

BASIC RESEARCH

**GAGGING THE LEAKY
BLADDER IN IC**

New research from the Oklahoma University Health Sciences Center has shown that glycosaminoglycan (GAG) replenishment therapy in rats can inhibit the inflammatory response commonly seen in patients with interstitial cystitis (IC), providing a possible mechanism for the success of this therapy in some patients.

Although the exact causes of IC are unknown, much evidence has amassed supporting the 'leaky bladder' theory, which suggests that the disease is characterized by loss of the GAG layer lining the bladder. Loss of this layer renders the bladder permeable to K⁺ ions present in urine, which can cause pain and urinary urgency via their depolarizing effect on deep sensory nerves. IC is also associated with long-term inflammation, with increased levels of mast cells and neutrophils in the bladder.

The study, published in *Urology*, used a rat model of IC—produced by physical damage to the bladder using dilute acid—to assess GAG replenishment with chondroitin sulfate. The researchers found that chondroitin sulfate treatment in rats with IC significantly reduced the inflammatory response compared with untreated rats, with evidence of a response just 2 days after treatment. During this time the number of mast cells increased fourfold in rats who did not receive treatment. At 4 days after chondroitin sulfate treatment, the difference in number of mast cells was highly significant between the two groups ($P=0.0004$).

"Using our bladder damage model, we demonstrated that intravesical administration of chondroitin sulfate substantially inhibited the recruitment of inflammatory cells to the suburothelial space," lead investigator Robert Hurst told *Nature Reviews Urology*. "This clearly demonstrates that GAG replenishment therapy is effective in inhibiting the inflammatory response resulting from a leaky bladder and provides a strong rationale for this therapeutic approach."

Although these results are encouraging and show promise for similar therapy in humans, it is unclear how accurately the acute IC rat model replicates human disease, and the dosing regimen of chondroitin sulfate—and, indeed, other GAGs—still needs optimization.

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Original article Engles, C. D. *et al.* Intravesical chondroitin sulfate inhibits recruitment of inflammatory cells in an acute acid damage "leaky bladder" model of cystitis. *Urology* doi:10.1016/j.urology.2011.10.010