Urinary symptoms and the neurological features of bladder dysfunction in multiple sclerosis

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Abstract
One hundred and seventy patients with multiple sclerosis and bladder dysfunction were evaluated. Emphasis was placed on the relationship between their neurological features and urinary symptoms. The severity of the urinary symptoms was related to the degree of pyramidal impairment in the lower limbs so that both problems are thought to reflect the extent of spinal involvement. No other neurological features correlated with bladder dysfunction. Detrusor hyperreflexia was the commonest finding on cystometry and no patient had areflexia. More than half of the patients had a significantly raised post-micturition residual volume but symptoms were largely unreliable in predicting poor bladder emptying. In this series only two patients had evidence of upper tract disease: both men with severe, longstanding neurological disease who had indwelling catheters. Detrusor hyperreflexia can be anticipated in patients with MS who have irritative urinary symptoms and pyramidal signs in their lower limbs. After measurement of the residual volume appropriate treatment can be instituted.

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Bladder dysfunction can cause some of the most distressing symptoms in multiple sclerosis (MS). Unpredictable urgency combined with poor mobility has a highly adverse effect on any patient's morale and ability to function in society. Fortunately, the symptoms are not an indication of sinister urological disease and upper tract complications and renal failure in MS¹⁻³ is extremely uncommon.

The neural control of the bladder is complex and requires the coordinated action of the autonomic and somatic nervous systems.

Neural pathways which modulate bladder function traverse the length of the spinal cord between the pons and the sacral spinal cord and are particularly vulnerable in diseases which affect the cord. An area in the dorsal tegmentum of the pons is thought to act upon a spino-bulbo-spinal pathway and "switch" between the storage and voiding phases of micturition.⁴ Higher centres, especially the medial frontal lobes, influence the pontine micturition centre mainly in an inhibitory manner.⁵ As the pathways which control bladder behaviour extend throughout the central nervous system, physiological control is likely to be affected by a disease characterised by disseminated lesions.

The high incidence of bladder dysfunction in MS was first recognised by Oppenheim.⁶ Several series since have reported an incidence of urinary symptoms in approximately 75% of all patients with MS.⁷⁻¹²

The commonest symptom is urgency of micturition, which occurs in 24-86% of all those with bladder dysfunction^{8 10 11 13-18} (see table 1). Urinary frequency has been reported in slightly fewer patients, the incidence varying between 17-65%^{10 17} and urge incontinence between 34-72% of patients with bladder dysfunction.^{8 17}

The term "retention" has been applied to both difficulty with and hesitancy of micturition and consequently the incidence of complete urinary retention is unclear. From the data available, however, it seems that a complete failure to void in MS is unusual.^{11 15} Hesitancy of micturition is common and has been reported between 25%¹⁵ and 49% of patients,¹³ and is more common in male patients.^{11, 14}

Formerly the diagnosis of MS could only be established several years after the onset of the first neurological symptoms, and therefore, data or urinary symptoms in the early stages of the disease has depended largely upon patient recall and may thus be question-

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Table 1 The urinary symptoms in 9 studies of patients with MS and bladder dysfunction

	Number of patients	% with urgency	% with frequency	% with urge incontinence	% with hesitancy	% with retention
Sachs (1921) ¹³	57	31%		37%	49%	
Langworthy (1938) ⁸	97	54%	33%	34%	40%	
Carter (1950) ¹⁰	36	24%	17%	50%		17%
Miller (1965) ¹¹	231	60%	50%	36%	33%	2%
Bradley (1973) ¹⁴	90	86%	60%		28%	20%
Philp (1981) ¹⁵	52	61%	59%	47%	25%	8%
Goldstein (1983) ¹⁶	86	32%	32%	49%		
Awad (1984) ¹⁷	47	85%	65%	72%	36%	
Gonor (1985) ¹⁸	64	70%	48%	56%	30%	

able. Miller *et al*¹¹ and Goldstein *et al*¹⁶ stated that urinary symptoms were the sole presenting symptoms of MS in 2% and 2.3% of their series of patients, respectively. Estimates of urinary symptoms occurring as part of the presenting symptom complex are mostly higher, varying from 2.8–14%.^{9 11 16 19 20}

Despite the large number of patients with MS who have urinary symptoms, few investigators have considered the bladder dysfunction in relation to the neurological features. Most studies have been carried out by urologists who have placed greatest emphasis on the results of urodynamic studies.

Hyperreflexia has been the commonest abnormality of detrusor function, found with a frequency between 52–78% (table 2).^{1 12 14–18 21–29} In contrast to the universal finding of a high incidence of detrusor hyperreflexia, urodynamic studies have shown a variable incidence of detrusor areflexia, that is, bladder acontractility.³⁰ The reported incidence of detrusor areflexia varies widely from 0%¹⁵ to 40%.^{14, 25} Some investigators have proposed that detrusor areflexia results from demyelination in the conus medullaris¹³¹ but Philp *et al*¹⁵ who did not find any cases of areflexia in their series, carried out a histological study of MS spinal cords and found that plaques in the conus occurred in only 18% of cases. These authors argued that demyelination in the conus could not account for the previously reported incidence of areflexia and that earlier urodynamic studies may have included patients who did not have MS.¹⁵

The relationship between the patients' neurological features and bladder symptoms has been the least studied aspect of the problem. Bladder symptoms were reported by Miller *et al*¹¹ to be associated with the presence of pyramidal signs in the lower limbs. In the same study, a high correlation between bladder dysfunction and bilateral impairment of vibration sense was demonstrated. In another study¹⁷ the patients' Kurtzke scores were compared with their urinary symptoms; the presence of urge incontinence, urgency, nocturia and frequency correlated with the scores for pyramidal and sensory dysfunction and with the total disability scores.

We report the results of a uro-neurological study to examine the nature of the urinary

symptoms and the urodynamic findings together with the neurological features.

Methods

We studied 170 patients with definite MS (Poser criteria) who were referred to the Department of Uro-Neurology for advice on the management of their urinary symptoms. The patients' demographic details, duration of the illness, duration of urinary symptoms and results of neurological examination were recorded and corroborated when necessary by reviewing the case notes. Patients were assessed on the Kurtzke system and disability in each functional group scored accordingly.

Post micturition residual volumes were measured in all patients by catheterisation. A total of 70 patients had cystometric studies using a slow filling technique (20mls/minutes). In many patients immobility precluded uroflowmetric studies and analysis of the urinary flow pattern was only possible in 45 patients. Intravenous urography (IVU) was carried out in 56 patients (12 female and 44 male).

Results

The study included 170 MS patients (97 females and 89 males) with urinary symptoms. Their mean age was 44 years (range 20–78 years). The mean duration of MS was 12 years (range 6 months–48 years). Patients had experienced urinary symptoms for an average of 6 years (range 2 months–31 years). The mean time between the first symptoms of MS and the onset of bladder dysfunction was 8 years (range 0–29 years). Most patients developed bladder dysfunction several years after the first neurological symptoms but in 4 the urinary symptoms were part of the presenting symptom complex. Urinary dysfunction was not the sole presenting symptom of MS in any patient.

Features of patients' urinary symptoms are summarised in table 3. Urgency and frequency of micturition were the commonest symptoms occurring in 85% and 82% of patients respectively. Urge incontinence affected 63%, and 14% of the patients had nocturnal enuresis. A total of 43% complained either of a

Table 2 Summary of the urodynamic findings in 16 studies of the bladder dysfunction in MS.

	Number of patients	Hyperreflexia	Hyporeflexia	Normal
Bradley (1973) ¹⁴	99	59%	40%	
Anderson (1976) ²¹	52	63%	33%	4%
Bradley (1978) ¹	302	62%	34%	4%
Summers (1978) ²²	50	52%	12%	18%
Schoenburg (1979) ²³	39	69%	5%	15%
Piazza (1979) ²⁴	31	74%	6%	9%
Blaivas (1979) ²⁵	41	56%	40%	4%
Philp (1981) ¹⁵	52	99%	0%	
Goldstein (1982) ¹⁶	86	76%	19%	
Van Poppel (1983) ¹²	160	66%	24%	10%
Awad (1984) ¹⁷	57	66%	21%	12%
Hassouna (1984) ²⁶	37	70%	18%	11%
Petersen (1984) ²⁷	88	83%	16%	1%
McGuire (1984) ²⁸	46	72%	28%	
Gonor (1985) ¹⁸	64	78%	20%	2%
Weinstein (1988) ²⁹	91	70%	16%	12%

Table 3 The urinary symptoms in 170 patients with MS and bladder dysfunction

	% of patients
Urgency	85%
Frequency	82%
Urge incontinence	63%
Hesitancy	49%
Interrupted stream	43%
Sensation of incomplete bladder emptying	34%
Nocturnal enuresis	14%

reduced or interrupted urinary stream and 34% had a sensation of incomplete bladder emptying. A complete failure to void occurred in 2 patients. One of these had become acutely tetraplegic and the other had been given a tricyclic antidepressant.

The great majority of these patients with MS and bladder dysfunction had pyramidal signs in their lower limbs; 95% of the patients had bilateral extensor plantar responses and pathologically brisk lower limb tendon reflexes. Flexor plantar responses were found in only 8 patients (4%), 4 of whom were thought to have abnormally brisk lower limb reflexes. The Kurtzke scores for bladder symptoms and the other functional group scores are shown in fig 1. All patients had urinary symptoms and therefore no patient had a zero bladder function score. Many patients with urinary symptoms had zero scores in the cerebellar, brainstem, visual, mental or sensory functional groups.

Figure 2 shows the patients' pyramidal and bladder function scores. There was an obvious association between the degree of pyramidal tract dysfunction and the severity of the urinary symptoms. Few patients had marked urinary symptoms and low pyramidal scores.

An apparent relationship was also found between the expanded Kurtzke disability status score (EDSS)³² and the severity of the bladder dysfunction, which is to be expected as the EDSS depends largely on the degree of pyramidal dysfunction in the lower limbs. Most patients in the series who were wheelchair dependent (EDSS score > 6.5) had reported at least one episode of urge incontinence.

An internuclear ophthalmoplegia (INO) was found in 16 patients but in 14 of these there were, in addition, signs of pyramidal tract disease. In 2, however, there were no pyramidal features, suggesting that a pontine lesion might be responsible for both their bladder and eye movement disorder. Both these patients appear as exceptions in the apparently linear relationship between pyramidal and bladder dysfunction, shown in fig 2.

A total of 107 (63%) patients had post-micturition residual volumes greater than 100 mls and their mean residual volume was 220 mls (range 100–700 mls). An important observation was that only 47% of the patients with a significantly raised residual volume actually had sensations of incomplete bladder emptying. However, 83% of the patients who thought their bladder emptying was incomplete, had residual volumes of more than 100 mls.

Filling cystometry showed hyperreflexia in 63 patients (91% of those in whom urodynamics were carried out). The remaining 7 had normal detrusor activity. No patient had detrusor areflexia. Of those patients with normal detrusor activity, 3 had pyramidal function scores of 2, and 3 had scores of 1. Of the 2 patients with zero pyramidal scores, 1 was

Figure 1 The Kurtzke functional group scores in 170 patients with MS and urinary symptoms. The Y axis represents the number of patients with each Kurtzke functional group score.

Figure 2 The Kurtzke pyramidal and bladder function scores in 170 patients with MS.

found to have detrusor hyperreflexia. Most patients with detrusor hyperreflexia had pyramidal scores of 3 or more.

The urodynamic finding of hyperreflexia correlated well with the symptoms of urgency, frequency and urge incontinence. Patients with stable detrusor activity had Kurtzke bladder function scores of 1 or 2 and their symptoms included mild hesitancy, frequency and urgency (Kurtzke bladder function score 1) with rare episodes of urge incontinence (Kurtzke bladder function score 2). The majority of patients in whom hyperreflexia was demonstrated had more severe urinary symptoms, with bladder function scores of 2, 3 or 4. All patients with moderate or severe pyramidal dysfunction in their legs (pyramidal scores of 3 or greater), complaining of frequency and urgency or urge incontinence, were found to have detrusor hyperreflexia.

No patient had biochemical evidence of renal impairment. Of the 56 patients who had intravenous urograms, normal upper tracts were demonstrated in 54. Two male patients had bilateral hydroureters and hydronephrosis. Both had long established MS with neurological symptoms for 22 and 48 years and urinary symptoms for 15 and 19 years, respectively. They had both been confined to a wheelchair for more than 5 years. Their bladder dysfunction had been managed by indwelling catheters for several years and they had had several episodes of urinary tract sepsis.

Discussion

Our study demonstrates that in MS the occurrence and severity of the urinary symp-

toms are related to the extent of pyramidal dysfunction in the lower limbs. This agrees with the findings of Miller *et al*¹¹ and Awad *et al*.¹⁷ The mean age of the patients and the mean duration of disease in this series were similar to those of previous studies of bladder dysfunction in MS.^{11,17} One notable difference in this series was that in none of our patients was bladder dysfunction the sole presenting feature of MS, in contrast to 2% found in other series.^{11,20} In other reports^{7,9,19,20} only a small proportion of MS patients had urinary symptoms in the early stages of the disease and then always in association with other neurological features of MS. In the past, urinary retention in young women has been attributed to MS and this could account for the reports that patients diagnosed as having MS presented with only urinary symptoms. The identification of an alternative cause for isolated urinary retention in young women³³ and the rarity of a complete failure of voiding in MS, means that urinary retention without other neurological signs should probably not be regarded as a symptom of MS. Furthermore, no woman with isolated urinary retention and abnormal sphincter EMG activity as described by Fowler *et al*,³⁴ has subsequently developed MS.

The coordinating centre of micturition is thought to be in the dorsal tegmentum of the pons and disorders of micturition have been described in patients with various pontine lesions.^{35,36} The role of pontine lesions in causing bladder dysfunction in MS appears to be relatively insignificant because most patients with an internuclear ophthalmoplegia also had a pyramidal lesion (14 out of 16). In 2 there was no pyramidal deficit, suggesting that pontine pathology in the vicinity of the

micturition centre was a significant factor.

The commonest urinary symptoms were irritative in nature (that is, urgency, frequency and urge incontinence) and difficulty in initiating voluntary voiding was a concurrent symptom in approximately half of the patients. Patients with more advanced bladder dysfunction became unable to void voluntarily and could empty only when they experienced spontaneous hyperreflexic detrusor contractions.

The recognition of incomplete bladder emptying is important since anticholinergic medication given for hyperreflexia may be ineffective if the residual volume is large. Symptoms of retention provide some guide to the likelihood of incomplete bladder emptying but were found not to be sufficiently reliable to exclude the problem. Measurement of the post-micturition residual volume is therefore an essential part of the assessment of a patient with MS who has urinary symptoms. More than half of the patients were found to have significant residual volumes and this has important therapeutic implications in patients with MS.

The commonest urodynamic finding was detrusor hyperreflexia and the results indicate that MS patients with irritative bladder symptoms and lower limb pyramidal involvement are highly likely to have detrusor hyperreflexia.

The explanation of detrusor areflexia in MS remains uncertain. Several investigators have reported that in some patients with MS the initial urodynamic tests showed detrusor areflexia but subsequent studies demonstrated hyperreflexia.^{16 23 28 37} The neurological basis for this complete change in detrusor activity remains obscure.

Of particular importance in the modern concept of the neural control of the bladder are long loop reflexes via the pontine tegmentum.⁴ Interruption of pathways between the sacral cord and pons may result in detrusor hyperreflexia and loss of the coordinated action of the detrusor and the external striated urethral sphincter during voiding, a condition known as detrusor sphincter dyssynergia (DSD).³⁸ The reported incidence of DSD in MS patients varies from 18%²⁹ to 66%.³⁹ DSD is important in the management of MS patients because of the resulting tendency to incomplete bladder emptying, compounded by poorly sustained detrusor contractions. Hesitancy of micturition, an interrupted urinary stream and the finding of a high post-micturition residual volume in a patient with spinal cord disease suggest DSD.

The risk of patients with MS developing serious renal impairment may have been over emphasised in the past. In two studies of the causes of death in patients with MS,^{40,41} no patient was reported to have died from renal failure. However, Samellas and Rubin⁴² reported an extraordinarily high mortality rate from urological complications; 12 of 20 deaths in patients with MS from either "hydronephrosis, pyelonephritis or septicaemia arising in the urinary tract". In a later

study,⁴³ 4 of 73 deaths were said to have been due to urological problems. Other investigators have concluded that renal impairment and upper urinary tract problems are uncommon in patients with MS.^{1-3 12} This study suggests that only male patients with very longstanding urinary symptoms and severe neurological disability in their lower limbs are at risk of developing dilatation of their upper urinary tracts.

Although we have not specifically addressed the question of treatment, the two main disorders which arise in MS patients with urinary symptoms are detrusor hyperreflexia and incomplete emptying. The post-micturition residual volume cannot be predicted from the urinary symptoms but is easily measured by catheterisation or ultrasound. The majority of MS patients with bladder dysfunction are managed by non-surgical means; anticholinergics to control hyperreflexia and intermittent catheterisation if there is a significant post-micturition residual volume. Thus in a patient with MS and symptoms of bladder dysfunction who has pyramidal signs in the lower limbs, detrusor hyperreflexia with a variable degree of incomplete emptying can be anticipated and appropriate treatment instituted after measuring the post-micturition residual volume.

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