

Pain, epigenetics and endometriosis: Research team wants to know how molecular tweaks affect which women hurt the most

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Most of us probably know at least one woman, and maybe quite a few more, with endometriosis. Despite the disease's prevalence, there is no consensus on the cause of it, the existing treatment options leave a lot to be desired, and there are too few ways for women to, at the very least, effectively numb the pain that the disease provokes.

Scientists – who over the years have suspected hormones, the immune system, [environmental toxins](#), genetics or some combination – still have a long way to go in terms of better understanding the disease's molecular bases. Researchers at the Joan C. Edwards School of Medicine at Marshall University, in Huntington, W.V., say that a great deal more attention should be paid to the daily [pain](#) suffered by endometriosis patients.

"Endometriosis is a not a well understood disease ," says Nalini Santanam, who is heading up the West Virginia research team looking into the [epigenetics](#) of pain in endometriosis. Santanam, who has studied the disease for more than 20 years, expresses disappointment in the lack of notice given to the pain associated with the disease.

"First of all, even though it's highly prevalent, we don't really have people talking about the disease. It's a woman's disease. It's pain," she says. "Women have [menstrual pain](#), and in most countries we don't even talk about this. It's taboo. People say, 'It's just pain. Get over it. In a few

days, it's gone.' And they don't think that there's actually an underlying disease there."

About the disease

Endometriosis occurs when cells normally present within the uterus migrate outside the organ and attach to other parts in the [pelvis](#). This outgrowth causes scarring, nodules of bumps on [pelvic organs](#), or [ovarian cysts](#). In some cases, organs can become fused by the [scar tissue](#). The disease affects about one out of every seven women, but, because some don't exhibit symptoms, the actual number could be larger.

A common cause of [infertility](#), endometriosis usually presents itself during the teen years in the form of pain in the pelvic region and lower back, but it's not usually diagnosed till women are in their mid-20s, often because they are having difficulty having babies. Hormones, including birth-control pills, can ease the symptom. Over-the-counter painkillers are often recommended.

"Unfortunately, there are few options for treatment," says Kristeena Ray, a doctoral student in Santanam's lab. "More complex treatment can involve surgeries to remove the damaged tissue or, in extreme cases, a complete hysterectomy." It's not uncommon for endometriosis to recur after surgery.

Pain can't be ignored

Much like the tissue does when situated correctly in the [uterus](#), the misplaced endometriosis grows, breaks down and sloughs off; however, because of its location, the detritus cannot exit the body, and it is believed that this misplaced chemical cocktail causes pain.

"It is extremely common for the pain suffered by these women to interfere with their day-to-day activities," says Ray.

Women often report pain during and after sexual intercourse. Interestingly, the stage of endometriosis is not necessarily indicative of the amount of pain.

When Santanam was working at Emory University a few years ago, her group looked into how nutritional supplementation affects potential endometriosis biomarkers. "One of the projects was a clinical study where we'd given patients vitamin E and C to see if it changes any markers related to endometriosis, and we found that it did," she explains. "What also was interesting was that it also decreased pain in these women. So in our mind, there must be something else, some other pain-related markers. So over the past few years I've been trying to concentrate on that particular aspect: What are the pain-related markers? And then there's the epigenetics."

The epigenetics of endometriosis and pain

Though several large gene-expression studies have identified many deregulated genes in endometriosis patients, the specific genetic factors remain elusive. The West Virginia group, meanwhile, is focusing on epigenetic mechanisms, the changes caused to DNA and gene expression by the environment and lifestyle.

Ray is heading up the group's investigation. Her preliminary findings will be presented Tuesday, April 22, at the annual meeting of the American Society for Biochemistry and Molecular Biology, which is being held in conjunction with the Experimental Biology conference in Boston.

"We're looking at epigenetic markers in patients with endometriosis,"

Ray explains. "We believe that our continuing research in this area will help us better understand what leads to endometriosis in some women and find alternate treatment options for its symptoms."

Unlike DNA mutations, epigenetic modifications are dynamic, constantly affected by environmental and lifestyle factors, which makes enzymes that affect epigenetic changes sought-after targets for drug development.

Santanam emphasizes that so little is known about the epigenetics of pain. "When you look at pain research, they mostly focus on back pain, fibromyalgia – those types of diseases. There are only now looking at epigenetics of pain," says Santanam. "If you look at all the other fields, there are already epigenetic-related drugs available in the market."

But, if epigenetic aberrations are found by her group or others, Santanam says, that could go a long way toward narrowing down biomarkers to be used in diagnostics and perhaps a personalized approach to [endometriosis](#) and its associated symptoms such as pain.

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