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Abstract Reproduction Form B-1

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Title (type in CAPITAL LETTERS): **THE ROLES OF THE CYCLOOXYGENASE AND LIPOXYGENASE PATHWAYS IN INCREASED CONTRACTILITY OF THE ISCHEMIC BLADDER SMOOTH MUSCLE**

Aims of Study: We have reported that chronic moderate ischemia causes noncompliance and structural changes of the bladder as well as bladder overactivity and supersensitivity to carbachol and electrical field stimulation (EFS) in the male rabbit. Eicosanoids, products of cyclooxygenase (COX), and leukotrienes, products of lipooxygenase (LOX), have been shown to interfere with bladder smooth muscle contractility. Their role in noninfectious urinary bladder inflammation and bladder instability has also been suggested. The aim of this study was to compare the effects of chronic ischemia on bladder contractility in male and female rabbits. Another goal was to study the roles of the COX and LOX pathways in ischemia-induced increased bladder contractility.

Methods: Male (n=16) and female (n=10) New Zealand white rabbits were divided into chronic bladder ischemia (CBI) and control groups. The CBI group underwent balloon endothelial injury of the iliac arteries and received a 0.5% cholesterol diet. The control group received a regular diet. After 16 weeks, iliac artery and bladder wall blood flows were measured and cystometrograms were obtained. After this, the bladder tissues were processed for isometric tension measurement in the organ bath. The sensitivity of bladder strips to electrical field stimulation (EFS, 10 V, 0.8 msec, 0.5-40 Hz) and to carbachol (10-9 to 10-4 M) was examined with and without the presence of COX inhibitor indomethacin and LOX inhibitor REV 5901.

Results: Iliac artery and bladder blood flows were significantly decreased in the CBI group compared with the control group. On cystometry, chronic ischemia caused bladder overactivity and noncompliance in the female rabbits similar to that observed in the male rabbits. In both sexes, bladder tissues from the CBI group showed significant supersensitivity to carbachol and EFS when compared with the control group. Tissue treatment with indomethacin failed to diminish ischemia-induced supersensitivity of bladder tissues in both sexes. In the control groups, tissue treatment with REV 5901 did not affect contraction to carbachol but decreased contraction to EFS. In the CBI group, treatment with REV 5901 alone significantly diminished

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supersensitivity of bladder tissues to carbachol while treatment with indomethacin and REV 5901 significantly decreased supersensitivity to EFS in both sexes.

Conclusions: Chronic ischemia leads to bladder overactivity and smooth muscle supersensitivity to carbachol and EFS in male as well as female rabbits. Pretreatment with the lipooxygenase inhibitor REV 5901 diminished supersensitivity to carbachol in ischemic tissue. The mechanism of chronic ischemia-induced supersensitivity of bladder smooth muscle appears to involve changes in the LOX pathway.