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Heather G. Kuruvilla

Cedarville University, [heatherkuruvilla@cedarville.edu](mailto:heatherkuruvilla@cedarville.edu)

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# Interstitial Cystitis: The Estrogen Connection

Heather G. Kuruvilla, Ph.D.

Department of Science and Mathematics, Cedarville University, Cedarville, OH USA

## Abstract

Interstitial cystitis (IC), or painful bladder syndrome, is an autoimmune condition with an unknown etiology. Common symptoms include urinary urgency, frequency, and bladder and urethral pain and burning. This condition, like many autoimmune disorders, disproportionately affects females; therefore, female sex hormones are hypothesized to play a role in the disorder. My hypothesis is that estrogen, both endogenous and synthetic, affects the severity of IC symptoms. Through surveying the available literature on interstitial cystitis, I have found that IC symptoms often correlate with low estrogen. My hope is that by understanding more about how hormones affect IC, we can come up with better treatment plans for IC sufferers.

## Introduction

Interstitial cystitis (IC) is a painful autoimmune disorder characterized by urinary urgency, frequency, and burning, along with bladder pain. IC is recognized as a disability under the Americans with Disabilities Act, and an estimated 50% of IC sufferers are unable to work due to their pain.

The cause of IC remains unknown, and currently, there is only one drug, Elmiron, which has been approved by the FDA to treat this disorder. Elmiron is hypothesized to work by coating the bladder lining, though its mechanism of action is unknown. However, Elmiron can interfere with liver function, cause hair loss, and lead to internal bleeding. Because of these side effects, and because Elmiron does not work for everyone, many patients are seeking alternative treatment methods.

Symptoms of IC can often be ameliorated by following a strict elimination diet. However, this is not always effective. As a result, many IC patients are treated using narcotics, vaginal valium, or antidepressants.

Since many women report a worsening of IC symptoms that correlates with the onset of their menstrual period, it is my hypothesis that IC symptoms correlate with low blood estrogen levels.

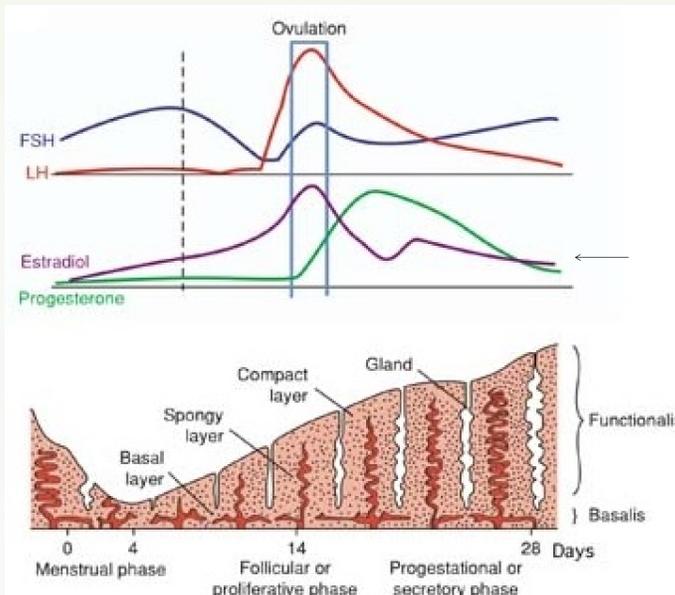
## Methods

Literature survey was conducted using Google Scholar. Search terms were "interstitial cystitis" and "estrogen", and "estrogen" and "autoimmunity". The dates of the referenced publications ranged from 2007 to 2015.

## Results

**Table 1. Low estrogen is likely to play a role in interstitial cystitis.** The perimenstrual phase of the menstrual cycle, as seen in Figure 1, which is characterized by low estrogen correlates with the highest prevalence of IC pain. In addition, mice who lacked an estrogen receptor developed a phenotype resembling IC, implying that estrogen signaling is required for normal bladder homeostasis.

Reference	Findings
He. <i>et al.</i> , 2015	Estrogen is likely to play a role in interstitial cystitis
Yamamoto <i>et al.</i> , 2015	An increase in interstitial cystitis symptoms is associated with the perimenstrual phase of the menstrual cycle.
Powell-Boone <i>et al.</i> , 2007	The perimenstrual phase of the menstrual cycle is associated with the highest amount of interstitial cystitis pain.
Imamov <i>et al.</i> , 2007	Female mice who were deficient in estrogen receptor $\beta$ developed a bladder phenotype resembling human interstitial cystitis.



**Figure 1. From Wikimedia Commons. The Human Menstrual Cycle.** The perimenstrual phase is characterized by low estrogen levels.

## HOW DOES ESTROGEN AFFECT IMMUNE CELLS?



**Table 2. Estrogen plays various roles within the immune system, depending upon its concentration, the estrogen receptor type expressed by the immune cell in question, and the type of immune cell.**

Reference	Immune Cell Type	Estrogen's Effect
Tan. <i>et al.</i> , 2015	Th <sub>1</sub> , T <sub>reg</sub>	Concentration-dependent; stimulated Th <sub>1</sub> cells at low concentration and T <sub>reg</sub> cells at high concentrations
Andersson <i>et al.</i> , 2015	Th <sub>17</sub>	Increases migration of Th <sub>17</sub> cells to lymph nodes during early stages of autoimmune arthritis, but decreases migration of Th <sub>17</sub> cells to joints during the later stages of the disease.
Laffont and Guéry, 2015	Dendritic Cells	Estrogen activates dendritic cells.
Muñoz-Cruz <i>et al.</i> , 2015	Mast cells	Estrogen caused histamine release from mast cells of female rats, but not male rats.

## Conclusions

- The relationship between estrogen and the immune system is highly complex.
- The correlation between IC symptoms and the perimenstrual phase of the menstrual cycle suggest that using a form of birth control which uses a constant level of estrogen and skips the menstrual phase may provide symptom relief. Anecdotal evidence from the #icstrong support group suggest that some women are already doing this, and find it helpful in alleviating their IC symptoms.
- A controlled study using the method suggested above would be helpful to IC patients and their healthcare providers.

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## Contact Information

Heather G. Kuruvilla, Professor of Biology  
Cedarville University  
[heatherkuruvilla@cedarville.edu](mailto:heatherkuruvilla@cedarville.edu)