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Interstitial cystitis: a neuroimmunoendocrine disorder.

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Interstitial cystitis (IC) is a sterile bladder condition occurring primarily in females. It is characterized by frequency, nocturia, and suprapubic pain. IC symptoms are exacerbated during ovulation and under stress, thus implicating neurohormonal processes. The most prevalent theories to explain the pathophysiology of IC appear to be altered bladder lining and increased number of activated bladder mast cells. A defective bladder glycosaminoglycan (GAG) layer could allow penetration of allergic triggers, as well as chemicals, food preservatives, drugs, toxins, and adherent bacteria, all of which can activate bladder mast cells. Vasoactive, nociceptive, and proinflammatory molecules released can lead to immune cell infiltration and can sensitize neurons to secrete neurotransmitters or neuropeptides that can further activate mast cells. Mast cell-derived proteases can directly cause tissue damage, and it is noteworthy that urine tryptase is elevated in IC. Bladder mast cells are located close to neuronal processes, which are increased in IC, and they can be activated in situ by acetylcholine (ACh) and substance P (SP). Such activation is augmented by estradiol, which acquires significance in view of the fact that human bladder mast cells express estrogen receptors, but few progesterone receptors, which may explain the worsening of IC symptoms during ovulation. Finally, acute psychological stress in rats leads to mast cell activation that can be reduced by depletion of SP or neutralization of peripheral immunocorticotropin-releasing hormone (CRH). These findings suggest that IC could be a

syndrome with neural, immune, and endocrine components, in which activated mast cells play a central role.

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