Nursing Science 护理学, 2024, 13(2), 141-148
Published Online February 2024 in Hans. https://www.hanspub.org/journal/ns
https://doi.org/10.12677/ns.2024.132021

Hans汉斯

催乳素与产妇泌乳关系的研究进展

李星星[1]，周梦佳[2]，刘　李[2]，肖　归[2]，张婷婷[3]，张　瑜[1]，秦春香[3*]，陈正英[1*]

[1]吉首大学医学院，湖南 湘西
[2]中南大学湘雅医学院，湖南 长沙
[3]中南大学湘雅三医院，湖南 长沙

收稿日期：2023年12月27日；录用日期：2024年1月27日；发布日期：2024年2月2日

摘　要

泌乳是乳腺分泌乳汁的过程，其过程与内分泌系统有错综复杂的联系。催乳素是与泌乳有关的主要激素之一，了解其在泌乳过程中的激素变化对泌乳障碍的妇女具有临床应用价值；因此，本文对催乳素与泌乳的启动、维持及泌乳量之间的关系进行综述，为进一步确定开展相关研究提供参考依据。

关键词

泌乳，催乳素，泌乳启动，泌乳量

Research Progress on the Relationship between Prolactin and Maternal Lactation

Xingxing Li[1], Mengjia Zhou[2], Li Liu[2], Gui Xiao[2], Tingting Zhang[3], Yu Zhang[1], Chunxiang Qin[3*], Zhengying Chen[1*]

[1]School of Medicine, Jishou University, Xiangxi Hunan
[2]Xiangya School of Medicine, Central South University, Changsha Hunan
[3]The Third Xiangya Hospital, Central South University, Changsha Hunan

Received: Dec. 27th, 2023; accepted: Jan. 27th, 2024; published: Feb. 2nd, 2024

Abstract

Lactation is a process in which the mammary gland secretes milk, which is intricately related to the endocrine system. Prolactin is one of the main hormones related to lactation. Understanding its hormonal changes during lactation is of clinical value for women with lactation disorder. Therefore, this article reviewed the relationship between prolactin and initiation, maintenance

*通讯作者。

文章引用: 李星星, 周梦佳, 刘李, 肖归, 张婷婷, 张瑜, 秦春香, 陈正英. 催乳素与产妇泌乳关系的研究进展[J]. 护理学, 2024, 13(2): 141-148. DOI: 10.12677/ns.2024.132021

and milk production, and provided a reference for further research.

Keywords

Lactation, Prolactin, Initiation of Lactation, Milk Yield

1. 引言

母乳作为婴儿最佳喂养方式已成为共识，纯母乳喂养能满足6个月内婴儿全部能量及营养素的需要，母乳喂养对母婴健康具有诸多益处[1] [2]。但我国的母乳喂养总体水平距《母乳喂养促进行动计划(2021~2025年)》[3]提出的50%目标还有一定距离。母乳供应不足是早期停止母乳喂养的一个常见原因，泌乳的激素调节很大程度可以影响泌乳的启动以及维持，其中催乳素是与泌乳有关的主要激素之一，关于催乳素与泌乳之间的关系的研究以国外为主，且研究方法与结果存在较大不一致，因此，本文对催乳素与泌乳的启动、维持及泌乳量之间的关系进行综述，为进一步确定开展相关研究提供参考依据。

2. 泌乳的概述

2.1. 泌乳启动机制

乳腺是泌乳的载体，发挥着分泌和储存乳汁的功能，其中乳腺导管负责运输和储存乳汁，成熟的乳腺导管由外层的肌上皮细胞和内层的管腔上皮细胞组成，肌上皮细胞末端被基底膜包裹，并嵌入基质中，其未发育的末端增殖并形成复杂的多层上皮结构，被称为末端芽[4]；分泌分化发生在妊娠中晚期，此期管腔上皮细胞会分化成产奶的分泌细胞，具有合成和分泌特定的乳成分的能力[5] [6]，从而产生乳汁并将其储存在腺泡腔中。这一过程很大程度上是由雌激素和孕激素的循环水平驱动的，这些雌激素和黄体酮不仅刺激乳腺导管发育，而且还抑制催乳素在妊娠期间对乳汁分泌的作用[7]。分泌激活发生在分娩后，胎盘的娩出导致黄体酮、雌激素、人胎盘生乳素水平迅速下降，并伴有高水平的循环催乳素，触发乳汁大量分泌[8] [9]。最后，乳汁的释放由催产素调节，乳汁通过肌上皮细胞的收缩被释放到导管系统中，从而在母乳喂养或吸奶器吸奶期间分泌乳汁[10] [11]。乳腺从分泌分化到分泌激活的转变发生短暂，但涉及到全身激素的剧烈变化、乳腺上皮的解剖变化和乳汁成分的改变。

2.2. 与泌乳相关激素

泌乳受复杂的激素环境调节，包括多种生殖激素(例如雌激素、孕激素、催乳素、催产素)和代谢激素(例如糖皮质激素、胰岛素、胰岛素样生长因子1 (IGF-I)、生长激素和甲状腺激素) [12]。其中生殖激素的水平在生殖发育或功能过程中发生变化，并直接作用于乳腺，导致乳腺发育变化或协调泌乳；代谢激素主要作用是调节对营养摄入或应激的代谢反应，通常对乳腺也有直接影响[13]。雌激素可促进乳腺导管上皮细胞增生，使乳腺导管的延伸和分支，同时会间接促进催乳素的释放，增加乳腺催乳素受体的数量[14]，雌激素可能还会直接影响乳腺对钙离子的吸收，因此哺乳期雌激素的缺乏可能会导致骨吸收障碍[15]；催产素主要通过收缩乳腺腺泡周围的肌上皮细胞和放松乳管括约肌，从而释放乳汁[16]；而生长激素也有明显的催乳作用，其作用可能是通过胰岛素样生长因子介导间接作用于乳腺，从而调控乳腺上皮细胞的增

殖和分化[17]；催乳素可直接影响乳腺发育，还可通过激活 Jak2/Stat 通路从而影响乳腺上皮细胞乳糖、乳脂和乳蛋白的合成及分泌[8] [18]。一旦开始哺乳，催乳素作用于管腔上皮细胞以维持乳汁分泌[19]。

3. 催乳素的概述

3.1. 下丘脑对催乳素的分泌机制

催乳素是一种由垂体前叶合成和分泌的多肽激素，它的分泌机制复杂，由下丘脑－垂体轴控制[20]。一般来说，下丘脑－垂体轴的调节包括刺激或抑制各种激素[21]的释放，以应对环境变化；催乳素的分泌由下丘脑神经分泌细胞向垂体提供的催乳素释放因子和抑制因子来调节[22]，其中多巴胺可抑制催乳素的释放，其他一系列激素可刺激催乳素的产生，包括催产素、促甲状腺激素释放激素和皮质醇。

多巴胺(DA)是最主要的下丘脑催乳素抑制因子，多巴胺作用于泌乳细胞，由结节漏斗多巴胺能(TIDA)，结节垂体多巴胺能(THDA)和脑室周围垂体多巴胺能(PHDA)神经元三个神经内分泌多巴胺能(NEDA)神经元释放；其中 TIDA 神经元为垂体前叶提供主要的多巴胺能输入。在没有下丘脑刺激的情况下泌乳细胞会表现出自发的电活动，触发钙离子通过电压门控钙通道(VGCC) [23]，从而发生催乳素分泌。而 DA 与 2 型 DA 受体的结合会使 VGCC 失活，抑制钙离子的内流，从而抑制催乳素分泌[24]；同时 DA 会抑制催乳素的释放[25]与基因表达[26]。此外，在缺乏靶向性腺体激素来提供对泌乳细胞的反馈控制的情况下，PRL 通过作用于下丘脑多巴胺能系统来调节自身的释放，这种现象被称为“短环反馈”[27]。因此可通过 D2 受体激动剂[28] (如溴隐亭和卡麦角林)或 D2 受体拮抗剂(如甲氧氯普胺) [29]来控制催乳素的释放。

针对催乳素的释放，大多数调节催乳素分泌的因素都是通过直接或间接影响下丘脑多巴胺神经元分泌的多巴胺来实现的；催乳素本身可刺激多巴胺释放以抑制自身分泌[30]；雌激素可通过再增加催乳素基因表达而刺激催乳素的释放[31]；催产素也可刺激催乳素的释放[32]，可以通过刺激 TIDA 神经元来调节催乳素的分泌，这可能起到前馈抑制催乳素释放的作用[33] [34]；催乳素的分泌与 DA 和催产素对泌乳细胞的作用有关，有研究证明 DA 的减少和催产素对泌乳细胞的刺激共同作用以维持催乳素分泌的节律性[35] [36]。

3.2. 催乳素对泌乳的作用

催乳素在乳腺发育、开始泌乳、维持乳汁分泌的过程中起着不可取代的作用。在女性乳房发育初期，催乳素通过与乳腺上皮细胞的催乳素受体结合直接影响乳腺发育[37] [38]，有助于乳腺从末端芽生长到成熟乳腺，成熟乳腺的标志就是没有末端芽，由高度发育的分支结构组成；有研究表明催乳素缺乏会导致乳腺发育状态停滞在青春期未成熟状态，在催乳素基因被靶向破坏的未生育小鼠乳腺中存在许多末端芽，而正常小鼠成熟乳腺腺体无末端芽[39] [40]；在妊娠期，催乳素的分泌可直接影响乳腺腺泡的发育，并通过激活 JAK2-STAT5 信号通路在乳腺中发挥作用，催乳素与催乳素受体结合后，可以刺激 JAK2，使 STAT5 磷酸化，与乳腺组织中的许多乳蛋白基因的启动因子结合，从而引发泌乳[41] [42]。

3.3. 女性各个阶段的催乳素水平

3.3.1. 产前催乳素相关水平

正常未妊娠妇女催乳素水平大于 20 ng/ml 为异常[43]；妊娠期间催乳素来源包括母亲垂体和宫腔蜕膜，几乎所有的母体血清催乳素都来源于垂体，从妊娠三个月开始，血清催乳素水平开始增加，在整个妊娠期呈直线上升状态，几乎达到非妊娠妇女的 10 倍，血清催乳素从第 8 周的 45.3 ± 14 ng/ml 持续上升至第 36 周的 224 ± 20 ng/ml [44]。羊水中的催乳素由宫腔蜕膜分泌，通过羊膜-羊膜腔运输并聚集到羊膜

腔中[45]，妊娠初期一直保持在低水平，直到第 14 周(33.1 ± 0.8 ng/ml)，随后在第 18 周至第 26 周期间急剧显著增加至 3750 ± 200 ng/ml 的平台，在第 36 周下降到 500 ± 50 ng/ml 的第二个平台；在妊娠 14 周至 18 周期间，平均每周羊水体积增加一倍，这与羊水催乳素浓度的急剧增加相对应；17 周之后羊水催乳素浓度逐渐减少，到 30~32 周时明显降低，可能与胎儿肾功能成熟和蜕膜的分泌减少有关[46] [47]。

3.3.2. 产后催乳素相关水平

催乳素水平在产褥期呈现多阶段模式，第一个阶段在分娩期，产程中催乳素水平显著下降，在分娩前 2 小时左右降至最低点；分娩后，催乳素立即激增，并在产后 2 小时内达到峰值，可达 150 ng/ml [48]。此后，催乳素水平下降，并在产后 9 小时左右达到第二次最低点；这一低水平维持在一个可变的时期内，直到产后 24 小时结束；造成产程中催乳素水平的快速下降的原因可能是由于催产素的快速而剧烈的释放[49]；第二个阶段在开始哺乳后，基础催乳素水平开始升高，哺乳刺激能刺激催乳素的释放，并在母乳喂养开始后 15~30 分钟达到峰值，可以达到基础浓度的 50 倍[50]，在母乳喂养开始后 3 小时内，血清催乳素水平恢复到喂养前水平[51]；大约到产后 2~3 周，不哺乳妇女的血清催乳素水平可恢复到非妊娠妇女正常水平的较高水平[47]；产后 60 天达到第三阶段，催乳素基线水平与峰值自分娩以来随着时间的推移而下降[28] [52]；进一步研究表明在血清催乳素浓度下降的情况下，催乳素脉冲频率是稳定的，催乳素脉冲高度和脉冲幅度在产后 3 周至 3 个月内显著减少[53]。

通过放射免疫法[54]测量血清催乳素水平，发现初产妇血清催乳素水平高于经产妇，可能与经产妇血液中催乳素受体与催乳素结合相对较多有关，导致血清催乳素较低[55]；在一项关于早产儿母亲和足月儿母亲催乳素水平的研究中[56]，早产婴儿母亲催乳素基线水平在 2 周、4 周、6 周均明显低于足月婴儿母亲；对比纯母乳喂养的母亲，其产后 24 小时内催乳素水平显著高于补充喂养组[57]；有学者认为哺乳期停经时间与血清催乳素水平有关，在产后持续哺乳的母亲中，长停经组血清催乳素水平明显高于短时间停经组，且长停经组催乳素生物活性明显增加[58] [59]。

4. 催乳素与泌乳之间的关系

4.1. 催乳素对泌乳启动的影响

成功的分泌激活依赖于分娩时高水平的催乳素、胰岛素和皮质醇，因此考虑泌乳失败的女性是否与催乳素不足有关[60]；有研究认为乳腺催乳素抵抗可能是泌乳失败的原因[61]；并且有研究对因自身抗体破坏垂体导致催乳素缺乏的女性进行催乳素替代疗法，结果该母亲成功泌乳，但药物一旦停止使用，泌乳也立即停止[62]。

4.2. 催乳素对泌乳维持的作用

母乳供应的维持取决于催乳素的间歇性激增以及乳房对不断产生的乳汁的足够储存能力[63]。哺乳行为是催乳素分泌最重要的生理刺激，在哺乳期维持较高频率的母乳喂养次数以维持较高水平的催乳素水平，同时维持催乳素稳定的催乳素脉冲频率，这是泌乳维持的关键[52]；有证据表明，乳腺排空不及时会导致泌乳反馈抑制剂的积累，减少催乳素的释放，从而导致接下来的产奶量减少[64]。有研究[65]发现产后 3~4 个月的基础催乳素水平仍处于较高水平，与长期母乳喂养有关，可以通过催乳素水平预测哺乳期的剩余时间。

4.3. 催乳素与泌乳量的关系

虽然泌乳必须有催乳素的参加，但催乳素水平与泌乳量之间的关系尚未明确，有研究表明，妊娠期间较高的催乳素水平与产后一周泌乳量增加有关[55]，Aono 等的研究[66]中也认为产后 5 天内的总泌乳

量与催乳素水平相关；也有研究认为催乳素水平与泌乳量无显著相关性[57] [65] [67]；通过测量产后 1~6 月内 24 小时泌乳量和血清催乳素的关系，发现在保持泌乳量相对不变的情况下，血清催乳素水平在逐渐下降[68]；通过测量 24 小时内每次母乳喂养泌乳量、催乳素水平，发现血清催乳素不能调节乳汁的生成或乳汁合成的速度，并发现血清催乳素水平存在昼夜节律模式，夜间催乳素水平高于白天[69] [70]。已有研究尝试使用药物诱导催乳素的分泌，增加泌乳量；结果表示催乳剂可能在短期内改善泌乳量，但对长期的泌乳量是否有改善尚不清楚[71] [72]。并且有报道显示有孕产妇在垂体手术后呈现催乳素低水平状态，但仍能成功泌乳[73]。

5. 小结

泌乳与内分泌系统关系错综复杂，催乳素正在其中起着关键作用，催乳素在泌乳开始和维持过程中的重要性已经毋庸置疑，但催乳素水平与泌乳量之间的联系需要进一步探究；值得注意的是，不同研究对催乳素和泌乳量的测量方法不同，包括测量血清催乳素水平、母乳催乳素水平、哺乳前后催乳素水平，以及对产奶量的计算包括婴儿喂养前后的体重对比，但也有研究并没有计算乳房内剩余的奶量；因此在未来的研究中可通过进一步研究确定是否可以根据催乳水平判断泌乳启动成功或泌乳启动延迟，并通过更完善、精准的测量方法催乳素水平与泌乳量之间的联系。

基金来源

吉首大学校级项目科研项目(Jdy22091)。

参考文献

[1] 王朕，王欢欢，肖梦杰，等. 我国母乳喂养现状与护理对策分析[J]. 中国生育健康杂志, 2018, 29(2): 200-202.

[2] 李玲，王小青，魏满荣，等. 中国 6 个月内婴儿纯母乳喂养影响因素 Meta 分析[J]. 中国妇幼保健，2021，36(22): 5359-5363.

[3] 关于印发母乳喂养促进行动计划(2021-2025 年)的通知[J]. 中华人民共和国国家卫生健康委员会公报，2021(11): 12-15.

[4] Luzardo-Ocampo, I., Dena-Beltrán, J.L., Ruiz-Herrera, X., *et al.* (2023) Obesity-Derived Alterations in the Lactating Mammary Gland: Focus on Prolactin. *Molecular and Cellular Endocrinology*, **559**, Article ID: 111810. https://doi.org/10.1016/j.mce.2022.111810

[5] Medina, Poeliniz, C., Engstrom, J.L., Hoban, R., *et al.* (2020) Measures of Secretory Activation for Research and Practice: An Integrative Review. *Breastfeeding Medicine*, **15**, 191-212. https://doi.org/10.1089/bfm.2019.0247

[6] Schuler, L.A. and O'leary, K.A. (2022) Prolactin: The Third Hormone in Breast Cancer. *Frontiers in Endocrinology*, **13**, Article 910978. https://doi.org/10.3389/fendo.2022.910978

[7] Alex, A., Bhandary, E. and Mcguire, K.P. (2020) Anatomy and Physiology of the Breast during Pregnancy and Lactation. In: Alipour, S. and Omranipour, R., Eds., *Diseases of the Breast during Pregnancy and Lactation*, Springer, Cham, 3-7. https://doi.org/10.1007/978-3-030-41596-9_1

[8] Golan, Y. and Assaraf, Y.G. (2020) Genetic and Physiological Factors Affecting Human Milk Production and Composition. *Nutrients*, **12**, Article 1500. https://doi.org/10.3390/nu12051500

[9] Truchet, S. and Honvo-Houeto, E. (2017) Physiology of Milk Secretion. *Best Practice & Research Clinical Endocrinology & Metabolism*, **31**, 367-384. https://doi.org/10.1016/j.beem.2017.10.008

[10] Farah, E., Barger, M.K., Klima, C., *et al.* (2021) Impaired Lactation: Review of Delayed Lactogenesis and Insufficient Lactation. *Journal of Midwifery & Womens Health*, **66**, 631-640. https://doi.org/10.1111/jmwh.13274

[11] 庞艳，林芳初，李媛，等. 母乳生物标志物在泌乳启动测定中的应用进展[J]. 广西医学, 2021, 43(13): 1636-1639.

[12] Lee, S. and Kelleher, S.L. (2016) Biological Underpinnings of Breastfeeding Challenges: The Role of Genetics, Diet, and Environment on Lactation Physiology. *American Journal of Physiology-Endocrinology and Metabolism*, **311**, E405-E422. https://doi.org/10.1152/ajpendo.00495.2015

[13] Neville, M.C., Mcfadden, T.B. and Forsyth, I. (2002) Hormonal Regulation of Mammary Differentiation and Milk Se-

cretion. *Journal of Mammary Gland Biology and Neoplasia*, **7**, 49-66. https://doi.org/10.1023/A:1015770423167

[14] Blasiak, M. and Molik, E. (2015) Role of Hormones and Growth Factors in Initiating and Maintaining the Lactation of Seasonal Animals. *Medycyna Weterynaryjna-Veterinary Medicine-Science and Practice*, **71**, 467-471.

[15] Veerkamp, R.F., Beerda, B. and Van Der Lende, T. (2003) Effects of Genetic Selection for Milk Yield on Energy Balance, Levels of Hormones, and Metabolites in Lactating Cattle, and Possible Links to Reduced Fertility's. *Livestock Production Science*, **83**, 257-275. https://doi.org/10.1016/S0301-6226(03)00108-8

[16] Uvnas-Moberg, K., Ekstrom-Bergstrom, A., Buckley, S., *et al.* (2020) Maternal Plasma Levels of Oxytocin during Breastfeeding—A Systematic Review. *PLOS ONE*, **15**, e0235806. https://doi.org/10.1371/journal.pone.0235806

[17] Bonefeld, K. and Møller, S. (2011) Insulin-Like Growth Factor-I and the Liver. *Liver International*, **31**, 911-919. https://doi.org/10.1111/j.1478-3231.2010.02428.x

[18] Patel, S., Sparman, N.Z.R., Arneson, D., *et al.* (2023) Mammary Duct Luminal Epithelium Controls Adipocyte Thermogenic Programme. *Nature*, **620**, 192-199. https://doi.org/10.1038/s41586-023-06361-5

[19] Neville, M.C., Mcfadden, T.B. and Forsyth, I. (2002) Hormonal Regulation of Mammary Differentiation and Milk Secretion. *Journal of Mammary Gland Biology and Neoplasia*, **7**, 49-66. https://doi.org/10.1023/A:1015770423167

[20] Buhimschi, C.S. (2004) Endocrinology of Lactation. *Obstetrics and Gynecology Clinics of North America*, **31**, 963-979. https://doi.org/10.1016/j.ogc.2004.08.002

[21] Erickson, E.N., Carter, C.S. and Emeis, C.L. (2020) Oxytocin, Vasopressin and Prolactin in New Breastfeeding Mothers: Relationship to Clinical Characteristics and Infant Weight Loss. *Journal of Human Lactation*, **36**, 136-145. https://doi.org/10.1177/0890334419838225

[22] Li, H., Wei, J., Ma, F., *et al.* (2020) Melatonin Modulates Lactation by Regulating Prolactin Secretion via Tuberoinfundibular Dopaminergic Neurons in the Hypothalamus- Pituitary System. *Current Protein & Peptide Science*, **21**, 744-750. https://doi.org/10.2174/1389203721666200511093733

[23] Kennett, J.E. and Mckee, D.T. (2012) Oxytocin: An Emerging Regulator of Prolactin Secretion in the Female Rat. *Journal of Neuroendocrinology*, **24**, 403-412. https://doi.org/10.1111/j.1365-2826.2011.02263.x

[24] Gregerson, K.A. (2003) Functional Expression of the Dopamine-Activated K^+ Current in Lactotrophs during the Estrous Cycle in Female Rats: Correlation with Prolactin Secretory Responses. *Endocrine*, **20**, 67-74. https://doi.org/10.1385/ENDO:20:1-2:67

[25] Ben-Jonathan, N. and Hnasko, R. (2001) Dopamine as a Prolactin (PRL) Inhibitor. *Endocrine Reviews*, **22**, 724-763. https://doi.org/10.1210/edrv.22.6.0451

[26] Ishida, M., Mitsui, T., Yamakawa, K., *et al.* (2007) Involvement of CAMP Response Element-Binding Protein in the Regulation of Cell Proliferation and the Prolactin Promoter of Lactotrophs in Primary Culture. *American Journal of Physiology-Endocrinology and Metabolism*, **293**, E1529-E1537. https://doi.org/10.1152/ajpendo.00028.2007

[27] Araujo-Castro, M., Marazuela, M., Puig-Domingo, M. and Biagetti, B. (2023) Prolactin and Growth Hormone Signaling and Interlink Focused on the Mammosomatotroph Paradigm: A Comprehensive Review of the Literature. *International Journal of Molecular Sciences*, **24**, Article 14002. https://doi.org/10.3390/ijms241814002

[28] Stuebe, A.M., Meltzer-Brody, S., Pearson, B., *et al.* (2015) Maternal Neuroendocrine Serum Levels in Exclusively Breastfeeding Mothers. *Breastfeeding Medicine*, **10**, 197-202. https://doi.org/10.1089/bfm.2014.0164

[29] Tabrizi, S.O., Mirghafourvand, M. and Seyedi, R. (2017) The Effect of Metoclopramide on Prolactin Levels in Breastfeeding Mothers: A Systematic Review and Meta-Analysis. *International Journal of Pediatrics-Mashhad*, **5**, 5827-5838.

[30] Grattan, D.R. (2015) 60 Years of Neuroendocrinology: The Hypothalamo-Prolactin Axis. *The Journal of Endocrinology*, **226**, T101-T122. https://doi.org/10.1530/JOE-15-0213

[31] Wood, C.E. and Keller-Wood, M. (2011) Influence of Estradiol and Fetal Stress on Luteinizing Hormone, Follicle-Stimulating Hormone, and Prolactin in Late-Gestation Fetal Sheep. *Neonatology*, **100**, 1551-61. https://doi.org/10.1159/000324431

[32] Xu, C., Papadakis, G.E. and Pitteloud, N. (2020) Normal Endocrine Physiology of Hypothalamic Hormones during Ovulation, Pregnancy, and Lactation. In: Kovacs, C.S. and Deal, C.L., Eds., *Maternal-Fetal and Neonatal Endocrinology*, Academic Press, Cambridge, 7-14. https://doi.org/10.1016/B978-0-12-814823-5.00001-5

[33] Villegas-Gabutti, C.M., Pennacchio, G.E., Vivas, L., *et al.* (2018) Role of Oxytocin in Prolactin Secretion during Late Pregnancy. *Neuroendocrinology*, **106**, 324-334. https://doi.org/10.1159/000480669

[34] Briffaud, V., Williams, P., Courty, J. and Broberger, C. (2015) Excitation of Tuberoinfundibular Dopamine Neurons by Oxytocin: Crosstalk in the Control of Lactation. *Journal of Neuroscience*, **35**, 4229-4237. https://doi.org/10.1523/JNEUROSCI.2633-14.2015

[35] Liang, S.-L. and Pan, J.-T. (2012) An Endogenous Dopaminergic Tone Acting on Dopamine D_3 Receptors May Be Involved in Diurnal Changes of Tuberoinfundibular Dopaminergic Neuron Activity and Prolactin Secretion in Estrogen-Primed Ovariectomized Rats. *Brain Research Bulletin*, **87**, 334-339. https://doi.org/10.1016/j.brainresbull.2011.11.018

[36] Mckee, D.N.T., Poletini, M.O., Bertram, R. and Freeman, M.E. (2007) Oxytocin Action at the Lactotroph Is Required for Prolactin Surges in Cervically Stimulated Ovariectomized Rats. *Endocrinology*, **148**, 4649-4657. https://doi.org/10.1210/en.2007-0646

[37] Oakes, S.R., Rogers, R.L., Naylor, M.J. and Ormandy, C.J. (2008) Prolactin Regulation of Mammary Gland Development. *Journal of Mammary Gland Biology and Neoplasia*, **13**, 13-28. https://doi.org/10.1007/s10911-008-9069-5

[38] Berryhill, G.E., Trott, J.F. and Hovey, R.C. (2016) Mammary Gland Development—It's Not Just about Estrogen. *Journal of Dairy Science*, **99**, 875-883. https://doi.org/10.3168/jds.2015-10105

[39] Geiger, A.J. and Hovey, R.C. (2023) Development of the Mammary Glands and Its Regulation: How Not All Species Are Equal. *Animal Frontiers*, **13**, 44-54. https://doi.org/10.1093/af/vfad029

[40] Naylor, M.J., Lockefeer, J.A., Horseman, N.D. and Ormandy, C.J. (2003) Prolactin Regulates Mammary Epithelial Cell Proliferation via Autocrine/Paracrine Mechanism. *Endocrine*, **20**, 111-114. https://doi.org/10.1385/ENDO:20:1-2:111

[41] Khan, M.Z., Khan, A., Xiao, J., *et al.* (2020) Role of the JAK-STAT Pathway in Bovine Mastitis and Milk Production. *Animals*, **10**, Article 2107. https://doi.org/10.3390/ani10112107

[42] Shin, H.Y., Hennighausen, L. and Yoo, K.H. (2019) STAT5-Driven Enhancers Tightly Control Temporal Expression of Mammary-Specific Genes. *Journal of Mammary Gland Biology and Neoplasia*, **24**, 61-71. https://doi.org/10.1007/s10911-018-9418-y

[43] Benjamin, F. (1994) Normal Lactation and Galactorrhea. *Clinical Obstetrics and Gynecology*, **37**, 887-897. https://doi.org/10.1097/00003081-199412000-00015

[44] Rana, M., Jain, S. and Choubey, P. (2022) Prolactin and Its Significance in the Placenta. *Hormones*, **21**, 209-219. https://doi.org/10.1007/s42000-022-00373-y

[45] Flores-Espinosa, P., Méndez, I., Irles, C., *et al.* (2023) Immunomodulatory Role of Decidual Prolactin on the Human Fetal Membranes and Placenta. *Frontiers in Immunology*, **14**, Article 1212736. https://doi.org/10.3389/fimmu.2023.1212736

[46] Kletzky, O.A., Rossman, F., Bertolli, S.I., *et al.* (1985) Dynamics of Human Chorionic Gonadotropin, Prolactin, and Growth Hormone in Serum and Amniotic Fluid throughout Normal Human Pregnancy. *American Journal of Obstetrics and Gynecology*, **151**, 878-884. https://doi.org/10.1016/0002-9378(85)90665-9

[47] Tyson, J.E., Hwang, P., Guyda, H., *et al.* (1972) Studies of Prolactin Secretion in Human Pregnancy. *American Journal of Obstetrics and Gynecology*, **113**, 14-20. https://doi.org/10.1016/0002-9378(72)90446-2

[48] Neville, M.C. (2001) Anatomy and Physiology of Lactation. *Pediatric Clinics of North America*, **48**, 13-34. https://doi.org/10.1016/S0031-3955(05)70283-2

[49] Rigg, L.A. and Yen, S.S. (1977) Multiphasic Prolactin Secretion during Parturition in Human Subjects. *American Journal of Obstetrics and Gynecology*, **128**, 215-218. https://doi.org/10.1016/0002-9378(77)90692-5

[50] Johnston, J.M. and Amico, J.A. (1986) A Prospective Longitudinal Study of the Release of Oxytocin and Prolactin in Response to Infant Suckling in Long Term Lactation. *The Journal of Clinical Endocrinology and Metabolism*, **62**, 653-657. https://doi.org/10.1210/jcem-62-4-653

[51] Healy, D.L., Rattigan, S., Hartmann, P.E., *et al.* (1980) Prolactin in Human Milk: Correlation with Lactose, Total Protein, and α-Lactalbumin Levels. *The American Journal of Physiology*, **238**, E83-E86. https://doi.org/10.1152/ajpendo.1980.238.1.E83

[52] Stuebe, A.M., Grewen, K., Pedersen, C.A., *et al.* (2012) Failed Lactation and Perinatal Depression: Common Problems with Shared Neuroendocrine Mechanisms? *Journal of Women's Health*, **21**, 264-272. https://doi.org/10.1089/jwh.2011.3083

[53] Nunley, W.C., Urban, R.J., Kitchin, J.D., *et al.* (1991) Dynamics of Pulsatile Prolactin Release during the Postpartum Lactational Period. *The Journal of Clinical Endocrinology and Metabolism*, **72**, 287-293. https://doi.org/10.1210/jcem-72-2-287

[54] Zuppa, A.A., Tornesello, A., Papacci, P., *et al.* (1988) Relationship between Maternal Parity, Basal Prolactin Levels and Neonatal Breast Milk Intake. *Biology of the Neonate*, **53**, 144-147. https://doi.org/10.1159/000242775

[55] Ingram, J.C., Woolridge, M.W., Greenwood, R.J. and McGrath, L. (1999) Maternal Predictors of Early Breast Milk Output. *Acta Paediatrica*, **88**, 493-499. https://doi.org/10.1111/j.1651-2227.1999.tb00164.x

[56] Chatterton, R.T., Hill, P.D., Aldag, J.C., *et al.* (2000) Relation of Plasma Oxytocin and Prolactin Concentrations to

Milk Production in Mothers of Preterm Infants: Influence of Stress. *Journal of Clinical Endocrinology & Metabolism*, **85**, 3661-3668. https://doi.org/10.1210/jc.85.10.3661

[57] Aisaka, K., Mori, H., Ogawa, T., *et al.* (1985) Effects of Mother-Infant Interaction on Maternal Milk Secretion and Dynamics of Maternal Serum Prolactin Levels in Puerperium. *Nihon Sanka Fujinka Gakkai Zasshi*, **37**, 713-720.

[58] Campino, C., Ampuero, S., Díaz, S., *et al.* (1994) Prolactin Bioactivity and the Duration of Lactational Amenorrhea. *The Journal of Clinical Endocrinology and Metabolism*, **79**, 970-974. https://doi.org/10.1210/jcem.79.4.7962307

[59] Díaz, S., Serón-Ferré, M., Cárdenas, H., *et al.* (1989) Circadian Variation of Basal Plasma Prolactin, Prolactin Response to Suckling, and Length of Amenorrhea in Nursing Women. *The Journal of Clinical Endocrinology and Metabolism*, **68**, 946-955. https://doi.org/10.1210/jcem-68-5-946

[60] Marasco, L.A. (2014) Unsolved Mysteries of the Human Mammary Gland: Defining and Redefining the Critical Questions from the Lactation Consultant's Perspective. *Journal of Mammary Gland Biology and Neoplasia*, **19**, 271-288. https://doi.org/10.1007/s10911-015-9330-7

[61] Zargar, A.H., Salahuddin, M., Laway, B.A., *et al.* (2000) Puerperal Alactogenesis with Normal Prolactin Dynamics: Is Prolactin Resistance the Cause? *Fertility and Sterility*, **74**, 598-600. https://doi.org/10.1016/S0015-0282(00)00691-9

[62] Iwama, S., Welt, C.K., Romero, C.J., *et al.* (2013) Isolated Prolactin Deficiency Associated with Serum Autoantibodies against Prolactin-Secreting Cells. *The Journal of Clinical Endocrinology and Metabolism*, **98**, 3920-3925. https://doi.org/10.1210/jc.2013-2411

[63] Eglash, A. and Malloy, M.L. (2015) Breastmilk Expression and Breast Pump Technology. *Clinical Obstetrics and Gynecology*, **58**, 855-867. https://doi.org/10.1097/GRF.0000000000000141

[64] Hernandez, L.L., Stiening, C.M., Wheelock, J.B., *et al.* (2008) Evaluation of Serotonin as a Feedback Inhibitor of Lactation in the Bovine. *Journal of Dairy Science*, **91**, 1834-1844. https://doi.org/10.3168/jds.2007-0766

[65] Uvnas-Moberg, K., Widstrom, A.M., Werner, S., *et al.* (1990) Oxytocin and Prolactin Levels in Breast-Feeding Women. Correlation with Milk Yield and Duration of Breast-Feeding. *Acta Obstetricia et Gynecologica Scandinavica*, **69**, 301-306. https://doi.org/10.3109/00016349009036151

[66] Aono, T., Shioji, T., Shoda, T. and Kurachi, K. (1977) The Initiation of Human Lactation and Prolactin Response to Suckling. *The Journal of Clinical Endocrinology and Metabolism*, **44**, 1101-1106. https://doi.org/10.1210/jcem-44-6-1101

[67] Howie, P.W., Mcneilly, A.S., Mcardle, T., *et al.* (1980) The Relationship between Suckling-Induced Prolactin Response and Lactogenesis. *The Journal of Clinical Endocrinology and Metabolism*, **50**, 670-673. https://doi.org/10.1210/jcem-50-4-670

[68] Cox, D.B., Owens, R.A. and Hartmann, P.E. (1996) Blood and Milk Prolactin and the Rate of Milk Synthesis in Women. *Experimental Physiology*, **81**, 1007-1020. https://doi.org/10.1113/expphysiol.1996.sp003985

[69] Stern, J.M. and Reichlin, S. (1990) Prolactin Circadian Rhythm Persists Throughout Lactation in Women. *Neuroendocrinology*, **51**, 31-37. https://doi.org/10.1159/000125312

[70] Cregan, M.D., Mitoulas, L.R. and Hartmann, P.E. (2002) Milk Prolactin, Feed Volume and Duration between Feeds in Women Breastfeeding Their Full-Term Infants over a 24 h Period. *Experimental Physiology*, **87**, 207-214. https://doi.org/10.1113/eph8702327

[71] Grzeskowiak, L.E., Wlodek, M.E. and Geddes, D.T. (2019) What Evidence Do We Have for Pharmaceutical Galactagogues in the Treatment of Lactation Insufficiency?—A Narrative Review. *Nutrients*, **11**, Article 974. https://doi.org/10.3390/nu11050974

[72] Barguño, J.M., Del Pozo, E., Cruz, M., *et al.* (1988) Failure of Maintained Hyperprolactinemia to Improve Lactational Performance in Late Puerperium. *The Journal of Clinical Endocrinology and Metabolism*, **66**, 876-879. https://doi.org/10.1210/jcem-66-4-876

[73] Narita, O., Kimura, T., Suganuma, N., *et al.* (1985) Relationship between Maternal Prolactin Levels during Pregnancy and Lactation in Women with Pituitary Adenoma. *Nihon Sanka Fujinka Gakkai Zasshi*, **37**, 758-762.