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Narrative Review

Endometrial Preparation Useful to Embryo Implantation

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Abstract

Endometrial preparation is crucial in IVF protocols to create optimal conditions for embryo implantation and pregnancy. Successful embryo nidation requires a receptive endometrium, influenced by factors such as endometrial thickness, hormonal environment, autocrine and paracrine growth factors, and resident stem cells in the endometrium basalis. Synchronization between embryonic and endometrial development is essential. However, identifying the precise Window of Implantation (WOI) is challenging due to variability in estrogen and progesterone production, metabolism, and metabolic clearance rates (MCR). This review aims to outline a clinical approach that, though not absolute, assists in understanding complementary phenomena and provides useful guidance for practice.

Keywords: *Endometrium; Basalis; Functionalis; Estradiol; Progesterone; Metabolic Clearance Rate; Transport; Growth Factors; Endometrial Thickness; Markers of Decidualization; Pinopodes; Endometrial Assessment; Embryo Implantation*

Capsule

Endometrial preparation is critical for successful IVF. This review discusses how hormonal regulation, thickness, and synchronization between embryo and endometrium impact implantation. Although there is no absolute guideline, this review provides clinicians with insights on optimizing IVF outcomes through a multifactorial approach.

Introduction

Endometrial preparation is essential for IVF protocols, aiming to create an optimal environment for embryo implantation and subsequent pregnancy. Successful nidation requires a receptive endometrium, influenced by factors such as thickness, hormonal environment, and synchronization with embryonic development [1-3]. Despite numerous studies linking endometrial thickness (ET) with implantation, evidence remains inconclusive, and ET is not yet an established marker for determining receptivity [4,5].

Studies have shown that endometrial thickness of ≥ 9 mm at the time of hCG administration is associated with higher pregnancy rates, but variability exists across studies [6-8]. Women with ET between 10 - 12 mm tend to have the highest pregnancy rates, although over 500 studies on ET and ART outcomes highlight the challenges in establishing a consistent relationship [9-12].

The clinical significance of small differences in ET, such as 0.5 mm, is debatable due to measurement variability. While extensively studied, ET's role in predicting implantation success remains controversial and requires cautious interpretation.

This study critically examines factors influencing endometrial adequacy for embryo implantation, aiming to balance the role of the endometrial interface at implantation. Although no single factor, procedure, or molecule significantly impacts embryo implantation alone, endometrial progesterone-mediated differentiation is essential for early pregnancy [13].

Materials and Methods

This narrative review synthesizes findings from multiple studies investigating endometrial preparation methods, including natural cycles, ovulation induction, and hormone replacement therapies (HRT). Pub Med, Google Scholar, Cochrane library, Scopus, Embase, Web of Science, and ClinicalTrials.gov databases helped in compiling a comprehensive literature review that covers both theoretical and clinical research on endometrial preparation, taking into account various study designs and methodologies. No date limit was used for our search. Particular attention is given to randomized controlled trials (RCTs) examining how various factors, such as biochemical conditions, estrogen and progesterone variability, and endometrial thickness, influence implantation rates. Key issues in study design, such as stimulation protocol variations, sample size limitations, and the influence of ultrasound variability, are critically analyzed [11,14-16].

Results

Studies show higher implantation rates in gestational carriers compared to intentional mothers during the first embryo transfer, suggesting a functional syncytium between the endometrium and myometrium that is involved in successful embryo implantation [17-19].

The debate persists on the impact of endometrial preparation on embryo implantation. Tailored treatments should not solely rely on sequential euploid embryo transfer due to age and ovarian reserve constraints but also consider extra-embryonic causes of implantation failure.

Recommendations include sequential euploid embryo transfer (SEET) as a strategy when possible, ensuring all known extra-embryonic causes of implantation failure are excluded or corrected [1]. Without excluding these potential causes, SEET can be considered an add-on rather than a primary strategy.

Collected studies suggest that optimal endometrial thickness is significant for embryo implantation and pregnancy success following embryo transfer. However, it is not the sole determinant. Other factors, including endometrial receptivity, embryo quality, and overall uterine health, also play crucial roles. This study emphasizes a comprehensive approach to assessing and optimizing endometrial conditions for successful embryo implantation, recognizing the complexity and multifactorial nature of implantation success.

Endometrial thickness and IVF outcomes: Numerous studies suggest an optimal ET of 8 - 14 mm correlates with higher pregnancy rates, with the best outcomes seen in women with an ET of 10 - 12 mm [6,8]. However, discrepancies exist, as earlier studies with smaller sample sizes showed inconsistent results [20,21]. Recent studies highlight that ET alone is not a definitive predictor of implantation success due to confounding variables such as embryo quality and synchronization with endometrial receptivity [16,22]. The issue remains debated with differing evaluations among authors [4,23,24]. A trilaminar or "triple-line" pattern on ultrasound around the time of embryo

transfer indicates a receptive endometrium [25]. This pattern, showing a central echogenic line surrounded by hypoechoic regions, correlates with higher implantation and pregnancy rates [26]. The trilaminar endometrial pattern is a key indicator of endometrial receptivity, associated with higher implantation success rates in IVF treatments.

Challenges in ET measurement: The variability in ultrasound technology and timing of ET measurements across cycles (IVF or IUI) complicates result comparability. Moreover, small differences in thickness (e.g. 0.5 mm) may not be clinically significant due to observer variability [27]. Additionally, differences in stimulation protocols and the number of embryos transferred further confound study results [28].

Biochemical and molecular markers: Endometrial thickness alone cannot fully predict implantation success. Biochemical markers such as VEGF, TGF-β, and IGF, and molecular markers like HOXA10 and LIF, play crucial roles in ensuring a receptive environment for embryo implantation [29,30]. Studies also highlight the importance of estrogen and progesterone in transforming the proliferative endometrium into a secretory state essential for implantation [3,31,32].

Hormonal environment and synchronization: Proper synchronization between the embryo and endometrium is critical, and this can be achieved through hormonal support. However, factors such as metabolic clearance rates of exogenously administered hormones affect their efficacy [33]. The balance between estrogen and progesterone is necessary to ensure a receptive endometrium and successful implantation [3,34].

Endometrial dating: Histological dating of an endometrial biopsy assesses the tissue's readiness for embryo implantation, particularly during the luteal phase [35-38]. Key features assessed include tortuous glands with secretory activity, increased stromal fluid, transformation of stromal cells, and coiling of spiral arteries. Histological dating helps ensure embryo transfer aligns with the receptive phase, increasing implantation and pregnancy success. Newer methods like molecular markers of endometrial receptivity and transcriptomic assays (e.g. the Endometrial Receptivity Array) aim to provide more precise assessments but have yet to significantly advance clinical diagnostics.

Immunohistochemical (IHC) evaluation assesses specific markers indicating the endometrium's readiness for implantation.		
Marker	**Assessment**	**Reference**
PR (Progesterone Receptor):	Decreases in the secretory phase	39
ER (Estrogen Receptor):	Downregulated in the secretory phase	32
LIF (Leukemia Inhibitory Factor):	Peaks during the mid-secretory phase.	40
Glycodelin:	Levels increase during the secretory phase.	41
Integrins:	Levels increase during the secretory phase.	42
Ki-67:	High in the proliferative phase, decreases in the secretory phase.	43
HOXA10:	Increases in the secretory phase, indicating receptivity.	44
VEGF (Vascular Endothelial Growth Factor):	Upregulated during the secretory phase for increased vascularization.	45
MUC1 (Mucin 1):	High levels during the mid-secretory phase suggest receptivity.	46

Table 1: *These markers help in dating the endometrium and determining its adequacy for embryo nidation.*

Strategies for low endometrial thickness

When the endometrium does not respond adequately to ovarian stimulation, it can negatively impact embryo implantation and pregnancy. Hormonal supplementation, such as oral, transdermal, or injectable estradiol, is commonly used to improve thickness. Higher doses or extended administration may be necessary [47,48]. Human chorionic gonadotropin (hCG) at low doses has also been shown to stimulate endometrial growth [49]. Insufficient endometrial growth can lead to implantation failure, miscarriage, and conditions like intrauterine growth restriction [50].

Several potential reasons for inadequate growth include hormonal imbalances, poor uterine blood flow, chronic endometritis, structural damage from surgeries or infections like Asherman's syndrome, and molecular abnormalities in growth factors [51,52]. Lifestyle factors such as smoking, stress, and poor nutrition also contribute to poor growth.

Management strategies focus on hormonal adjustments, increasing estrogen and progesterone, and improving blood flow with agents like aspirin or pentoxifylline [53]. Treating underlying infections such as endometritis with antibiotics is also crucial for restoring normal growth [54]. Surgery may be required to remove adhesions, and lifestyle changes like a healthier diet and stress reduction may help improve reproductive health [55].

Adjuvant therapies include the use of platelet-rich plasma (PRP) to stimulate vascularization, granulocyte-colony stimulating factor (G-CSF) to increase endometrial thickness, and sildenafil to enhance uterine blood flow [56,57]. Despite these interventions, large-scale RCTs are still required to validate these methods, especially with controversial therapies like endometrial scratching, which has shown mixed results in studies [58,59].

Endometrial thickness is critical for embryo implantation success, but achieving the right hormonal environment and improving blood flow are equally important. Both vascularization and hormonal factors like estradiol and progesterone balance are vital for proper endometrial preparation [31]. Growth factors like VEGF and nitric oxide regulate vascularity, enhancing blood flow for successful embryo implantation [60].

Cellular and molecular markers, such as pinopodes, stromal decidualization, and integrins, play crucial roles in determining endometrial receptivity. Inadequate development can prevent successful implantation, and continuous research is essential for improving outcomes in IVF cycles [31,61].

Here is a simplified and rephrased version of the table content, with clear and concise text.

Feature	Details
Endometrial Thickness	Ideal range is 7-14 mm for successful implantation. Thickness below 7 mm increases the risk of miscarriage.
Triple-Line Pattern	A trilaminar pattern on ultrasound near embryo transfer indicates a receptive endometrium.
Hormonal Environment	Adequate estrogen stimulates growth; progesterone converts the lining to support implantation. Synchronization with the embryo is essential.
Receptive Window	The "window of implantation" occurs 6-10 days post-ovulation, marking the best time for embryo attachment.
Molecular Markers	Key markers like integrins and LIF help create a favorable environment for the embryo.

Table 2: *Key features determinant for endometrial adequacy for embryo implantation.*

Method	Intervention
Hormonal Supplementation	Estradiol via oral, transdermal, or injectable routes increases thickness. Progesterone, delivered vaginally or via injections, also helps.
Adjuvant Therapies	Low-dose aspirin and pentoxifylline improve blood flow. Platelet-rich plasma (PRP) can stimulate growth.
Granulocyte-Colony Stimulating Factor (G-CSF)	Injected directly into the uterus to improve thickness and pregnancy outcomes.
Endometrial Scratching	A minor procedure that stimulates tissue repair, enhancing receptivity.
Lifestyle Changes	Healthy diet, exercise, stress management, and yoga can promote overall endometrial health.

Table 3: *Strategies to improve the endometrial thickness and possible euploid embryo implantation.*

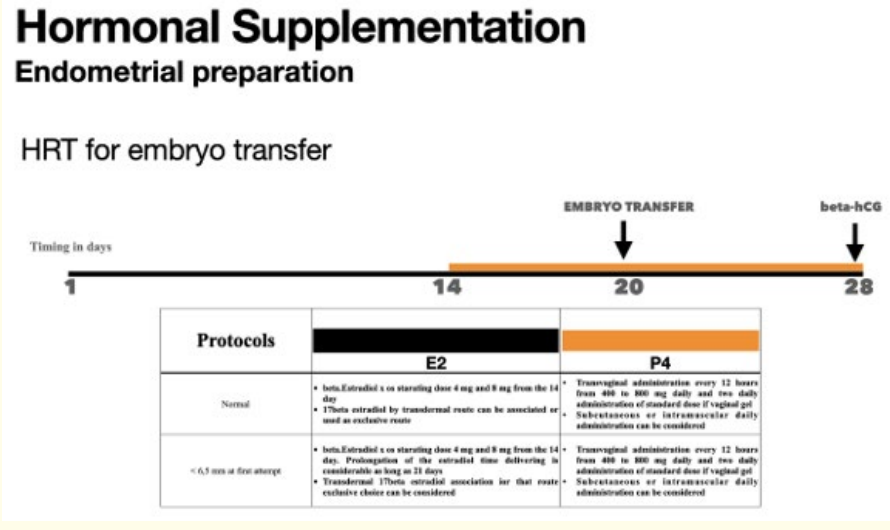

Figure 1: *Schematic view of endometrial preparation for embryo transfer by HRT.*

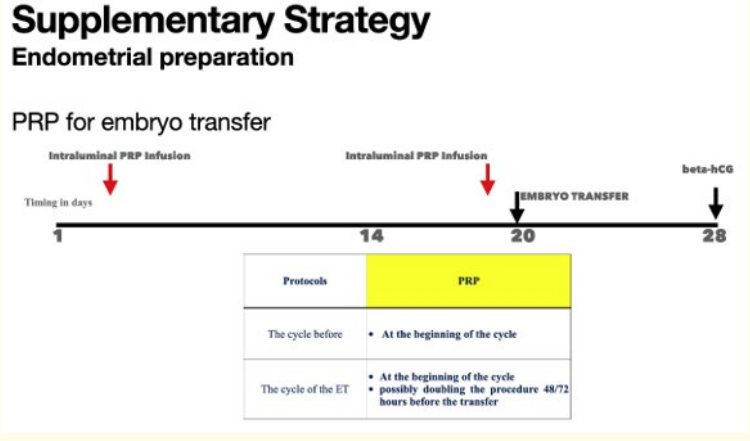

Figure 2: *Schematic view of second line endometrial preparation strategy after failure of endometrial growth and receptivity after several euploid embryo transfer.*

Discussion

Despite the large body of research, no single factor-such as endometrial thickness-can independently predict embryo implantation success [69,70]. Studies highlight the complexity of implantation, where a multitude of factors, including hormonal environment [62-64], synchronization between embryo and endometrium [65-67], abnormal uterine contractility [68] and molecular markers of receptivity [61], must be considered.

Variations in study design, differences in stimulation protocols, and sample size issues contribute to inconsistent results across studies. Large-scale, well-designed trials are necessary to refine our understanding of how best to optimize endometrial preparation for successful embryo transfer.

Clinical interventions, such as estradiol supplementation, PRP therapy [56,71,72] and G-CSF [73] injections, show promise in improving endometrial receptivity. However, these interventions should be personalized based on individual patient profiles and broader contextual factors such as embryo quality and uterine health.

Conclusion

Endometrial preparation for embryo transfer involves a complex interplay of factors, including thickness, hormonal environment, and synchronization with embryonic development. While no single factor guarantees implantation success, the review emphasizes a comprehensive, multifactorial approach to optimizing endometrial receptivity. Future research should focus on integrating molecular diagnostics and personalized therapeutic approaches to further improve IVF outcomes.

Authors Contribution

- Francesco Maria Bulletti and Carlo Bulletti contributed equally to this article in terms of conceptualization and first draft of the manuscript. Francesco Maria Bulletti wrote the last version of the manuscript.
- Antonio Palagiano, Veronica Bianchi and Maurizio Guido provided to search and first selection of the studies required and remark the more realistic pathogenetic concept reported.
- Maria Elisabetta Coccia and Romualdo Sciorio revised the second and third draft.

Bibliography

1. Gill P., *et al*. "Does recurrent implantation failure exist? prevalence and outcomes of five consecutive euploid blastocyst transfers in 123,987 patients". *Human Reproduction* 39.5 (2024): 974-980.
2. Strowitzki Thomas., *et al*. "The human endometrium as a fertility-determining factor". *Human Reproduction Update* 12.5 (2006): 617-630.
3. Bulletti C., *et al*. "Progesterone: The key factor of the beginning of life". *International Journal of Molecular Sciences* 23.22 (2022): 14138.
4. Mathyk B., *et al*. "A critical appraisal of studies on endometrial thickness and embryo transfer outcome". *Reproductive Biomedicine Online* 47.4 (2023): 103259.
5. Brodeur TY., *et al*. "Increasing endometrial thickness beyond 8 mm does not alter clinical pregnancy rate after single euploid embryo transfer". *Reproductive Sciences* 31.4 (2024): 1045-1052.
6. Chen SL., *et al*. "Endometrial thickness is a reliable predictor of pregnancy in *in vitro* fertilization and embryo transfer cycles". *Fertility and Sterility* 94.6 (2010): 1960-1963.

7. Kovacs, P., *et al*. "The effect of endometrial thickness on IVF/ICSI outcome". *Human Reproduction* 18.11 (2003): 2337-2341.

8. Demirol A and T Gurgan. "Effect of endometrial thickness on implantation rates during *in vitro* fertilization". *Fertility and Sterility* 82.3 (2004): 431-434.

9. Craciunas L., *et al*. "Conventional and modern markers of endometrial receptivity: A systematic review and meta-analysis". *Human Reproduction Update* 25.2 (2019): 202-223.

10. Gao G., *et al*. "Endometrial thickness and IVF cycle outcomes: A meta-analysis". *Reproductive Biomedicine Online* 40.1 (2020): 124-133.

11. Kasius A., *et al*. "Endometrial thickness and pregnancy rates after IVF: A systematic review and meta-analysis". *Human Reproduction Update* 20.4 (2014): 530-541.

12. Momeni M., *et al*. "A meta-analysis of the relationship between endometrial thickness and outcome of *in vitro* fertilization cycles". *Journal of Human Reproductive Sciences* 4.3 (2011): 130-137.

13. Csapo AI., *et al*. "Effects of luteectomy and progesterone replacement therapy in early pregnant patients". *American Journal of Obstetrics and Gynecology* 115.6 (1973): 759-765.

14. Gallos ID., *et al*. "Optimal endometrial thickness to maximize live births and minimize pregnancy losses: analysis of 25,767 fresh embryo transfers". *Reproductive Biomedicine Online* 37.5 (2018): 542-548.

15. Lv H., *et al*. "Effect of endometrial thickness and embryo quality on live-birth rate of fresh IVF/ICSI cycles: a retrospective cohort study". *Reproductive Biology and Endocrinology* 18.1 (2020): 89.

16. Liu KE., *et al*. "The impact of a thin endometrial lining on fresh and frozen-thaw IVF outcomes: an analysis of over 40,000 embryo transfers". *Human Reproduction* 33.10 (2018): 1883-1888.

17. "Assisted Reproductive Technology (ART) and Surrogacy Abroad". U.S. Department of State (2024).

18. "Surrogacy by State". American Society for Reproductive Medicine (2024).

19. "Recommendations for Practices Using Gestational Carriers: A Committee Opinion". American Society for Reproductive Medicine (2022).

20. Fleischer AC., *et al*. "Sonography of the endometrium during conception and nonconception cycles of *in vitro* fertilization and embryo transfer". *Fertility and Sterility* 46.3 (1986): 442-447.

21. Gonen Y., *et al*. "Endometrial thickness and growth during ovarian stimulation: a possible predictor of implantation in *in vitro* fertilization". *Fertility and Sterility* 52.3 (1989): 446-450.

22. Mahutte N., *et al*. "Optimal endometrial thickness in fresh and frozen-thaw *in vitro* fertilization cycles: an analysis of live birth rates from 96,000 autologous embryo transfers". *Fertility and Sterility* 117.4 (2022): 792-800.

23. ESHRE Working Group on Recurrent Implantation Failure., *et al*. "ESHRE Good Practice Recommendations on Recurrent Implantation Failure". *Human Reproduction Open* (2023): hoad023.

24. Groenewoud Eva R., *et al*. "Influence of endometrial thickness on pregnancy rates in modified natural cycle frozen-thawed embryo transfer". *Fertility and Sterility* 97.7 (2018): 808-815.

25. Ju W., *et al*. "Endometrial compaction is associated with the outcome of artificial frozen-thawed embryo transfer cycles: a retrospective cohort study". *Journal of Assisted Reproduction and Genetics* 40.7 (2023): 1649-1660.

26. Check JH., *et al*. "The effect of endometrial thickness and echo pattern on pregnancy rates during assisted reproduction". *Fertility and Sterility* 80.5 (2003): 1130-1135.

27. De Geyter C., *et al*. "Prospective evaluation of the ultrasound appearance of the endometrium in a cohort of 1,186 infertile women". *Fertility and Sterility* 73.1 (2000): 106-113.

28. Shakerian B., *et al*. "Endometrial thickness is not predictive for live birth after embryo transfer, even without a cutoff". *Fertility and Sterility* 116.1 (2021): 130-137.

29. Al-Jefout M., *et al*. "Vascular endothelial growth factor and endometriosis". *Obstetrics and Gynecology International* (2009).

30. Stewart CL., *et al*. "Blastocyst implantation depends on maternal expression of leukaemia inhibitory factor". *Nature* 359.6390 (1992): 76-79.

31. Marquardt RM., *et al*. "Progesterone and estrogen signaling in the endometrium: what goes wrong in endometriosis?" *International Journal of Molecular Sciences* 20.15 (2019): 3822.

32. Marquardt Rebecca M., *et al*. "Contemporary understanding of the genetic basis of endometrial receptivity". *Fertility and Sterility* 111.3 (2019): 620-628.

33. Bulletti C., *et al*. "Targeted drug delivery in gynaecology: the first uterine pass effect". *Human Reproduction* 13.4 (1998): 998-1004.

34. Mackens S., *et al*. "Frozen embryo transfer: A review on the optimal endometrial preparation and timing". *Human Reproduction* 32.11 (2017): 2234-2242.

35. Díaz-Gimeno P., *et al*. "A genomic diagnostic tool for human endometrial receptivity based on the transcriptomic signature". *Fertility and Sterility* 95.1 (2011): 50-60.

36. Noyes N., *et al*. "Endometrial thickness appears to be a significant factor in embryo implantation in *in-vitro* fertilization". *Human Reproduction* 10.4 (1995): 919-922.

37. Noyes RW., *et al*. "Dating the endometrial biopsy". *Fertility and Sterility* 1.1 (1950): 3-25.

38. Lessey BA and SL Young. "What exactly is endometrial receptivity?" *Clinical Obstetrics and Gynecology* 62.2 (2019): 356-367.

39. Lessey Bruce A. "Assessment of endometrial receptivity". *Fertility and Sterility* 96.3 (2011): 522-529.

40. Stewart Colin L., *et al*. "Blastocyst implantation depends on maternal expression of leukaemia inhibitory factor". *Nature* 359.6390 (1992): 76-79.

41. Seppala Markku, *et al*. "Glycodelin in reproductive physiology and pathology". *Current Opinion in Obstetrics and Gynecology* 14.3 (2002): 275-281.

42. Lessey Bruce A., *et al*. "Integrin adhesion molecules in the human endometrium. correlation with the normal and abnormal menstrual cycle". *Journal of Clinical Investigation* 90.1 (1992): 188-195.

43. Bulun Serdar E., *et al*. "Regulation of Ki-67 proliferation index in normal and abnormal endometrium". *Obstetrics and Gynecology International* (2010): 1-8.

44. Bagot Catherine N and Linda C Troy. "HOXA10 and uterine receptivity". *Reproductive Biomedicine Online* 4.3 (2001): 303-307.

45. Sher Gur., *et al*. "Endometrial vascularity during controlled ovarian hyperstimulation and the outcome of *in vitro* fertilization". *Fertility and Sterility* 71.5 (1999): 870-875.

46. Aplin John D., *et al*. "MUC1, glycans and the cell-surface barrier to embryo implantation". *Biochemical Society Transactions* 36.6 (2008): 1470-1474.

47. Lutjen P., *et al*. "The establishment and maintenance of pregnancy using *in vitro* fertilization and embryo donation in a patient with primary ovarian failure". *Nature* 307.5947 (1984): 174-175.

48. Simón C., *et al*. "Clinical evidence for a detrimental effect on uterine receptivity of high serum oestradiol concentrations in high and normal responder patients". *Human Reproduction* 10.9 (1995): 2432-2437.

49. Eftekhar M., *et al*. "Effect of low-dose HCG on endometrial thickness and ivf outcomes: a randomized controlled trial". *Human Fertility* 17.2 (2014): 130-135.

50. Margalioth EJ., *et al*. "Investigation and treatment of repeated implantation failure following IVF-ET". *Human Reproduction* 21.12 (2006): 3036-3043.

51. Santamaria X and C Simon. "Endometrial receptivity: Cell adhesion molecules and implantation of the human embryo". *Human Reproduction Update* 18.3 (2012): 219-232.

52. Xu B., *et al*. "Vascular endothelial growth factor (VEGF) gene polymorphisms in endometriosis: a meta-analysis". *Molecular Biology Reports* 40.6 (2013): 4743-4751.

53. Rubinstein M., *et al*. "Low-dose aspirin treatment improves ovarian responsiveness, uterine and ovarian blood flow velocity, implantation, and pregnancy rates in patients undergoing *in vitro* fertilization: a prospective, randomized, double-blind placebo-controlled assay". *Fertility and Sterility* 71.5 (1999): 825-829.

54. Lédée-Bataille N., *et al*. "Concentration of leukaemia inhibitory factor (LIF) in uterine flushing fluid is highly predictive of embryo implantation". *Human Reproduction* 17.1 (2002): 213-218.

55. Domar AD., *et al*. "Impact of group psychological interventions on pregnancy rates in infertile women". *Fertility and Sterility* 73.4 (2000): 805-811.

56. Huniadi A., *et al*. "Autologous platelet-rich plasma (PRP) efficacy on endometrial thickness and infertility: a single-centre experience from Romania". *Medicina* 59.9 (2023): 1532.

57. Stewart A., *et al*. "Determining a threshold measurement of endometrial thickness for asymptomatic postmenopausal women: a tertiary centre case series". *Australian and New Zealand Journal of Obstetrics and Gynaecology* 62.6 (2022): 887-893.

58. Barash A., *et al*. "Local injury to the endometrium doubles the incidence of successful pregnancies in patients undergoing *in vitro* fertilization". *Fertility and Sterility* 79.6 (2003): 1317-1322.

59. "Randomized controlled trial of the effect of endometrial injury on implantation and clinical pregnancy rates during the first ICSI cycle". *Cochrane Database of Systematic Reviews.*

60. Raine-Fenning NJ., *et al*. "The relationship between endometrial vascularity and endometrial thickness during the peri-implantation period in women undergoing assisted conception". *Human Reproduction* 19.5 (2004): 1045-1051.

61. Roberto da Costa RP., *et al*. "Endometrial nitric oxide production and nitric oxide synthases in the equine endometrium: relationship with microvascular density during the estrous cycle". *Domestic Animal Endocrinology* 32.4 (2006): 287-302.

62. Bulletti C., *et al*. "Paracrine regulation of menstruation". *Journal of Reproductive Immunology* 39.1-2 (1998): 89-104.

63. Bulletti C., *et al*. "Basement membrane components in normal, hyperplastic, and neoplastic endometrium". *Cancer* 62.1 (1988): 142-149.

64. Bulletti C., *et al*. "Extraction of estrogens by human perfused uterus". *American Journal of Obstetrics and Gynecology* 159.2 (1988): 509-515.

65. Bulletti C., *et al*. "Uterine contractility during the menstrual cycle". *Human Reproduction* 17.4 (2002): 877-883.

66. Bulletti C., *et al*. "The role of progesterone in uterine contractility and embryo implantation". *Journal of Assisted Reproduction and Genetics* 18.7 (2001): 443-446.

67. Bulletti C., *et al*. "Electromechanical activities of human uteri during extra-corporeal perfusion with ovarian steroids". *Human Reproduction* 8 (1998): 1558-1563.

68. Bulletti, C., *et al*. "Uterine contractility and embryo implantation". *Current Opinion in Obstetrics and Gynecology* 17.3 (2005): 265-276.

69. Doyle N., *et al*. "Effect of timing by endometrial receptivity testing vs. standard timing of frozen embryo transfer on live birth in patients undergoing *in vitro* fertilization: a randomized clinical trial". *JAMA* 328.21 (2022): 2117-2125.

70. Doyle JO., *et al*. "Double-blind, multicenter, randomized clinical trial to compare the live birth rate in patients who had era or not in their single EET cycle". *Journal of Assisted Reproduction and Genetics* (2022).

71. Tang Y., *et al*. "An update on experimental therapeutic strategies for thin endometrium". *Endocrines* 4.4 (2023): 672-684.

72. Shalma NM., *et al*. "The efficacy of intrauterine infusion of platelet rich plasma in women undergoing assisted reproduction: a systematic review and meta-analysis". *BMC Pregnancy and Childbirth* 23 (2023): 843.

73. Kamath MS., *et al*. "Granulocyte-colony stimulating factor administration for subfertile women undergoing assisted reproduction". *Cochrane Database of Systematic Reviews* 1.1 (2020): CD013226.

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