

# Nitric Oxide Synthase—Its Distribution and Alteration in the Intramural Ganglia of the Urinary Bladder in Normal and Urethra-obstructed Guinea Pigs

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## Abstract

*Nitric oxide (NO) has been proposed to function as an inhibitory neurotransmitter in the lower urinary tract. This study investigates the distribution of NO-containing neurons and its changes following urethral obstruction in the guinea-pig. By using nicotinamide adenine dinucleotide phosphate diaphorase (NADPH-d) histochemistry and NO synthase (NOS) immunohistochemistry, the highest frequency of NO-containing neurons was observed in the bladder base. Double labelling studies showed that 70.9% of NADPH-d reactive neurons co-expressed NOS immunoreactivity. Acetylcholinesterase reactivity was present in the majority of the intramural neurons with 54% of them expressed NOS immunoreactivity. NADPH-d reactivity was colocalized with vasoactive intestinal polypeptide, calcitonin gene-related peptide and substance P immunoreactivities in both neurons and fibres. Colocalization study also revealed that NADPH-d reactive neurons formed a distinct cell population from tyrosine hydroxylase positive neurons. At 12 hours after urethral obstruction, NADPH-d reactivity in the intramural ganglion cells was noticeably enhanced and this was sustained till 24 hours whence some intensely stained neurons appeared to undergo degenerative changes. Neuronal degeneration was more drastic at 48 hours so that the number of NADPH-d positive neurons was significantly reduced. The present study suggests that NO is an important neurotransmitter in the urinary bladder and that it may be involved in the relaxation activity in the bladder base during micturition. It is speculated that the increased NADPH-d reactivity in intramural ganglion cells elicited by urethral obstruction may be responsible for the cell death. It is suggested that the resulting cell loss or bladder denervation may account for the urinary dysfunction such as frequency and urgency of micturition in patients with urethral obstruction.*

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*Key words: Guinea pigs, Intramural ganglia, Nitric oxide synthase, Urethral obstruction, Urinary bladder*