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Neuronal nitric oxide synthase in the canine prostate: aging, sex steroid, and pathology correlations

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Nitric oxide synthase (NOS) is expressed in the prostate of various species, including humans. NOS catalyzes the production of nitric oxide (NO), which may function in prostatic smooth-muscle relaxation. To investigate further the role of NO in the prostate, we examined neuronal NOS expression in the aging canine prostate, after hormonal perturbation, and correlated these results with histopathologic findings. The study comprised the following treatment groups: intact dogs (treatment group 1, n = 6); dogs who were castrated at 7 days of age and received testosterone and estrogen replacement at 2 years of age (treatment group 2, n = 10); and dogs who were castrated at 2 years of age and received testosterone and estrogen replacement at 2 years of age (treatment group 3, n = 9). Studies were done on prostates removed from dogs after euthanasia at 6 years of age. In treatment group 1, complex benign prostatic hyperplasia (BPH) was observed in all specimens. In treatment group 2, atrophy was observed in 70%, normal prostate with small areas of hyperplasia in 20%, and BPH in 10% of specimens. In treatment group 3, atrophy was observed in 78%, normal histology with small areas of hyperplasia in 11%, and BPH in 11% of specimens. Neuronal NOS localizations were confirmed by western blot analysis and by immunohistochemistry in 0% and 17%, respectively, of specimens in treatment group 1, in 60% and 70%, respectively, of specimens in treatment group 2, and in 67% and 71%, respectively, of specimens in treatment group 3. Neuronal NOS immunoreactivity was localized in histologically normal prostates of four intact, young-adult control dogs (2 years of age). For all treatment groups, neuronal NOS immunoreactivity was confirmed by western blot in 86% of atrophic prostates but in no prostates with BPH ($P < 0.001$), and it was confirmed by immunohistochemistry in 75% of atrophic prostates but in only 13% of prostates with BPH ($P < 0.02$). These data suggest that, in the canine prostate, NO release relates to growth and pathology. Low levels of neuronal NOS expression in BPH tissue, compared with higher levels in atrophic tissue, suggest that neuronal NOS expression is down-regulated in the prostate with benign cellular proliferation whereas it is maintained or possibly up-regulated in the prostate with prostatic involution. Whether altered neuronal NOS expression contributes to the pathogeneses of BPH and prostatic involution or whether it occurs as a consequence of these processes requires further investigation.