

# Could Endometriosis Be Caused by Bacteria?

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February 23, 2024

## STORY AT-A-GLANCE

- › A 2023 study found *Fusobacterium* could be linked to the development of endometriosis, which is a proliferation of uterine endometrial tissue in areas of the abdomen outside the uterus
- › The condition causes pain, heavy and irregular periods, fatigue and gastrointestinal symptoms during a menstrual period, such as diarrhea, constipation and pain with urination or bowel movements
- › Certain species of *Fusobacterium* are commonly found in the human gut and oral flora, but infections with other invasive species have been linked to a wide range of clinical presentations from non-severe pharyngitis to life-threatening abscesses and sepsis
- › Endometriosis places women at an increased risk of other health problems, including infertility, cancer, cutaneous melanoma, Non-Hodgkin's lymphoma, autoimmune diseases, cardiovascular disease, asthma, obesity, migraine headaches and irritable bowel syndrome
- › Women can take several steps to reduce the risk of developing endometriosis or help reduce the symptoms, including avoiding endocrine-disrupting chemicals as the condition is hormone dependent, avoiding sugar to reduce inflammation and pain, and considering several nutraceuticals that may help reduce symptoms

There is a good and a bad side to bacteria. One 2023 study<sup>1</sup> published in *Science Translational Medicine* revealed data suggesting one genus of an anaerobic, gram-negative bacteria,<sup>2</sup> *Fusobacterium*, plays an influential role in the development of

endometriosis. This genus of bacteria has species that live symbiotically with humans and others that develop invasive infections.

The inappropriate use of antibiotics and bacterial infections has culminated in the "greatest public health challenge of our time"<sup>3</sup> – antimicrobial resistance. One important focus of attaining and maintaining optimal health is supporting a balanced gut microbiome. When bacteria develop the ability to avoid the drugs designed to kill them, resistant infections can proliferate and become difficult or impossible to treat.

Your gut microbiome is a major contributor to a wide range of physical, mental and emotional health conditions. Research links gut microbial dysbiosis to obesity, Type 2 diabetes, cardiovascular disease,<sup>4</sup> athletic performance,<sup>5</sup> cognitive impairment,<sup>6</sup> depression and anxiety.<sup>7</sup> It should then come as no surprise that bacteria may play a role, regardless of how significant, in many of the prevalent chronic health conditions that plague society.

The film, "The Invisible Extinction,"<sup>8</sup> highlights the work of microbiologists Dr. Martin Blaser and Gloria Dominguez-Bello – a husband-wife team – who warn that the [human microbiome is endangered](#), putting human health at risk.

As data indicating the significance of a healthy microbiome to overall health continues to mount, researchers are also identifying ways in which harmful bacteria play a role in noninfectious disease development. And, one particular bacterial infection associated with endometriosis, Fusobacterium, may suggest a potential treatment pathway for this painful disorder.<sup>9</sup>

## **Could This Bacteria Trigger Endometriosis?**

The 2023 study<sup>10</sup> found that Fusobacterium, a bacterial type that's commonly found in the human gut and oral flora, may be linked to endometriosis. The study included 155 women in Japan<sup>11</sup> and found 64% of women presenting with endometriosis had Fusobacterium within ovarian endometriotic lesions. However, less than 10% of women without endometriosis had the Fusobacterium in their endometrium.<sup>12</sup>

The researchers used an animal model and inoculated Fusobacterium into mice which then increased myofibroblasts and the weight and number of endometriotic lesions. The mice were treated with antibiotics and researchers found this could, in large part, not only prevent endometriosis from developing, but help reduce the endometriotic lesions that were already established.

The researchers believe the data support a potential mechanism for the development of endometriosis and suggest it could be an approach to treating the disease.<sup>13</sup>

In addition to evaluating for the presence of Fusobacterium within human endometrial tissue and testing an animal model, the researchers also used cell culture experiments to find that the bacteria initiated a substance called TGF-beta, which appeared to activate normally dormant cells.

Although certain species of Fusobacterium live symbiotically within the oral and gut microflora, this species of Fusobacterium is invasive and has been linked to other infections and diseases.<sup>14</sup> Although the infections with Fusobacterium are uncommon,<sup>15</sup> they tend to infect younger and older individuals and cause a wide range of clinical symptoms from non-severe pharyngitis to life-threatening abscesses and sepsis.

## **What Is Endometriosis?**

The word "endometriosis" is derived from the name of the tissue that lines the uterus, which is the endometrium. This lining is what the body releases with each menstrual cycle. Each month, the body grows a new endometrium in preparation for a potential pregnancy. Endometriosis occurs when this tissue grows in areas of the abdomen outside of the uterus.

According to Johns Hopkins Medicine, the condition affects up to 10% of women.<sup>16</sup> The endometrial tissue most often grows on or around the reproductive organs, such as the ovaries, fallopian tubes, space between the uterus and the rectum, or the lining of the pelvic cavity. Less frequently, it can also grow around the bladder, intestines, rectum and stomach.

The condition increases pain associated with menstrual cramps and can cause pain during or after sex. Women may also experience heavy or irregular periods, fatigue and gastrointestinal symptoms during a menstrual period such as diarrhea, constipation and pain with urination or bowel movements.

Although the condition has no known cause, data does show certain factors increase the risk, including starting menstruation before age 11, a family history of endometriosis and periods that last more than 7 days. Although in many cases, a diagnosis of endometriosis begins with severe symptoms, some women can have endometriotic lesions outside the uterus but have no symptoms.<sup>17</sup>

While data from the featured study is encouraging, as it helps to at least point to a potential trigger, it's important to note that endometriosis is likely multifactorial and may have cultural or environmental differences. A 2021 study<sup>18</sup> published in *Reproductive Sciences* evaluated a group of 371 fertile women with endometriosis, 175 from China and 196 from Italy. Symptoms and quality of life were compared, which revealed significant differences between the two groups.

Italian women presented with symptoms at a younger age, more frequently with severe pain, were more often diagnosed with deep infiltrating endometriosis and had more systemic comorbidities at the time of diagnosis than women from China. Scores on tests also showed the Italian group of women had worse health-related quality of life.

In the group of Chinese women, there was less pain, diagnosis at an older age, ovarian and superficial endometriosis and better quality of life scores. The researchers suggested that the differences may be related to ethnicity, healthcare system or social and cultural background.<sup>19</sup>

## **Endometriosis and Comorbidities**

Endometriosis is debilitating. According to *Science Alert*,<sup>20</sup> women in the U.K. often wait an average of 7.5 years before seeing their physician for a diagnosis and Yale

Medicine<sup>21</sup> estimates that women in the U.S. may experience symptoms for 10 years before getting a proper diagnosis.

Unfortunately, this places these women at risk of more health problems, including infertility. In some cases, endometriosis causes complete infertility, but in other cases, fertility may not be affected. Research<sup>22</sup> also suggests that women with endometriosis have a higher risk of pregnancy-related complications, including preterm delivery, miscarriage, preeclampsia, bowel perforation and uterine rupture.

When left untreated, endometriosis not only leads to infertility, but other organ damage. A 2015 systematic review<sup>23</sup> of the literature identified studies that looked at the association between endometriosis and specific diseases.

They found increasing evidence that women with endometriosis have a higher risk of several chronic diseases, suggesting that the condition is not harmless with respect to long-term health. According to this review, women with endometriosis had a "higher risk of ovarian and breast cancers, cutaneous melanoma, asthma, and some autoimmune, cardiovascular and atopic diseases, and at decreased risk of cervical cancer."<sup>24</sup>

In a separate article,<sup>25</sup> one of the scientists postulated potential explanations for the associations, including that studies may have had a methodological bias. Other explanations included the potential that endometriosis induces physiological changes that increase the risk of chronic disease, that women with endometriosis share specific risk factors for chronic disease, or that the treatment for endometriosis could increase the risk of some chronic diseases.

Analysis of data from Taiwan<sup>26</sup> identified similar associations between endometriosis and chronic diseases. In this population, the researchers also found an association with irritable bowel syndrome, migraine headaches, pelvic inflammatory disease, obesity, chronic liver disease, cardiovascular disease, diabetes, rheumatoid arthritis and chronic renal disease.

A 2023 study<sup>27</sup> published in the journal Nature Genetics may help explain the comorbidity with other inflammatory and pain-related conditions. In a genome-wide

association meta-analysis of European and East Asian participants, the researchers:

*"... observed significant genetic correlations between endometriosis and 11 pain conditions, including migraine, back and multisite chronic pain (MCP), as well as inflammatory conditions, including asthma and osteoarthritis."*

The severity of the symptoms can affect mental health<sup>28</sup> and may compromise social relationships, which in turn influences support systems. Depression and anxiety can also amplify the perception of pain. In one study,<sup>29</sup> researchers estimated that at least one-third of women with endometriosis suffer from depression and anxiety.

## Reducing Symptoms of Endometriosis

Insulin sensitivity may also play a role in endometriosis. A 2019 review<sup>30</sup> looked at the likelihood of the coexistence of Type 1 diabetes and endometriosis, including the prospect that therapeutic strategies could help reduce complications. While Type 1 diabetes is an autoimmune disease, endometriosis is not.

However, according to the paper, they share similar pathophysiological pathways, including an association with chronic inflammation and an overactive immune response. A 2002 study<sup>31</sup> also showed women with endometriosis more frequently had mechanical dysfunction in the gastrointestinal system and reactive hypoglycemia with normal insulin levels.

According to the researchers, the nerve dysfunction found in women with endometriosis was identical to that found in individuals with insulin resistance and resulted in debilitating gastrointestinal symptoms. In addition to strategies that improve insulin sensitivity and reduce resistance, women with endometriosis may consider addressing other factors that contribute to symptoms of endometriosis, such as:

- **Avoiding endocrine disruptors** – Endometriosis is hormone dependent, and data has linked exposure to environmental endocrine disrupting chemicals (EDCs) with the development of endometriosis. A 2023 study<sup>32</sup> looked at epidemiological and experimental data of four EDCs and found:

*"The available information strongly indicates that environmental exposure to EDCs such as PCBs, dioxins, BPA, and phthalates individually or collectively contribute to the pathophysiology of endometriosis."*

One commonly used EDC is oxybenzone, found in many sunscreen formulations. The Environmental Working Group (EWG) calls oxybenzone "the most worrisome sunscreen active ingredient,"<sup>33</sup> as the chemical is readily absorbed through the skin, is associated with skin reactions and has demonstrated hormone-disrupting properties.

A 2012 study<sup>34</sup> associated benzophenone, the class of drugs to which oxybenzone belongs,<sup>35</sup> as an EDC that has a high likelihood of increasing the risk of endometriosis. EDC chemicals are found in many everyday products, including pesticides, plastics and food storage materials, and antibacterial soaps.<sup>36</sup>

- **Avoiding sugar** – Dysregulated blood sugar has a significant influence on endometriosis as it promotes an inflammatory response in the body,<sup>37</sup> which may contribute to a flare-up of the disease and raise pain levels. As blood sugar rises, cortisol can also rise which lowers progesterone levels and sets the stage for higher levels of estrogen.<sup>38</sup>
- **Considering physical activity** – Physical activity and exercise is an important factor in attaining and maintaining optimal health. Yet, for women with endometriosis, they may want to consider physical activity a prescription to help lower inflammation and painful symptoms. While the literature examining endometriosis is not conclusive, data does reveal that physical activity helps lower the inflammatory response.<sup>39</sup>

One review of the literature<sup>40</sup> was unable to find enough quality studies to produce a quantitative meta-analysis, but did identify a couple studies showing activity improved pain intensity and decreased stress levels. The researchers suggested future high-quality randomized controlled trials were necessary to determine if physical activity improved symptoms and quality of life.

A 2023 study<sup>41</sup> in the International Journal Gynecology and Obstetrics, reviewed the benefits of physical therapy in women with endometriosis, doing a meta-analysis on six studies that evaluated pain intensity and quality of life measures. The data show these non-pharmacological therapies "are a therapeutic option for women with endometriosis for improving pain intensity and physical function."

- **Considering supplements** – Women with endometriosis may also consider nutraceuticals that have demonstrated a beneficial effect against the pain and symptoms of endometriosis. N-acetylcysteine (NAC), chasteberry and melatonin may all offer some relief.

In a 2013 Italian study,<sup>42</sup> women who took 600 mg of NAC three times a day for three consecutive days per week, for three months, saw such significant improvement that half of the treatment group were able to cancel their surgeries. Eight of the 47 women in the intervention group had complete remission. The researchers concluded that:<sup>43</sup>

*"Our results are better than those reported after hormonal treatments ... NAC actually represents a simple effective treatment for endometriosis, without side effects, and a suitable approach for women desiring a pregnancy."*

Chasteberry is known as "the woman's herb," and has a long history of use in female fertility and hormonal health. A leaf decoction has demonstrated a reduction in symptoms of endometriosis within clinical practice and reduction in endometrial cyst size.<sup>44</sup> Chasteberry may also help reduce inflammation and balance reproductive hormones.<sup>45</sup>

Chasteberry may help increase progesterone production, which affects the luteal phase of the menstrual cycle, the time from ovulation until bleeding starts. These issues are often linked to menstrual irregularities, including endometriosis.

Melatonin has also shown some promise for pain control. In one study,<sup>46</sup> 10 mg per day of **melatonin** helped decrease pain by 39.8% and dysmenorrhea by 38.01%.



## Sources and References

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