has no effect on development of the mammary gland before the calf weighs 90 kg, but between that weight and puberty, high feeding leads to reduced growth of the mammary gland and also reduced milk yield (102). After puberty and during pregnancy, high feeding does not affect mammary development (102), which is complete at calving (102). The negative effects of high feeding on mammary development appear to be driven by the energy, not the protein, component of the diet offered (11).

In the dairy cow, high feeding disproportionately increases the mass of the mammary stroma, a matrix of connective and adipose tissue, but inhibits growth of the parenchyma, which consists of epithelial cells (107). Sejrsen and coworkers (102) have investigated whether growth hormone, which is required for mammary gland development during puberty in the dairy cow and is affected by feeding level, might be involved. Based on the results of several experiments, they concluded that the "reduced sensitivity of the mammary tissue to IGF-I is the most logical explanation for the reduced mammary growth due to high feeding level" (102). More recently, they and others (107) have considered the additional hypothesis that leptin, which rises in response to high feeding, might be an important mediating factor. Although Thorn et al. (107) were able to show that leptin synthesis is increased in heifers fed at a high plane of nutrition, they also showed that leptin did not act directly on mammary epithelial cells. Thus, the exact cause of the inhibition of the growth of the mammary parenchyma with high feeding in dairy cows remains unknown.

Although there is no recognized "fat pig syndrome," some attention has been given to the association between nutritional status and the success of lactation in this species, with findings similar to those in dairy cows. Pigs that were overfed during pregnancy and, thus, were too fat at farrowing ate significantly less and had significantly higher concentrations of nonesterified fatty acids in their plasma during lactation than controls of normal fatness (89). In this same experiment, the milk production of the overfat sows was 10% and 15% lower than that of the control animals at 2 and 4 wk of lactation, respectively (88). The authors speculated that the poorer milk production of the overfat animals may have resulted from poor mammary development during pregnancy. There is support for this possibility because increased dietary energy was detrimental to the development of secretory tissue in the mammary gland in another experiment in which gilts were overfed during the last quarter of pregnancy and during lactation (112). In this study, mammary parenchymal weight as well as DNA, RNA, and protein concentrations in the parenchyma were significantly lower in the overfed than in normally fed animals; this was not the case in the mammary stroma (112).

There is one report (109) of an association between overnutrition and an indicator of lactation performance in sheep. In this study, ewes were overfed after breeding, and at parturition, were 20 kg heavier and produced significantly less colostrum. In horses, there is a positive association between condition score, a measure of body fatness (36), and reproductive performance, including success in lactation (20, 35). Although there did not appear

to be reproductive difficulties among the relatively few obese mares studied, researchers have noted that there is "no reproductive advantage" to keeping animals in this condition and that it can be "economically prohibitive" (32).

In summary, it is not surprising that the association between maternal overfatness and milk production has been most thoroughly studied in the dairy cow, where the economic consequences of this association are the greatest. Poor milk production results from the metabolic sequelae of especially severe negative energy balance among so-called fat cows. Poor milk production may also result from impaired development of the mammary gland when overfeeding occurs before puberty in dairy cows. In pigs, poor milk production results from impaired development of the mammary gland when overfeeding occurs during pregnancy. The mechanism by which excess body fatness impairs the development of the mammary gland in these species has not yet been determined.

Experimental Species

Nearly all of the research on obesity and lactational performance in experimental species has been carried out in rodents, particularly rats, and has used either "cafeteria" feeding or high-fat diets to produce obesity before breeding. In cafeteria feeding, rats are offered a selection of high-fat snack items. As a result, the composition of the diet differs from rat to rat and the diet consumed may or may not provide adequate protein. With a high-fat diet, each rat consumes a diet of the same composition, which can be constructed to provide adequate dietary protein for animals at all life stages. Although it is easier to know what the rat has consumed and also to meet the relatively high protein requirements for lactation in rats with a high-fat diet than with cafeteria feeding, results obtained using these two approaches are concordant so they are considered together. Genetically obese rats and mice generally are infertile and, thus, not suitable for studying the association between obesity and lactation. Obese rats are significantly heavier and fatter than are their nonobese counterparts, but there is no cut-off point—as there is for human beings—for declaring a rat to be "obese." Studies in rodents have provided data to support many of the elements of the underlying conceptual framework for this review (82).

Development of the mammary glands. In a study of mice fed a high-fat diet for 2 mo before conception, Flint et al. (28) found that they were heavier throughout the reproductive period than controls, with heavier mammary glands during pregnancy and immediately after parturition. This difference in mammary gland weight was no longer evident at mid-lactation because adipose tissue had been mobilized from the mammary glands of the obese animals. There was no difference between the obese and control animals in the DNA content or the total amount of parenchymal tissue in the mammary glands during this experiment. The ductal structures had invaded the entire mammary fat pad in both obese and control animals. However, there were a number of abnormal aspects of the mammary glands of the obese mice, such as abnormal side branching of the ductules and abnormal alveolar development at mid-pregnancy. Taken together, these findings suggest that the problem caused by obesity is not one of growth or proliferation of epithelial tissue in the mammary gland but rather one of development or differentiation of the alveoli (28).

The growth and development of the parenchyma of the mammary gland is regulated by both systemic and local factors, and the mammary fat pad is central to this regulation (42). The mammary fat pad is a matrix of adipose and connective tissue that can mediate hormone action and synthesize compounds that regulate growth. Whether the excess fat that is deposited in the mammary gland as the animal becomes obese influences the development or differentiation of the gland is

unknown at present. However, it is known that the lipids (or their derivatives) stored in the adipose tissue that is part of the fat pad could influence the growth of mammary epithelial cells (42). Thus, the results of Flint et al. (28) suggest that additional attention to the role of the mammary fat pad in obesity could prove to be informative.

Complications of pregnancy. In both rats (94, 95, 103, 110) and mice (28), a lower proportion of obese animals conceive and, among those that do become pregnant, obese animals deliver fewer pups in each litter and have lower pup survival than controls (84). Even with fewer pups in the litters, mean weight at birth for pups born to obese dams is either not different (94, 96, 103) or even less (19, 28)—not more—than those of normal-weight dams, as might be expected from excess maternal adiposity and lower litter number.

Metabolic conditions postpartum. Rodents dramatically increase their food and energy intakes during lactation. Surprisingly, obesity dampens these increases in rats (95, 96). This may be because heat production in the lactating rat is already maximal (30) and obesity exacerbates the animal's problem with heat disposal. Body weight (94, 96) and carcass fat (82) decrease substantially from late pregnancy to mid-lactation, but remain higher in obese rats in mid-lactation than in control animals. As was the case for the dairy cow, obese rats may develop fatty livers (1). In the single study in mice (28), obese animals decreased their food intake more than controls around the time of parturition, but remained heavier than controls throughout the remainder of lactation. Although these obese mice lost more parametrial fat than controls during lactation, they still had more fat in this depot in mid-lactation.

The transition from pregnancy to lactation is associated with numerous metabolic changes that permit the nursing animal to direct the substrates that are needed for milk production to the mammary gland. For example, concentrations of plasma insulin decrease while those of prolactin increase between day 20 of pregnancy and day 3 of lactation (87). These changes also occur in obese animals, but they are significantly reduced (103). Agius et al. (1) observed that by 6–10 d postpartum, blood concentrations of glucose and ketone bodies were higher in obese than in control animals. This combination may have contributed to the remarkably reduced rate of fatty acid synthesis that they observed in mammary tissue in the obese rats (1). Similar observations have been made in mice (28). In the experiment of Agius et al. (1), the obese rats also developed fatty livers, which the investigators attributed to increased mobilization of fat from their excessive amount of adipose tissue. This greater mobilization of adipose tissue during lactation in rats fed a high-fat diet has been confirmed by others (105).

Progress of lactation. In both rats and mice, obesity causes an initial impairment in milk production. This may result in the death of the litter because the pups may receive no milk at all in the first day of life (103). Alternatively, the milk volume may be low but still sufficient for the pups to survive, and then may increase over the next few days (28). Both of these findings suggest that obesity interferes with lactogenesis.

In their photomicrographs, Flint et al. (28) have provided visual evidence of impaired lactogenesis in mice: Lipid droplets remained within the alveolar cells of the obese animals but had moved to the lumen of the ductules of the controls at day 1 of lactation. Impaired lactogenesis is consistent with the observation of impaired alveolar development in these animals (28). Moreover, Flint et al. (28) also documented changes in mRNA expression that were consistent with a decrease in milk secretion at this time. On day 1 of lactation, the expression of major milk proteins—α-lactalbumin, β-casein, and whey acid protein—was reduced as was the expression of acetyl-CoA carboxylase, which indicates

that the de novo synthesis of fatty acids in the mammary gland was also reduced (28).

Both milk production and composition are affected by obesity in rats. Obese animals produce less milk than controls (91). This is also seen in animals fed high-fat diets only during lactation who are not yet "obese," and is thought to result from ketosis in the dams (30). The milk of the obese rats contains a lower concentration of protein (93) and a higher concentration of fat (73, 92, 93) than that of control animals. The fatty acid composition of the milk reflects the diet fed to produce obesity and, thus, also the composition of the animals' adipose tissue (92, 93). The effects of these simultaneous changes in milk volume and composition have been inconsistent, with investigators reporting lower (94) or higher (5, 73, 96) pup weights at weaning among those nursed by obese dams compared with control animals.

In the single report in mice (28), the expression of α-lactalbumin and acetyl-CoA carboxylase remained depressed on day 10 of lactation. These changes in expression were associated with lower concentrations of protein and higher concentrations of fat in the milk of the obese dams. The litters nursed by obese dams grew less well than did those nursed by controls on the first day of life, but their growth was equivalent thereafter (28).

In one report in rats, maternal obesity was accompanied by changes in maternal behavior. Pups born to obese rat dams "were observed in contact with their mothers, but not suckling, and they were being licked more frequently than pups of control mothers" (110). From this single report, it is difficult to know how important changes in maternal behavior might be, but it may be fruitful to explore this possibility further.

Amelioration of the effects of obesity on lactation. Studies in experimental species also provide information about whether changes in diet during lactation can ameliorate the effects of pre-existing obesity on lactation. In these studies, the type of high-fat diet that was used to induce maternal obesity before conception appeared to matter. When rats fed a cafeteria diet were switched to a closed-formula, low-fat rat diet at delivery, they lost more weight during lactation than those who continued to be fed the cafeteria diet. Their pups also grew poorly (96) in spite of the fact that the milk energy concentration did not differ between these two groups of dams. Milk production was not measured in this experiment (93). In contrast, when rats fed an open-formula, high-fat diet were switched to an open-formula, low-fat diet, they lost less weight during lactation than those that continued to be fed the high-fat diet. In addition, the litters of the animals that switched diets grew better than the litters of those that continued to be fed the high-fat diet (87). Thus, the higher milk volume in the dams that were switched to the low-fat diet appeared to have compensated for lower milk lactose and lipid concentrations (87) to permit better growth of the pups.

In summary, the findings in production and experimental species are consistent: Consumption of a diet that is sufficient to cause excess maternal fatness is deleterious for lactation. In production species, excess maternal fatness is also deleterious for maternal health and survival. In experimental species, the deleterious effects of excess fatness occur during pregnancy and immediately after giving birth (when milk production is just beginning) and may be accompanied by poor growth and survival of the litter.

STUDIES IN LACTATING WOMEN

Development of the Mammary Glands

To date, the possibility that obesity might directly affect the development of the human mammary gland at any stage has not been studied in women. More generally, "little is known about the development of the normal human mammary gland" (43). The

development and function of the mammary gland are controlled by both reproductive and metabolic hormones (70). Moreover, adipose tissue should be considered an endocrine organ (65) (although perhaps only a "feeble" one at the whole-body level) (18). Thus, evaluating this link is warranted. The data from mice suggest that obesity affects development of the mammary gland during periods of morphological change and cellular differentiation (28). Thus, it reasonable to expect that obesity might act during similar periods in women. After puberty, these periods are during the menstrual cycle and, particularly, pregnancy (43). This expectation is in accord with the long-recognized positive association between increase in breast size during pregnancy (reflecting an increase in parenchymal breast tissue) and milk production early in lactation (44).

Women who are obese at conception can be assumed to have been so for some time. As a result, they could have experienced effects of their obesity on the proliferation and differentiation of the mammary parenchymal tissue that occur during each menstrual cycle (43). However, this possibility has not yet been evaluated.

Changes in their breasts are among the earliest signs of pregnancy that women notice. Proliferation of mammary gland tissue "begins very early after conception and is maximal during the first trimester of pregnancy, significant during the middle trimester, and moderate in the final trimester of gestation" (45). In early pregnancy, there is proliferation of the distal epithelial elements of the ductal tree in addition to an increase in the number of ductules. These changes increase the secretory potential of the gland. In later pregnancy, proliferation is less but the epithelial cells grow and the alveoli become distended as secretory material accumulates (45). The timing and pattern of mammary gland development suggest that being too fat at conception is likely to be important for later readiness to secrete milk. These findings also suggest that women who are of normal weight at concep-

tion but who subsequently gained excess adipose tissue during pregnancy could also compromise their readiness to secrete milk. As described below, this is what we and others have observed.

Obese women have excess adipose tissue in their breasts as well as in fat depots elsewhere in their bodies. Thus effects on lactation of excess fat in each of these locations should be considered, but to date have not been studied separately. In human beings, epithelial cells are not in direct contact with adipocytes in the mammary fat pad, rather "they are continuously ensheathed by multiple layers of connective tissue and fibroblasts" (42). Nonetheless, "epithelial cells grow within a depot of adipose tissue enriched with lipid and its derivatives" (42). Data from experimental species establish clearly that "fat cells and fibroblasts of the mammary gland are potentially capable of exerting a regulatory influence on the growth potential of the epithelium" (45). Recently a proteomic analysis of the adipose tissue in the human mammary gland was conducted using biopsy samples from women being treated for breast cancer. The tissue used for this analysis was collected at a site far from the tumor. These investigators found that a wide variety of cytokines (leptin, TNF-α, and components of the caspase cascade) as well as estrogen receptors and growth factors were present there (15). Estrogen receptors have previously been observed in autopsy samples of mammary gland tissue from normal women (7). The implications of this environment of adipose tissue for the development of human mammary epithelial cells are only beginning to be understood (71). The effects of obesity in amplifying or modifying this environment have not yet been explored.

Moreover, the behavior of adipose tissue itself changes as obesity becomes more severe, with macroscopic and histologic changes occurring in the tissue as well as changes in the secretion of endocrine and paracrine factors, among others (18). This suggests that as obesity becomes more severe so too might the

effects of obesity on pregnancy and lactation. As described below, this is what we and others have observed.

An important issue is whether the hormonal and metabolic characteristics of obesity have the capacity to influence the next two major stages of mammary gland development after the proliferative stage of early pregnancy. The first stage is secretory differentiation, which begins in mid-pregnancy; this is the period (also called lactogenesis I) during which "the gland becomes competent to secrete milk" (69). The second stage is secretory activation, which occurs after birth, when milk secretion actually begins (also called lactogenesis II).

Compared with normal-weight women, obese women exhibit many differences in circulating concentrations of hormones and metabolites [see (4) for a review]. Among asymptomatic, eumenorrheic women, obesity is associated with accelerated androgen metabolism but normal plasma steroid values, an "extremely enlarged body steroid pool," and insulin resistance (4). The increase in estrogen values that is associated with obesity is still much less than basal estrogen values in premenopausal women (4). In addition, obese individuals respond differently to standard challenges to hormone secretion. For example, the response of prolactin to insulin hypoglycemia and stimulation by thyrotropin-releasing hormone may be reduced in obese compared with normal-weight individuals (13, 50).

There is some debate in the literature about whether basal prolactin concentrations in obese individuals are higher (13, 49), lower (78), or not different (51) from those of lean controls. The recent work of Kok et al. (49) may provide some explanation for these inconsistent findings. They showed that the daily release of prolactin was more highly correlated with visceral fat mass than body mass index [BMI, weight/(height^2)] among obese women. In contrast, there is no debate about the reduction in the release of prolactin in response to various standard stimuli (hy-

poglycemia, thyrotropin-releasing hormone, etc.) that occurs among obese individuals compared to lean controls (13, 50, 51). The interaction of prolactin with adipose tissue in nonlactating individuals is complex. Prolactin binds to receptors on the adipocyte and affects lipid metabolism by inhibiting lipoprotein lipase and suppressing fatty acid synthetase. It also inhibits the secretion of adiponectin and IL-6 and, depending on the conditions, may increase or stimulate leptin (8). In addition, prolactin is produced by adipose tissue in the breast as well as in subcutaneous and visceral fat depots (8, 114). Thus, prolactin may have an autocrine/paracrine role in both of these tissues (8).

In contrast to the detailed information available in the mouse (37, 69), among women the "hormonal regulation of lactogenesis [I] is poorly understood" (70). At this point, it is clear that prolactin is involved in secretory differentiation in women, although other hormones may also be involved, including progesterone and placental lactogen (69). Prolactin is stimulated by the increasing concentrations of estrogen that also occur at this time (70). In many species, a variety of paracrine factors are also involved in secretory differentiation (69), but their potential role has not been studied in women.

Compared to secretory differentiation, the control of secretory activation after delivery is much better understood in women. Initially, the plasma concentration of progesterone must fall while that of prolactin must remain high. It is still unclear whether the increase in glucocorticoid concentration that occurs around parturition is also a trigger for lactation (69). After the third or fourth day postpartum, milk removal is also required for the continuation of copious milk secretion (72). In women, the infant's demand controls the rate of milk secretion during the remainder of lactation (69). Prolactin "is required for maintenance of all alveolar cell processes associated with milk secretion as well as cell survival" (69)—even though its concentration is poorly correlated with milk volume. This

is because prolactin is secreted in a pulsatile fashion in response to infant suckling and the amount released is a function of both the interval between feeds and the time after delivery (106).

Both estrogen and progesterone values fall rapidly in the first week after parturition (46, 60). Our small study provided no evidence that this pattern of change differed between normal-weight and overweight/obese women (85). However, there were too few subjects in this investigation to determine if values for these two hormones differed between normal-weight and heavier women.

We proposed that the reduction in release of prolactin in response to stimulus that has been observed among obese individuals might extend to the prolactin response to infant suckling (85). If true, this would help to explain why obesity is associated with a shorter duration of breastfeeding. We observed no difference between normal-weight and overweight/obese lactating women in basal prolactin values at 2 or 7 d postpartum. However, the prolactin response to suckling (the difference between basal and postsuckling values of prolactin, adjusted for confounding factors) was significantly lower in the overweight/obese women than in the normal-weight comparison group at both of these times (85). These times bracket the period of secretory activation and coincide with the period during which many overweight/obese women cease breastfeeding.

As is the case for nonlactating women (34), leptin values are correlated with maternal adiposity and BMI among normal-weight lactating women (12, 67, 100). As a result, it is not surprising that leptin values differ between normal-weight and overweight/obese lactating women (85). In addition to being produced in adipose tissue, leptin is produced by the placenta (62). As a result, plasma leptin values fall rapidly following the delivery of the placenta (33, 62, 67, 100). An inverse relationship between leptin and prolactin values has been observed in normal-weight lactating women (12, 67), although the consequences

of this association remain unexplored. Leptin also appears in human milk in amounts that reflect maternal adiposity (41, 108). The leptin in human milk appears to be derived both from maternal plasma as well as from mammary epithelial cells, but its functional significance for maternal health or milk production is unknown (104).

Another adipocytocine, adiponectin, also appears in human milk (10, 59). Its concentration in milk is much lower than its concentration in serum. In serum, adiponectin is positively associated with BMI but, in milk, the opposite is true (59). Whether the adiponectin in human milk is produced locally in the mammary gland or comes from the blood is unknown at present. As was the case for leptin, its functional significance is not understood but merits further study as both of these adipocytokines are regulated by prolactin (3, 8).

In summary, although the possibility exists that maternal obesity affects the development of the mammary glands before and during pregnancy as well as early in the postpartum period, direct evidence for this is quite limited in women. Although plasma hormone values change in response to obesity, the evidence to show that such changes are important for the success of breastfeeding is also quite limited. The finding that the prolactin response to suckling is blunted in obese women is intriguing and provides support for there being a biological basis for an association between maternal obesity and the duration of breastfeeding. However, additional factors are likely to be involved, so further study of these factors is also warranted.

Complications of Pregnancy

Women who are obese at the time of conception have an excess risk of suffering from many complications during pregnancy and at delivery. This association has been known for many years and has been reviewed elsewhere [see, for example, (2, 23, 31, 83)]. Recently it has received additional attention from researchers with access to exceptionally

large datasets covering all deliveries in a large region (101) or country (14). Sebire et al. (101), for example, studied 287,213 women who delivered in the North West Thames Region (which includes London) from 1989 to 1997. Compared to normal-weight women (BMI $20 - < 25$ kg/m^2), those who were obese (BMI ≥ 30 kg/m^2) at the time of conception were significantly more likely to experience gestational diabetes and preeclampsia during pregnancy and were less likely to become anemic during this period (101). These obese women were more likely to experience induction of labor and cesarean section (emergency or elective) as well as infection and hemorrhage after delivery (101). Using national data from Sweden (805,275 pregnancies that occurred from 1992 to 2001), Cedergren (14) found that the risk of these same complications of pregnancy and delivery increased with the severity of obesity. Some similar associations have been observed in large samples of American births (24, 111).

The complications of pregnancy are important because several of them, including cesarean section, are known to interfere with establishing breastfeeding. Cesarean section is now more common than ever (occurring in 27.5% of deliveries in the United States in 2003) (58) and is a more difficult procedure with more postpartum complications in obese than normal-weight women (2). Women who have undergone a cesarean delivery have a longer recovery postpartum than do women who have not had this procedure and also put their babies to the breast later to suckle for the first time (16). Moreover, there is some evidence that undergoing a cesarean section may interfere with ever putting the newborn to the breast (77). The mechanism by which having a cesarean section leads to no breastfeeding or shorter breastfeeding has not been established, although both the delay in initially putting the baby to the breast, which by itself is associated with shorter breastfeeding (99), or a delay in the onset of secretory activation (lactogenesis II) (22, 26) may be contributing factors. However, cesarean section has not uniformly been associated with a delay in lactogenesis II (54, 76).

Condition of the Infant at Birth

The condition of babies born to obese women may also be compromised. For example, Sebire et al. (101) found that the babies of obese women were more likely to be born after 42 weeks of gestation, be stillborn, have a birthweight >90th percentile, be in poor condition at birth, and be admitted to the special care nursery than were babies of normal-weight women. Correspondingly, the babies of obese women were also less likely than were those of normal-weight women to be born before 32 weeks of gestation, to have a birthweight <5th percentile, and to be breastfed. In studies in Denmark and Sweden that also included large samples, researchers have observed that the fetuses and infants of obese women were more likely to die before or after 28 weeks of gestation or in the neonatal period (17, 52, 74). As maternal obesity becomes more severe, so too do the problems experienced by the infants born to these women. Cedergren (14) observed that the risk of preterm birth, stillbirth, and death within 7 d of delivery as well as shoulder dystocia and being large-for-gestational age rose progressively with the severity of maternal obesity.

Babies who are macrosomic (usually defined as having a birthweight >4000 g) or who are large (>90th percentile) for their gestational age are more likely to be in poor condition at birth (e.g., low APGAR score, admitted to the special care nursery, etc.), but they are not less likely to be breastfed (48). It is often routine practice to take blood samples from large-for-gestational age babies to screen them for neonatal hypoglycemia (C.L. Kjolhede & R.J. Schanler 2005, personal communication). Babies whose blood glucose values are too low are then given a dextrose-water solution or infant formula until their blood glucose values normalize. This practice is contrary to expert recommendations (55) and may make it more difficult to establish

breastfeeding (9, 61, 64). Moreover, these babies can also be difficult to feed because of their size and their likelihood of having been delivered somewhat early to make birth easier. A more complete description of the infants of obese women and the challenges they present for breastfeeding is provided elsewhere (83). Although the unique needs of infants of diabetic mothers have been well characterized, the needs of infants born to nondiabetic, obese mothers have not. Inasmuch as the proportion of pregnant women who are obese has increased, it is time for further study of the needs of their babies, with particular attention to improving the success of breastfeeding.

In summary, obese women may experience complications during pregnancy and at delivery that affect their health and lead to difficulties in establishing breastfeeding. Similarly, infants born to these women may themselves have problems in the early neonatal period that make it more difficult to establish breastfeeding. These challenges are above and beyond those that might be related to inadequate development of the mammary glands during pregnancy.

Progress of Lactation

In production and experimental species, the progress of lactation is largely determined by biological factors; social, demographic, and psychological factors are not involved. Among women, the evidence discussed above supports the concept that at least one of the ways that obesity affects lactation in women may be through a biological pathway, the prolactin response to suckling (85). Obese women also may experience other kinds of challenges that act through more proximal biological pathways. In addition to the condition of the mother and baby at birth, these include difficulty in positioning the infant because of their overall body shape and size as well as difficulty with latching on because of the size of their breasts, areolas, and nipples. Infants who are poorly positioned or latched on can create nipple pain for the mother—a stress that

is a disincentive to continue breastfeeding—and may fail to elicit an adequate prolactin response to suckling (16). Such factors are associated with delayed lactogenesis (16, 21), but whether they have a specific role in lactation failure among obese women has not been studied directly. In our recent study, some health care providers who work with lactating women reported that they thought that large breasts were more of a problem than obesity itself (86). Investigators have reported that obesity is not associated with breast size before pregnancy (79), and it has long been known that it is the increase in breast size during pregnancy that predicts milk production (44). Thus, the scientific evidence on this point is quite limited, but what is available does not support the viewpoint that breast size is more important than obesity in determining the progress of breastfeeding.

Among those women who ever gave their infants a chance to suckle, we found that obese white women living in a rural area (38) and obese Hispanic women living in an urban area (53) were more likely to fail to initiate breastfeeding (defined as continuing to breastfeed through the time of hospital discharge) than normal-weight women. This was not true of the black women living in an urban area whom we also studied (53). Among the women in the Danish National Birth Cohort, there was a dose-response relationship between maternal prepregnant BMI and the risk of early cessation of breastfeeding (6). Given the social support for breastfeeding that exists in Denmark, this is compelling evidence that a biological mechanism may underlie this association.

Among both white and Hispanic women we studied (38, 53), many obese women ceased to breastfeed their babies within the first days after delivery. This may be because overweight or obese women experience a delay in the timing of lactogenesis II (22, 39), which may result from the reduced prolactin response to suckling that we have observed in such women (85). These findings are concordant with the possibility that obese women

may have difficulty with positioning their newborns and with proper latching on. The clear implication of these results is that obese women may benefit from extra support for breastfeeding in the immediate postpartum period (85).

Much more information is available about the duration of breastfeeding than its initiation (**Figure 2**). Ferris et al. (27) noted a "tendency" for heavier women not to have continued breastfeeding beyond 10 wk. Rutishauser & Carlin (98) observed that, among primiparous Australian women who had breastfed their infants for at least 14 d, being heavier (BMI $>26\,\text{kg/m}^2$) at this time was a risk factor for early cessation of breastfeeding. Obesity was also associated with shortened breastfeeding in a national sample of Australian women who provided information by recall (25) as well as in a sample of 1601 Italian women (90) who were interviewed within a month of delivery and followed for 12 months. In two other recent studies from Australia, high prepregnant BMI was also associated with reduced duration of breastfeeding (29, 75). Maternal obesity was associated with a shortened duration of breastfeeding (56) or with a lower proportion of women still breastfeeding at 6 and 12 mo postpartum (57) in large samples of American women. From a review of medical records, we evaluated the duration of exclusive and any breastfeeding separately in our studies of women in upstate New York. Both of these outcomes were negatively affected by maternal obesity among white (38) and Hispanic (53) but not black (53) women. The reason for this difference is unknown but may result from differences in commitment to breastfeeding or to differences in the effect of obesity in black compared to white women (53). In national samples (56, 57), black women breastfeed for much shorter periods than white women, but the association of obesity with their duration of breastfeeding has not been reported.

It is possible that maternal prepregnant BMI is an inadequate proxy for maternal adiposity, not only because BMI itself is an im-

perfect measure of adiposity but also because maternal adiposity changes substantially during pregnancy in response to maternal weight gain. Li et al. (56) found that the duration of any breastfeeding was indeed shorter among women who gained more than the amount recommended by the Institute of Medicine for their prepregnant BMI, but this did not modify the negative association of prepregnant BMI with the duration of any breastfeeding. For their analysis, they used a large sample of low-income American women from the pediatric and pregnancy surveillance systems. In our sample of 2783 white women from rural New York State, we also observed an additive relationship between maternal prepregnant BMI and category of gestational weight gain on the initiation of breastfeeding as well as both the duration of exclusive and any breastfeeding (40). In contrast, we found no independent association between gestational weight gain and the risk of early termination of breastfeeding in a much larger sample of women from the Danish National Birth Cohort when prepregnant BMI was also in the regression model (6). This was likely because prepregnant BMI and gestational weight gain were negatively associated in this sample. Taken together, these conflicting findings don't permit us to resolve if the additional adipose tissue that is gained during pregnancy, whether deposited in the breast or elsewhere (as this cannot be determined from the available data), interferes with lactation in some important way. The mechanism by which excessive gestational weight gain could contribute to lactation failure is unknown at present, but it is reasonable to conclude from the timing of this additional weight gain that it might particularly affect the development changes in the mammary gland that occur during pregnancy. Until this possible relationship is more fully understood, it is reasonable to continue to counsel women to gain an appropriate—not an excessive—amount of weight during pregnancy.

Unlike production and experimental species, however, social, demographic, and

psychological factors are also likely to be important determinants of the duration of breastfeeding among women. Inasmuch as they represent possible targets for interventions to improve the success of obese women at breastfeeding, they merit attention. In the United States, overall support for breastfeeding is relatively low and the lack of any or adequate maternity leave are barriers to breastfeeding for all women (80). This creates a culture in which it is acceptable—even expected—for women to feed their babies infant formula instead of human milk. It also makes it socially acceptable for women not to breastfeed at all and, for women who are experiencing difficulties with breastfeeding, to supplement with infant formula or cease breastfeeding entirely. In this cultural context, motivation and self-efficacy for breastfeeding, attitudes toward body size and shape, and social support for breastfeeding—among other related factors—take on additional importance. The important issue here is whether these kinds of social factors affect obese women differentially. Only limited data are available with which to investigate this possibility.

One socially—not biologically—determined aspect of breastfeeding is the choice to do so at all. In nationally representative data collected as part of the National Health and Nutrition Examination Survey (57), only 44.8% of obese women ever breastfed their babies compared with 58.1% of normal-weight women. In a large sample of low-income women drawn from the pediatric and pregnancy surveillance data in the United States (57), the picture was more complicated as there was an interaction between prepregnant BMI and gestational weight gain. In this sample (56), obese women, regardless of their weight gain, were less likely to choose to breastfeed than the reference group, normal-weight women who gained appropriately. In our data, in contrast, obese women were as likely as were normal-weight women to ever put their babies to the breast (38). Thus, the available data suggest that there is both complexity and controversy about whether maternal prepregnant BMI is associated with the choice to breastfeed.

In the studies of obesity as a determinant of the initiation and continuation of breastfeeding cited above, analyses were adjusted for the various social and demographic determinants of breastfeeding. As a result, these studies provide no information about the separate role of these factors with respect to the success or failure of breastfeeding. We have investigated this possibility in more detail in a study of 151 women who were enrolled during pregnancy (39). Obese women planned to breastfeed for a shorter period and were less satisfied with their appearance than were normal-weight women, but other psychosocial characteristics, such as behavioral beliefs and knowledge about breastfeeding, exposure to models for breastfeeding, as well as maternal confidence and support for breastfeeding, did not differ between obese and normal-weight women. Some of these factors attenuated but did not eliminate the relationship between obesity and the duration of breastfeeding.

In summary, it is possible that maternal obesity affects development of the mammary glands before and during pregnancy as well as early in lactation, but evidence to support or refute this proposition is lacking. However, evidence is available to confirm an association between maternal obesity and the initiation as well as the continuation of breastfeeding in nearly all of the population groups that have been studied. This association appears to be derived from biological as well as sociocultural factors that are as yet poorly defined and understood. The deleterious effects of maternal obesity and excessive gestational weight gain on complications of pregnancy and delivery as well as the condition of the infant at birth may also contribute to this association.

CONCLUSIONS

There is clear evidence of an association between maternal obesity and lactation failure in production and experimental species as well as

in women. A number of biological factors have been identified that contribute to this association. In women, sociocultural, demographic, and psychosocial factors may also be important. Given the high rate of obesity among women of reproductive age around the world and the central importance of breastfeeding for infant health, interventions are needed to address this challenge. Many interventions are possible—from the provision of more adequate maternity leave, to assistance to women to help them to conceive at a healthy weight and gain weight appropriately during pregnancy, to additional assistance with breastfeeding in the early postpartum period, among other possibilities.

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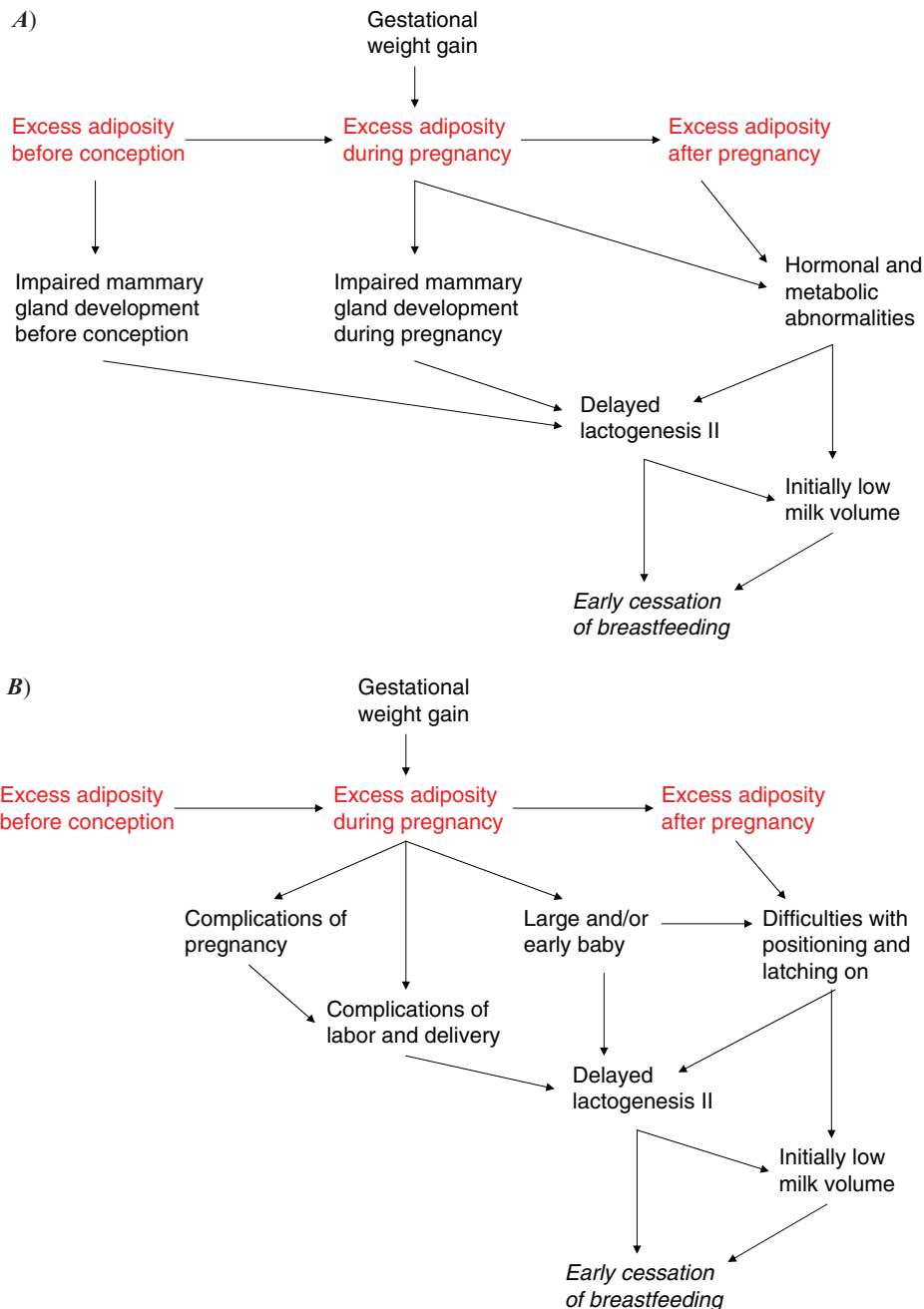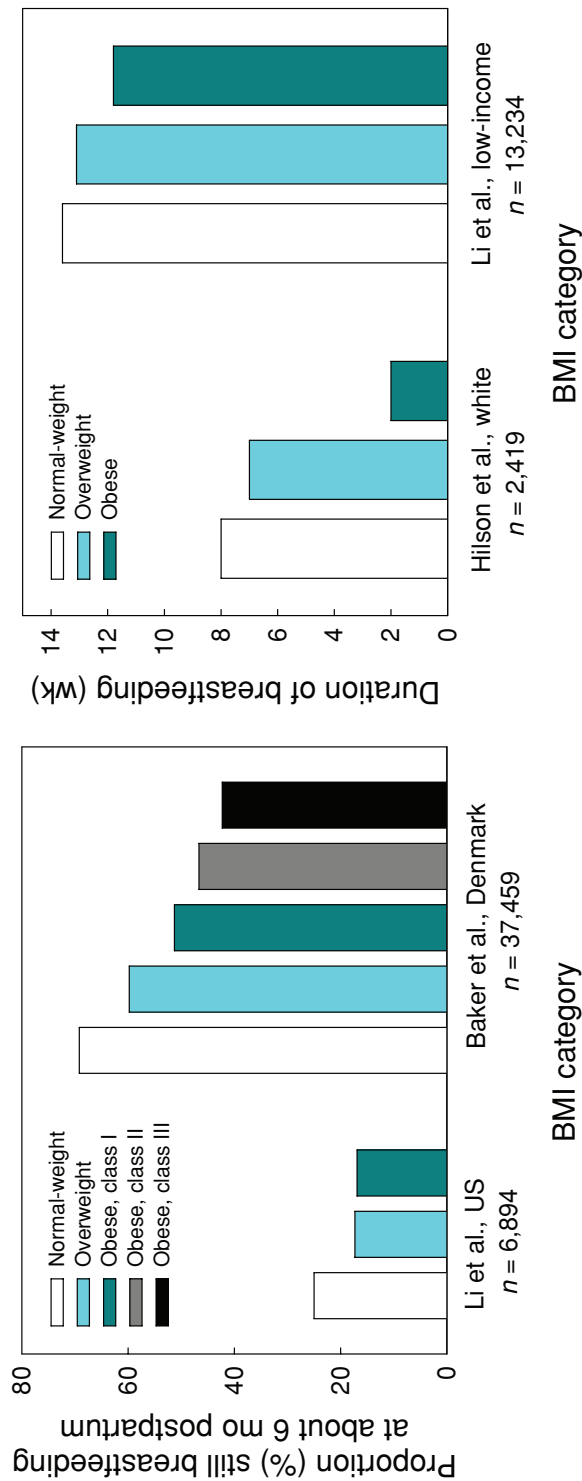
Figure 1

Possible pathways by which maternal obesity could lead to early cessation of breastfeeding.
(*A*) Biological factors related to mammary gland development as well as physiological factors in the
postpartum period. (*B*) Medical factors in pregnancy and mechanical and physiological factors in the
postpartum period. (*C*) Modification of the choice to breastfeed and to continue to breastfeed by
sociodemographic and psychosocial factors as well as mechanical and physiological difficulties with
establishing breastfeeding.

C)

Gestational
weight gain

Excess adiposity
before conception → Excess adiposity
during pregnancy → Excess adiposity
after pregnancy

Sociodemographic and
psychosocial factors

Choice to breastfeed

Sociodemographic and
psychosocial factors

Mechanical and physiological
difficulties with establishing
breastfeeding

*Early cessation
of breastfeeding*

Figure 1

(*Continued*)

Figure 2

Association between maternal prepregnant body mass index (BMI) and the proportion of women still breastfeeding at 6 mo postpartum (*left panel*) and the duration of breastfeeding (*right panel*). The data of Li et al. (57) are from a nationally representative sample of American women, Hilson et al. (40) are from white women living in a rural area, and Li et al. (56) are from low-income women; all used the Institute of Medicine's categories (47) for overweight (26.1–29.0 kg/m²) and obesity (>29 kg/m2). The data of Baker et al. (6) are from a national sample of Danish women and used the World Health Organization criteria (113) for overweight (BMI 25.0–29.9 kg/m²) and obesity (BMI >30 kg/m²).

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Errata

An online log of corrections to *Annual Review of Nutrition* chapters
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