

—discrete inflammatory lesions, previously believed to be ulcers, that have a well-characterized inflammatory profile on histologic and pathologic analysis. While Hunner lesions are easily identified under direct vision by cystoscopy, a spectrum of other, less obvious inflammatory patterns in the bladder is associated with infiltration of acute and chronic inflammatory cells and mast cells. This inflammation observed on histologic analysis can be so subtle that it cannot be recognized under direct visual examination of the bladder with cystoscopy.

Investigators in the Multidisciplinary Approach to the Study of Chronic Pelvic Pain (MAPP) Research Network have found that, among patients with UCPPS, women exhibit more robust inflammatory responses to stimulation of Toll-like receptor 2 (TLR2) and TLR4. Furthermore, an increased response to stimulation of TLR4 predicts more severe symptoms, widespread pain (vs pelvic/bladder pain only), and a higher number of chronic overlapping pain conditions (COPCs). Further studies aimed at a better understanding of these findings are under way.

■ UROTHELIAL DYSFUNCTION

Urothelial Permeability and the Glycosaminoglycan Layer The stratified epithelium of the bladder—the urothelium—is composed of basal precursor cells, intermediate cells, and a layer of specialized, superficial epithelial cells called *umbrella cells*. Collectively, these layers are responsible for the various functions of the bladder lining. One important function of the urothelium is to provide a robust barrier layer. This function is fulfilled by the dense layering of glycosaminoglycans (GAGs) on the luminal surface of the urothelium along with a complex arrangement of numerous intercellular tight junctions among urothelial cells that protects the underlying bladder interstitium from the constituents of the urine resting in the bladder.

Defects in this barrier function—either disruptions in the GAG layer or disruptions in the epithelial layer itself or its cellular junctions—have been proposed as a possible mechanism for bladder pain in IC/BPS patients. This theory, while still popular, lacks definitive evidence supporting it as the etiology of this disease.