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A Watershed Year for Interstitial Cystitis

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A watershed is occurring in our understanding of interstitial cystitis (IC). Recent publications in *The Journal of Urology*® and others have added explanations of genetic¹ and epigenetic² influences, documented the time course of the appearance of comorbid disorders³ and shown again how much systemic involvement occurs in most patients.⁴

A disorder once described as “a hole in the air” may be yielding to investigators looking beyond the bladder to consider the whole individual. The most recent contributions to this expanded view of IC as a problem affecting the bladder rather than as a bladder problem include contributions to an expanded view of phenotyping of IC cases. A recent group concluded, “(Clinically relevant) domains that function outside of the bladder (psychosocial, neurological, tenderness) predict a significant impact on symptoms.”⁴ A new review added additional evidence for an overlap between urological and nonurological unexplained clinical conditions.⁵

The article by Ogawa et al (page 1206) in this issue of *The Journal* focuses on the ulcerative form of IC, which may be different from the nonulcerative form in its extent of systemic involvement. Although their gene expression studies are limited to urothelium, others have reported increased circulating chemokines in patients with IC.⁶

Concurrent events also are under way at the National Institute of Diabetes, Digestive and Kidney Diseases (NIDDK), which recently established the Multidisciplinary Approach to the Study of Chronic Pelvic Pain research network (<http://www.mappnetwork.org>). The network is charged to take a new look at urological chronic pelvic pain and is undertaking comprehensive phenotyping activities in patients with these syndromes. Another recently reported systemic biomarker may eventually assist in diagnosing IC in humans and animals.⁷

However, new knowledge cannot always be accepted and integrated easily. For example, revision of the nosology of the syndrome has been under way for some time. Although IC no longer captures the extent of the problem, if it ever did, it is less clear what the most appropriate name may be. A number of suggestions have been offered, including painful bladder syndrome, bladder pain syndrome and bladder hypersensitivity syndrome. They remain focused on the end organ, still reflecting the perspective of the specialty rather than current understanding of the syndrome. Feinstein recently concluded, “An important principle in naming apparently new ailments is to avoid etiologic titles until the etiologic agent has been suitably demonstrated. A premature causal name can impair a patient’s recovery from the syndrome and impede research that may find the true cause.”⁸ Regardless

of the name eventually chosen, we have reached a time when the description of patients with IC (and these 2 letters may be name enough for the time being) in research and clinical presentations and publications may no longer be restricted to urinary symptoms.

A research implication of this new view is the choice of appropriate animal models for studying IC. Acute bladder injury in otherwise healthy animals cannot adequately model the systemic aspects of IC. Fortunately various models in other disciplines are available that exploit the effects of early adverse experience on adult physiology and behavior.⁹ Although to my knowledge reports of the effects of these maneuvers on voiding function have not yet appeared, the results of evaluating other organs suggest that isolated abnormalities are unlikely. Collaboration with groups that have established these models could rapidly screen for influences on bladder function using relatively simple methods.

What has also occurred recently is the retirement of a major driving force behind this renaissance of knowledge about IC, Dr. Lee Nyberg. Leroy M. Nyberg, M.D. and Ph.D., was Director of Urology Programs at NIDDK from 1989 until retirement in September 2009. His portfolio included directing basic and clinical research into IC, and he led NIDDK efforts to understand its etiopathogenesis. Doctor Nyberg was instrumental in developing research programs, mentoring and collaborating with investigators, and speaking at conferences around the world about IC. As an indicator of his influence, there were 317 IC citations in PubMed® from 1929 to the end of 1989 and from 1989 to the end of 2009 a total of 1,678 were added (53 vs 839 per decade), a 16-fold increase. Because of his efforts and those of many others, new leaders in IC research and treatment will emerge. They and their patients have Doctor Nyberg's determination and persistence to thank for getting us to this new place in the evolution of our understanding of IC.

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