Breast Hypoplasia and Polycystic Ovary Syndrome: Is There a Link?

Renee L. Kam, BPhysio, IBCLC, RLC[a]
Meabh Cullinane, BSc, PhD[b]
Lisa H. Amir, MBBS, MMed, PhD, IBCLC, RLC[c,d]

Background: *Low milk production is a common reason for early breastfeeding cessation. Breast hypoplasia is one possible reason for an inability to make a full milk supply.*

Method: *This article explores endocrinological changes which may link polycystic ovary syndrome (PCOS) and breast hypoplasia.*

Results: *Stein-Leventhal syndrome—named after two American gynecologists—was the original name for PCOS, and minimal mammary gland tissue was included in the syndrome. Common characteristics of PCOS, including insulin resistance, obesity, hyperandrogenism, and low progesterone levels, may be involved in the pathogenesis of breast hypoplasia.*

Conclusion: *Lactation professionals should be aware of breast hypoplasia markers and common features of PCOS to help identify women at risk of low milk production to facilitate timely and optimal support for infant feeding.*

Keywords: polycystic ovarian syndrome; PCOS; insufficient glandular tissue; IGT; breastfeeding; low milk supply

Causes of Low Milk Production

Low milk production (or "not enough milk") is the most common reason women give for ceasing breastfeeding prematurely around the world (Newby & Davies, 2016; Stuebe et al., 2014). Primary insufficient milk supply describes when mothers are inherently unable to make a full milk supply (Galipeau et al., 2017). Secondary insufficient milk supply stems from inadequate lactation management (Galipeau et al., 2017). Perceived insufficient milk supply is when mothers believe they are not making enough breast milk regardless of whether a true insufficient milk supply is present or not (Galipeau et al., 2017). It is not known what proportion of mothers cease breastfeeding due to a perceived primary or secondary insufficient milk supply.

a. Judith Lumley Centre, School of Nursing and Midwifery, La Trobe University, Bundoora, VIC, Australia. renee.kam@latrobe.edu.au

b. Judith Lumley Centre, School of Nursing and Midwifery, La Trobe University, Bundoora, VIC, Australia. M.Cullinane@latrobe.edu.au

c. Judith Lumley Centre, School of Nursing and Midwifery, La Trobe University, Bundoora, VIC, Australia. L.Amir@latrobe.edu.au

d. Breastfeeding Service, Royal Women's Hospital, Parkville, VIC, Australia.

There are various possible reasons for primary insufficient milk supply. Previous breast surgery may impact a woman's milk production capacity, as might conditions (such as diabetes and obesity) which may interfere with hormones involved with breast development and milk synthesis (Amir & Donath, 2007; Marasco et al., 2000; Riddle & Nommsen-Rivers, 2016). It is important for lactation consultants to be aware of possible reasons for primary insufficient milk supply so that they can identify infants potentially at risk of low intake, and support women to maximize their milk supply, discuss strategies and options for supplementation, and help women reach realistic breastfeeding goals.

Breast Hypoplasia

Hypoplasic breasts have deficient lobular development (Winocour & Lemaine, 2013) and is one possible reason for a primary insufficient milk supply (Riddle & Nommsen-Rivers, 2017). Kam, Amir et al. (2021) identified seven studies (all case studies or case series), which evaluated breastfeeding outcomes in a total of 42 women with breast hypoplasia. Most women in this systematic review (40/42) ceased exclusive breastfeeding prior to one month postpartum and the features associated with insufficient milk production due to hypoplasia are shown in Table 1 (Kam, Amir et al., 2021).

Clinical Lactation, 2021, *12*(4), http://dx.doi.org/10.1891/CLINLACT-D-21-00019

TABLE 1. Features Associated With Insufficient Milk Production Due to Breast Hypoplasia (Huggins et al., 2000)
Noticeable breast asymmetry
A wide intra-mammary width (≥3.8 cm or 1.5 inches)
Stretch marks on one or both breasts
Little or no breast growth in pregnancy
A lack of postpartum engorgement
Minimal breast tissue in the inferomedial and inferolateral breast quadrants

The causes of breast hypoplasia are not well understood, but it is thought that hormonal irregularities may impair glandular tissue development during puberty and/or pregnancy (Kirigin Biloš, 2017; Nommsen-Rivers, 2016). According to an international guideline, the diagnosis of polycystic ovary syndrome (PCOS) requires the presence of two of the following three factors: (i) biochemical or clinical evidence of hyperandrogenism (as demonstrated by serological investigations and calculating free testosterone, free androgen index, or calculated bioavailable testosterone or clinical signs such as hirsutism, alopecia, and acne), (ii) ovulatory dysfunction (usually oligoamenorrhea), or (iii) polycystic ovaries on ultrasound (Teede et al., 2018). PCOS affects 8%–13% of reproductive-age women (Teede et al., 2018).

Breastfeeding and PCOS

The original name of PCOS was Stein-Leventhal syndrome and was first described in 1935 by American gynecologists Dr Stein and Dr Leventhal (Azziz & Adashi, 2016; Stein & Leventhal, 1935). Balcar et al. (1972) examined the breasts of 61 women (mean age of 23 years) with Stein–Leventhal syndrome (characterized by polycystic ovaries and varying combinations of irregular menstruation or amenorrhoea, sterility, hirsutism, and obesity) by soft tissue radiography. They compared the breast films to normal breast radiographs from 256 women of various age groups examined for "cancerophobia" (a fear of cancer) as well as 23 women with congenital changes without any hormonal disorder (Balcar et al., 1972). The breasts of 87% (53/61) of women with Stein–Leventhal syndrome had reduced glandular tissue, with 64% (34/53) described as having a "marked" reduction in glandular tissue compared to women in the other two groups (Balcar et al., 1972).

Observational studies have investigated a possible link between women with PCOS and breastfeeding rates with conflicting results (Marasco et al., 2000; Vanky et al., 2008; Vanky et al., 2012). Marasco et al. (2000) presented three case studies of women with PCOS and insufficient milk supply. McGuire and Rowan (2015) reported a woman with PCOS and breast hypoplasia, and low milk supply. A retrospective case analysis reported breastfeeding patterns after gestational metformin use in 164 women with PCOS; 76% (124/164) initiated breastfeeding, 78% (97/124) of whom "succeeded" and 22% (27/124) "failed" (Thatcher & Jackson, 2006 p. 1006). A case-control study by Riddle and Nommsen-Rivers (2016) investigated a link between low milk supply and gestational impaired glucose tolerance and found that women with low milk supply (n = 175) were no more likely to have PCOS compared to women without low milk supply (n = 226). Conversely, another case-control study by Vanky et al. (2008) of 36 women with PCOS and 99 controls found that 75% of the women with PCOS exclusively breastfed at one month postpartum compared to 89% of controls. However, in this study, the controls were not matched for body mass index (BMI) (Vanky et al., 2008). A cross-sectional study of 4,989 women, aged 31–36, from the Australian Longitudinal Study on Women's Health (Lee et al., 2005), found that women reporting PCOS (6.5%) had a lower median duration of breastfeeding compared to women not reporting PCOS (Joham et al., 2016). However, when the researchers adjusted for BMI, there was no difference in the breastfeeding rates between the women reporting PCOS or not (Joham et al., 2016).

In a follow-up of their randomized controlled trial comparing metformin with placebo in pregnant women with PCOS (Vanky et al., 2010), Vanky et al. (2012) compared breastfeeding rates between women with PCOS who reported an increase in their bra size during pregnancy and women with PCOS who did not. Women with PCOS who reported no bra size increase during pregnancy had lower rates of exclusive and partial breastfeeding compared to women whose bra size increased (Vanky et al., 2012). In addition, women whose bra size did not increase had higher BMIs, blood pressure, serum triglycerides, and fasting insulin levels compared to women whose bra size did increase (Vanky et al., 2012).

The reasons why some women with PCOS are thought to struggle to produce sufficient milk relate to endocrine alterations and clinical manifestations associated with the syndrome including insulin resistance, obesity,

hyperandrogenism, and low progesterone levels (Kirigin Biloš, 2017). Not all women with PCOS experience insufficient milk supply; this may reflect the heterogeneity in the clinical criteria and severity of factors involved in the diagnosis of PCOS (Ramezani Tehrani & Amiri, 2019; Teede et al., 2018).

Insulin Resistance

Carbohydrates are broken down to glucose in the bloodstream. The normal function of insulin is to manage blood glucose levels by transferring glucose from the blood into liver and muscle cells, to be used as energy. With insulin resistance, the cells resist the action of insulin and so glucose cannot enter muscle and liver cells easily (Cefalu, 2001). Therefore glucose levels build up in the blood and the pancreas releases more insulin to try to deal with the increased glucose levels (Cefalu, 2001). Insulin resistance has been associated with the development of type 2 diabetes, atherosclerosis, and hypertension (Lebovitz, 2001). It has been estimated that 50% of women with PCOS have insulin resistance (Nawrocka-Rutkowska et al., 2013). Insulin plays important roles in breast development during pregnancy and milk synthesis throughout lactation (Kirigin Biloš, 2017; Nommsen-Rivers, 2016). A rodent study (Berlato & Doppler, 2009) and a human study (Lemay et al., 2013) have shown that the mammary gland is highly sensitive to insulin during lactation, demonstrating that insulin function is an important contributor to timely secretory activation and milk production, and confirming the relationship between insulin resistance and insufficient milk. A pilot randomized controlled trial investigated the feasibility and acceptability of metformin to help overcome insufficient milk supply (Nommsen-Rivers et al., 2019). The researchers measured milk production by mothers, test-weighing their infants on a specialized scale immediately before and after feeding on each breast and weighing all milk expressed over 24 hours (Nommsen-Rivers et al., 2019). Baseline data from this study showed strong evidence that milk production was lower in women with signs of insulin resistance (e.g., the presence of gestational diabetes, PCOS, or abdominal obesity) than those without signs of insulin resistance ($p = .002$) (Nommsen-Rivers et al., 2019).

Obesity

Obesity is a common clinical manifestation of PCOS, with 30%–75% of women with PCOS estimated to have a high BMI (Kataoka et al., 2019). Regardless of the presence of PCOS, women with high BMIs are less likely to initiate or sustain breastfeeding (Turcksin et al., 2014). Insulin resistance is a physiological hallmark of obesity and, as described previously, may be a factor underlying lactation challenges faced by obese women (Nommsen-Rivers, 2016). In addition, animal studies demonstrated that obesity is associated with abnormal mammary gland development (Flint et al., 2005; Zanton & Heinrichs, 2005). Therefore, some women with PCOS may be at an increased risk for insufficient milk production due to their excess weight.

Hyperandrogenism

Hyperandrogenism is a key diagnostic feature of PCOS affecting between 60% and 100% of women with the condition (Teede et al., 2018). In the past, androgens such as testosterone (in combination with estrogens) were used to suppress lactation (De Gezelle et al., 1979; Kochenour, 1980). Despite high circulating levels of estrogen in women with PCOS, hyperandrogenism may down-regulate estrogen receptors (Kirigin Biloš, 2017) and result in poorer breast development, especially during puberty when estrogen (and progesterone) are the main influences on breast development (Macias & Hinck, 2012). Studies on rodents have demonstrated an inhibitory effect of androgens on mammary gland development during puberty (Walters et al., 2016).

In women, studies have revealed conflicting results regarding a link between androgen levels and breastfeeding outcomes. Vanky et al. (2008) demonstrated that third-trimester pre-androgen dehydroepiandrosterone-sulphate (DHEA) levels were negatively correlated with breastfeeding rates at 1 and 3 months postpartum. However, another study by Vanky et al. (2012) showed that maternal androgen levels during late pregnancy were *not* associated with breast size increase during pregnancy or breastfeeding duration. Also, a prospective cohort study by Carlsen et al. (2010) evaluated an association between pregnancy maternal androgen levels (at 25 weeks gestation) and breastfeeding at 6 weeks, 3 months, and 6 months postpartum in two groups of women. One group included a random sample of pregnant women ($n = 63$) and the other group was comprised of women at increased risk of giving birth to a small-for-gestational age newborn ($n = 118$) (Carlsen et al., 2010). After adjusting for maternal age, education, and smoking, breastfeeding was negatively associated with the free testosterone index (calculated as total testosterone/sex hormone binding globulin × 100) at 3 and 6 months postpartum in the healthy sample, and with dehydroepiandrosterone levels at 6 weeks and 3 months postpartum in the small-for-gestational age group (Carlsen et al., 2010).

Low Progesterone Levels

The anovulatory status of some women with PCOS results in overall lower progesterone (Teede et al., 2018). Low levels of progesterone during pregnancy in women with PCOS could interfere with gestational breast alveolar growth (Marasco et al., 2000). There may be a minimum level of progesterone required to keep a pregnancy viable that is lower than what is needed to trigger the formation and development of the alveoli during pregnancy (Cassar-Uhl, 2014).

Consultation With Women With Low Milk Supply

Taking a history is an important aspect of a breastfeeding consultation. It identifies what the patient's concerns are and possible contributing factors while assisting to build rapport (Williams, 2017). Aspects of taking a good history include encouraging patient narratives, asking questions, active listening, using empathy, and understanding the patient's psychosocial context (Williams, 2017). Patient narratives can be encouraged by a friendly demeanor, verbal encouragement (e.g., "Can you tell me more about ..."), silent pauses, and eye contact when appropriate. The questions asked at the start are typically open-ended, although close-ended questions can be useful to help identify specific factors not elicited by the open-ended questions or if a topic needs to be explored more thoroughly (Williams, 2017). Active listening by picking up on aspects of what the patient says (e.g., "Why did you ...?") and empathy ("I can understand how that would have been very upsetting...") are important aspects of history taking that help patients feel supported (Williams, 2017). Signposting during an interview indicates the clinician's plan (e.g., "I'd like to ask some more questions before letting you know what I think is going on here") and is helpful to minimize patient uncertainty, allowing them to concentrate and contribute more effectively (Williams, 2017). Finally, understanding the psychosocial context of the patient's breastfeeding concerns is important because, often, the contributing factors (or possible aid) to breastfeeding problems lie within this context (Williams, 2017).

Taking a good history also assists with implementing shared decision-making by providing clinicians with insight into the patient's values and preferences. Shared decision-making describes a form of nondirective counselling where a clinician and patient come together as experts in their own right (Haiek et al., 2021; Légaré et al., 2011). The end goal of shared decision-making is a patient making informed decisions that are consistent with their personal values and acted upon (Haiek et al., 2021).

In addition to PCOS and associated conditions, there are various other factors that may be involved with the development of breast hypoplasia. Table 2 is a guide for taking a history to help identify possible risk factors for a primary insufficient milk supply due to breast hypoplasia.

The management of low milk supply depends on the likely causes and requires "timely, empathetic, and effective support to the mother struggling with her milk production" (Riddle & Nommsen-Rivers, 2017, p. 254). Guidelines are available for health professionals (Brodribb, 2018; Royal Women's Hospital 2020), and families may find Marasco and West's book for a general audience useful (Marasco & West, 2020).

TABLE 2. Questions to Ask to Identify Risk Factors for Primary Insufficient Milk Supply Due to Breast Hypoplasia

Question	Rationale
1. Do you have any medical or hormonal conditions?	
Prompts:	
• Do you have polycystic ovary syndrome (PCOS)?	The various endocrinological alterations associated with PCOS may impact breast development (Kirigin Biloš, 2017).
• Do you have type 2 diabetes?	Insulin is an important hormone associated with breast development during pregnancy (Kirigin Biloš, 2017; Nommsen-Rivers, 2016). Therefore, insulin resistance can hamper breast development during this period (Kirigin Biloš, 2017; Nommsen-Rivers, 2016).

(*Continued*)

TABLE 2. Questions to Ask to Identify Risk Factors for Primary Insufficient Milk Supply Due to Breast Hypoplasia (*Continued*)

Question	Rationale
• Did you have gestational diabetes?	As above.
• Do you have type 1 diabetes?	Prolactin and human placental lactogen can be lower in pregnancy in women with type 1 diabetes and this may affect breast tissue development (Botta et al., 1984).
• Do you have any problems with your thyroid gland?	Mice models suggest a link between hypothyroidism and altered mammary gland morphological development (Hovey et al., 2002; Vonderhaar & Greco, 1979).
2. Has your weight changed from puberty to now?	
Prompts:	
• Would you describe yourself as being overweight between 8 and 16 years of age?	A high body mass index (BMI) is associated with altered breast development due to insulin resistance (Flint et al., 2005; Nommsen-Rivers, 2016; Sejrsen et al., 2000; Zanton & Heinrichs, 2005).
• Would you describe yourself as being overweight just prior to pregnancy?	As above.
3. Have you ever had any surgery or injury to your breasts? or chest	Women with breast hypoplasia may have had cosmetic breast surgery to correct the deformity (Knackstedt et al., 2020; Marasco & West, 2020, p. 140). If any chest surgery cuts through budding glandular tissue, this may result in breast hypoplasia (Goyal & Mansel, 2003). Chest trauma may result in altered breast development, leading to breast hypoplasia (Arabi et al., 2019; Foley et al., 2008; Sadove & van Aalst, 2005).
4. Did you have any difficulty getting pregnant?	If the cause of infertility is an underlying hormonal problem, it is possible for breast development to be impacted (Marasco & West, 2020, p. 158).
5. Are your periods usually regular?	
Prompts:	
• Do you have a history of an eating disorder that delayed or stopped you from getting your period?	This may impact hormones involved in breast development (Marasco & West, 2020, p. 136).
• Do you have a history of extreme athleticism that delayed or stopped you from getting your period?	This may impact breast development in the same way as indicated above.
• Did you ever use hormonal birth control between 8 and 16 years of age for reasons other than to prevent pregnancy?	A "yes" answer to this question may uncover additional avenues to enquire about.
• Do you have a close biological female relative with low milk supply?	Breast hypoplasia may have a genetic link in some cases and so it is worthwhile asking about family history (Arbour & Kessler, 2013; Vaccari et al., 2014).

(*Continued*)

TABLE 2. Questions to Ask to Identify Risk Factors for Primary Insufficient Milk Supply due to Breast Hypoplasia (*Continued*)

Question	Rationale
6. Other questions to ask regarding less common factors	
• Have you had to have radiation to your breast?	Radiation to the breast (especially prior to complete development) may result in breast hypoplasia (Skalkeas et al., 1972).
• Have you experienced a breast infection?	Scarring post a breast infection may result in skin restriction and breast hypoplasia (Eser et al., 2015).
• Have you lived in agricultural towns where you may have been exposed to high levels of hormone-disrupting chemicals when your mother was pregnant or between the ages of 8 and 16 years?	Endocrine-disrupting chemical exposure during key stages of breast development is a possible risk factor for altered morphological mammary gland development (Kam, Ingman et al., 2021).
• Do you have a history of congenital syndromes involving the chest wall?	A history of Poland, Jeune, or ulnar-mammary syndrome or chest wall deformities (e.g., pectus excavatum and pectus carinatum) can result in breast hypoplasia (Bamshad et al., 1996; Winocour & Lemaine, 2013).
• Do you have a history of a breast hemangioma?	A history of a breast hemangioma may impact breast development and result in breast hypoplasia (Theiler et al., 2016; Velter et al., 2017).
• Do you have a history of congenital adrenal hyperplasia?	Untreated (or a delay in treatment for) congenital adrenal hyperplasia can impair breast development and result in breast hypoplasia (Kulshreshtha et al., 2012; Schwarz et al., 1995).

Conclusion

When lactation professionals identify women at risk of primary insufficient milk supply due to breast hypoplasia, they can provide women with timely and optimal support in the critical early postpartum period. In addition, lactation professionals being able to recognize factors involved in the development of breast hypoplasia can result in a timely diagnosis and therefore implementation of appropriate medical investigation, management strategies, and psychological support.

References

Amir, L. H., & Donath, S. (2007). A systematic review of maternal obesity and breastfeeding intention, initiation and duration. *BMC Pregnancy & Childbirth*, *7*, 9. https://doi.org/10.1186/1471-2393-7-9

Arabi, Z., Md Monoto, E. M., & Bojeng, A. (2019). Impact of childhood burn injuries on breastfeeding: A case report. *International Breastfeeding Journal*, *14*, 17. https://doi.org/10.1186/s13006-019-0210-4

Arbour, M. W., & Kessler, J. L. (2013). Mammary hypoplasia: Not every breast can produce sufficient milk. *Journal of Midwifery & Women's Health*, *58*(4), 457–461. https://doi.org/10.1111/jmwh.12070

Azziz, R., & Adashi, E. Y. (2016). Stein and Leventhal: 80 years on. *American Journal of Obstetrics & Gynecology*, *214*(2), 247.e1–247.e11. https://doi.org/10.1016/j.ajog.2015.12.013

Balcar, V., Silinkova-Malkova, E., & Matys, Z. (1972). Soft tissue radiography of the female breast and pelvic pneumoperitoneum in the Stein-Leventhal syndrome. *Acta Radiologica: Diagnosis*, *12*(3), 353–362. https://doi.org/10.1177/028418517201200310

Bamshad, M., Root, S., & Carey, J. C. (1996). Clinical analysis of a large kindred with the Pallister ulnar-mammary syndrome. *American Journal of Medical Genetics*, *65*(4), 325–331. https://doi.org/10.1002/(SICI)1096-8628(19961111)65:4<325::AID-AJMG15>3.0.CO;2-W

Berlato, C., & Doppler, W. (2009). Selective response to insulin versus insulin-like growth factor-I and -II and up-regulation of insulin receptor splice variant B in the differentiated mouse mammary epithelium. *Endocrinology*, *150*(6), 2924–2933. https://doi.org/10.1210/en.2008-0668

Botta, R. M., Donatelli, M., Bucalo, M. L., Bellomonte, M. L., & Bompiani, G. D. (1984). Placental lactogen, progesterone, total estriol and prolactin plasma levels in pregnant women with insulin-dependent diabetes mellitus. *European Journal of Obstetrics & Gynecolology and Reproductie Biology*, *16*(6), 393–401. https://doi.org/10.1016/0028-2243(84)90020-0

Brodribb, W. (2018). ABM clinical protocol #9: Use of galactogogues in initiating or augmenting maternal milk production, second revision 2018. *Breastfeeding Medicine*, *13*(5), 307–314. https://doi.org/10.1089/bfm.2018.29092.wjb

Carlsen, S. M., Jacobsen, G., & Vanky, E. (2010). Mid-pregnancy androgen levels are negatively associated with breastfeeding. *Acta Obstetrica et Gynecologica Scandinavica*, *89*(1), 87–94. https://doi.org/10.3109/00016340903318006

Cassar-Uhl, D. (2014). *Finding Sufficiency: Breastfeeding with Insufficient Glandular Tissue*. Praeclarus Press.

Cefalu, W. T. (2001). Insulin resistance: Cellular and clinical concepts. *Experimental Biology and Medicine*, *226*(1), 13–26. https://doi.org/10.1177/153537020122600103

De Gezelle, H., Dhont, M., Thiery, M., & Parewyck, W. (1979). Puerperal lactation suppression and prolactin. *Acta Obstetrica et Gynecologica Scandinavica*, *58*(5), 469–472. https://doi.org/10.3109/00016347909154069

Eser, C., Temiz, G., Dulgar, A. G., Gencel, E., & Yavuz, M. (2015). Reconstruction of acquired breast hypoplasia by subcutaneous scar releasing and repeated fat grafting combination. *Plastic and Reconstructive Surgery*, *3*(6), e408. https://doi.org/10.1097/GOX.0000000000000385

Flint, D. J., Travers, M. T., Barber, M. C., Binart, N., & Kelly, P. A. (2005). Diet-induced obesity impairs mammary development and lactogenesis in murine mammary gland. *American Journal of Physiology-Endocrinology and Metabolism*, *288*(6), E1179–E1187. https://doi.org/10.1152/ajpendo.00433.2004

Foley, P., Jeeves, A., Davey, R. B., & Sparnon, A. L. (2008). Breast burns are not benign: Long-term outcomes of burns to the breast in pre-pubertal girls. *Burns*, *34*(3), 412–417. https://doi.org/10.1016/j.burns.2007.05.001

Galipeau, R., Dumas, L., & Lepage, M. (2017). Perception of not having enough milk and actual milk production of first-time breastfeeding mothers: is there a difference? *Breastfeeding Medicine*, *12*(4), 210–217.

Goyal, A., & Mansel, R. E. (2003). Iatrogenic injury to the breast bud causing breast hypoplasia. *Postgraduate Medical Journal*, *79*(930), 235. https://doi.org/10.1136/pmj.79.930.235

Haiek, L. N., LeDrew, M., Charette, C., & Bartick, M. (2021). Shared decision-making for infant feeding and care during the coronavirus disease 2019 pandemic. *Maternal and Child Nutrition*, *17*(2), e13129. https://doi.org/10.1111/mcn.13129

Hovey, R. C., Trott, J. F., & Vonderhaar, B. K. (2002). Establishing a framework for the functional mammary gland: From endocrinology to morphology. *Journal of Mammary Gland Biology and Neoplasia*, *7*(1), 17–38. https://doi.org/10.1023/A:1015766322258

Huggins, K. E., Petok, E. S., & Mireles, O. (2000). Markers of lactation insufficiency: A study of 34 mothers. *Current Issues in Clinical Lactation*, *1*, 25–35.

Joham, A. E., Nanayakkara, N., Ranasinha, S., Zoungas, S., Boyle, J., Harrison, C. L., Forder, P., Loxton, D., Vanky, E., & Teede, H. J. (2016). Obesity, polycystic ovary syndrome and breastfeeding: An observational study. *Acta Obstetrica et Gynecologica Scandinavica*, *95*(4), 458–466. https://doi.org/10.1111/aogs.12850

Kam, R. L., Amir, L. H., & Cullinane, M. (2021). Is there an association between breast hypoplasia and breastfeeding outcomes? A systematic review. *Breastfeeding Medicine*, *16*(8), 594–602. https://doi.org/10.1089/bfm.2021.0032

Kam, R. L., Ingman, W. V., Bernhardt, S. M., & Amir, L. H. (2021). Modern, exogenous exposures associated with altered mammary gland development: A systematic review. *Early Human Development*, *156*, 105342. https://doi.org/10.1016/j.earlhumdev.2021.105342

Kataoka, J., Larsson, I., Bjorkman, S., Eliasson, B., Schmidt, J., & Stener-Victorin, E. (2019). Prevalence of polycystic ovary syndrome in women with severe obesity - effects of a structured weight loss programme. *Clinical Endocrinology*, *91*(6), 750–758. https://doi.org/10.1111/cen.14098

Kirigin Biloš, L. S. (2017). Polycystic ovarian syndrome and low milk supply: Is insulin resistance the missing link? *Endrocrine Oncology and Metabolism*, *3*(2), 49–55.

Knackstedt, R., Deross, A., & Moreira, A. (2020). Congenital breast deformities: Anatomical basis and surgical approaches for optimal aesthetic outcomes. *The Breast Journal*, *26*(7), 1302–1307. https://doi.org/10.1111/tbj.13798

Kochenour, N. K. (1980). Lactation suppression. *Clinical Obstetrics and Gynecology*, *23*(4), 1045–1059. https://doi.org/10.1097/00003081-198012000-00008

Kulshreshtha, B., Eunice, M., & Ammini, A. C. (2012). Pubertal development among girls with classical congenital adrenal hyperplasia initiated on treatment at different ages. *Indian Journal of Endocrinology and Metabolism*, *16*(4), 599–603. https://doi.org/10.4103/2230-8210.98018

Lebovitz, H. E. (2001). Insulin resistance: definition and consequences. *Experimental and Clinical Endocrinology & Diabetes*, *109*(Suppl. 2), S135–148. https://doi.org/10.1055/s-2001-18576

Lee, C., Dobson, A. J., Brown, W. J., Bryson, L., Byles, J., Warner-Smith, P., & Young, A. F. (2005). Cohort profile: The Australian longitudinal study on women's health. *Internataional Journal of Epidemiology*, *34*(5), 987–991. https://doi.org/10.1093/ije/dyi098

Légaré, F., Stacey, D., Pouliot, S., Gauvin, F., Desroches, S., Kryworuchko, J., Dunn, S., Elwyn, Frosch., D, Gagnon., M, Harrison., B, M., Pluye, P., & Graham, I. D. (2011). Interprofessionalism and shared decision-making in primary care: A stepwise approach towards a new model. *Journal of Interprofessional Care*, *25*(1), 18–25. https://doi.org/10.3109/13561820.2010.490502

Lemay, D. G., Ballard, O. A., Hughes, M. A., Morrow, A. L., Horseman, N. D., & Nommsen-Rivers, L. A. (2013). RNA sequencing of the human milk fat layer transcriptome reveals distinct gene expression profiles at three stages of lactation. *PLoS One*, *8*(7), e67531. https://doi.org/10.1371/journal.pone.0067531

Macias, H., & Hinck, L. (2012). Mammary gland development. *Wiley Interdisciplinary Reviews. Developmental Biology*, *1*(4), 533–557. https://doi.org/10.1002/wdev.35

Marasco, L., Marmet, C., & Shell, E. (2000). Polycystic ovary syndrome: A connection to insufficient milk supply? *Journal of Human Lactation*, *16*(2), 143–148.

Marasco, L., & West, D. (2020). *Making more milk: The breastfeeding guide to increasing your milk production* (2nd ed.). McGraw Hill.

McGuire, E., & Rowan, M. K. (2015). PCOS, breast hypoplasia and low milk supply: A case study. *Breastfeeding Review*, *23*(3), 29–32.

Nawrocka-Rutkowska, J., Ciecwiez, S., Marciniak, A., Brodowska, A., Wisniewska, B., Kotlega, D., & Starczewski, A. (2013). Insulin resistance assessment in patients with polycystic ovary syndrome using different diagnostic criteria–impact of metformin treatment. *Annals of Agricultural and Environmental Medicine*, *20*(3), 528–532.

Newby, R. M., & Davies, P. S. (2016). Why do women stop breast-feeding? Results from a contemporary prospective study in a cohort of Australian women. *European Journal of Clinical Nutrition*, *70*(12), 1428–1432. https://doi.org/10.1038/ejcn.2016.157

Nommsen-Rivers, L. (2016). Does insulin explain the relation between maternal obesity and poor lactation outcomes? An overview of the literature. *Advances in Nutrition*, *7*(2), 407–414. https://doi.org/10.3945/an.115.011007

Nommsen-Rivers, L., Thompson, A., Riddle, S., Ward, L., Wagner, E., & King, E. (2019). Feasibility and acceptability of metformin to augment low milk supply: A pilot randomized controlled trial. *Journal of Human Lactation*, *35*(2), 261–271. https://doi.org/10.1177/0890334418819465

Ramezani Tehrani, F., & Amiri, M. (2019). Polycystic ovary syndrome in adolescents: Challenges in diagnosis and treatment. *Internataionl Journal of Endocrinology and Metabolism*, *17*(3), e91554.

Riddle, S. W., & Nommsen-Rivers, L. A. (2016). A case control study of diabetes during pregnancy and low milk supply. *Breastfeeding Medicine*, *11*(2), 80–85. https://doi.org/10.1089/bfm.2015.0120

Riddle, S. W., & Nommsen-Rivers, L. A. (2017). Low milk supply and the pediatrician. *Current Opinion in Pediatrics*, *29*(2), 249–256. https://doi.org/10.1097/MOP.0000000000000468

Royal Women's Hospital. (2020, July 29). *Infant feeding - Management of low breast milk supply*. https://thewomens.r.worldssl.net/images/uploads/downloadable-records/clinical-guidelines/infant-feeding-management-of-low-breast-milk-supply_280720.pdf

Sadove, A. M., & van Aalst, J. A. (2005). Congenital and acquired pediatric breast anomalies: A review of 20 years' experience. *Plastic and Reconstructive Surgery*, *115*(4), 1039–1050. https://doi.org/10.1097/01.PRS.0000154214.99641.72

Schwarz, H. P., Jocham, A., & Kuhnle, U. (1995). Rapid occurrence of thelarche and menarche induced by hydrocortisone in a teenage girl with previously untreated congenital adrenal hyperplasia. *European Journal of Pediatrics*, *154*(8), 617–620. https://doi.org/10.1007/BF02079062

Sejrsen, K., Purup, S., Vestergaard, M., & Foldager, J. (2000). High body weight gain and reduced bovine mammary growth: Physiological basis and implications for milk yield potential. *Domestic Animal Endocrinology*, *19*(2), 93–104. https://doi.org/10.1016/S0739-7240(00)00070-9

Skalkeas, G., Gogas, J., & Pavlatos, F. (1972). Mammary hypoplasia following irradiation to an infant breast. Case report. *Acta Chirurgiae Plasticae*, *14*(4), 240–243.

Stein, I. F., & Leventhal, M. L. (1935). Amenorrhea associated with bilateral polycystic ovaries. *American Journal of Obstetrics & Gynecology*, *29*, 181–191. https://doi.org/10.1016/S0002-9378(15)30642-6

Stuebe, A. M., Horton, B. J., Chetwynd, E., Grewen, K. G., & Meltzer-Brody, S. (2014). Prevalence and risk factors for early, undesired weaning attributed to lactation dysfunction. *Journal of Women's Health*, *23*(5), 404–412. https://doi.org/10.1089/jwh.2013.4506

Teede, H. J., Misso, M. L., Costello, M. F., Dokras, A., Laven, J., Moran, L., Piltonen, T., & Norman, R. J. (2018). Recommendations from the international evidence-based guideline for the assessment and management of polycystic ovary syndrome. *Fertility and Sterility*, *110*(3), 364–379. https://doi.org/10.1016/j.fertnstert.2018.05.004

Thatcher, S. S., & Jackson, E. M. (2006). Pregnancy outcome in infertile patients with polycystic ovary syndrome who were treated with metformin. *Fertility and Sterility*, *85*(4), 1002–1009. https://doi.org/10.1016/j.fertnstert.2005.09.047

Theiler, M., Hoffman, W. Y., & Frieden, I. J. (2016). Breast hypoplasia as a complication of an untreated infantile hemangioma. *Pediatric Dermatology*, *33*(2), e129–e130. https://doi.org/10.1111/pde.12742

Turcksin, R., Bel, S., Galjaard, S., & Devlieger, R. (2014). Maternal obesity and breastfeeding intention, initiation, intensity and duration: A systematic review. *Maternal and Child Nutrition*, *10*(2), 166–183. https://doi.org/10.1111/j.1740-8709.2012.00439.x

Vaccari, C. M., Romanini, M. V., Musante, I., Tassano, E., Gimelli, S., Divizia, M. T., Torre, M., Morovic, C. G., Lerone, M., Ravazzolo, R., & Puliti, A. (2014). De novo deletion of chromosome 11q12.3 in monozygotic twins affected by Poland Syndrome. *BMC Medical Genetics*, *15*, 63.

Vanky, E., Isaksen, H., Moen, M., & Carlsen, S. (2008). Breastfeeding in polycystic ovary syndrome. *Acta Obstetrica et Gynecologica Scandinavica*, *87*(5), 531–535. https://doi.org/10.1080/00016340802007676

Vanky, E., Nordskar, J. J., Leithe, H., Hjorth-Hansen, A. K., Martinussen, M., & Carlsen, S. M. (2012). Breast size increment during pregnancy and breastfeeding in mothers with polycystic ovary syndrome: A follow-up study of a randomised controlled trial on metformin versus placebo. *BJOG*, *119*(11), 1403–1409. https://doi.org/10.1111/j.1471-0528.2012.03449.x

Vanky, E., Stridsklev, S., Heimstad, R., Romundstad, P., Skogoy, K., Kleggetveit, O., Hjelle, S., von, Brandis., P, Eikeland., T, Flo., K, Berg., F, K., Bunford, G., Lund, A., Bjerke, C., Almas, I., Berg, A. H., Danielson, A., Lahmami, G., & Carlsen, S. M. (2010). Metformin versus placebo from first trimester to delivery in

polycystic ovary syndrome: A randomized, controlled multicenter study. *Journal of Clinical Endocrinology and Metabolism*, *95*(12), E448–E455. https://doi.org/10.1210/jc.2010-0853

Velter, C., Gronier, C., & Lipsker, D. (2017). Small infantile hemangioma and breast hypoplasia. *Journal of the European Academy of Dermatology and Venereology*, *31*(8), e355–e356. https://doi.org/10.1111/jdv.14158

Vonderhaar, B. K., & Greco, A. E. (1979). Lobulo-alveolar development of mouse mammary glands is regulated by thyroid hormones. *Endocrinology*, *104*(2), 409–418. https://doi.org/10.1210/endo-104-2-409

Walters, K. A., Simanainen, U., & Gibson, D. A. (2016). Androgen action in female reproductive physiology. *Current Opinion in Endocrinology, Diabetes and Obesity*, *23*(3), 291–296. https://doi.org/10.1097/MED.0000000000000246

Williams, D. (2017). The clinical history. *Medical Journal of Australia*, *207*(11), 473–475. https://doi.org/10.5694/mja16.00493

Winocour, S., & Lemaine, V. (2013). Hypoplastic breast anomalies in the female adolescent breast. *Seminars in Plastic Surgery*, *27*, 42–48. https://doi.org/10.1055/s-0033-1343996

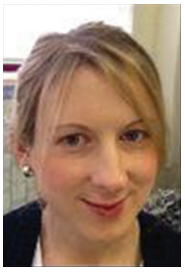
Zanton, G. I., & Heinrichs, A. J. (2005). Meta-analysis to assess effect of prepubertal average daily gain of Holstein heifers on first-lactation production. *Journal of Dairy Science*, *88*(11), 3860–3867. https://doi.org/10.3168/jds.S0022-0302(05)73071-X

Disclosure. The authors have no relevant financial interest or affiliations with any commercial interests related to the subjects discussed within this article.

Funding. The author(s) received no specific grant or financial support for the research, authorship, and/or publication of this article.

Renee L. Kam, BPhysio, IBCLC, qualified as a physiotherapist in 2000 and has experience in the areas of women's health, pediatrics, and musculoskeletal physiotherapy. She became an IBCLC in 2012 and has worked in private practice ever since. Renee is currently undertaking a PhD exploring breast hypoplasia as a reason for insufficient milk production. Her supervisors for this degree are Professor Lisa Amir and Dr Meabh Cullinane.

Lisa H. Amir, MBBS, MMed, PhD, IBCLC, FABM, FILCA, is a general practitioner and lactation consultant. She works in breastfeeding medicine at The Royal Women's Hospital. She is a Principal Research Fellow at the Judith Lumley Centre, La Trobe University, Australia. She is the author of over 120 peer-reviewed articles and the Editor-in-Chief of *International Breastfeeding Journal.*



Meabh Cullinane, BSc, PhD, is involved in maternal and infant health research at the Judith Lumley Centre, La Trobe University. She is currently coordinating a randomized trial investigating whether caseload midwifery reduces preterm birth among women considered socially vulnerable. She has worked, and continues to work, with Professor Amir on a number of breastfeeding projects, and is currently exploring general practitioners' experiences of treating breastfeeding conditions including mastitis.