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A NEW GENETIC RAT MODEL OF DIABETES MELLITUS (DM) FOR STUDIES OF LOWER URINARY TRACT (LUT) DYSFUCTION.

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(Presentation by Dr. Daneshgari)

INTRODUCTION- A transgenic rat model of insulin deficient DM in which an anti-sense mRNA for mitochondrial carnitine palmitoyltransferase I (CPT I) is expressed in the pancreas has recently been created in our laboratory. The goal of the current study was to investigate physiologic indices of bladder function in these rats.

METHODS- Fifteen transgenic diabetic and 3 wild type (WT) rats underwent: a) cystometrogram (CMG) under anesthesia evaluating for bladder capacity, compliance, and vesical pressure at leak; and b) in-vitro muscle physiology studies evaluating contractile responses to acetylcholine, electeric field stimulation and KCl

RESULTS- The table below shows the range of CMG findings in both DM and WT animals. In general, diabetic rats show an increase in bladder capacity (3-6 fold) and compliance, and decreased detrusor contractility that worsened with longer exposure to untreated diabetic conditions. In the muscle bath experiments, there was an initial increase in contractile responses, which declines with both advancement of age and diabetes progression if untreated.

| Rat Type/age (weeks) | Bladder Capacity (cc) | Compliance at 50% | Pdet at Leak mm $H_2O$ | Contractility | Time to Leak 0 6 cc/m |
|---|---|---|---|---|---|
| WT/10 | 0 48-1 92 | 0 13-1.37 | 3 8-4 5 | Normal | 0.8-2 |
| DM/10 | 3 2-6 | 6.5-30 | 1-2 8 | Normal | 6 5-10 |
| WT/20 | 1-1.5 | 0.02-0 06 | 10-33 | Decreased | 1.5-1 7 |
| DM/20 | 6 7-8 5 | 3 5-4 5 | 15-25 | Decreased | 11-13 5 |

CONCLUSIONS- 1) The cystometric and contractile properties of the transgenic rat bladders are characteristic of clinical type-I DM in human. 2) This model is distinguished from other currently available models of rodent type I-like DM (e.g. the BB rat, NOD mouse and chemically-induced DM) by being monogenic and free from side effects typically associated with chemically-induced DM.