PHARMACOLOGICAL STUDY ON SYMPATHETIC INHIBITION OF THE URINARY BLADDER IN DOGS

Minoru OHTSUKA, Jo MORI, Keiji TSUJIOKA
and Shigenobu KUMADA
Research Laboratories, Fujisawa Pharmaceutical Co., Ltd.,
Yodogawa-ku, Osaka 532, Japan
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Abstract—The sympathetic inhibitory mechanism in dog urinary bladder was studied. The bladder contractions induced by electrical stimulation of the pelvic nerve both proximal and distal to the pelvic plexus and by intraarterial administration of tetramethylammonium (TMA) were inhibited by stimulation of the hypogastric nerve and intraarterial injection of catecholamines. The inhibition by hypogastric nerve stimulation was more potent at the low frequency of pelvic nerve stimulation than at the high frequency. The inhibition of contraction induced by stimulation of the pre-plexal pelvic nerve was antagonized by phentolamine and propranolol, whereas the inhibition of contraction induced by stimulation of the post-plexal pelvic nerve and by TMA treatment were antagonized only by propranolol. It is concluded that inhibition by hypogastric nerve stimulation of bladder contraction induced by pelvic nerve stimulation is composed of two different components. One occurs at the ganglia in the pelvic plexus and is mediated by α-adrenoceptors. The other occurs at the post-plexal pelvic pathway, probably at the ganglia in the bladder wall or on the muscle cells, and is mediated by β-adrenoceptors. Moreover, the α-adrenergic action facilitated the pelvic nerve excitation in its pathway from the ganglionic cell bodies to the muscle cells.

In dogs, the pelvic nerve carries parasympathetic fibres to the urinary bladder via the pelvic plexus located on the lateral surface of the rectum, and its ganglion cells are found in the bladder wall and the plexus (1). Many of these ganglia lie in conjunction with the adrenergic cell clusters and fibres (unpublished data). The present experiments were carried out to determine whether the sympathetic regulatory mechanism which has been found in the superior cervical ganglion (2-4) exists in the bladder ganglion of dogs.

MATERIALS AND METHODS

Female mongrel dogs, weighing 7–15 kg, were anesthetized with 35 mg/kg of i.p. pentobarbital sodium. The lower abdomen was opened along the midline to fully expose the urinary bladder. A urethral catheter was inserted and secured in place by a ligature around the urethra. The catheter was filled with physiological saline and connected to a pressure-transducer (Toyo-Baldwin, LPU-0.1) for recording isometric intravesical pressure developed by the detrusor muscle. The bladder was emptied and then refilled with physiological saline of a volume which caused a resting pressure of about 100 mmH2O. The bladder was carefully packed with a cotton-wool pad soaked in warm saline and kept warm. The ureters were ligated and cut, and the proximal cut end was cannulated with polyethylene...
tubing and the urine was led outside. For intra-arterial and -venous injections of drugs, polyethylene tubes were inserted into the lower portion of the abdominal aorta from the right femoral artery and into the left femoral vein respectively. Systemic blood pressure and heart rate were monitored from the left femoral artery, and all the parameters were simultaneously recorded on a polygraph (Nihon Kohden, RM-85).

Prior to all experiments, the pelvic and hypogastric nerves on both sides were freed and sectioned 2–4 cm proximal to the pelvic plexus, and then about 30 min were allowed to elapse before any recording was made. The following nerve stimulations were given via bipolar platinum electrodes in all cases.

**Pelvic nerve stimulation and tetramethylammonium (TMA) treatment:** The distal end of the cut pelvic nerve or the post-plexal nerve which was freed at a point 1–2 cm from the pelvic plexus on the right side was stimulated for 5 seconds every 2–3 min with rectangular pulses of 3–5 V and 1 msec at varying frequencies. In the initial experiment, frequency-response curves for both nerves were obtained using pulse frequencies in two- to four-fold steps from 0.2 to 20 Hz. In both experiments, the optimal low and the submaximum responses were obtained at pulse frequencies of 2 and 10 Hz respectively, and then these responses were chosen to assess the influence of drugs and hypogastric nerve stimulation. In the experiment with TMA, 32 and 100 μg were selected as doses which would produce almost the same amplitude of contractions as those induced by pelvic nerve stimulation at 2 and 10 Hz. TMA was given intraarterially at intervals of 2–3 min.

**Hypogastric nerve stimulation:** When the response to pelvic nerve stimulation became constant, the distal end of the cut hypogastric nerve on the right side was stimulated for about 2 min with rectangular pulses of 10 msec, 4–6 V and 30 Hz. The next pelvic nerve stimulation was applied during the 2-min stimulation of the hypogastric nerve, and the response was compared with that before the hypogastric nerve stimulation. The hypogastric nerve stimulation itself, however, usually produced a transient contraction in the initial part of the stimulation period (see text). Therefore, the pelvic nerve stimulation was performed when the initial contractions almost disappeared. Then, recovery from sympathetic influence was followed by repeated stimulation of the pelvic nerve after interruption of the hypogastric nerve stimulation. The above procedure was repeated at intervals of not less than 10 min, and when reproducible sympathetic influences were obtained, saline or one or more adrenoceptor antagonists were given intravenously. Then, at least 10 min were allowed to elapse and the next simultaneous stimulation of the hypogastric and the pelvic nerves was given within the next 20 min. Experimental procedure for studying the influence of hypogastric nerve stimulation on TMA-induced contraction before and after adrenoceptor antagonists was essentially the same as that described above.

**Catecholamines:** When the response to pelvic nerve stimulation or TMA injection was reproducible, catecholamine was given i.a., with immediate influence on the pelvic nerve- or TMA-induced contraction. Catecholamines themselves in the used doses usually caused a transient contraction immediately after dosing (see text). Therefore, pelvic nerve stimulation or TMA injection was given 30 sec after dosing with catecholamine.
amine was given to each animal in doses of 0.25 to 16 or 64 μg. The order of administration was random at intervals of not less than 10 min. With this procedure, dose-influence curves for catecholamines were obtained in untreated and adrenoceptor antagonist-treated animals. In the treated animals, at least 10 min were allowed to elapse after dosing with the antagonist and varying doses of catecholamine were given within the next 60 min.

Statistical evaluation: Data were analyzed by Student’s t-test, and differences were accepted as significant at 0.05 and 0.01 levels of probability.

Drugs: The following drugs were used: 1-epinephrine bitartrate (Sigma), 1-norepinephrine hydrochloride (Sigma), phentolamine mesylate (Regitine injection, CIBA), propranolol hydrochloride (Sigma), tetramethylammonium iodide (Sigma), atropine sulfate (Merck), hexamethonium bromide (Methodbromin injection, Yamanouchi), reserpine (Serpasil injection, CIBA). All the drugs except those in injection form were dissolved in physiological saline. Doses were given in terms of salts except for reserpine. Catecholamines and tetramethylammonium solutions were injected in a constant volume of 0.5 ml. Reserpine in a dose of 0.5 mg/kg was given s.c., 24 hr before the experiment. Atropine and hexamethonium were given i.v.

RESULTS

Effect of hypogastric nerve stimulation on bladder contraction induced by stimulation of the pelvic nerve proximal to the pelvic plexus: As shown in Figure 1, electrical stimulation of the pelvic nerve proximal to the pelvic plexus caused a rapid contraction of the detrusor muscle which lasted for the duration of the stimulation. The intensity of the contraction was correlated with the frequency of the stimuli. Maximum contraction was obtained at 20 Hz, which gave an increase in bladder pressure by 431 ± 28 mmH2O (mean ± s.e., n = 7). The pressure rises caused by stimulus frequencies of 2 and 10 Hz were 109 ± 15 (n = 7) and 389 ± 35 mmH2O (n = 7), respectively, and were not affected by atropine (1 mg/kg). These increases were, however, completely inhibited by hexamethonium (2 mg/kg). The results
suggest that the bladder contractions are preganglionic and atropine-resistant.

Electrical stimulation of the hypogastric nerve, on the other hand, caused a biphasic response consisting of a rapid transient contraction followed by no response or a slight relaxation. Maximum contractile response was obtained at a stimulus frequency of 30 Hz, which caused a pressure rise not exceeding 200 mmH₂O for about 50 seconds. When the pelvic nerve was stimulated in the latter part of the hypogastric stimulation period of 30 Hz stimuli, the contraction was less than that without hypogastric nerve stimulation. The inhibition was more potent at the low frequency of pelvic nerve stimulation than at the high frequency, and percentage inhibitions at 2 and 10 Hz were respectively 85 ± 1 (n = 20) and 34 ± 6% (n = 10). In dogs pretreated with reserpine, the hypogastric nerve stimulation revealed no inhibition, even on the contraction induced by a low frequency of 2 Hz (n = 5). Sympathetic inhibition of the pelvic nerve-induced contractions at 2 Hz was blocked, but only partially, by either phentolamine (4 mg/kg) or propranolol (2 mg/kg) and was completely blocked by the two in combination (Fig. 2). In all cases there were no significant changes in either the resting intravesical pressure or the pelvic nerve-induced contraction immediately before the hypogastric nerve stimulation. The hypogastric nerve-induced contraction, however, was lowered by phentolamine or by combined treatment with phentolamine and propranolol, whereas it was unaltered or slightly prolonged by propranolol. Systemic blood pressure was also lowered by 5–35 mmHg after phentolamine or concomitant dosing with both drugs, while no such change was obtained with propranolol alone. Heart rate increased by 5–30 beats/min after dosing with phentolamine, whereas it decreased by 20–45 beats/min after dosing with propranolol or concomitant dosing with both drugs. The results on sympathetic inhibition are summarized in Figure 3. The mean percentage in-

![Fig. 2](image-url)  
**Fig. 2.** Effect of hypogastric nerve stimulation on bladder contraction induced by electrical stimulation of the pelvic nerve proximal to the pelvic plexus at a stimulus frequency of 2 Hz, and antagonism by adrenoceptor antagonists against hypogastric nerve-induced inhibition. Hypogastric nerve stimulation was applied during the period indicated by the bar under each record.
Inhibitions before and after the antagonist were respectively, 86±4 and 85±3% in animals given saline, 83±2 and 58±2% in animals given phentolamine, 84±3 and 56±11% in animals given propranolol and 86±2 and 16±9% in animals given both drugs. All values after dosing, except after saline, were significantly different from the corresponding control value.

**Effect of catecholamines on bladder contraction induced by stimulation of the pelvic nerve proximal to the pelvic plexus:** Intraarterial dosing with lower doses of norepinephrine (0.25–1 µg) or epinephrine (0.25–4 µg) failed to significantly alter the resting tone of intravesical pressure, systemic blood pressure and heart rate. Higher doses of norepinephrine (4–64 µg), however, usually caused a biphasic bladder response which consisted of a slight contraction of a few sec duration followed by relaxation of 5–20 mmH2O for 2–4 min. Higher doses of epinephrine (16–64 µg), however, induced bladder contractions of 5–20 mmH2O at a peak, which for the greater number disappeared 30 sec after dosing. These responses to higher doses of catecholamines were usually accompanied by a rise in arterial blood pressure not exceeding 10–15 mmHg. Adrenergic bladder contraction and hypertension did not occur in animals dosed with phentolamine (4 mg/kg), whereas relaxation by norepinephrine did not occur in propranolol (2 mg/kg)-treated animals.

In the case of intraarterial administration, both catecholamines inhibited dose-dependently the bladder contraction induced by stimulation of the pelvic nerve proximal to the pelvic plexus at 2 Hz (Fig. 4). Effects of the drugs were apparent even at doses below those which produced a detectable change on the resting tone of intravesical pressure, and nearly 90% inhibition was obtained at a dose of 64 µg. After dosing with either phentolamine (4 mg/kg) or propranolol (2 mg/kg), the inhibitory effect of norepinephrine was significantly reduced and the dose-inhibition curve shifted correspondingly to the right. On the other hand, the dose-inhibition curve for epinephrine shifted farther to the right on treatment with phentolamine than on treatment with propranolol. In the case of propranolol, the inhibitory

**Fig. 3.** Inhibitory effect of hypogastric nerve stimulation on bladder contraction induced by electrical stimulation of the pelvic nerve proximal to the pelvic plexus at a stimulus frequency of 2 Hz. Mean percentage inhibition before (open column) and after blocker or saline (stippled column). Vertical lines indicate the s.e. means; n=5 in each experiment. *p<0.05, **p<0.01 against corresponding control (paired t-test).
Effect of epinephrine with some doses did not significantly differ from the corresponding control effect.

*FIG. 4. Inhibitory effect of intraarterial catecholamines on bladder contraction induced by electrical stimulation of the pelvic nerve proximal to the pelvic plexus at a stimulus frequency of 2 Hz, and antagonism by adrenoceptor antagonists against catecholamine-induced inhibition. Mean percentage inhibition in untreated dogs (○), phentolamine 4 mg/kg i.v.-pretreated dogs (●) and propranolol 2 mg/kg i.v.-pretreated dogs (▲). The s.e. means (n=5 in each experiment) are indicated by vertical lines. *p<0.05, **p<0.01; significantly different from the control value using the same dose.

Effect of hypogastric nerve stimulation on bladder contraction induced by stimulation of the pelvic nerve distal to the pelvic plexus: Electrical stimulation of the pelvic nerve distal to the pelvic plexus also caused a rapid contraction of the bladder (Fig. 5). The intensity of bladder contraction obtained with various stimulus frequencies was much the same as that by stimulation of the pelvic nerve proximal to the pelvic plexus; the maximum pressure response obtained with a frequency of 20 Hz was 390±48 mmH₂O (n=7). The pressure rises at 2 and 10 Hz were respectively, 101±10 (n=7) and 335±39 mmH₂O (n=7), and were

*FIG. 5. Pressure response of dog urinary bladder to various frequencies of electrical stimulation of the pelvic nerve distal to the pelvic plexus, and the effect of atropine and hexamethonium given i.v., on bladder contractions induced by frequencies of 2 and 10 Hz.
significantly affected by hexamethonium (2 mg/kg) but not by atropine (1 mg/kg). The results suggest that this stimulation is also preganglionic and atropine-resistant. Bladder contraction was also counteracted by stimulation of the hypogastric nerve at 30 Hz, and the sympathetic inhibition disappeared in reserpine-pretreated animals (n=5). However, the percentage inhibitions on the bladder contractions caused by 2 and 10 Hz were respectively, 63 ± 3% (n=25) and 12 ± 4% (n=6), which were apparently smaller than those on the pre-plexal pelvic nerve-induced contractions (p<0.01). In experiments on adrenoceptor antagonists, likewise, a qualitative difference between sympathetic inhibitions on the pre- and post-plexal pelvic nerve-induced contractions was evident. Sympathetic inhibition of the post-plexal pelvic nerve-induced contraction at 2 Hz was antagonized by propranolol (2 mg/kg) but not by phentolamine (4 mg/kg). Phentolamine only slightly enhanced sympathetic inhibition (Fig. 6). In this experiment, application of adrenoceptor antagonists did not produce a significant change in post-plexal pelvic nerve-induced contraction, without hypogastric nerve stimulation. The results are summarized in Figure 7. The mean percentage inhibitions before and after the antagonist were respectively, 56 ± 7 and 57 ± 6% in animals given saline, 63 ± 7 and 73 ± 3% in those given phentolamine, 63 ± 6 and 15 ± 7% in those given propranolol and 67 ± 5 and 21 ± 6% in those given both drugs. The value after propranolol or the two in combination was significantly different from the corresponding control inhibition.

Effect of catecholamines on bladder contraction induced by stimulation of the pelvic nerve distal to the pelvic plexus: The mode of action of catecholamine on the post-plexal pelvic nerve-induced contraction was considerably different from that on the pre-plexal pelvic nerve-induced contraction. Although both norepinephrine (0.25–64 μg) and epinephrine
(1-64 μg) inhibited dose-dependently the bladder contraction at 2 Hz, epinephrine was apparently less active than norepinephrine (Fig. 8). Moreover, the dose-inhibition curves for norepinephrine and epinephrine were shifted to the right only by propranolol (2 mg/kg), and even the inhibitory effect of epinephrine was not affected by phentolamine (4 mg/kg).

**Effect of hypogastric nerve stimulation on bladder contraction induced by tetramethylammonium (TMA):** As shown in Figure 9, intraarterial doses of 32 and 100 μg of TMA produced much the same intensity of bladder contraction as response to stimulation of the pre-plexal pelvic nerve, at 2 and 10 Hz, respectively. The mean pressure increases seen with 32 and 100 μg were respectively, 115±9 (n=5) and 367±28 mmH₂O (n=5), and were
not significantly affected by atropine (1 mg/kg). Hexamethonium (2 mg/kg), however, completely inhibited the contractions.

The contraction caused by 32 μg of TMA was also inhibited by stimulation of the hypogastric nerve at 30 Hz. Like the sympathetic inhibition of the contraction induced by stimulation of the post-plexal pelvic nerve, the potency was moderate and the mean percentage inhibition was 32 ± 2% (n=20). As shown in Figure 10, the sympathetic inhibition was significantly enhanced from 31 ± 2% to 44 ± 6% after phentolamine (4 mg/kg, n=5), and was significantly reduced from 29 ± 6% to 6 ± 2% after propranolol (2 mg/kg, n=5). After concomitant dosing with both drugs, the inhibition was also significantly reduced from 35 ± 3% to 12 ± 8% (n=5). Treatment with adrenoceptor antagonists produced no significant effect on the TMA-induced contraction, without hypogastric nerve stimulation.

Effect of catecholamines on bladder contraction induced by TMA: Norepinephrine in doses of 0.25 to 16 μg inhibited dose-dependently the bladder contraction induced by 32 μg of TMA (Fig. 11). On the contrary, epinephrine in doses of 1 to 16 μg produced no inhibition, rather the contraction was enhanced. The inhibitory effect of norepinephrine was antagonized only by propranolol (2 mg/kg), the antagonism was complete and the TMA-induced contraction was conversely enhanced. In contrast, the enhancement by epinephrine was completely antagonized and inhibition occurred with application of phentolamine (4 mg/kg).

DISCUSSION

Electrical stimulation of the pelvic nerve both proximal and distal to the pelvic plexus produced urinary bladder contractions of the same extent. A similar bladder contraction
was obtained with an intraarterial dose of TMA. These contractions were readily blocked by hexamethonium, suggesting that activation of the ganglion cells is involved in the bladder contractions induced by stimulation of the pelvic nerve and intraarterial injection of TMA.

Electrical stimulation of the hypogastric nerve inhibited bladder contractions, which prevailed when the parasympathetic excitatory input to the bladder was low, i.e. pelvic nerve stimulation at 2 Hz or dosing with 32 µg of TMA. These findings suggest the presence of a hypogastric regulatory mechanism in the pelvic excitatory pathway to the bladder, which is functionally of considerable significance under conditions of lower pelvic activity. Since the hypogastric nerve stimulation did not produce inhibition in animals pretreated with reserpine, the inhibition is probably due to the action of catecholamine released by stimulation of the hypogastric nerve.

The possible sites of the sympathetic inhibition were also evident in the present investigation. The observation that the sympathetic inhibition was more potent on the bladder contraction induced by stimulation of the pre-plexal pelvic nerve than on the contractions induced by stimulation of the post-plexal pelvic nerve and by injection of TMA indicate that the pelvic excitatory pathway is inhibited by the hypogastric nerve at least at two sites, i.e. in the pelvic plexus and the post-plexal pathway. The results from the experiments using α- and β-adrenoceptor antagonists provided additional evidence of the difference in character of the sympathetic inhibitions which occur at such sites. The inhibition of the pre-plexal pelvic nerve-induced contraction was partially antagonized by phentolamine and propranolol, and completely blocked by the two in combination, suggesting that the inhibition was mediated by both α- and β-adrenoceptors. On the other hand, the inhibition of the post-plexal pelvic nerve-induced contraction was antagonized only by propranolol. Similarly, the inhibition of the TMA-induced contraction was antagonized only by propranolol, and a slight enhancement of the inhibition occurred after phentolamine. These results strongly suggest that the sympathetic inhibition in the pelvic plexus is mediated by only the α-adrenoceptors.

The role of the α- and β-adrenoceptor-mediated actions in sympathetic inhibition was more clearly demonstrated in the experiments using catecholamines. Norepinephrine inhibited the contractions induced by both pre- and post-plexal pelvic nerve stimulations to the same extent. This inhibition of pre-plexal nerve-induced contractions was equally counteracted by both α- and β-adrenoceptor antagonists, while that of the post-plexal nerve-induced contraction was blocked only by β-adrenoceptor antagonist. On the other hand, epinephrine, by which inhibition of the pre-plexal nerve-induced contraction was dominantly blocked by an α-adrenoceptor antagonist, produced only a slight inhibition of the post-plexal nerve-induced contraction, which was antagonized by β-adrenoceptor antagonist alone. These findings also suggest that the adrenergic inhibition in the post-plexal pelvic pathway is mediated by β-adrenoceptors.

In our histochemical studies (unpublished data), we found that many of parasympathetic ganglion cells in the pelvic plexus and the body of the bladder are densely conjugated with adrenergic nerves and chromaffin-like cells. In contrast, in the muscular layers throughout
the whole bladder except the neck, which contain abundant cholinergic nerve terminals, 
adrenergic nerve terminals are either scarce or absent. In the neck part, however, there 
is a rich supply of adrenergic nerve terminals of the muscular layers which clearly exceeds 
that of other areas in the bladder. Therefore, it seems likely that the site of the α-
adrenoceptor-mediated inhibition is the plexal ganglia, whereas the site of the β-
adrenoceptor-mediated inhibition is the ganglia in the bladder wall and/or the muscle cells.

Inhibition of synaptic or junctional transmission by activation of α-adrenoceptors in 
the superior cervical ganglion has been reported (2–6) and the intramural neuronal structures 
of the visceral organs (7–9), whereas inhibition by β-adrenoceptors, which may occur in the 
neuronal structure, is considered to be a unique finding. Concerning the β-adrenoceptor-
mediated inhibition, however, the possibility of counteraction on the muscle cells (10–11) 
cannot be ruled out.

The experiment with TMA and catecholamines provided further new evidence. The 
TMA-induced bladder contraction was enhanced by epinephrine and the enhancement was 
reverted to an inhibitory response after treatment with an α-adrenoceptor antagonist. 
Thus, an α-adrenergic action facilitated the parasympathetic nerve excitation in its pathway 
from the ganglionic cell bodies to the muscle cells. α-Adrenergic facilitation of the TMA-
induced contraction was also demonstrated by concomitant injection of norepinephrine and 
a β-adrenoceptor antagonist.

In brief, the sympathetic inhibition of the bladder contraction induced by stimulation 
of the pelvic nerve is evident under the condition of lower pelvic activity and is composed 
of two different components. One occurs at the ganglia in the pelvic plexus and is mediated 
by α-adrenoceptors, whereas the other occurs at the post-plexal pelvic pathway, probably 
at the ganglia in the bladder wall or on the smooth muscular cells, and is mediated by β-
adrenoceptors. Moreover, the α-adrenergic action facilitated pelvic nerve excitation in the 
pathway from the ganglionic cell bodies to the muscular cells.

REFERENCES
1) MILLER, M.E., CHRISTENSEN, G.C. AND EVANS, H.E.: The autonomic nervous system. 
   Anatomy of the dog, p. 626–644, W.B. Saunders Company, Philadelphia and London 
   (1964)
2) DE GROAT, W.C. AND VOLLE, R.L.: The actions of the catecholamines on transmission in 
   the superior cervical ganglion of the cat. J. Pharmacol. exp. Ther. 154, 1–13 (1966)
3) MCISAAC, R.J.: Ganglionic blocking properties of epinephrine and related amines. Int. 
   J. Neuropharmacol. 5, 15–26 (1966)
4) CHRIST, D.D. AND NISHI, S.: Effects of adrenaline on nerve terminals in the superior cervical 
   ganglion of the rabbit. Brit. J. Pharmacol. 41, 331–338 (1971)
5) LIBET, B. AND KOBAYASHI, H.: Generation of adrenergic and cholinergic potentials in 
   sympathetic ganglion cells. Science N.Y. 164, 1530–1532 (1969)
6) LIBET, B.: Generation of slow inhibitory and excitatory postsynaptic potentials. Fedn. Proc. 
   29, 1945–1956 (1970)
7) BEANI, L., BIANCHI, C. AND CREMA, A.: The effect of catecholamines and sympathetic 
   stimulation on the release of acetylcholine from the guinea-pig colon. Brit. J. Pharmacol. 
   36, 1–17 (1969)
8) PATON, W.D.M. AND VIZI, E.S.: The inhibitory action of noradrenaline and adrenaline on 
   acetylcholine output by guinea-pig ileum longitudinal muscle strip. Brit. J. Pharmacol.
9) Knoll, J. and Vizi, E.S.: Effect of frequency of stimulation on the inhibition by noradrenaline of the acetylcholine output from parasympathetic nerve terminals. *Brit. J. Pharmacol.* **42**, 263–272 (1971)

10) Dave, K.C. and Dhattiwala, A.S.: Adrenoceptors of the guinea-pig urinary bladder. *Brit. J. Pharmacol.* **58**, 37–41 (1976)

11) de Groat, W.C. and Saum, W.R.: Sympathetic inhibition of the urinary bladder and of pelvic ganglionic transmission in the cat. *J. Physiol.* **220**, 297–314 (1972)