New Concepts Emerge for Treatment of IC

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San Antonio — Highly effective treatments for interstitial cystitis remain elusive, but new concepts are enlivening the field, Deborah R. Erickson, M.D., said at the annual meeting of the American Urological Association.

Some of the concepts build on old ones, while others are completely new. But all are off-label, and with two exceptions they have not been subjected to placebo-controlled trials, cautioned Dr. Erickson, of the University of Kentucky (Lexington).

Here is a rundown of some interstitial cystitis (IC) treatment concepts she presented at the meeting:

► Finding ways to restore the deficient bladder epithelium is an old approach; several drugs are being developed with this in mind, but none is yet available.

► Another old concept focuses on mast cells—either inhibiting mast cell activation or blocking mast cell mediators. Ketotifen, a mast cell stabilizer, has proved effective when used topically in the eye and may be developed for IC. Montelukast, a leukotriene receptor blocker, has been the subject of one open-label trial in IC. Among 10 patients with IC and detrusor mastocytosis who had at least 28 mast cells per square millimeter of muscle tissue, 3 months of treatment with montelukast was associated with significant improvements in nocturia, day voids, and pain scores (J. Urol. 2001;166:1734-7).

► Immunosuppression is another old concept that's getting a fresh look. Until now, immunosuppression has not been popular for treating IC because it's too risky to apply to all patients, it's unclear which patients would do best with this strategy, and it's unclear when treatment can be stopped.

Patients with evidence of inflammation or autoimmune involvement may do best on immunosuppression. Such patients include those with the ulcer type of IC, those with evidence of inflammation on bladder biopsy, and those with high levels of urine mediators such as interleukin-6. High levels of nitric oxide gas also suggest inflammation, but special equipment is needed to measure gas levels.

In several recent open-label trials of patients selected for at least one of these signs, prednisone, prednisolone, and low-dose cyclosporine all have shown evidence of efficacy.

"The current status of immunosuppression in 2005 is [that] it's a valid concept, it's not a standard treatment, and the best drugs and doses are not well defined," Dr. Erickson said. "The best patients are the ones who have failed conventional treatment, are well-informed and compliant, and have some evidence for the autoimmune or inflammatory type of IC."

Another concept is to focus on nerves.

► Some patients with IC may have neuropathic pain, and gabapentin and pregabalin, which are well-studied treatments for neuropathic pain, may help. Several small open-label trials of gabapentin in IC have seemed to demonstrate efficacy.

► Many physicians have put lidocaine into the bladders of IC patients, but often this doesn't help, possibly because the acidic form of lidocaine is ionized and doesn't penetrate the epithelium very well. Two different formulations of alkalinized lidocaine appear to reduce bladder pain, but one of those forms seems to cause urethral pain on voiding.

► Sacral nerve stimulation has been approved by the Food and Drug Administration for significant symptoms of urgency/frequency. Some IC patients have this symptom. Three short-term studies and three longer-term studies appear to demonstrate efficacy in some patients.

► Lumbar epidural injections, typically with bupivacaine, have shown promise in three small trials. The methods varied widely, as did the duration of the effect (ranging from 0 to 75 days), so Dr. Erickson said more research clearly is needed.

► The only two drugs that have performed well in randomized, placebo-controlled trials are cimetidine and amitriptyline. Their mechanisms of action are unclear, and as a result neither fits into one of Dr. Erickson's concept categories.

In one study of 36 patients, cimetidine 400 mg b.i.d. resulted in significant improvements in suprapubic pain, nocturia, and total symptom score. The drug may work through histamine$_2$ receptors on mast cells or on T cells, or through reduced stomach acid secretion, which may translate into less acid excreted in urine. ■