

# Central effect of bladder filling and voiding<sup>1</sup>

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**SYNOPSIS** In normal subjects and in patients with spasticity and/or urological complaints changes in somatic muscle reflexes associated with filling of the urinary bladder were observed. Two different patterns of reflex changes occurred. One pattern was associated with easy initiation of voiding: it consisted of increasing H and T reflexes and decreasing flexor reflexes with concomitant decreasing sphincter muscle activity. The other pattern was associated with difficulty in initiation of voiding: it consisted of increasing flexor reflexes including sphincter muscle activity and decreasing H and T reflexes. The importance of these reflex patterns in disturbances of micturition is discussed. During voiding, decreasing flexor reflexes with increasing H and T reflexes occur as the general pattern.

The level of excitation of the central nervous system is determined by influences from many different sources, both central and peripheral.

Among the peripheral structures influencing the level of excitation, the urinary bladder must be supposed to be of importance. This applies, in particular, to changes in the inflow in relation to the degree of filling of the bladder and the act of voiding.

Knowledge of such influences is of general interest. We have, for example, encountered the problem in testing leg reflexes, both for the purpose of quantitating clinical spasticity (Pedersen, 1969, 1974) and in pharmacological studies of certain drugs (Pedersen *et al.*, 1974a).

In spite of this common interest in the central effect from the bladder receptors, few studies in man are available (McPherson and Skorpil, 1966; Marsden *et al.*, 1969). The scarcity of reports on this problem prompted us to study the effect of the inflow from the bladder during filling and voiding through the changes in the H and T reflexes (Pedersen and Mai, 1975), but later it proved necessary to include other investigations—for example, on flexor reflexes and activity of the sphincter muscles. The results of these studies are presented below.

## METHODS

A total of 53 adult persons was investigated, 17 normal volunteers and 36 patients who were admitted to the clinic with disturbances of micturition. Of the patients, 25 were spastic, the spasticity being caused either by multiple sclerosis or trauma. Eleven patients had urological complaints, but showed no signs of upper motor neurone involvement.

Thirty patients, including the 11 urological patients and 19 of the spastic patients, were investigated in the supine position by reflex measurements while simultaneous recording was made of a pressure-volume curve of the bladder (cystometry). Sterile water was filled into the bladder at a very slow rate (10 ml/min) through one of the tubes of a double urethral catheter. Pressure was recorded through the other catheter tube, and during detrusor spasms the filling was discontinued. Reflex series were measured at a bladder filling of zero and for every increment of 100 ml.

Of the 11 urological patients, five had a cystometry within the normal range and six showed large-capacity bladders with a shift in sensibility to the right. Of the 19 spastic patients investigated by cystometry, 13 proved to have hyperactive bladders, two showed a cystometry within normal limits, and four had large-capacity bladders with disturbed sensibility.

Twenty-three subjects, including the 17 normal volunteers and six spastic patients with multiple sclerosis, were not catheterized. They were placed in the sitting position in a specially designed chair permitting them to void into a DISA mictrometer while simultaneous reflex recordings were made. They

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emptied their bladder before the start of the investigation and were given ample amounts of water together with furosemide, 40 mg by mouth, to promote natural bladder filling. Reflex series were measured at intervals of about five minutes during the filling and post-voiding phases, and during voiding as many single reflexes as possible were measured, with due regard to the necessary intervals (Desmedt *et al.*, 1973; Pedersen *et al.*, 1974a).

Electromyographic investigations and reflex measurements were performed in the various groups as described below. Before the start of any investigation a period of 15–20 minutes was allowed to pass. During this period, the test person accommodated to the stimulation, and adjustments of the electrode placement and stimulation intensity, etc., were performed.

The following measurements were made:

**ELECTROMYOGRAM FROM ANAL SPHINCTER** The electromyogram was detected continuously by needle electrodes (DISA 13K57) placed intramuscularly in the external anal sphincter.

**T REFLEX (ACHILLES TENDON REFLEX)** This reflex was elicited by applying taps of constant force from an electromagnetic hammer to the same site of the Achilles tendon (Pedersen *et al.*, 1974b). The force exerted by the hammer was adjusted to produce a reflex about midway between threshold and maximum. The reflexes were elicited in series of 10 to 20 single reflexes, each separated by an interval of 10 seconds (Desmedt *et al.*, 1973).

**H REFLEX (HOFFMANN REFLEX)** This reflex was elicited by square-wave electrical pulses of 1 ms duration (Veale *et al.*, 1973), fed through a constant-current unit and applied to the posterior tibial nerve in the popliteal fossa by a slightly modified Simon electrode (Simon, 1962). After the determination of a recruitment curve, the stimulation current was adjusted to produce an H reflex of about 50% of maximum, and only H reflexes with unchanged M responses were included in the study. This reflex was also elicited in series of 10–20 single reflexes at an inter-reflex interval of 10 seconds.

**FLEXOR REFLEX** This was elicited by a train of five square-wave electrical pulses, each of a duration of 1 ms and separated by 10 ms, fed through a constant-current unit to the posterior tibial nerve behind the medial malleolus (Pedersen, 1954). Here, series of three single reflexes were performed, each separated by three minutes to avoid habituation (Pedersen *et al.*, 1974a).

The electromyographic reflex responses were detected by surface electrodes glued to the skin after

the skin had been appropriately treated. For the recording of the H and T reflexes the electrodes were placed 3 cm apart in the midline over the soleus muscle, and for the flexor reflex over the tibialis anterior muscle.

All electromyographic responses were fed to DISA EMG amplifiers (type 14A10), monitored, and stored on video-tape for later assessment (Pedersen and Klemar, 1974). During the investigation, all subjects tested in the supine position had the leg well supported with the knee joint slightly flexed (160°) and the foot fixed in a transducer pedal with the ankle joint at 100°.

Subjects tested in the sitting position were investigated with the knee joint flexed (120°), and they also had the foot fixed in the transducer pedal at 100°. The voiding pattern was determined in these subjects. According to the shape of the voiding curve obtained from the mictometer supplemented by the subjects' own observations as to straining, the subjects were divided into two groups—namely, (a) one with easy initiation of voiding without initiating straining and good maximal flow (above 10 ml/s) and (b) another with difficulty in initiation of voiding requiring abdominal straining and resulting in poor urine flow of about 5 ml/s.

## RESULTS

The T reflex was investigated during cystometric bladder filling in 20 patients. It increased in 11 and decreased in five, often preceded by an initial increase. The pattern showed no significant correlation either with the neurological status or with the type of cystometrogram, although four of the five patients with decreasing T reflexes were spastic including three with hyperactive bladders.

The flexor reflex assessed in 13 patients during cystometry was found to increase in three, all with spasticity and two of them with hyperactive bladders; it decreased in nine cases and was unchanged in one. Thus, the general pattern was the reciprocal of the T reflex—that is, the flexor reflexes decreased during cystometric bladder filling. This reciprocity was also demonstrated in three patients in whom T reflexes and flexor reflexes were elicited during the same cystometry. In two of them, both with hyperactive bladders, we found increasing flexor reflexes and concomitantly decreasing T reflexes, while the third, with a large-capacity bladder and disturbed sensibility, had increasing T reflexes and decreasing flexor reflexes (Fig. 1).

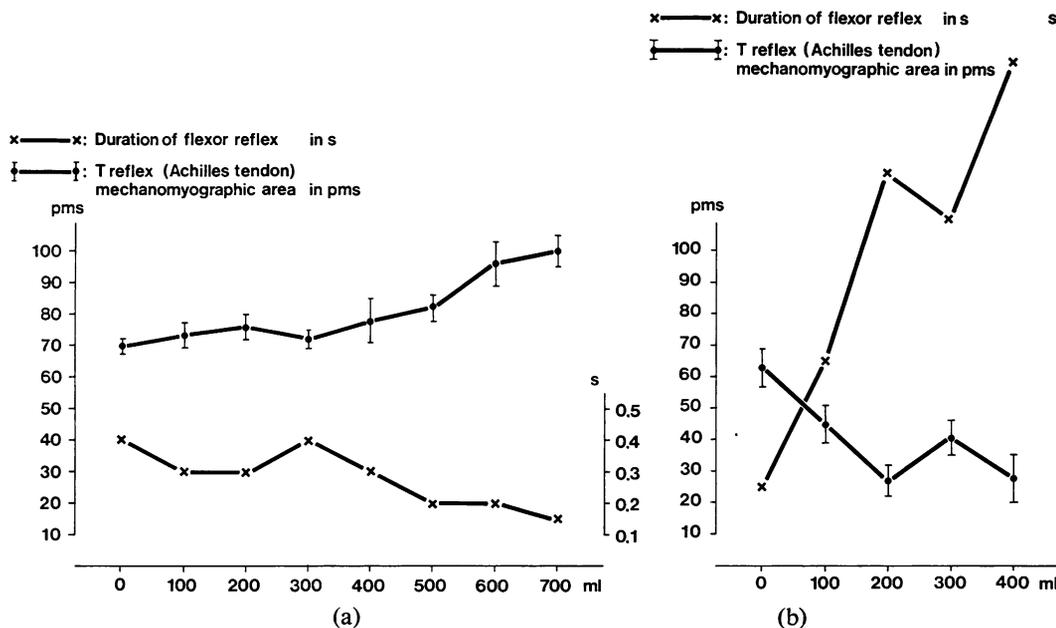


FIG. 1 Opposing patterns of flexor reflex and T reflex changes during cystometric bladder filling. (a) represents the pattern in a patient with a large-capacity bladder and disturbed sensibility, while (b) was found in a patient with hyperactive bladder. Ordinate: T reflex mechanomyographic area in pms (left). Duration of flexor reflex in seconds (right). Abscissa: bladder filling in milliliters.

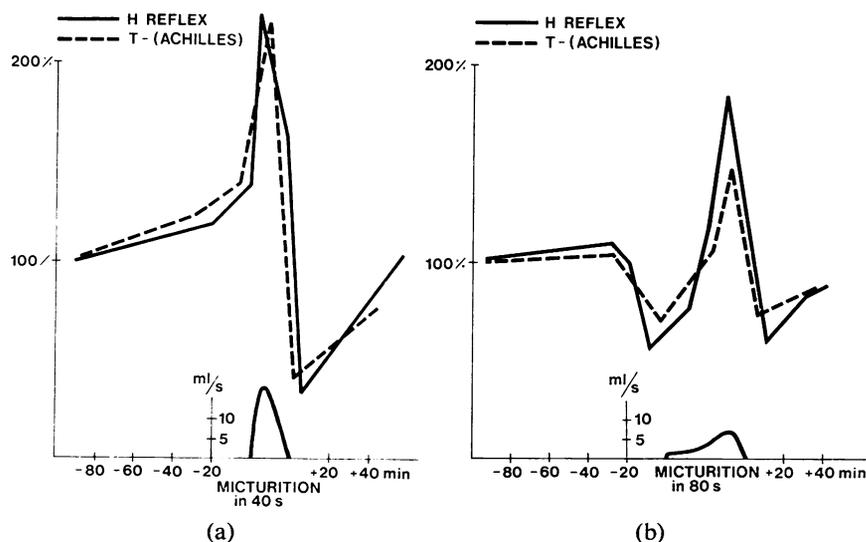


FIG. 2 Patterns of H and T reflex changes during natural bladder filling, micturition, and post-voiding phase. (a) represents the averaged pattern in test persons with easy initiation of voiding (type a), while (b) represents the averaged pattern in persons with difficulty in initiation of voiding (type b). Ordinate: electromyographic amplitudes of H and T reflexes in per cent of the basic value. Urine flow in ml/s. Abscissa: time scale in minutes. Note that another time scale is used during micturition.

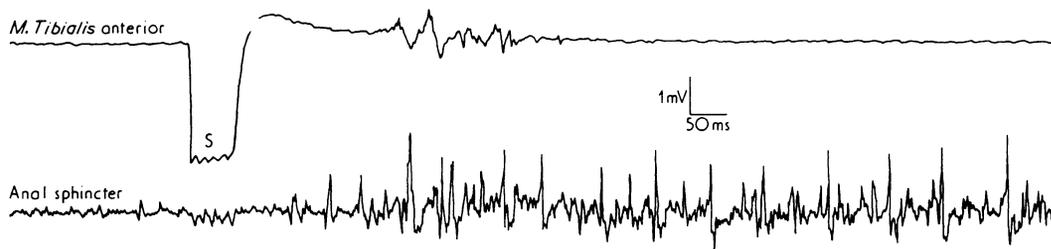
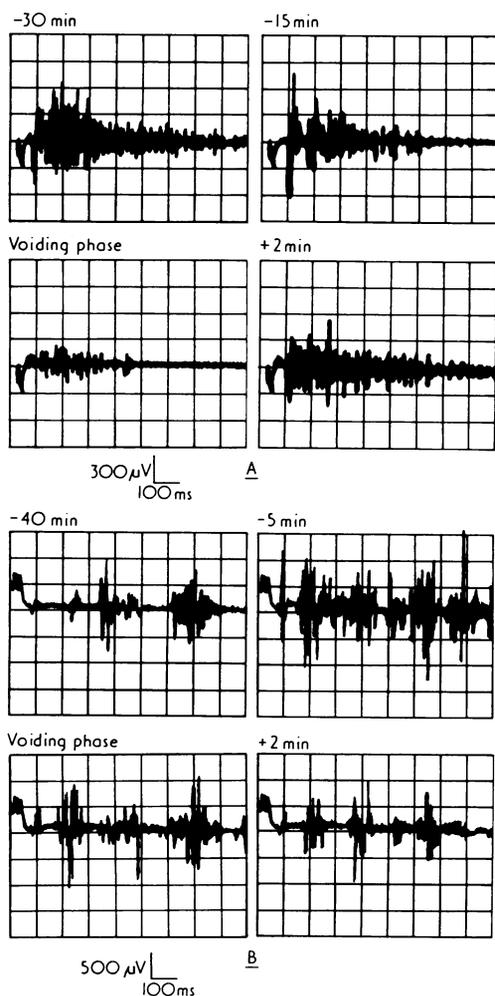


FIG. 3 Simultaneous EMG recordings of reflex responses in the tibialis anterior muscle (upper trace) and in the external anal sphincter (lower trace) in response to electrical stimulations of the posterior tibial nerve behind the medial malleolus. The response from the tibialis anterior muscle was picked up by two surface electrodes, while the sphincter response was picked up by a monopolar intramuscular needle electrode.



In all 17 normal volunteers, we investigated both the H and the T reflex. We found the same pattern of changes in both the H and T reflexes in the individual person, both during natural bladder filling, voiding, and in the post-voiding phase. During the filling phase, the mono-synaptic extensor reflexes (H and T reflexes) increased in eight and decreased in nine of the test persons (often after an initial increase) (Fig. 2). During voiding, increasing H and T reflexes were found as the general pattern. When comparing the initiation of micturition (types a and b) with the pattern of reflex changes during bladder filling, we found a significant correlation between easy initiation of micturition (type a) and increasing extensor reflexes during filling, and between difficulty in initiation of micturition (type b) and falling H-T reflexes during the filling phase ( $P < 0.02$ ). During micturition it was observed that, even though it started with a poor flow, it often increased later in the voiding phase, which gave rise to increasing reflexes—that is, the larger the flow, the higher were the extensor reflexes. In the post-voiding period, the reflexes remained at the increased level for a couple of

FIG. 4 Flexor reflex recordings during natural bladder filling, voiding, and post-voiding phases. (A) Patient with type a voiding pattern and satisfactory flow. (B) Patient with type b voiding pattern. During the reflex elicitation, the flow here was very poor and was accompanied by abdominal straining and considerable anal sphincter EMG activity.

minutes, then often fell below the initial value, after which the pattern observed during the filling phase was repeated.

Three of the normal volunteers, all medical students, were asked to contract the urethral sphincter. During this procedure, we observed a strong reduction in the H and T reflexes.

In the six patients with multiple sclerosis investigated in the sitting position, we assessed the flexor reflex and anal sphincter activity. During the filling phase, we found increased flexor reflexes in three and reduction in three. In a comparison with their urine flow pattern, we found that all with easy initiation of voiding (type a) had decreasing flexor reflexes and decreasing activity of the anal sphincter, and all with difficulty in initiation of voiding (type b) had increasing flexor reflexes during natural bladder filling with a concomitant increase in the sphincter electromyogram. It was also found that the elicitation of a flexor reflex always gave rise to a reflex contraction of the anal sphincter (Fig. 3). During voiding, the flexor reflexes were depressed when the flow was good and the sphincter EMG was reduced or abolished, and only slightly depressed when the flow, often initiated by straining, was poor and the sphincter EMG unaffected (Fig. 4). In the post-voiding period, the reflexes returned to about their initial level.

#### DISCUSSION

This study shows that both monosynaptic extensor reflexes and polysynaptic flexor reflexes of the lower extremities are affected during filling of the urinary bladder in normal subjects, in neurological patients with bladder dysfunction, and in urological cases. This result is not in agreement with the observations reported by McPherson and Skorpil (1966), who did not find any influence on the H reflex during filling of the bladder. The explanation of this discrepancy may be that they measured the reflexes only during a relatively short period towards the end of bladder filling, during which period two opposing patterns of reflex changes may occur as shown in our study. Such opposing patterns will tend to cancel out each other, when they are measured in a group of patients.

Both during filling of the bladder and during voiding, the pattern of changes in the H and T

reflexes was always the same in the individual subject. This parallelism between the H and T reflexes suggests that the observed changes are due to a direct influence from bladder receptors on the alpha motoneurons and are not exerted through the gamma system as assumed by McPherson and Skorpil (1966) on the basis of H reflex studies and by Marsden *et al.* (1969), who studied the tonic vibration reflex during micturition in a few cases. Our observation that the flexor reflex is also affected, and always in the direction opposite to the monosynaptic extensor reflex, is in support of the assumption of a direct influence of bladder receptors on the alpha motoneurons.

As early as 1906, Sherrington demonstrated that the elicitation of a stretch reflex *per se* gives rise to a reciprocal influence on agonist and antagonist. The flexor reflex, too, can influence the stretch reflex, as shown by Lundberg (1966), who found in cats that the flexor-reflex afferent nerve fibres can inhibit Ia afferent fibre impulses. In our own laboratory, we have observed inhibition of the monosynaptic reflexes for about one minute after the elicitation of a flexor reflex. We have, however, avoided this spinal interaction by allowing a sufficiently long time interval after the elicitation of a reflex: 10 s after monosynaptic and 3 min after flexor reflexes in agreement with the minimum values recommended by Desmedt *et al.* (1973) and Pedersen *et al.* (1974a).

We thus think that the inflow from the bladder exerts a reciprocal effect on the monosynaptic extensor reflexes and on the flexor reflex, as appears both directly from our simultaneous measurements of T reflexes and flexor reflexes in three patients and indirectly from the fact that the monosynaptic and the flexor reflexes were inversely related to the voiding pattern.

Voluntary contraction of the urethral sphincter depresses the extensor reflexes as shown in the three medical students. In the six patients with multiple sclerosis, the anal sphincter was always influenced in the same way by bladder filling and micturition as the flexor reflex, which in other cases was found to change opposite to the extensor reflexes. In normal subjects and in patients with supranuclear lesions, the anal sphincter would be expected to represent also the urethral sphincter. These observations may thus be helpful in the elucidation of the mechanisms of the voiding

difficulties often encountered in neurological patients.

We assume that the reflex pattern, consisting of increasing extensor reflexes on the one hand and depression of the flexor reflexes and the activity of the sphincter muscles on the other (pattern A), is induced through impulses from the detrusor muscle stretch receptors. If, in man, they are coupled in series as has been demonstrated in the cat (Iggo, 1955), this pattern should be exaggerated during voiding. Here the detrusor contraction will stretch these receptors further. This was found to be the case in most of the normal volunteers and in the three sitting multiple sclerosis patients with type a voiding pattern.

The inverse reflex pattern, consisting of depressed monosynaptic reflexes, increased flexor reflexes and increased sphincter activity (pattern B), often coming into action at a later stage of bladder filling, may then be induced by another receptor type, giving rise to sphincter contraction and flexor alpha-motoneurone hyperactivity, reciprocally inhibiting the extensor alpha-motoneurons and thus the H and T reflexes. Normal persons with intact central pathways should then be able to depress the impulses from this receptor type, responsible for the sphincter contraction preventing voiding from a relatively full bladder. When the impulses are depressed, the voiding should start with concomitant sphincter and flexor muscle relaxation and extensor muscle hyperactivity. That only some of our test persons showed the type B pattern of reflex changes during bladder filling may be due to bladder evacuation at an earlier stage of filling in the persons with pattern A. If the afferent pathways are disrupted, or if the mechanism of depression is defective, as may be expected in some cases of spasticity, this 'security reflex' for preventing voiding at an inconvenient time or place will still be in action when the patient tries to micturate, and the 'detrusor-sphincter dyssynergia' of spasticity (Scott *et al.*, 1967) with unrelaxed sphincter activity during efforts of voiding will be present. However, it is not yet clear where this second receptor type is actually placed, although our test persons with type B reflex patterns reported sensations from the bladder outlet. Nor is it clear whether the improvements in the voiding pattern often

seen in spastic patients after bladder-neck resection (Pedersen *et al.*, 1972) are due to surgical removal of some of these receptors, although this might be a plausible explanation.

Anyhow, the observed patterns of changes of the reflexes during bladder filling, occurring both in normal persons and in patients, should be kept in mind during reflex measurements of fairly long duration, and we therefore recommend that, before such measurements are commenced, the subject to be tested should be requested to empty the bladder.

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