



Published in final edited form as:

*J Urol.* 2009 January ; 181(1): 13–14. doi:10.1016/j.juro.2008.10.078.

## Diabetic Cystopathy—What Does it Mean?

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TYPE 2 diabetes and lower urinary tract dysfunction in women increase with age, and are common, chronic and costly disorders.<sup>1</sup> The prevalence of diabetes appears to be increasing in recent years with an estimated 19.3 million American adults having diabetes and another 54 million having pre-diabetes or impaired fasting glucose as defined by a fasting glucose between 100 and 125 mg/dl.<sup>2</sup> Total estimated diabetes costs in the United States in 2002 were \$132 billion including medical care and services, short-term and permanent disability, and premature death. Approximately 12.7 million women have weekly incontinence in the United States including approximately 1.9 million with impaired fasting glucose and another 2.5 million with diabetes.<sup>3</sup> Costs for incontinence may be as high as \$32 billion per year in the United States, greater than the annual direct costs for breast, ovarian, cervical and uterine cancers combined.<sup>4,5</sup>

Although lower urinary tract dysfunction is a common health problem in women with diabetes, there is a lack of clarity, understanding and standardization of the term diabetic cystopathy.<sup>6</sup> Bladder cystopathy has been classically described as decreased bladder sensation, poor contractility and increased post-void residual urine diagnosed with urodynamics, uroflow and measurement of post-void residual urine. Prevalence estimates of urodynamically diagnosed bladder cystopathy have ranged from 25% to 90%.<sup>7</sup> The wide variation in estimates reflects the lack of validated or standardized clinically significant measures used to diagnose bladder cystopathy as well as the selected referral based populations that have often been studied. It has commonly been thought that in older women with diabetes diabetic cystopathy leads to a flaccid, hypotonic or atonic bladder. However, an atonic bladder does not appear to comprise the majority of bladder dysfunction in older women with diabetes but is rather a relatively uncommon end organ effect of diabetes. Current literature suggests a broad spectrum of lower urinary tract dysfunction including urinary urgency, frequency, nocturia and incontinence that may or may not progress to an atonic or flaccid bladder.<sup>7</sup>

Recent epidemiological evidence strongly suggests that urinary incontinence is 50% to 200% more common in women with type 2 diabetes than in those with normal glucose levels.<sup>8</sup> Relatively few studies have investigated the incidence of and risk factors for new onset incontinence and, therefore, our understanding of the natural history and possible mechanisms for incontinence among women with type 2 diabetes is limited. In this issue of *The Journal* Danforth et al (page 193) report a methodologically sound, prospective, observational study persuasively showing that type 2 diabetes is a strong independent risk factor for new onset weekly incontinence in community dwelling middle-aged and older women. In particular, diabetes was more strongly associated with incident urge incontinence. These findings support their prior finding of nearly double the increased risk of incident incontinence in women with diabetes.<sup>8</sup>

While it is known that incontinence is more common in women with diabetes, mechanisms by which type 2 diabetes may contribute to its development or severity are not well understood.<sup>9</sup> A likely etiology for incontinence is microvascular damage, similar to the disease process involved in the development of retinopathy, nephropathy and peripheral neuropathy. Microvascular complications associated with diabetes might damage the innervation of the bladder, alter detrusor muscle function or cause urothelial dysfunction.

Also in this issue of *The Journal* Lee et al (page 198) report on a cross-sectional study using urodynamics with intravesical current perception threshold testing. They present data suggesting A[H9254] and C fiber bladder afferent pathways may be damaged resulting in early diabetic bladder dysfunction. This interesting finding is important in identifying mechanisms involved in diabetic bladder dysfunction that may potentially lead to innovative interventions for treatment or prevention. Further testing in a broad spectrum of patients followed prospectively seems appropriate to determine the clinical usefulness of intravesical current perception threshold testing as a screening instrument.

Recent findings of a similarly high prevalence of incontinence in women with pre-diabetes and in those with diabetes suggest that incontinence may be an earlier and more common consequence of hyperglycemia than other microvascular complications such as retinopathy, neuropathy or nephropathy.<sup>3</sup> As the population ages, diabetes and lower urinary tract dysfunction will increase markedly in prevalence. Physicians should be alert for lower urinary tract dysfunction because it is often unrecognized and, therefore, undertreated in women with diabetes and pre-diabetes.

New research initiatives are needed to further understand the dimensions, including possible basic disease mechanisms and evidence for supporting the accurate diagnosis and treatment of diabetic cystopathy. The reproducibility, accuracy and clinical outcomes if treatment were based on diagnostic tests have not been evaluated in a generalizable community dwelling population of women with type 2 diabetes. Clinical outcomes of common treatments for lower urinary tract dysfunction in women with pre-diabetes and diabetes have not been critically examined, and randomized controlled trials are needed to assess the efficacy and safety of conservative, pharmacological and surgical treatments. With the current lack of evidence supporting the accurate diagnosis, clinical significance and treatment of diabetic cystopathy, it is time to clarify what we are talking about.

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