Can germs cause premenstrual syndrome?

Each month a woman's body prepares itself for pregnancy. Monthly hormonal cycles alter immunological defenses to allow survival of sperm cells, the fertilized egg, and the developing embryo. At the onset of each cycle immune defenses are broadly competent. About two weeks later when her egg cell is released, renewing possibilities for fertilization and pregnancy, the cell-killing arsenal of the immune system is suppressed. This immunological shift leaves a woman vulnerable to flares of persistent infections that may be smoldering but held in check by a fully balanced immune system. During the day or so just before each new cycle many women experience symptoms of illness. When a persistent infection is not an accepted cause of the symptoms, they are collected into an umbrella category referred to as premenstrual syndrome - PMS.

Over 300 different symptoms have been associated with PMS. Some can be debilitating. If PMS were just a quirky side-effect of a woman's hormonal system, debilitating aspects of PMS should have been weeded out by natural selection. The debilitating nature of PMS therefore requires looking deeply into this condition to determine why it exists.

Nearly a decade ago we hypothesized that PMS symptoms were, in fact, flares of unrecognized persistent infections that arose because of the monthly shift in a woman's immune system. To test this hypothesis, we reviewed medical records from an urban population to determine whether debilitating symptoms of PMS were associated with infectious agents. We suspected sexually transmitted pathogens because sexual transmission favors evolution of long-term persistence within individuals to allow for transmission to future sexual contacts. We focused on headache, nausea, pain and depression.

The results showed depression and pain were significantly associated with *Chlamydia trachomatis* infection. Headache was associated with the protozoal pathogen, *Trichomonas vaginalis*, and nausea with the bacterium, *Gardnerella vaginalis*. The patients were unaware that they were infected prior to reporting their symptoms; therefore knowledge of the infection did not affect their likelihood of reporting any specific symptom (i.e. knowledge of being infected did not lead to depressive symptoms simply because the woman was aware she had a sexually transmitted infection).

We found the association with depression particularly intriguing, because *C. trachomatis* was higher on our suspect list for depression than the other pathogens for a simple reason. The body sequesters tryptophan during infection to "starve" pathogens. Women rely on this depletion of tryptophan particularly during the last half of the menstrual cycle, because it does not pose a hazard for sperm cell, egg cell and developing embryo. But *C. trachomatis* can make its own tryptophan and may therefore persist indefinitely in the face of tryptophan restriction. *Chlamydia* may therefore persist easily from cycle to cycle. The continued presence *C. trachomatis* may therefore lead to persistent depletion of tryptophan. This depletion is important because tryptophan

is converted to serotonin in the brain--and serotonin helps to maintain positive mood. The body's persistent suppression of tryptophan in a vain attempt to control *Chlamydia* may therefore generate depression as a response to this pathogen.

Trichomonas vaginalis is predominantly controlled by tryptophan-rich antimicrobial compounds. It could therefore persist under conditions of tryptophan restriction. Although *Trichomonas* resides in the vaginal tract, it manufactures putrescene which increases the permeability of the blood-brain barrier, leading to headaches.

Gardnerella vaginalis is relatively understudied. The mechanism for *its* association with nausea is still a mystery.

Overall these findings cast new light on the symptoms of PMS. Practically it suggests that some women suffering from depression, pain, headache or nausea may benefit from the control of persistent infections through use of antibiotics.

Publication

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