Neurourology and Urodynamics 12:463–471 (1993)

New Concepts in Relation to Urge and Detrusor Activity

Bo L.R.A. Coolsaet, Wim A. Van Duyl, Pooran Van Os-Bossagh, and Hans V. De Bakker

Department of Urology, Klina Hospitals, Kapellen, Belgium (B.L.R.A.C.); Department of Biomedical Physics and Technology, Erasmus University Rotterdam, The Netherlands (W.A.V.D., P.V.O.-B., H.V.D.B.)

Investigations of micromotion characteristics of bladder wall strips and pressure wave phenomena in total bladders in vitro and in vivo indicate that micromotion phenomena occur in the bladder wall. Local contractions can occur without an increase in tension or pressure, because other parts are in antiphase. Local contractions stretch surrounding tissues, which can stimulate fast stretch receptors. Synchronisation of these micromotion phenomena appears to be possible. Hence, above threshold levels urge can theoretically occur, even in the absence of a pressure increase. This hypothesis could explain the weak relation between urge and pressure. The distinction between motor and sensory urge could be artifactual based on a misunderstanding of fundamental bladder wall processes.

Key words: instability, bladder wall, spontaneous activity

INTRODUCTION

Urge is the sensation of the inability to voluntarily postpone micturition. It usually causes frequency, sometimes nocturia, and interferes with the quality of life, especially when it causes incontinence. Its incidence and clinical significance increase with age [Abrams, 1985]. Changes at the proximal urethra have been repeatedly reported to be associated with these complaints. Stress incontinence [McGuire and Savastano, 1985], as well as affections of the prostate, either obstructive or unobstructive, are frequently related to urge symptoms [Coolsaet and Blok, 1986]. Bladder properties during filling have been reported [Coolsaet, 1985].

The causal relation between these symptoms and detrusor overactivity has been clinically evaluated in several studies. Knowledge about the clinical "urge" problem has made little progress during recent years. This is due to the fact that detrusor pressure has been accepted as the key factor. Pressure increases during the bladder filling phase which exceed 15 cm H_2O have been arbitrarily labeled as *detrusor instability* or *motor urge*. Patients who did not fullfil this criterion were labelled as having *sensory urge*. Most authors still use these criteria, although the clinical rele-

Received for publication December 10, 1992; accepted March 5, 1993.

Address reprint requests to Wim A. Van Duyl, Erasmus University Rotterdam, Department of Biomedical Physics and Technology, P.O. Box 1738, 3000 DR Rotterdam, The Netherlands.

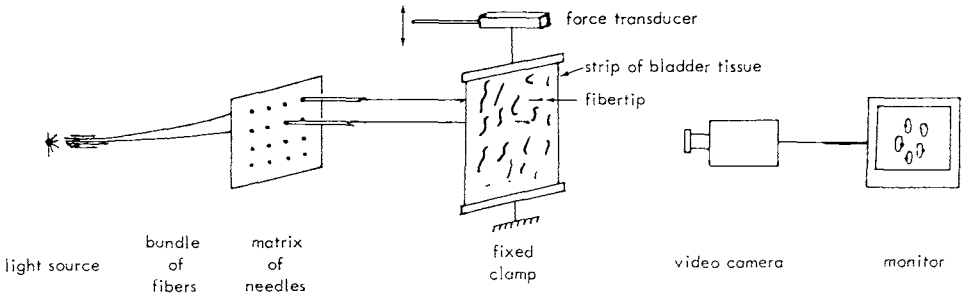

Fig. 1. Principle of the technique used for the observation of micromotion in bladder strips in vitro.

vance of subthreshold pressure increases has been demonstrated [Coolsaet et al., 1985]. The International Continence Society adapted the definition accordingly. The main interest of urodynamic research has been to find techniques to confirm the patient's complaint of urge in terms of pressure: ambulatory urodynamics and provocative tests such as changes of diuresis, position, catheter position, and many others.

The relation between detrusor pressure and urge was recently questioned. Notwithstanding the use of "instability indices," there appears to be a poor correlation between pressures and symptoms [Murray et al., 1982; Jorgenson et al., 1987]. Abrams [1985] reported that in a group of benign prostatic hypertrophy (BPH) patients, only 47% with preoperative unstable bladders complained of urgency and only 16% of them complained of instability after the operation. It is a common experience that pressure increases occur without urge and that pharmacotherapy can cure the symptom without changing the pressure and vice versa.

In this contribution we will try to go back from the bladder lumen to the bladder wall, an essential part of the musculoneuronal urge problem.

OBJECTIVES OF THE STUDY

The aim of the study was to further investigate the spontaneous micromotion activity of bladder wall strips and total bladders. The observation of the presence of contracting and relaxing areas provides fundamental information on local wall mechanisms which produce afferent input to the central nervous system. This input does not necessarily need to be coupled with significant pressure increases.

IN VITRO OBSERVATIONS ON BLADDER WALL STRIPS

Methods

The technique to study patterns of spontaneous microdisplacements (<0.1 mm) have been described earlier [Van Duyl, 1985a]. Strips of pig bladder wall are connected to an isometric force transducer, while microdisplacements are measured by means of thin fibers, which are stuck through the tissue and follow the local motions. The fibertips are lighted, and the motions of the light spots are analysed (Fig. 1).

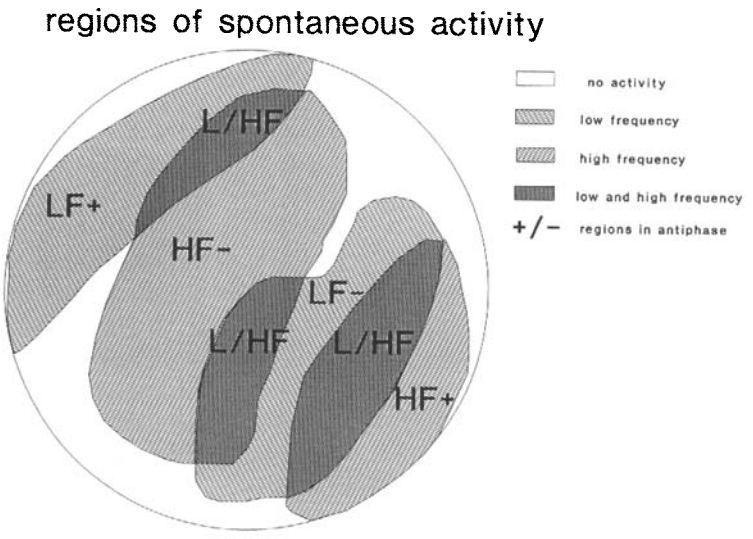

Fig. 2. Illustration of spontaneous activity in bladder tissue: regions of low frequency (LF) and high frequency (HF), in phase (+) and antiphase (−). Regions of different frequencies may overlap each other.

Results

As the results of this study have been published earlier [Van Der Hoeven et al., 1990; Van Duyl et al., 1990], here we will only summarize the conclusions. Spontaneous activity is distributed in the bladder wall and is composed of two frequency components, the lower frequency component in the range of 0.02–0.05 per second and the higher at about twice this frequency. Areas of synchronized motion of the two frequency components coexist independently of each other and are independently distributed in the tissue. Figure 2 is a snapshot showing the regions of spontaneous activity of both frequency components. The study on a large series of such snapshots reveals several fundamental aspects of spontaneous detrusor activity:

(a) the two frequency components occur in different areas
(b) the areas of the two frequencies may overlap
(c) these micromotion areas migrate over the course of time
(d) for each frequency component, different areas are in antiphase, which means that some regions are in the contracting phase while others are relaxing
(e) the two different frequency components are generated separately
(f) the two frequency components have different characteristics: the lower frequency component is inhibited by oxyphenomiumbromide [Hak et al., 1988]
(g) local contractions may occur without a rise in force across the strip

IN VITRO OBSERVATIONS ON TOTAL PIG BLADDERS

Methods

A fast stretch generates a contraction of smooth muscle by depolarising the cell membrane. Based on this property, Van Duyl et al. [1992] postulated that rhythmic straining of the bladder wall in the frequency of one of the components of micromo-

tion activity might interfere with this activity in such a way that synchronization occurs. In order to investigate this phenomenon, fresh total pig bladders with partly intact urethra were suspended in a metabolic solution (Krebs solution at 37°C, bubbled with 95% O_2/5% CO_2. A catheter was introduced in the bladder lumen via the urethra, which was subsequently sutured around the catheter.

The catheter was connected to a pressure transducer via a Y-connector. The other limb of the Y-connector was connected to a homemade controlled infusion pump. The bladder was filled with the same metabolic solution of 37°C, to a baseline volume of 100 ml. Then the bladder was allowed to equilibrate for 30 minutes. Subsequently volume changes of 20 ml were applied blockwise by means of the controlled infusion pump at a frequency in the range of 0.01–0.10/sec. Intravesical pressure was registrated during the period of equilibration, during application of volume changes, and after stopping of the volume changes.

Similar series of measurements have been performed on four pig bladders.

Results

During the period of equilibration, the detrusor pressure shows some irregular spontaneous variations (Fig. 3a). Figure 3b shows the pressure during and after blockwise volume changes. As appears from Figure 3b, the detrusor activity indeed has become more rhythmic, with larger amplitudes during and after blockwise volume changes. After stopping the volume changes, while the intravesical volume is kept at the baseline volume of 100 ml, large phasic pressure variations are observed at a remarkably stable frequency (Fig. 3c). The experiments have shown that spontaneous phasic rhythmic pressure waves can be evoked and increased by blockwise variation of bladder volume on total pig bladders in vitro.

IN VIVO OBSERVATIONS ON HUMAN BLADDERS

Methods

The observation in total pig bladders in vitro that spontaneous phasic variations in detrusor pressure can be induced by rhythmic variation of bladder volume motivated us to perform similar studies on human bladders in vivo. For this investigation we selected patients whose bladders showed obvious detrusor overactivity in a previous urodynamic investigation.

In principle, we used the same setup and followed the same procedure as for measurements on total pig bladders in vitro. A catheter (8 Fr) was introduced in the bladder via the urethra. The catheter was connected to a pressure transducer via a Y-connector (Fig. 4). The other limb of the Y-connector was connected to a controlled infusion pump. A baseline volume of 200 ml was introduced into the bladder. Blockwise volume variations of 30 ml were applied at a frequency of 0.025/sec during periods of 5–10 minutes. Detrusor pressure was recorded before, during, and after the applied volume changes.

Results

Figure 5 shows the pressure recording obtained in a female patient. The bladder was filled via the urethra, until a baseline volume of approximately 200 ml was reached. Figure 5a shows some spontaneous activity previous to stimulation by rhythmic volume changes. Figure 5b shows that rhythmic contractions are increased by

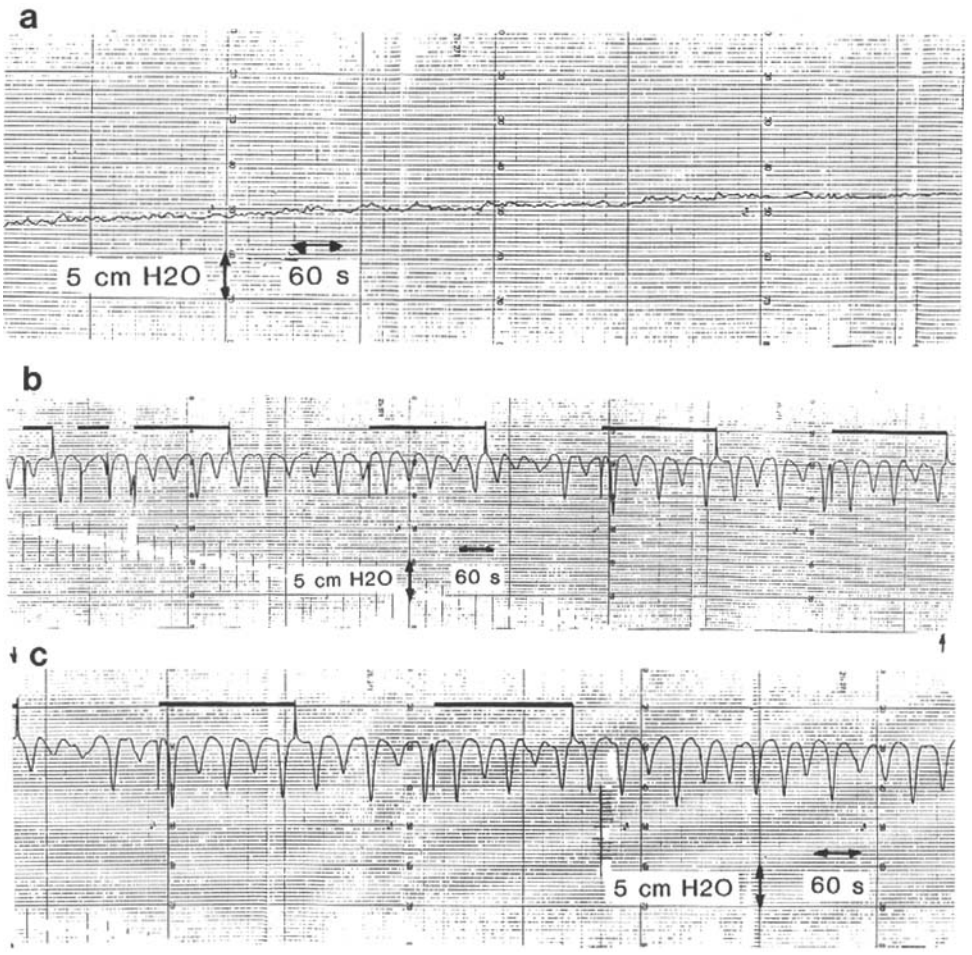

Fig. 3. Recording of intravesical pressure of pig bladder in vitro: —indicates periods of increased bladder volume. (**a**) Recording showing spontaneous activity previous to stimulation. (**b**) Recording of pressure variation during rhythmic blockwise volume changes. (**c**) Recording after stopping rhythmic volume changes showing manifest spontaneous rhythmic activity.

rhythmic straining; however, the contractions are not synchronized to the frequency of the applied straining.

In Figure 5c it is shown that after stopping the applied rhythmic straining, phasic rhythmic contractions continue for some time, and this spontaneous activity is considerably larger than in the period previous to stimulation. After a period of approximately 10 minutes, rhythmicity seems to be lost, indicating that the spontaneous activity becomes less synchronized. In Figure 5d the situation is restored after re-applying a period of rhythmic straining.

DISCUSSION

Bladder wall properties have been evaluated extensively. The passive and active properties have been taken as characteristics of two bladder conditions: the fully passive state [Van Mastrigt et al., 1978] and the fully activated state [Griffiths et al.,

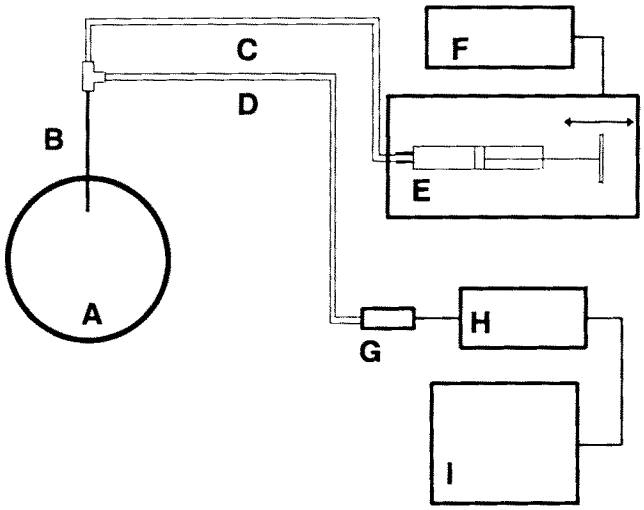

Fig. 4. Set up for the measurement of intravesical pressure and application of rhythmic volume changes in a patient. A, bladder of patient; B, urethral catheter (Ch 8); C, infusion channel; D, pressure channel; E, electrically controlled infusion pump; F, square-wave generator; G, pressure transducer; H, low-pass filter; I, chart recorder.

1979]. In situ, both extreme bladder conditions are very rare. Van Duyl [1985a] introduced the concept of spontaneous micromotion. It was postulated that in a normal bladder wall, a certain degree of spontaneous micromotion continuously exists. Depending on the degree of micromotion, the actual condition of the bladder is situated along a bladder performance scale (BPS) between the extreme conditions of fully passive and fully activated [Van Duyl, 1985b]. According to this concept, detrusor activity, either spontaneous or stimulated, is a gradual phenomenon and will change during filling and micturition phase. This phenomenon is probably under the control of substances outlined by De Groat and Kawatani [1985]. Detrusor pressure is only a partial reflection of detrusor wall phenomena [Coolsaet and Elhilali, 1988].

Recent studies on bladder wall strips revealed that micromotion in areas of the wall is the origin of spontaneous activity, which can be observed as variations of force across a strip or as pressure waves in detrusor pressure [Van Der Hoeven et al., 1990; Van Duyl et al., 1990]. The amplitude of the contraction in a certain area of the bladder wall depends on the degree of synchronization of micromotions within that area.

The absence of waves in the overall force across a strip, or of waves in the detrusor pressure, does not mean that there is no spontaneous activity in the bladder wall. Spontaneous wall activity patterns probably are the key phenomenon in the origin of symptoms. Urge is not necessarily coupled to pressure variations in the bladder lumen. Local contractions can occur in the absence of an increase in pressure. The contraction per se is not necessarily the origin of urge. Local contractions can stretch the surrounding tissues, which can stimulate fast receptors [Kuru, 1965; Talaat, 1937]. The distinction between motor and sensory urge has probably been based on a misunderstanding of the fundamental process. Pressure in the bladder lumen ought to be dealt with primarily as a consequence of bladder wall phenomena.

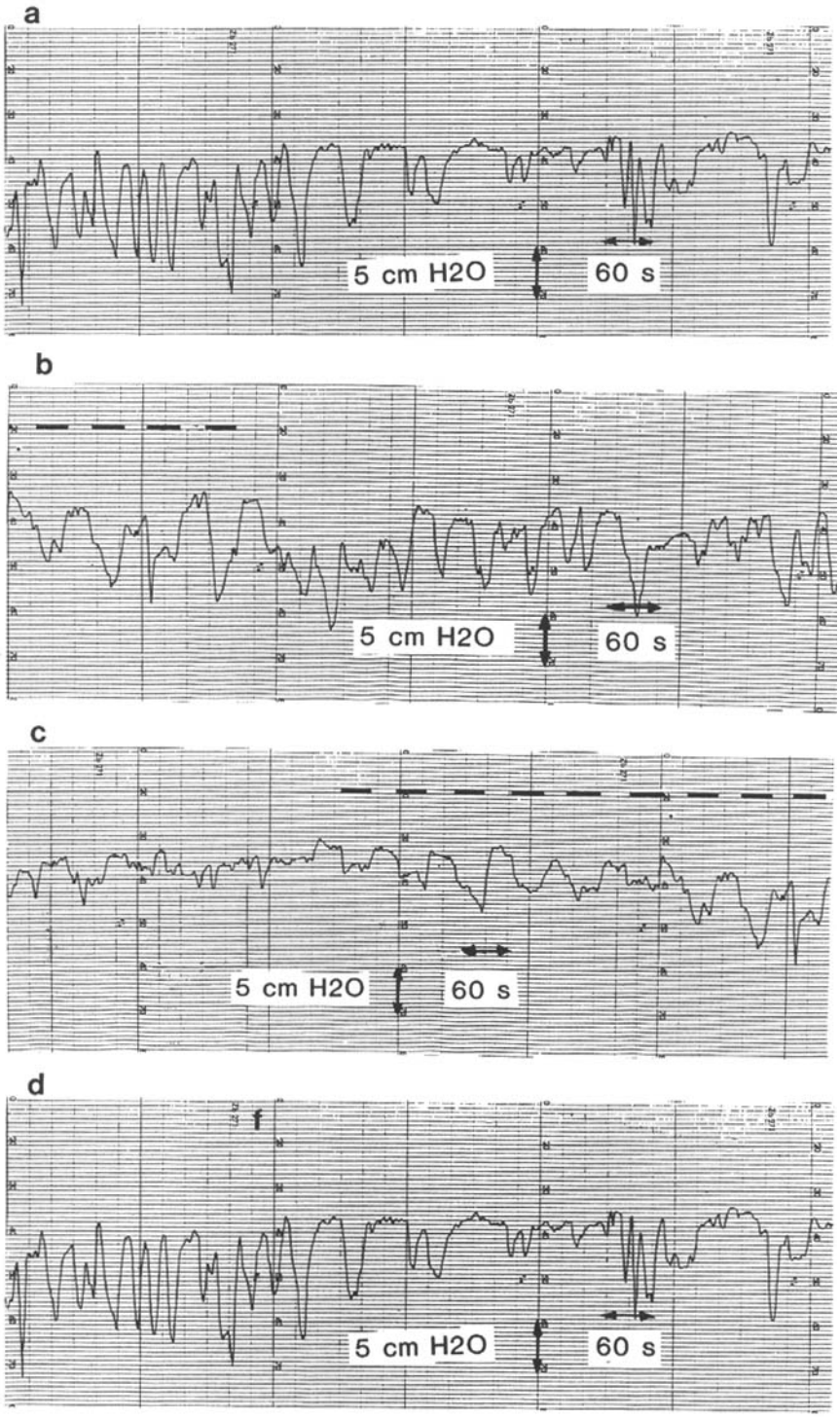

Fig. 5. ——indicates periods of increased bladder volume. Recording of intravesical pressure in a patient. (**a**) Recording showing spontaneous activity previous to stimulation. (**b**) Recording during rhythmic blockwise volume changes. (**c**) Recording after stopping stimulation, which demonstrates enhancement of spontaneous activity after stimulation and subsequent loss of synchronisation. (**d**) Recording during and after restimulation, which demonstrates recovery and subsequent loss of synchronization.

This conclusion confirms the statements made earlier that, strictly speaking, no detrusor is stable [Coolsaet and Blaivas, 1985]. The consequences are important. The apparently fundamental pathophysiologic difference between sensory and motor urge appears to be rather misleading. It is possible, indeed, that the origin of urge symptoms is in local stretch, detected by fast stretch receptors and transported to the cortical areas via fibers, with the C-fibers possibly playing an important role. It is not necessarily the contraction per se, as a source of tension and pressure, which causes the symptom, although the symptom can be correlated with these contractions. In relation to our concept, we can furthermore assume that a well-coordinated contraction with total bladder wall involvement does not necessarily cause urge. Indeed, although pressure is increased, no parts of the wall are stretched. On the contrary, a localized contraction can stretch parts of the wall which are in a relaxed state, generating afferent pulses and subsequently urge.

Our concept explains why the correlation between detrusor pressure and symptoms is weak, notwithstanding bladder wall activity. The results on total bladders explain the clinical observation that fast stretch can evoke urge. The conditions under which local stretch and symptoms can be evoked are posture change, stepwise bladder filling [Susset, 1983], and hyperdiuresis cystometry [Coolsaet and Elhilali, 1988; Van Venrooy et al., 1987]. In harmony with the concept of synchronizable spontaneous micromotion, rhythmic spontaneous contractions can be induced and enhanced by rhythmic straining of the pig bladder wall in vitro. The results obtained from similar experiments on human unstable bladders are consistent with this observation in vitro. Our results show that spontaneous activity observed in vitro is more than an artifact, as was concluded by Levin et al. [1986]. Phasic spontaneous pressure waves may be induced by blockwise straining of the bladder wall. A neurogenic mechanism is probably responsible for the loss of synchronization observed after a period of induced rhythmic contraction activity.

Regional stretching phenomena can generate different input to the central nervous system via C-fibers, which appear to be enhanced in urge conditions [De Groat and Kawatani, 1985].

Steers [1990] observed morphological and electrophysiological alterations in neural pathways in hypertrophic bladders, which are supposed to be related to sensory symptoms. Similarly, Elbadawi [1991] suggests that more attention be paid to the microstructural basis of detrusor contractility.

The above considerations suggest that detrusor pressure has been overestimated as a key criterion in the urge symptom complex. Indeed, contraction phenomena in the wall can cause detrusor pressure increases, but they do not necessarily do so. The classical definition of motor urge (detrusor instability) has to be interpreted within a range of the BPS. The threshold of 15 cm H_2O is just an arbitrarily chosen mark on the BPS but it has no pathophysiologic basis.

CONCLUSIONS

A new theory on the relation between bladder wall phenomena and urge symptoms has been presented. According to this theory the key factor might be local stretch, caused by locally synchronized contracting areas, as demonstrated in vitro by micromotion dynamics. Detrusor pressure variations are not only incomplete reflections of bladder wall phenomena, they mislead the clinician away from the basic

problem, which concerns local stretch. Contractions per se do not necessarily cause symptoms. Synchronization of local micromotions is possible by stretch stimulation, as demonstrated in these investigations and as clinically observed. The pathophysiologic localisation of the patient's complaint "urge" can be in the bladder wall, neurotransport and neurocontrol [de Groat and Kawatani, 1985], and perception. Further research has to be shifted from complicated pressure-monitoring systems (ambulatory cystometry) towards the investigation of bladder wall phenomena and their neural control.

REFERENCES

Abrams P (1985): Detrusor instability and bladder outlet obstruction. Neurourol Urodyn 4:317–328.

Coolsaet B (1985): Bladder compliance and detrusor activity during the collection phase. Neurourol Urodyn 4:263–273.

Coolsaet BLRA, Blaivas JG (1985): No detrusor is stable. Neurourol Urodyn 4:259–261.

Coolsaet BLRA, Blok C (1986): Detrusor properties related to prostatism. Neurourol Urodyn 5:435–447.

Coolsaet BLRA, Elhilali MM (1988): Detrusor overactivity. Neurourol Urodyn 7:541–561.

Coolsaet BLRA, Blok C, Van Venrooy GEPM, Tan B (1985): Subthreshold detrusor instability. Neurourol Urodyn 4:309–311.

De Groat WC, Kawatani M (1985): Neural control of the urinary bladder. Neurourol Urodyn 4:285–300.

Elbadawi A (1991): Microstructural basis of detrusor contractility: The MIN-approach to its understanding and study. Neurourol Urodyn 10:77–85.

Griffiths DJ, Van Mastrigt R, Van Duyl WA, Coolsaet BLRA (1979): Active mechanical properties of the smooth muscle of the urinary bladder. Med Biol Eng Comput 17:281–290.

Hak J, Griffiths DJ, Van Mastrigt R, Koopal B, Kluck P (1988): Quantitative study in vitro of the spontaneous contractions of the pig detrusor muscle and their frequency-selective inhibition by drugs. Neurourol Urodynam 7:471–481.

Jorgenson L, Lose G, Molsted-Pederson L (1987): Vaginal repair in female motor urge incontinence. Eur Urol 13:382–387.

Kuru M (1965): Nervous control of micturition. Physiol Rev 45:425–494.

Levin RB, Ruggerie MR, Velagapudi S, Gordou D, Altman B, Wein AJ (1986): Relevance of spontaneous activity to urinary bladder function: An in vitro and an in vivo study. J Urol 136:514–521.

McGuire, Savastano (1985): Stress incontinence and detrusor instability. Neurourol Urodyn 4:313–316.

Murray K, Howell S, Lewis P (1982): The effect of apoid blockade on idiopathic detrusor instability. Proceedings of the 12th Annual Meeting, Leiden, pp 85–87.

Steers WD (1990): Neuroplasticity secondary to infravesical obstruction. Neurourol Urodyn 9:559–561.

Susset J (1983): Relation between clinical urodynamics and pathologic findings in prostatic obstruction. In Hinman F, Jr. (ed): "Benign Prostatic Hypertrophy." New York: Springer Verlag, pp 613–626.

Talaat M (1937): Afferent impulses in the nerves supplying the urinary bladder. J Physiol 89:1–13.

Van Der Hoeven AAM, Van Duyl WA, De Bakker JV (1990): Detection of spontaneous motion patterns in urinary bladder tissue in vitro. In Kerrebroeck and Debruyne (eds): "Dysfunction of the Lower Urinary Tract." Bussum: Medicom Europe, pp 10–13.

Van Duyl WA (1985a): Spontaneous contractions in urinary bladder smooth muscle: Preliminary results. Neurourol Urodyn 4:301–308.

Van Duyl WA (1985b): A model for both the passive and active properties of urinary bladder tissue related to bladder function. Neurourol Urodyn 4:275–283.

Van Duyl WA, Van der Hoeven AAM, De Bakker JV (1990): Synchronization of spontaneous contraction activity in smooth muscle of urinary bladder. Neurourol Urodyn 9:547–550.

Van Duyl WA, Coolsaet BLRA, De Bakker JV (1992): Evocation of synchronouc spontaneous contraction activity of the bladder in-vitro. In preparation.

Van Mastrigt R, Coolsaet BLRA, Van Duyl WA (1978): The passive properties of the urinary bladder in the collection phase. Med Biol Eng Comput 16:471–482.

Van Venrooy GEPM, Kamphuis ET, Wolfhagen M (1987): Diuresis cystometry versus filling cystometry Neurourol Urodyn 6:29–36.