in organ baths containing Kreb's solution maintained at 37°C. The amplitude and frequency of spontaneous activity as well as the response to field stimulation were determined. The response of detrusor tissue strips to heptanol (10^{-9} to 10^{-3}M), a gap junction uncoupler, or tetraethylammonium (TEA: 10^{-6} to 10^{-3}M) a gap junction up-regulator were obtained. A carbachol dose response curve (10^{-9} to 10^{-5}M) was generated before and after exposure to heptanol (10^{-4} to 10^{-3} M).

RESULTS: Electric field stimulation produced a consistent, frequency dependent increase in contractile force. The contractile response to electric field stimulation was significantly attenuated in the presence of heptanol in a dose dependent manner (figure 1). Exposure to heptanol also resulted in a significant decrease in the frequency and amplitude of spontaneous activity (figure 2). In addition, the carbachol dose response was significantly attenuated following heptanol exposure (figure 3). Conversely, TEA increased the frequency and amplitude of spontaneous activity.

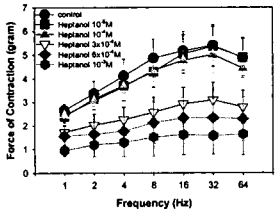

Figure 1: Effect of heptanol on the response to electric field stimulation.

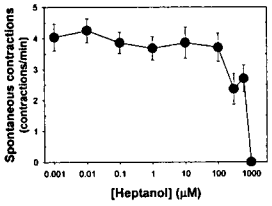

Figure 2: Effect of heptanol on frequency of spontaneous activity.

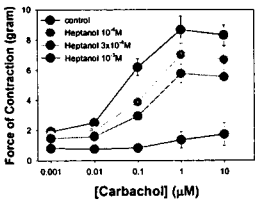

Figure 3: Effect of heptanol on carbachol dose response curve.

CONCLUSION: The effect of heptanol on spontaneous activity and on the responses to field stimulation and carbachol suggest that gap junctions may play an important role in bladder contractility by facilitating propagation of electrical signals. Furthermore, changes in gap junctional activity may contribute to altered detrusor smooth muscle function observed in detrusor instability or detrusor underactivity. Studies to identify and localize specific gap junction proteins are ongoing to support these findings.

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2. Am J Physiol. 249:C20-C31, 1985.
3. Life Sci 49:PL195-200, 1991.

134

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Title (type in CAPITAL LETTERS, leave one blank line before the text):

ALTERATIONS IN THE PROFILE AND TRANSLOCATION OF PROTEIN KINASE C (PKC) IN NORMAL AND DIABETIC DETRUSOR MUSCLE OF RAT.

INTRODUCTION- Published data suggest that diabetes mellitus (DM) complications in the lower urinary tract (LUT) may be due to specific malfunctions in signal transduction pathways in LUT. PKC has been recognized as a prominent intracellular signaling pathway that modulates the effects of cholinergic and adrenergic neurotransmission in many tissues/cells. The goal of the current study was to evaluate the changes in profile and translocation of PKC in the bladder of diabetic rat.

METHODS- Detrusor muscle strips from a transgenic rat model of DM (n=15) and similar age-matched

control rats (n=3) were isolated in OCT compound after sacrifice. The frozen sections were incubated with the diluted rabbit polyclonal antibody against PKC isoenzymes η, β, and ξ, Sections were further stained to visualize the isoform of interest (red channel with Cy-3) together with the surface glycoproteins (green channel stained with wheat germ agglutinen conjugated to Oregon Green) and nuclei (blue channel with bisbenzimide). Sections are viewed and photographed with a confocal microscope equipped with fluorescence optics.

RESULTS- 1) There is significantly increased presence of PKC βI at extended sarcolemmal contact faces between diabetic detrusor muscle cells and interstitial cells. 2) The presence of PKC βI at the nuclei of detrusor muscle cells do not appear to be different between diabetes and control. 3) In diabetic detrusor muscle cells, PKC η intensity at the cell membrane is decreased compared to the intensity in the cytoplasmic structure. 4) The mean intensity of PKC ξ in the diabetic diabetic detrusor cell is twice as great as in the control.

CONCLUSIONS-1) Isolation and translocation of PKC isoforms in detrusor muscle cells of normal and diabetic rat are reported for the first time; 2) Profile and translocation of PKC isoforms η, β, and ξ are markedly different in diabetic detrusor muscle cell compared to control.