Enikő A Széll M.D. (Dept. of Pediatrics): Regulation of the contractility of the urinary bladder under healthy and diseased condition

1. Neurally evoked contractions and release of 3H-acetylcholine (ACh) during electrical field stimulation were measured in rat urinary bladder strips. The α1 agonist phenylephrine (PE) increased the amplitude of neurally evoked contractions, facilitated the release of ACh and increased the baseline tone of the bladder strips. Low concentrations of specific α_{1A} antagonists, 5-methyl urapidil (5-MU), REC15/2739 and WB-4101 competitively inhibited the facilitation of the neurally-evoked contractions. WB-4101 (100 mM) inhibited the PE-induced facilitation of ACh release. The irreversible α_{1B} antagonist chloroethyl-clonidine (CEC) inhibited the PE-evoked rise in base line tone, but did not affect the PE-induced facilitation of the neurally evoked contractions nor the facilitation of ACh release. However, CEC increased the area and amplitude of the neurally-evoked contractions. Atropine significantly inhibited the CEC evoked increase in area and amplitude of the electrically evoked contractions indicating that CEC facilitated the cholinergic responses of the electrically stimulated bladder strips.
   It is concluded that α_{1A} and CEC sensitive α_{1B} and/or α_{1D} adrenoceptors are expressed in the rat bladder in different locations. On the cholinergic nerve terminals α_{1A} adrenoceptors mediate prejunctional facilitation, whereas postjunctional $\alpha_{1B/1D}$ adrenoceptors mediate smooth muscle contraction.
2. Changes in spontaneous activity of the urinary bladder during postnatal development were examined in muscle strips from the base and dome of bladders from 1- to 5-week-old rats. Activity was analyzed using fast Fourier transformation (FFT) and nonlinear tests. Spontaneous activity was not detected in strips from 1- to 5-day-old rats but was observed in 50% of strips from 6- to 7-day-old rats and was prominent in strips from 2-week-old animals. FFT analysis revealed one peak in activity, which was significantly faster in the bladder base than in the dome. A second peak was detected at 3–5 week of age. Atropine but not tetrodotoxin decreased the amplitude of spontaneous contractions, whereas carbachol, a muscarinic agonist, unmasked or stimulated spontaneous activity.
   These data suggest that slow rhythmic activity observed previously in neonatal whole bladders is generated by pacemaker cells in the bladder base or dome. The emergence of faster activity in bladders from older animals may reflect the development of multiple pacemaker sites, which would reduce coordination within the bladder wall and improve storage function in the mature bladder.
3. In anesthetized rats, the bladder was exposed and cryoinjury was induced by abruptly freezing the serosal side of the bladder wall with dry ice. Five days later, the rats were euthanized, and strips were prepared from the area adjacent to the injury. Neurally and *α*,*β* methylene-ATP (*α*,*β*-mATP)-evoked contractions were measured in bladder strips from cryoinjured or intact bladders prepared from sham-operated rats. Cryoinjured bladder strips produced significantly lower contractile forces than intact strips to electrical stimulation at higher (10–40 Hz) frequencies. The contractile response to *α*,*β*-mATP was smaller in the cryoinjured preparations indicating that the changes may have also occurred at the postjunctional site. In addition, atropine was more effective at inhibiting the neurally evoked contractions in the cryoinjured bladder strips suggesting that a cholinergic dominance occurs after cryoinjury.
   It is concluded that cryoinjury is a viable method of causing a defined, reproducible injury to the urinary bladder resulting in impaired function of both the cholinergic transmission and the smooth muscle. The bladder cryoinjury can be used as a model for studying impaired bladder compliance and detrusor contractility as well as treatments that may improve bladder function such as tissue engineering.