

Close to a revolution in the treatment of endometriosis

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Translated from Le Journal de Montréal, December 18th, 2023.

Japanese researchers report that the presence of a pro-inflammatory bacteria in the uterine lining could play a crucial role in the development of endometriosis, a very painful disease that affects one in ten women.

Endometriosis is a disease caused by the migration and development of tissues of the uterine lining outside the uterus (ovaries, fallopian tubes, peritoneum, among others). These abnormal locations cause chronic inflammatory reactions and internal lesions which cause violent pain to those who suffer from them, especially during periods and sexual intercourse, and can represent a cause of infertility.

Although endometriosis is very common, affecting around one in ten women, there are still very few effective treatments for this debilitating disease.

RETROGRADE FLOW

The migration of endometrial cells out of the uterus is thought to be largely caused by retrograde menstruation, which is when menstrual blood flows backward through the fallopian tubes and into the pelvic cavity instead of out of the vagina.

However, studies indicate that most women of childbearing age have retrograde periods, meaning other factors are responsible for the development of endometriosis.

PRO-INFLAMMATORY BACTERIA

A major advance in the understanding of this phenomenon has just been published by a Japanese research team (1). By examining endometrial samples taken during a hysterectomy (excision of the uterus) of women with or without endometriosis, researchers observed that two-thirds of women with the disease had infiltration of bacteria of the *Fusobacterium* genus in the endometrium, while this bacteria was rarely observed in the control samples.

Further analysis revealed that certain growth factors produced by these bacteria were also present in high quantities and stimulated the multiplication and migration of myofibroblasts, a class of cells found in connective tissue (the supporting tissue that holds together endometrial cells).

This observation is very interesting, because we know that myofibroblasts actively contribute to endometriosis due to their inflammatory properties and their abundant production of collagen responsible for fibrosis.

It therefore appears that bacterial infection of the endometrium by *Fusobacterium* causes chronic inflammation which activates myofibroblasts and promotes their migration outside the uterus to form foci of endometriosis.



This bacterial contribution to the development of endometriosis is also suggested by the observation that lesions typical of endometriosis were larger and more frequent in mice infected with *Fusobacterium* and that antibiotic treatment, vaginally, slowed the development of the disease and made it possible to reduce the size and number of lesions already present.

ANTIBIOTICS

Like any bacterial infection, *Fusobacterium* infection can be treated with antibiotics. However, this class of bacteria is not sensitive to usual antibiotics and is known to be able to survive for a long time inside tissues (it is frequently observed in colorectal tumors, for example). The bacteria, however, remains sensitive to certain antibiotics such as metronidazole, which demonstrated good effectiveness in the study on mice mentioned earlier.

A clinical trial is underway to determine whether antibiotics of this type can also relieve symptoms in humans.

Recognition of a contribution of a bacterial infection to the development of a disease is often the prelude to a spectacular improvement in its treatment. We only have to think of stomach ulcers caused by *Helicobacter pylori*, a discovery which revolutionized the treatment of this condition and earned Barry Marshall and Robin Warren the Nobel Prize in Medicine in 2005.

It is hoped that the identification of a bacterial origin in a high proportion of cases of endometriosis could also prove to be a huge step forward in the effective treatment of this disease. This is an important scientific revolution in our understanding of this pathology.

- (1) Muraoka A et al. *Fusobacterium* infection facilitates the development of endometriosis through the phenotypic transition of endometrial fibroblasts. *Sci. Transl. Med.* 2023; 15(700):eadd1531.