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Review

Microbiota dysbiosis and probiotic interventions in endometriosis: Current evidence and therapeutic perspectives

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Abstract

Background: Endometriosis is a chronic, estrogen-dependent inflammatory disorder characterized by the presence of endometrial-like tissue outside the uterine cavity, leading to pelvic pain, infertility, and reduced quality of life. Emerging evidence suggests that dysbiosis of the gut and female reproductive tract microbiota may contribute to immune dysregulation, chronic inflammation, and disease progression.

Main body: This narrative review synthesizes current evidence on microbiota alterations in endometriosis and evaluates the therapeutic potential of microbiome-targeted interventions, particularly probiotics, prebiotics, and synbiotics. Available data indicate that women with endometriosis frequently exhibit reduced abundance of Lactobacillus spp. and increased representation of opportunistic or pro-inflammatory bacteria in the female reproductive tract and, in some studies, the gut microbiota. Microbial products such as lipopolysaccharide may activate Toll-like receptor 4-mediated inflammatory signaling, promoting cytokine production, immune dysfunction, and lesion persistence. Probiotic administration, especially with Lactobacillus and Bifidobacterium strains, has shown potential to restore microbial balance, enhance natural killer cell activity, modulate macrophage responses, and reduce pro-inflammatory mediators including TNF-α\alphaα and IL-6. Preclinical studies suggest that probiotics may reduce lesion size and improve inflammatory profiles, whereas early clinical studies indicate possible benefits for pain-related symptoms. However, evidence for prebiotics and synbiotics in endometriosis remains limited.

Conclusion: Microbiota dysbiosis may represent an important component of endometriosis pathophysiology. Microbiome-targeted therapies, particularly probiotics, are promising adjunctive strategies; however, robust, well-designed clinical trials are required to determine optimal strains, dosing regimens, treatment duration, safety, and patient selection before routine clinical use can be recommended.

Keywords: Dysbiosis, Endometriosis, Female reproductive tract, Inflammation, Microbiota, Prebiotics, Probiotics, Synbiotic

Introduction

Endometriosis (EM) is a chronic, estrogen-dependent inflammatory disease defined by the ectopic presence of endometrial glands and stroma outside the uterine cavity (1). It affects approximately 10% of reproductive-aged women worldwide, corresponding to nearly 190 million individuals (2). The disorder is clinically associated with dysmenorrhea, chronic pelvic pain, dyspareunia, infertility, and substantial impairment in quality of life (3, 4). In addition to its clinical burden, endometriosis imposes considerable socioeconomic costs because of delayed diagnosis,

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long-term symptom recurrence, reduced work productivity, and repeated medical and surgical treatment (5).

The pathogenesis of endometriosis is multifactorial and remains incompletely understood. Retrograde menstruation is widely regarded as a major initiating event, allowing endometrial cells to enter the peritoneal cavity and potentially implant at ectopic sites (6). However, because retrograde menstruation also occurs in many women who do not develop the disease, additional pathogenic mechanisms must be involved. These include altered immune surveillance, genetic predisposition, hormonal dysregulation, angiogenesis, oxidative stress, and stem cell-related mechanisms (7-9). Familial aggregation further supports a hereditary contribution to disease susceptibility (10, 11).

Recently, increasing attention has been directed toward the role of the microbiota in endometriosis. The upper female reproductive tract was once considered sterile; however, molecular sequencing studies have demonstrated the presence of microbial communities throughout the female reproductive tract (FRT), including the endometrium (12, 13). Under physiological conditions, these communities are often dominated by Lactobacillus species, which promote mucosal homeostasis through lactic acid production, pathogen exclusion, and immune regulation (14-16). Emerging evidence indicates that women with endometriosis may exhibit disturbances in both FRT and gut microbiota, including reduced Lactobacillus abundance and increased prevalence of opportunistic bacterial taxa (12, 13, 17).

Such dysbiosis may influence endometriosis through several mechanisms. Bacterial products such as lipopolysaccharide (LPS) can activate inflammatory signaling pathways, particularly through Toll-like receptor 4 (TLR4), thereby promoting cytokine release and immune activation (13, 18). In addition, gut microbial communities may influence estrogen metabolism through the estrobolome, which may be particularly relevant in an estrogen-dependent disease (19). These observations have led to growing interest in microbiome-targeted strategies, especially probiotics, as potential adjunctive therapies in endometriosis.

The present narrative review summarizes current evidence on microbiota dysbiosis in endometriosis and critically evaluates the therapeutic potential of probiotics, prebiotics, and synbiotics (Table 1).

Main body

Microbiota alterations in endometriosis:

Advances in sequencing technologies have enabled increasingly detailed characterization of microbial communities within the female reproductive tract and gastrointestinal system (20). In healthy women, the lower reproductive tract is typically dominated by Lactobacillus species, which contribute to defense against pathogens through maintenance of a low vaginal pH, production of antimicrobial metabolites, and reinforcement of mucosal barrier function (15, 21). However, several studies suggest that women with endometriosis exhibit altered microbial profiles.

In the female reproductive tract, decreased abundance of Lactobacillus spp. together with increased prevalence of opportunistic or potentially pathogenic bacteria has been reported in women with endometriosis (13). Higher levels of taxa such as Streptococcaceae and Moraxellaceae have been identified in affected individuals (17), while other genera, including Pseudomonas, Acinetobacter, Vagococcus, and Comamonas, have also been detected (13). These findings support the possibility that reproductive tract dysbiosis may be associated with the disease.

Gut microbiota alterations have also been described, particularly in patients with advanced endometriosis (17, 22). Some studies have reported increased abundance of Escherichia/Shigella, suggesting a shift toward a more inflammatory microbial pattern (22). Given the role of the gut microbiota in immune regulation, epithelial barrier integrity, and estrogen recirculation, such changes may be biologically relevant to endometriosis pathogenesis (19, 23).

Nevertheless, interpretation of these findings requires caution. Microbiota composition is influenced by menstrual cycle phase, age, hormonal status, sexual activity, infertility, prior antibiotic exposure, and sampling methodology (19, 21, 24, 25). Furthermore, studies of low-biomass niches such as the endometrium are particularly susceptible to contamination and technical variation (15, 21). Thus, although an association between dysbiosis and endometriosis is increasingly supported, a consistent microbial signature has not yet been established.

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Table 1. High-level critical appraisal of probiotic studies in endometriosis

Study	Study type	Intervention	Main findings	Strengths	Limitations	Overall appraisal
Itoh et al. (23)	Preclinical murine model	Lactobacillus gasseri OLL2809	Inhibited development of ectopic endometrial lesions; effect associated with NK-cell activation	Mechanistic relevance; biologically plausible immune pathway; experimental control	Animal model; limited direct clinical generalizability; dose and translational applicability uncertain	Strong preclinical support for immunomodulatory probiotic effects, but not sufficient for clinical recommendation
Itoh et al. (26)	Randomized, double-blind, placebo-controlled clinical study	Lactobacillus gasseri OLL2809	Improved menstrual pain and dysmenorrhea in women with endometriosis	Controlled design; clinically relevant pain outcome; human population	Likely small sample size; limited duration; strain-specific findings; unclear effects on lesion biology	Promising early clinical evidence for symptom relief, but requires replication in larger trials
Khodaverdi et al. (27)	Pilot placebo-controlled randomized clinical trial	Oral Lactobacillus supplementation	Reduced pain severity in women with endometriosis	Randomized placebo-controlled design; patient-centered outcome	Pilot scale; underpowered; strain composition and mechanistic endpoints limited; short follow-up	Suggestive of benefit, but evidence remains preliminary
Chouzenoux et al. (28)	Review/conceptual therapeutic report with preclinical emphasis	Oral probiotic treatments	Proposed probiotics as a novel therapeutic strategy and summarized supportive preclinical observations	Highlights translational rationale; integrates mechanistic and experimental evidence	Not a primary interventional trial; limited direct clinical data	Useful for conceptual framing, but not confirmatory evidence
Jiang et al. (18)	Mechanistic/review evidence	Probiotic-related microbiota modulation	Summarized links between microbiota, inflammation, cytokine signaling, and probiotic potential	Strong mechanistic synthesis; relevant to disease biology	Secondary source; not direct therapeutic eve	

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Mechanistic links between dysbiosis and endometriosis:

The biological plausibility of a microbiota endometriosis axis is supported by several interconnected mechanisms. One of the most studied pathways involve activation of innate immune signaling by bacterial endotoxins. LPS can activate TLR4 signaling and downstream inflammatory cascades, leading to increased production of cytokines such as TNF-α\alphaα and IL-6 (13, 18). These mediators are known to contribute to angiogenesis, cellular proliferation, lesion survival, and pain in endometriosis.

Dysbiosis may also affect immune cell behavior. Macrophages in endometriosis exhibit altered phagocytic capacity and polarization states that may favor tissue remodeling and lesion maintenance rather than efficient clearance of ectopic endometrial tissue (29-31). Likewise, reduced NK-cell cytotoxicity is a well-recognized feature of endometriosis (32) . Because microbial signals can influence both innate and adaptive immune responses, disturbances in host–microbe interactions may contribute to the aberrant inflammatory and immune landscape characteristic of the disease.

A further mechanistic consideration is the role of the gut microbiota in estrogen metabolism. Microbial enzymes can deconjugate estrogens in the intestine, affecting enterohepatic circulation and systemic estrogen exposure (19). Since endometriosis is strongly estrogen dependent, dysbiosis within the gut microbiome may influence disease activity through hormonal as well as inflammatory pathways. However, direct evidence linking microbiome-mediated estrogen metabolism to clinical endometriosis remains limited.

Conventional treatment and the rationale for microbiome-targeted therapy:

Current treatments for endometriosis primarily aim to suppress ovarian estrogen production, control pain, and remove lesions surgically (33, 34). First-line medical therapies include nonsteroidal anti-inflammatory drugs, combined hormonal contraceptives, and progestins (34). Second-line options include GnRH agonists, GnRH antagonists, aromatase inhibitors, and danazol (35-40). Although these strategies are often effective for symptom control, they may be associated with adverse effects, poor long-term tolerability, and frequent recurrence after treatment discontinuation (36).

These limitations have prompted investigation of non-hormonal and adjunctive approaches, including anti-inflammatory and metabolic therapies such as metformin and dichloroacetate (41). In parallel, microbiome-targeted strategies have emerged as a potentially attractive option because they may modulate inflammation, mucosal barrier function, and immune responses without directly suppressing reproductive endocrine function. Animal data showing attenuation of endometriosis progression after antibiotic treatment further support a role for host–microbiota interactions in disease biology (42).

Mechanisms of probiotic action relevant to endometriosis

Probiotics are live microorganisms that confer a health benefit when administered in adequate amounts (43). The most extensively studied strains belong to the genera Lactobacillus and Bifidobacterium, which have demonstrated beneficial effects in multiple gastrointestinal and immune-mediated conditions (43-46).

Their proposed mechanisms of action are highly relevant to endometriosis. First, probiotics can inhibit pathogen colonization through competitive exclusion, acidification of the local environment, and production of antimicrobial compounds (47). Second, they may strengthen epithelial barrier function and reduce microbial translocation, thereby limiting exposure to inflammatory stimuli (48, 49). Third, probiotics can modulate host immune responses by affecting dendritic cell maturation, T-cell polarization, macrophage activation, and cytokine production (50-52). Some strains have also been shown to attenuate TLR4-mediated signaling and suppress downstream inflammatory pathways (49).

In endometriosis, these mechanisms may be advantageous because the disease is characterized by chronic inflammation, impaired immune surveillance, and altered cytokine networks. Thus, the therapeutic potential of probiotics may extend beyond simple correction of microbial imbalance to include broader immunomodulatory and anti-inflammatory effects.

Evidence for probiotic interventions in endometriosis:

Current evidence for probiotic use in endometriosis derives from both preclinical and early clinical studies. Preclinical data are particularly informative. In a

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murine model, Lactobacillus gasseri OLL2809 inhibited the development of ectopic endometrial lesions, an effect associated with activation of NK cells (19). This is of particular interest because reduced NK-cell activity is a recognized feature of endometriosis (32). Other experimental findings suggest that probiotics may reduce lesion burden, attenuate oxidative stress, and improve inflammatory profiles (18).

Human evidence remains limited but encouraging. A pilot placebo-controlled randomized clinical trial reported that oral Lactobacillus reduced pain severity in women with endometriosis (27). Likewise, a randomized, double-blind, placebo-controlled study found that Lactobacillus gasseri OLL2809 improved menstrual pain and dysmenorrhea in affected patients (23). These data suggest a possible role for probiotics in symptom relief, particularly in pain-related outcomes.

Potential mechanisms underlying these benefits include restoration of Lactobacillus-dominant microbial communities, reduction of pro-inflammatory cytokines such as TNF-α\alphaα and IL-6, enhancement of NK-cell activity, and modulation of macrophage responses (50). Broader evidence from other pain-related disorders also suggests that probiotics may influence neuroimmune pathways and visceral sensitivity (53, 54). However, whether these findings translate consistently to endometriosis-associated pain requires further clarification.

At present, the clinical evidence remains insufficient to support routine use of probiotics in standard endometriosis care. Existing studies are limited by small sample size, short follow-up, heterogeneity in probiotic strain and dose, and variability in clinical endpoints. Moreover, probiotic effects are strain specific, and results obtained with one formulation should not be generalized to others (65). Accordingly, larger and more rigorously designed randomized controlled trials are required.

Prebiotics and synbiotics:

Prebiotics are non-digestible substrates that selectively stimulate the growth or activity of beneficial microorganisms (43). Examples such as inulin, oligofructose, and lactulose can alter microbial metabolism and promote the production of beneficial metabolites (55-57). In theory, prebiotics may improve inflammatory and metabolic pathways relevant to endometriosis by supporting a more favorable gut microbial environment.

Synbiotics combine probiotics with prebiotics and may provide synergistic benefits by improving survival, colonization, and functional activity of administered strains (58). This approach may be particularly useful where sustained microbiome modulation is desired. However, direct evidence for prebiotics or synbiotics in endometriosis is currently sparse.

Some related data suggest that modulation of reproductive tract microbial composition may be feasible. For example, lactoferrin supplementation has been associated with increased Lactobacillus abundance in the endometrium of infertile women with dysbiosis (59), and beneficial effects have also been reported in refractory bacterial vaginosis (60). Although these findings cannot be directly extrapolated to endometriosis, they support further evaluation of microbiome-supportive interventions in gynecologic disorders.

Current limitations and future directions:

Despite growing interest in the microbiome–endometriosis axis, several limitations constrain the current evidence base. Most human microbiome studies are observational and cross-sectional, precluding causal inference. It remains unclear whether dysbiosis is a driver of endometriosis, a consequence of the disease environment, or both. In addition, substantial heterogeneity in sampling sites, sequencing approaches, bioinformatic pipelines, and patient characteristics has limited comparability across studies.

The therapeutic literature is also at an early stage. Probiotic studies in endometriosis are relatively few and typically underpowered. Important variables, including strain selection, dose, duration, route of administration, baseline microbiome composition, and disease phenotype, remain poorly defined. Standardized outcome measures, including pain, lesion progression, inflammatory biomarkers, and microbiome endpoints, will be essential for future trials.

Further work should also examine whether microbiome-targeted therapies exert their effects primarily through local changes in the reproductive tract, systemic immunomodulation, gut-derived metabolites, altered estrogen metabolism, or combined mechanisms. Integration of metagenomics,

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metabolomics, transcriptomics, and immune profiling may help identify biologically meaningful patient subgroups and improve therapeutic precision.

Limitations and future perspectives:

Current evidence linking microbiota dysbiosis to endometriosis is promising but remains preliminary. Most studies are observational, cross-sectional, and based on small, heterogeneous cohorts, limiting causal inference and reducing comparability across populations, specimen types, sequencing methods, and analytical pipelines. Interpretation is further complicated by important confounders, including menstrual cycle phase, hormonal therapy, antibiotic exposure, diet, and infertility status, as well as by contamination concerns in low-biomass reproductive tract samples. Likewise, probiotic studies remain limited by small sample sizes, short follow-up, and substantial variability in strain composition, dose, and outcome assessment, making it difficult to draw firm therapeutic conclusions. Future research should prioritize large, well-phenotyped multicenter cohorts, standardized sampling and analytical methods, longitudinal designs to clarify temporality, and adequately powered randomized trials evaluating strain-specific interventions with both clinical and mechanistic endpoints. Such advances will be essential to determine whether microbiome-targeted strategies have a reproducible and clinically meaningful role in endometriosis management.

Conclusion

Emerging evidence suggests that microbiota dysbiosis may contribute to the pathophysiology of endometriosis through interactions involving chronic inflammation, immune dysregulation, and possibly estrogen metabolism. Alterations in both gut and female reproductive tract microbiota, particularly reduced Lactobacillus abundance and enrichment of inflammatory taxa, support the concept of a microbiota-associated disease component.

Among microbiome-targeted interventions, probiotics have shown the greatest promise. Preclinical studies indicate that selected strains, particularly Lactobacillus gasseri OLL2809, may reduce lesion development and modulate immune responses, while early clinical studies suggest potential benefits for pain-related symptoms. However, evidence remains preliminary, and no microbiome-based intervention can yet be recommended as standard therapy.

Well-designed clinical trials with adequate power, standardized probiotic formulations, mechanistic endpoints, and long-term follow-up are needed to determine the clinical utility of probiotics, prebiotics, and synbiotics in endometriosis. Until such evidence is available, these approaches should be regarded as promising adjunctive strategies rather than established therapeutic options.

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Conflicts of Interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

References

1. Kennedy S, Bergqvist A, Chapron C, D'Hooghe T, Dunselman G, Greb R, et al. ESHRE guideline for the diagnosis and treatment of endometriosis. Human reproduction (Oxford, England). 2005;20(10):2698-704.
2. Zondervan KT, Becker CM, Missmer SA. Endometriosis. The New England journal of medicine. 2020;382(13):1244-56.
3. Sinaii N, Plumb K, Cotton L, Lambert A, Kennedy S, Zondervan K, et al. Differences in characteristics among 1,000 women with endometriosis based on extent of disease. Fertility and sterility. 2008;89(3):538-45.
4. Agarwal SK, Chapron C, Giudice LC, Laufer MR, Leyland N, Missmer SA, et al. Clinical diagnosis of endometriosis: a call to action. American journal of obstetrics and gynecology. 2019;220(4):354.e1-.e12.
5. Ellis K, Munro D, Clarke J. Endometriosis Is Undervalued: A Call to Action. Frontiers in global women's health. 2022;3:902371.
6. D'Hooghe TM, Bambra CS, Raeymaekers BM, De Jonge I, Lauweryns JM, Koninckx PR. Intrapelvic injection of menstrual endometrium causes endometriosis in baboons (Papio cynocephalus and Papio anubis). American journal of obstetrics and gynecology. 1995;173(1):125-34.

[DOI: 10.22088/caspjrm.11.2.50]

7. Du H, Taylor HS. Contribution of bone marrow-derived stem cells to endometrium and endometriosis. Stem cells (Dayton, Ohio). 2007;25(8):2082-6.
8. Vassilopoulou L, Matalliotakis M, Zervou MI, Matalliotaki C, Krithinakis K, Matalliotakis I, et al. Defining the genetic profile of endometriosis. Experimental and therapeutic medicine. 2019;17(5):3267-81.
9. Becker CM, Laufer MR, Stratton P, Hummelshoj L, Missmer SA, Zondervan KT, et al. World Endometriosis Research Foundation Endometriosis Phenome and Biobanking Harmonisation Project: I. Surgical phenotype data collection in endometriosis research. Fertility and sterility. 2014;102(5):1213-22.
10. Nouri K, Ott J, Krupitz B, Huber JC, Wenzl R. Family incidence of endometriosis in first-, second-, and third-degree relatives: case-control study. Reproductive biology and endocrinology : RB&E. 2010;8:85.
11. dos Reis RM, de Sá MF, de Moura MD, Nogueira AA, Ribeiro JU, Ramos ES, et al. Familial risk among patients with endometriosis. Journal of assisted reproduction and genetics. 1999;16(9):500-3.
12. Winters AD, Romero R, Gervasi MT, Gomez-Lopez N, Tran MR, Garcia-Flores V, et al. Does the endometrial cavity have a molecular microbial signature? Scientific reports. 2019;9(1):9905.
13. Wei W, Zhang X, Tang H, Zeng L, Wu R. Microbiota composition and distribution along the female reproductive tract of women with endometriosis. Annals of clinical microbiology and antimicrobials. 2020;19(1):15.
14. Moore DE, Soules MR, Klein NA, Fujimoto VY, Agnew KJ, Eschenbach DA. Bacteria in the transfer catheter tip influence the live-birth rate after in vitro fertilization. Fertility and sterility. 2000;74(6):1118-24.
15. Baker JM, Chase DM, Herbst-Kralovetz MM. Uterine Microbiota: Residents, Tourists, or Invaders? Frontiers in immunology. 2018;9:208.
16. Pelzer ES, Willner D, Buttini M, Huygens F. A role for the endometrial microbiome in dysfunctional menstrual bleeding. Antonie van Leeuwenhoek. 2018;111(6):933-43.
17. Svensson A, Brunkwall L, Roth B, Orho-Melander M, Ohlsson B. Associations Between Endometriosis and Gut Microbiota. Reproductive sciences (Thousand Oaks, Calif). 2021;28(8):2367-77.
18. Jiang I, Yong PJ, Allaire C, Bedaiwy MA. Intricate Connections between the Microbiota and Endometriosis. International journal of molecular sciences. 2021;22(11).
19. Baker JM, Al-Nakkash L, Herbst-Kralovetz MM. Estrogen-gut microbiome axis: Physiological and clinical implications. Maturitas. 2017;103:45-53.
20. Moreno I, Simon C. Relevance of assessing the uterine microbiota in infertility. Fertility and sterility. 2018;110(3):337-43.
21. Altmäe S, Rienzi L. Endometrial microbiome: new hope, or hype? Reproductive biomedicine online. 2021;42(6):1051-2.
22. Ata B, Yildiz S, Turkgeldi E, Brocal VP, Dinleyici EC, Moya A, et al. The Endobiota Study: Comparison of Vaginal, Cervical and Gut Microbiota Between Women with Stage 3/4 Endometriosis and Healthy Controls. Scientific reports. 2019;9(1):2204.
23. Itoh H, Sashihara T, Hosono A, Kaminogawa S, Uchida M. Lactobacillus gasseri OLL2809 inhibits development of ectopic endometrial cell in peritoneal cavity via activation of NK cells in a murine endometriosis model. Cytotechnology. 2011;63(2):205-10.
24. Moreno I, Garcia-Grau I, Perez-Villaroya D, Gonzalez-Monfort M, Bahçeci M, Barrionuevo MJ, et al. Endometrial microbiota composition is associated with reproductive outcome in infertile patients. Microbiome. 2022;10(1):1.
25. Wang J, Li Z, Ma X, Du L, Jia Z, Cui X, et al. Translocation of vaginal microbiota is involved in impairment and protection of uterine health. Nature communications. 2021;12(1):4191.
26. Itoh H, Uchida M, Sashihara T, Ji ZS, Li J, Tang Q, et al. Lactobacillus gasseri OLL2809 is effective especially on the menstrual pain and dysmenorrhea in endometriosis patients: randomized, double-blind, placebo-controlled study. Cytotechnology. 2011;63(2):153-61.
27. Khodaverdi S, Mohammadbeigi R, Khaledi M, Mesdaghinia L, Sharifzadeh F, Nasiripour S, et al. Beneficial Effects of Oral Lactobacillus on Pain Severity in Women Suffering from Endometriosis: A Pilot Placebo-Controlled Randomized Clinical Trial. International journal of fertility & sterility. 2019;13(3):178-83.
28. Chouzenoux S, Jeljeli M, Bourdon M, Doridot L, Thomas M, Barbeito A. A new strategy against endometriosis: Oral probiotic treatments. Clin Obstet Gynecol Reprod Med. 2021;7(1):1-11.
29. Hogg C, Panir K, Dhami P, Rosser M, Mack M, Soong D, et al. Macrophages inhibit and enhance endometriosis depending on their origin. Proceedings of the National Academy of Sciences of the United States of America. 2021;118(6).
30. Wu J, Xie H, Yao S, Liang Y. Macrophage and nerve interaction in endometriosis. Journal of neuroinflammation. 2017;14(1):53.
31. Hudson QJ, Ashjaei K, Perricos A, Kuessel L, Husslein H, Wenzl R, et al. Endometriosis Patients Show an Increased M2 Response in the Peritoneal CD14(+low)/CD68(+low) Macrophage Subpopulation Coupled with an Increase in the T-helper 2 and T-regulatory Cells. Reproductive sciences (Thousand Oaks, Calif). 2020;27(10):1920-31.
32. Thiruchelvam U, Wingfield M, O'Farrelly C. Natural Killer Cells: Key Players in Endometriosis.

[DOI: 10.22088/caspjrm.11.2.50]

American journal of reproductive immunology (New York, NY : 1989). 2015;74(4):291-301.
33. Rice VM. Conventional medical therapies for endometriosis. Annals of the New York Academy of Sciences. 2002;955:343-52; discussion 89-93, 96-406.
34. Dunselman GA, Vermeulen N, Becker C, Calhaz-Jorge C, D'Hooghe T, De Bie B, et al. ESHRE guideline: management of women with endometriosis. Human reproduction (Oxford, England). 2014;29(3):400-12.
35. Ferrero S, Barra F, Leone Roberti Maggiore U. Current and Emerging Therapeutics for the Management of Endometriosis. Drugs. 2018;78(10):995-1012.
36. Abu Hashim H. Gonadotrophin-releasing hormone analogues and endometriosis: current strategies and new insights. Gynecological endocrinology : the official journal of the International Society of Gynecological Endocrinology. 2012;28(4):314-21.
37. Ferrero S, Remorgida V, Maganza C, Venturini PL, Salvatore S, Papaleo E, et al. Aromatase and endometriosis: estrogens play a role. Annals of the New York Academy of Sciences. 2014;1317:17-23.
38. Donaldson VH. Danazol. The American journal of medicine. 1989;87(3n):49n-55n.
39. Diamond MP, Carr B, Dmowski WP, Koltun W, O'Brien C, Jiang P, et al. Elagolix treatment for endometriosis-associated pain: results from a phase 2, randomized, double-blind, placebo-controlled study. Reproductive sciences (Thousand Oaks, Calif). 2014;21(3):363-71.
40. Taylor HS, Giudice LC, Lessey BA, Abrao MS, Kotarski J, Archer DF, et al. Treatment of Endometriosis-Associated Pain with Elagolix, an Oral GnRH Antagonist. The New England journal of medicine. 2017;377(1):28-40.
41. Leow HW, Koscielniak M, Williams L, Saunders PTK, Daniels J, Doust AM, et al. Dichloroacetate as a possible treatment for endometriosis-associated pain: a single-arm open-label exploratory clinical trial (EPiC). Pilot and feasibility studies. 2021;7(1):67.
42. Chadchan SB, Cheng M, Parnell LA, Yin Y, Schriefer A, Mysorekar IU, et al. Antibiotic therapy with metronidazole reduces endometriosis disease progression in mice: a potential role for gut microbiota. Human reproduction (Oxford, England). 2019;34(6):1106-16.
43. Liu Y, Tran DQ, Rhoads JM. Probiotics in Disease Prevention and Treatment. Journal of clinical pharmacology. 2018;58 Suppl 10(Suppl 10):S164-s79.
44. Szajewska H, Skórka A, Ruszczyński M, Gieruszczak-Białek D. Meta-analysis: Lactobacillus GG for treating acute gastroenteritis in children--updated analysis of randomised controlled trials. Alimentary pharmacology & therapeutics. 2013;38(5):467-76.
45. Wang Y, Li X, Ge T, Xiao Y, Liao Y, Cui Y, et al. Probiotics for prevention and treatment of respiratory tract infections in children: A systematic review and meta-analysis of randomized controlled trials. Medicine. 2016;95(31):e4509.
46. Zuccotti G, Meneghin F, Aceti A, Barone G, Callegari ML, Di Mauro A, et al. Probiotics for prevention of atopic diseases in infants: systematic review and meta-analysis. Allergy. 2015;70(11):1356-71.
47. Beachey EH. Bacterial adherence: adhesin-receptor interactions mediating the attachment of bacteria to mucosal surface. The Journal of infectious diseases. 1981;143(3):325-45.
48. Thomas CM, Versalovic J. Probiotics-host communication: Modulation of signaling pathways in the intestine. Gut microbes. 2010;1(3):148-63.
49. Liu Y, Fatheree NY, Mangalat N, Rhoads JM. Lactobacillus reuteri strains reduce incidence and severity of experimental necrotizing enterocolitis via modulation of TLR4 and NF-κB signaling in the intestine. American journal of physiology Gastrointestinal and liver physiology. 2012;302(6):G608-17.
50. Amar Y, Rizzello V, Cavaliere R, Campana S, De Pasquale C, Barberi C, et al. Divergent signaling pathways regulate IL-12 production induced by different species of Lactobacilli in human dendritic cells. Immunology letters. 2015;166(1):6-12.
51. Gao C, Ganesh BP, Shi Z, Shah RR, Fultz R, Major A, et al. Gut Microbe-Mediated Suppression of Inflammation-Associated Colon Carcinogenesis by Luminal Histamine Production. The American journal of pathology. 2017;187(10):2323-36.
52. Habil N, Al-Murrani W, Beal J, Foey AD. Probiotic bacterial strains differentially modulate macrophage cytokine production in a strain-dependent and cell subset-specific manner. Beneficial microbes. 2011;2(4):283-93.
53. Richter ON, Dorn C, Rösing B, Flaskamp C, Ulrich U. Tumor necrosis factor alpha secretion by peritoneal macrophages in patients with endometriosis. Archives of gynecology and obstetrics. 2005;271(2):143-7.
54. Rousseaux C, Thuru X, Gelot A, Barnich N, Neut C, Dubuquoy L, et al. Lactobacillus acidophilus modulates intestinal pain and induces opioid and cannabinoid receptors. Nature medicine. 2007;13(1):35-7.
55. Parnell JA, Reimer RA. Weight loss during oligofructose supplementation is associated with decreased ghrelin and increased peptide YY in overweight and obese adults. The American journal of clinical nutrition. 2009;89(6):1751-9.
56. Trautwein EA, Rieckhoff D, Erbersdobler HF. Dietary inulin lowers plasma cholesterol and triacylglycerol and alters biliary bile acid profile in hamsters. The Journal of nutrition. 1998;128(11):1937-43.
57. Pool-Zobel B, van Loo J, Rowland I, Roberfroid MB. Experimental evidences on the potential of

[DOI: 10.22088/caspjrm.11.2.50]

prebiotic fructans to reduce the risk of colon cancer. The British journal of nutrition. 2002;87 Suppl 2:S273-81.
58. López-Moreno A, Aguilera M. Probiotics Dietary Supplementation for Modulating Endocrine and Fertility Microbiota Dysbiosis. Nutrients. 2020;12(3).
59. Kyono K, Hashimoto T, Kikuchi S, Nagai Y, Sakuraba Y. A pilot study and case reports on endometrial microbiota and pregnancy outcome: An analysis using 16S rRNA gene sequencing among IVF patients, and trial therapeutic intervention for dysbiotic endometrium. Reproductive medicine and biology. 2019;18(1):72-82.
60. Otsuki K, Imai N. Effects of lactoferrin in 6 patients with refractory bacterial vaginosis. Biochemistry and cell biology = Biochimie et biologie cellulaire. 2017;95(1):31-3.

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