
The characterisation of the urodynamics of elderly people with lower urinary tract dysfunction

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MD Thesis 1991

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Summary

This thesis examined the age-related differences in the urodynamics of men and women presenting with symptoms of lower urinary tract dysfunction. In order to characterise the nature of the differences as precisely as possible the urodynamic data were analysed according to mechanically based mathematical principles derived by a number of physicists working the field. I developed a set of computer programmes which were used to collect and process the data. In addition, I constructed a computerised mathematical model of the micturition process which was used to illustrate the theory behind my approach to analysis as well as to aid in the interpretation of the data. A very large sample was used (2393 patients) so that age-related changes could be examined across the four decades of late life. Important differences were found, the most striking findings concerned voiding abilities which seemed to be markedly compromised in the elderly because of problems in sustaining micturition and reductions in the speed of detrusor shortening. Elderly men were found to show fewer differences from their younger counterparts than those shown by women. Many of the changes, similar to those seen in the elderly, were found to occur in a number of important illnesses which affect both the young and the old. A number of assumptions made about the elderly were refuted and I obtained data which contradicted the findings of some other workers in the field.

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Overview and Introduction

Overview

This is a detailed study of the urodynamics associated with lower urinary tract dysfunction in late life. Care has been taken to obtain data on a large number of patients so as to examine differences over the four decades of old age. In order to identify specific age associated changes I have studied a large sample of younger patients of adult years. Because intercurrent illness is such a common accompaniment to aging I have made a point of identifying groups of patients suffering from a number of common, relevant illnesses, irrespective of their age.

I did not believe that techniques such as videourodynamics or urethral pressure profilimetry would ever be applicable in geriatric departments (Turner-Warwick & Whiteside 1979). To this end I made use of mathematical techniques, derived from the work of a number of physicists, which allow the calculation of informative parameters from basic pressure/flow urodynamic data. I felt that in describing urodynamic data by means of specific parameters I would be able to facilitate accurate interpretation by less experienced investigators. Many of the calculations which I used were complicated and required microcomputers for their processing. To achieve them I developed a set of computer programmes which may be used in clinical departments to derive informative parameters without the requirement for a facility with the mathematics nor a deep understanding of urodynamic theory.

I have explained the derivation of the mathematical equations, used to describe the physics of micturition, in some detail. I have developed a few of my own refinements. In order to illustrate the principles, I created computerised mathematical models which generated data that could be compared with clinical observations. These served to ensure my own understanding, test the validity of the theory and hopefully, provide computer tools which could be used by urodynamisists to to educate themselves about the subtle aspects of their craft. c /

I have used mathematical principles to characterise my observations of urodynamic changes in the elderly. To my knowledge this thesis includes the most detailed analysis of age associated changes of disordered micturition in late life. I do not believe that my findings are conclusive. I believe that they may form a basis for future exploration and development in the mangement of incontinence in late life.

I am conscious of the danger of excessive discursion in a work of this kind. I have attempted to minimise the written text and maximise the use of illustrations, graphs and diagrams. In order to lay the foundations I have had to review, very briefly, the relevant anatomy and physiology of the lower urinary tract. So as to be succinct I have minimised the descriptions of the software techniques which I used, even though the work on this part of the project took the greatest time. In the end, it is the products of software which count.

Introduction

Urinary incontinence in the elderly is an important but very neglected issue. Although it is accepted as a common symptom the prevalence has been hard to establish. Milne (1979) reviewed seven population studies with prevalence figures for female urinary incontinence of between 1.6% and 42%. This disparity reflected the use of different interviewing techniques, with workers using varied definitions of incontinence. Yarnell and St Leger (1979), while studying an elderly population, found the prevalence of incontinence, defined as urinary leakage in the previous twelve months, to be 17% in women. Only 5.3% of their sample experienced daily leakage and this compares with the findings of Milne et al (1972) who reported a 5% incidence of severe incontinence amongst the elderly. The prevalence is higher in hospitalised patients, Milne (1979) describes prevalence figures of between 21.9% and 47%.

The most widely quoted study is that reported by Thomas et al (1980). They examined a sample taken from the population of two London boroughs. The prevalence of incontinence known to the health and social service agencies was 0.2% in women and 0.1% in men aged 15-64 and 2.5% in women and 1.3% in men aged 65 and over. However, when people themselves were asked about their symptoms the reported prevalence was very different. Urinary incontinence was experienced by

8.5% of women and 1.5% of men aged 15-64 and 11.6% of women and 6.9% of men aged 65 and over.

Despite the importance of these findings, our knowledge of the processes affecting the incontinent elderly are rather lacking, and data from large clinical studies are particularly meagre.The earliest investigative studies conducted on elderly patients with urinary incontinence were reported by Brocklehurst and Dillane (1966a, 1966b) who noted the high incidence of detrusor instability and its association with neurological disease, either cerebrovascular disease or dementia. In addition they also reported the presence of a residual urine volume in some patients with detrusor instability. Isaacs and Walkey (1964) reported a close association between mental and physical disability and the severity of urinary incontinence when studying hospitalised patients.

Castleden et al (1981) published a paper which examined the urodynamic findings in 100 elderly patients referred to an incontinence clinic, 48 attending as outpatients although ten of these were inpatients in other hospitals. Thirty eight of whole sample had clinically detectable neurological disease. These workers found that they were able to classify their patients into four groups, normal (16%), unstable (67%), underactive (11%) and irritable (5%) (Irritable is equivalent to sensory urgency). They pointed out that elderly patients with unstable bladders did not necessarily suffer from neurological disease. They were unable to identify any bladder capacity or pressure level which characterised any of their groups. Some difficulties arise over the interpretation of the results because the definitions used in this paper were not very clear. Little data concerning residual urine volume and the pressure flow relationship during voiding was described. The latter issue reflects the limitations of much current urodynamic equipment which does not facilitate and accurate assessment of the voiding phase.

Hilton and Stanton (1981) reported a series involving assessment of 100 elderly women (mean age 74.6 range 65-93) with urinary incontinence. They assigned their patients to different categories but where mixed diagnoses were considered "the patient was assigned to the diagnosis which warranted primary treatment". The criteria used to form this decision were not defined. They described detrusor instability in 29%, detrusor instability and urethral incompetence in 10%, urethral sphincter incompetence in 30%, voiding difficulties in 14% and no abnormality in 5%. The remainder were placed in a miscellaneous category. Thirteen patients had residual volumes over 100 ml. In 10 patients with residual urine volumes between 330 and 1250 ml the residual was evident on abdominal palpation, in the remainder they did not consider the residual significant but did not state their criteria for making this judgement. They found that stress incontinence in women with voiding difficulties was only found in those with palpable bladder enlargement. Vaginal prolapse was uncommon. On the basis of their findings they designed an algorithm for use in assessing elderly patients with urinary incontinence without the use of urodynamic investigation. However, the algorithm was not validated prospectively.

Resnick et al. (1987) reported on 19 women and 3 men with a mean age of 89 years from a chronic care hospital and eight women and two men with a mean age of 79 years who were outpatients. They proposed two entities "Detrusor hyperactivity" and "Detrusor hyperactivity with impaired contractile function", the two forming a bimodal distribution with the latter group emptying less than 25% of the bladder capacity. They noted that the patients with voiding difficulties demonstrated a reduction in contractility during voiding despite unstable activity during filling. The characteristics of this group included a tendency to use abdominal straining during voiding and a slower rise in the detrusor pressure during unstable activity. Unfortunately the numbers were very small and we cannot be confident about bimodal distributions without very large samples.

To date investigative studies on elderly patients with incontinence have been conducted on comparatively small samples of the population without specific reference to the four decades of late life. The variability of the diagnoses means that all workers have identified small subgroups but with data which is too limited to allow valid extrapolation. Elderly people are subject to a variety of diseases and these may influence bladder behaviour in may different ways. My own understanding of the changes associated with the elderly is that they form part of a broad continuum which evolves with only a moderate association with chronological age and in consequence will be impossible to understand without observations on very large numbers. However, this process will never fully resolve our ignorance over the consequences of aging, as we are only able to examine, in detail, cross-sectional samples. Large longitudinal samples, followed over many years, pose impossible logistical problems. By describing our data according to chronological age we can identify changes associated with late life. Even though we may show changes which seem to progress with each decade of late life we cannot claim to be identifying the true effects of aging. Longitudinal studies only, are capable of describing the course of progessive ageing.

At the moment urodynamic studies are used for diagnostic purposes, we do not know whether they have any prognostic value. We are unsure as to when we should perform a urodynamic investigation and when we should treat a patient on clinical impression. The definitions which we use to describe bladder changes are broad and not well suited to mapping therapeutic responses. Many of our methods of interpretation are very crude and fail to integrate the physics of the processes with the pathophysiology. We are also lax about defining the limitations of our methods and tend to license the use of poorly defined clinical judgement. In the process of developing this thesis I have attempted to address some of these problems.

The Anatomy

The urinary bladder performs a dual function by acting as a passive reservoir during filling and as an active contractile organ, expelling its contents during voiding.

The smooth muscle of the bladder, termed the detrusor, forms a large part of the bladder and is of particular interest in relation to continence. The muscle consists of numerous interlacing bundles of fibres. The detrusor muscle does not extend into the urethra (Gosling 1984) but merges with the urethral smooth muscle at the bladder neck. Contraction of the detrusor fibres results in a rise in bladder pressure and ultimately opening of the urethra. The trigone forms a triangular base-plate with its apex at the bladder neck and base running between both ureters. Muscle fibres run from the ureters into the trigone and at the apex trigonal muscle fibres are in contact with those of the urethra. Contraction of the muscle of the trigone results in funnelling of the bladder neck. There are some fibres which originate in the detrusor and are inserted into the external surface of the trigone distally. These fibres will pull the distal surfaces of the trigone apart and thus open the bladder neck (Brocklehurst,1978). The internal urethral sphincter is fully developed in the male and forms a circular collar continuous with the prostatic smooth muscle. This sphincter is not present in the female, indeed the muscle fibres at the bladder neck in the female are arranged longitudinally and could not provide a sphincteric function. We now recognise that an open bladder neck seen during cystometry is not necessarily associated with urinary incontinence (Versi et al 1990). In the male the internal sphincter functions to prevent the retrograde flow of semen during ejaculation and its failure to function is associated with passing semen in the urine after ejaculation and with infertility. Despite this primary function the internal sphincter still needs to relax during normal micturition. (Gosling et al,1981)

The external urethral sphincter is present in both sexes and is the site of maximum urethral resistance (Griffiths,1980). The circularly arranged muscle fibres are striated and extend into the anterior wall of the urethra proximally and distally. The striated fibres of the external sphincter are less dense posteriorly. The sphincter is quite separate from the periurethral striated muscle of the pelvic sling which passes lateral to the urethra and inserts into the inferior pubic rami. The sphincter does not contain any spindles and the fibres are slow twitch in character. With the support of the numerous elastic fibres in the wall of the urethra, the external sphincter is able to maintain a constant resting tone (Gosling 1984). On coughing or abdominal straining the pressure in the urethra at the external sphincter will normally rise higher than the abdominal pressure (Griffiths 1980), this results from transmission of the cough impulse from the abdomen to the proximal urethra and a reflex contraction in the sphincter.

The pelvic sling does not encircle the urethra as a sphincter would. This sling supports the bladder and proximal urethra posteriorly. Without this support the bladder neck becomes incompetent and abdominal pressure transmission and associated reflex sphincter activity fails (Hald,1984).

The prostate gland is present only in men, there has been a fruitless search for a prostate analogue in women. The organ consists of a mixture of glandular tissue and smooth muscle. The muscle has a constant resting tone which can vary and may influence the passage of urine through the prostatic urethra. Benign nodular hyperplasia of the prostate is universal over the age of forty but only 10% of men develop obstructive symptoms which are particularly common in caucasians and american negroes (McNeal,1983).

In both sexes continence is usually maintained at the bladder neck because of the passive closure that the smooth muscle and elastic tissue promote and because of its position in the abdominal cavity. The external sphincter plays a role when the bladder neck is open. Women, who have a short urethra and no prostate, have to depend heavily on the external sphincter, supported by the urethral elastic tissue and the pelvic floor muscle. The position of the female urethra is critical for the maintenance of continence (Hald, 1984).

The Pharmacological Anatomy

Most of the detrusor fibres carry muscarinic cholinergic receptors which are innervated by parasympathetic efferents originating in the intermedio-lateral columns of sacral segments two, three and four (Fletcher & Bradley 1978). Stimulation of these neurones results in a contraction.

There are a number of other receptors within the detrusor but their clinical significance is limited (Eaton et al 1981, Hindmarsh et al 1977, Khalof et al 1981). The bladder neck and internal sphincter are richly supplied with excitatory alpha-1 receptors, some excitatory cholinergic receptors and a few inhibitory beta-2 receptors (Gosling et al 1981, Caine et al 1975). The smooth muscle of the urethra has a similar receptor distribution (Gosling et al 1981). Cholinergic and alpha adrenergic stimulation cause a rise in pressure at the membranous urethra (Caine et al 1975). The female urethra has oestrogen receptors throughout its length with maximum concentration in the distal two-thirds (Wilson et al 1981). Progesterone receptors have not been detected though there is a sensitivity of the urethra to progesterone (Caine & Raz 1973). This subject has been reviewed in considerable detail in a separate publication (Malone-Lee 1984).

The Afferent Pathway Function

The most important receptors in the bladder are tension receptors. The afferents which pass to the lumbar segments of the cord are concentrated in the muscle coats and submucosa of the bladder neck and urethra. Afferents going to the sacral cord are distributed throughout the bladder. The receptors respond, with varying thresholds, to tension produced by distension or contraction (Fletcher & Bradley,1978). The sacral afferents start responding at low bladder volumes and from about two-thirds of bladder capacity they activate a short reflex arc which inhibits detrusor excitation thereby permitting bladder fill without a rise in pressure. The lumbar afferents respond to the extremes of distension and are stimulated at high bladder volumes. All tension afferents ascending to the brain do so in the lateral dorsal columns (Fletcher & Bradley,1978). Some sacral afferents are involved in a different reflex arc. The sensory neurones synapse with motor efferents either at sacral level or, more importantly, after traversing the spinal cord to the pontine reticular formation. This reflex, when activated, initiates micturition and is essential for voiding. It is usually suppressed by the influence of neurones from higher cerebral centres. The sensations of bladder fullness, touch and pain are conveyed from receptors in the submucosa via sacral and lumbar afferents up into the spinothalamic tracts with one third crossing to the opposite side (Fletcher & Bradley,1978)

Central nervous system control

The highest centres involved in the control of micturition are located on the supero-medial aspect of both frontal lobes adjacent to the genu of the corpus callosum. They receive sensory fibres from the brainstem nuclei and the ascending tracts. Motor neurones arising at these centres pass to other parts of the cortex, cross the corpus callosum, or descend in the internal capsule to the brainstem nuclei and reticulo-spinal tracts. If these cortical centres are stimulated experimentally the detrusor becomes activated but they also exert an inhibitory influence on the brainstem centres (Fletcher & Bradley,1978). The thalamus relays sensory signals from bladder, urethral and pelvic receptors to the cortical micturition centres. Some nuclei relay signals to other parts of the brain which mediate modifications of behaviour and autonomic function in response to bladder filling. Motor efferents from the cortical centres synapse in the basal ganglia which send communications to the brainstem motor nuclei. Electrical stimulation of the basal ganglia in experimental animals leads to suppression of the detrusor and ablation results in detrusor hyperreflexia. Distension of the bladder in experimental animals results in activity in the neurones of the posterior hypothalamus and neurones from the anterior hypothalamus communicate with motor neurones travelling to the detrusor. We do not however know what influence the hypothalamus exerts on the lower urinary tract. In man the limbic system would seem to be unassociated with bladder function as ablation of the temporal lobes is not associated with changes in bladder behaviour. The main brainstem motor nuclei governing detrusor activity are situated in the pontine reticular formation. Stimulation of these nuclei results in precipitant detrusor activity whereas ablation leads to detrusor inactivity. The anterior vermis receives sensory signals from the lower urinary tract via the spinocerebellar tracts. From here neurones pass to the fastigial nucleus and thence to the brainstem motor nuclei. Stimulation of the fastigial nucleus results in inhibition of these nuclei. The descending pathways from the brainstem motor nuclei become organised into three important tracts. Nerves originating in the pons, medulla oblongata and midbrain pass in the lateral spinoreticular tract to the motor nuclei of the sacral cord. They function to promote a sustained contraction of the detrusor with inhibition of the sphincters. Another group of fibres pass from the pons in the medial reticulospinal tract and function to inhibit the external sphincter. The third group of neurones arise in the medulla oblongata and travel in the anterior reticulospinal tract and function to inhibit the detrusor and stimulate the sphincters.

The method of urodynamic investigation

The basic urodynamic investigation using pressure-flow cystometry or video cystometry has been described in a number of texts (Griffiths,1980; Turner-Warwick & Whiteside, 1979).

Patients referred to my clinic with symptoms of lower urinary tract dysfunction are asked to attend with a comfortably full bladder. Great care is taken to ensure that they are welcomed to the clinic and not required to wait before being seen. They are interviewed by a carefully trained member of staff who will conduct the whole of the assessment. Occasionally one or two observers may be present. They are given a careful explanation of the procedure, along with the reasons for performing the investigation. Care is taken to reassure them and to allay their anxieties. They are then asked to empty their bladders in private.

The patients are undressed and examined. The rectum is examined and if a faecal impaction is detected the study is postponed until it is cleared. If the rectum is clear a french gauge 14 plastic tube, capped by a perforated latex sheath (to avoid faecal plugging) is passed into the rectum. This is referred to as the **rectal line**. A french gauge 10 plastic Jaques' catheter along with a plastic epidural catheter are passed into the bladder per urethra, after the urethral mucosa has been anaesthetised with 2% lignocaine jelly. The epidural catheter is referred to as the **bladder line** and the plastic Jaques' catheter as the **filling line**. The residual urine is drained and measured, a sample is tested with labstix and a specimen is sent for culture. Evidence of an obvious urinary infection, cloudy proteinous urine with associated pain, results in abandonment of the test.

The patient is then sat on a special commode with a urinary flow meter fitted to the base. The flow meter is a rotating drum flow meter (Abram/s et al 1983). The rectal line and bladder line are connected to force displacement strain gauge transducers, mounted at the level of the superior margin of the pubic symphysis (the zero point for pressure measurements), and filled with normal saline. The filling line is connected to a reservoir of normal saline via a peristaltic pump. The normal saline is at room temperature.

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The bladder line transmits the sum of the pressure generated by the walls of the bladder, the pressure head of fluid in the bladder above the pubic symphisis, and the pressure generated in the abdominal cavity. The rectal line transmits the pressure in the abdominal cavity. Both these pressures are recorded at sampling rate of 3 Hertz throughout the study and the rectal pressure is subtracted from the bladder pressure to give the **detrusor pressure**. Because of the position of the transducers the measurement of the pressure does not reflect the pressure head at the bladder neck and a small error will exist. In addition, the rectal pressure is not an ideal measure of the abdominal pressure and errors may occur in the subtraction process, especially if rectal contractions occur during the study. The operator must be very careful to ensure that excursions on the bladder and rectal line recorded, in response to coughing and blowing on the back of the hand by the patient, parallel each other. If this is not achieved the lines have to be re-positioned. In circumstances where this is not successful the test must be abandoned. In some patients, especially those who are obese, the rectal pressure reading shows a constant error in excess of the resting bladder pressure, this may be corrected by mathematical transformation, but only if the error is a constant. A linear or exponential error would not be acceptable.

The bladder is filled at the rate of 1 ml/sec. The patients are asked to declare the point at which they first experience the sensations which would normally cause them to seek to void. They are asked to retain the contents until 500 ml has been infused into the bladder or they are unable to tolerate any further filling, or when unstable bladder contractions preclude further filling despite effort to suppress them.

After bladder filling the filling catheter is removed but the bladder line is left in place. This operation requires considerable skill and failure to achieve the goal will obviate a successful voiding study. The patient is then asked to stand and to cough vigorously a number of times while the operator examines the external urethral meatus in order to identify any leakage. The pressures are recorded continuously during this process.

The patient is then sat on the commode and asked to void to completion in private, the operator leaves the room, but remains able to view the data screen through an observation window. We do not perform a "stop test", which involves asking the patient to interrupt micturition in mid void. It was thought that this manoeuvre could be used as a means of measuring the isometric detrusor pressure. Considerable doubt now affects this view (Griffiths 1980) because of inhibition of the detrusor during the process.

During the voiding process the pressures and voiding flow rate are recorded. At the end of voiding, the voided volume is measured and the residual urine calculated from the infused volume.

At the end of the test the patients are helped to clean themselves and then to dress again.

Errors in the method

This test is not physiological and is at best an approximation of the real life event. Failure to void because of inhibition is a very rare event our clinic. Auditing of our patients has demonstrated a very high tolerance of the procedure.

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The measurement of the flow rate is subject to a 5% error (Abrams et al 1983). The signal, which is a measure of the current required to maintain the rotation of the drum at a constant speed during impact with the urinary stream, has to be filtered in order to remove aberrant electrical interference.

Although great care is taken over the placement of the pressure lines and the positioning of the transducers we cannot be absolutely certain of the reliability of our measurements and some error must exist.

The use of the upper margin of the superior pubic ramus as the zero point for pressure readings means that the pressure head in the bladder is not properly measured. In addition anatomical differences between individuals may affect the comparablility of results. It is likely that an error of around 5 cm H_2O may be incurred as a result of these two issues.

We assess the end-test post micturition residual urine volume indirectly. We do not, therefore, take account of any urine production by the kidneys during the test.. The test takes about twenty minutes so the volume is likely to be very small.

The method of sampling

The sample source

I have examined a large sample of the population of interest. This helps in establishing confidence limits around conclusions which I may draw. I do not however, believe that I have obtained an unbiased sample, the processes of referral and treatment are subject to many influences and it would be foolhardy to expect to account for all confounding factors. I do believe that I have been able to obtain a sample of elderly people representative of those likely to be referred to an incontinence clinic. A description of my clinic is therefore important.

The Incontinence Clinic at St. Pancras Hospital, operating since 1981, is run by myself, a geriatrician, in a district with excellent urological and gynaecological surgeons who take a specific interest in the surgery of urinary incontinence. The Institutes of Urology and of Neurology as well as the London Spinal Injuries Unit are sited within the district.

The Incontinence Clinic is staffed by myself and three nurse continence advisors. There is also a substantial research team with a large interest in the science of absorbents.

A selection bias affects referrals. The elderly and people suffering from neurological disease are more likely to be referred to St. Pancras Hospital. The surgeons tend to refer patients who are thought to be suffering from non-surgical problems, or patients who have not responded to extensive surgical intervention. Specific contacts with the London Spinal Injuries Unit and certain neurologists have resulted in higher numbers of patients suffering from Parkinson's Disease, spinal injury or Multiple Sclerosis. A considerable number of gynaecologists refer patients with symptomatic stress incontinence associated with symptoms of detrusor instability. However, the majority of referrals come from general practitioners, these involve patients of all ages with incontinence who have not previously been treated.

I have analysed the patient attendance over a twelve month period from 20/09/1989 to 19/09/1990. Comparison with returns from previous years show us that the patterns of referral have not changed although there has been a steady increase in the number of referrals.

During the period analysed there were 482 new referrals 213 (48.6%) came from 132 different general practitioners; 199 (41.2%) came from 36 different gynaecologists and 86 (17.8%) came from 7 different neurologists; 65 (13.5%) came from physicians; the remainder were referred from a variety of other specialities such as psychiatry, orthopaedics and social services. There was only one referral from a urologist. The urologists have highly developed urodynamic services and in fact, for their urodynamics, use computer programmes which I wrote for them. Although their urodynamic data were offered to me for inclusion in this analysis I felt that instrumentation incompatibilities would compromise the validity of my sample. A comparison of patients' characteristics from my clinic and that run by the urologists, shows that my department attracts an overwhelming majority of patients with idiopathic detrusor instablilty and neurological disease whereas they are seeing very much more urinary tract outflow obstruction.

The sources of referral to my clinic involve a wide variety of geographical locations, reflecting the lack of this type of clinic within the Health Service. 42% came from my own health authority, 45% were referred from inside the regional health authority and 13% were referred from outside of the region.

Male patients accounted for 19% of referrals and females, 81%. This reflects a selection bias as well as a higher incidence of urinary incontinence amongst women.

The age distribution of patients is shown in Figure 1. The fact that a geriatrician specialising in incontinence attracts such a broad cross section of age groups is an illustration of how concentration on specific aspects of clinical geriatric medicine can serve so many others in our community.

The clinic is unusual in the fact that there is only one doctor on the team. This means that all patients are exposed to a similar management strategy and that data collected on their responses is very consistent. Because of the high referral rate there is considerable pressure to discharge patients as soon as they have recovered. During the twelve months examined there were 1573 review consultations so that the ratio of new patients to review patients was 1 : 3.2. The distribution of total review attendances (excluding first attendances) by invidiual patients is illustrated in Figure 2, the data includes some patients whose treatment had not been completed.

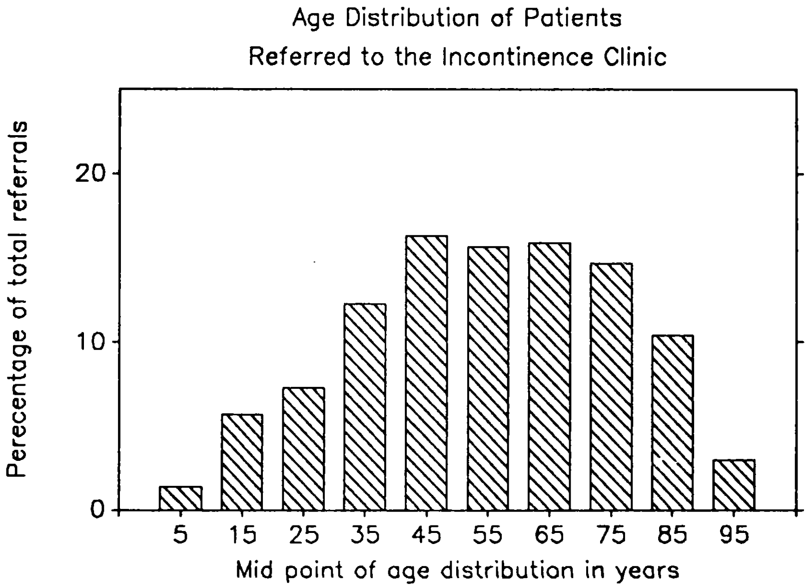

Age Distribution of Patients
Referred to the Incontinence Clinic

Figure 1

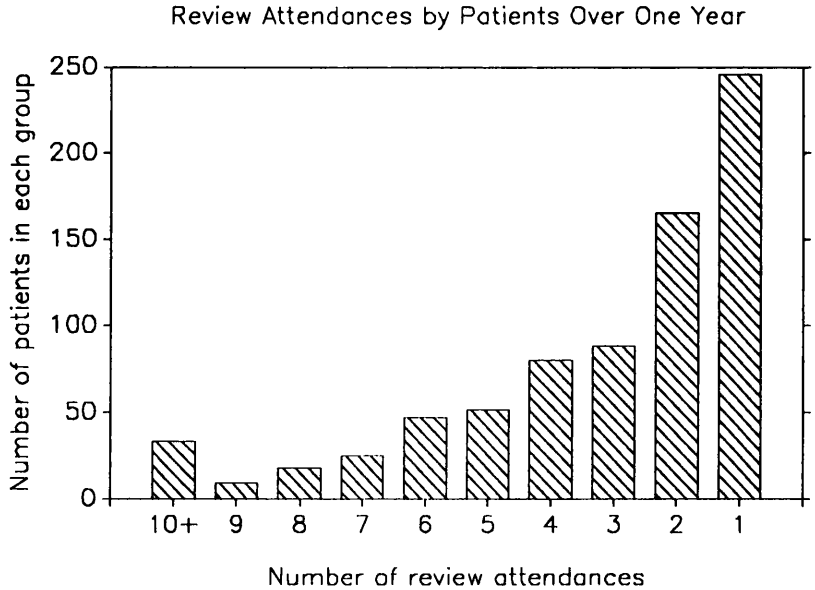

Review Attendances by Patients Over One Year

Figure 2

The sample characteristics:

I have collected urodynamic data on 2393 patients of whom 1824 were female and 569 were male.

At the beginning of this project I collected all of the urodynamic data by transcribing the following principle urodynamic parameters manually onto a computer database:

(1) The post micturition residual urine volume prior to testing

(2) The bladder capacity

(3) The end filling pressure

(4) The maximum detrusor pressure during filling

(5) The maximum flow rate

(6) The detrusor pressure at maximum flow rate

(7) The maximum voiding detrusor pressure

(8) The maximum detrusor pressure at no flow

(9) The voided volume

(10) The post micturition residual urine volume at end of testing

As I progressed it became clear that I stood little hope of unravelling the variety of changes exhibited by my patients unless I was able to analyse the urodynamic data in a more sophisticated manner than this system allowed. I therefore developed a computer programme which was used to run the urodynamic studies and which collected all of the analogue data, digitised them and transcribed them to disc for future analysis.

At a later date I attached a database to this programme which was used to collect a set of clinical data with each urodynamic study and thereby improve on the limited data which I had been collecting up to that point.

Incomplete data

There are two phases to a urodynamic study, the filling phase and the voiding phase. It is easier to collect data during the former than the latter. Some patients find it difficult to void in the test circumstances and in others it proves impossible to maintain the measuring catheters during voiding. This means that there will always be more complete filling data than voiding data. The data sets which I was able to collect using these techniques were are shown in table 1.

Table 1 Definition of sample groups

Data collected manually:

	666 patients	**Group A**
	400 females	
	266 males	
Voiding data on:	400 patients	Group Ai
	240 females	
	160 males	

Full analogue data collected by microprocessor:

	1727 patients	Group B
	1424 females	
	303 males	
Voiding data on:	1333 patients	Group Bi
	1124 females	
	209 males	

Patients with more detailed clinical history data:

	1194 patients	Group Bii
	1023 females	
	171 males	

The patient characteristics

The age distributions of the female and male patients are illustrated in Figures 3 and 4. These patients were referred to the incontinence clinic because they were suffering from symptoms of lower urinary tract dysfunction.

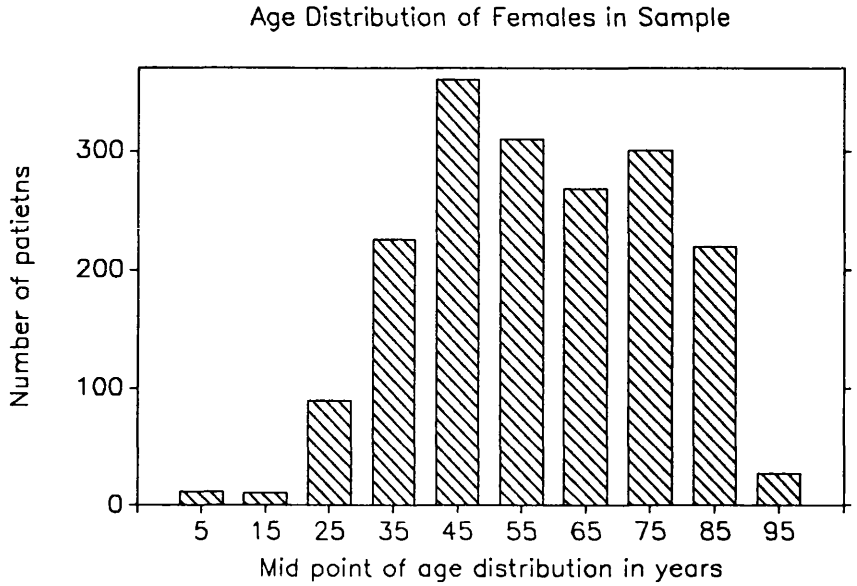


Figure 3

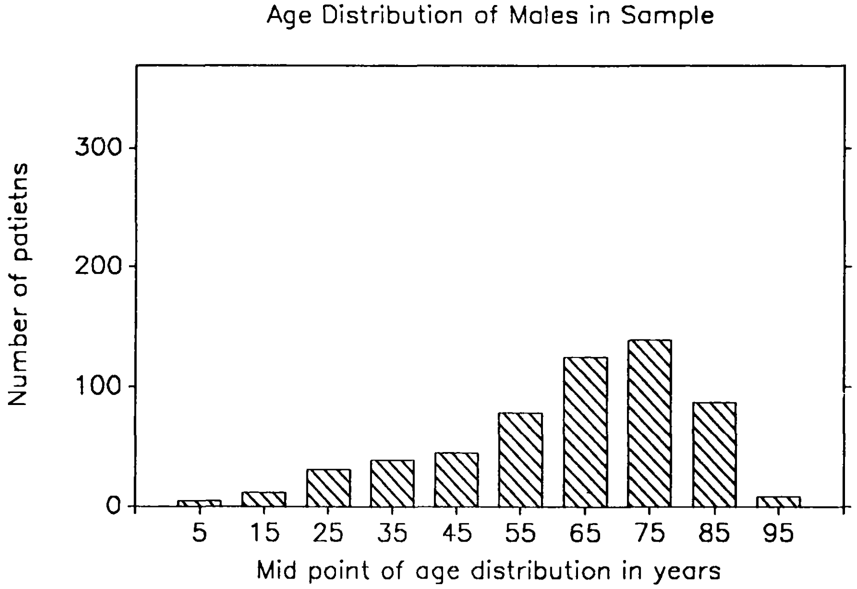


Figure 4

The symptom constellations collected from the sub-group of 1194 (Group Bii) patients are shown below in tables 2-A and 2-B. It should be remembered that patients tend to experience more than one symptom.

Table 2-A Female patients' presenting symptoms

Urgency of micturition	81%
Urge incontinence	79%
Stress incontinence	61%
Terminal dribbling	47%
Post micturition dribbling	35%
Sense of incomplete emptying	33%
Recurrent urinary infection	33%
Reduced urinary stream	32%
Nocturnal enuresis	19%
Straining on micturition	14%
Dysuria	12%
Painful micturition	11%
Continuous incontinence	7%
Haematuria	4%
Hesitancy	4%

Table 2-B Male patients' presenting symptoms

Urgency of micturition	68%
Urge incontinence	61%
Reduced urinary stream	61%
Terminal dribbling	54%
Post micturition dribbling	39%
Sense of incomplete emptying	38%
Nocturnal enuresis	27%
Straining on micturition	23%
Recurrent urinary infection	16%
Hesitancy	14%
Stress incontinence	8%
Painful micturition	7%
Haematuria	5%
Continuous incontinence	4%
Dysuria	2%

Not all of the patients presenting were incontinent. There was an age related increase in the proportion of patients with urinary incontinence (Females: ChiSq=39.5 df=9 $p<0.001$ Males: ChiSq=28.8 df=9 $p<0.001$). These trends are shown in Figures 5 and 6.

Amongst women urge incontinence was significantly more common in those aged 70 years and over (74%) compared with younger women (53%) (ChiSq=7.46 df=1 $p=0.01$). Men aged 80 years and over had a higher incidence of nocturnal enuresis (32%) than younger men (17%) (ChiSq=17.5 df=1 $p<0.001$). There was no age related difference in the incidence of the other symptoms.

I took special note of the presence of a number of key diseases. The incidences, for all patients in the study, are shown table 3.

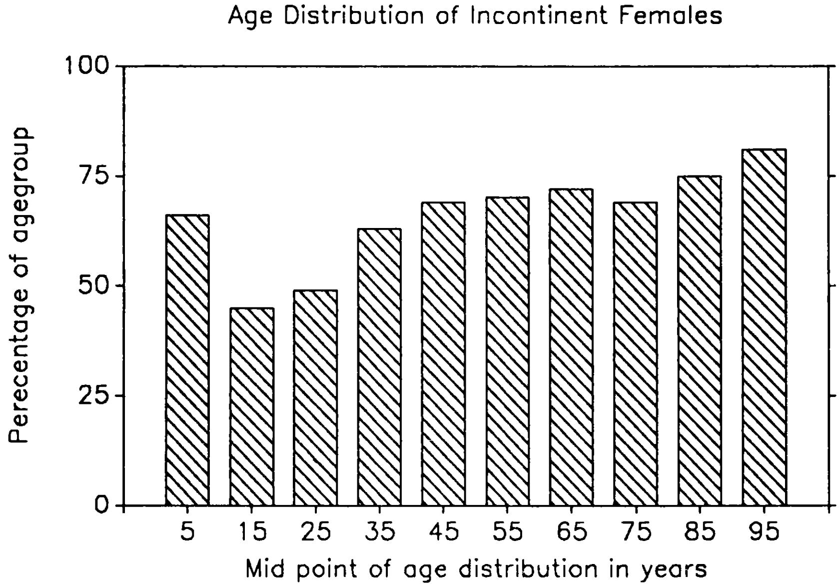


Figure 5

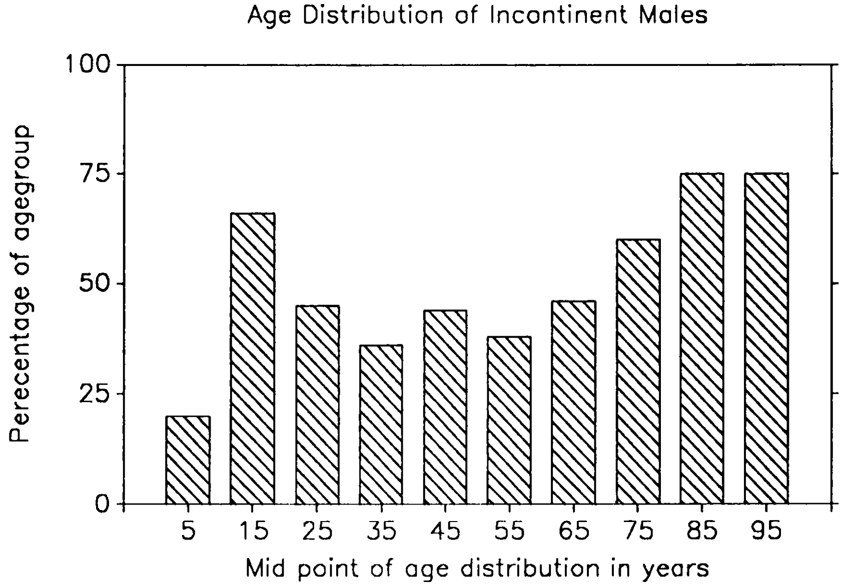


Figure 6

Table 3 The distribution of key illnesses amongst patients

Table 3-A Patients suffering from key illnesses

	Women	Men
Diabetes	88	33
Dementia	47	22
Parkinson's Disease	30	39
Cerebrovascular disease	83	73
Multiple Sclerosis	109	37
Spinal injury	29	23
Other Neurological illness	56	31
Patients with none of these	1407	332

Table 3-B Patients with key illnesses in combination

	Women	Men
Diabetes & Dementia	1	1
Diabetes & CVA	10	8
Diabetes & MS	1	1
Diabetes & other neurol.	4	2
Diabetes & Spinal	0	1
Diabetes & Parkinson's	0	1
Dementia & CVA	2	4
Dementia & MS	1	0
Dementia & other neurol.	2	0
Dementia & Parkinson's	1	1
Parkinson's & CVA	1	1
CVA & other neurol.	1	1
Spinal & other neurol.	1	1

CVA = Cerebrovascular disease, MS = Multiple Sclerosis, other neurol. = other neurological disease, Parkinson's = Parkinson's disease, Spinal = Spinal injury

Where analyses on specific disease groups were conducted the patients with combinations of problems were excluded. The age distributions of the patients with none or only one of these diseases are tabled below (table 4).

Table 4 The age distributions of patients with none or one key illness

Females - Ages by disease group

Disease	N	Mean	Median	Stdev
No disease	1407	55.9	54	18.3
Diabetes	71	63.6	67	17.4
Dementia	41	78.7	80	8.7
Parkinson's	28	74.2	75	10.3
CVA	69	71.6	75	15.4
MS	107	45.8	44	11.4
Spinal	28	47.3	48.5	21.3
Other neurol.	48	51.2	49	17.8

Males - Ages by disease group

Disease	N	Mean	Median	Stdev
No disease	331	62.7	66	18.4
Diabetes	19	66.6	69	14.4
Dementia	16	77.3	77	6.6
Parkinson's	36	71.8	75	13.1
CVA	60	66.9	69	14.3
MS	36	43.1	41	13.0
Spinal	21	38.8	40	16.0
Other neurol.	28	46.6	45	21.5

The physics, mathematical theory and related methods

The theory of urethral resistance

liquid /

In 1740 Bernoulli obtained a relation between the pressure and viscosity at different parts of a moving incompressible fluid. If the viscosity is negligibly small, which is the case with urine (Griffths 1980) there are no frictional forces to overcome. In this case the work done by the pressure difference per unit volume of a fluid flowing along a pipe steadily is equal to the gain of kinetic energy per unit volume plus the gain in potential energy per unit volume (Nelkon 1966). f /

The work done by a pressure in moving fluid through a distance is expressed as:

$$\text{Work} = \text{force} \times \text{distance moved} \qquad (1)$$

$$\text{Work} = \text{pressure} \times \text{area} \times \text{distance moved} \qquad (2)$$

$$\text{Work} = \text{pressure} \times \text{volume moved} \qquad (3)$$

assuming that the area is constant at a particular place for a short time of flow. At the beginning of the pipe where the pressure is p_1, the work done per unit volume on the fluid is thus p_1. At the other end, the work done per unit volume by the fluid is likewise p_2. Hence the net work done on the fluid per unit volume is $p_1 - p_2$.

The kinetic energy (KE) per unit volume ~~may~~ y be calculated from:

$$\text{KE} = 1/2 \text{ mass per unit volume} \times \text{velocity}^2 \qquad (4)$$

$$\text{KE} = 1/2\rho \times \text{velocity}^2 \qquad (5)$$

(where ρ is the fluid density)

Thus if v_2 and v_1 are the final and initial velocities respectively at the end and the beginning of the pipe, the kinetic energy gained per unit volume:

$$\text{dKE} = 1/2\rho\{v_2 - v_1\}^2 \qquad (6)$$

If h_2 and h_1 are the respective heights measured from a fixed level at the end and beginning of the pipe, the potential energy (PE) gained per unit volume:

$$PE = \text{mass per unit volume} \times g \times \{h_2 - h_1\} \tag{7}$$

$$PE = \rho g\{h_2 - h_1\} \tag{8}$$

Thus, from the principle of energy conservation

$$p_1 - p_2 = 1/2\rho\{v_2{}^2 - v_1{}^2\} + \rho g\{h_2 - h_1\} \tag{9}$$

$$\therefore\ p_1 + 1/2\rho v_1{}^2 + \rho g h_1 = p_2 + 1/2\rho v_2{}^2 + \rho g h_2 \tag{10}$$

$$\therefore\ p + 1/2\rho v^2 + \rho g h = \text{constant} \tag{11}$$

Where p is the pressure at any part and v is the velocity there. Hence, it can be said that, for streamline motion of an incompressible non-viscous fluid, "The sum of the pressure at any part plus the kinetic energy per unit volume plus the potential energy per unit volume at any part is always constant."

Bernuolli's principle shows that at points in a moving fluid where the potential energy change is very small, or zero as in flow through a horizontal pipe, the pressure is low where the velocity is high; conversely the pressure is high where the velocity is low.

Consider the steady flow of an non-viscous, incompressible fluid, of density ρ from a reservoir at pressure p_{rev} through a straight and uniform tube of cross sectional area A. The fluid velocity (v) is uniform over the cross section and is parallel to the axis. The volume flow rate Q, through the tube is given by :

$$Q = vA \tag{12}$$

The pressure at the exit of the tube is p_e. According to the Bernoulli equation:

$$p_e + 1/2\rho v^2 = p_{rev} \qquad (13)$$

Therefore by eliminating v

$$Q^2 = \{p_{rev} - p_e\}2A^2/\rho \qquad (14)$$

Figure 7 shows a sphere of radius r with a cylindrical outlet at its base of cross sectional area A.

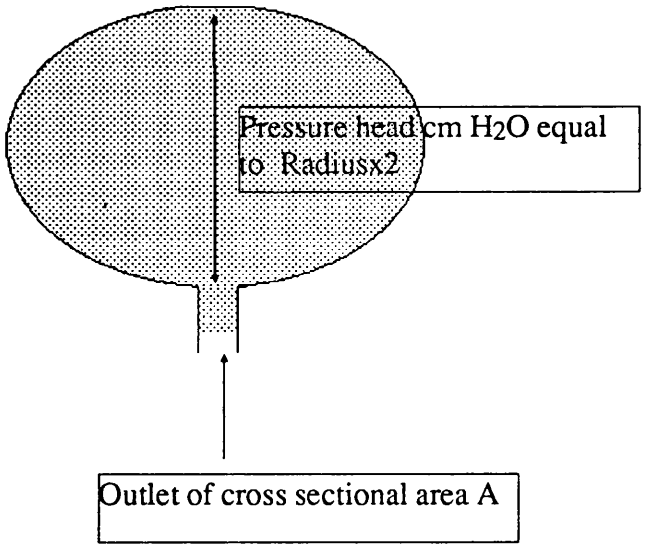


Figure 7

The volume of the sphere is calculated from the expression:

$$\mathrm{vol} = 4\pi r^3/3 \tag{15}$$

If the pressure at the outlet p_e = atmospheric pressure and the fluid in the sphere is water of density $\rho = 1$, the pressure head at the outlet may be expressed as $2r$ (the diameter of the sphere). An expression for this pressure head would therefore be:

$$2r=2\{3\mathrm{vol}/4\pi\}^{1/3} \tag{16}$$

At full capacity the volume flow rate through the outlet may be expressed by:

$$Q=\{\{2\{3\mathrm{vol}/4\pi\}^{1/3}\}2A^2\}^{1/2} \tag{17}$$

The flow rate is measured in ml/sec.

As water flows out of the sphere the change in volume with respect to time will be expressed as:

$$dv/dt = Q$$

$$dv/dt = \{\{2\{3\mathrm{vol}/4\pi\}^{1/3}\}2A^2\}^{1/2} \tag{17}$$

The change in pressure head at the outlet with respect to time may be expressed as:

$$dp_e/dt = 2\{3\{\{2\{3\mathrm{vol}/4\pi\}^{1/3}\}2A^2\}^{1/2}/4\pi\}^{1/3} \tag{18}$$

Using these expressions it is possible to plot the relationship between pressure and flow as the sphere empties under the influence of gravity from a finite capacity.

Example (1)

Let the radius of the outlet $r_o = 0.398$ cm such that the area of the outlet $\pi r_o^2 = 0.5\ \mathrm{cm}^2$. Let the capacity of the sphere be 500 ml. Figure 8 plots the relationship between pressure and flow as the sphere empties from 500 ml to 0 ml. The parameters are calculated to the nearest integer because the clinical data in this study were rounded to the nearest integer. At full capacity there is a fixed pressure head at the outlet, this will cause a certain flow rate of water out of the sphere. As the sphere empties the pressure head reduces and the flow rate consequently falls until the sphere is empty. The maximum flow is achieved at the beginning of emptying, I have placed arrows on the graph to indicate the direction of the plot in relation to time.

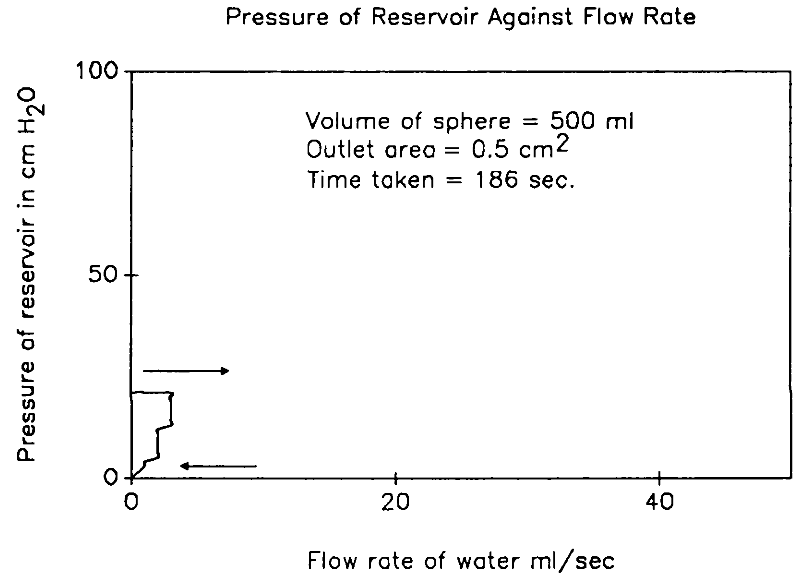


Figure 8

Figures 9 to 11 show the same relationship but with variations in the capacity of the sphere. It can be seen that with each increase in sphere capacity the pressure at the start of flow is higher, the maximum flow rate also increases but only slightly such that the integer rounding hides the increment between pairs of examples.

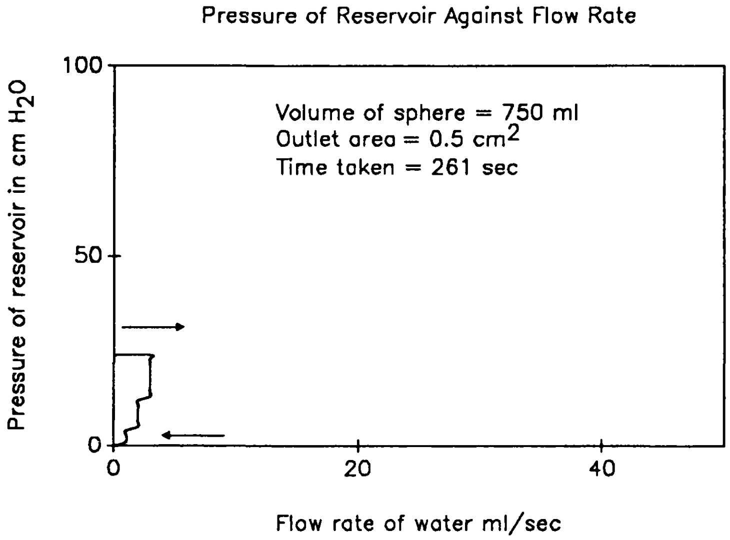


Figure 9

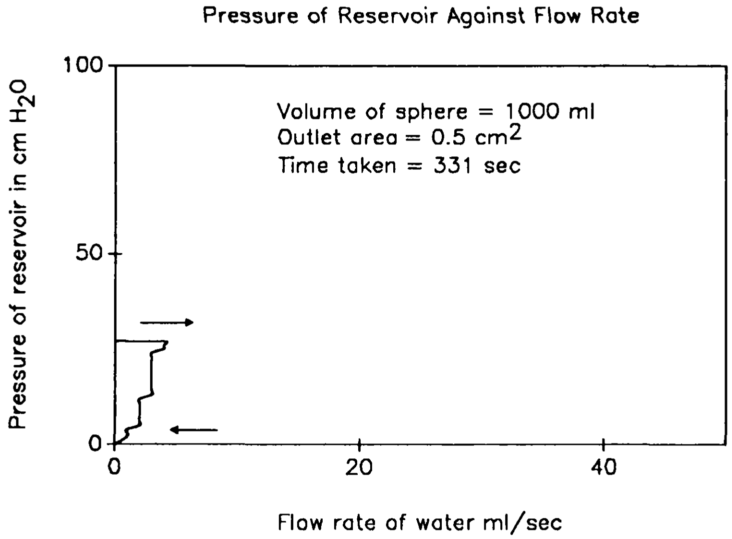


Figure 10

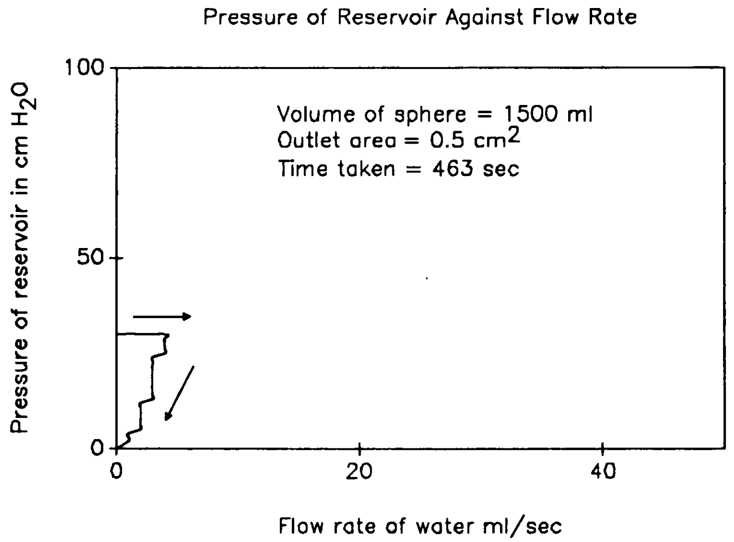


Figure 11

Because the outlet is of constant cross-sectional area there is a fixed flow rate for each value of the pressure head, which depends in turn on the volume of the sphere. The flow rate is defined by the equation

$$Q = \{2p_{rev}A^2/p\}^{1/2} \qquad (19)$$

A^2, in these circumstances, is kept constant.

Figure twelve is quite different to figures 8 to 11. It is a plot of equation (19) and describes the flow rate caused by any pressure head between 0 and 100 cm H_2O acting on an outlet of area 0.5 cm^2. It is not a time series plot of an emptying sphere, as in the previous examples. In this plot I have not used integer rounding so as to make the illustration as clear as possible. This curve includes the points plotted in figures 8 to 11, prior to integer rounding. It describes the pressure/flow relationship of a rigid tube. In urodynamics this relationship is shown in situations where there is a rigid urethral obstruction, provided that the contractility of the detrusor is well sustained. It is an extremely useful means of identifying in-elastic obstruction.

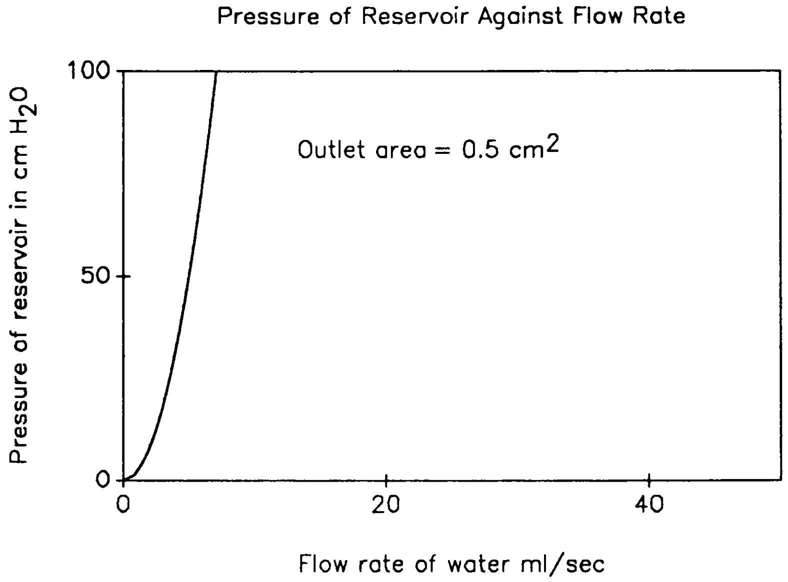


Figure 12

The relationship between pressure and flow for a rigid tube is a hyperbolic function.

Example 2

Let us now attach a valve to the outlet so that it becomes possible to vary the cross sectional area of the outflow (figure 13). Let us use a sphere of 500 ml and increase the cross sectional area of the outlet by 10% every second. The area will therefore by incremented using an arbitrary factor which is independent of volume and pressure. Figure 14 shows the relationship between pressure and flow in these circumstances. Note that it took less time for the sphere to empty, as previously there was a pressure drop over the whole period but in the early phase there was an increase in flow rate with a fall in pressure. The shape of the plot is very different to examples 8 to 11.

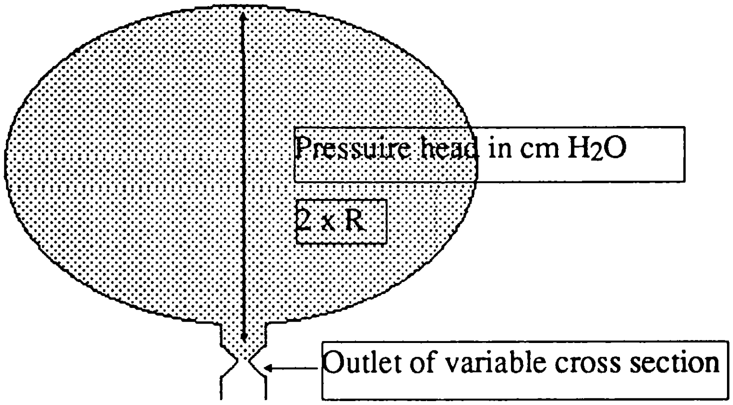


Figure 13

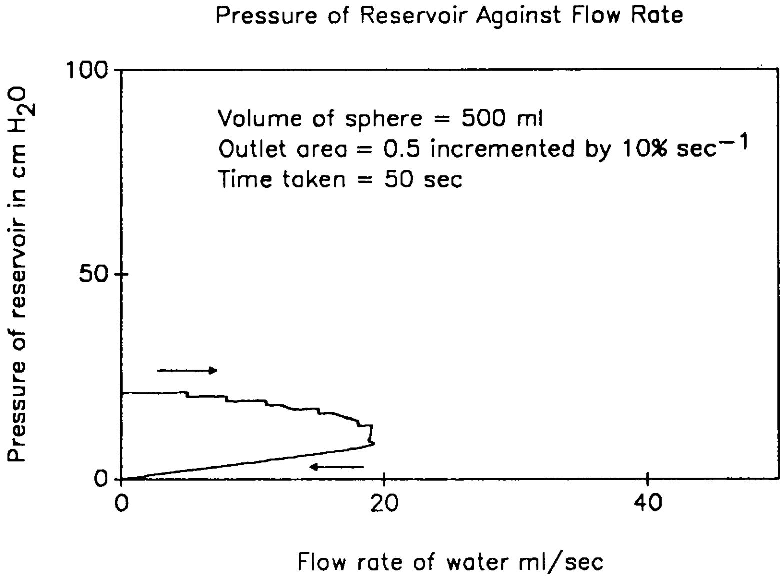


Figure 14

The relationship between pressure and flow for a tube with a changing cross-sectional area.

Example 3

Example 2 moved closer to the situation in real life and the pressure/flow relationship demonstrated may be seen in clinical practice. If this were to hold in all circumstances the corollary would be that the sphincter opens independently of the pressure in the bladder (sphere in these examples). This is in fact not usually the case. If we view our outlet as being an elastic tube then the cross sectional area of the outlet will be related to the pressure head which will cause the walls of the outlet to part in proportion to the pressure acting at the outlet. The cross sectional area of the outlet then becomes a function of pressure $A=A(p)$. Hooke's law of the elastic properties of materials relates the extension force (F) applied to a body to the elongation of that body (L_e) under the influence of that force. $F=K \times L_e$. Where K is a constant describing the elastic properties of the material (Nelkon 1966).

Let us use a very simplistic model in which we relate the pressure at the outlet to the cross section area of the outlet with an expression:

$$A(p_o) = p_o/K \qquad (20)$$

Figures 15 and 16 illustrate the pressure/flow relationship for two different values of K, K=2 and K=1.

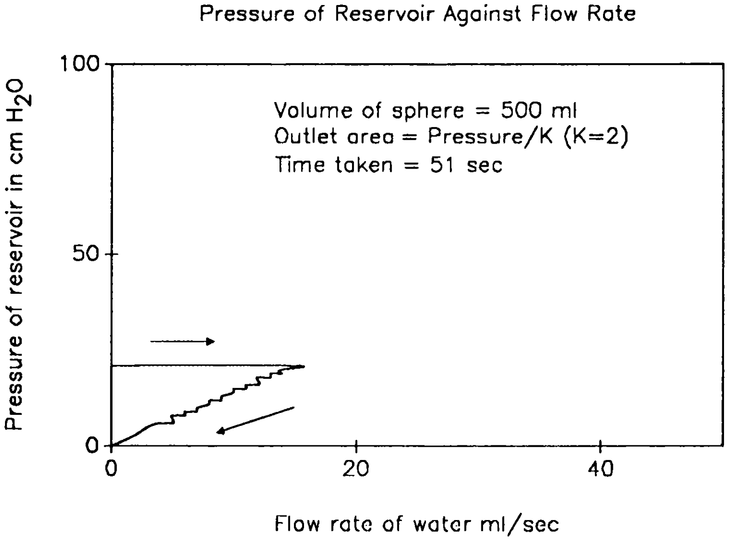


Figure 15

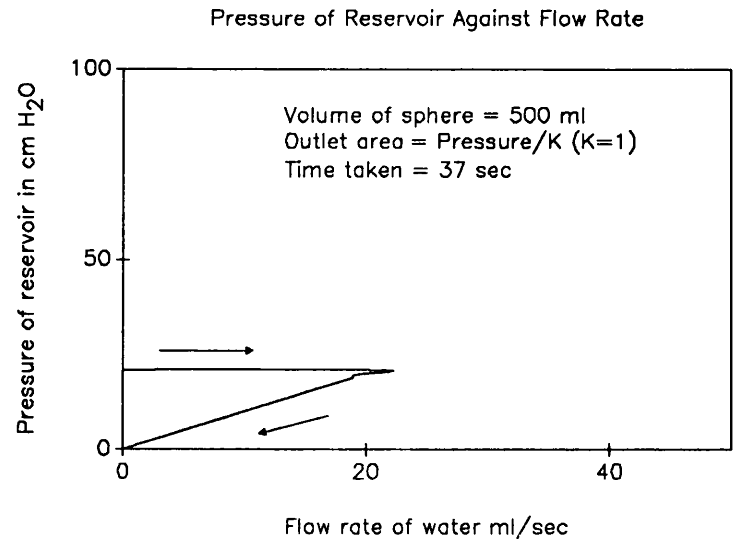


Figure 16

Example 4

We now need to relate the very simplistic model described in example 3 to the known elastic properties of the urethra, which we are developing in the model. Studies of the viscoelastic properties of the component elements of soft tissue have shown that the distribution of collagen and elastin in the tissue determine, to a large extent, the mechanical properties * (Yalla et al 1973, Fung 1981). Collagen is one of the stiffer tissues with a Young's modulus of elasticity of approximately 1.0×10^7 N/m^2. Elastin which is more elastic has a Young's modulus of about 1×10^5 N/m^2. Relaxed muscle tissue has a Young's modulus of about 1×10^5 N/m^2.

The elasticity of the tissue of the lower urinary tract has been studied by a number of workers who have examined the relationship between extension force and length for the tissue as opposed to its individual elements. It has been found that the force/elongation curves plotted from observed data may be described mathematically by means of exponential functions. (Fung 1967, Yin & Fung 1971, Bjerle 1974, van Mastrigt et al 1978, Fung 1981).

* No reference : I think : Resnick + Yalla '73

Yalla et al (1973) were able to show that the intraluminal pressure in the urethra may be related, exponentially, to the change in the cross sectional area at the point of reference. Griffiths (1973, 1980) was able to relate the pressure in the urethra at a point by means of the function:

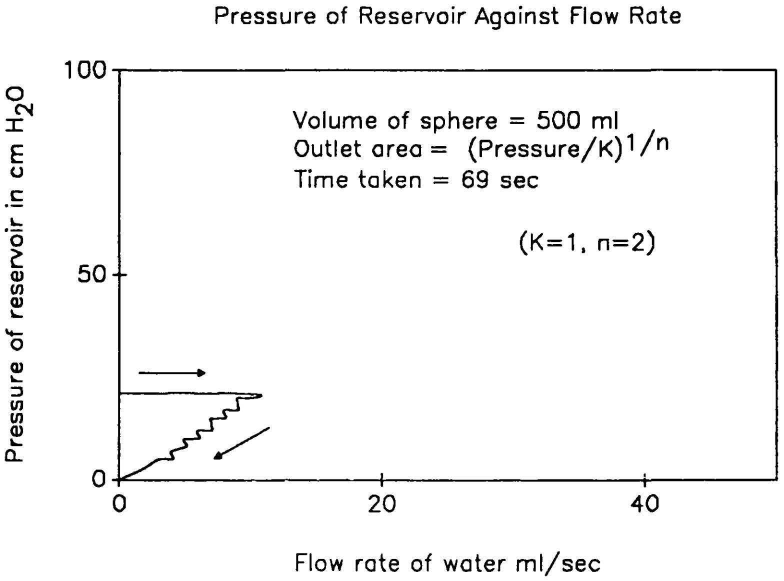
$$p(A) = p_{mo} + KA^n \tag{21}$$

p_{mo} is the pressure at the beginning of flow (the pressure at meatal opening) which I will return to discuss later. K and n are constants describing the elastic properties of the urethral tissue. These will vary between individuals.

Let us now return to the model described in example 3 and modify the elasticity equation in order to take account of the proven exponential function. Let us exclude p_{mo} for the moment by making $p_{mo} = 0$. We should modify the expression for the relationship between cross sectional area of the tube and pressure to:

$$A(p_o) = \{p_o / K\}^{1/n} \tag{22}$$

p_o is the pressure at the outlet and the function $A(p_o)$ is area as a function of outlet pressure, as opposed to $p(A)$, (pressure as a function of area) in equation (21) . Hence the inverse exponent ($^{1/n}$, "the nth root") in equation (22). Figure 17 illustrates the pressure/flow relationship in these circumstances when $K=1$ and $n=2$.



Pressure of Reservoir Against Flow Rate
100
50
0
0
20
40
Pressure of reservoir in cm H_2O
Flow rate of water ml/sec
Volume of sphere = 500 ml
Outlet area = $(\text{Pressure}/K)^{1/n}$
Time taken = 69 sec
(K=1, n=2)

Figure 17

Example 5

It is normal experience to note a threshold pressure below which the urethra will not open (Griffiths 1973, Schafer 1983). This pressure is called the urethral opening pressure and has already been referred to (p_{mo}). Up to this point I have not included it in the model which we have been building. Figure 18 shows a similar plot to that used in example 4 except that the urethral opening pressure has been set to $p_{mo} = 10$ cm H_2O. Once the pressure of the sphere fell below p_{mo} the outlet closed and emptying stopped leaving a residual in the sphere.

It is now clear that given a value of p_{mo} such that $p_{mo} > 0$ there can be no hope of emptying the sphere fully purely under the influence of gravity. This means that we must alter the walls of the sphere so that they are capable of generating a tension such that the resultant pressure $p_{det} > p_{mo}$ as the volume $V \rightarrow 0$. The walls must become contractile. We must start to examine the contractile properties of the muscle of the bladder wall (the detrusor) but before doing this I would like to round off the theory c/ concerning the behaviour of the urethra.

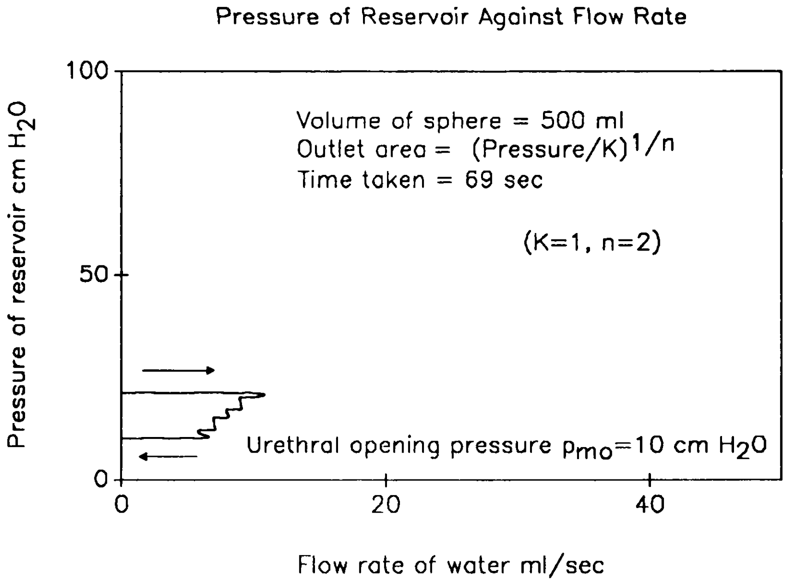


Figure 18

The formal characterisation of urethral resistance.

Griffiths (1969, 1971 a,b & 1980) dealt with properties of the elastic urethra in considerable detail. I would like to summarise the mathematical processes which he adopted. He was able to show that the flow through the urethra was controlled by an elastic constriction centred at the external sphincter. This was the case for normal females and males. The urethra proximal and distal to this maximal constriction zone, in normal circumstances, does not influence the urinary flow. This means that we may describe the properties of the urethra in terms of a very limited zone (the outlet used in our model so far).

If we consider the steady flow of a non-viscous, incompressible fluid, of density ρ from a reservoir at pressure p_o through a straight and uniform elastic tube. The fluid velocity v is uniform over the cross section and is parallel to the axis. The fluid pressure is uniform and is given by the expression, derived from the Bernoulli equation:

$$p_{det} + p_{head} = p(A) + \rho v^2/2 \qquad (23)$$

p_{det} refers to the "detrusor pressure" which is the pressure generated by the detrusor muscle, it should be contrasted with the "bladder pressure" which is the detrusor pressure + the intrabdominal pressure. p_{head} refers to the pressure head caused by the height of urine within the bladder. Other workers did not include an expression for p_{head} in their equations because of the view that it was negligible. In many circumstances this is the case but where p_{det} is very low this does not hold.

The volume of flow is given by the continuity equation:

$$Q = vA \qquad (24)$$

Where Q = the volume flow rate ml/sec and A is the cross sectional area of the constriction zone.

By combining equations (23) & (24) we get

$$Q^2 = \{p_{det} + p_{head} - p(A)\}2A^2/\rho \qquad (25)$$

If the only limitation on flow is the elastic constriction there will be a maximum flow. An expression for this may be found by differentiating (25) to give an expression for the gradient:

$$dQ^2/dA = p_{det} + p_{head} - p(A)4A/\rho - \{dp/dA\}2A^2/\rho \qquad (26)$$

This will be zero if A=0 which is the situation when the urethra is closed. The gradient will also be zero when:

$$p_{det} + p_{head} - p(A) = 1/2Adp/dA \qquad (27)$$

This will correspond to a maximum of Q if the second derivative {derivative of (26) } is greater than 0. ie:

$$A^2d^2\rho/dA^2 + 3Adp/dA > 0 \qquad (28)$$

From equations (25) and (27) we get an expression for the maximum value of Q:

$$Q_{max}{}^2 = \{A^3/\rho\}dp/dA \qquad (29)$$

We have already seen that the area at the constriction zone A(p) has been found to be an exponential function of the form $A(p_o) = \{p_o/K\}^{1/n}$ (22) provided that $p_{mo} = 0$. We know that this is not the case so the correct expression for the area as a function of pressure A(p) must be:

$$A(p) = p_{mo} + \{p_o/K\}^{1/n} \qquad (30)$$

We may use (21) to obtain an expression for the change in pressure as a function of area with respect to change in area dp(A)/dA:

$$dp(A)/dA = nKA^{n-1} \qquad (31)$$

we may then insert (31) into (29) to give an expression for flow rate:

$$Q_{max} = \{nK/\rho\}^{1/2} A^{\{n+2\}/2} \qquad (32)$$

We do not know the cross sectional area A so we use (21), (31) and (27) to provide and expression for A:

$$A = \{2\{p_{det} + p_{head} - p_{mo}\}/K\{n + 2\}\}^{1/n} \tag{33}$$

If we use this expression in (32) we get:

$$Q_{max} = \{nK/\rho\}^{1/2}\{2\{p_{det} + p_{head} - p_{mo}\}/K\{n + 2\}\}^{\{n+2\}/2n} \tag{34}$$

and we may also derive an expression for $p_{det} + p_{head}$:

$$p_{det} + p_{head} = p_{mo} + \{K\{n+2\}/2\}\{K/\rho\}^{-n/\{n+2\}}\, Q_{max}^{\ 2n/\{n+2\}} \tag{35}$$

These equations may be used to calculate the maximum flow rate through the urethral compression zone and the pressure required to achieve the maximum flow. Equation (35) may be simplified to

$$p_{det} + p_{head} = p_{mo} + HQ_{max}^{\ m} \tag{36}$$

$$\text{Where } H = \{K\{n+2\}/2\}\{K/\rho\}^{-n/\{n+2\}} \tag{37}$$

$$\text{and } m = 2n / \{n+2\} \tag{38}$$

If we plot a pressure/flow relation recorded while someone is passing urine (provided that the contractility of the bladder does not alter) we may attempt to calculate the parameters by fitting equation (36) to the curve (Spangberg et al 1989). In fact, in the clinical situation, the validity of such curve fitting is doubtful since it is not possible to be sure that the stimualtion and activity of the bladder are necessarily constant throughout micturition, nor is it certain that the H and m remain constant. Spangberg et al (1989) claim to be able to describe the parameters H and m by means of curve fitting. I believe that they would have to have been using very idealised situations for such an analysis (Schafer 1989). Griffiths calls this plot of equation (36) the "Urethral resistance relationship" (URR) since its form gives information about the physical influence of the urethra during voiding.

Example 6

Figure 19 illustrates a pressure/flow relationship (URR) using similar parameters as those used in example 5 but the flow rate for each pressure is calculated using equation (36). The pressure, in this example, is the pressure consequent on the head of water in the sphere. I have not, as yet, included a contractile element. As there is no time axis it is not possible to see that as the pressure fell with flow of water out of the sphere the rate of decrease in flow rate became progressively slower.

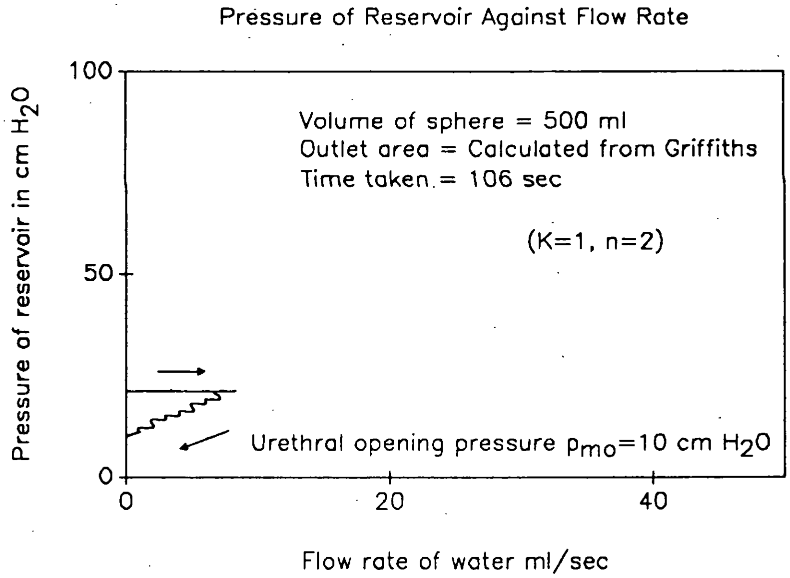


Figure 19

The theory of detrusor contractility.

Example 5 made it clear that the model which I had built up to that point was inadequate since it would not allow complete bladder emptying.

During micturition the detrusor muscle contracts and develops a tension which is registered as a rise in pressure within the bladder (the sphere will now evolve into a bladder just as the outlet evolved into the urethra)

Contraction force and muscle length

A muscle contraction depends on the chemical interaction between actin and myosin. Maximum contraction occurs when there is maximum overlap between the actin and myosin filaments and the cross bridges of the myosin filaments. If the actin filaments overlap with each other there is a decrease in contractile strength (Figure 20). When a muscle is at its normal resting stretched length and is then activated it contracts with maximum force of contraction.

If a resting muscle is stretched to greater than its normal length a tension develops caused by the elastic recoil properties of the connective tissue. However, this elastic tension does not lead to an increased tension during contraction because if a muscle is stretched beyond its normal length there is excessive separation of the actin and myosin and a decrease in the maximum tension generated by a contraction. (Point D figure 20)

Shortening of a muscle also affects the maximum tension generated during a contraction. If a resting muscle is shortened to less than its normal fully stretched length there is overlap between the actin and myosin (Point A figure 20).

The marked differences between resting tension and contractile tension for different lengths of a muscle are shown in Figure 21. The relationship between muscle length and tension developed during contraction is called the **length-tension relationship** (Guyton 1971, Wilkie 1978).

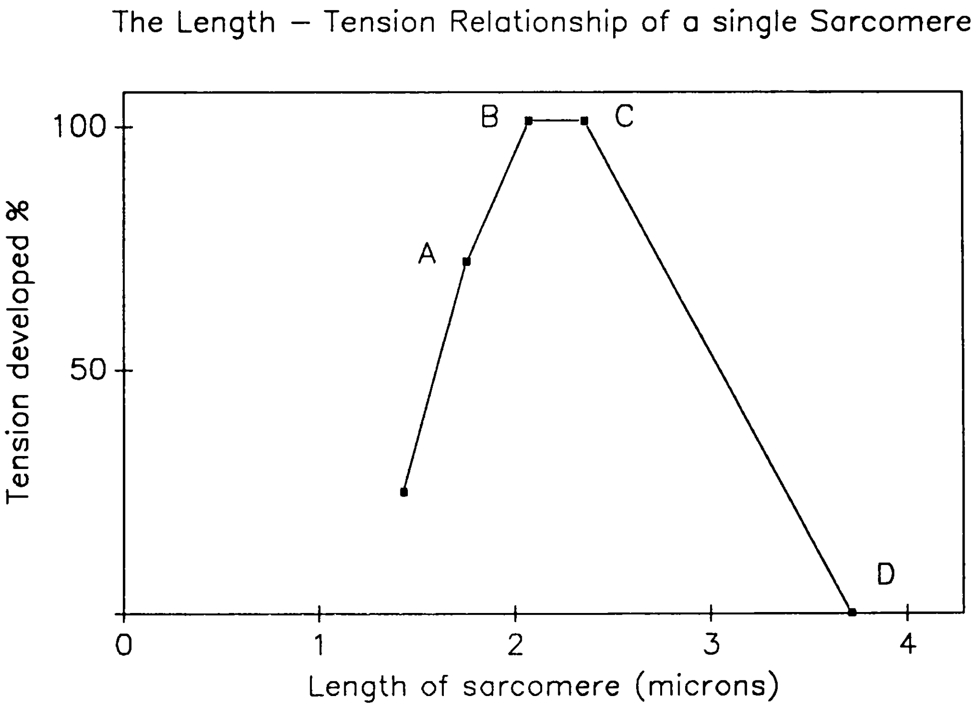


Figure 20

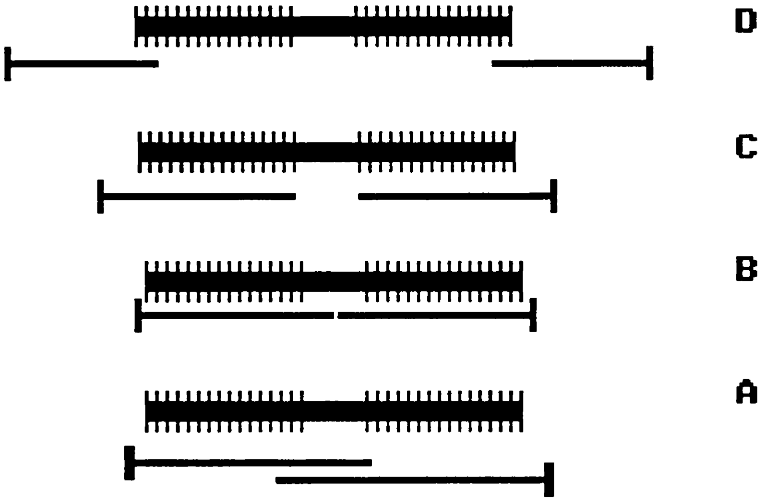


Figure 20a : The relationship between the actin and myosin filaments for each point on figure 20.

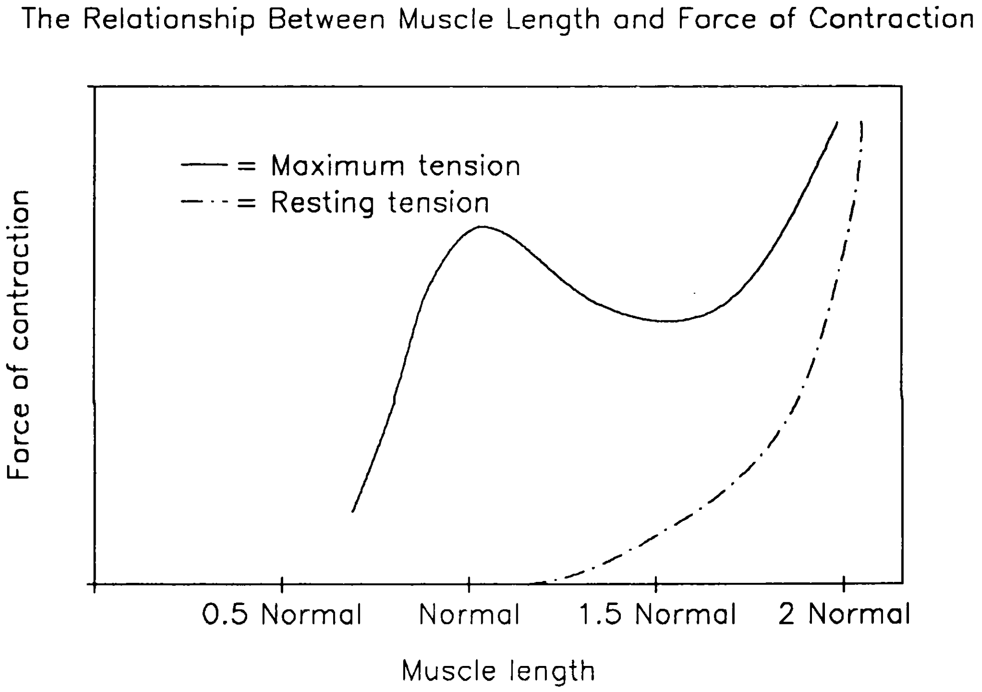

The Relationship Between Muscle Length and Force of Contraction
—— = Maximum tension
—·· = Resting tension
Force of contraction
0.5 Normal
Normal
1.5 Normal
2 Normal
Muscle length

Figure 21

Velocity of contraction and load

A muscle contracts extremely rapidly when it contracts against no load. When loads are applied the velocity of contraction becomes progressively less. If the load applied equals the maximum force that the muscle can exert then the velocity of contraction becomes zero and no contraction occurs (Guyton 1971, Wilkie 1978) (Figure 22).

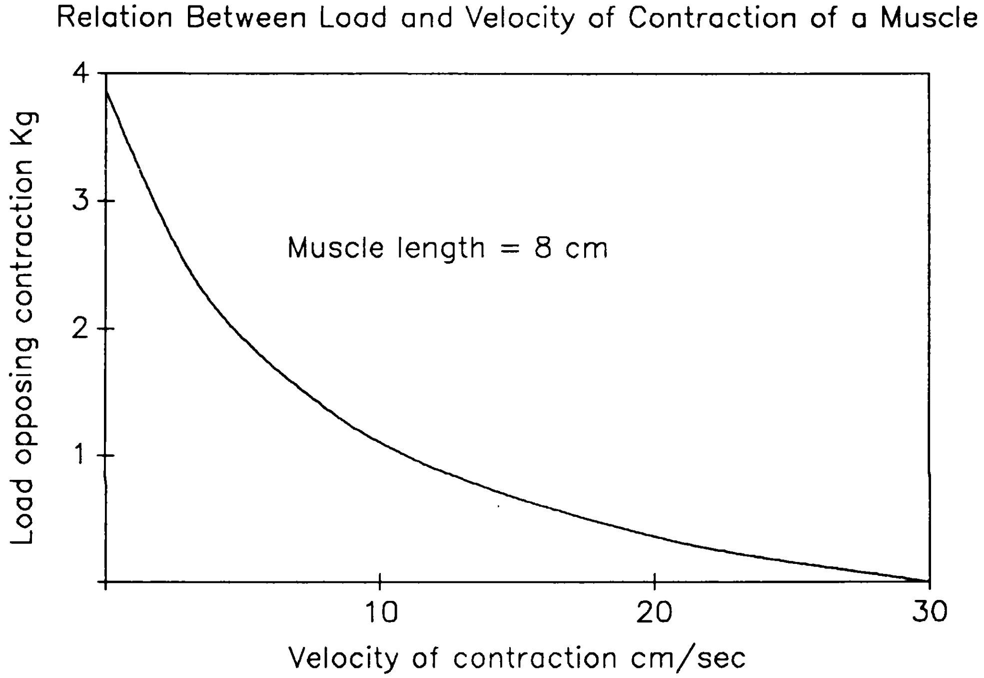


Figure 22

The relationship between the speed of shortening and load is called the **force-velocity** relation. Figure 23 shows two force-velocity relations. One is taken from a muscle with a high proportion of fast twitch muscle fibres and the other is taken from a muscle with a greater proportion of slow twitch fibres. The force-velocity relationship demonstrates how restraint effects the kinetics of the utilisation of ATP by the actin and myosin (Wilkie 1978).

a/

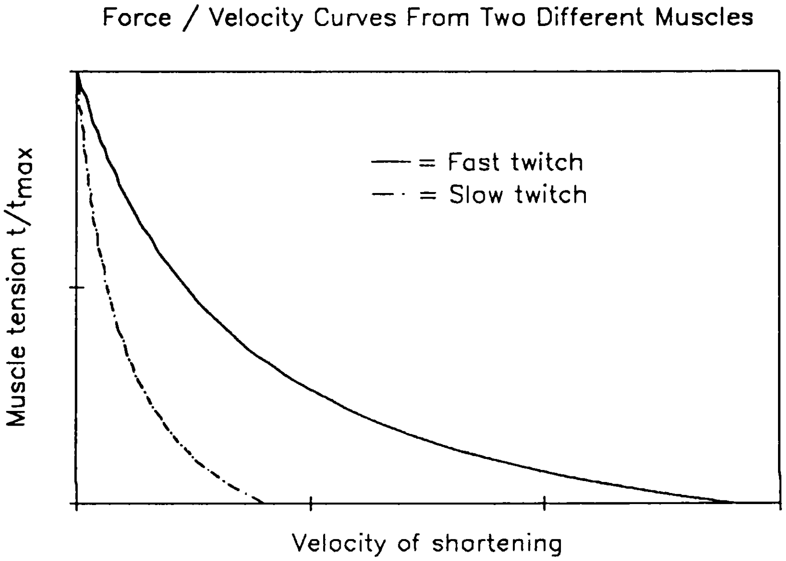


Figure 23

The Fenn effect

If a muscle contracts and moves an object against a force it performs work. The amounts of nutrients and oxygen consumed by the muscle are greater when it performs work as opposed to when it simply contracts without causing work. This is called the "**Fenn**" effect (Wilkie 1978).

Isometric and Isotonic Contractions

A muscle contraction is said to be isometric when the muscle does not shorten during contraction and isotonic when it shortens but the tension on the muscle remains constant.

There are several basic differences between isometric and isotonic contractions. Isometric contraction does not require the sliding of myofibrils among each other. In isotonic contractions a load is moved which involves the phenomenon of inertia. The load is accelerated to a velocity which gives it momentum which causes it to continue moving after the contraction has terminated. In consequence an isotonic contraction will last considerably longer than an isometric contraction of the same muscle. An isotonic contraction entails the performance of external work, because of the Fenn effect a greater amount of energy is utilised by the muscle. Most muscle contractions are a mixture of isotonic and isometric activity. Guyton (1971)

Contraction force and stimulation

Griffiths et al (1979) demonstrated the relationship between electrical stimulation and the force of contraction of bladder muscle strips. Stimulation by a train of electrical pulses gave a force which rose rapidly to a maximum and then decayed more slowly. If stimulation was continued long after the maximum was passed, the response to succeeding periods of stimulation was reduced, apparently persistently. If stimulation ceased as soon as the maximum was reached, similar maximum forces of contraction could be elicited by similar stimulations but only after a rest period of about fifteen minutes. Variation of the frequency and duration of pulses had minimal effect on the force of contraction. Maximum force was obtained with frequencies of about 20 s^{-1} and durations of 7 ms. With variation of the voltage of stimulation the force of contraction rose to a maximum plateau, this was achieved at 8 volts with a current of 250 milliamps.

The series elastic element

When a muscle contracts against a load a number of non-contractile tissues within the muscle and attached to it stretch elastically. As a result the muscles must contract an extra 3% to 5% to make up for these stretching elements. The elements of the muscle which stretch during a contraction are referred to as the series elastic element (Guyton 1971, Wilkie 1978).

The parallel elastic element

If a muscle is stretched elastic tissues within its structure will exert a tension related to their elastic properties and these will bear some relationship to Hooke's law. This tension will add to the tension generated by a contracting muscle during shortening and cause tension prior to shortening. This is referred to as the parallel elastic element. For soft body tissues the force/extension relationship governed by elastic properties has a slope which increases exponentially with extension (Fung 1967, Yin & Fung 1971, Bjerle 1974, van Mastrigt et al 1978, Fung 1981).

Relating muscle theory to the bladder.

Less is known about the behaviour of smooth muscle, but from what we do understand of experimental tests on bladder muscle (Griffiths 1980) many of the principles governing striated muscle apply to bladder muscle. Most of our knowledge is drawn from *in vitro* tests on pig bladder which behaves similarly to human bladder (Griffiths 1980)

(1) The parallel elastic component.

In order to understand how data obtained from muscle strip experiments relates to the behaviour of the bladder we have to express the results in realtion to a sphere.

The bladder is treated as a thin walled sphere with a of radius R with a thin outer wall. This can develop a tangential tension T. The wall encloses a volume of urine V with a volume V_t of wall tissue.

The tissue is assumed to be incompressible but sufficiently fluid as to be able to fill up the sphere as V approaches 0.

The volume of urine may be expressed as:

$$V=\{4\pi R^2/3\} - V_t \tag{39}$$

V_t lies between 10 and 50 ml. (Griffiths 1980).

If the tension in the wall of the bladder is T and this is opposed by an equal force, this force per unit area, may be expressed as:

$$p_{det} = T/\pi R^2 \tag{40}$$

p_{det} is an expression meaning "detrusor pressure" which is the conventional term used to describe the pressure in the bladder generated by the detrusor. It differs from the "Bladder pressure" which describes the detrusor pressure + the intra-abdominal pressure. When we were dealing with the urethral resistance I pointed out that in that situation p_{det} should be adjusted to account for the pressure head in the bladder. While dealing with bladder contractility it refers only to the tension generated by the detrusor.

If we take the natural unstretched circumference of the bladder to be $2\pi R_o$, then the tension T generated by the stretch in a bladder at a certain volume may be expressed as a function of the change in circumference:

$$T = T(2\pi R - 2\pi R_o). \qquad (41)$$

This tension T will depend on the elastic properties of the detrusor. We know that the stretching force applied to a muscle strip may be expressed as a function of the change in length from resting unstretched length:

$$F = F(l - lo) \qquad (42)$$

which is an exponential function. We need to relate equations (41) & (42) so as to extrapolate our understanding of muscle strips to the whole spherical bladder. If the length of a strip is a fraction λ of the circumference of the bladder then the change in volume may be expressed as:

$$2\pi R - 2\pi R_o = \{l - l_o\} / \lambda \qquad (43)$$

The extension force (and reactive tension) acts over the width of the muscle strip so that the total force acting on the bladder wall must be related to the width of the strip.

When a strip is extended its diameter usually decreases at the same time. This change in diameter is described by Poisson's ratio σ:

σ = {lateral contraction/original diameter}/{longitudinal extension/original length}

This is a constant for a given material. When the volume of a strip of material remains constant while extension and lateral contraction take place Poisson's ratio is 0.5.(Nelkon 1966). We assume that the volume of detrusor material does remain constant in these circumstances. For small strains the tensile stress for a given axial strain is increased by a factor $1/\{1 - \sigma\}$. Therefore if the breadth of a strip is a fraction β of the circumference we may express the the tension T developed in the wall of the bladder as a result of an extension force F applied to individual muscle strips:

$$T = F/\beta\{1 - \sigma\} \tag{44}$$

$$T = F/\beta\{1 - 0.5\} \tag{45}$$

$$T = 2F/\beta \tag{46}$$

(43) and (46) show that function (41) may be obtained from function (42).

$$T = T(2\pi R - 2\pi R_o). \tag{41}$$

$$F = F(l - lo) \tag{42}$$

$$2\pi R - 2\pi R_o = \{l - l_o\}/\lambda \tag{43}$$

$$T = 2F/\beta \tag{46}$$

As already stated the elastic force/extension relationship of body tissues is an exponential function so:

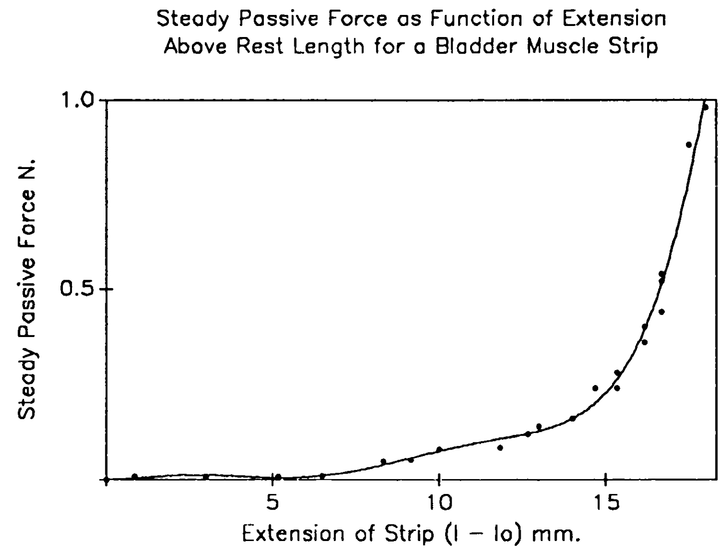
$$F = F(l - lo) = K(l - l_o)^n \tag{47}$$

By using equations (40), (43) and (46) we may obtain an expression for the equivalent change in detrusor pressure within a bladder:

$$d.p_{det} = 2F/\beta/\pi R^2 \tag{48}$$

K and n are constants dependent on the elastic properties of the detrusor muscle. They are obtained by fitting equation (48) to the results of in vitro experiments on muscle strips (Griffiths et al 1979). They may then be related to a whole sphereical bladder. Figure 24 is taken from results obtained by Griffiths et al. (1979) and illustrates the relationship between passive force and the change in extension length $(l - l_o)$ of muscle strips. The original muscle strips were set up so that the test length was 8 mm which was approximately 1/20 of the circumference of the sampled bladders. This means that the volumes of the empty sample bladders were around 70 ml (V_t = 70 ml). This means that $\lambda = 0.05$. The strips were approximately 9 mm breadth so that $\beta = 0.056$. Over the range $l - l_o = 0$ to 15 mm the equivalent change in bladder volume would have been approximtely 456 ml.

I have applied equation (48) using the gradient of Figure 24 to this range and have calculated a change in p_{det} of approximately 3 cm H_2O for $V + V_t = 70$ ml to $V + V_t = 530$ ml. Griffiths (1980) calculated a change in p_{det} of about 5 cm H_2O for a change in bladder volume between 50 and 600 ml. The gradient of the curve in Figure 24 over the range $l - l_o = 0$ to 15 mm is approximately linear. These calculations fit with clinical experience. Figure 25 shows a plot of p_{det} against bladder volume taken from a normal woman. Figure 26 shows a similar plot obtained from a patient who had undergone pelvic irradiation. The reduction in compliance associated with the post-irradiation change in the detrusor are clearly demonstrated by the form of the curve.



Griffiths et al. (1979)

Figure 24

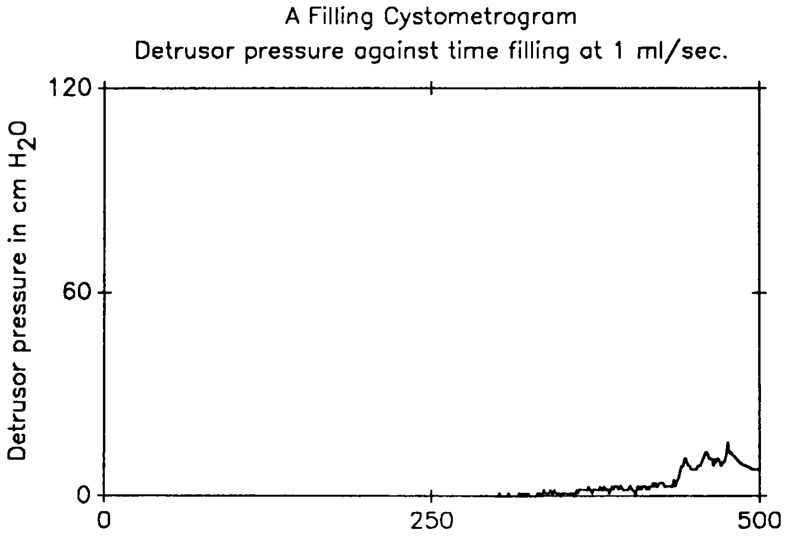


Figure 26

A filling study record of the detrusor pressure taken from a patient with a normal stable bladder

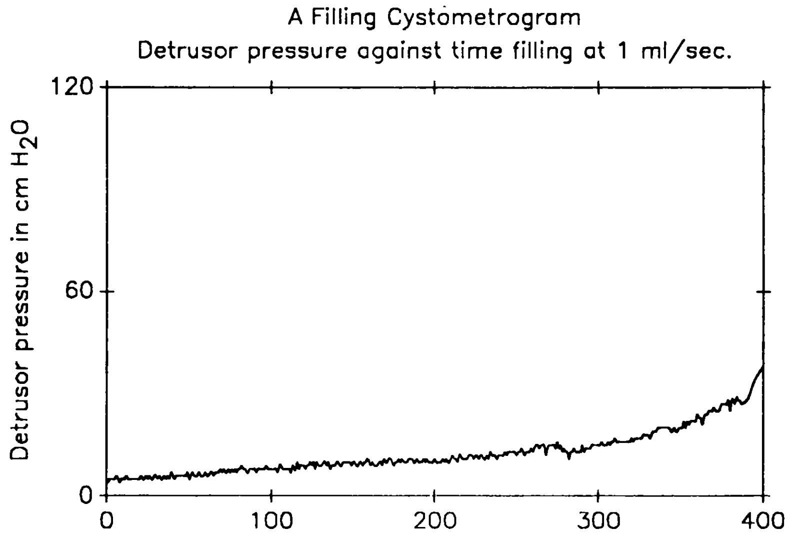


Figure 25

A filling study record of the detrusor pressure taken from a patient with a bladder of low compliance.

Griffiths et al (1979) also demonstrated the fact that the detrusor muscle has considerable plasticity and that the passive force relation is also time dependent and velocity dependent. All the patients who were studied by me, in this project, underwent bladder filling at a rate of 1 ml/sec. At very much faster rates changes will occur in the detrusor pressure which are related to the stress relaxation of a passive visceoelastic solid (Van Mastrigt et al 1978) as well as the properties described by Griffiths et al (1979).

This analysis explains the behaviour of the detrusor during passive filling in the absence of active detrusor contractions. In pathological situations, when the detrusor is unstable, active contractions of the detrusor will lead to pressure rises which will alter the pressure/volume relationship. These will require a different analysis but before exploring this area it is more sensible to analyse the contractile behaviour of the bladder in normal circumstances, during normal voiding.

(2) The contractile element.

We know that the force generated by a contracting muscle will depend on two variables; the extension (**length-tension relationship**) and the speed of shortening of the muscle fibres (**force-velocity relationship**).

Griffiths et al (1979) have shown that the isometric tension (F_o) depends on the extension of the strip above its resting length. They also showed that the ratio of force to isometic force (F/F_o) depends only on the velocity of shortening and is independent of extension.

The force/velocity relationship may be expressed by means of a modification of an equation first described by Hill (1938) which described the force/velocity relationship for striated muscle:

$$\{F + a\}\{v + b\} = \{F_o + a\}b \qquad (49)$$

Where a and b are constants, F is force, v is velocity of shortening and F_o is the isometric force (exerted at zero velocity). For striated muscle the ratio $a/F_o = 0.25$ (Hill 1938). We also know that the relation F/F_o

depends only on velocity (Griffiths et al 1979, Griffiths & van Mastrigt 1979,Griffiths 1980). It is therefore useful to divide equation (49) by F_o:

$$\{F/F_o + a/F_o\}\{v + b\} = \{a/F_o + 1\}b \qquad (50)$$

We need to relate force and velocity to the pressure and flow of a whole bladder. From (40):

$$F = p_{det}\pi R^2 \qquad (51)$$

Where pdet is the detrusor pressure and R is the radius of the bladder. $F \propto p_{det}$, so if the volume is kept constant:

$$F/Fo = p_{det}/p_{iso} \qquad (52)$$

where p_{iso} is the isometric detrusor pressure.

The velocity (v) which is the linear speed of shortening of a muscle strip now needs to be related to the rate of flow of urine out of the bladder. Let U be the speed of shortening of the circumference of the bladder:

$$U = d\{2\pi R\}/dt = -2\pi\{dR/dt\} \qquad (53)$$

remembering that the length of a strip of muscle is a fraction λ of the circumerference of the bladder, then:

$$U = v / \lambda \qquad (54)$$

where v is the velocity of shortening of a strip whose length is a fraction λ of the circumference.

During voiding the urine flow rate out of the bladder Q is the rate of change in volume $\{V + V_t\}$ of the bladder:

$$Q = -d(V+Vt)/dt = -d(4\pi R^3/3)/dt \qquad (55)$$

$$Q = -4\pi R^2\{dR/dt\} \qquad (56)$$

By substituting (53) into (56) we get:

$$Q = 2R^2U \tag{57}$$

By substituting (54) into (57) we get:

$$Q = 2R^2v/\lambda \tag{58}$$

$$v = Q\lambda/2R^2 \tag{59}$$

Substituting equation (59) and (52) into (50) we get:

$$\{p_{det}/p_{iso} + a/F_o\}\{Q\lambda/2R^2 + b\} = \{1 + a/F_o\}b \tag{60}$$

by multiplying through by $2R^2/\lambda$ we get:

$$\{p_{det}/p_{iso} + a/F_o\}\{Q + 2R^2b/\lambda\} = \{1 + a/F_o\}2R^2b/\lambda \tag{61}$$

$$\text{Let } Q^* = 2R^2b/\lambda \tag{62}$$

$$Q^* = 2\{3/4\pi\}^{2/3}\{V + Vt\}^{2/3}(b/\lambda) \tag{63}$$

β/λ is the value of the velocity parameter b when related to the whole of the circumference of the bladder then:

$$\{p_{det}/p_{iso} + a/F_o\}\{Q + Q^*\} = \{1 + a/F_o\}Q^* \tag{64}$$

Equation (64) expresses the relationship between detrusor pressure and urine flow out of a bladder in a manner that parallels the **force-velocity** relationship of individual muscle strips. The validity of the equation has been confirmed by experiments conducted on pig bladder (van Mastrigt & Griffiths 1979). They took the value of a/F_o to be 0.25 (Hill 1938). Note that they did not consider the influence of the parallel elastic element which would be insignificant during a detrusor contraction. We may rewrite (64) now as:

$$\{p_{det}/p_{iso} + 0.25\}\{Q + Q^*\} = \{1 + 0.25\}Q^* \tag{65}$$

This equation is referred to as the "Bladder output relation" (BOR). It is important to note that it is volume dependent since both p_{det}/p_{iso} and Q^* (which contains a volume expression in its equation) are both volume dependent. Griffiths (1980) using data from normal human micturitions suggested that p_{iso} be corrected for bladder volume by using the expression:

$$p_{iso} = p_o\{1 - k\{V + V_t\}\} \qquad (66)$$

where p_o is the isometric pressure generated at zero bladder capacity (typically 100 cm H_2O by extrapolation) and $k = 5 \times 10^{-4}$ ml^{-1}. I have included this correction in the mathematical models which I have set up as examples.

Q^* is a useful variable for studying the velocity properties of a bladder at a given volume. An interesting property of this variable is shown when p_{det} is zero:

$$\{0 + 0.25\}\{Q + Q^*\} = \{1 + 0.25\}Q^*$$

$$0.25Q + 0.25Q^* = Q^* + 0.25Q^*$$

$$0.25Q = Q^*$$

$$Q = 4Q^*$$

u/ If we plot eqation (65) the intercept on the flow rate axis will be equal to $4Q^*$. Figure 27 shows a plot of the bladder output relation using $Q^* = 40$. The intercept on the flow axis is 160 ml/sec.

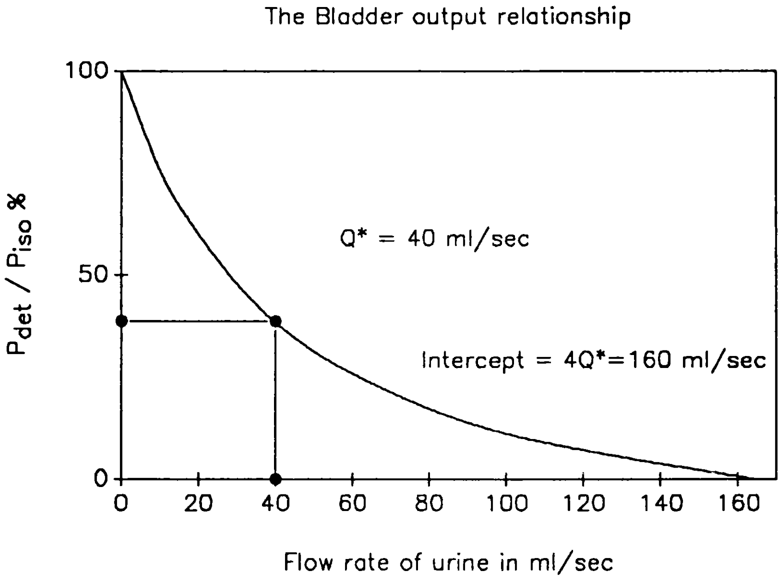


Figure 27

The bladder output relation describes the range of flow rates achieveable by a given bladder at a given bladder volume. The flow rate, from this range, which is achieved will be decided by the urethral resistance relationship equation (36). Therefore, the flow rate may be calculated from the intersection of equation (36) and equation (65).

If we express equation (36) in terms of flow rate:

$$Q_{max} = \{ p_{det} + p_{head} - p_{mo} / H\}^{1/m} \tag{36a}$$

and equation (65) in terms of flow rate:

$$Q = \{\{1 + 0.25\}Q^{*} / \{p_{det}/p_{iso} + 0.25\}\} - Q^{*} \tag{67}$$

The flow rate at a given pressure is the flow rate which has a value such that equation (36_a) = equation (67).

conversely if we take equation (36):

$$p_{det} = p_{mo} + HQ_{max}{}^{m} - p_{head} \tag{36}$$

and express (65) in terms of pressure:

$$p_{det} = \{\{1 + 0.25\}Q^{*} / \{Q + Q^{*}\}\} - 0.25 / p_{iso} \tag{68}$$

The pressure at a given flow rate is the pressure which has a value such that equation (36) = equation (68).

Figure 28 demonstrates the solutions of the BOR equation plotted during voiding. As the bladder volume decreases the BOR changes and moves to the left. Each BOR curve marks out the range of flow rates which a bladder, of pre-defined isotonic and isometric capabilities, would be able to achieve when contracting maximally at a certain volume. As the volume of the bladder falls the flow rate at a given pressure reduces. The actual flow rate which is achieved during voiding depends on the resistance of the urethra. If the resistance is low the flow rate will be high but the pressure low. If the urethral resistance is high the pressure will be high but the flow rate low. We may describe the actual flow rate throughout voiding by ploting the intersections of the URR curve with the series of different BOR curves.

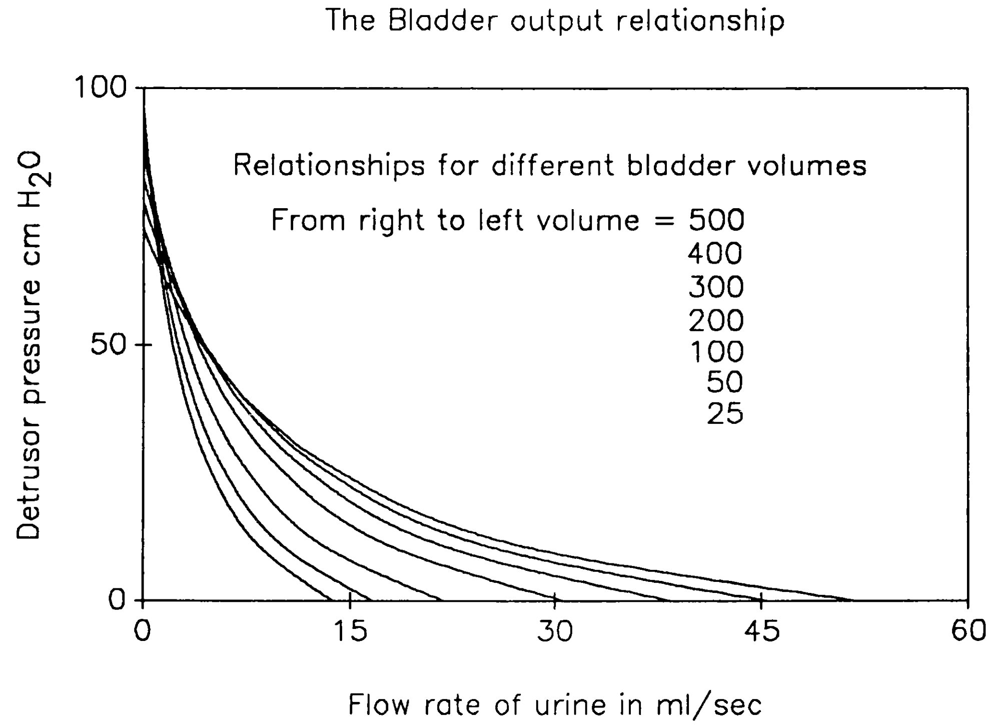


Figure 28

Figure 29 shows the BOR curves as in figure 28 but I have included the actual flow rate curve (dashed line with black dots) which is defined by intersections of the URR curve on the BOR curves. This curve traces the course of micturition. In this example I have not included p_{head} in the URR equation in line with the method used by others (Griffiths et al 1979, Spangberg et al 1989). Note how the pressure rises towards the point at maximum flow rate. Figure 30 shows a similar plot but the URR is calculated with the correction for p_{head}. The pressure falls between the commencement of voiding and the point of maximum flow rate. This feature is seen in clinical practice in women with very elastic urethras. In these circumstances the pressure head p_{head} acting on the urethra is particularly significant. Because we measure the pressure in the bladder with reference to the upper margin of the superior pubic ramus we fail to take full account of p_{head} and an apparent fall in pressure below the urethral opening pressure, despite an increase in flow rate, is observed. This picture is a helpful sign of good urethral elasticity.

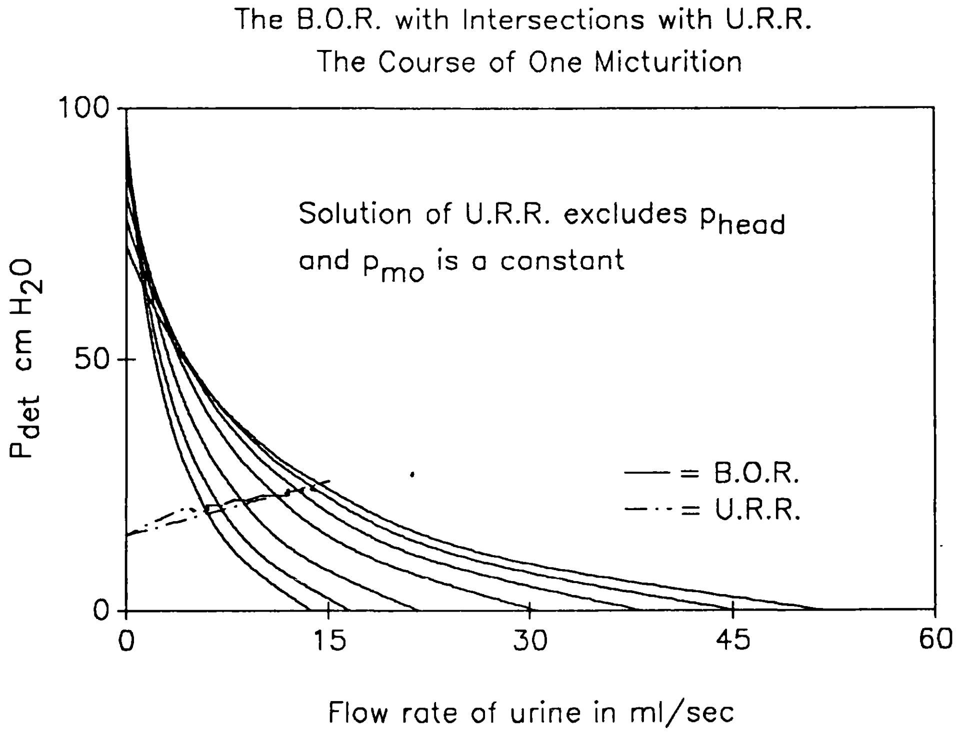


Figure 29

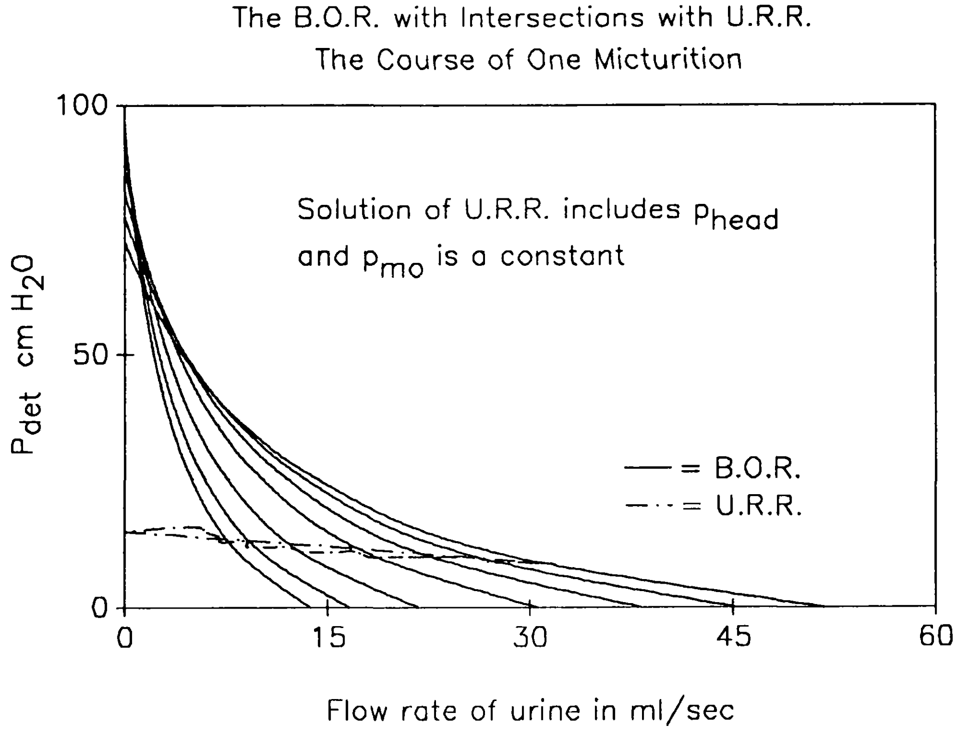


Figure 30

An important observation made in clinical practice is that p_{mo} does not remain constant during the course of micturition but decreases by a varying degree so that the urethral opening pressure at the end of micturition is lower than at the beginning (Griffiths 1980). In other words it is usual for the sphincter to continue to relax after the initiation of micturiton. Figure 31 uses the same data as in the previous two examples but in the course of the micturition p_{mo} was decremented from 15 cm H_2O to 10 cm H_2O, there by emulating the active relaxation of the sphincter during the early stages of micturition. The curve has now opened up a little with the first part of micturition being traced above that showing the later part.

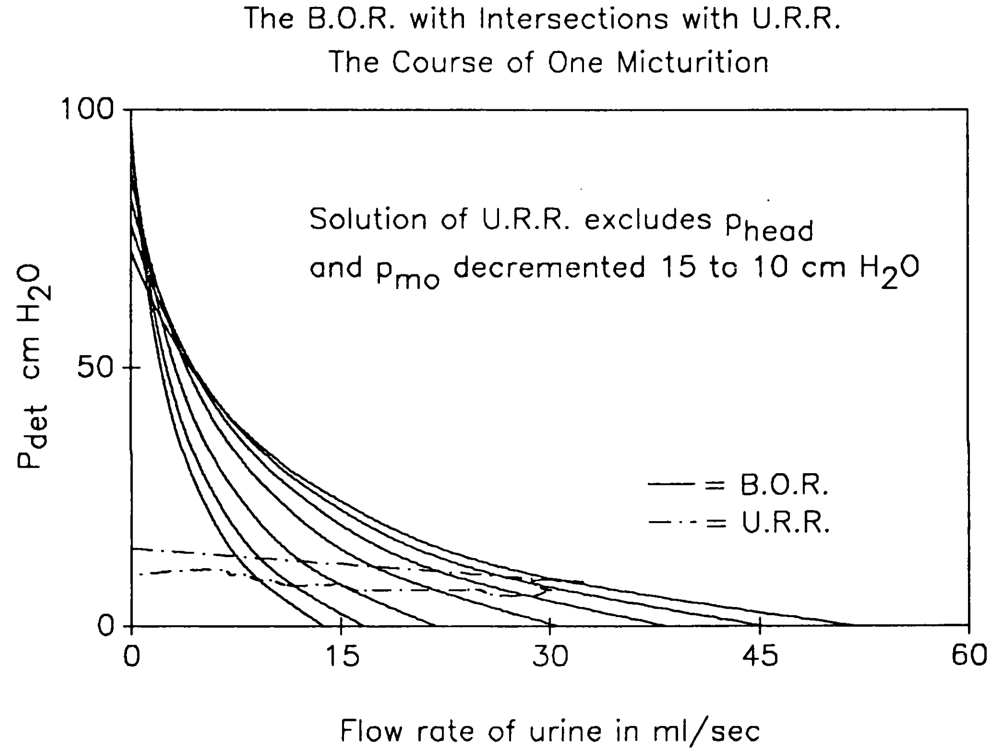


Figure 31

Figure 32 shows a plot of the voiding detrusor pressure against voiding flow rate recorded from a normal woman voiding from 500 ml. The detrusor pressure is delayed by one second relative to the flow rate in order to correct for an inverse delay in the recording apparatus (Griffiths & Van Mastrigt 1985). There is slight interference due to urethral kinking which causes the two loops on the upper part of the curve but the relation to the mathematical models is clear. Voiding pressure / flow plots of the kind shown in Figure 32 give important information about the urethral resistance relationship (URR), because pressure is used on the y axis they also give some data on the strength of the bladder, although the isometric pressure is needed to give a fuller description. It is less reliable for deducing the detrusor shortening velocity which must be assessed by calculating a velocity parameter. Figures 33 to 44 illustrate a series of pressure/flow plots which have been generated by computer using the URR and BOR equations with all of the corrections used in figure 31. In each one different constants have been changed. The aim is to illustrate the varying plots which are seen in clincal practice.

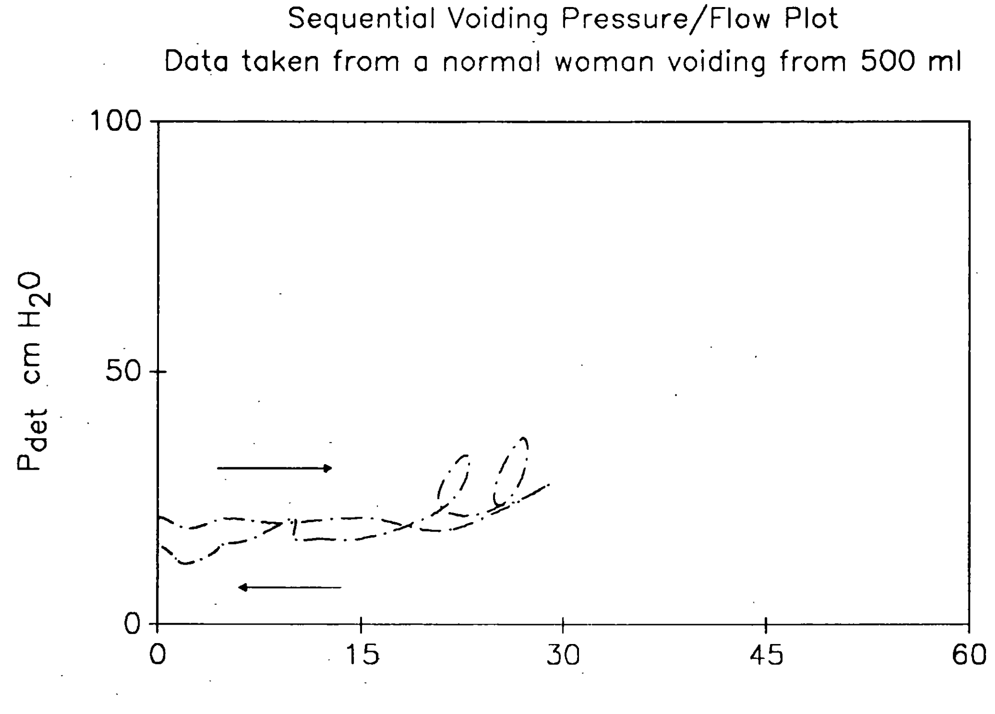


Figure 32

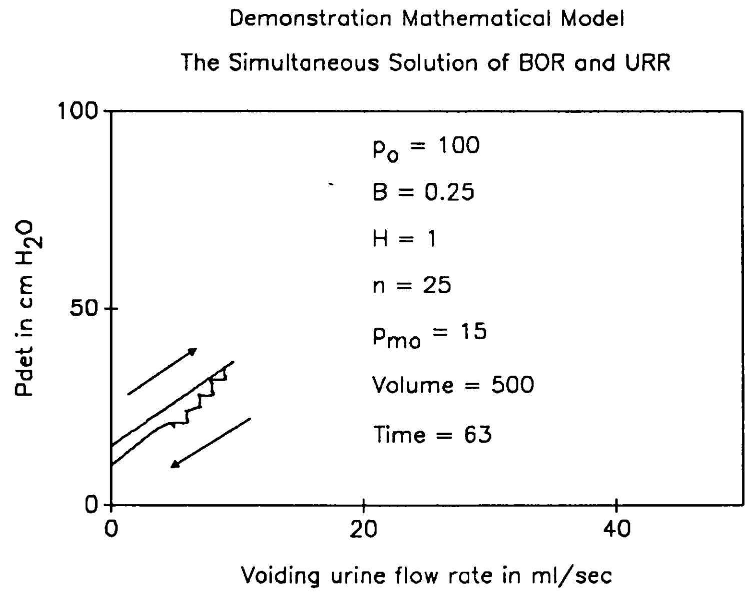


Figure 33

Isometric and isotonic activity are set to normal values (B=0.25 and p_o=100). The urethral compliance is increased by raising the value of the exponential elasticity constant n (n=25). The urethral opneing pressure p_{mo} is set to a normal value (p_{mo}=15).

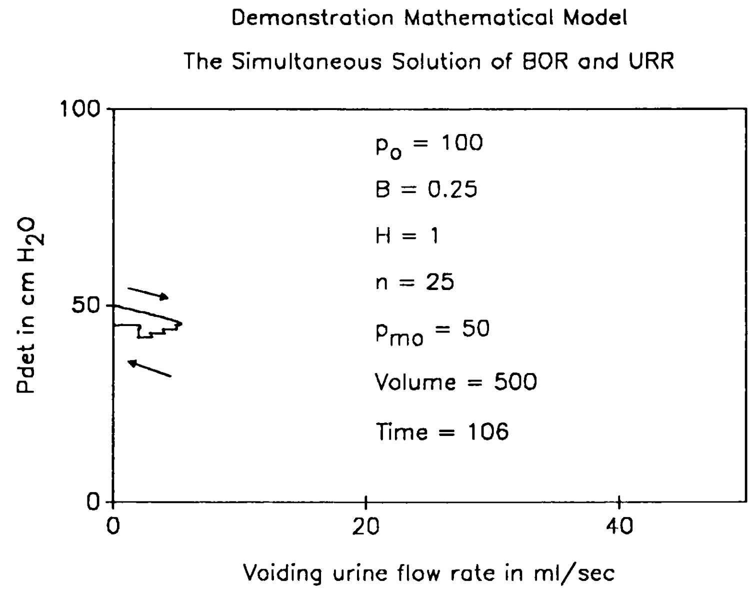


Figure 34

This figure is similar to figure 33 but the urethral opening pressure p_{mo} is elevated (p_{mo}=50).

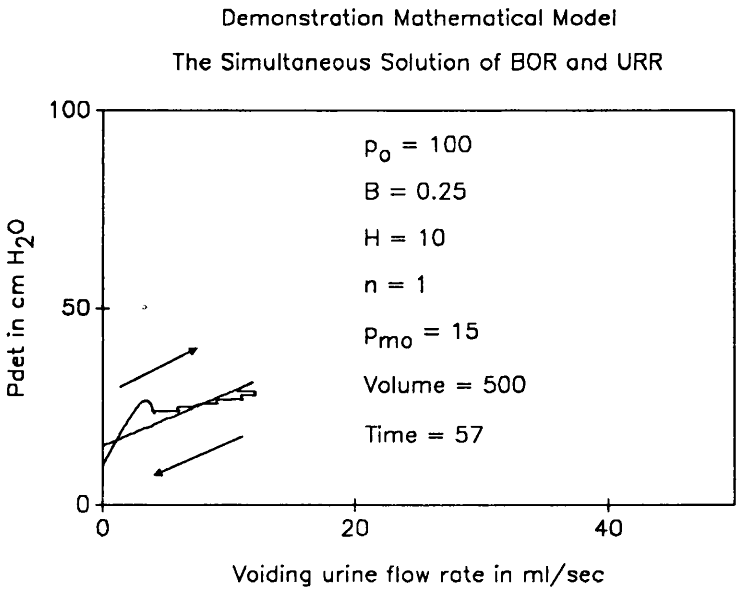


Figure 35

This figure is similar to figure 33 but in this case the compliance of the urethra is increased by elevating the value of the linear urethral elasticity constant H whilst keeping the exponential elasticity constant n at a normal value . In clinical practice it is not possible to differentiate the influence of these two elasticity constants.

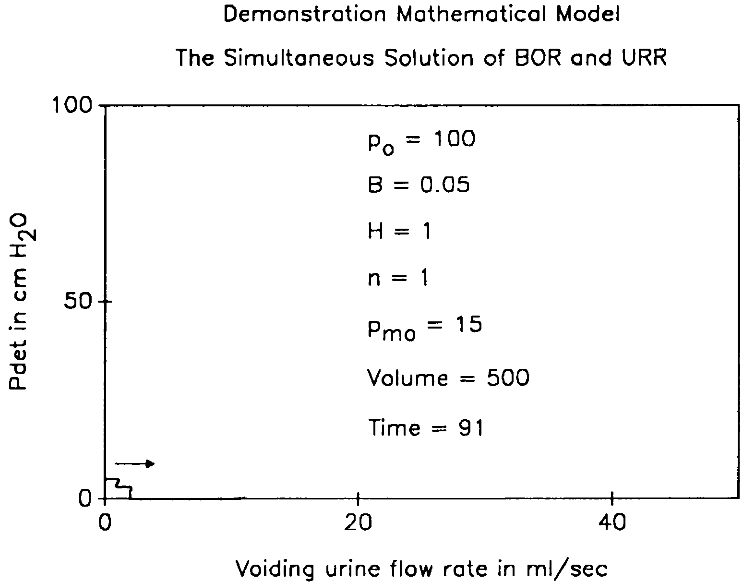


Figure 36

In this case all of the constants are set to normal values appart from the velocity constant B, which is set to a very low value (B=0.05). This models a low velocity bladder, a common finding amongst the elderly.

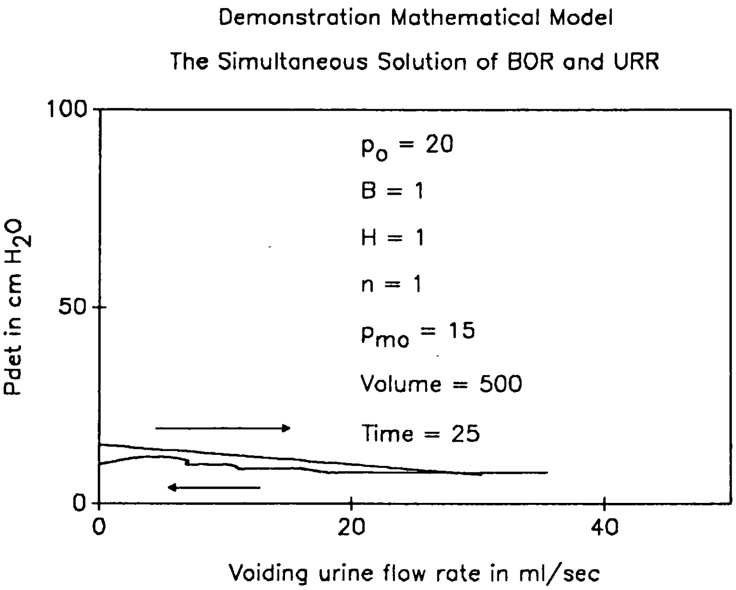


Figure 37

The velocity constant B is elevated (B=1), modelling a fast bladder and the isometric component of detrusor contractilityy is reduced by using a low value for p_o (p_o=20). This is commonly seen amogst women. The fall in pressure towards maximum flow models good urethral elasticity.

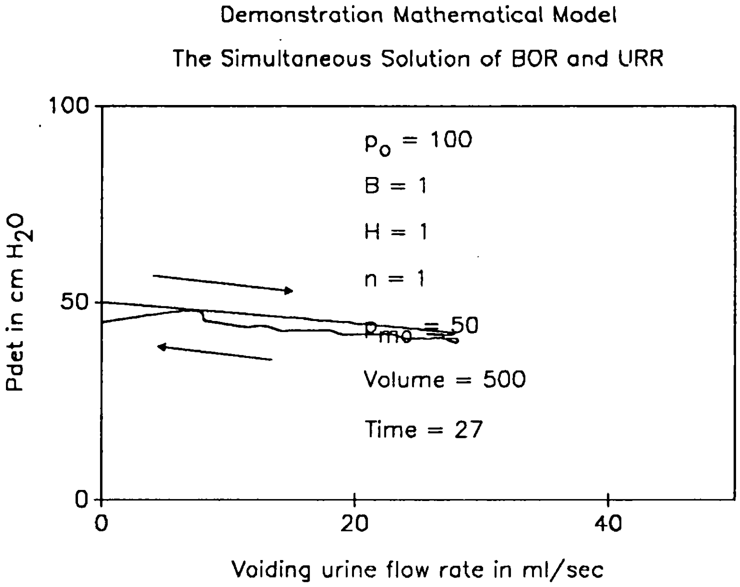


Figure 38

This figure is similar to figure 37 but the isometric detrusor activity is set higher (p_o=100) the urethral opening pressure is also elevated (p_{mo}=50). This type of picture is often seen in young adults, especially men.

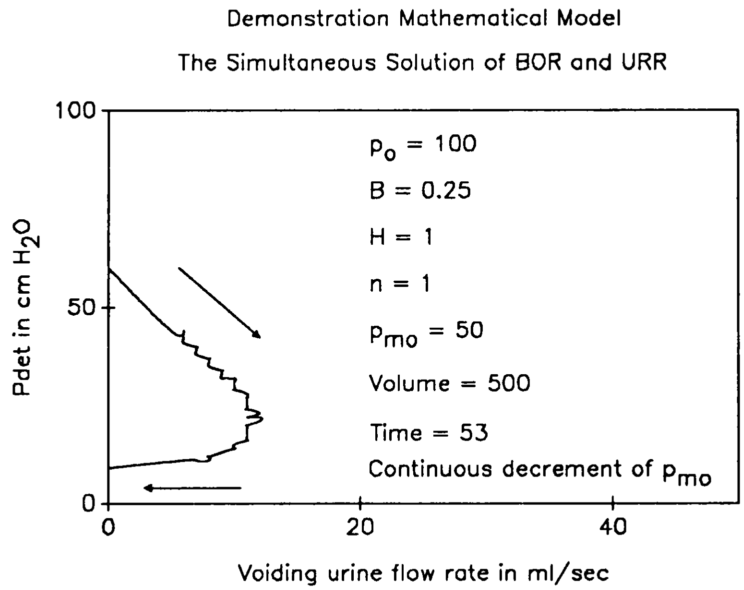


Figure 39

The various constants are set to normal values except the urethral opening pressure which starts at 50 cm H_2O. However, the p_{mo} is decremented during voiding down to 15 cm H_2O. This models a delay in sphincter opening with relaxation progressing during voiding.

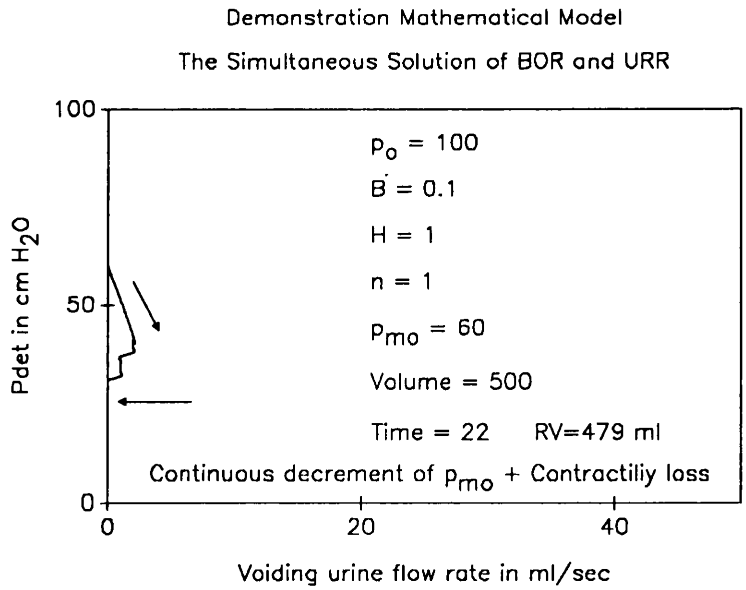


Figure 40

This figure is very similar to figure 39 but in this case the detrusor is much slower (B=0.1) and the detrusor contractility is reduced incrementally during voiding. This models a poorly sustained slow contraction working against a urethral obstruction.

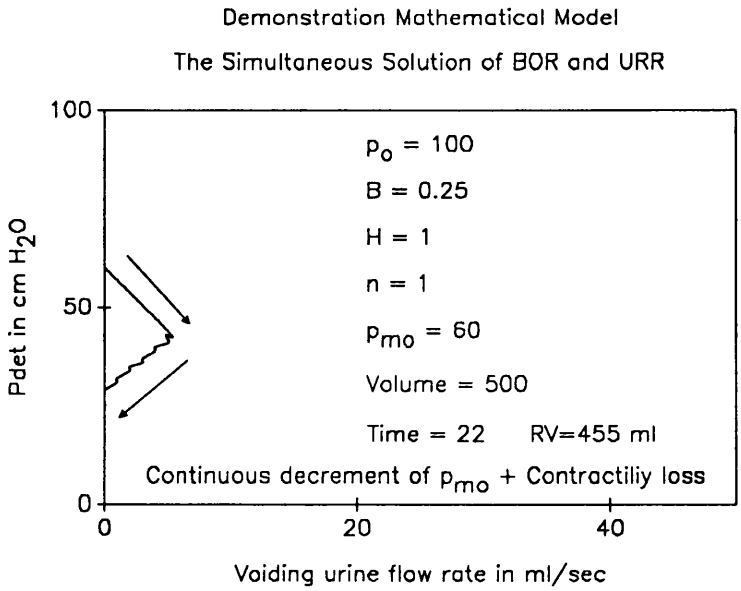


Figure 41

This is identical to figure 40 but in this case the velocity constant B is set to normal values (B=0.25). This models a poorly sustained detrusor with normal velocity working against an obstruction.

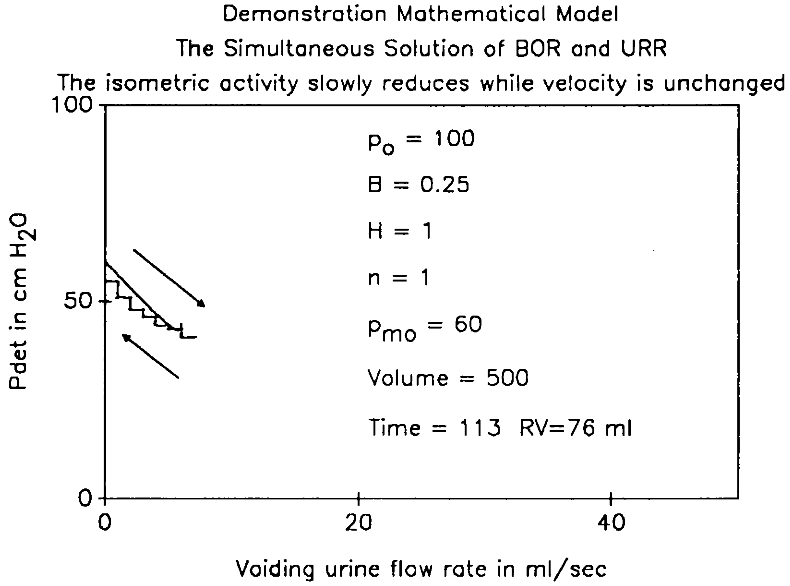


Figure 42

This is similar to figure 41 but the decrement in contractility during voiding applies to the isometric activity only (p_o), the velocity is maintained (B=0.25).

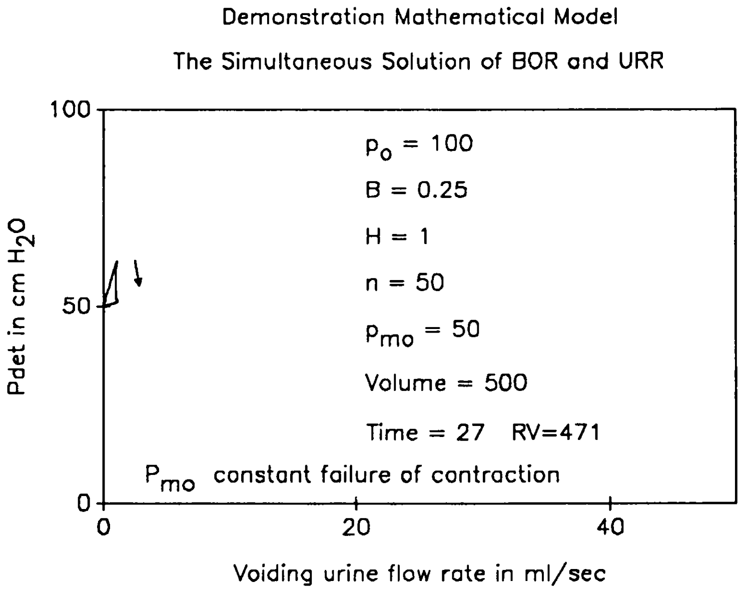


Figure 43

In this case the p_{mo} is set high and remains the same throughout voiding. This models a very rigid obstruction. The isometric and isotonic detrusor activity are decremented during the void thus modelling a failure to sustain the contraction.

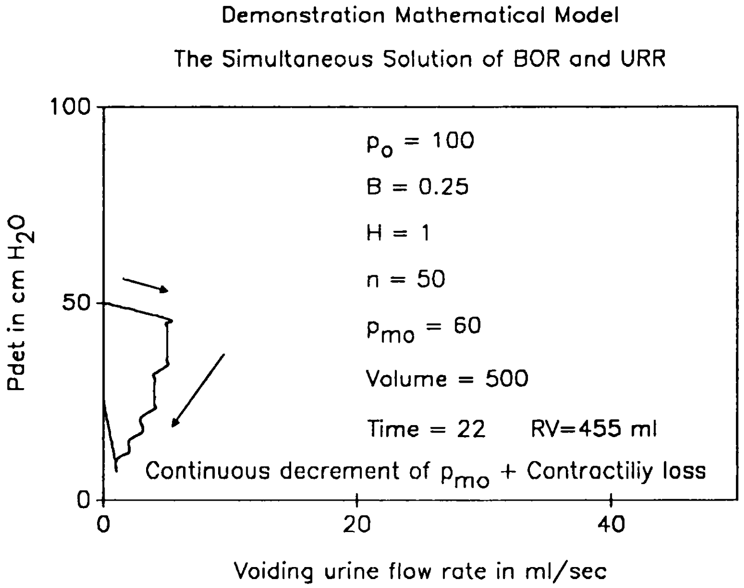


Figure 44

This is similar to figure 43 but the urethral opening pressure p_{mo} is decreased continuously during voiding. As previously the contraction is also decremented. This models a poorly sustained contraction with a delay in sphincter opening. This feature is more common amongst patients with neurological disease.

Q^* is a useful variable for comparing the detrusor speeds between individuals. As it is dependent on bladder volume we will need to modify it for comparison between individuals voiding from different volumes. From equation (63) it can be seen that $Q^* \propto \mathrm{vol}^{1/2}$. Griffiths (1980) has suggested that Q^* be normalised to a standard volume V_{std} = 200 ml using the equation:

$$Q^*_{std} = \{200/\mathrm{vol}\}^{1/2} Q^* \qquad (69)$$

Normal values for Q^*_{std} lie between 30 and 100 ml s^{-1} in both sexes (Griffiths 1980). Q^*_{std} is proportional to β/λ of equation (63)

(3) The Series elastic element

Up to this point we have not included an expression for the series elastic element in the contractitily equations. The truth is that not much is known about the series elastic element in the detrusor. Our assumption is that ~~like~~ the elastic elements of most body tissues can be approximately represented by an exponential spring so that the force generated by the spring is related to the extension of the spring: (Van Mastrigth et al 1978)

$$F_{spring} = k\Delta L^{(\mu\Delta L)} \qquad (70)$$

where k and μ are positive constants independent of bladder volume and ΔL is the extension of the series elastic element above its rest length measured around the whole circumference of the bladder. Griffiths et al (1979) fitted this expression into the voiding equations already described and compared the results from their mathematical models to those found by clinical observation. Their results suggest that the series elastic element acts as a sort of baffle during bladder contraction. Figure 45 shows two voiding flow curves related to the same patient, one is calculated from the mathematical model using data from the patient applied to the URR and BOR equations, the other is the actual recording during urodynamic testing. There is a difference in the two curves. The rise in flow rate in the live recording has a slower gradient than that achieved by the model. The live flow curve has a better defined plateau than the model curve and a slower decline. The slower rise in flow rate can be accounted for by the elongation of the series elastic element during the initial period of detrusor contraction. The plateau and slow decline in the flow curve can be explained by a delay in the decay of muscle shortening at the end of the contraction as the series elastic element shortens back towards resting length. These changes would be easier to see if we plotted the detrusor shortening velocity against time rather than the flow rate.

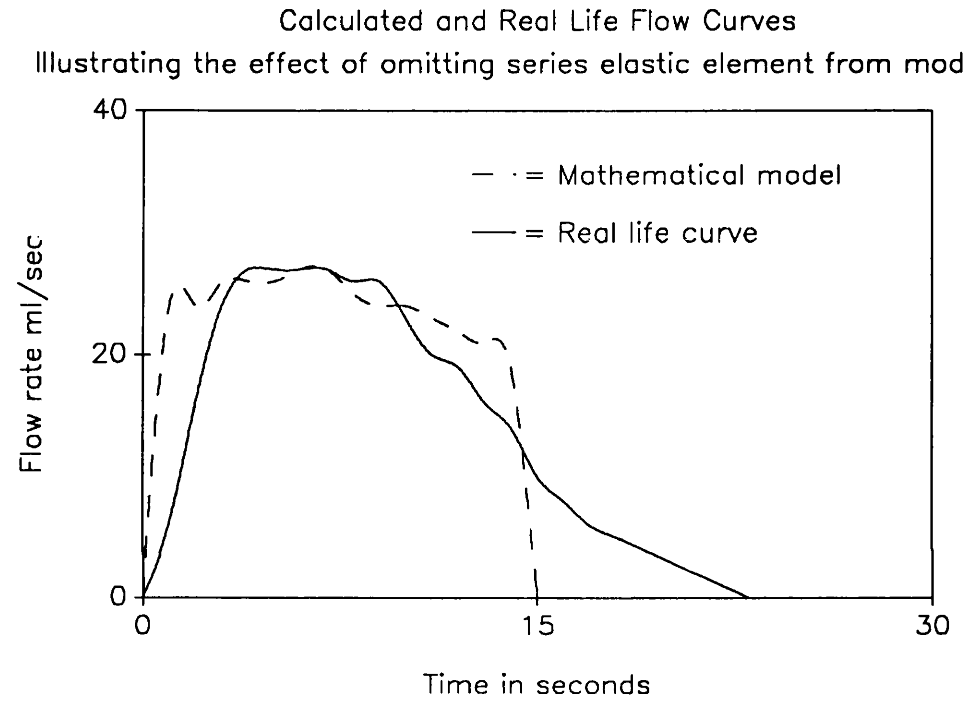


Figure 45

The equation for the velocity of shortening of the bladder circumference is derived as follows. The velocity is the rate of shortening of the bladder circumference:

$$\text{vel} = -d(2\pi R)/dt = -2\pi dR/dt \tag{71}$$

During voiding the flow rate Q is the rate of change of bladder volume

$$Q = -dV/dt = -d(4\pi R^3/3)/dt \tag{72}$$

differentiating this equation

$$Q = -4\pi R^2 dR/dt \tag{73}$$

replacing (71) into (73)

$$\therefore\ Q = 2R^2 vel \tag{74}$$

$$\therefore\ vel = Q/2R^2 \tag{75}$$

The bladder volume may be calculated from:

$$V = 4\pi R^3/3 \tag{76}$$

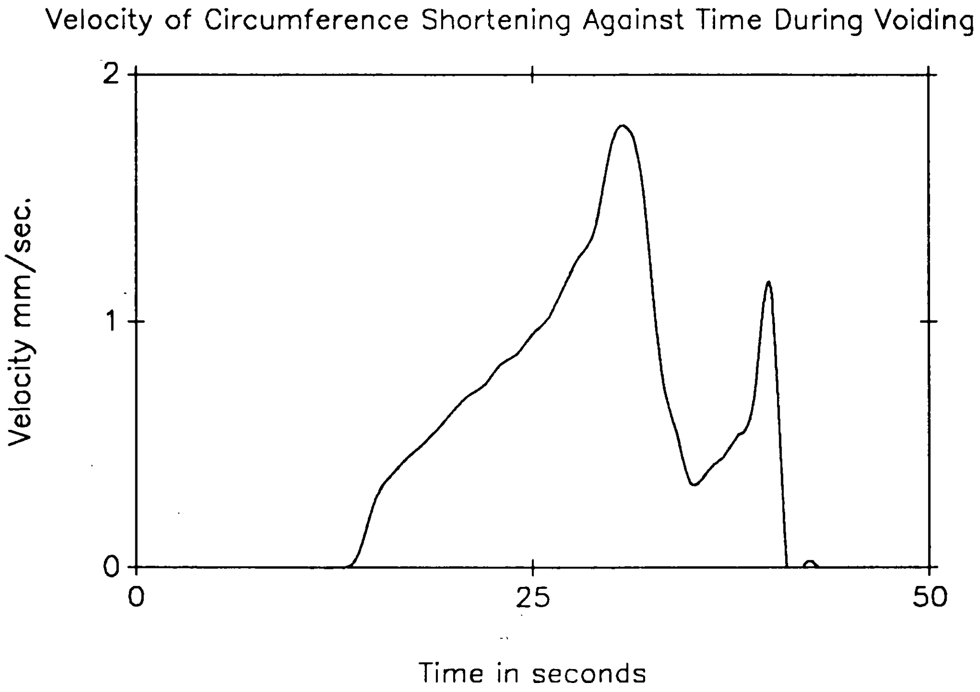
so

$$R = \{3V/4\pi\}^{1/3} \tag{77}$$

so velocity vel may be calculated by replacing (77) into (75):

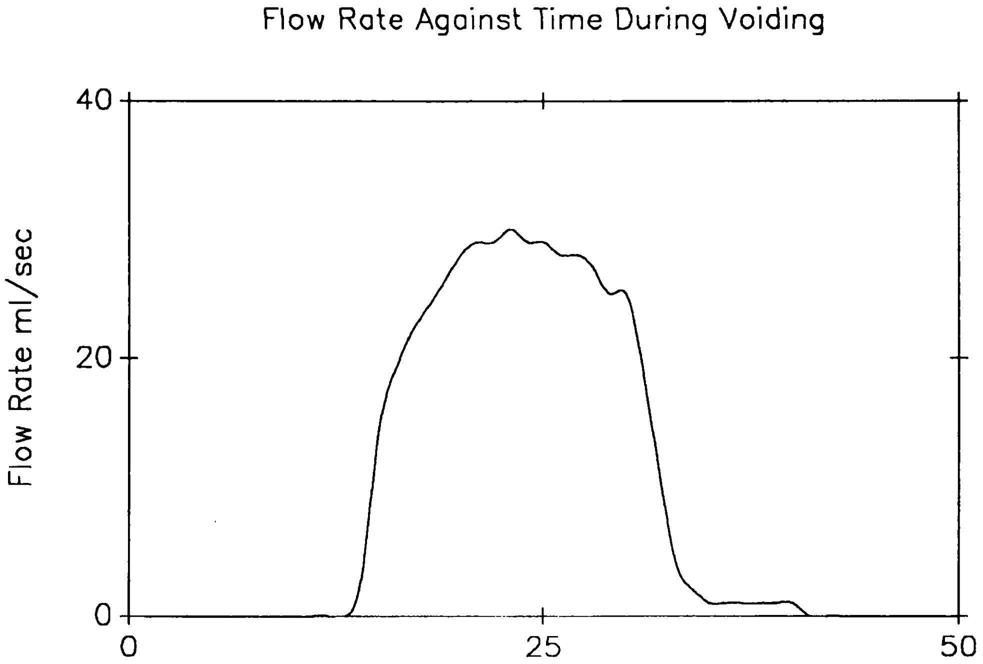
$$vel = Q/2\{3V/4\pi\}^{2/3} \tag{78}$$

Figure 46 shows a plot of the velocity of shortening of the detrusor circumference during a micturtion from 450 ml accomplished by a female patient. The peak is thought to be due to contraction of the series elastic element. Figure 47 shows the voiding flow rate plotted against time , and figure 48 shows the pressure/flow plot, taken from the same patient. The more gradual rise and plateau on the flow curve is well shown. The pressure/flow plot shows a terminal rise in pressure due to a contraction of the urethral sphincter which caused a rise in detrusor pressure at the end of micturition. It is interesting to note that in clinical practice a spontaneous sphincter contraction causing such a terminal rise in pressure is not commonly seen.



Velocity of Circumference Shortening Against Time During Voiding

Figure 46



Flow Rate Against Time During Voiding

Figure 47

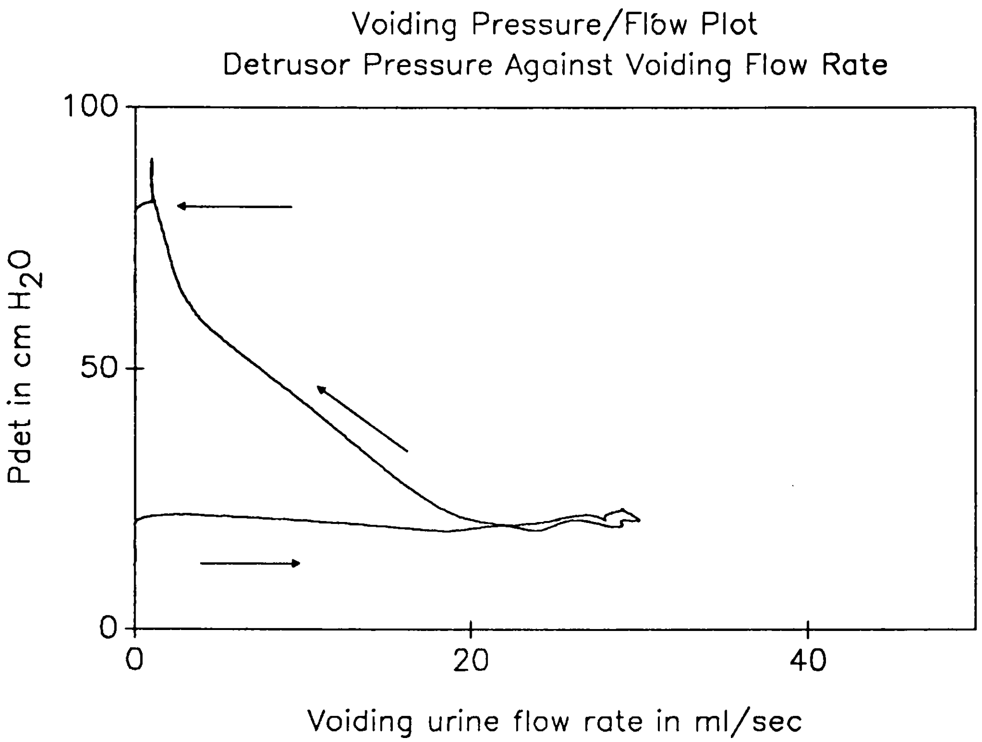

Voiding Pressure/Flow Plot
Detrusor Pressure Against Voiding Flow Rate
100
50
0
Pdet in cm H_2O
0
20
40
Voiding urine flow rate in ml/sec

Figure 48

Deriving a voiding contractilty parameter

The contractility of the bladder has been described according to the force/velocity relationship by means of equation (65). Because of the length/tension relationship the value of this equation will vary according to bladder volume. It would be helpful to express the contractility of the bladder muscle during voiding according to a single parameter which describes the force and velocity of contraction together. If this parameter would decribe the mechanical power developed by the detrusor per unit bladder area it would be possible to compare values between indivuals voiding from different capacities without having to plot a curve.

Consider a rectangle of bladder with width b and length l which is stretched a distance x such that and the new length $l_{new} = l + x$. The work done will be Tbx Where T is the tension opposing the force used to stretch the rectangle. T is the stored energy per unit area as well as force per unit length.

Now, if a bladder is stretched (or contracted) from radius R to radius $R + dR$ and T remains constant then the surface area changes by $dA = 8\pi R dR$ ------ $(A = 4\pi R2)$

Therefore the extra energy stored by stretching = $8\pi R dR T$ this energy comes from the work done by the pressure inside the bladder which is equal to $4\pi R^2 dR p_{det}$

Therefore:

$$8\pi R dR T = 4\pi R^2 dR p_{det} \qquad (79)$$

$$p_{det} = 2T/R \qquad (80)$$

Let the parameter WF = the mechancial power developed by the detrusor muscle per unit bladder area.

Consider a unit area of bladder with each side of unit length contracting by a distance dx while the tension T remains constant (Figure 49).

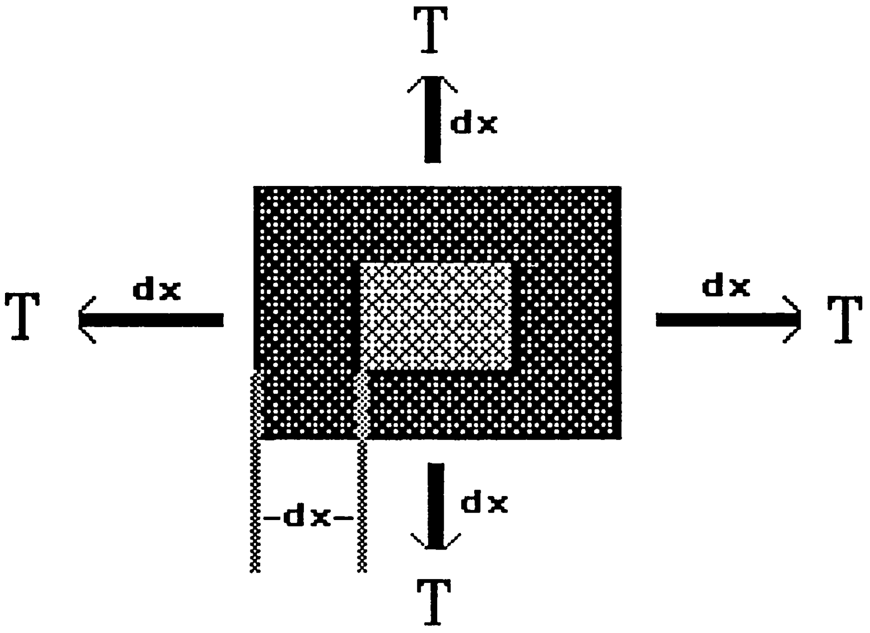


Figure 49

$$\text{The work done} = 2Tdx \qquad (81)$$

(2 because work is done in two orthogonal directions)

Power = rate of doing work

Therefore:

$$WF = 2Tdx/dt \qquad (82)$$

The velocity of shortening of the detrusor will be equal to the change in circumference with respect to time, dC/dt (where C = circumference). The change in length dx of our strip may be expressed in terms of the circumference as $dx=dC/2\pi R$ (where R is the radius of the bladder).

$$WF = 2T\,dx/dt \tag{83}$$

$$dx = dC/2\pi R$$

$$WF = \{2T/2\pi R\}\{dC/dt\} \tag{84}$$

But

$$p_{det} = 2T/R \tag{80}$$

and

$$v_{det} = dC/dt \tag{85}$$

(where v_{det} is the velocity of shortening of the detrusor circumference)

Therefore

$$WF = P_{det}v_{det}/2\pi \tag{86}$$

This equation poses certain problems; it will equal zero when the flow rate is zero which will occur when there is no contraction and when the detrusor contracts against a closed sphincter. It will also equal zero when the contraction is entirely isotonic and the pressure is therefore zero but the flow rate reaches a theoretical maximum.

This may be circumvented by adding two constants to the variables:

$$WF = \{P_{det} + a\}\{v_{det} + b\}/2\pi \tag{87}$$

This however will not be zero when there is no contraction at all, so to ensure this we need to subtract ab from the equation:

$$WF = \{\{P_{det} + a\}\{v_{det} + b\}-ab\}/2\pi \tag{88}$$

van Mastrigt and Griffiths (1987), who developed equation (88), studied this relationship by plotting the detrusor pressure against the contraction velocity during voiding in 86 patients. By fitting curves to the part of the trace which seemed to describe a hyperbolic function of the form of (88) they established v~~la~~ues for a and b such that 4b = the maximum theoretical velocity of the contraction (in other words b=Q of equation (65) expressed as velocity of shortening) and 4a = the isovolumetric detrusor presure (which is p_{iso} of equation (65)). When van Mastrigt and Griffiths (1986) first described this equation they suggested using approximate median values for a and b, namely a = 25 cm H_2O and b = 6 mm/s respectively. They also set V_t to V_t = 10 ml. I used the same values when applying equation (88) to my patients. Figure shows a plot of WF against bladder volume during voiding. Since the bladder is emptying the plot moves from right to left. The data are taken from the same patient featured in figures 46 to 48. The contractility is shown to be approximately constant throughout voiding ap~~p~~art from a terminal peak which coincides with the peak on the velocity curve.

N

δ?

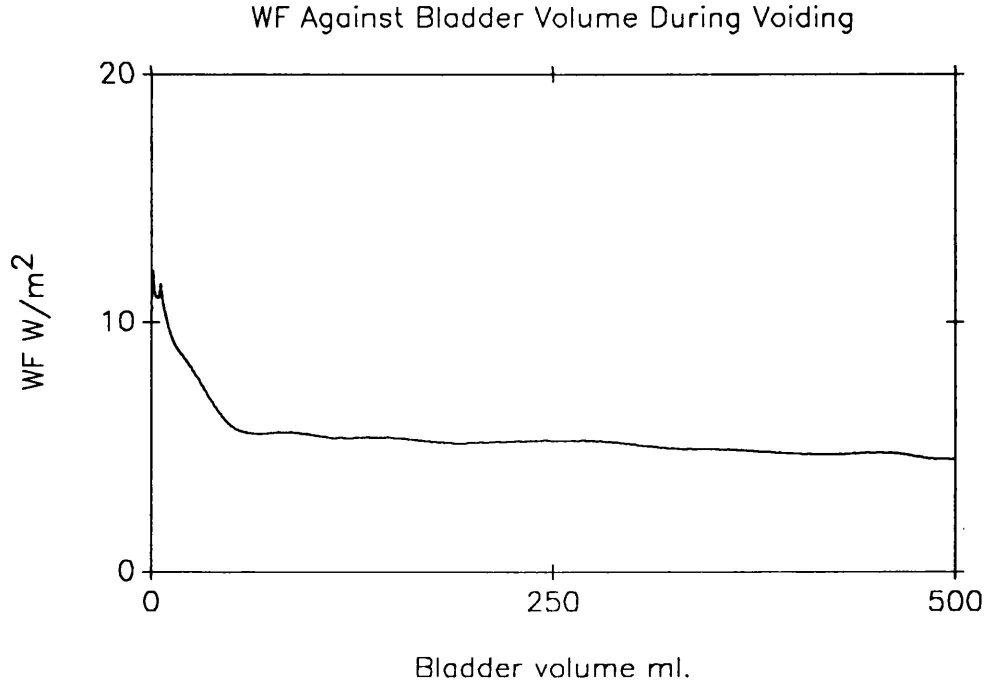


Figure 50

Maximising voiding study interpretation without a microcomputer

The application of the mathematical principles described so far is only feasible if the urodynamic data are collected by a microcomputer and stored for further processing. The majority of urodynamic departments do not have these facilities and the first cohort in my sample could not be studied in these ways. It is however possible to enhance understanding of the maximum flow rate and detrusor pressure at maximum flow by plotting the the point defined by these two parameters on a graph with pressure on the Y axis and flow on the X axis (Abrams & Griffiths 1979). Some caution should be used in interpreting these plots in patients voiding less than 100 ml or more than 400 ml because of the dependence of flow rate on bladder volume and, to a lesser extent, a similar dependence of detrusor pressure. Figures 51 and 52 illustrate these plots with areas marked out according to the recommendations of the International Continence Society (1989) and after Abrams & Griffiths (1979) and Griffiths (1980). There are zones suggesting the presence or absence of obstruction and zones indicating the degree of detrusor contractility. It should be this/ remembered that/is approach is an approximation based on limited data.

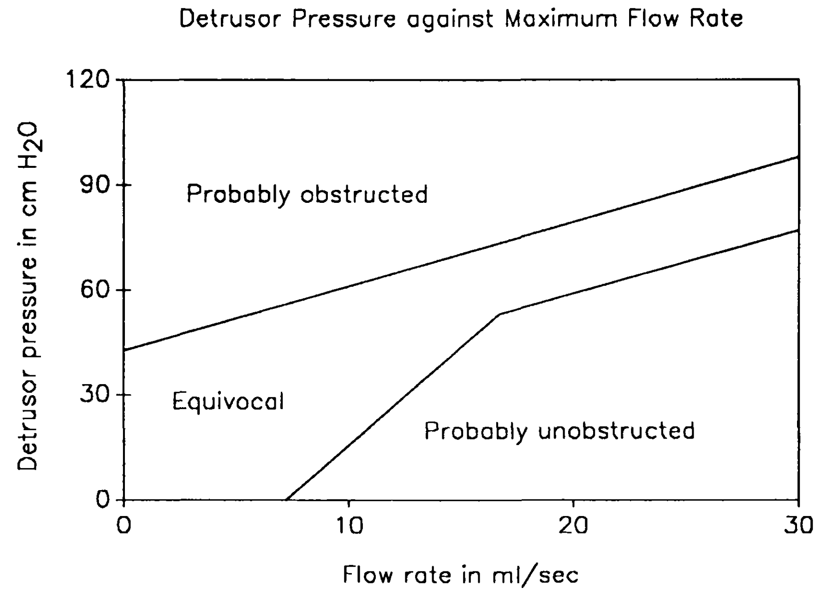


Figure 51

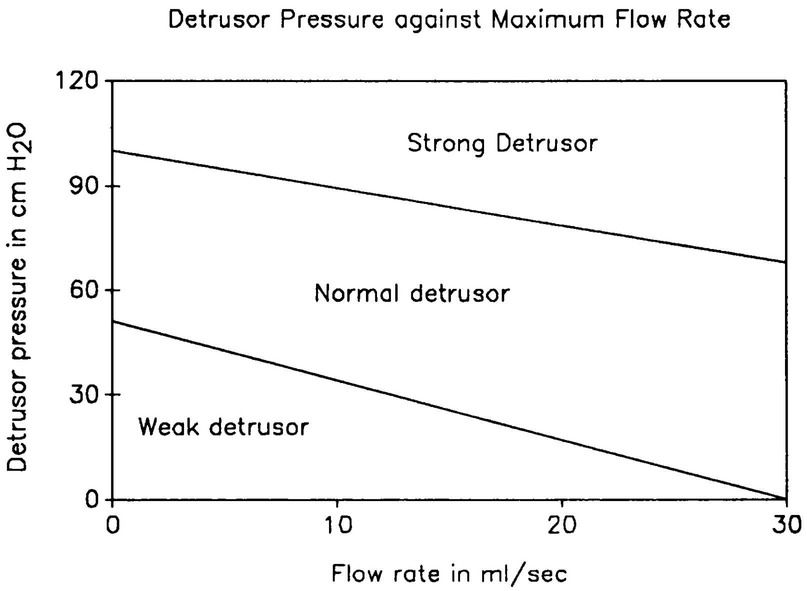

Detrusor Pressure against Maximum Flow Rate
Detrusor pressure in cm H_2O
120
90
60
30
0
0
10
20
30
Flow rate in ml/sec
Strong Detrusor
Normal detrusor
Weak detrusor

Figure 52

Describing detrusor pressure changes during bladder filling.

If we fill a bladder from 0 ml to 500 ml and the detrusor does not contract during the process, the relationship between the detrusor pressure and bladder volume may be described by equation (48). This allows us to to assess the compliance of the bladder during filling while it is unstimulated.

In pathological situations, when the bladder is unstable, contractions of the detrusor occur which cause a rise in detrusor pressure. According to the International Continence Society, the unstable detrusor is one that is shown objectively to contract, spontaneously or on provocation, during the filling phase while the patient is attempting to inhibit micturition (International Continence Society 1989). Until recently a pressure of 15 cm H_2O was considered as a threshold to be achieved by a contraction before it could be considered to be unstable. Some of the mathematical methods which I used to analyse unstable activity required a threshold, where this was necessary I used a threshold of 15 cm H_2O.

This contractile activity is often described in terms of the maximum filling detrusor pressure and the detrusor pressure at the end of fill (end filling pressure). These parameters are inadequate since they do not take account of bladder volume. Because pressure is force per unit area a given pressure will have different energy implications at different volumes. I would maintain that it is better to describe unstable activity in terms of the tension T acting in the detrusor and calculated from the equation (80):

$$p_{det} = 2T/R \qquad (80)$$

where R may be calculated from the volume:

$$vol = 4\pi R^3/3 \qquad (76)$$

$$R = \{3/4\pi\}^{1/3}vol \qquad (77)$$

so that:

$$T = p_{det}\{3/4\pi\}^{1/3}vol/2 \qquad (89)$$

If equation (89) is used to calculate the force of unstable contractions during filling the unstable activity may be described in terms of maximum tension and total tension. However this does not satisfy all of our requirements. Figure 53 shows the relationship between p_{det} and time during a filling study (filling rate = 1 ml/sec.) taken from a patient with an unstable bladder. Figure 54 is from another patient with the same diagnosis. The two studies are qualitatively and quantitatively very different. Equation (89) addresses the latter difference but to my knowledge no parameter has been derived to address the qualitative difference. I therefore needed to develop a parameter which would describe the qualitative nature of unstable detrusor activity.

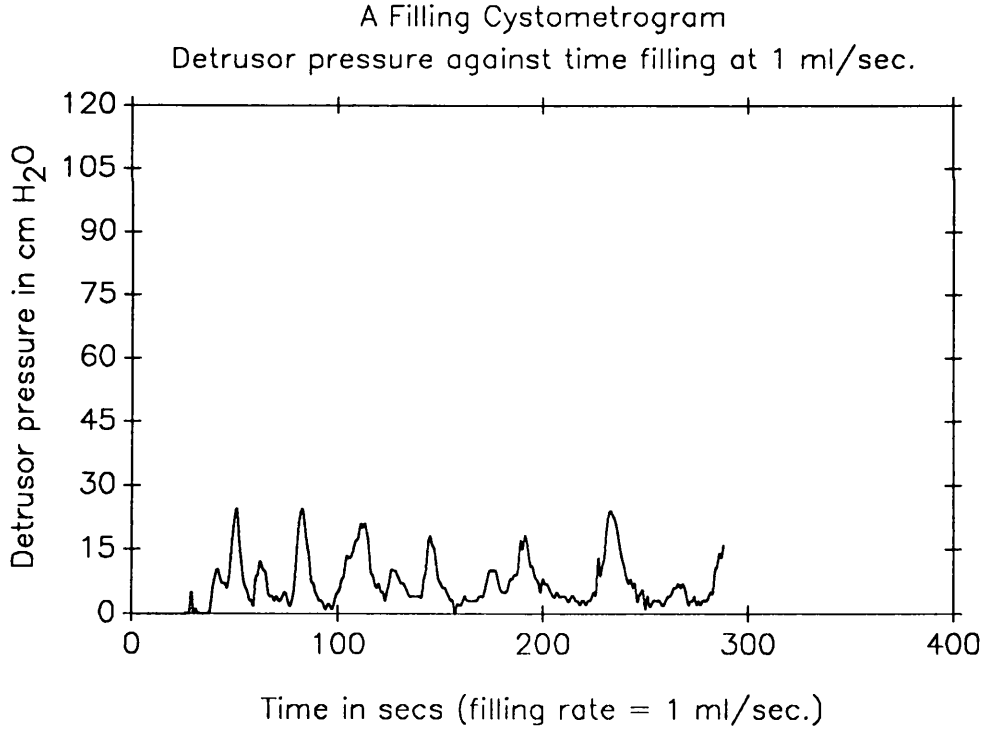


Figure 53

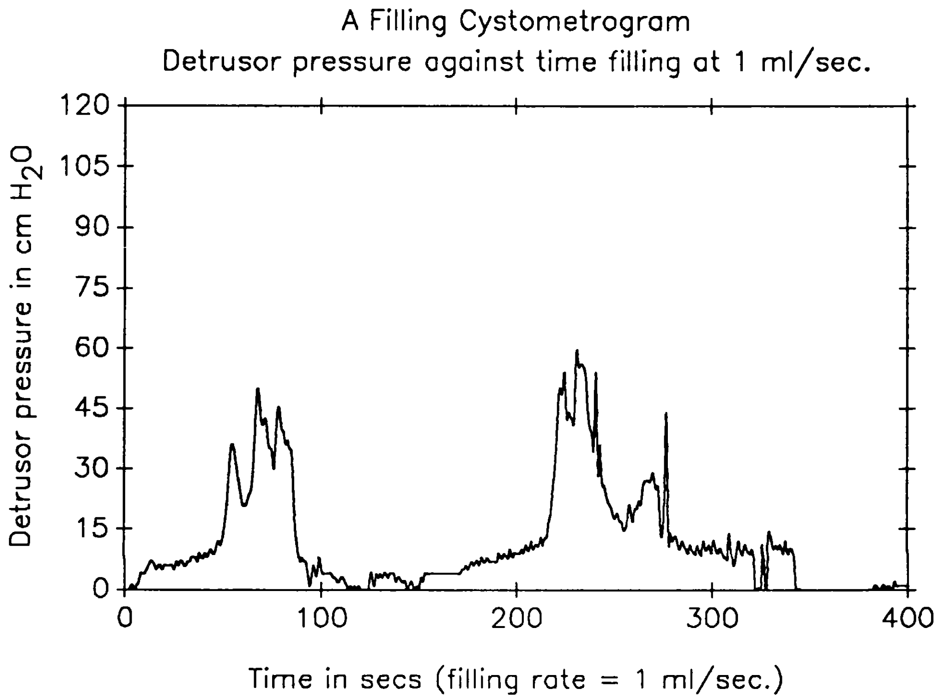

A Filling Cystometrogram
Detrusor pressure against time filling at 1 ml/sec.
Detrusor pressure in cm H_2O
120
105
90
75
60
45
30
15
0
0
100
200
300
400
Time in secs (filling rate = 1 ml/sec.)

Figure 54

My first approach was to calculate a linear regression equation across all of the data points obtained during a filling study in patients with unstable bladders ie:

$$p_{det} = MT + C \qquad (90)$$

Where T = time, M is the gradient and C is the intercept on the p_{det} axis.

$$M = \{\Sigma T p_{det} - \{\{\Sigma T\}\{\Sigma p_{det}\}/n\}\}/\{\Sigma T^2 - \{\{\Sigma T\}^2/n\}\} \qquad (91)$$

Where n = the number of sample pairs.

$$C = p_{det\mu} - MT_\mu \qquad (92)$$

Where $p_{det\mu}$ = the mean pdet and T_μ = the mean time

The correlation coefficient r_{corr} was calculated from the equation:

$$r_{corr} = \Sigma\{T_i - T_\mu\}\{p_{deti} - p_{det\mu}\}/\sqrt{}\Sigma\{T_i - T_\mu\}^2\Sigma\{p_{deti} - p_{det\mu}\}^2 \qquad (93)$$

Where T_i = ith value of T, p_{deti} = ith value of p_{det},

The standard deviation of $p_{det\mu}$ was calculated from the equation:

$$p_{detsd} = \sqrt{}\{\{1/n-1\}\{\Sigma p_{deti}{}^2 - \{\{\Sigma\ p_{deti}\}^{2/n}\}\}\} \qquad (94)$$

These parameters prove capable of providing information on the filling study which is not supplied from the bladder capacity, maximum filling pressure and end filling pressure. An important limitation is that I am applying a linear equation to data which is freqently non-linear. u /

The correlation coefficient r_{corr} measures the strength of the relationship between the two variables time and pressure. Thus r_{corr} approaches unity in circumstances when systolic detrusor contractile activity is minimal. This occurs in a bladder of low compliance and in a bladder with minimal detrusor activity. The gradient M and the intercept C reflect the integrated trend in contractile activity, whether it is crescendo, decrescendo or consistent. The intercept C falls as the bladder capacity falls (we fill at a constant rate of 1 ml/sec) and the contractile activity becomes more precipitant and crescendo. The standard deviation of the mean pressure, P_{detsd} increases as the systolic detrusor activity becomes more varied. The number of data points is directly proportional to the bladder capacity, given the limitation that filling was discontinued at 500 ml if not previously interrupted.

These parameters are incomplete as they do not describe the amount of energy put into the unstable activity. This may be defined by integrating the results of equation (89), applied to unstable contractions, over the whole course of the filling study so as to find the total unstable filling force.

I calculated all of these variables for patients with unstable bladders. The integral of force was the total unstable force, which I took to be that produced by contractions of 15 cm H2O and over.

I wanted to describe these data by means of one or two parameters. There are a variety of statistical techniques available for reducing data in this way and I selected a principal components analysis because I was most familiar with this technique. I performed such an analysis on the mean pressure, standard deviation of the mean pressure, the r_{corr}, the intercept, the slope coefficient, the total number of data points, reflecting fill volume, and the total unstable force.

A principal components analysis involves the combination of a finite set of variables into linear models so as to describe, with fewer variables, as much of the variance in all of the variables as possible. The process results in a number of linear equations equal to the number of variables used. Each equation examines the data from a different mathematical perspective. By using subsets of these models it may be possible to describe data in a meaningful way using a small number of parameters. The calculations are performed using correlation matrices. I standardized the variables before entering them into the models. This meant that from each variable I subtracted the mean of the whole sample and divided the result by the standard deviation. The means and standard deviations for each variable are shown below.

Table 5

The variables used in the principal components analysis

	N	MEAN	STDEV
Mean pressure	1161	9.5	6.50 (cm H_2O)
Standard deviation	1161	7.9	6.12
Rcorr	1161	0.6	0.31
Intercept (M)	1161	1.3	6.72
Coefficient (C)	1161	0.09	0.17
Data point count	1161	330	151
Total unstable force	1161	6.9	11 (dynes x 10^{-5})

? Below are tabled the results of the principal components analysis. The eigenvalues are the variances of the principal component, the proportion and the cumulative proportion of the total variance explained by each principal component is also shown. In adition, I list the coefficients for each principal component. d /

Table 6

The eigenvalues and explained variance of the principal components

	PC1	PC2	PC3
Eigenvalue	2.62	1.89	1.18
Proportion	0.37	0.27	0.16
Cumulative proportion	0.37	0.64	0.80

	PC4	PC5	PC6	PC7
Eigenvalue	0.62	0.36	0.24	0.06
Proportion	0.10	0.03	0.03	0.01
Cumulative proportion	0.90	0.96	0.99	1.00

Table 7

Coefficients of each variable in the principal component model

	PC1	PC2	PC3
Mean pressure	**-0.448**	**0.448**	0.025
Standard deviation	**-0.516**	0.131	-0.200
Rcorr	-0.216	-0.241	0.718
Intercept (M)	0.223	**0.552**	-0.299
Coefficient (C)	**-0.497**	-0.244	-0.117
Data point count	0.365	0.272	0.443
Total unstable force	-0.238	**0.534**	0.381

	PC4	PC5	PC6	PC7
Mean pressure	-0.251	-0.174	-0.246	0.667
Standard deviation	0.446	0.243	-0.518	-0.387
Rcorr	-0.461	0.028	-0.294	-0.285
Intercept (M)	-0.486	-0.235	-0.123	-0.500
Coefficient (C)	0.047	-0.720	0.338	-0.211
Data point count	0.513	-0.511	-0.269	0.007
Total unstable force	0.156	0.274	0.618	-0.176

I chose to use only the first two principal components which between them explained 65% of the total variance. I have highlighted the variables which were maximally weighted in each. It can be seen that the first principal component concentrates on the variability and relative crescendo of the unstable acitivty, the gradient M plays an important part, whereas the second component focuses on the energy generated. I did not find that the third and subsequent principal components provided any additional benefit to interpretation.

I calculated the two principal components (PC1 & PC2) for 1161 patients with unstable bladders who had suitable computerised urodynamic data. I then sorted a random sample of 514 traces according to the calculated scores. The classification achieved proved better than I had ever expected and a useful classification of the unstable detrusor activity was achieved. The descriptive statistics of these two components are shown below.

Table 8

The descriptive statistics of PC1 and PC2

	N	**Mean**	**Median**	**Stdev**	**S.E. Mean**
PC1	1161	0.32	0.61	1.44	0.04
PC2	1161	-0.15	-0.48	1.24	0.04

	Minimum	**Maximum**	**Quartile 1**	**Quartile 3**
PC1	-10.05	4.34	-0.25	1.25
PC2	-2.0	7.9	-0.9	0.23

These new variables may be used as a convenient way to describe the quality of the filling studies from patients with unstable bladders. As they are mathematical creations they do not necessarily have clinical significance. However, I did find some important relationships and these are detailed in the results section.

As PC1 moves from the maximum towards the minimum the pattern of unstable bladder activity changes from variable peaks of inconsistent amplitude, to more consistent peaks, to more crescendo contractions, to more precipitant and rapidly progressive contractions. Although the regression gradient plays an important role in influencing the value of

PC1, the consistency of the amplitude of the contractions is also influential. As PC2 moves from the maximum towards the minimum the amount of energy expended in the contractions decreases. The bladder capacity falls as both paramaters move from maximum to minimum.

Figure 55 shows a graph with PC1 on the Y axis and PC2 on the X axis. Different points on this graph are derived from filling study traces shown as figures 56 to 67. The filling studies have the same time axis so as to demonstrate the difference in the length of separate studies. The length of the study is directly proportional to the bladder capacity. On each figure I have included the calculated regression line.

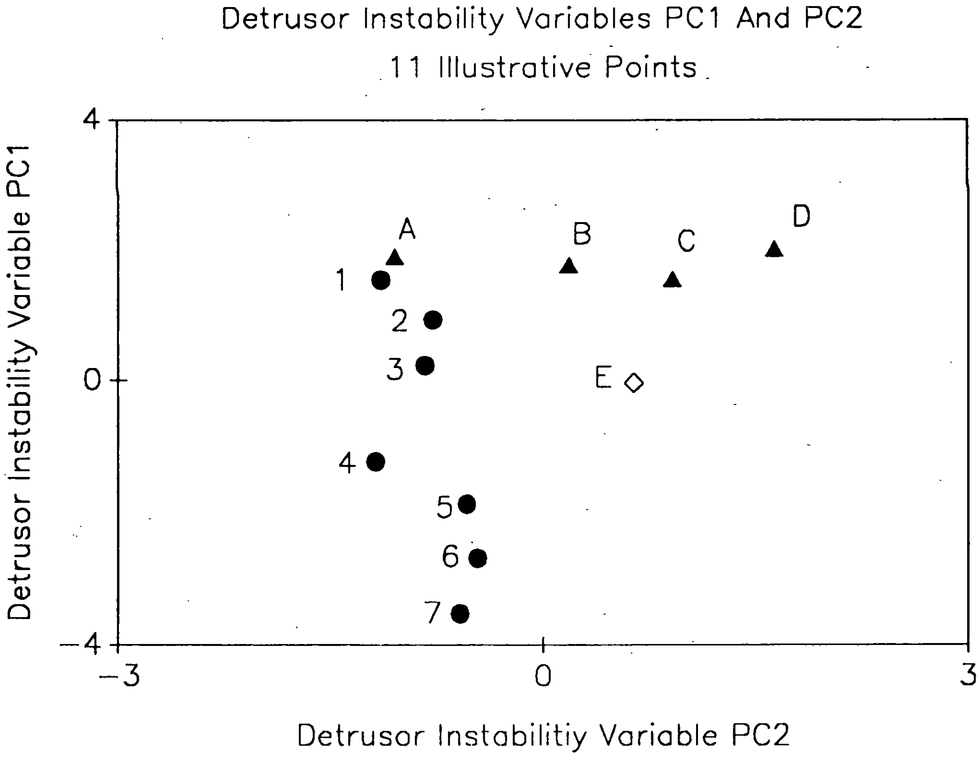


Figure 55

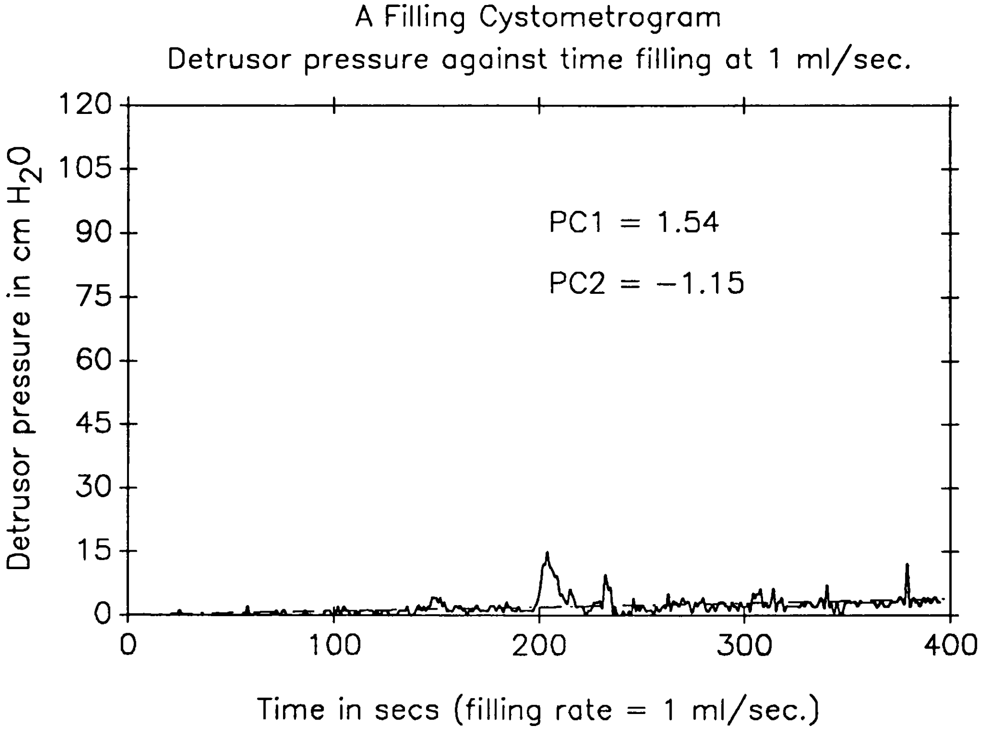

A Filling Cystometrogram
Detrusor pressure against time filling at 1 ml/sec.

Figure 56 (Point 1)

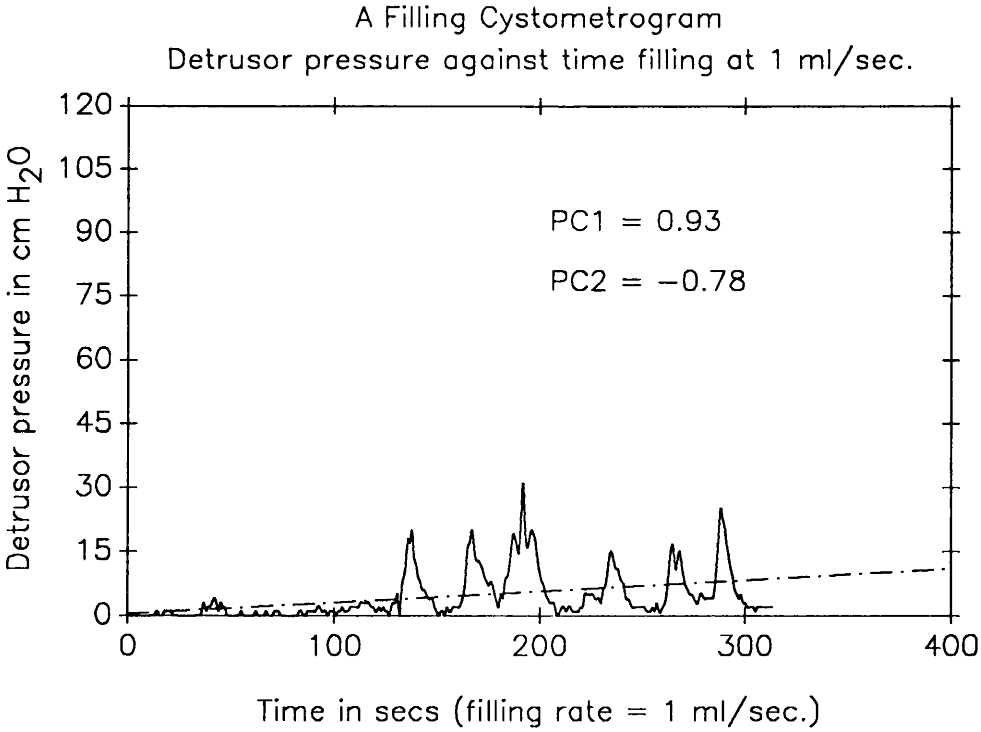
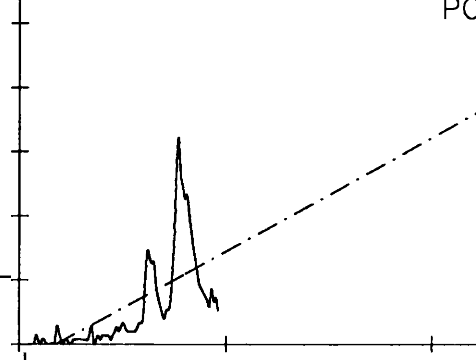

A Filling Cystometrogram
Detrusor pressure against time filling at 1 ml/sec.

Figure 57 (Point 2)



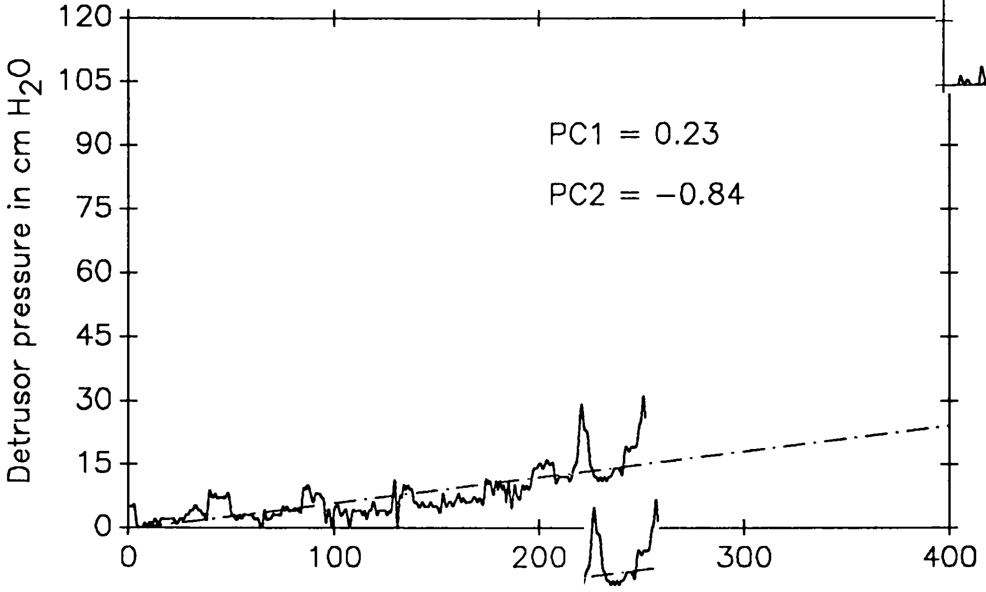

A Filling Cystometrogram
Detrusor pressure against time filling at 1 ml/sec.

Figure 58 (Point 3)

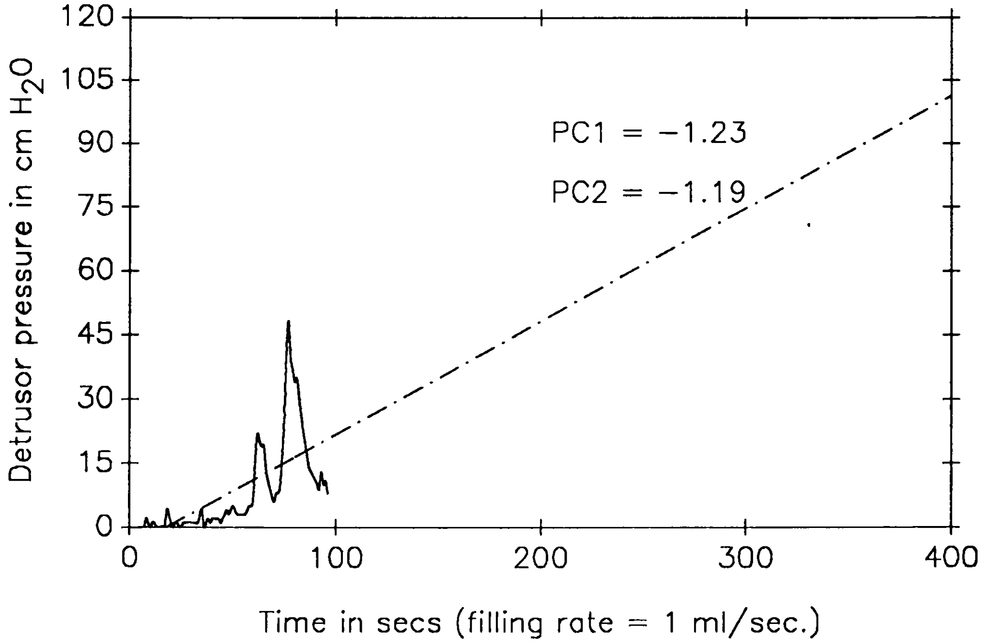

A Filling Cystometrogram
Detrusor pressure against time filling at 1 ml/sec.

Figure 59 (Point 4)

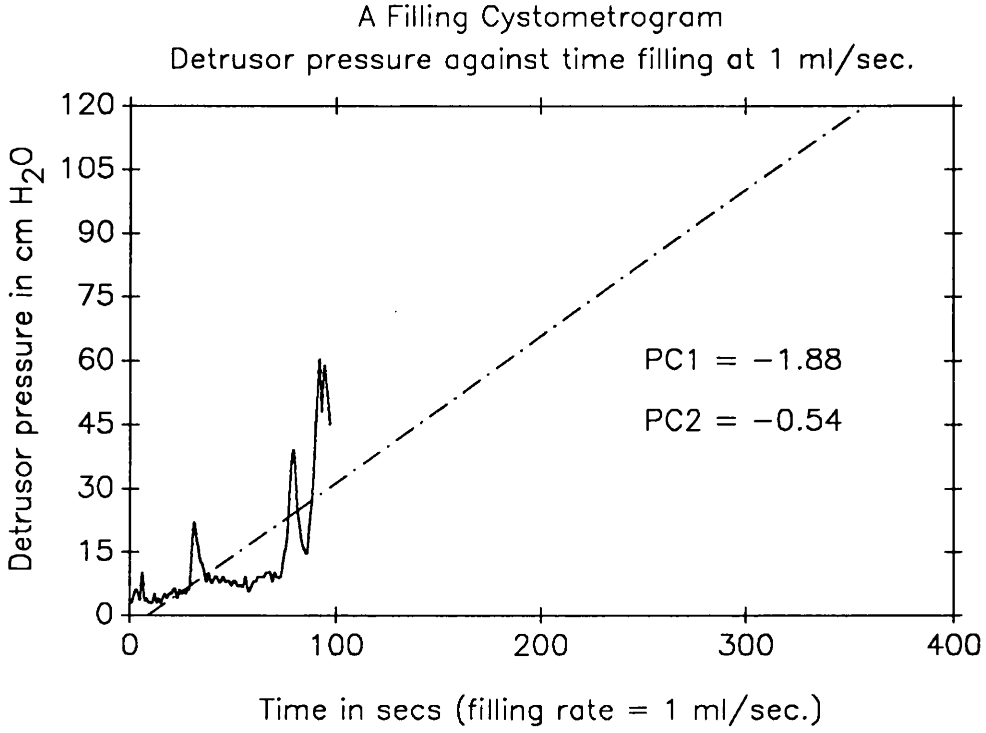
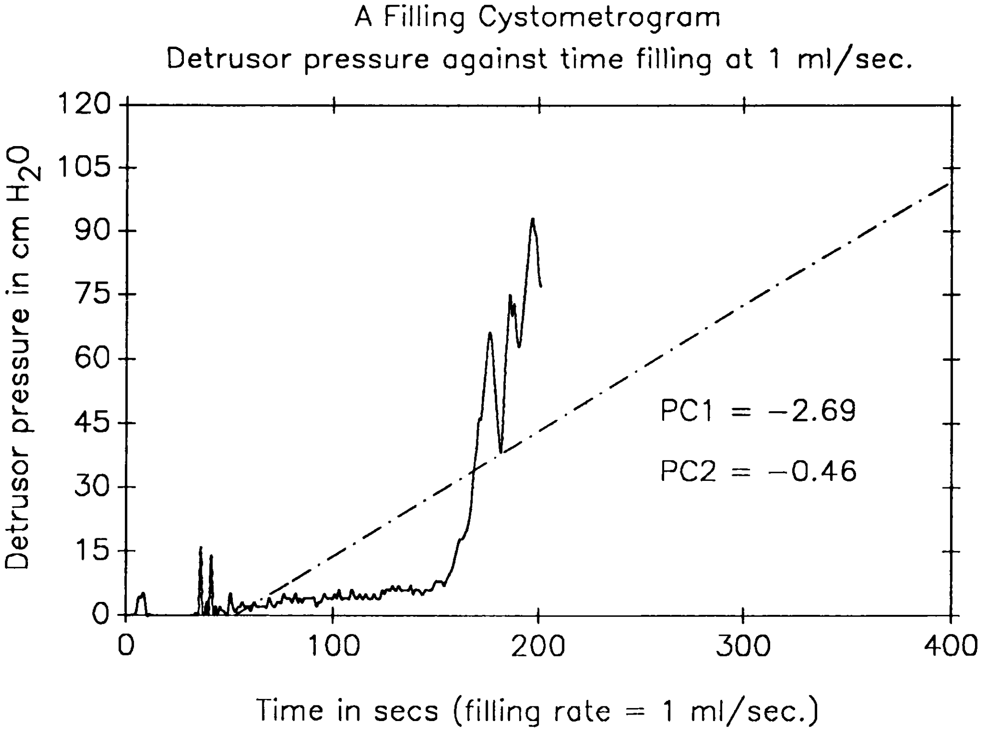


Figure 60 (Point 5)



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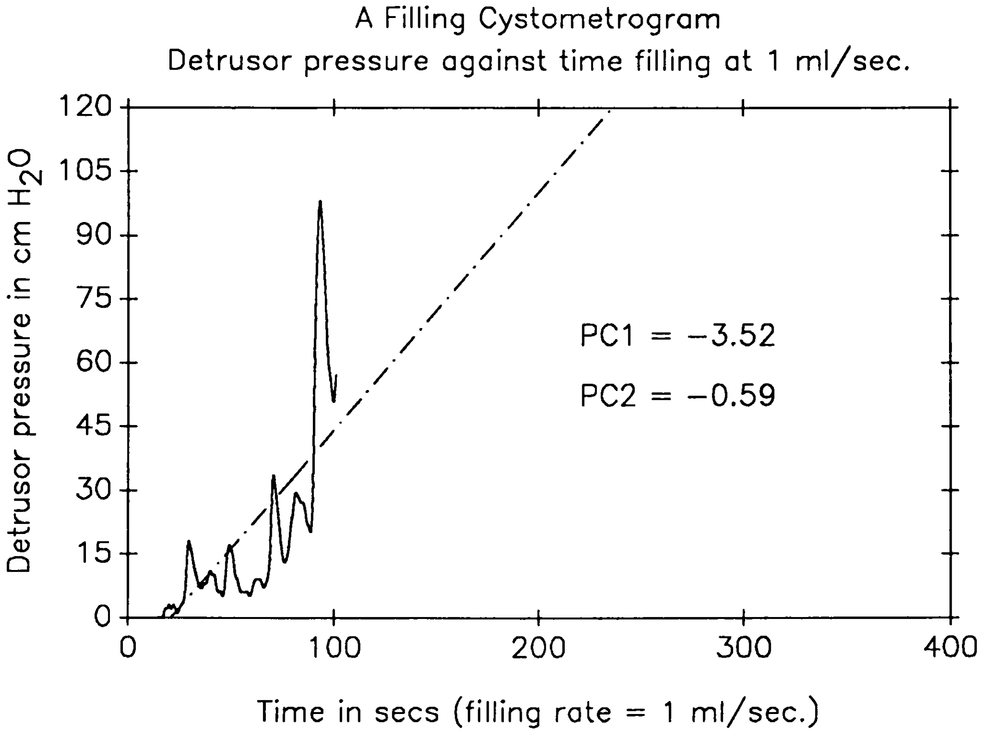

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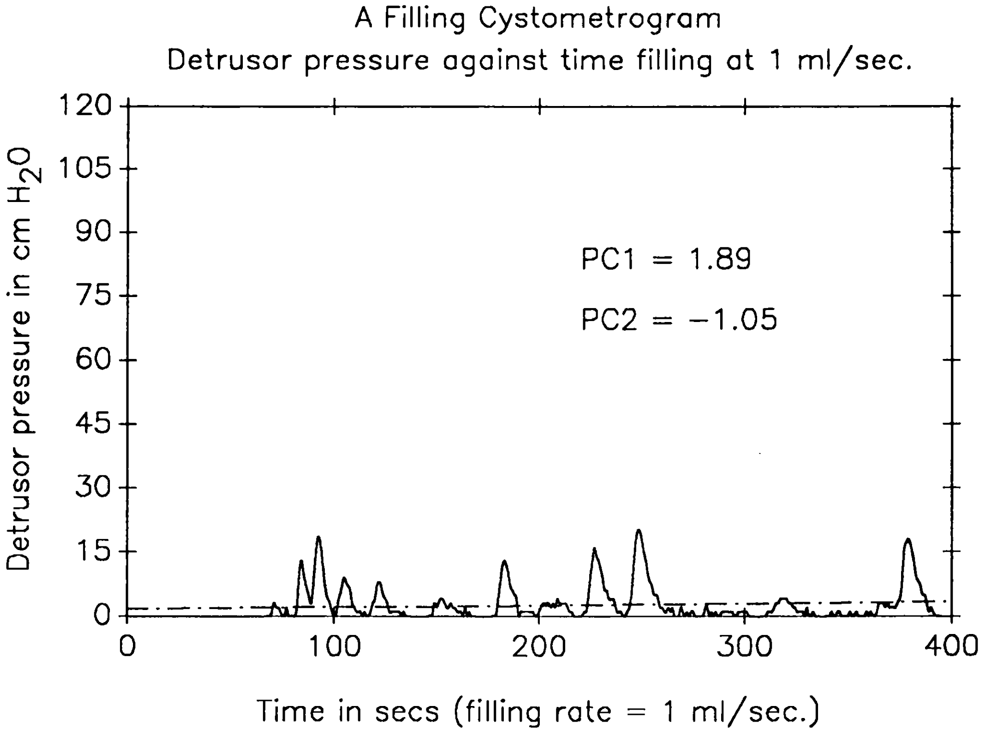
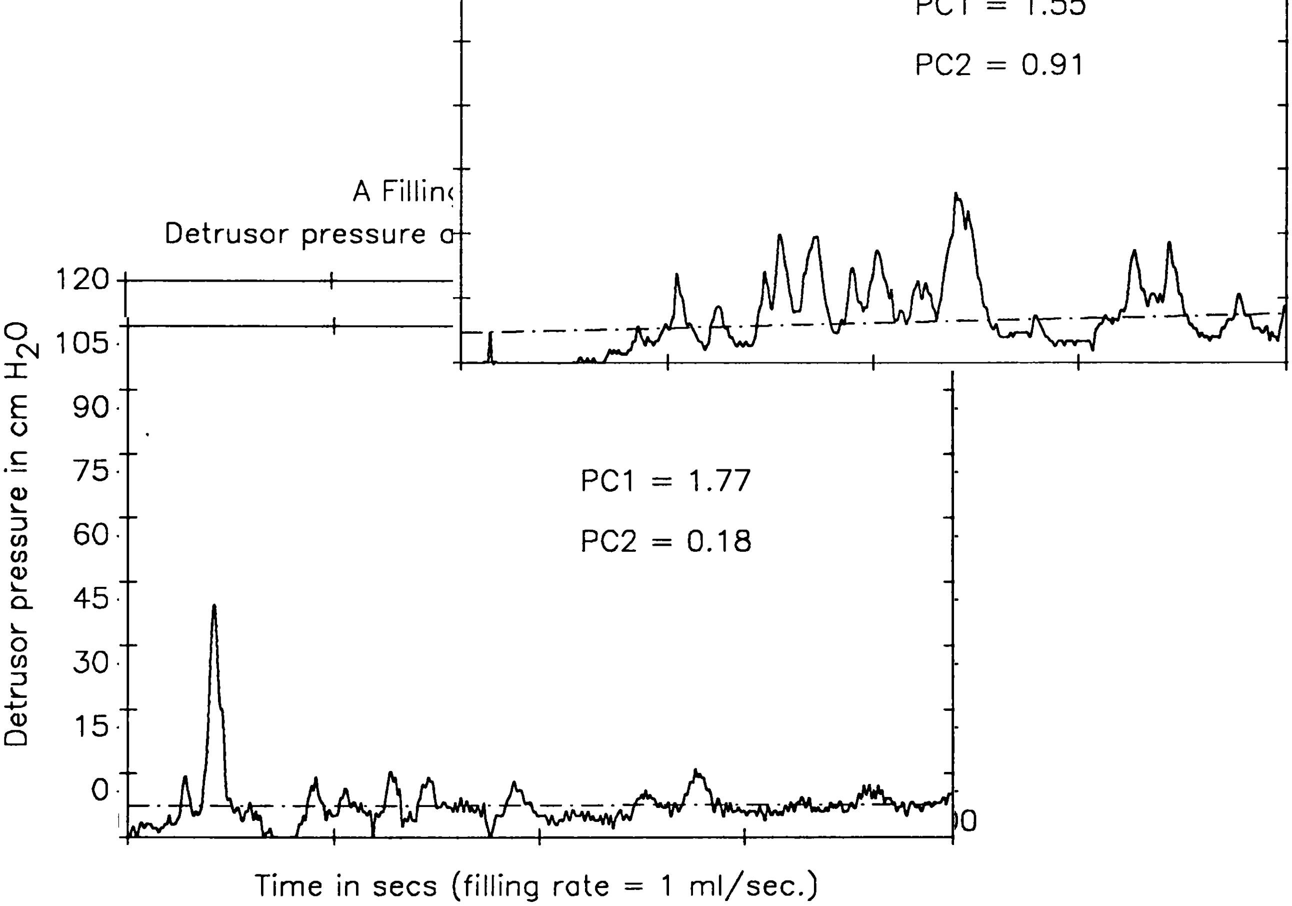


Figure 63 (Point A)



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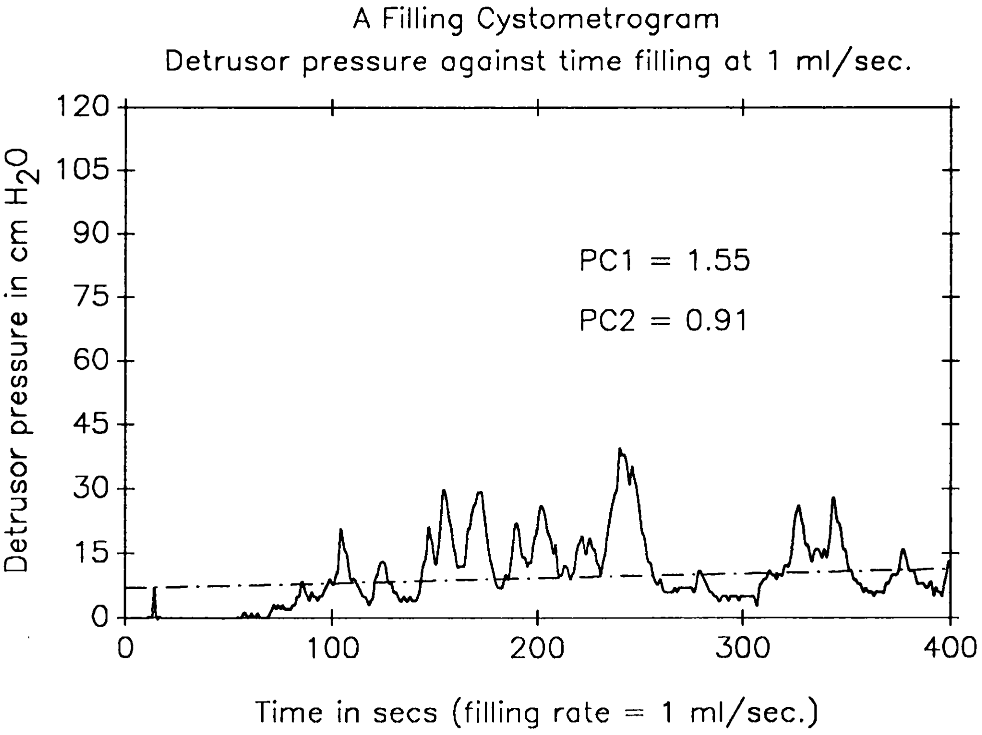

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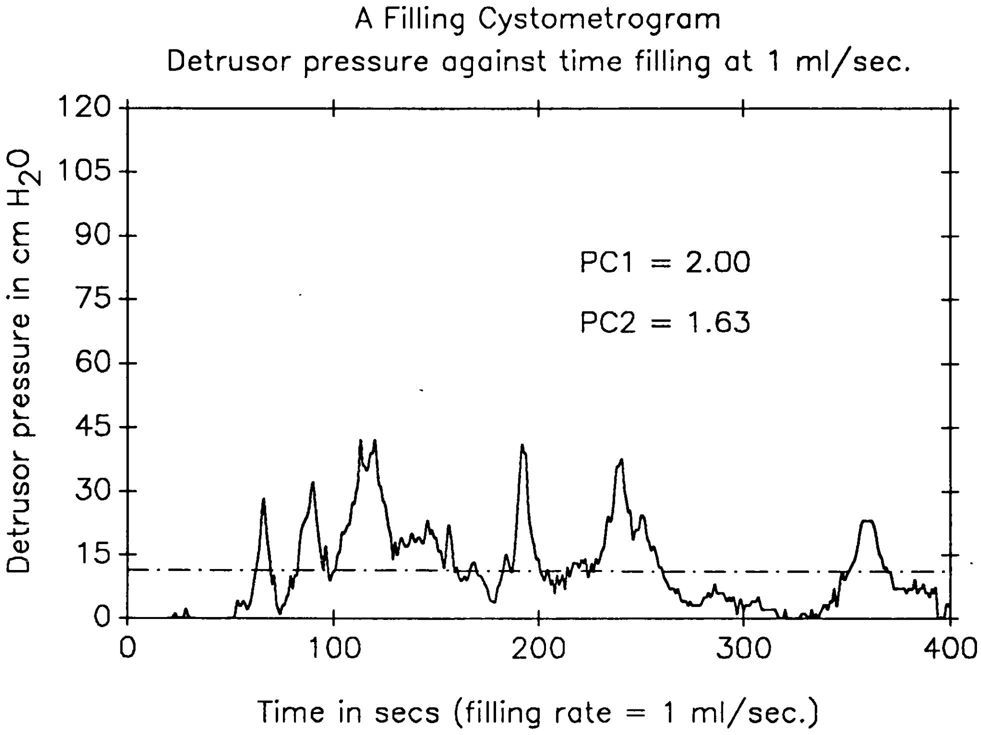

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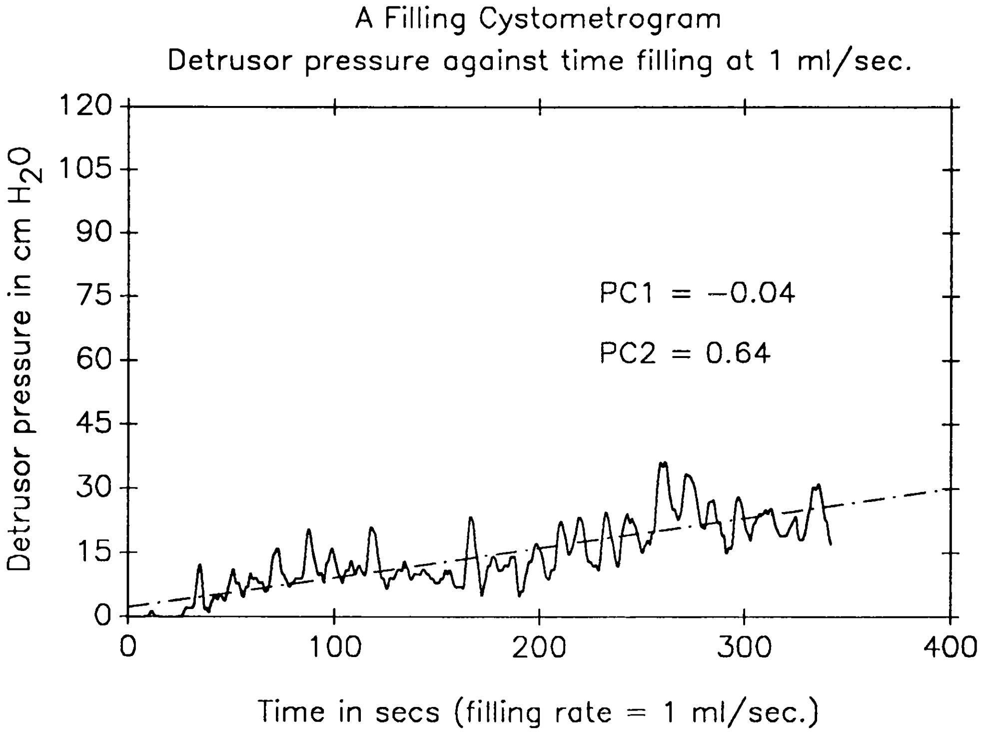


Figure 67 (Point E)

Conclusion of mathematical theory and methods

The mathematical treatment of urodynamic data which I have described allows a more informative scrutiny of the studies. A summary of the strategy may be helpful.

The filling study

The basic data from the filling study are the residual urine volume prior to initiation of the study, the bladder capacity at the point of a first desire to void, the actual bladder capacity and the presence or absence of detrusor instability or reduced compliance. These standard data may be supplemented by using the newer approaches to calculate the force of unstable detrusor activity (equation 89) and by defining the quality of the unstable contractions using PC1 and PC2.

The voiding study

Traditional approaches to the voiding study rely on measuring the maximum flow rate, the detrusor pressure at maximum flow, the maximum voiding detrusor pressure, the voided volume and the post-micturition residual urine volume. I have now augmented this interpretation by measuring voiding contractility with the parameter WF (equation 88), the velocity of shortening of the detrusor curcumference (equation 78), which may be used to examine the series elastic component and the isotonic detrusor activity by means of the standardised Q* (equations 65 and 66). In addition inspection of the voiding pressure/flow plot, with a mind to the theory which lies behind it and the computer models which illuminate the patterns which are formed, permits a very much more sophisticated appreciation of what we are seeing.

Other methods

The method of treating detrusor instability

Because detrusor instability proves to be such an important part of the pathophysiology of the elderly with lower urinary tract dysfunction, I examined the response to treatment of a sub-group of the patients whose urodynamic data was sampled. A description of the treatment method is therefore required.

All patients are treated by the same doctor and the protocol remains very consistent. Once detrusor instability has been diagnosed the patients are instructed on a bladder retraining regime (Jarvis & Millar 1980). They are given a simple diary chart to use to record their micturition patterns. They are asked to record each episode of micturition and/or incontinence to the nearest hour by placing a tick in a column on the chart. They are advised to attempt to delay micturition, on the first sensation of a need to urinate, for as long as possible. The aim is for them to reduce their frequencies to between four and six times in twenty four hours. I explain that this will be difficult and that they are likely to experience incontinence during the initial stages of this exercise. I advise them not to attempt to delay during the night since this leads to sleep deprivation. I emphasise the extreme importance of this bladder retraining and make it clear that I believe that without it they are unlikely to recover.

volume?

Wherever possible I attempt to treat them with bladder retraining on its own. However, where patients are unable to cope with this I will use some anticholinergic medication. I will start with terodiline (Wiseman et al 1990), unless there is evidence of a low urethral resistance or nocturnal symptoms in which case I will start with imipramine (Castleden al 1981). If these drugs fail I will then use oxybutynin (Moisey et al 1980).If nocturia or nocturnal enuresis proves to be a persistent problem and the patient is not elderly I will treat them with DDAVP (Hilton & Stanton 1981). If an established voiding problem presents, then this will be managed with intermittent catheterisation (Lapides 1979).

Patients are followed up two to three weekly until their symptoms have settled. They are then seen once more after three months and if all is well they are discharged. All patients are free to book in for review if their symptoms are deteriorating or they experience problems. At each review I obtain records of their daily frequency and the incidence of incontinence.

This policy is used for patients who are mobile and independent and capable of cooperating with the regime. The consistency of the programme and method of follow up, along with data recording, allow a reasonable assessment of response within sample populations by counting the number of attendances, the change in frequency and nocturia, and the number of incontinence episodes. The measures are essentially audit parameters but they will give a guide as to how people are progressing.

Computational methods

Earlier sections of this thesis have made it clear that microcomputers have played a very important part in this study. I will therefore give a brief overview of the methods which I used.

Originally, it was hoped that a physicist would provide the software for the urodynamic measurements. This policy proved problematic. I found that the time required was more than my financial resources could afford and the physicists had great difficulties in catering successfully for the needs of a clinical department. It was therefore decided that I would have to learn how to write software and create the programmes myself.

I started by learning to programme in BBC Basic using an early Acorn BBC model B microcomputer. Progress was slow and difficult. As time passed I was able to upgrade my hardware and the final urodynamics package runs on an Acorn BBC Master Series microcomputer. I am in no doubt that an eight bit microcomputer such as the type I have been using, although remarkably effective, is not up to the tasks which will be demanded by an active clinical department. (On completion of this thesis, the software designed on the BBC microcomputers will be adapted for IBM (use on IMB compatible microcomputers). Calculations performed on the urodynamic data were conducted using real numbers but storage limitation meant that I had to file the data as integers. This meant that I lost on precision by rounding to the nearest whole number. I was able to sample the analogue data from the urodynamic studies, at 3 Hertz but stored averaged data at 1 Hertz. A more powerful computer would resolve this problem.

The analogue data collected, simultaneously during the urodynamic tests, were transmitted to the analogue ports of the microprocessor through an interface connected to the amplifiers. The data were written to floppy disc during the study and stored for future analysis. The BBC microcomputer was used to calculate the various urodynamic parameters, which have been described, by re-reading the data stored on discs into programmes written for specific calculations. The data were then passed onto an IBM AT 286 compatible microcomputer for further analysis.

I transferred data from the BBC micromputer to the IBM machine using the interface package "KERMIT" with my own software redefining the data in American Standard Code for Information Interchange. The statistical analyses were performed using the statistical package "MINITAB" (Minitab 1989) interfaced with my own data extraction programme. I constructed the graphs using the scientific graphics package "SIGMA-PLOT", once again interfaced with my own software.

Part of this study involved the construction of mathematical models of micturition, based on the equations described in a previous section, and run on the IBM compatible microcomputer. I wrote the programmes required for these models by using the database compiler "CLIPPER" (Clipper, Nantucket 1987).

Statistical methods

Urodynamic data is not continuous and tends to be skewed and unresponsive to methods of transformation. I therefore used non parametric techniques. The principal tests used were the Mann-Whitney test for the difference between two population medians and the Kruskall-Wallis test of the difference between two or more population medians. Where these are used I state the test statistic ("W" for Mann-Whitney and "H" for Kruskall-Wallis), the degrees of freedom and the p value. I adopted the median as the measure of central tendency and illustrate many of the findings by plotting the median with 95% confidence intervals. On some classification data I used the Chi-square test with Yates' correction. I conducted a very limited number of correlation tests using linear regression and quoting the correlation coefficient r. The specific use of the principal components analysis has already been described. I used the 95% level of confidence for tests of significance.

The results

I have collected a large quantity of data and there is a danger that the presentation of the results may become clouded in the details. In order to avoid this problem I have placed a certain amount of basic background information, which should be quoted but is not germa~~i~~ne to the main thrust of the argument, into a set of appendices which are referenced in the text. I have made considerable use of graphs in order to clarify the data and avoid too much discursion. 8)

To accomplish this analysis I separated out the patients according to sex and conducted all age related analyses on patients who were not suffering from any of the key diseases. I did not include the small number of patients below the age of twenty. When examining the influence of the key illnesses I analysed the data from patients with none or only one key illness, separating them according to sex.

Different data were available from sub-groups of individuals. Patients from Group A did not have their analogue data collected and stored by microcomputer, so certain variables could not be cacluated for them. The numbers of patients analysed and the age groups relevant to each part of this analysis are tabled in Appendix A.

Analysis of the filling phase

The basic filling urodynamic variables, which were collected on all of the patients in this study, are defined in Appendix B they are:

1. First residual volume

2. Bladder volume at first sensation

3. Bladder capacity

4. Maximum filling detrusor pressure

5. End filling detrusor pressure

The frequencies of different age and illness groups with basic filling study data (Groups A and B) are shown in tables 9 and 10 of Appendix A. Similarly, the frequencies of patients from groups A and B with unstable bladders are shown in tables 11, 12 and 13.

The first residual volume

The first residual volume showed evidence of a voiding problem affecting older women with a definite trend towards higher values whether they had an unstable bladder or not (Stable: $H=16.5$ $df=7$ $p=0.02$, unstable: $H=28.54$ $df=7$ $p<0.001$). Men did not show this trend although there were insufficient of them with stable bladders (55) to perform an age related analysis. The findings are well illustrated in figures 68, 69 and 70.

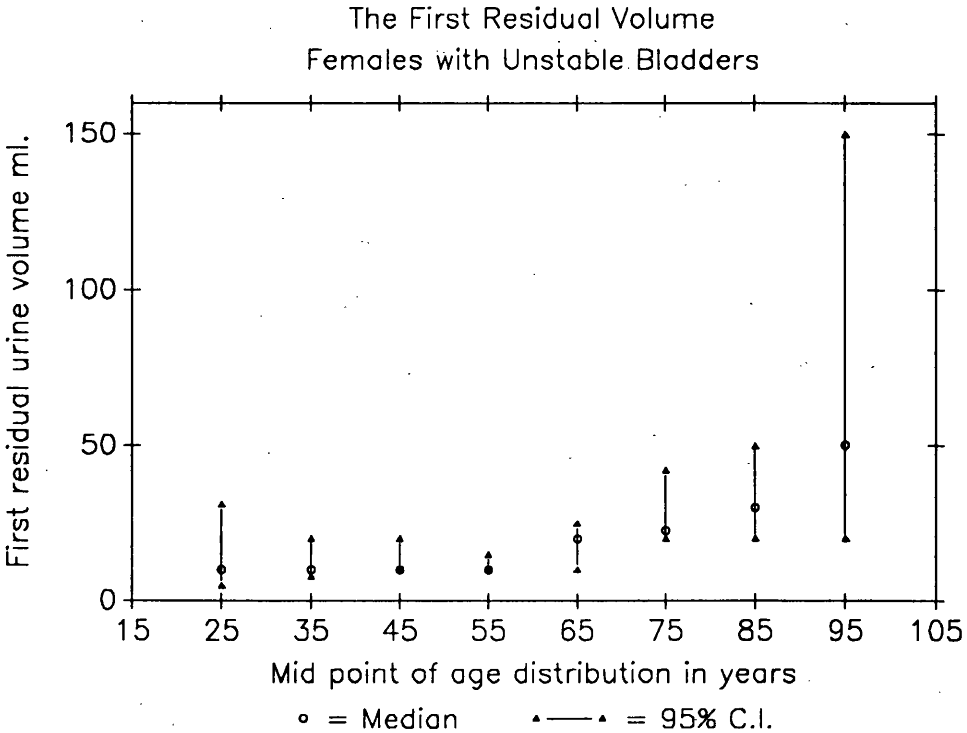
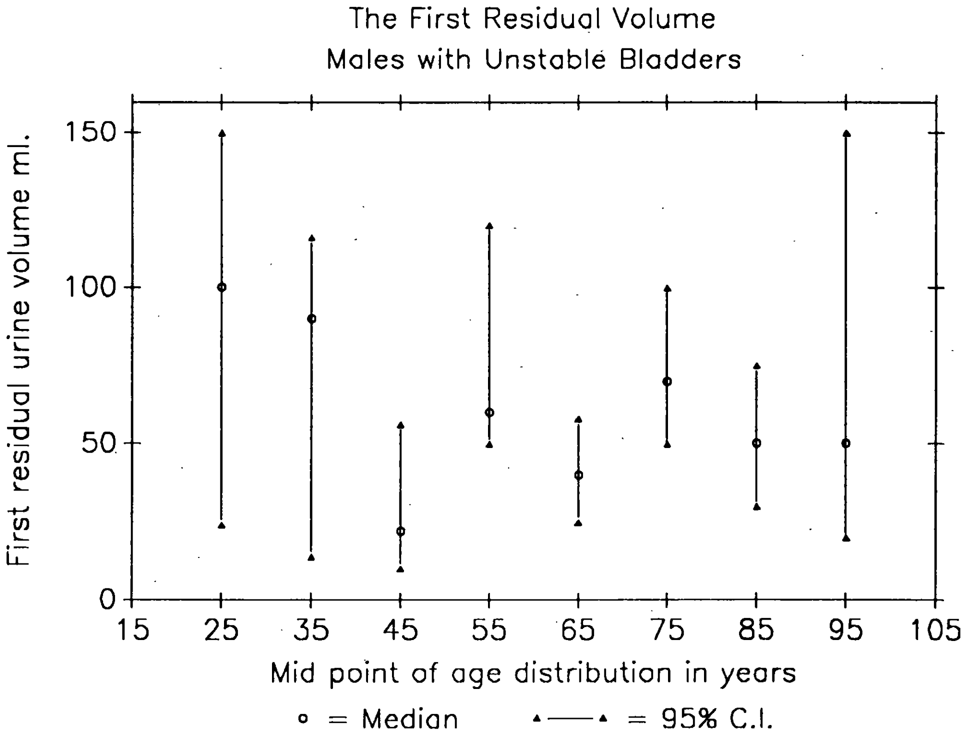


Figure 68



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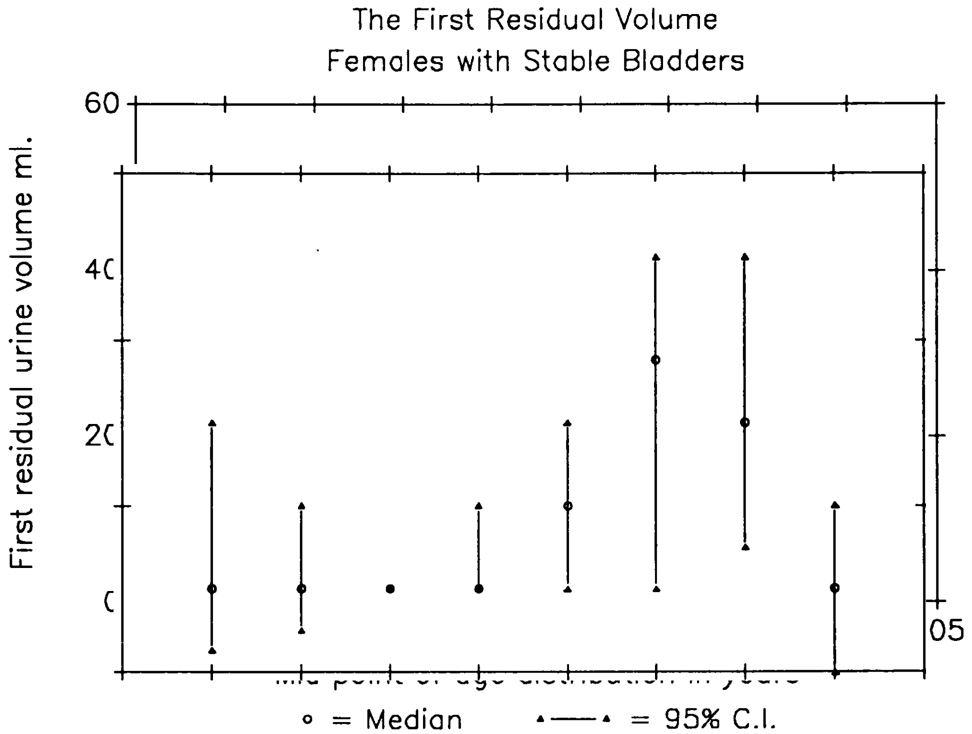


Figure 70

Analysis of the disease groups was limited to patients with detrusor instability because of the very small numbers with stable bladders. Amongst women higher residual urine volumes were found in those suffering from dementia (median=100 ml, 95%CI=73-135) and multiple sclerosis (median=100 ml, 95%CI=100-140), (H=84.41 df=7 p<0.001), see figure 71. Amongst men there was an elevated first residual urine volume most notably in patients with spinal injury see Figure 72, (H=36.89 df=7 P<0.001).

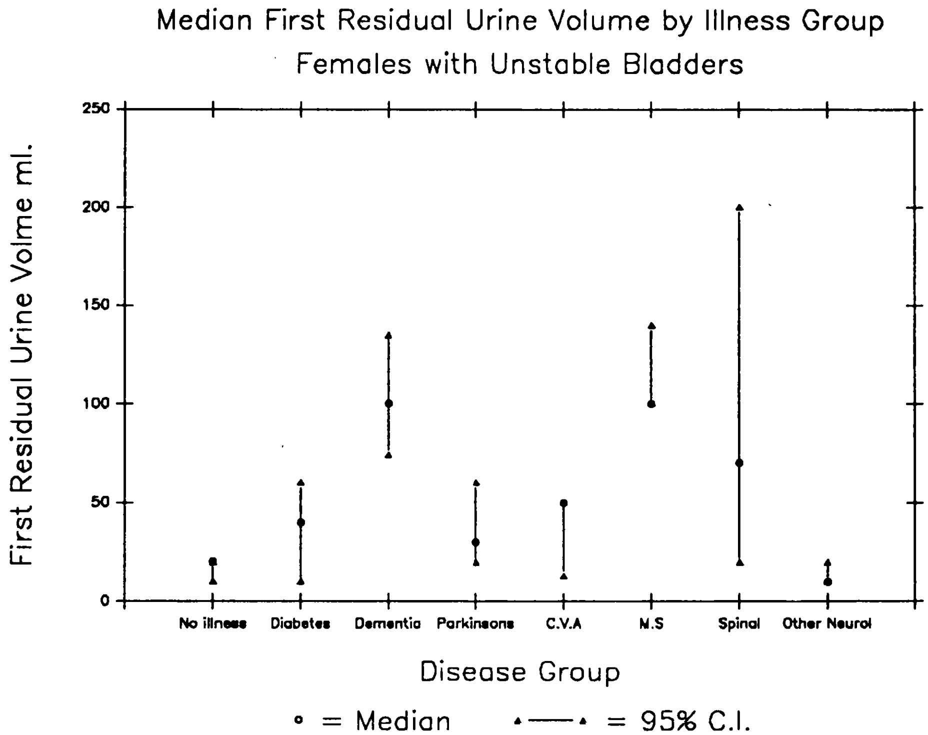


Figure 71

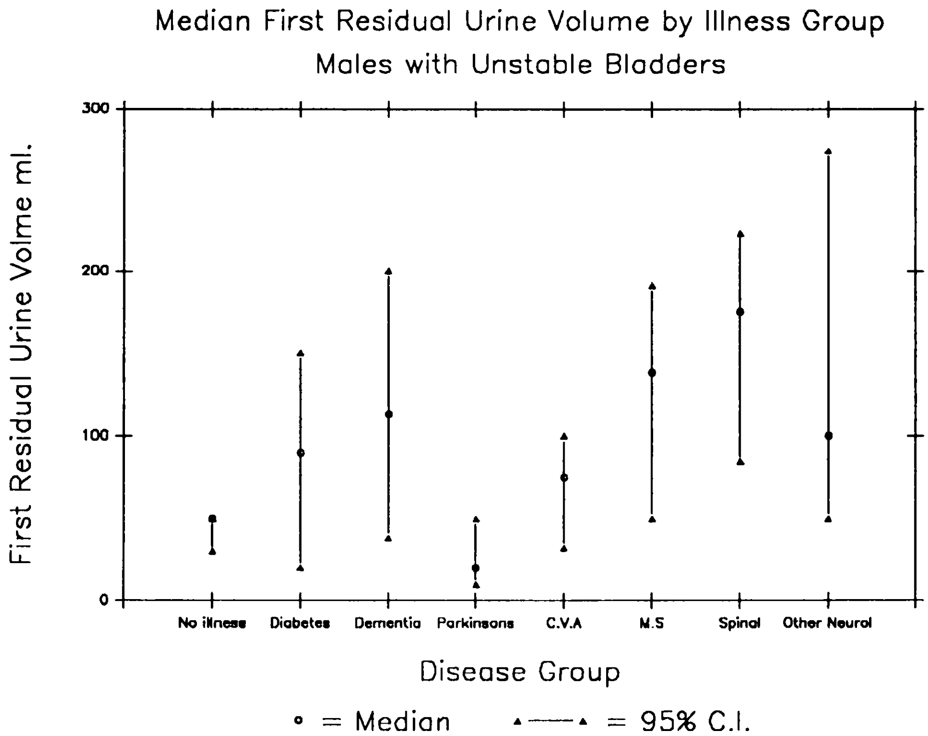
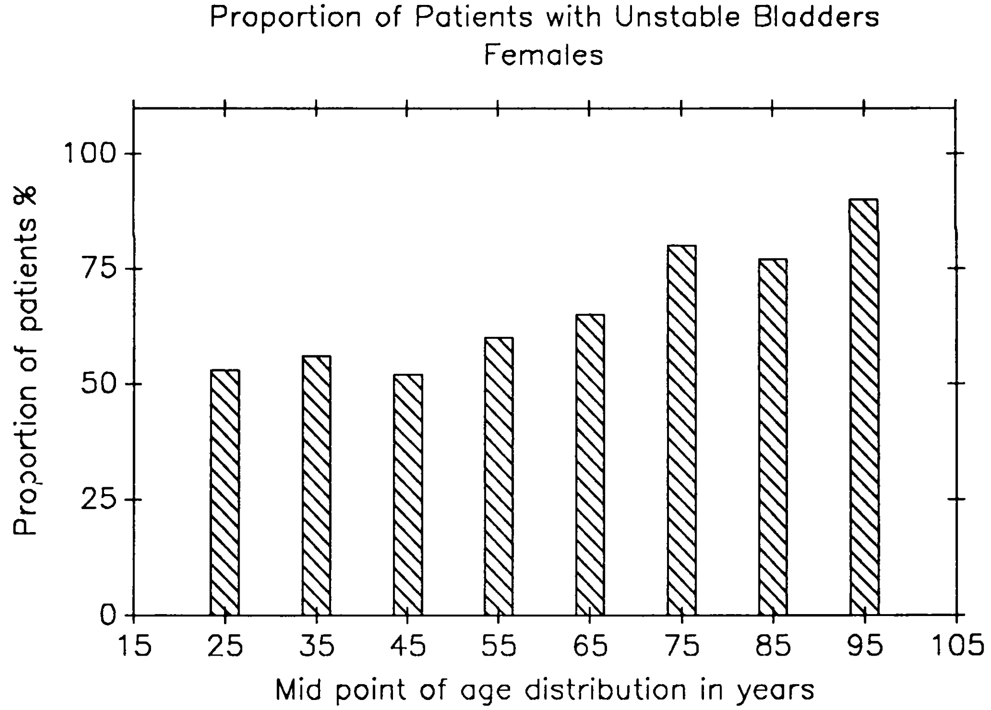


Figure 72

Detrusor instability

The diagnosis of detrusor instability was more common amongst the elderly in both sexes, (Females: Chisq=72.66 df=7 p<0.001; Males: Chisq=30.4 df=7 p<0.001), see figures 73 and 74. It should be noted however, that if patients were suffering from any of the key illnesses, the incidence of detrusor instability was similar to that found amongst the elderly in both sexes, see Figures 75 and 76.



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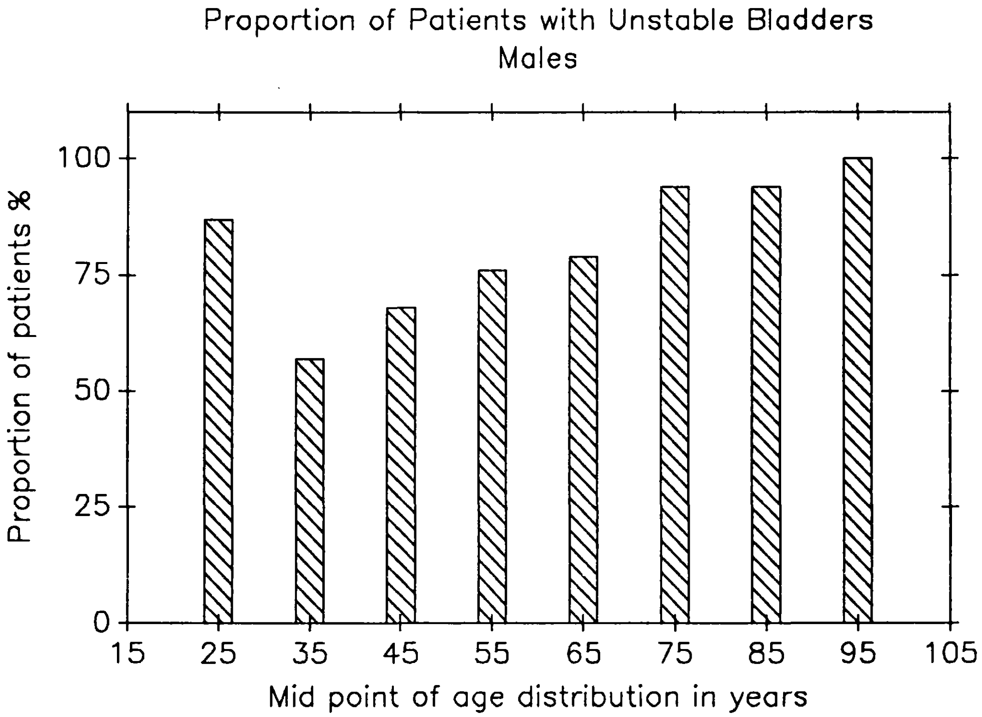


Figure 74

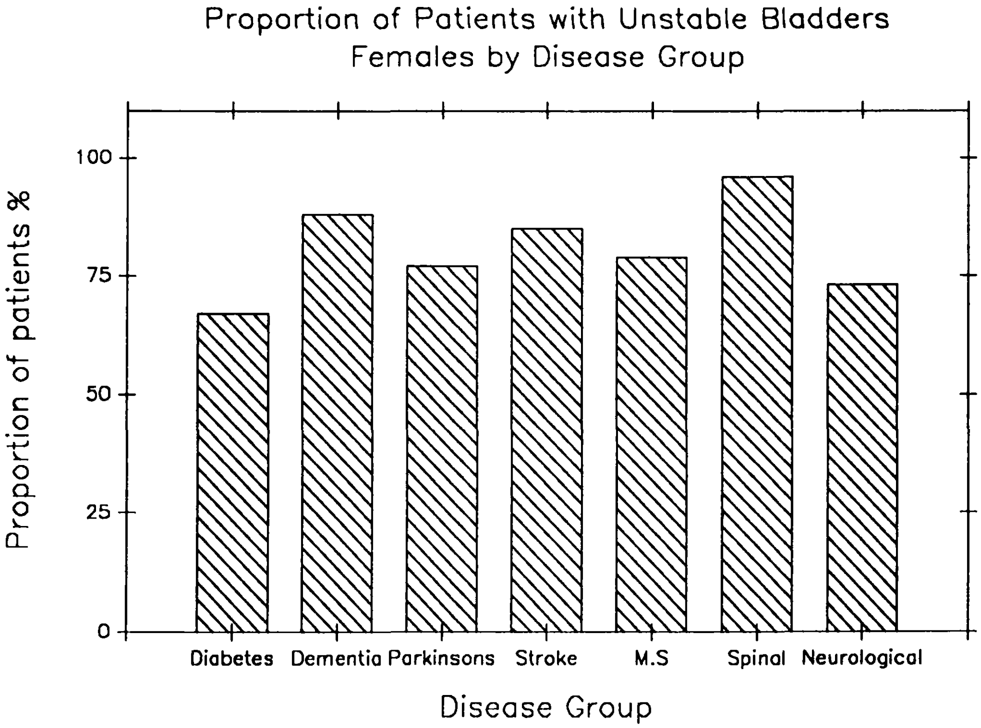
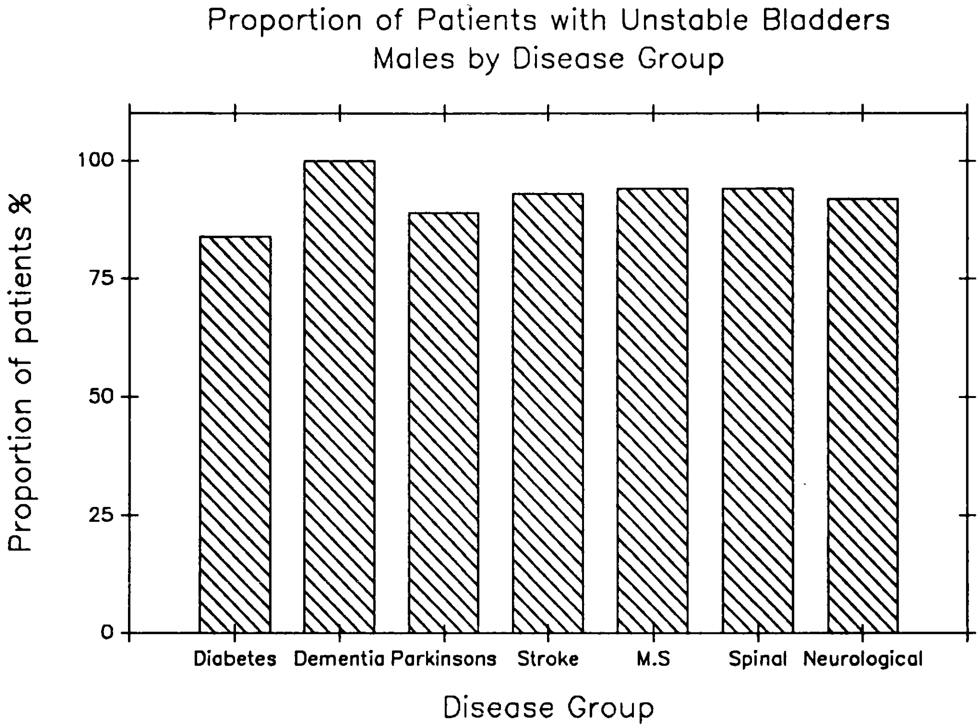


Figure 75



Proportion of Patients with Unstable Bladders
Males by Disease Group
Proportion of patients %
100
75
50
25
0
Diabetes
Dementia
Parkinsons
Stroke
M.S
Spinal
Neurological
Disease Group

Figure 76

The bladder capacity at first desire to void

The process of a filling urodynamic study results in an occasional omission, when the operator fails to log the patient's declaration of the first sensation of bladder fullness. There are some disease states which may prevent a patient declaring this experience, typically dementia. This means that the bladder capacity at first sensation was recorded on a sub-group of patients. The distributions of these patients are shown in tables 14 and 15 in Appendix A.

An interesting finding is illustrated in Figures 77 and 78. In women only there was an age associated change in the proportion of maximum bladder capacity at which the first sensation of bladder fullness was noted. The sensation was experienced at higher proportions of the bladder capcaity. This finding was seen in women with stable bladders ($H=25.79$ $df=7$ $p<0.001$) and women with unstable bladders ($H=58.1$ $df=7$ $p<0.001$). No similar change was noted amongst men ($H=7.33$ $df=7$ $p=0.396$). This would suggest that older women have less time available to them once they experience a desire to void. Among women, certain disease groups showed similar changes, with first sensation recorded at a higher proportion of bladder capacity in patients with cerebrovascular disease, multiple sclerosis, spinal injury and other neurological diseases ($H=27.689$ $df=7$ $p<0.001$). Figures 79 and 80 show median proportions for each disease group in men and women.

+ the converse?

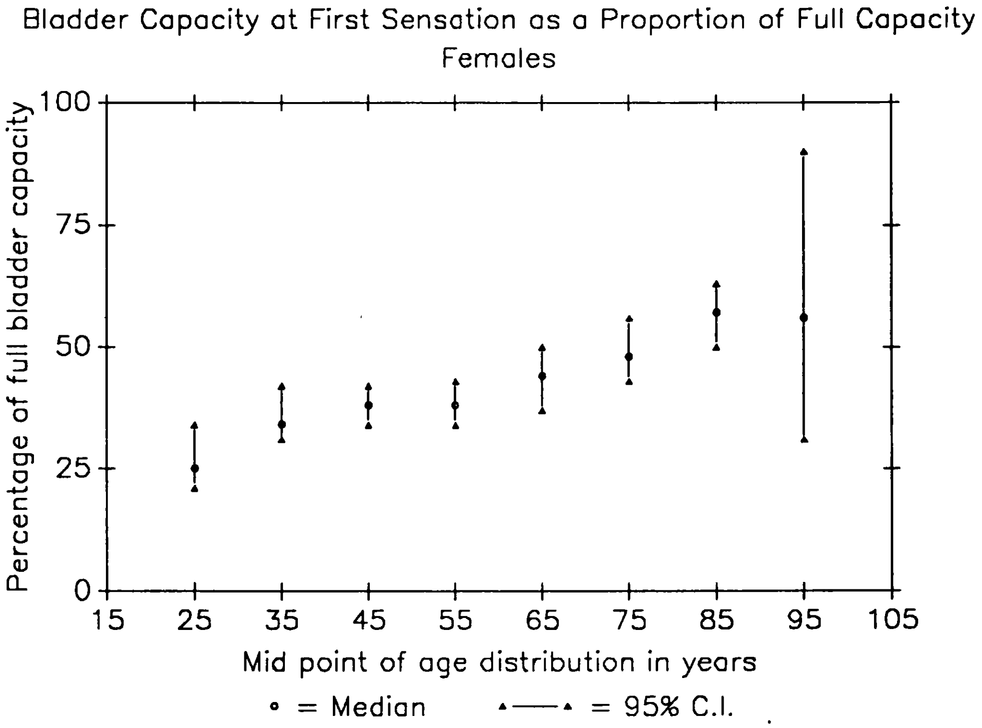


Figure 77

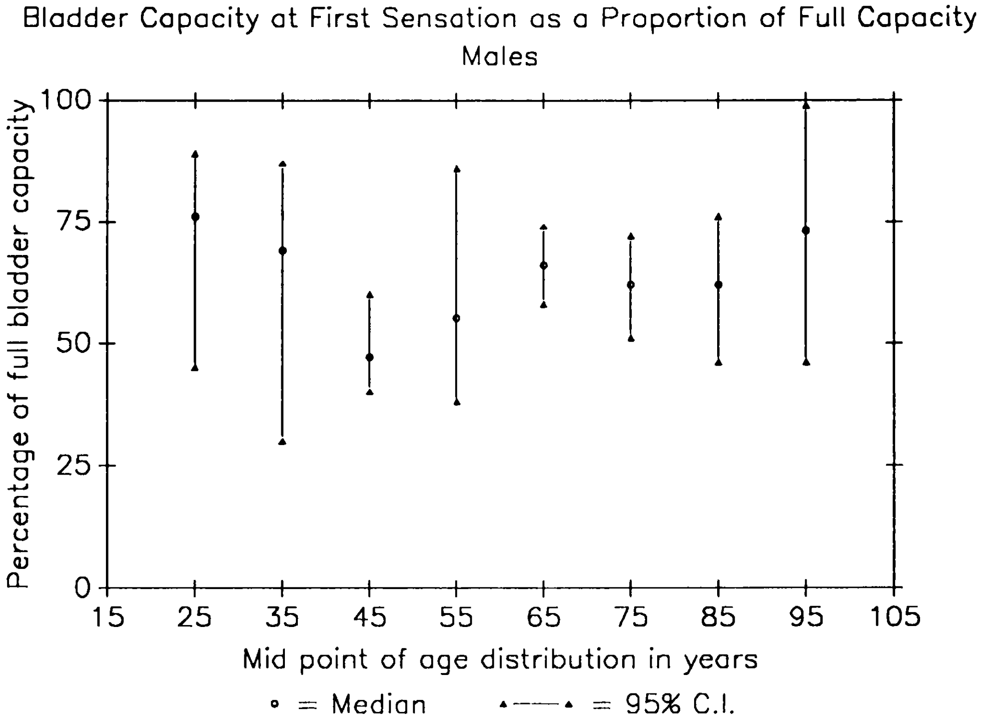


Figure 78

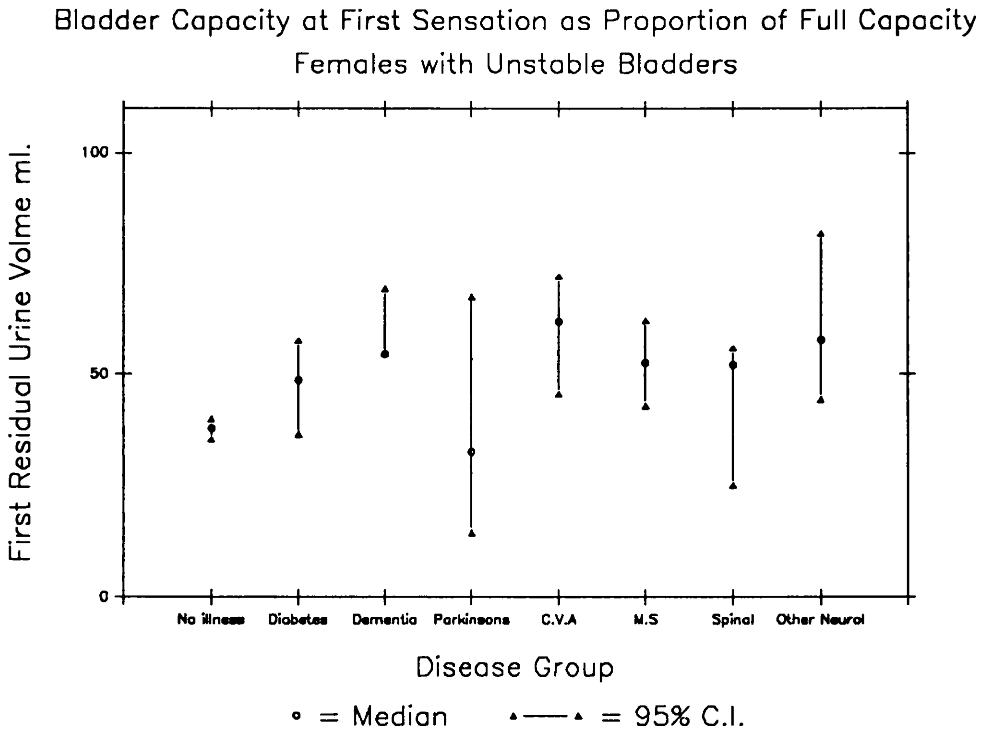


Figure 79

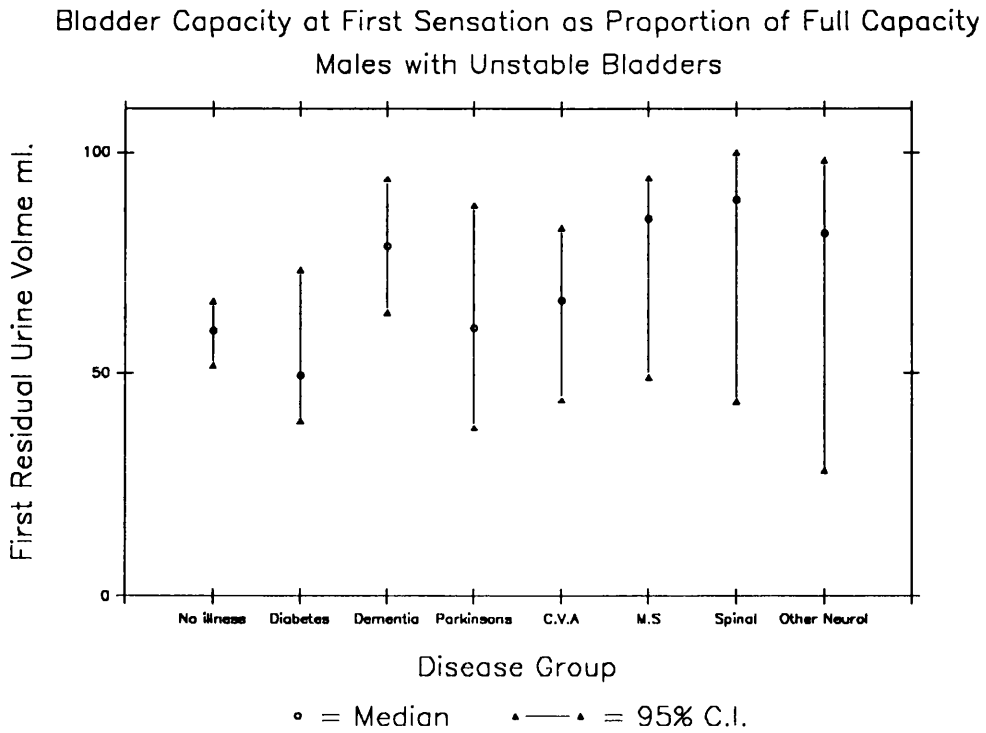


Figure 80

The Bladder capacity

The median bladder capacities measured in both men and women with unstable bladders are shown in Figures 81 and 82. In addition, Figure 83 shows the median bladder capacities recorded in women with stable bladders. Because of the small numbers I have not included a similar plot for men. The median bladder capacities according to key disease groups for men and women are shown in Figures 84 and 85. There is a very clear trend towards a lower bladder capacity in late life in both sexes. (Females stable H=34.99 df=7 p<0.001; females unstable H=73.09 df=7 p<0.001; males unstable H=25.03 df=7 p<0.001). However, it is clear that certain diseases are associated with particularly low bladder capacities. In both sexes Parkinson's disease and cerebrovascular disease patients had particularly low bladder capacities (Females H=54.05 df=7 p<0.001; males H=27.14 df=7 p<0.001).

Median Bladder Capacities with 95% Confidence Intervals

Women with unstable bladders

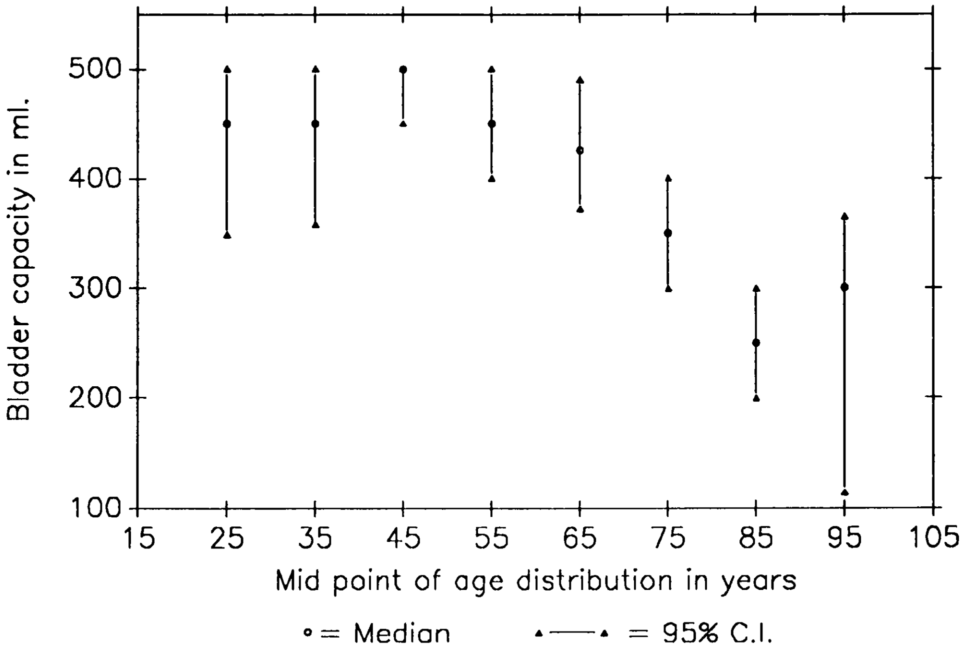


Figure 81

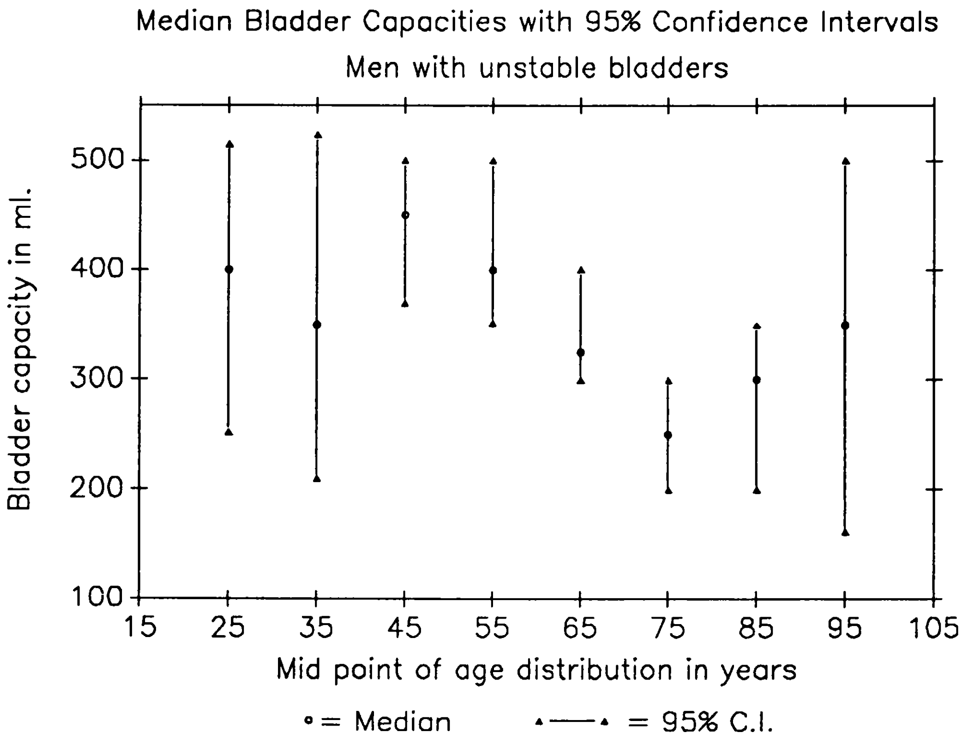


Figure 82

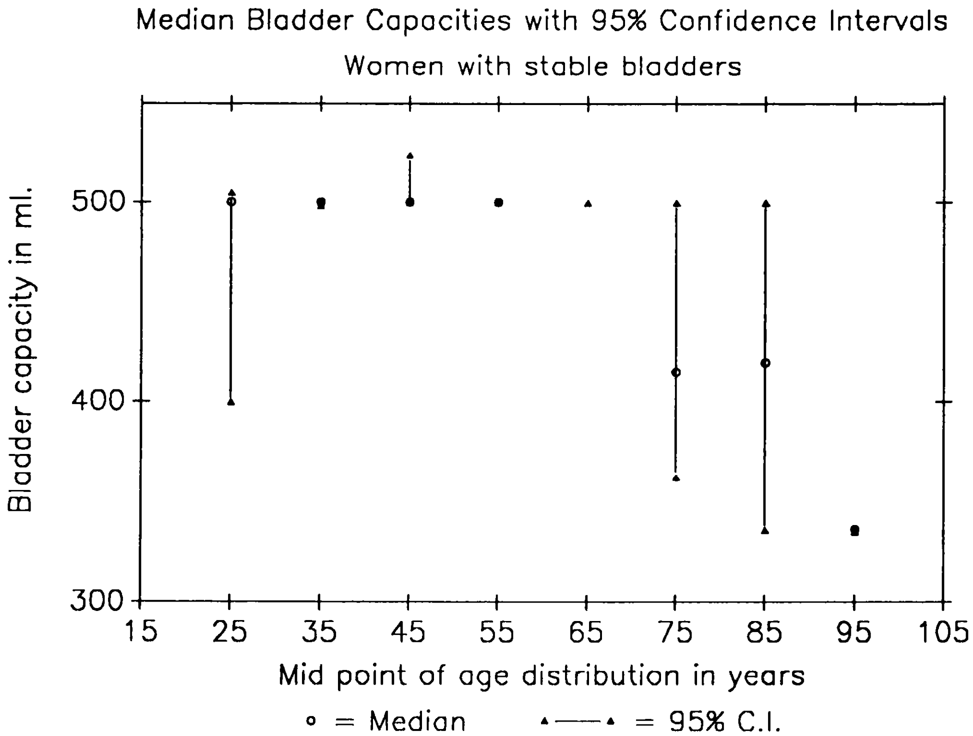


Figure 83

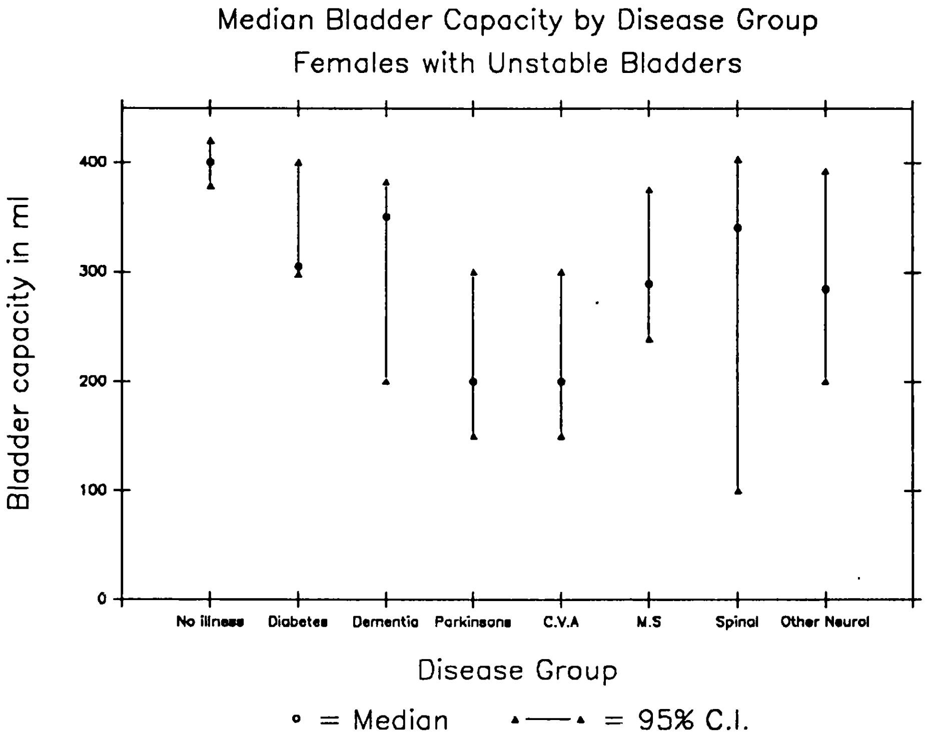


Figure 84

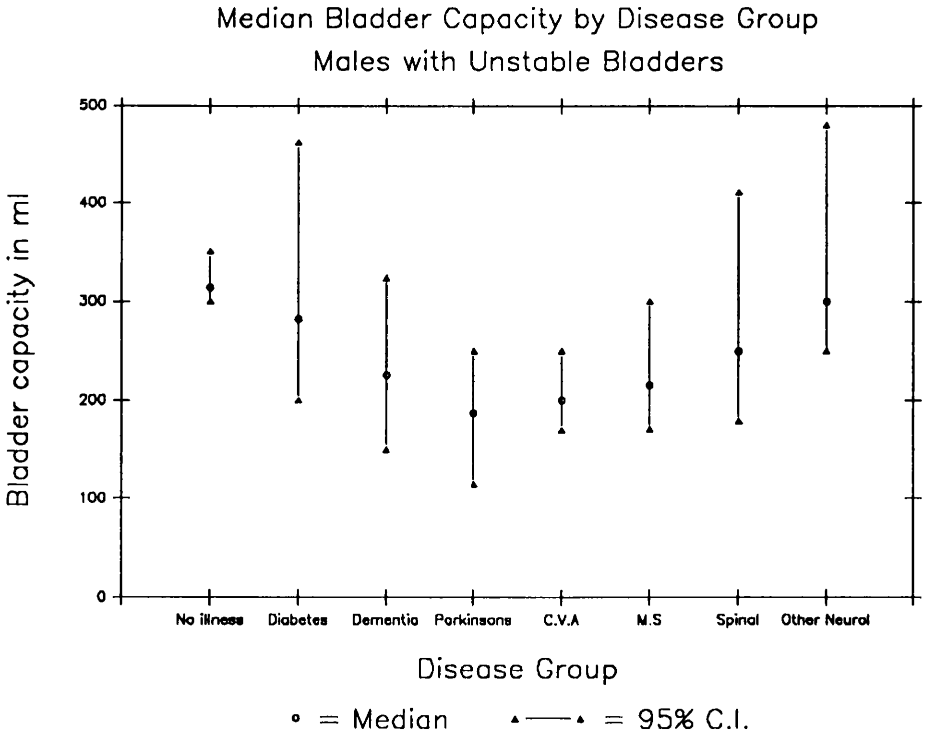


Figure 85

The maximum filling and end filling detrusor pressures

In Figures 86 and 87 I illustrate the median maximum filling pressures in men and women with unstable bladders according to age group. For both sexes the maximum filling pressure is higher in the late decades but differences across the decades are statistically significant in men only (Females H=12.53 df=7 p=0.086; males H=20.11 df=7 p=0.006). In Figures 88 and 89 I illustrate the median end filling pressures in the same way. For this variable the same trend is present in both sexes, although this reaches statistical significance in women only (Females H=28.91 df=7 p<0.001; males H=12.20 df=7 p=0.096). These findings are of limited import because no account was taken of bladder capacity which was lower amongst the elderly.

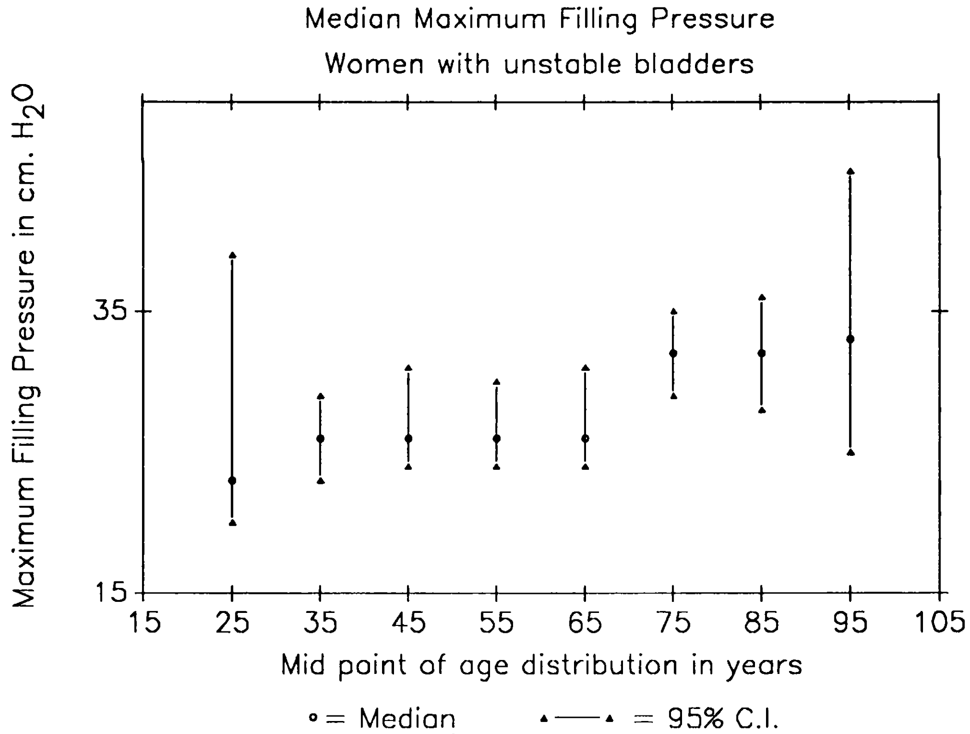


Figure 86

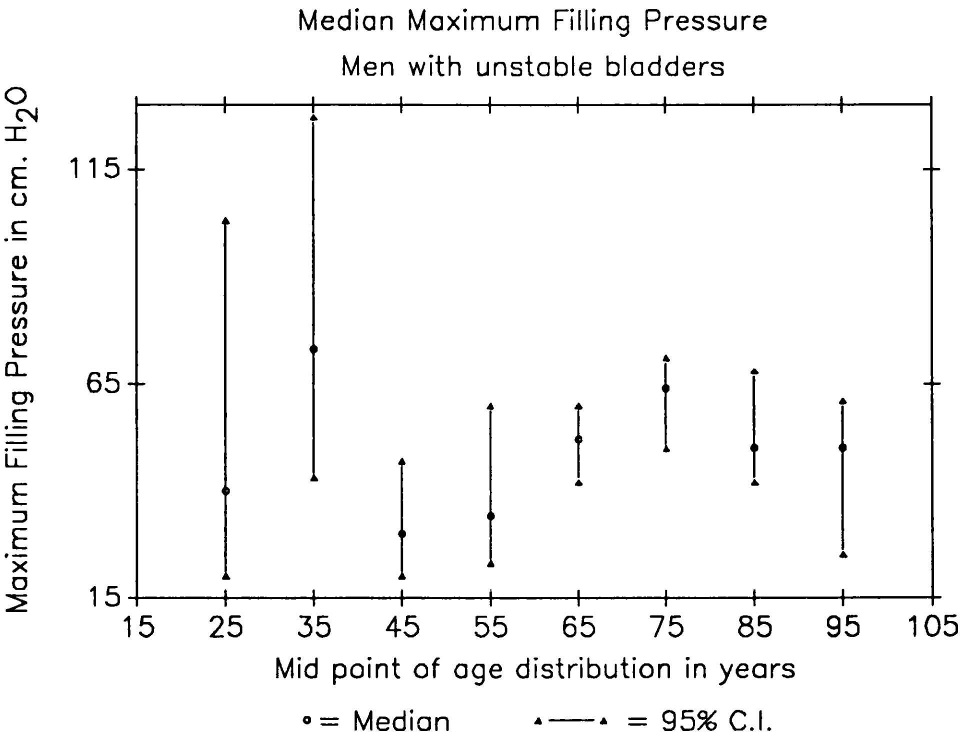


Figure 87

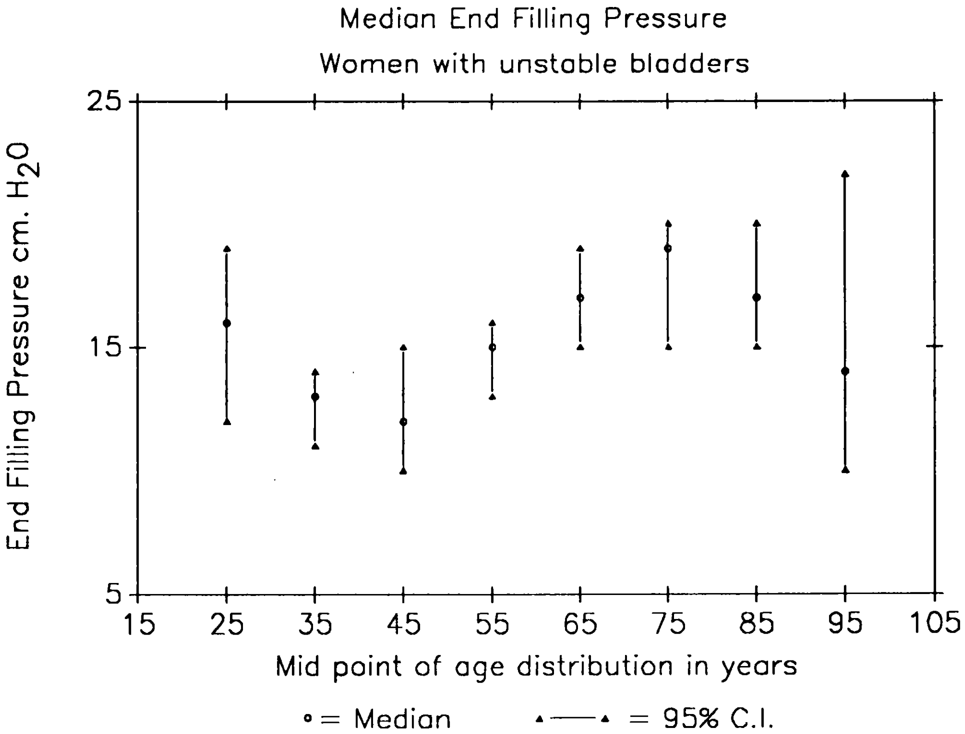


Figure 88

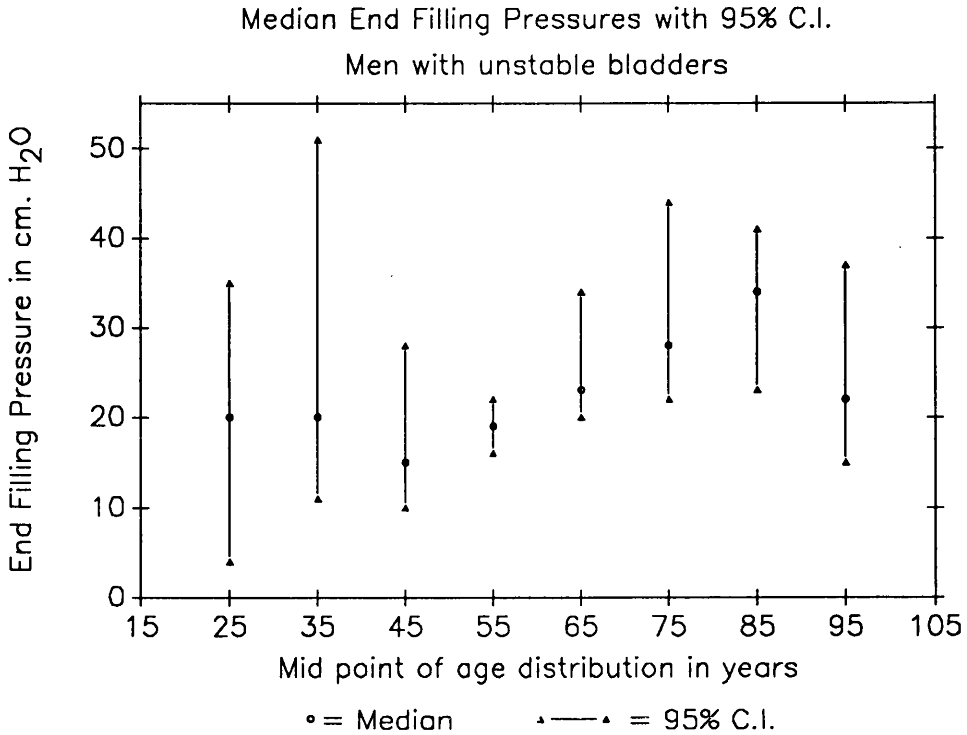


Figure 89

I analysed, in greater detail, the filling studies of patients in group B who showed unstable detrusor contractions and for whom full analogue data were recorded onto magnetic discs. The distributions of these patients are shown in tables 16 and 17 in Appendix A.

The force of unstable contractions

I calculated the force of unstable contractions by applying equation (89) to the data where detrusor contractions occurred which were greater than 14 cm H_2O. In this way I calculated the maximum unstable force and the integral, total force, in dynes.

Not surprisingly, there was a distinct sex difference amongst patients with no key illness, for both total unstable force and maximum force which are higher in men (Total force W=14.58 df=1 p<0.001 95% C.I. of difference 3.1, 6.9 dynes x 10^{-5}; Maximum force W=29.21 df=1 p<0.001 95% C.I. of difference 0.3, 0.8 dynes x 10^{-5}). These findings are illustrated in figures 90 and 91. A within sex analysis, comparing both variables according to age group, showed that there was no age associated difference in these vairables as shown in Figures 92 to 95. The statistical results are shown in table 18. These findings indicate that elderly people, even though they do seem to experience a voiding problem, demonstrate robust isometric detrusor activity comparable with the young. The data also show the error in attributing significance to the detrusor pressure, which was higher amongst the elderly, without considering the underlying force being generated, which was not different amongst the elderly.

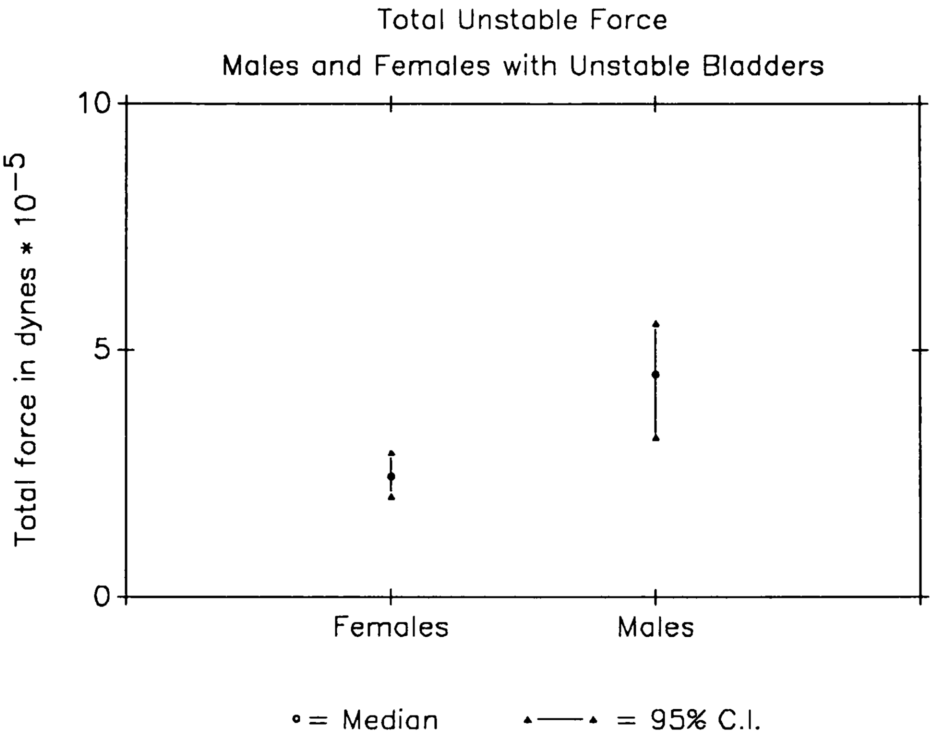


Figure 90

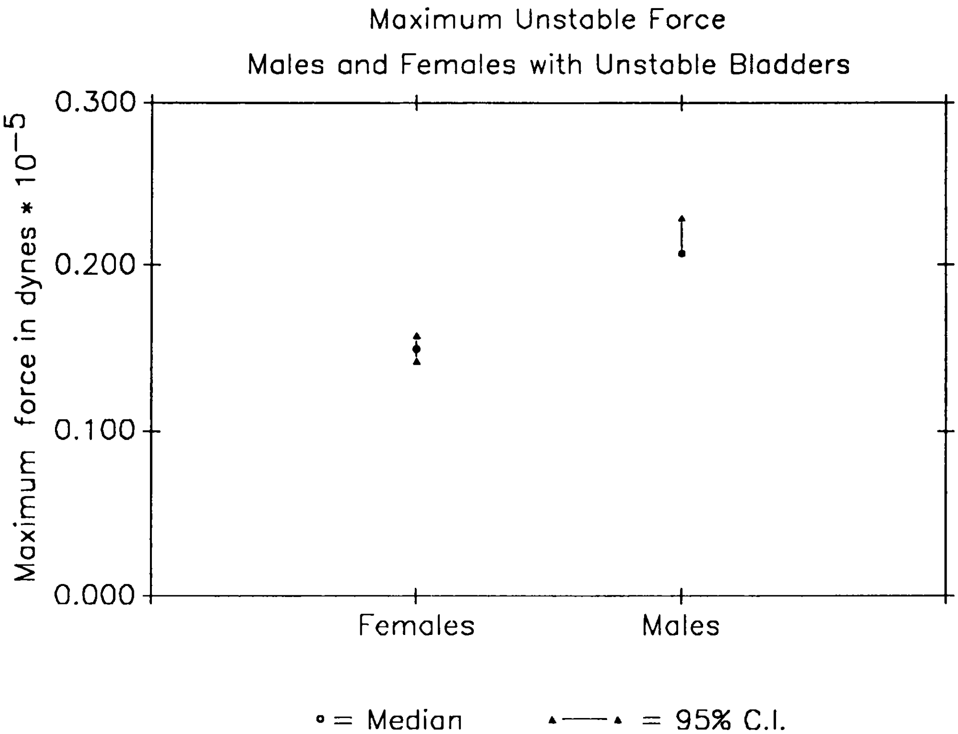


Figure 91

Table 18

The analysis of unstable forces by age group and sex

Statistics

Analysis	H	df	p
Total force, females by age groups	5.49	7	0.6
Maximum force, females by age groups	7.13	7	0.42
Total force, males by age groups	7.98	7	0.34
Maximum force, males by age groups	10.19	7	0.18

Figure 92

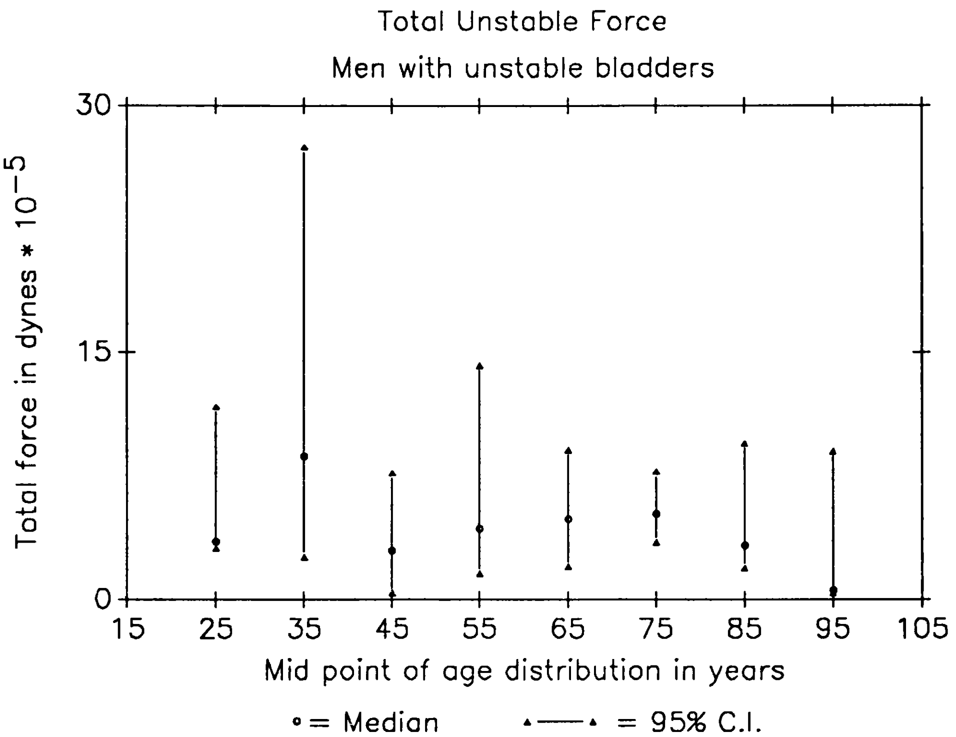


Figure 93

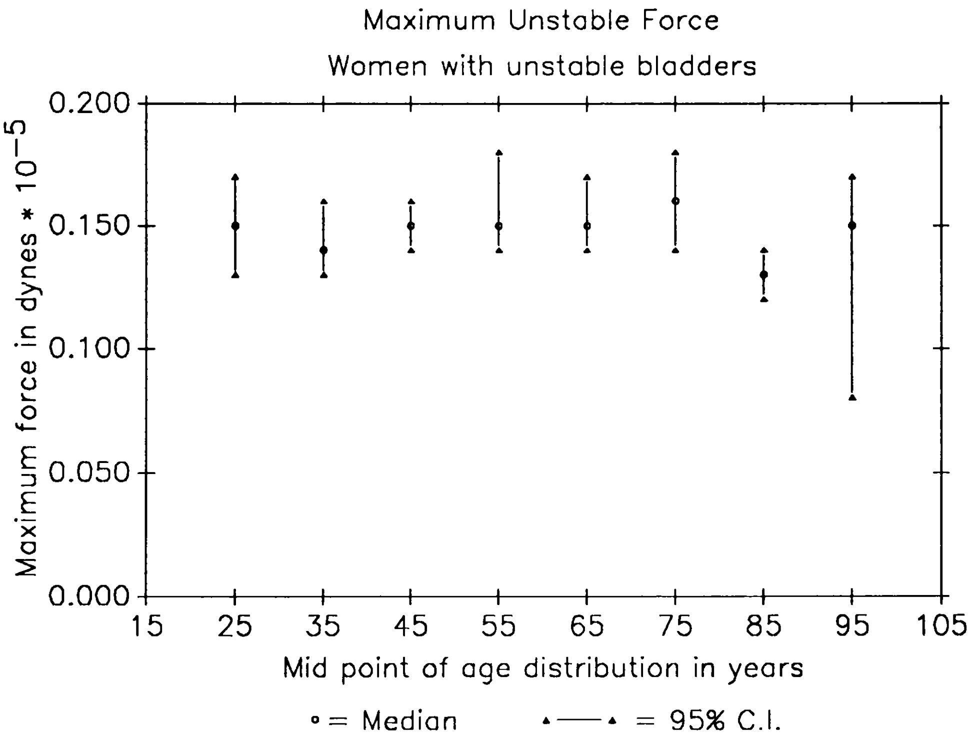


Figure 94

Figure 95

A similar analysis, according to disease groups, demonstrated little of clinical significance. Amongst women there was a definite difference in maximum unstable force between patients with cerebrovascular disease and patients with multiple sclerosis. This is illustrated in figure 96 in which I have left out demented patients because of their low numbers. This difference can be explained by the lower bladder capacities found in patients with cerebrovascular disease. The statistical results for this analysis are shown in table 19, below.

Table 19

Unstable forces according to disease group

Analysis	H	df	p
Total force, females by disease	10.84	7	0.14
Maximum force, females by disease	16.1	7	0.025
Total force, males by disease	8.6	7	0.28
Maximum force, males by disease	8.9	7	0.26

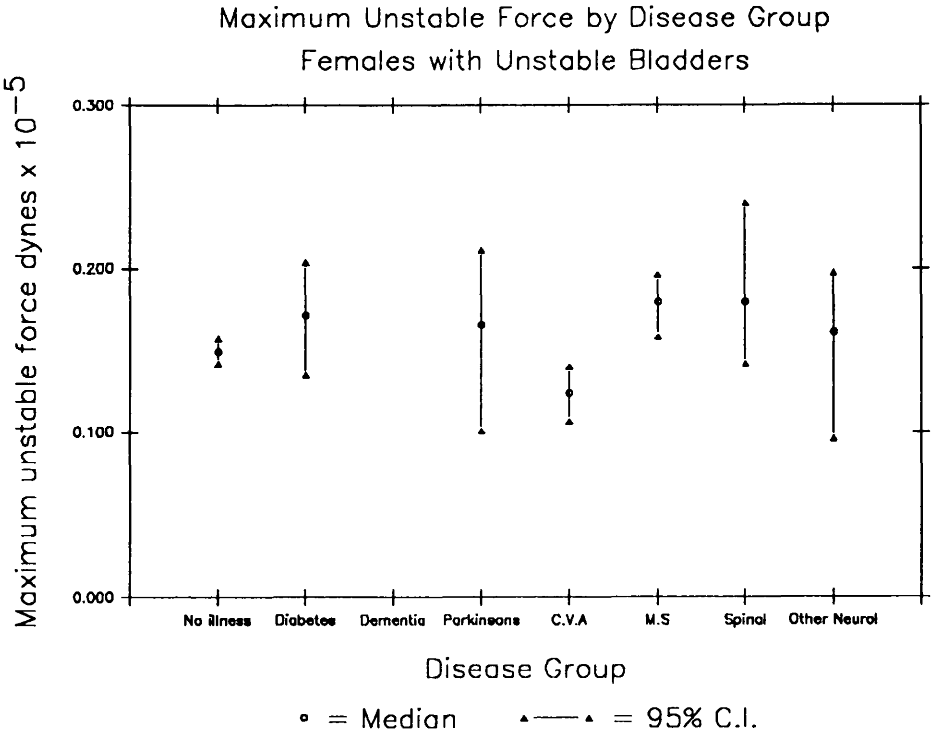


Figure 96

The total unstable force was found to be higher in patients with post micturition residual urine volumes of greater than 200 ml in both sexes, see figures 97 & 98 (Females W=4.71 df=1 p=0.03; males W=22.69 df=1 p<0.001). This separation increased as the cut off residual urine volume was set to higher values. This suggests that lower energy unstable activity is not indicative of a voiding problem, an assumption which many of us in the field have made (personnal communication Griffiths 1990).

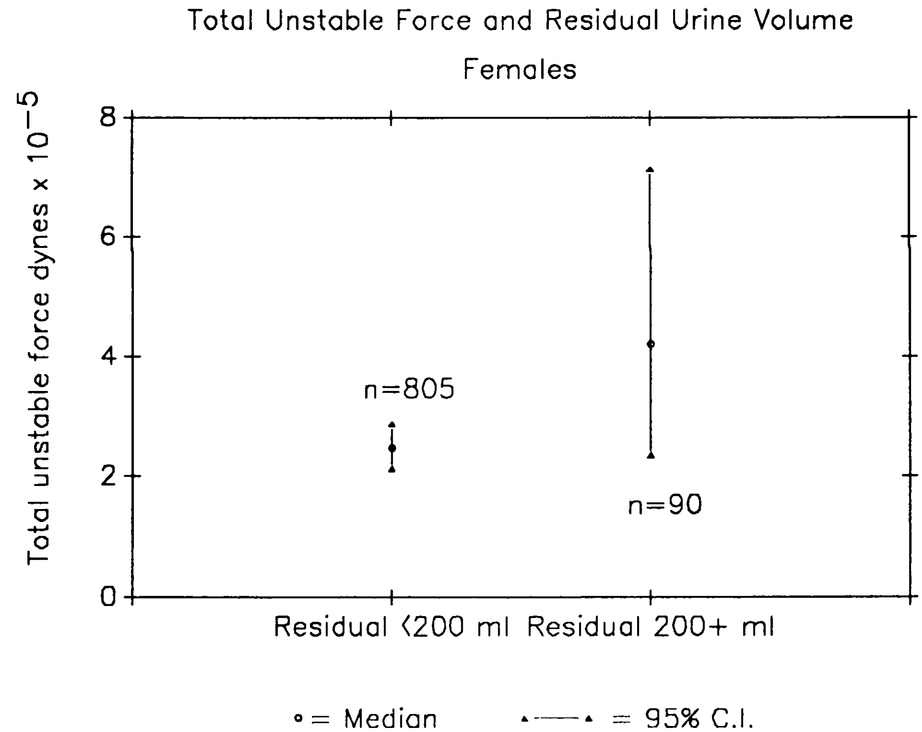


Figure 97

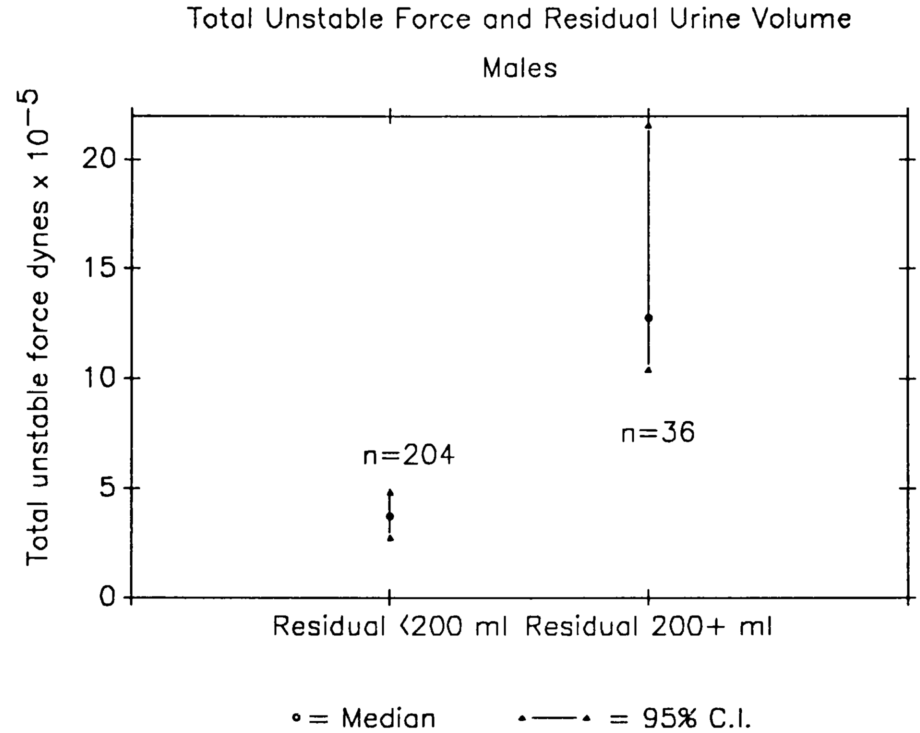


Figure 98

The instability variables PC1 and PC2

I also used the data from these patients to analyse the difference in the quality of the unstable activity by calculating the two variables PC1 and PC2 (equations 90 to 94) derived from principal components analysis. This demonstrated very important differences between the various patient groups.

I will deal with the parameter PC1 first. This describes the form of the unstable activity. If the detrusor contractions are of variable height and unprogressive PC1 tends to be higher with a positive value. If the contractions are more consistent PC1 tends towards zero, if the contractions crescendo PC1 falls below zero and the value is lower the steeper the gradient of the crescendo. At very low values of PC1 , -3 and below, the contractions tend to involve one precipitant high gradient contraction which terminates the filling study.

There was a sex related difference in the distributions of PC1 in patients with no key illness, see figure 99 (H=36.28 df=1 p<0.001 95% C.I. of difference 0.37, 1.00). PC1 was lower in men than in women.

In females with no key illness, there was a clear age related difference in the value of PC1 which was lower in the elderly. Although there was a statistically significant difference between age groups in men this was not clinically significant. These differences are illustrated in figures 100 and 101. The relevant statistics are shown below in table 20.

Table 20

The age differences in PC1

Result	**H**	**df**	**p**
PC1, females by age group	36.23	7	<0.001
PC1, males by age group	16.57	7	0.021

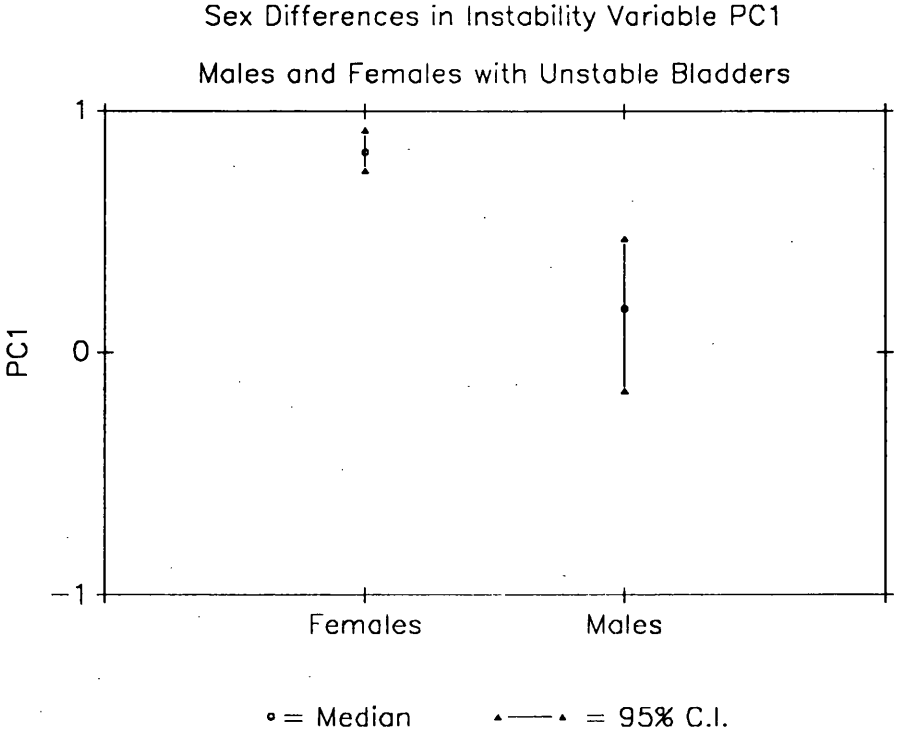
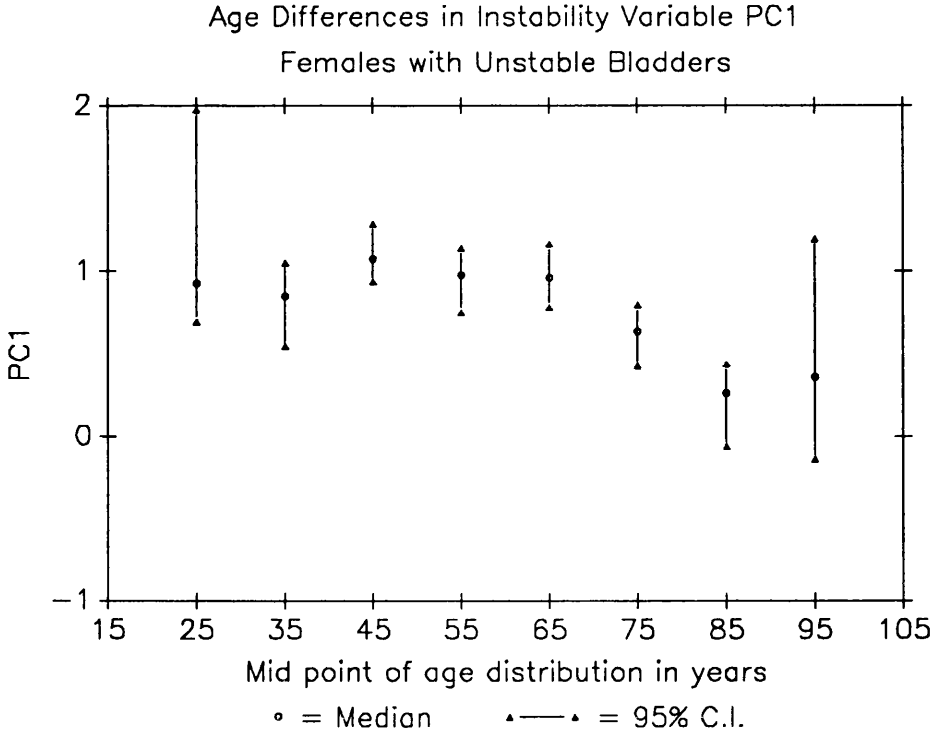
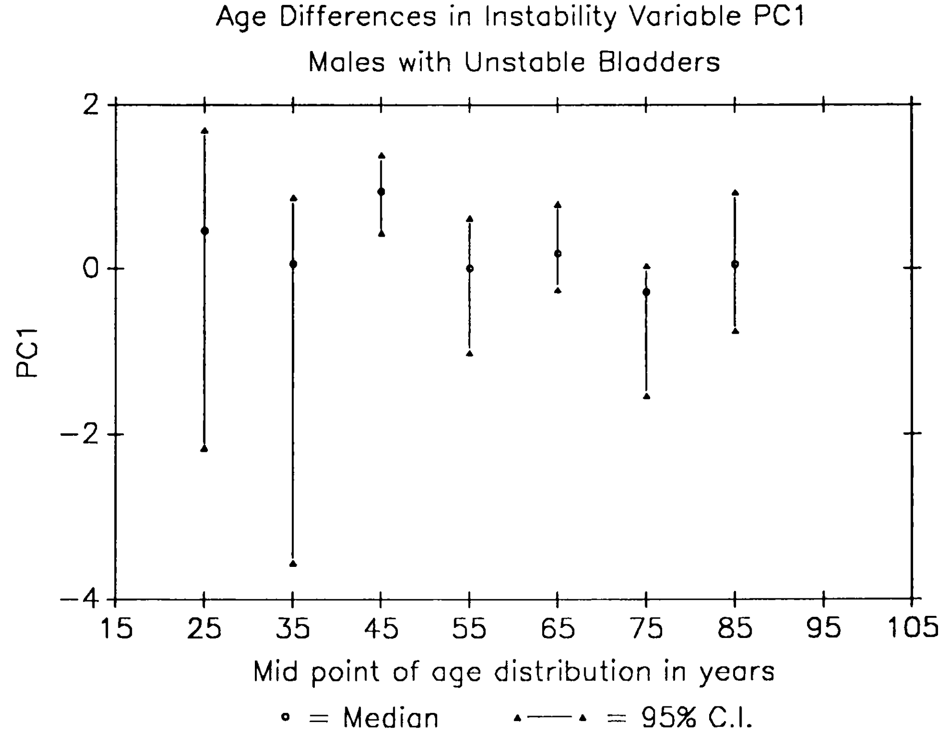


Figure 99


Age Differences in Instability Variable PC1

Females with Unstable Bladders

Figure 100


Age Differences in Instability Variable PC1

Males with Unstable Bladders

Figure 101

Amongst women there was a difference in the values of PC1 between disease groups, see figure 102. It is only possible to feel sure about the lower values in patients with multiple sclerosis compared to women with no key illness ($H=34.83$ $df=7$ $p<0.001$). The female patients with multiple sclerosis showed similar values to those found in older women without a key illness. No differences between the disease groups were found in men.

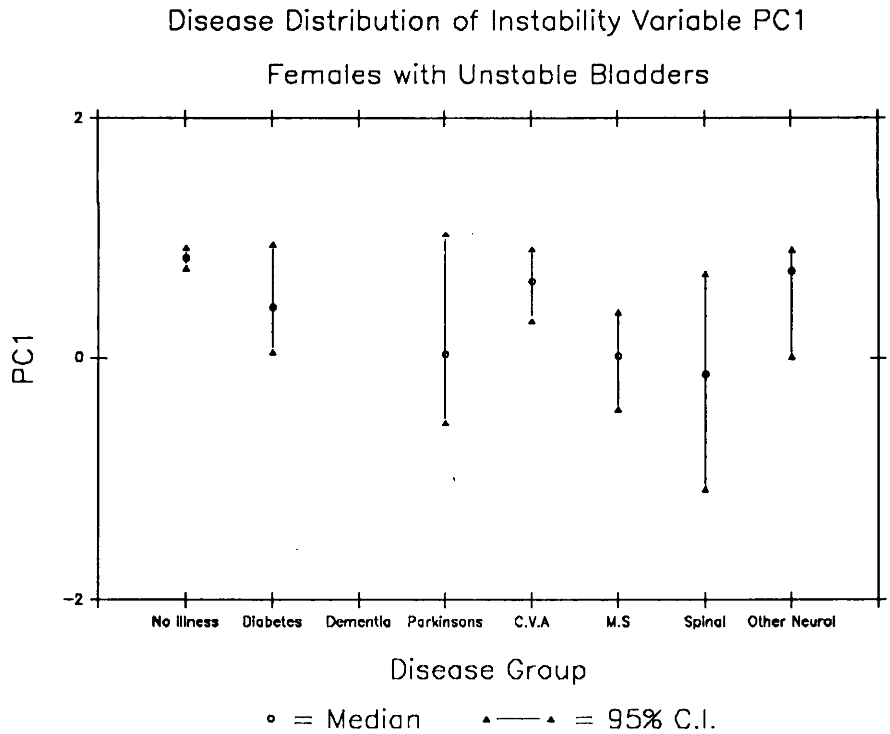


Figure 102

PC1 seemed to show some important properties in its relationship with other urodynamic variables. Figures 103 and 104 illustrate the relationship between bladder capacity and PC1 in both sexes. Lower values of PC1, reflecting more persistent and crescendo activity, were associated with lower bladder capacities (Females H=394.91 df=6 p<0.001; males H=86.62 df=6 p<0.001). Women with urgency or urgency and urge incontinence showed lower values for PC1, see figure 105, (Urgency W=10.01 df=1 p=0.002; urge incontinence W=13.73 df=1 p<0.001). PC1 did not seem to change in association with frequency and nocturia but women with nocturnal enuresis had a lower PC1, see figure 106, (W=5.56 df=1 p=0.019). Similar differences were not detected amongst men.

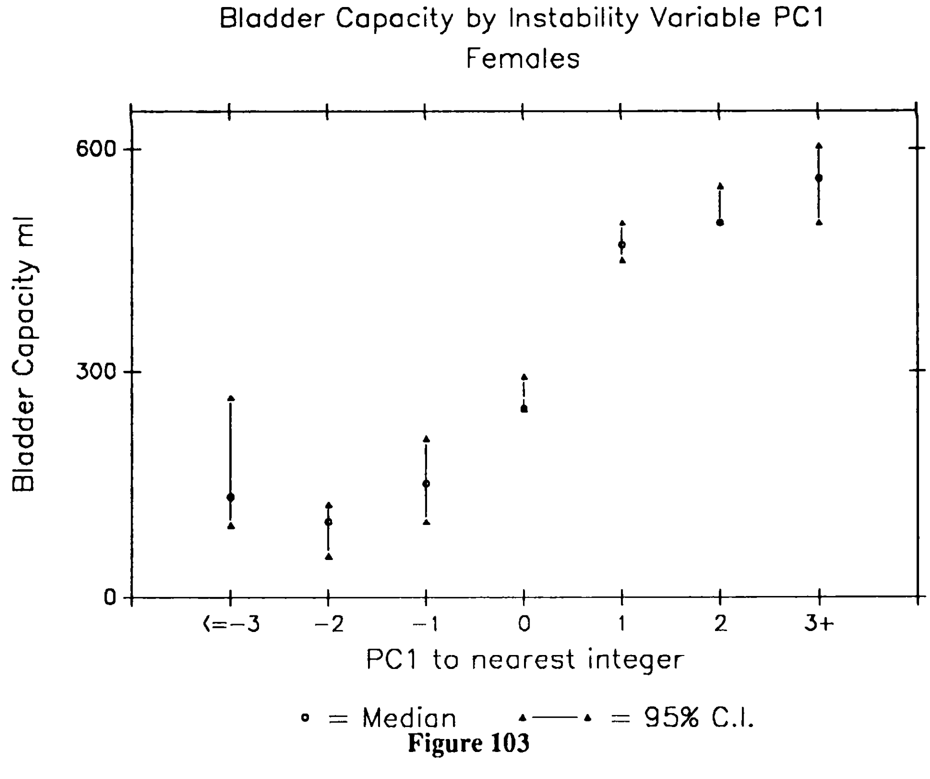


Figure 103

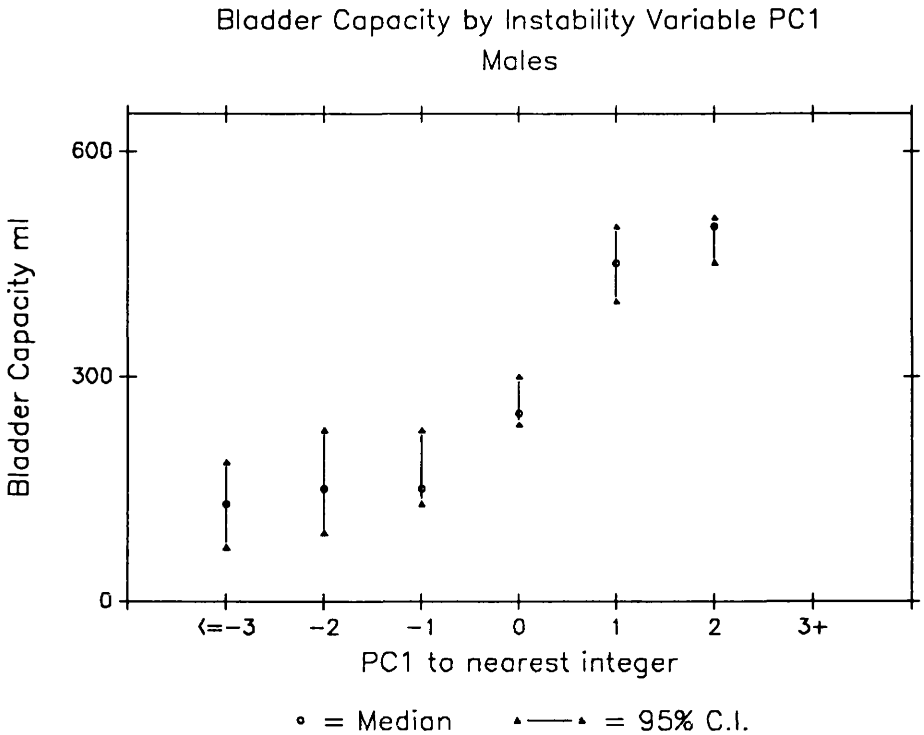


Figure 104

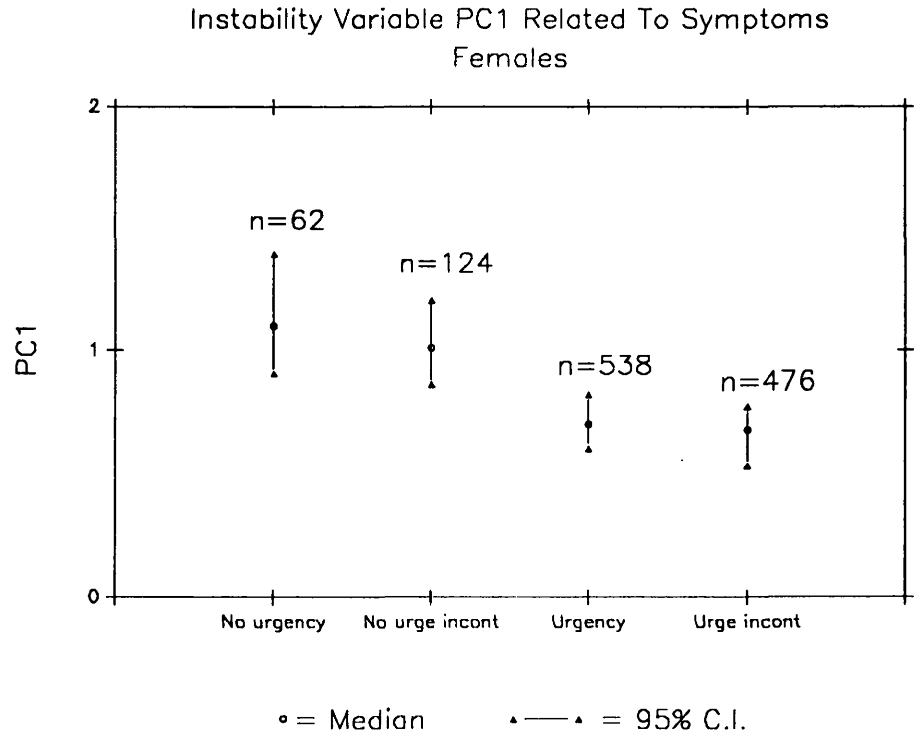


Figure 105

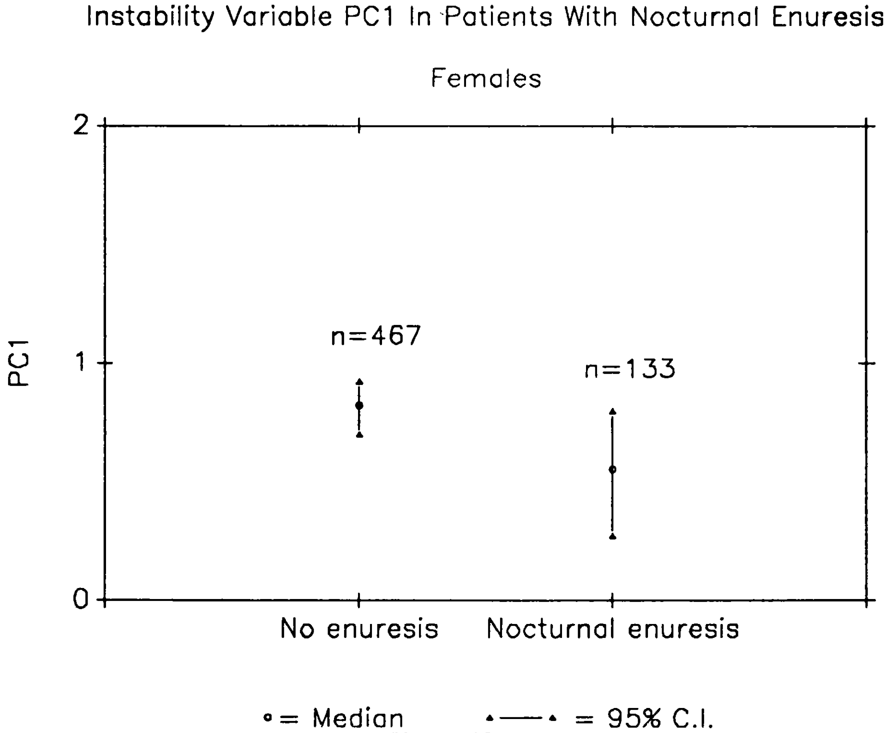


Figure 106

PC1 was higher amongst patients with residual urine volumes, at the end of the test, greater than 100 ml, but this was a meaningless aberration since a higher PC1 was associated with a higher bladder capacity and you required a higher bladder capacity to achieve a higher residual urine volume.

PC2 had a more meaningful relationship with the end-test post micturition residual urine volume amonst women. If the residual volume was expressed as a proportion of the bladder capacity, patients with higher proportionate residuals tended to higher values of PC2. This finding is illustrated in figure 107. The same variable correlated strongly with the total unstable force in both sexes (Females r=0.84 p<0.001; males r=0.75 P<0.001).

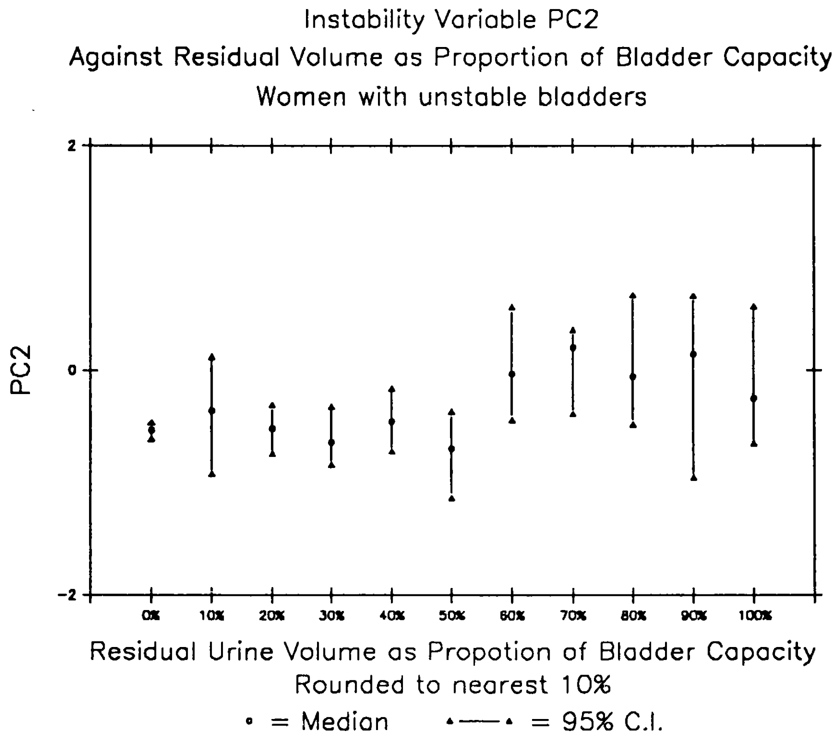


Figure 107

Summary of the the analysis of the filling phase

The age related changes noted are more clearly seen in women. Older men have lower bladder capacities and a higher incidnece of detrusor instability compared to younger counterparts. Older women show more a widespred differences compared to younger women. Their first residual urine volumes are higher, their bladder capacities lower and they perceive bladder fullness later. The incidence of detrusor instability is greater and older women tend to show more persistent and precipitant unstable detrusor activity, a similar combination being noted amongst patients with multiple sclerosis. In both sexes the unstable forces are not reduced and are very similar to those found in the young.

Certain diseases mirror these age related changes, particularly amongst women. Dementia and multiple sclerosis are notably associated with higher first residual urine volumes, whereas Parkinson's disease and cerebrovascular disease are associated with low bladder capacities. All of the key illnesses show an incidence of detrusor instability equivalent to that found in the elderly.

In women, higher energy unstable activity during filling is associated with higher residual urine volumes at the end of the test.

Analysis of the voiding phase

I was able to obtain data from patients in groups Ai and Bi on the following voiding parameters:

1. Maximum voiding flow rate

2. Detrusor pressure at maximum voiding flow rate

3. Maximum voiding detrusor pressure

4. Voided volume

5. Residual urine volume at the end of the test.

The terms used to describe these parameters define their nature such that an expanded explanation is not required.

The age, sex and key illness distribution of the patients studied are tabled in Appendix A tables 21 and 22, very small numbers of elderly men in their nineties were studied.

Maximum voiding flow rate

There was evidence of a very clear breakdown in voiding ability associated with late life. These changes affect both sexes but they are very much more obvious amongst women. Figures 108 and 109 show the maximum voiding flow rates according to age group for women and men. It can be seen that I found a trend downwards in association with aging (Females $H=121.97$ $df=7$ $p<0.001$; males $H=43.99$ $df=6$ $p<0.001$). We need to be cautious of interpreting these changes as the flow rate is volume dependent and the elderly patients had lower bladder capacities. This problem is addressed later.

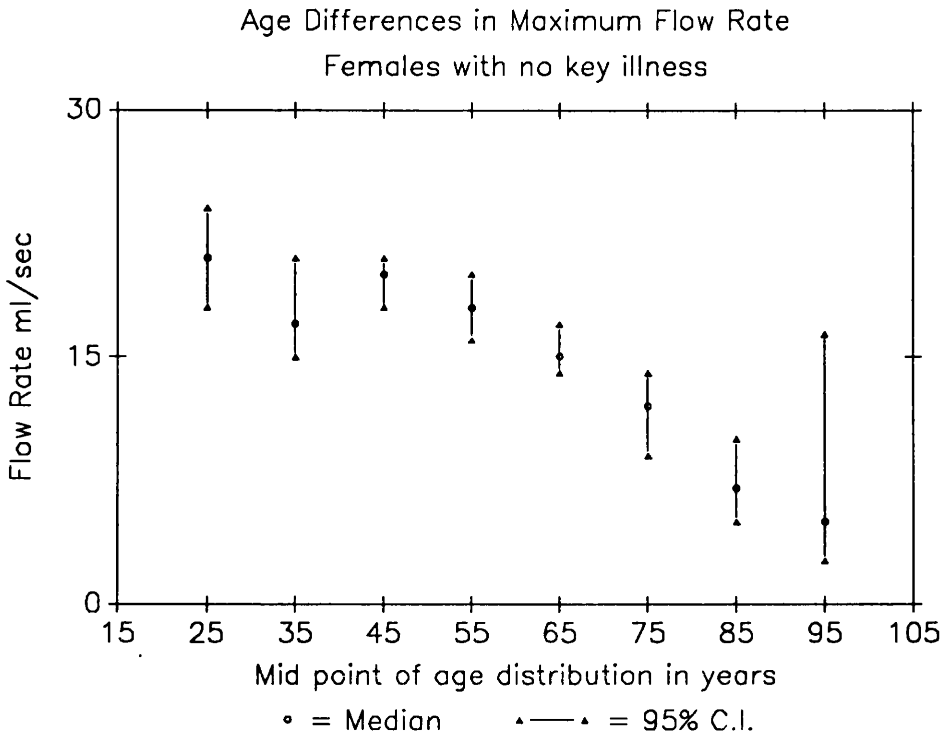

Age Differences in Maximum Flow Rate
Females with no key illness

Figure 108

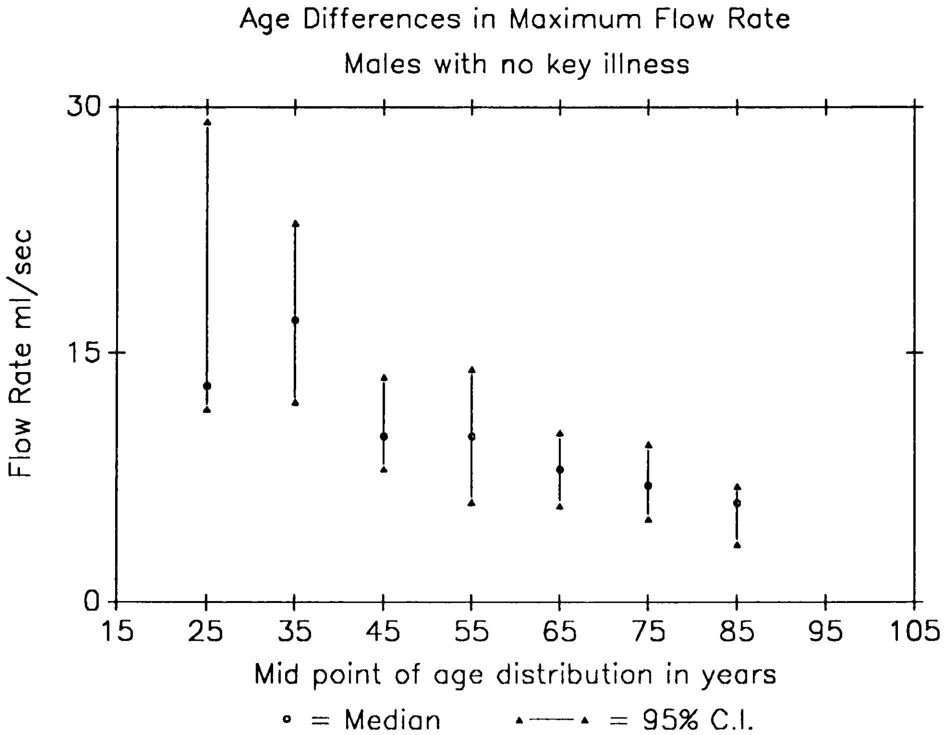

Age Differences in Maximum Flow Rate
Males with no key illness

Figure 109

Detrusor pressure at maximum flow and maximum voiding pressure

Figures 110 to 113 illustrate the age related differences in the detrusor pressure at maximum flow and the maximum voiding detrusor pressure. Men did not show any difference across the decades but elderly women certainly did show lower values for these parameters. The statistical results related to these variables are shown below in table 23.

Table 23

The principle voiding pressure variables compared by age group

Result	H	df	p
Detrusor Pressure at maximum flow rate, females	30.69	7	<0.001
Maximum voiding detrusor pressure, females	55.62	7	<0.001
Detrusor pressure at maximum flow rate, males	5.61	6	0.59
Maximum voiding detrusor pressure, males	3.86	6	0.80

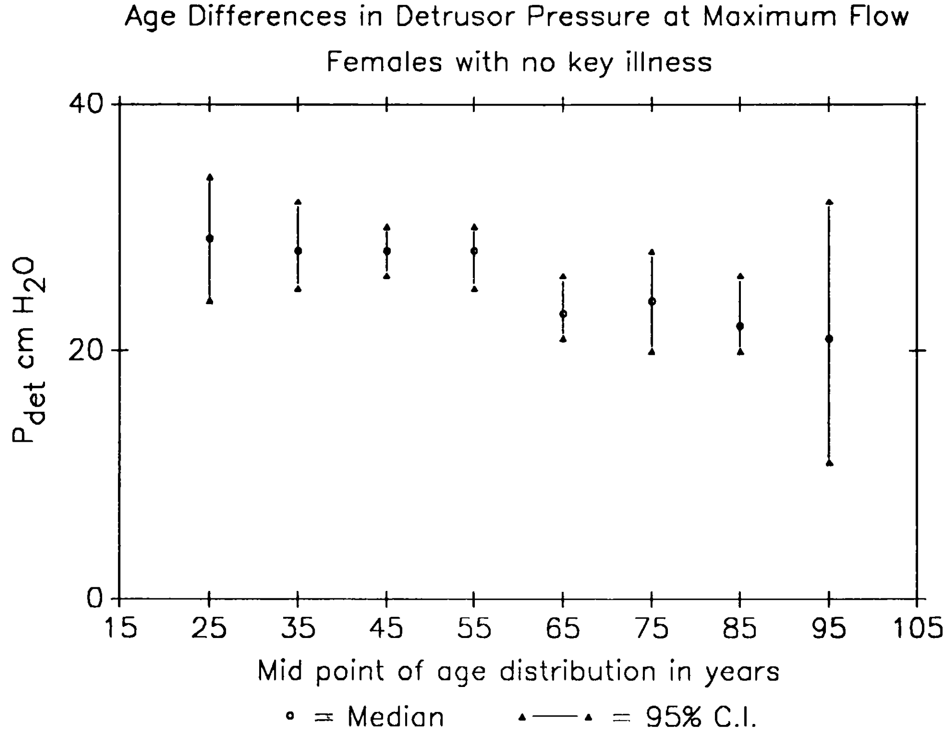


Figure 110

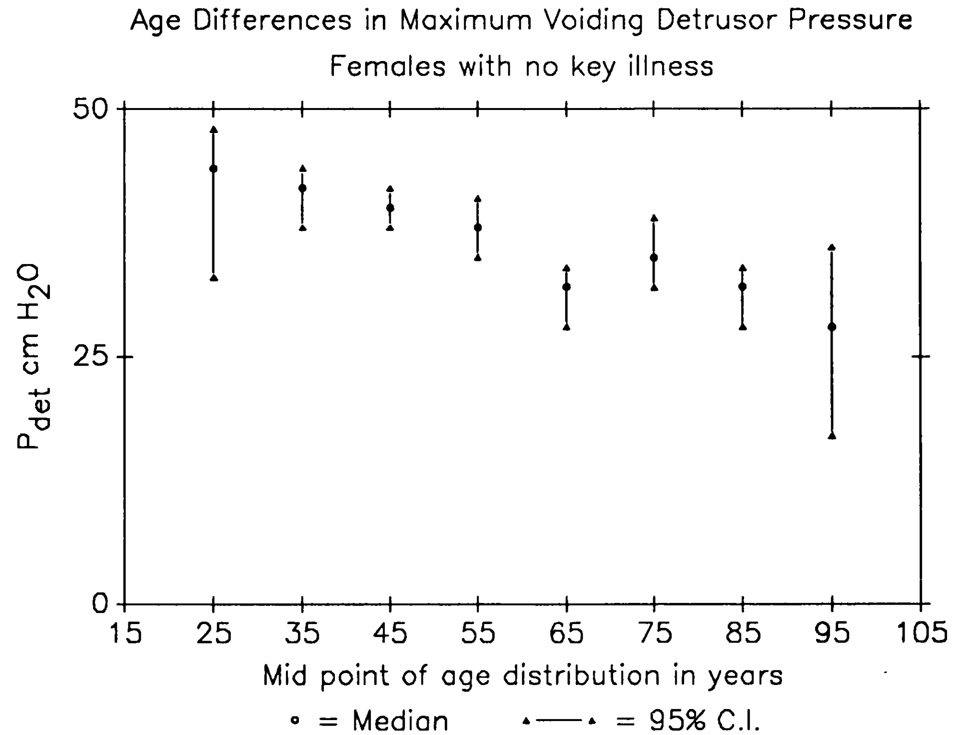


Figure 111

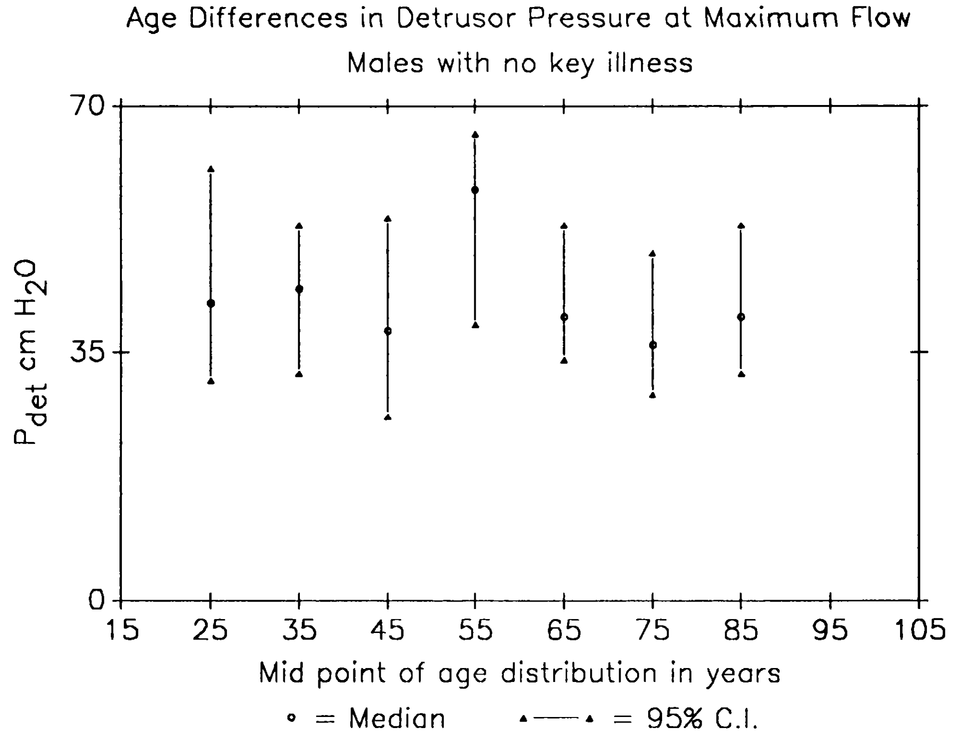


Figure 112

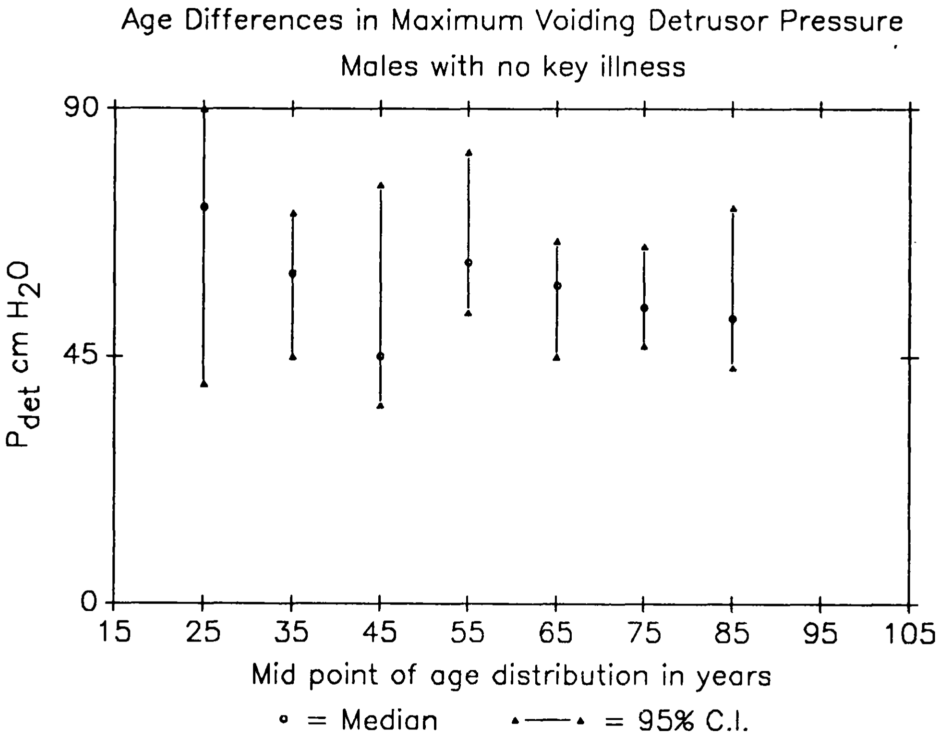

Age Differences in Maximum Voiding Detrusor Pressure
Males with no key illness
P_{det} cm H_2O
90
45
0
15
25
35
45
55
65
75
85
95
105
Mid point of age distribution in years
° = Median
▲—▲ = 95% C.I.

Figure 113

The voided volume

The voided volume was the difference between the bladder capacity and the residual urine volume at the end of the test. I have therefore not included a description of the analysis of this variable as it did not add extra information to the data set.

The residual volume at the end of the test (second residual volume)

The fact that a genuine voiding difficulty existed amongst the elderly patients in both sexes is illustrated by plotting the proportion of patients with residual volumes of 100 ml and more, and the proportion of patients retaining more than 10% of the bladder capacity, according to age group. The proportion is higher amongst the elderly in both sexes. These histograms are shown in figures 114 to 117. The statistical analyses for these variables against age are tabled below.

Table 24

Age group comparisons of residual urine volumes

Result	Chisq	df	p
Females with residuals of 100 ml +	26.13	7	<0.001
Females with residuals > 10% of capacity	36.67	7	<0.001
Males with residuals of 100 ml +,	13.68	6	0.05
Males with residuals > 10% of bladder	16.98	6	0.01

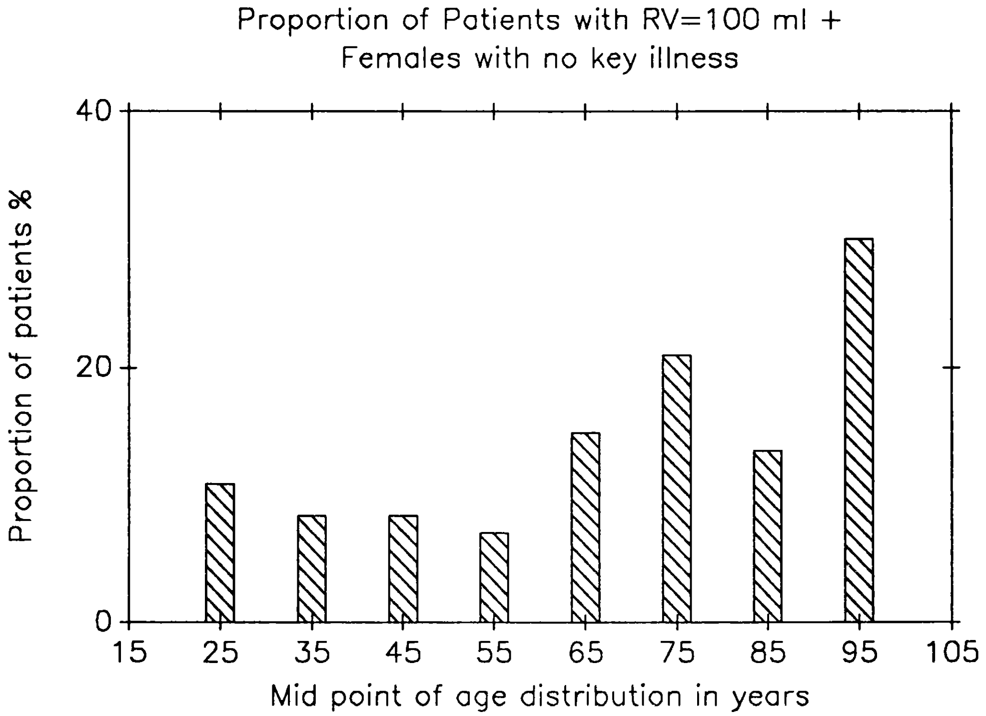


Figure 114

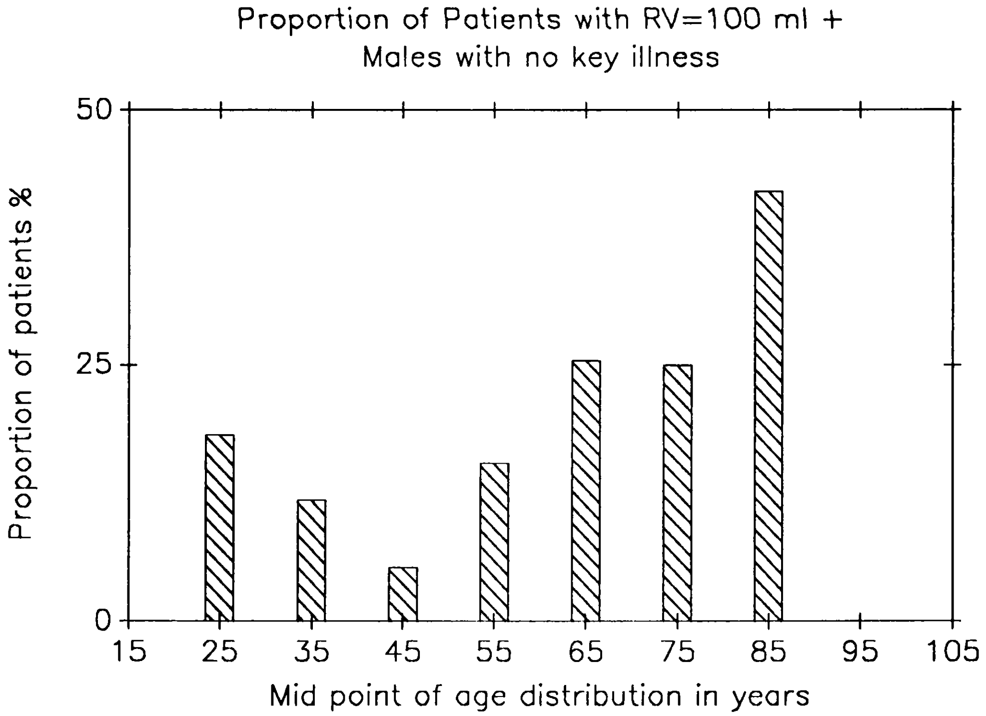


Figure 115

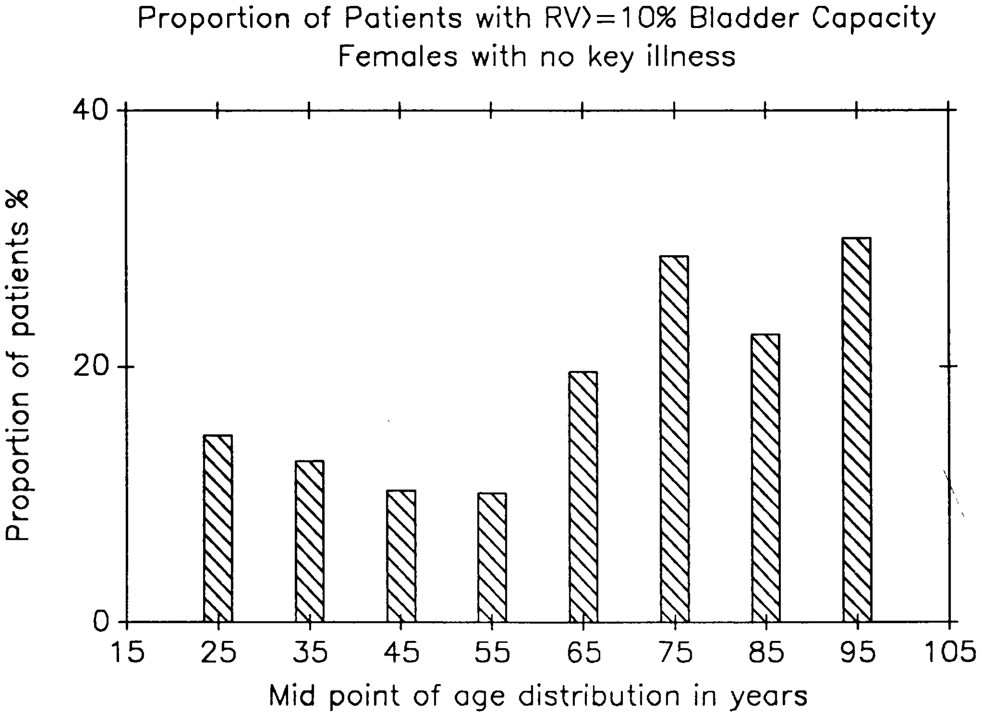


Figure 116

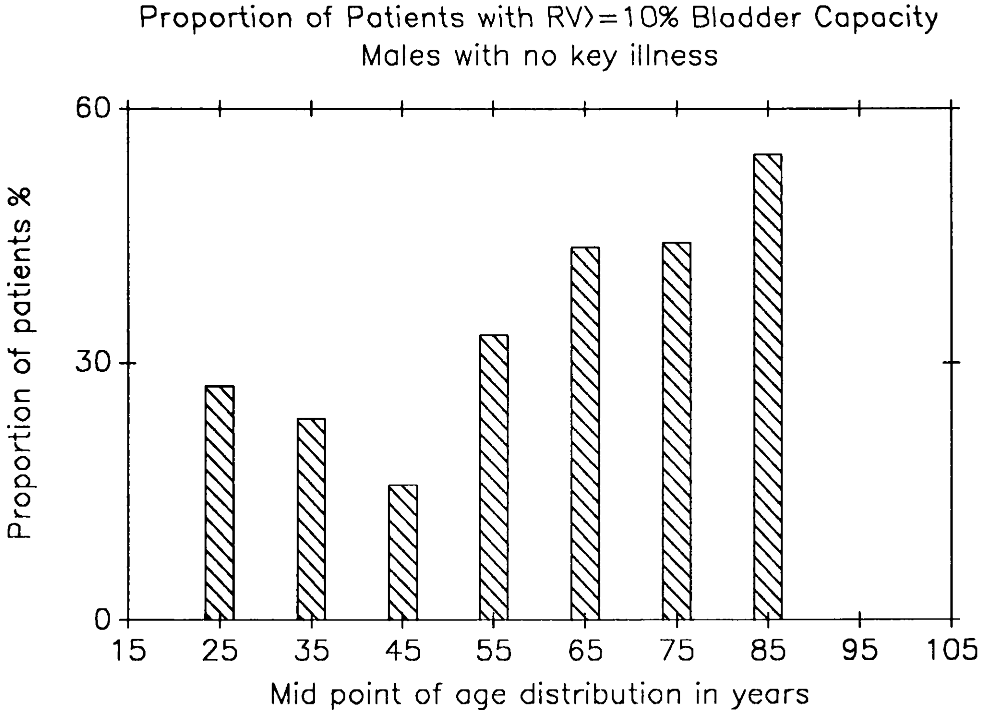


Figure 117

Figure 118 shows the frequency distribution of the proportion of bladder capacity voided in women aged 70 years and over who had unstable bladders and incomplete emptying. I excluded those who emptied completely in order to obtain better scaling of the Y axis. It can be seen that there is no evidence of the bimodal distribution described by Resnick et al (1987).

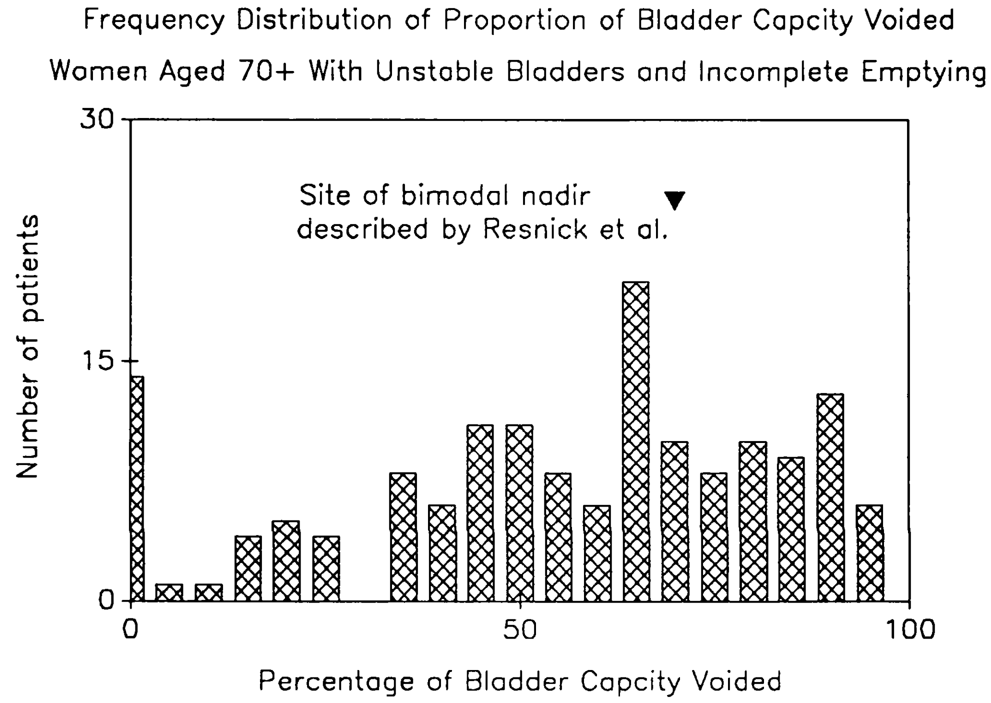


Figure 118

The relationship between detrusor pressure and maximum flow

At this point I have shown evidence of voiding difficulties affecting the flow rate in both sexes in late life, in women this appears to be associated with lower voiding pressures. Figures 119 to 122 plot the detrusor pressure at voiding maximum flow rate against the maximum voiding flow rate for men and women aged 75+ and for the same sexes aged 74 and below.

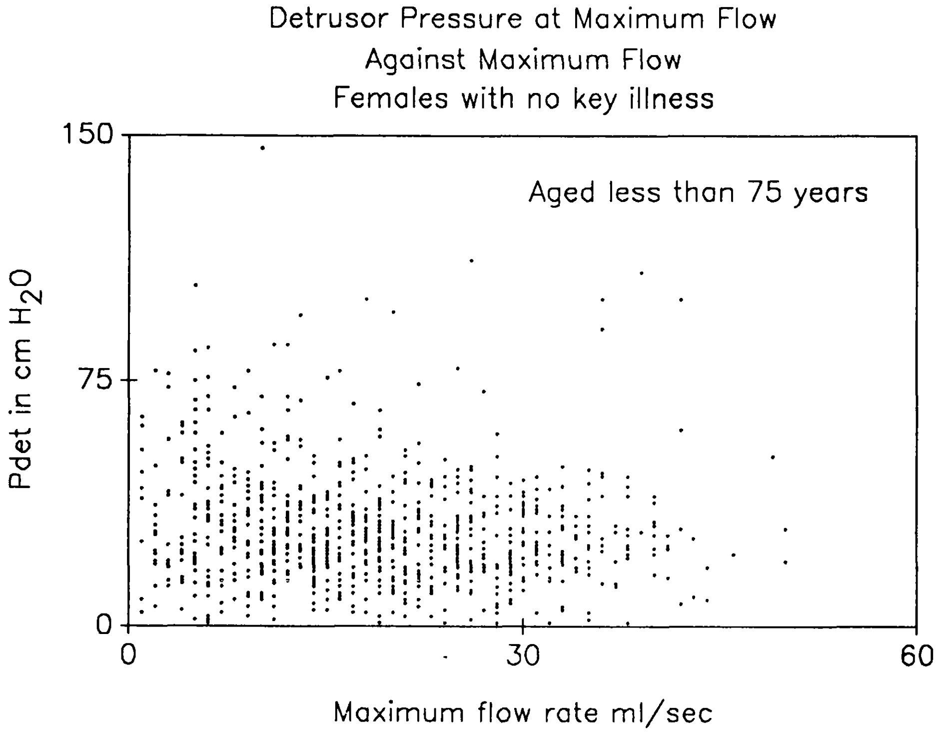


Figure 119

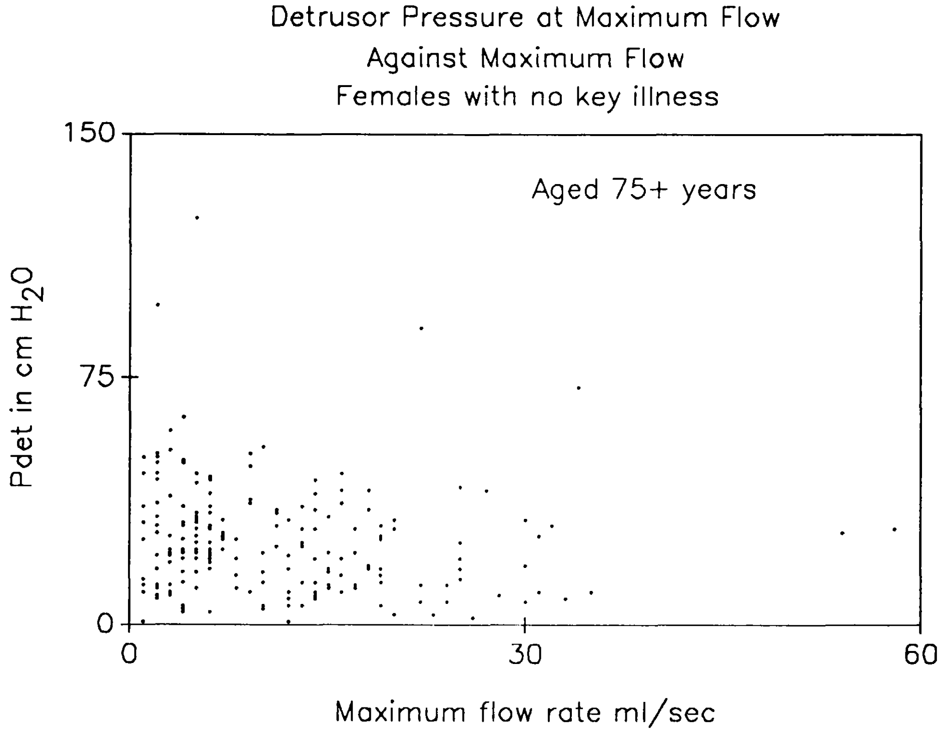


Figure 120

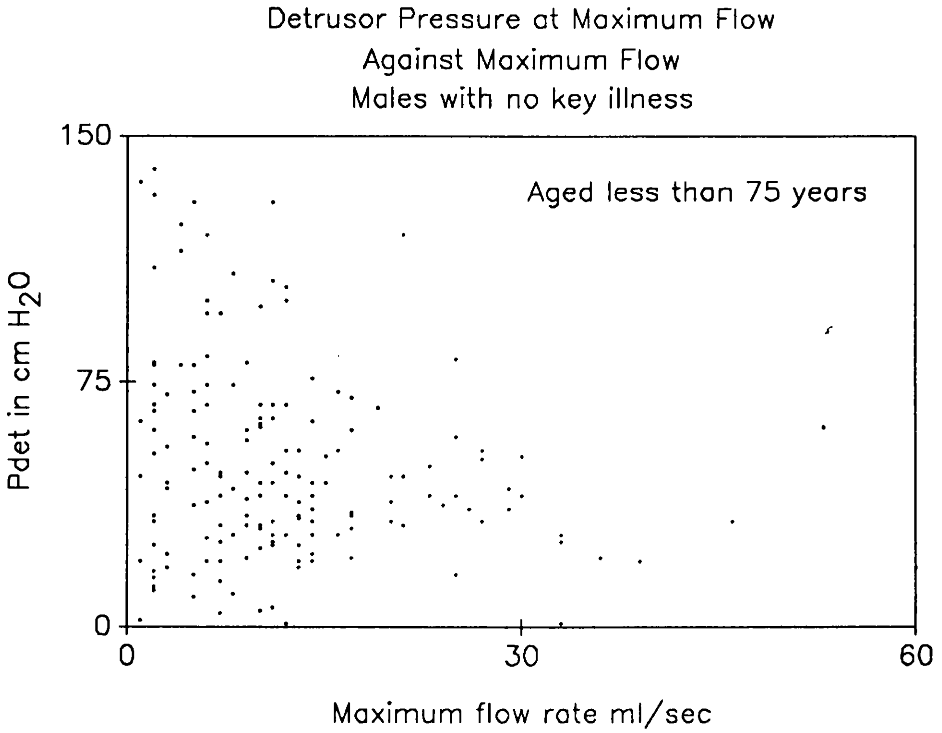


Figure 121

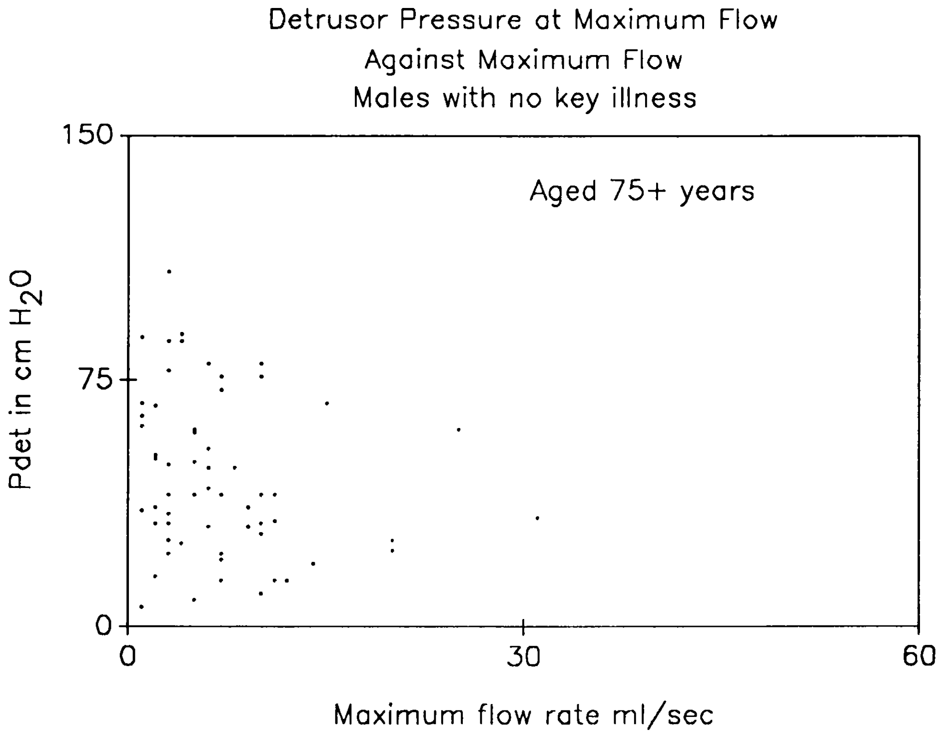


Figure 122

For each pair of values on these plots I calculated the position in relation to the zones defining contractility and obstruction. In this way I classified the voiding studies as showing strong detrusors, normal detrusors or weak detrusors and as showing probable obstruction, equivocal evidence and no obstruction. I would not consider these classifications as absolute although there are very clear sex differences and they do serve to show trends associated with late life. Figures 123 to 125 show the distributions of the groupings in relation to age group. These apply to patients without any of the key illnesses.

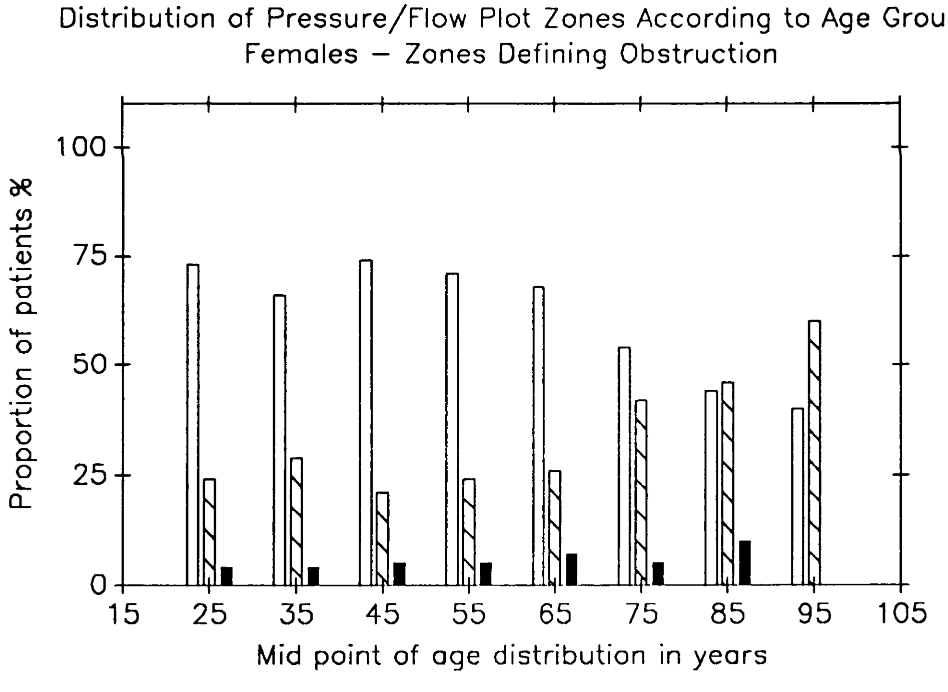


Figure 123

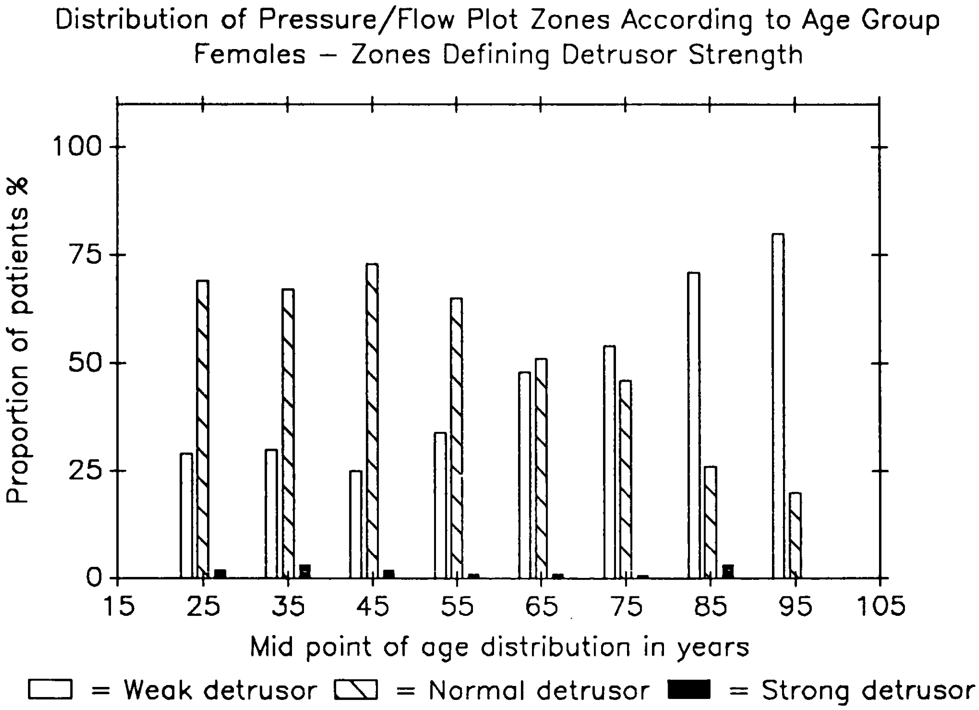


Figure 124

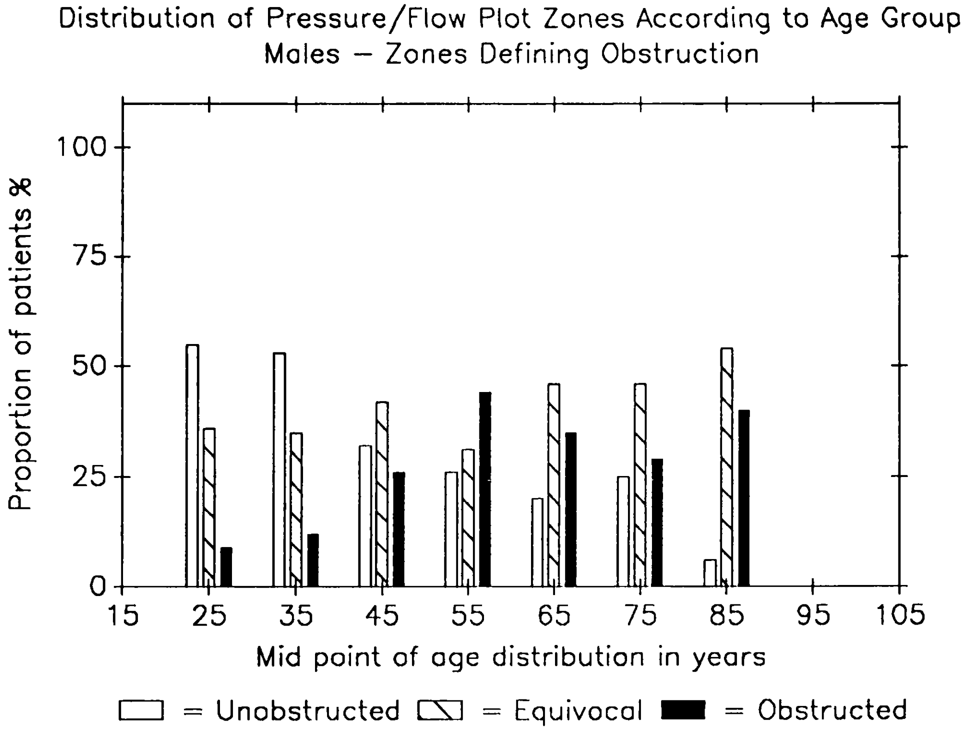


Figure 125

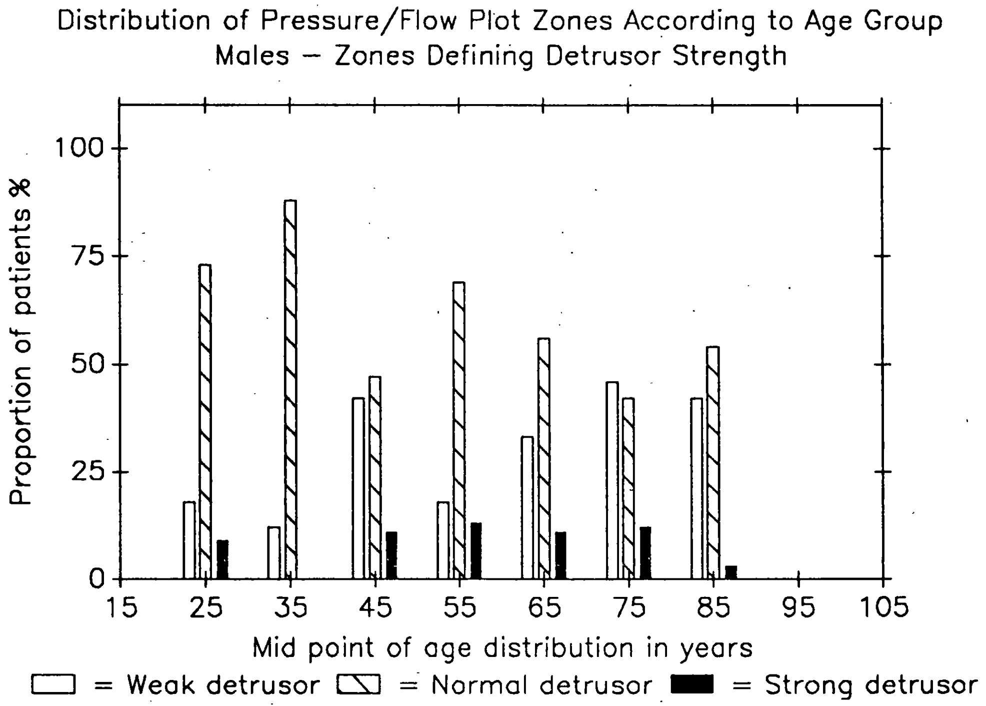


Figure 126

It can be seen that with age, amongst women, the proportion of patients with "weak detrusors" increased at the expense of proportion with "normal detrusors". A similar shift was shown amongst men but, in addition, there was also a reduction in the proportion showing evidence of "strong detrusors". Amongst older women there was a shift from the "unobstructed" zone into the "equivocal" whereas in men there was a shift in the proportion showing evidence of "obstruction" into the "equivocal" zone. The statistical analyses related to these findings are tabled below.

Table 25

Age group comparisons of detrusor strength and obstruction

Result	**Chisq**	**df**	**p**
Females, detrusor strength	106.9	14	<0.001
Females, outflow obstruction	52.7	14	<0.001
Males, detrusor strength	20.39	12	0.05
Males, outflow obstruction	24.24	12	0.013

I was able to extend the analysis of voiding in a subset of patients on whom I had been able to collect digitised analogue data throughout the voiding study. I used this data to calculate the following parameters.

1. The maximum velocity of shortening of the bladder circumference using equation (78)

2. The maximum WF using equation (88)

3. The mean WF using equation (88)

I used the mean WF because the plateau form of the WF plot during voiding makes this a meaningful measure.

The age, sex and key illness distribution of the patients who had sufficient data for these variables to be calculated are shown in tables 26 and 27 Appendix A. In addition to the velocity of shortening of the bladder circumference and WF I was also able to calculate the value of the standardised Q^* in a subset of patients from groups Ai and Bi in whom it was possible to identify an isometric contraction indicating p_{iso}. I calculated the standardised Q^* using equations (64) and (69).

The age, sex and key illness distribution of the patients who had sufficient data for standardised Q^* to be calculated are shown in tables 28 and 29 Appendix A.

Maximum shortening velocity of bladder circumference

Figures 127 and 128 show the median maximum velocities for both sexes according to age group. In both sexes there is a clear fall with increasing age (Females H=86.72 df=7 p<0.001; males H=20.28 df=6 p=0.003). The maximum velocity usually reflects a peak in the velocity plot at the end of micturition which is thought to be caused by the terminal contraction of the series elastic element. If the elasticity of the series elastic element is reduced so this peak will be reduced.

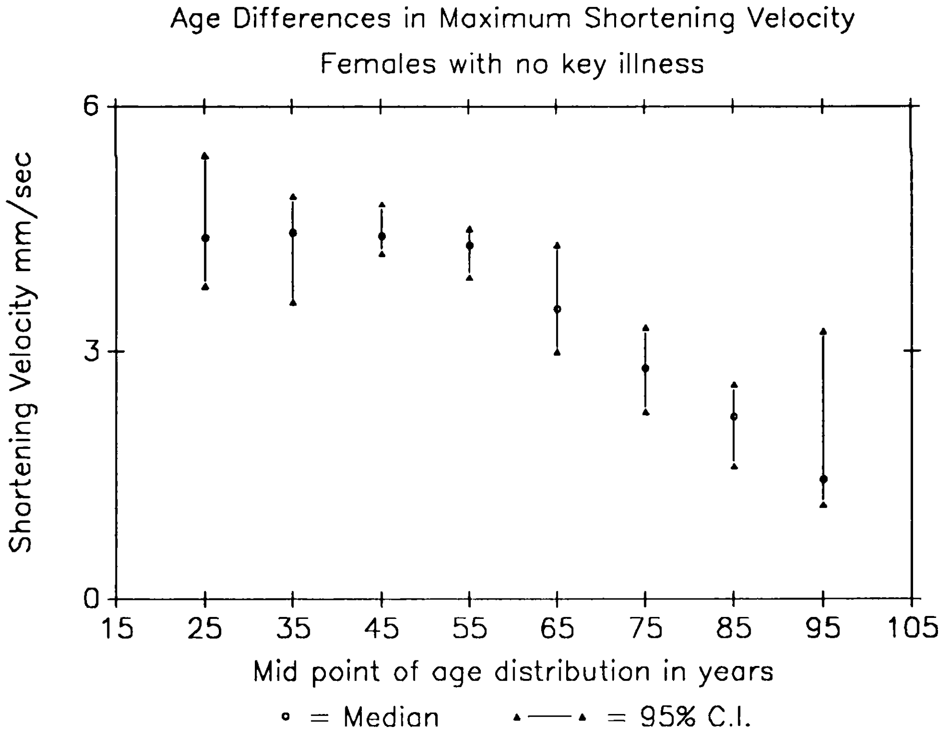


Figure 127

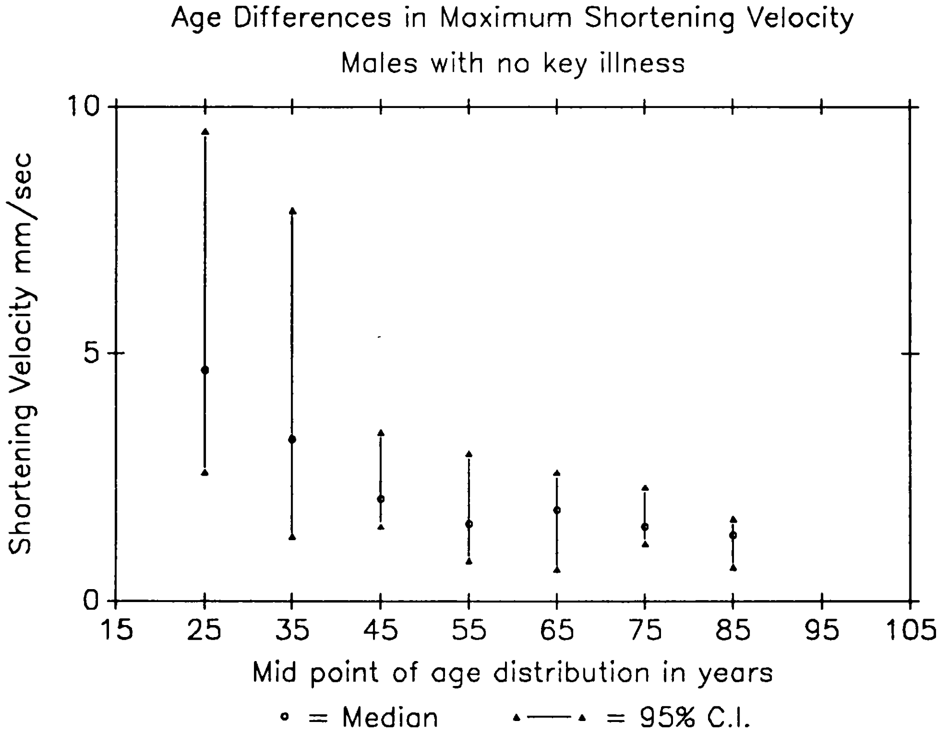


Figure 128

Voiding contractility WF

The maximum WF is normally manifest as a rise in contractility at the end of micturition and reflects the pressure and velocity of shortening generated by the terminal contraction of the series elastic element. Figures 129 and 130 show the age relationship of this parameter for females and males, the fall noted among men is not statistically significant (Females H=94.45 df=7 p<0.001; males H=9.28 df=6 p=0.16).

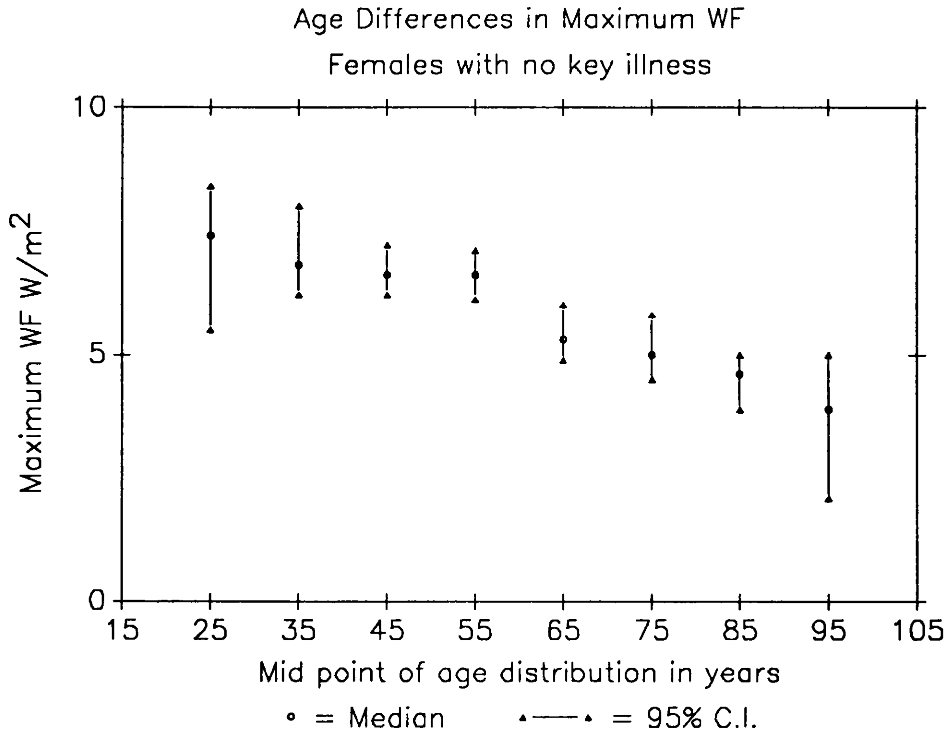


Figure 129

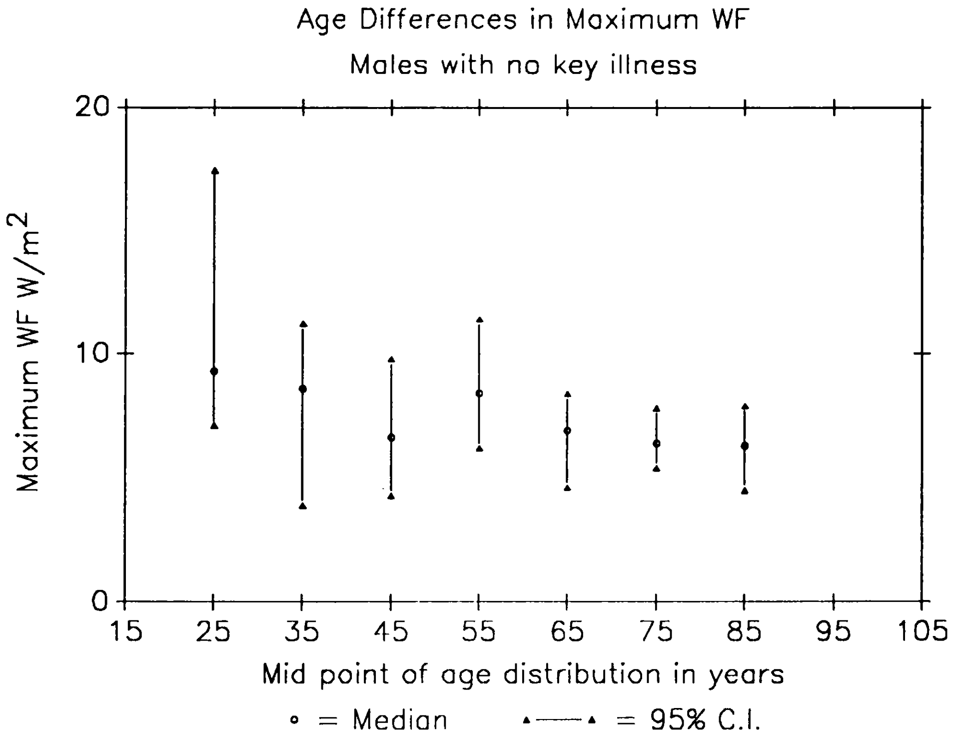


Figure 130

The mean WF reflects the contractility of the detrusor in terms of isometric and isotonic activity throughout voiding. Once again the median of this parameter is illustrated according to age group for females and males in figures 131 and 132. Men do not show an age related difference whereas women do (Females H=25.86 df=7 p=0.001; males H=6.17 df=6 p=0.405).

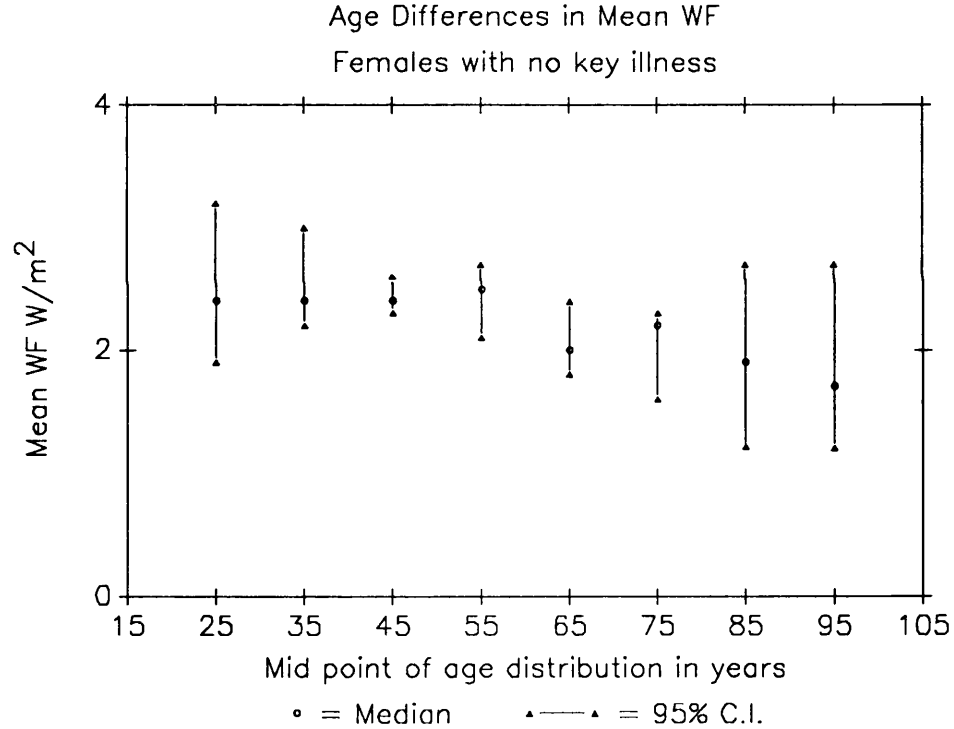

Age Differences in Mean WF
Females with no key illness

Figure 131

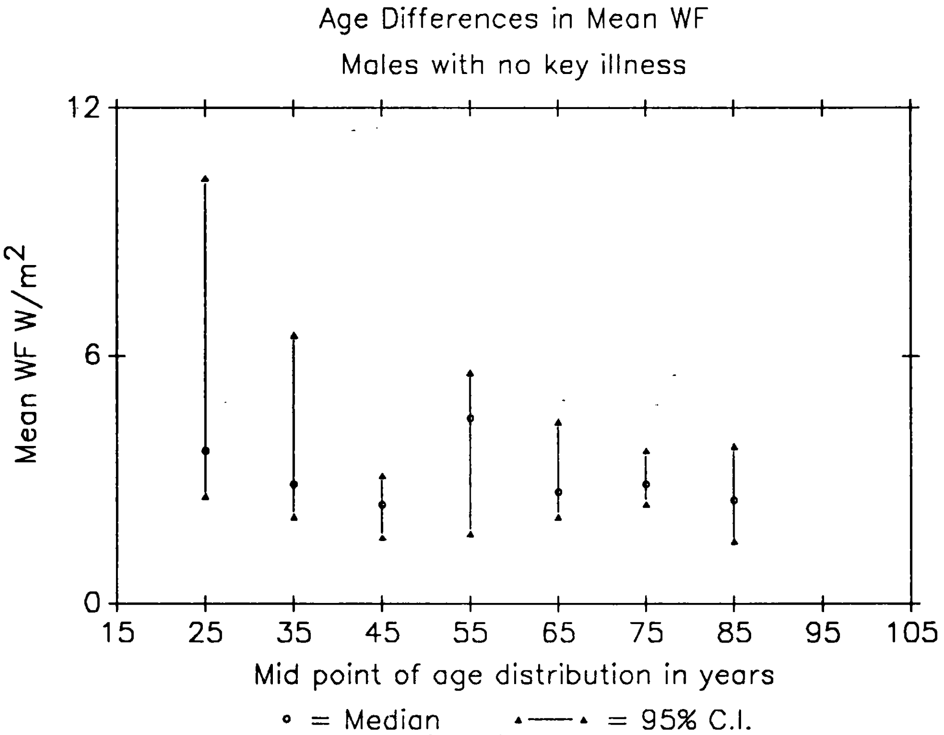


Figure 132

Standardised Q*

Standardised Q* is probably the best reflection of the isotonic detrusor activity available to us. This is illustrated, according to age group, in figures 133 and 134. Very little difference is noted amongst men whereas women show a very distinct progressive decline (females H=39.62 df=7 p<0.001; males H=11.08 df=6 p=0.137).

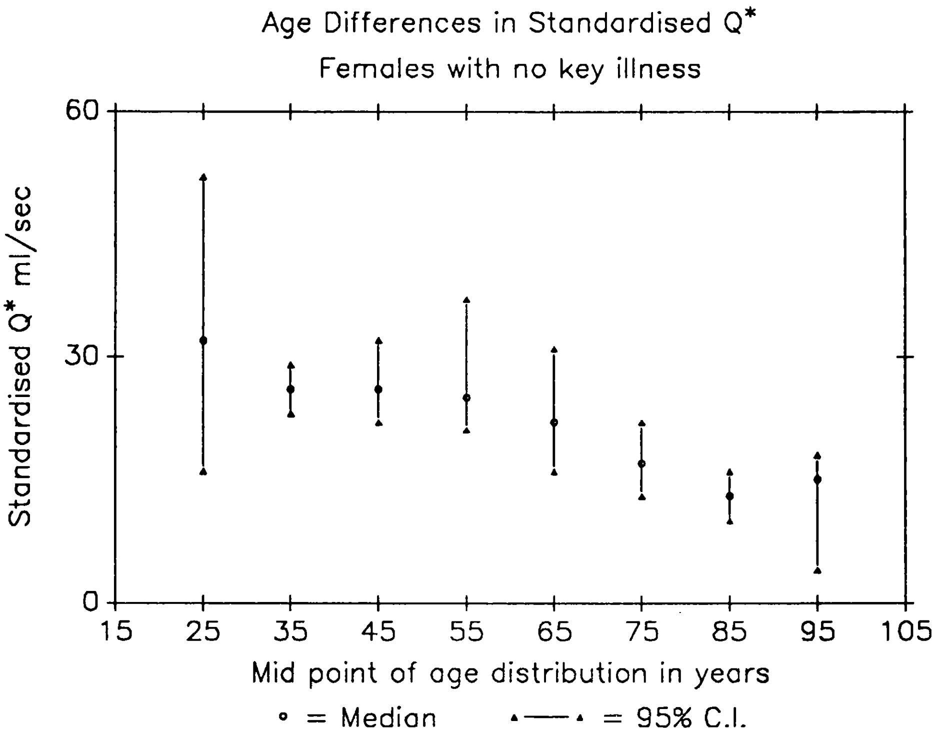


Figure 133

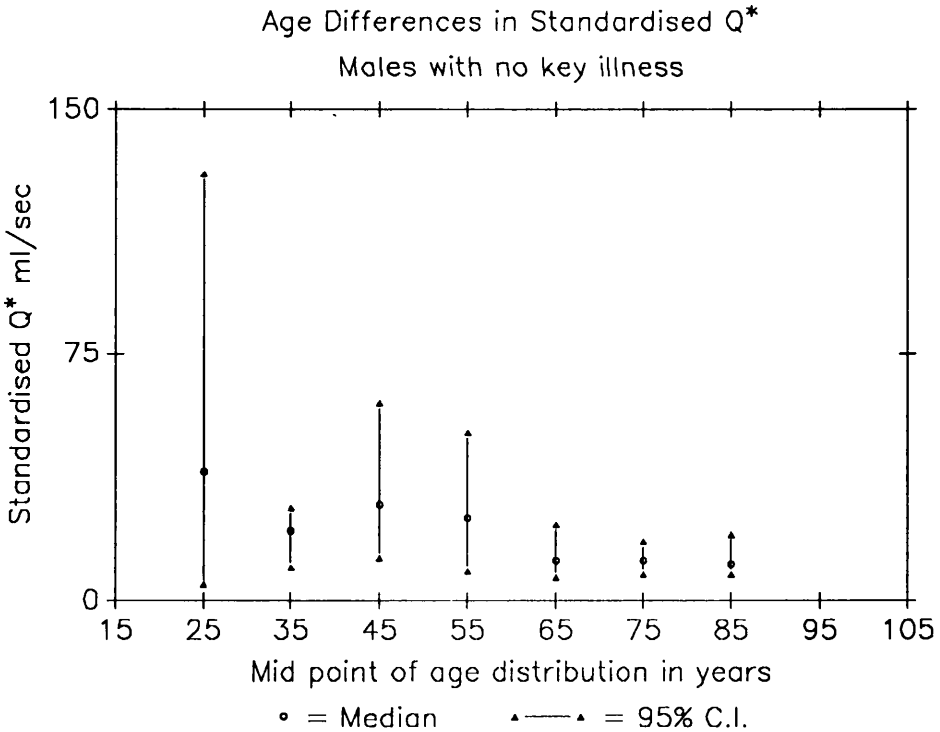


Figure 134

Voiding and the key illnesses

Figures 135 to 139 illustrate a number of the voiding measures in relation to the key illnesses. There are a number of statistically significant differences which are not clinically significant. I think that the differences of note are the low flow rates seen in women with Parkinson's disease and multiple sclerosis and the very low Standardised Q* found in women with Parkinson's disease which is less evident in men. The statistical analyses by disease group for these variables are shown below in table 30.

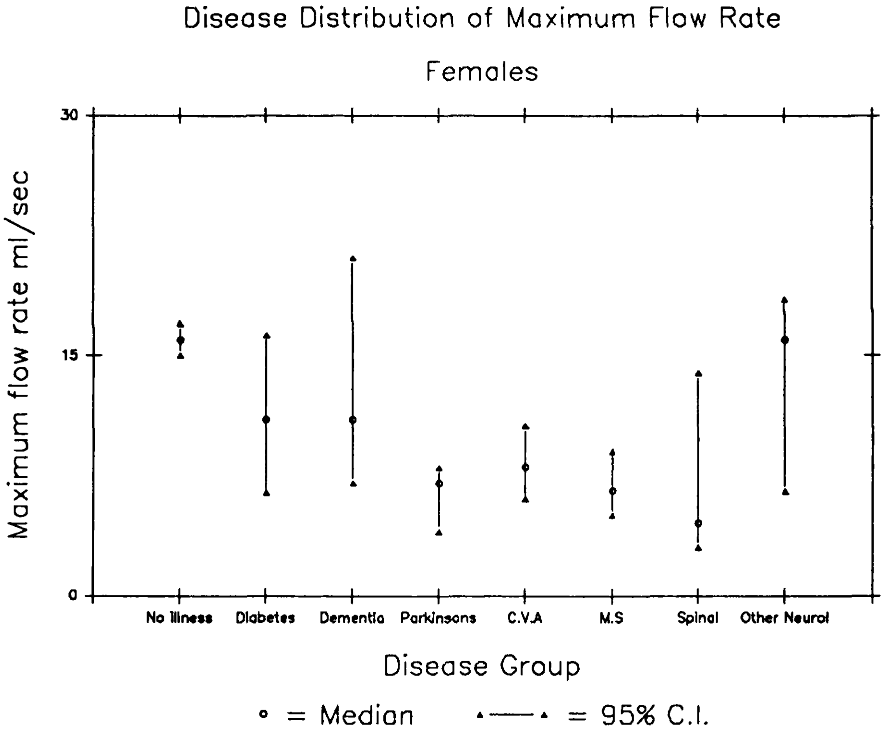


Figure 135

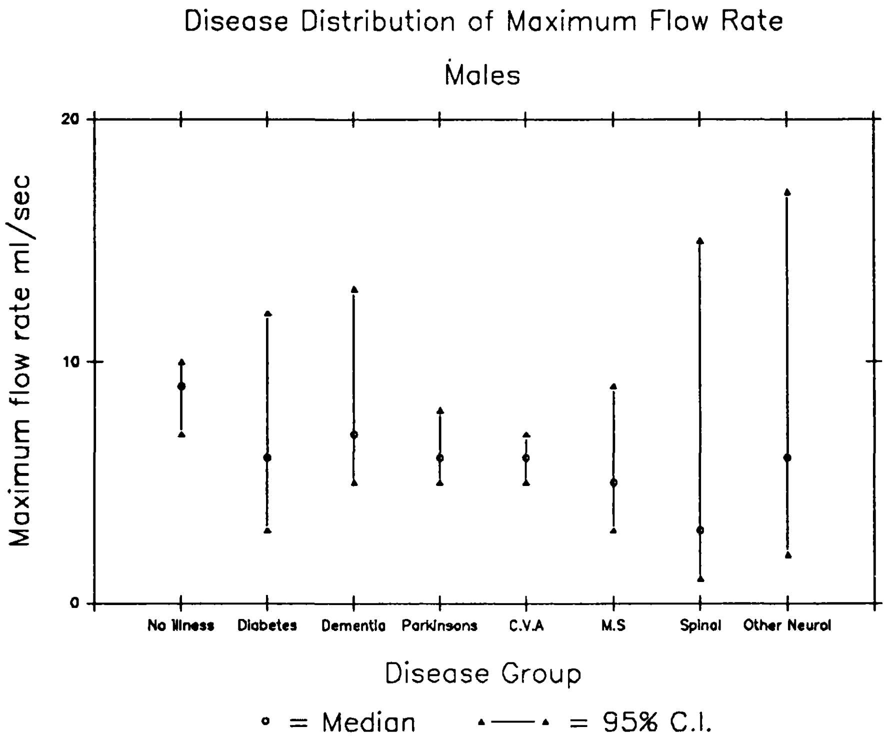


Figure 136

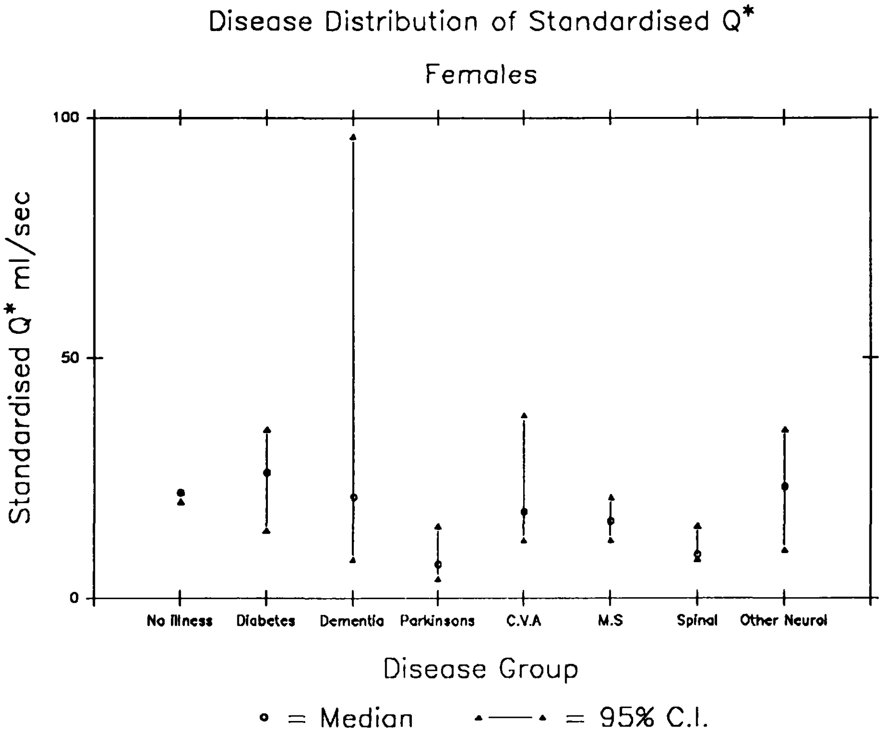


Figure 137

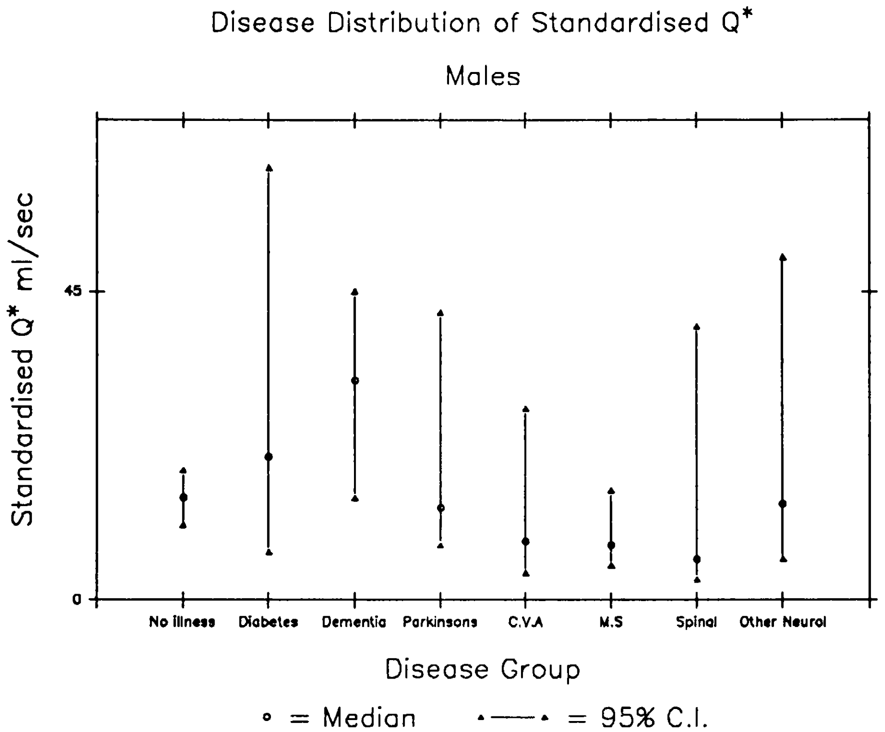


Figure 138

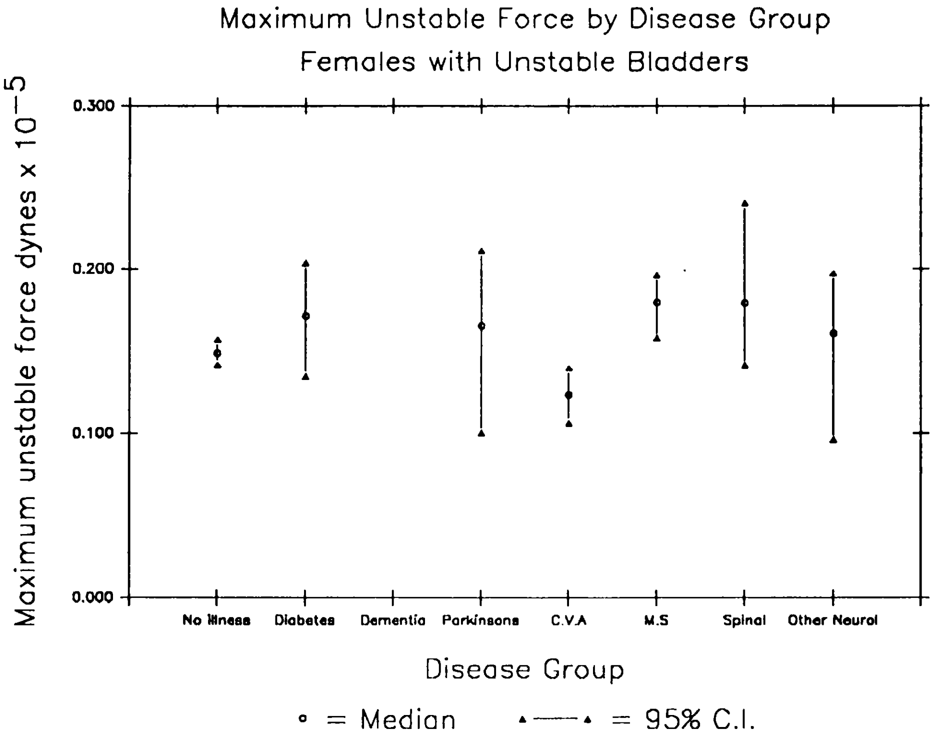


Figure 139

Table 30

Disease comparisons of voiding measures

Result	H	df	p
females maximum flow rate	78.76	7	<0.001
females detrusor pressure at maximum flow rate	20.73	7	0.004
females maximum voiding detrusor pressure	15.15	7	0.035
males maximum velocity of shortening	50.48	7	<0.001
females maximum WF	24.69	7	0.001
females mean WF	12.09	7	0.099
females standardised Q^*	20.48	7	0.005
males maximum flow rate	14.88	7	0.039
males Detrusor pressure at maximum flow rate	10.62	7	0.158
males maximum voiding detrusor pressure	10.81	7	0.148
males maximum velocity of circumference	5.6	7	0.579
males maximum WF	5.65	7	0.581
males mean WF	6.15	7	0.523
males standardised Q^*	11.08	7	0.137

Voiding and inadequate bladder emptying

I performed a careful analysis of the relationship of the various voiding measures to the completeness of emptying expressed as residual urine at the end of voiding as a proportion of bladder capacity. I could find no measure which was even remotely predictive of the eventual outcome of voiding and this agrees with the findings of other workers (personal communication Griffiths 1990). In addition, I found that the residual urine volume measured immediately prior to the test correlated somewhat weakly with the residual measured at the end of the test ($r=0.65$ $p<0.001$)

Analysis of the voiding pressure flow plots

The voiding pressure/flow plot traces the voiding phase of the urodynamic investigation by plotting the detrusor pressure against the voiding urinary flow rate. Ideally the pressure recording should be delayed by 0.8 secs with respect to the flow rate (Griffiths 1980) in order to correct for latency in the measuring apparatus. I was only able to achieve a delay of 1 second because my sample storage rate to disc was 1 Hertz. I collected interpretable pressure/flow plots on 1036 patients aged 20 and over. I used voiding studies in which the operator had clearly marked the instruction to start voiding. Some data to be included in this sample was lost because of accidental damage to three discs.

The age, sex and key illness distribution of the patients who were included in this sample are shown in tables 31 and 32 in appendix A.

I printed out the traces and then classified them into groups according to appearance. I achieved this by running the classification three times building up a system which coped with the data available. I was able in consequence, to achieve the following groupings.

(1) Patients showing a flat trace indicating an elastic urethra but varying contraction velocities (eg figure 140).

(2) Patients showing a flat trace with isotonic activity but superimposed distortions due to intermittent urethral narrowing consequent on movement and kinking of the urethra (eg figure 141).

(3) Patients with well established flow but gross distortion of the trace associated with movement of the urethra and abdominal straining. Voiding occurring through a sequence of poorly sustained attempts. (eg figure 142).

(4) Patients with low pressures and low flows with poorly developed isotonic and isometric activity (eg figure 143).

(5) Patients with higher pressures but low flows and traces indicative of obstruction and poorly sustained contractions (eg figure 144).

(6) Patients showing evidence of good contractility with reduced urethral compliance (eg figure 145).

(7) Patients demonstrating evidence of reducing contractility during the voiding phase in assocation with poorly coordinated sphincter activity (eg figure 146)

(8) Patients with well established contractility but premature sphincter closure (eg figure 147).

I tabulated the results of this classification and found that there was no clear difference in the patterns of distribution between age groups and disease groups, other than those which were expected from the analysis of the voiding parameters already discussed. The curve forms associated with very elastic urethras were certainly absent amongst the elderly who also demonstrated lower velocity and contractility within each classification. It would be quite impossible to identify a person's general pathophysiological state by simple pattern recognition of the voiding pressure/flow plot only because no pattern is typical of a specific group. However, in clinical practice I do find these traces helpful in describing in detail the characteristics of voiding for individual patients.

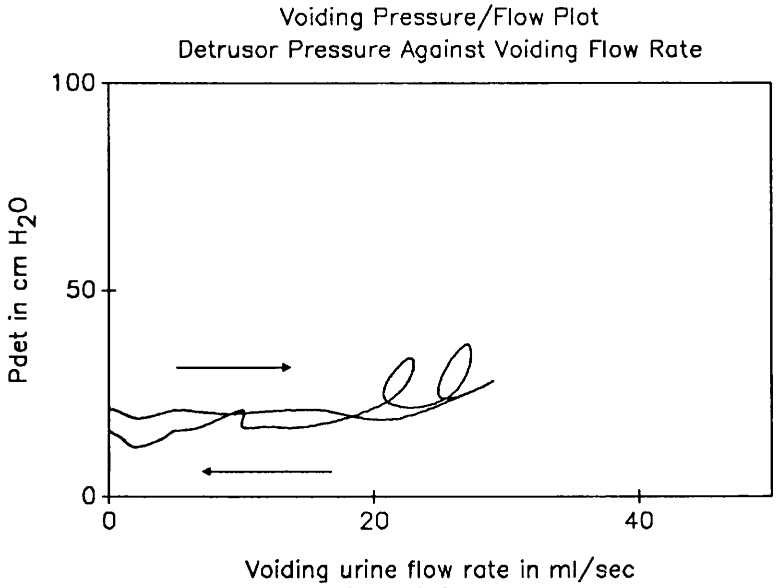


Figure 140

A trace taken from a patient with an elastic urethra. There is some slight interference due minor urethral kinking. This is a normal trace. Differences in bladder speed will influence the maximum flow rate.

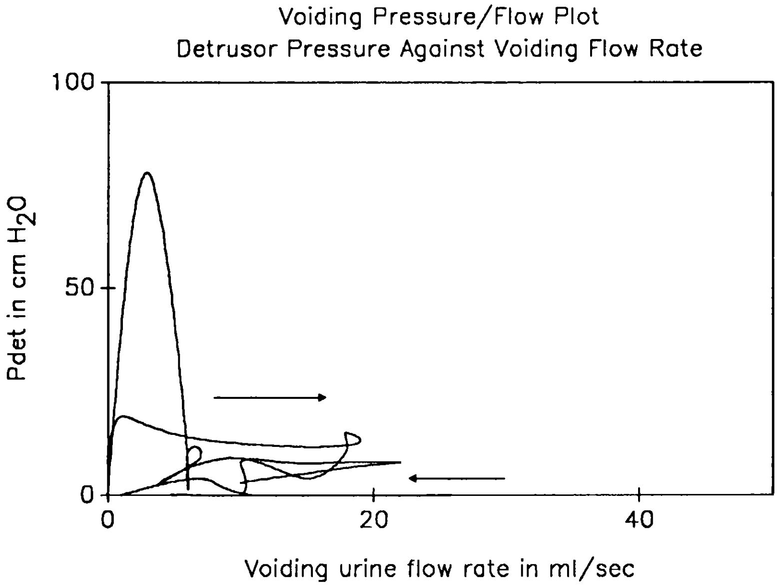


Figure 141

The basic plot is a flat trace similar to figure 140 but there is very marked distortion caused by descent of the bladder neck and urethral kining during voiding.

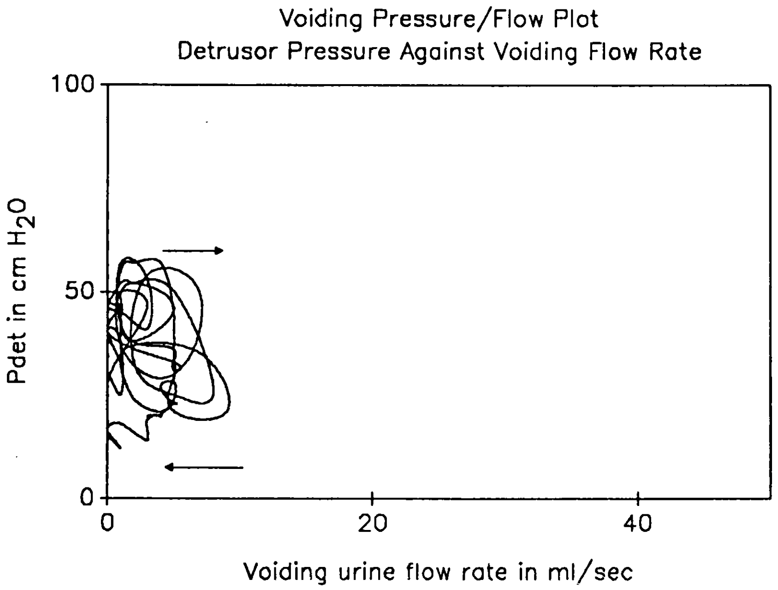


Figure 142

There is obstruction due to descent of the bladder neck and urethral kinking. In addition the detrusor contraction is poorly sustained and voiding is achieved by a series of attempts assisted by abdominal straining. The shortening velocity is reduced.

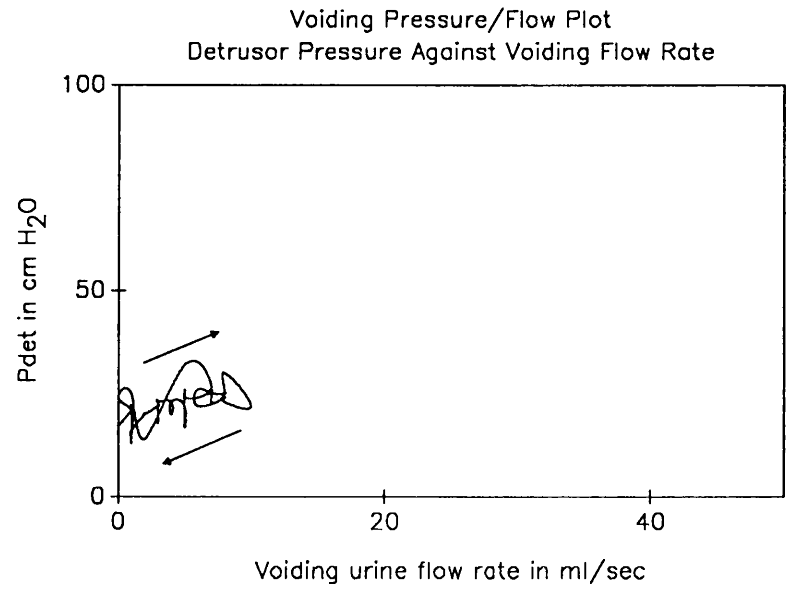


Figure 143

The detrusor is rather underactive and of low velocity. A very poor flow rate is achieved but the voiding pressures are not elevated. This is a common occurence in late life.

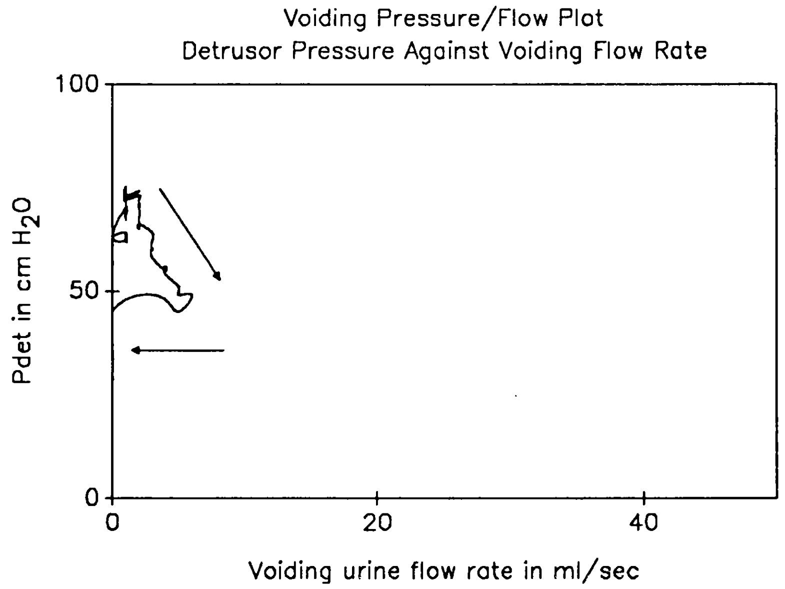


Figure 144

This shows an obstructed void. Some of the resistance to flow is caused by sphincteric activity at the onset. The contraction is poorly sustained and there is a rapid decay in the detrusor pressure. This was taken from a man with a prostatic obstruction.

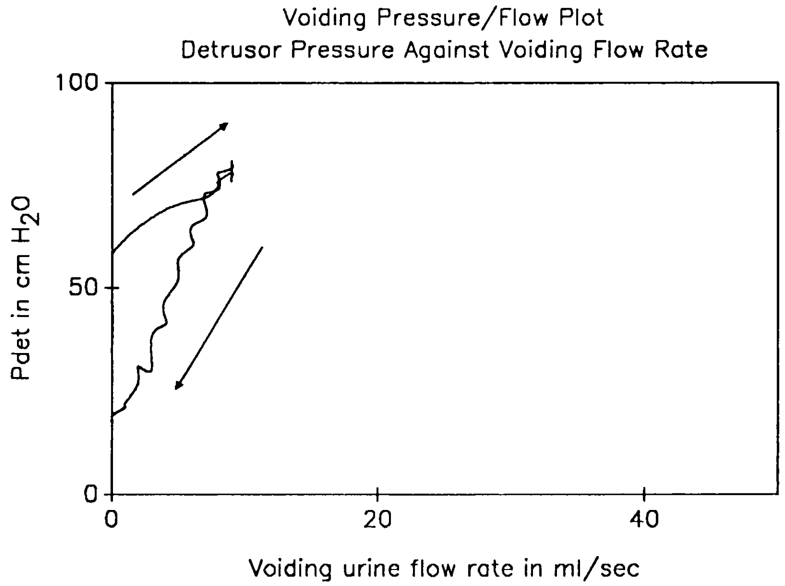


Figure 145

This also shows an obstruction caused by a urethra with low compliance. The very marked difference in the p_{mo} at the beginning and end of voiding suggests that the obstrtuction was due to sphincteric activity which reduced at the end of voiding.

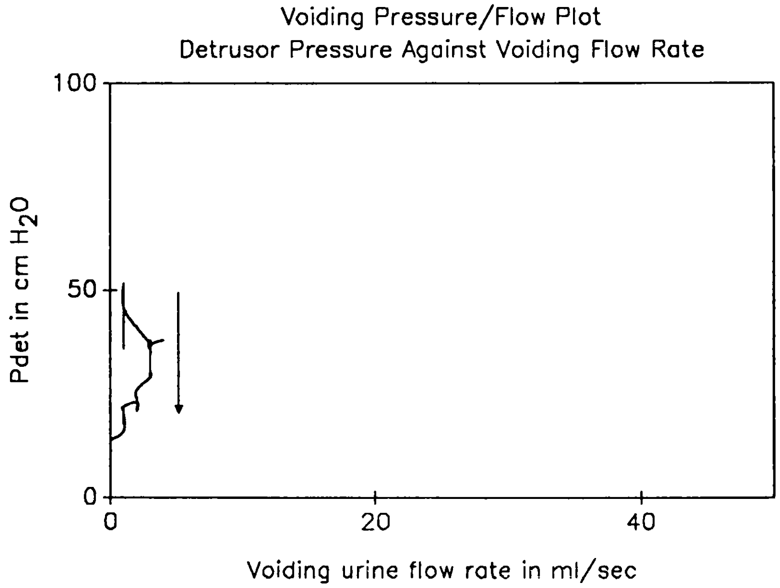


Figure 146

The contraction is poorly sustained and decays rapidly after the onset of voiding. The sphincter opening was delayed and continued after the onset of micturition.

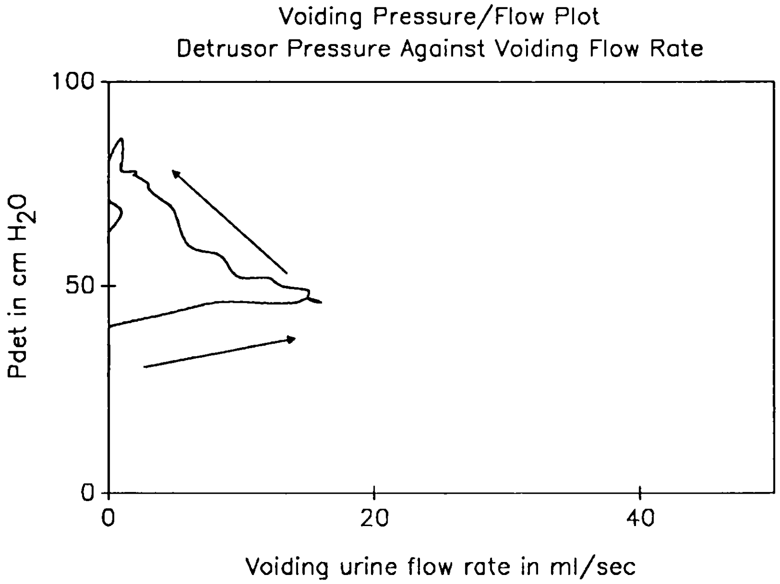


Figure 147

In this situation the voiding was terminated prematurely by a sphincter contraction whilst the detrusor contraction was well sustained.

One important point is illustrated by a sub-analysis. I measured the detrusor pressure immediately before sphincter opening, ie 2 seconds prior to first measuring a flow rate. I called this the **prior pressure** and I subtracted it from the detrusor pressure at maximum flow. In most cases, especially amongst women, there is a slight rise in pressure between the two points, see figure 140. There will be a fall if the detrusor contraction fails (figure 143), if the urethra is particularly distensible or if sphincter opening is slightly delayed. Figure 148 shows the proportions of females in different age groups showing a fall in pressure, no change or a rise in pressure. The older people more often show a fall (H=23.06 df=7 p<0.001). A similar difference was not evident amongst men in whom just over 50% demonstrated a rise. Figures 149 and 150 show the proportions demonstrating these changes according to disease groups for males and females. In both sexes, patients with multiple sclerosis show a predilection for a fall as do men with cerebrovascular disease and women with spinal injury (Females Chisq= 29.88 df=7 p<0.001; males Chisq=10.54 df=6 p=0.05).

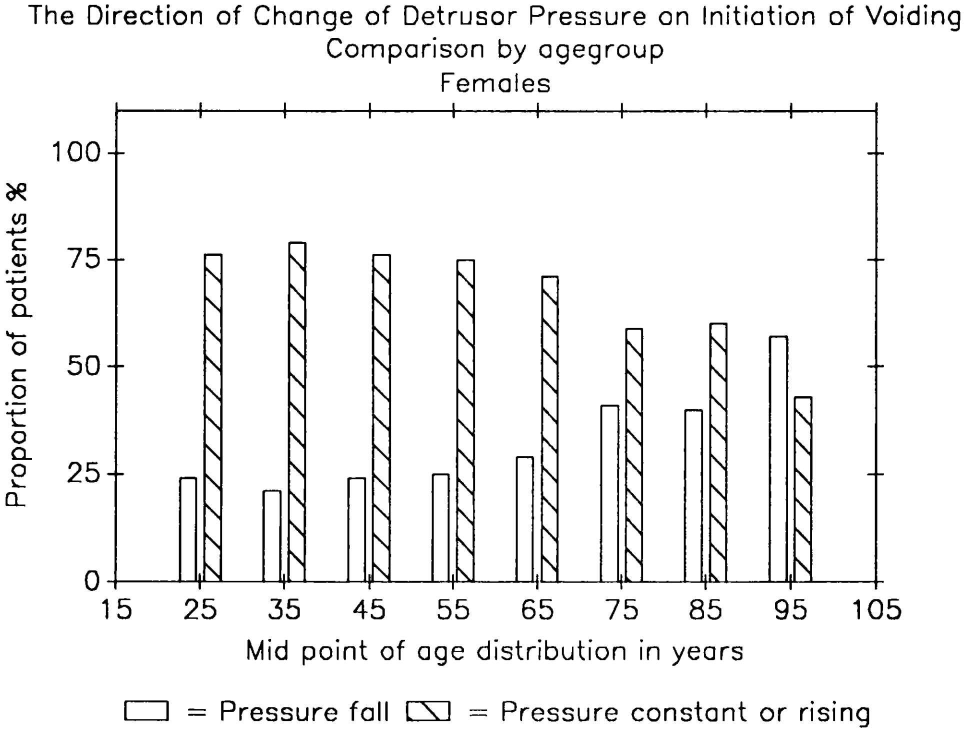


Figure 148

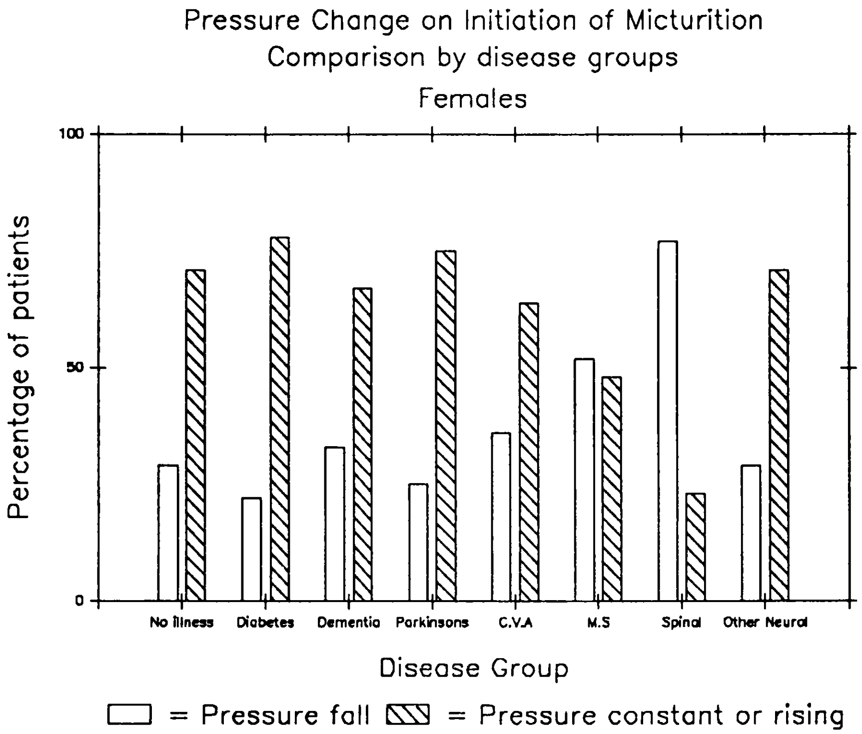


Figure 149

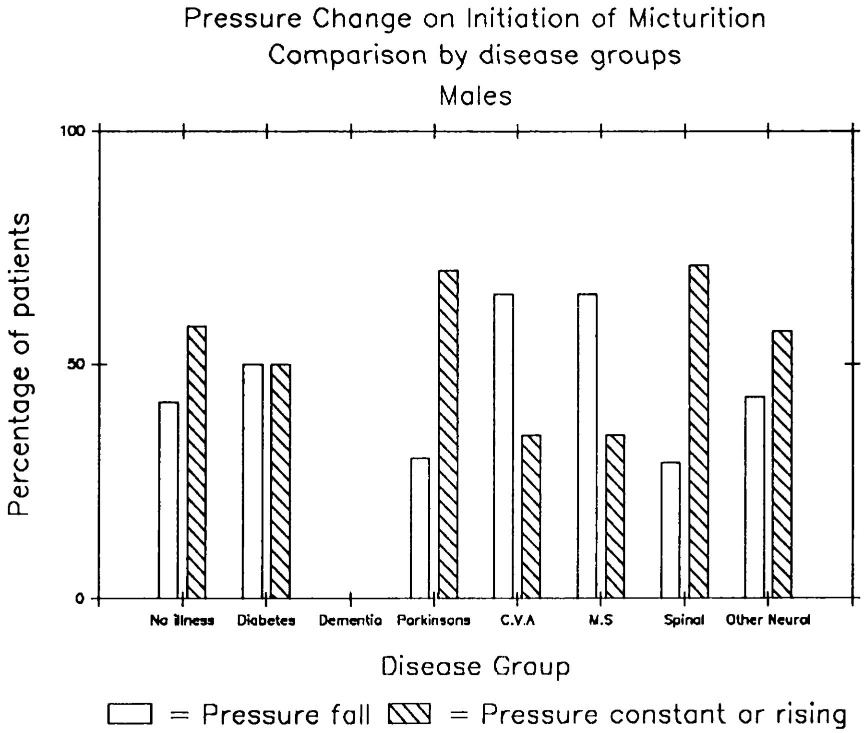


Figure 150

In figures 151 and 152 I illustrate the median change in pressure by age group for men and women with no key illness. Older women demonstrate a reduction in the rise, men show no difference between age groups (Females H=30.25 df=7 p<0.001; males H=6.14 df=6 p=0.408).

A majority of patients with evidence of an obstruction demonstrated an initial rise in the pressure up to maximum flow but 80% of these patients showed problems with maintaining the detrusor pressure during voiding and usually accomplished this through a sequence of poorly sustained contractions. These data suggest that a detrusor confronted with an obstruction has problems in sustaining the contraction.

could not

could not

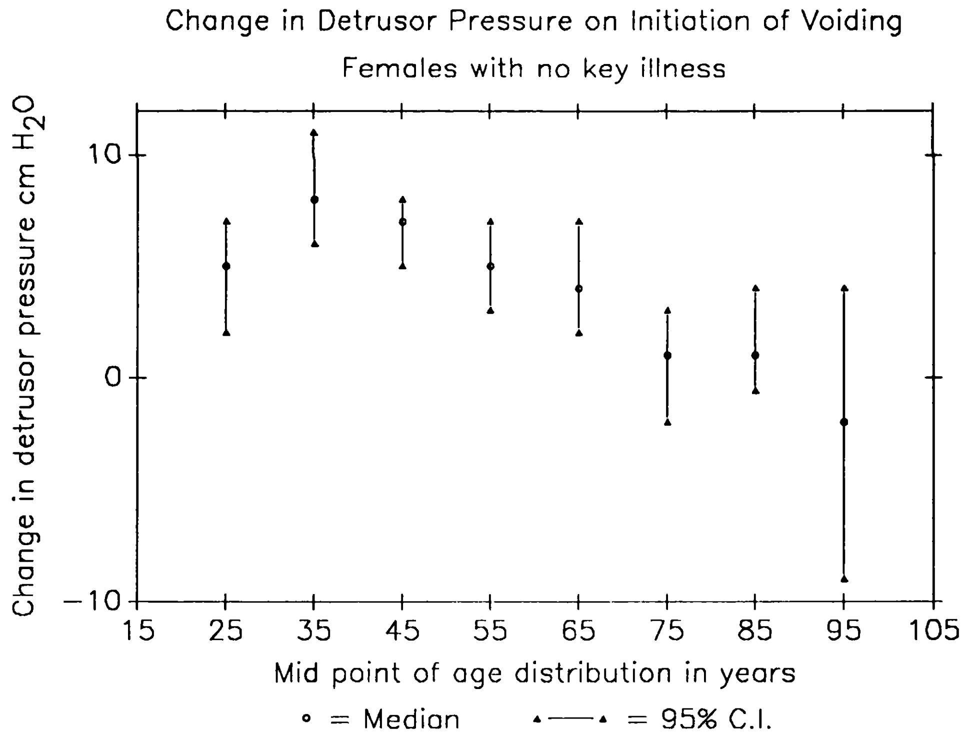


Figure 151

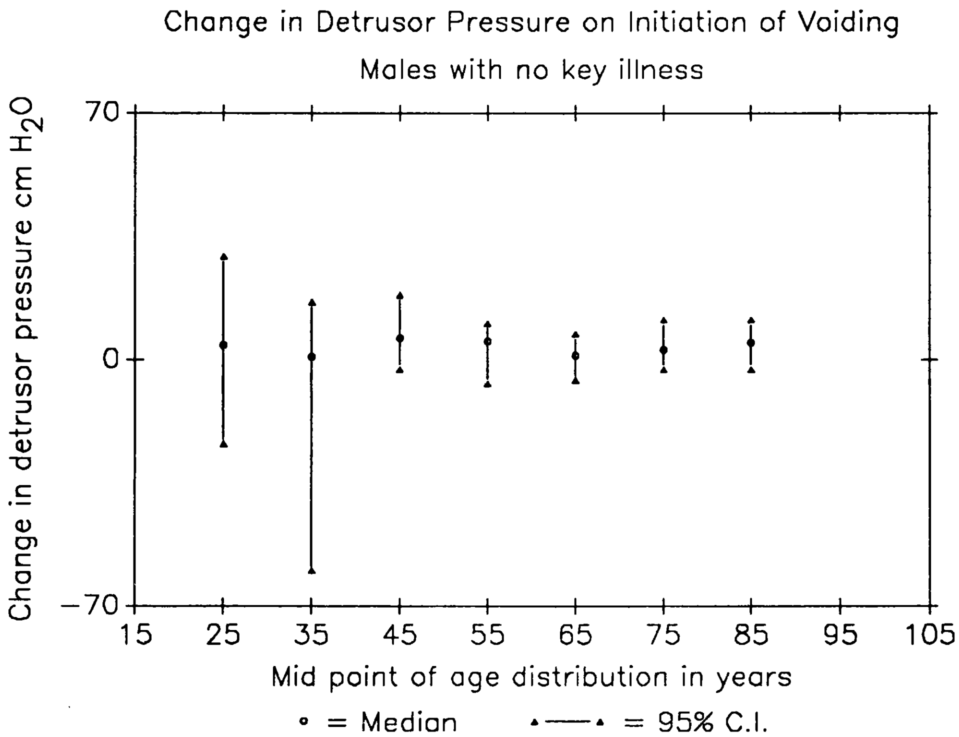


Figure 152

Summary of the analysis of the voiding phase

The elderly in both sexes produced lower flow rates which were associated with voiding inadequacy and incomplete bladder emptying. Elderly women and elderly men both had lower values of the maximum speed of shortening of the bladder circumference, which suggests a stiffening of the series elastic element. The velocity of detrusor muscle shortening expressed as standardised Q^* was lower amongst elderly women but men, who had lower values anyway, did not show this age-related change. Similarly, elderly women demonstrated a reduction in detrusor contractility expressed as WF which elderly men did not demonstrate with males as a whole having higher WF values. Elderly women differed from their younger counterparts by demonstrating a much greater tendency for the detrusor contraction to fail shortly after the initiation of voiding, with voiding frequently occuring by means of a series of poorly sustained efforts. Although similar findings occured amongst men there was no age associated difference. The graphical interpretation of the maximum flow and detrusor pressure at that point, for both sexes, showed a shift towards zones of lower contracitility in the elderly. The shift of elderly women away from the unobstructed zone towards the equivocal zone was accompanied by the absence of voiding pressure/flow plots indicating high urethral elasticity.

Female patients with Parkinson's disease were noted to have markedly slow bladders. Patients with multiple sclerosis frequently showed evidence of poorly sustained voiding contractions as did men with cerebrovascular disease.

The demonstration of totally inactive bladders

In both sexes there is a very small subgroup of patients who demonstrate no detrusor activity during filling and then failed to void. These people will not have been included in the analysis conducted so far because their data were inappropriate for inclusion. There were 23 females and 7 males who showed this feature. In both sexes they were evenly distributed over the age groups and disease groups.

The demonstration of genuine stress incontinence

At the end of the filling study it is normal practice to ask the patient to stand and to cough while the operator examines the urethra for urinary leakage. Often unstable contractions preclude this operation. I found no age related difference in the incidence of genuine stress incontinence amongst women of different age groups. The incidence ranged between 7 and 15%. The symptom of stress incontinence proved remarkably common (around 61% of female patients) with no age related differences and 64% of women complaining of stress incontinence had detrusor instability. These are well recognised phenomena. Although the incidence of vaginal atrophy rose with age (figure 153, Chisq=226.34 df=7 p<0.001) the incidence of anterior vaginal wall prolapse decreased amongst the elderly, figure 154 (Chisq=40.44 df=7 p<0.001).

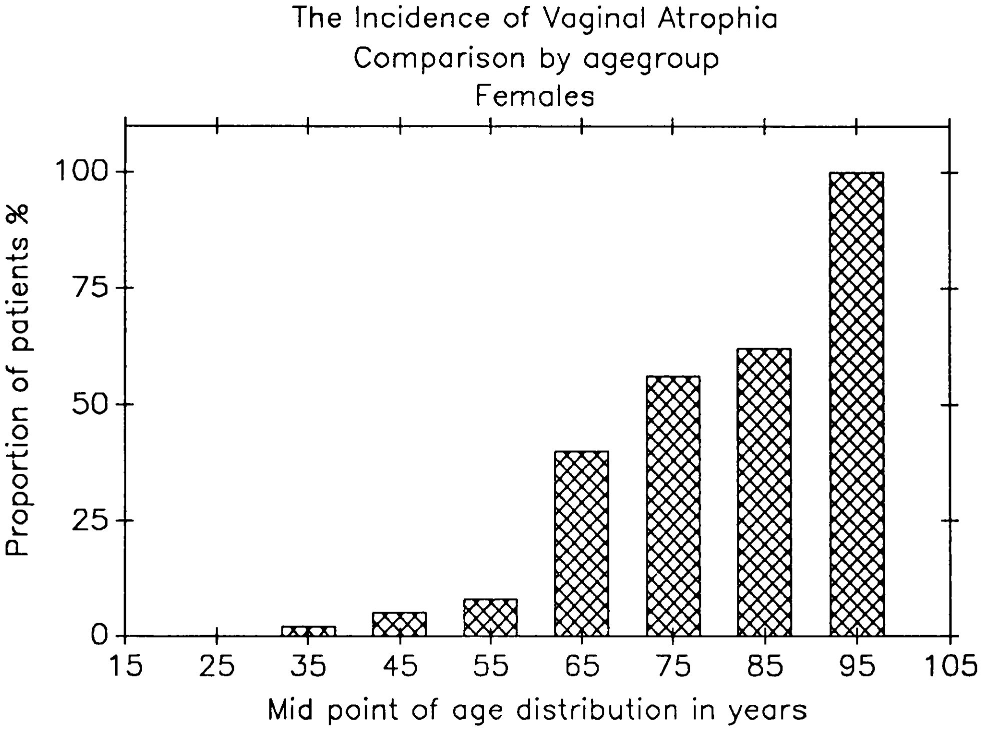


Figure 153

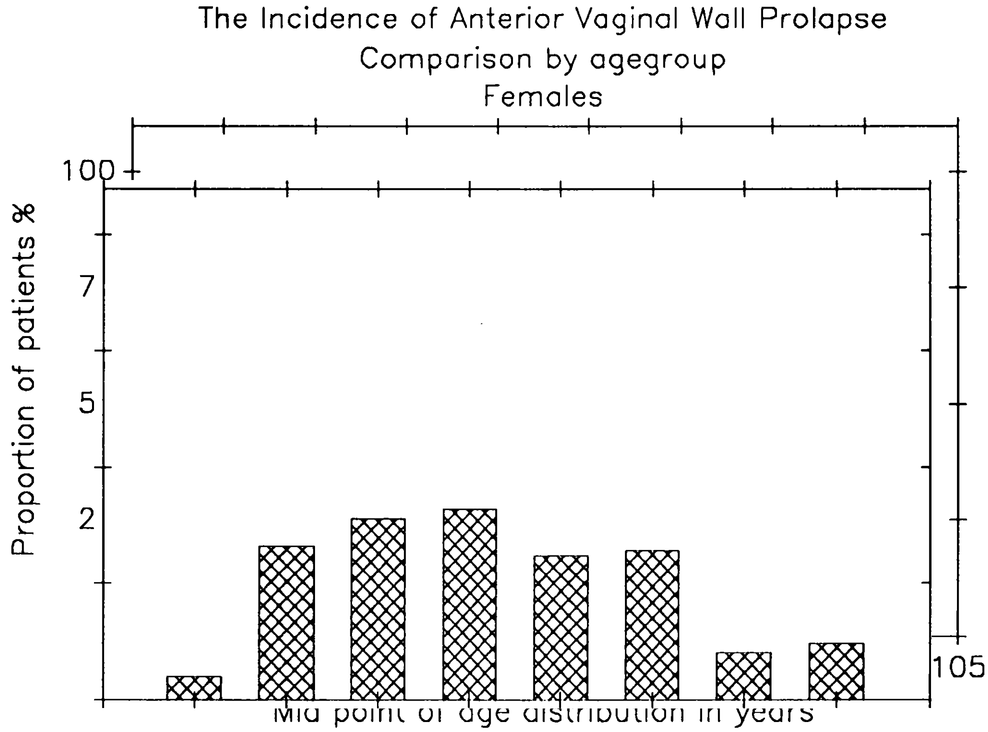


Figure 154

The outcome measures on the treatment of detrusor instability

I collected data on 275 patients, who were treated for detrusor instability, which described their course and response to treatment. The characteristics of this sample are tabled below.

Table 33

Patients on whom treatment data as collected

Age group	**Number**
0	2
10	1
20	11
30	33
40	49
50	42
60	42
70	61
80	32
90	2

Sex	**Number**
Females	236
Males	39

Table 34

Patients with none or one key illness and treatment data

Key Illness	**Number**
No illness	177
Diabetes	10
Dementia	2
Parkinson's	6
Cerebrovascular disease	13
Multiple Sclerosis	51
Spinal disease	6
Other Neurological	5

I obtained data on the following:

1. The change in incontinence: Worse, no change, improvement but not cured, cured.

2. The number of attendances before the conclusion of therapy.

3. The daytime frequency and nocturia at the start and at the end of treatment.

I illustrate the grading of the change in incontinence in figure 155. I analysed the data according to age-group (age either side of 75 years) sex, bladder capacity, residual urine, instability variable PC1 and instability variable PC2. There was no evidence of a difference in the measures between any of the groupings. The median number of clinic attendances was 4 (95% CI 4,5). The median nocturia at the end of treatment was 0 (95% CI 0,1) and the median daytime frequency at the end of treatment was 5 (95% C.I. 4,6).

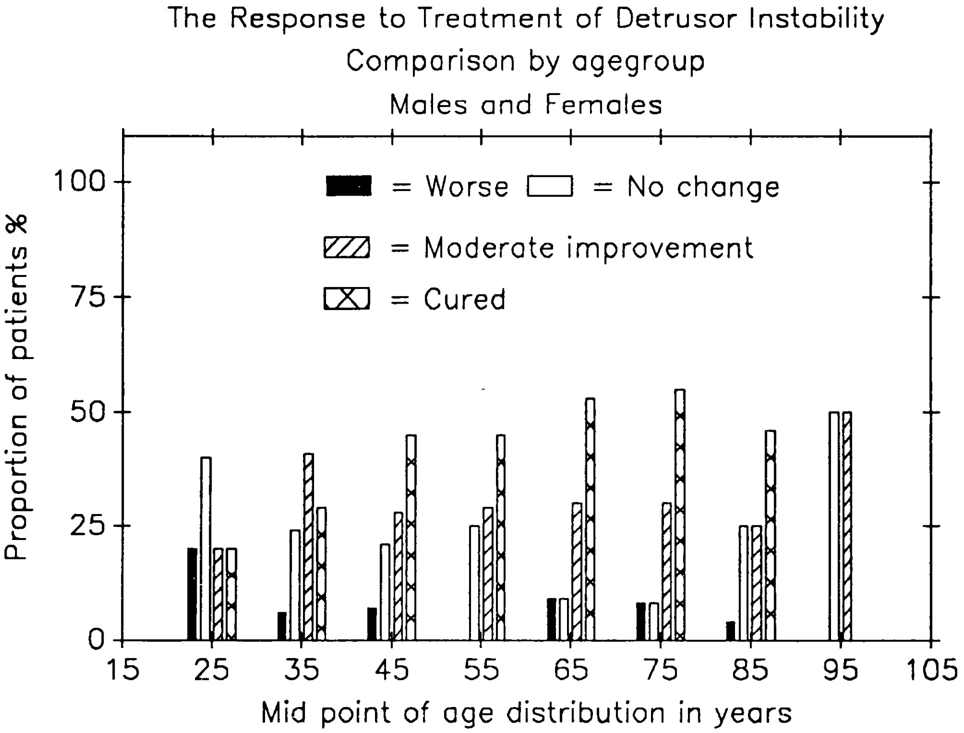

The Response to Treatment of Detrusor Instability
Comparison by agegroup
Males and Females
■ = Worse
☐ = No change
▨ = Moderate improvement
☒ = Cured
Proportion of patients %
0
25
50
75
100
15
25
35
45
55
65
75
85
95
105
Mid point of age distribution in years

Figure 155

Discussion and Conclusions

This study is the largest investigation of urodynamics in late life to date. In addition the analysis of the data using the mathematical techniques adopted has not been used at all. The main reason for this has been the lack of available computer resources for performing the calculations required. The developmental work associated with this thesis has resulted in a set of programmes which can be used successfully in clinical urodynamic departments so that other workers will have the opportunity to explore their findings in a similar way. I would hope that future work will improve our understanding, which remains far from complete.

There are problems with the methods which I have used and these should be taken into account when interpreting the results. The signal sampling and storing rates were low. This resulted from hardware limitations which have now been addressed by transferring the programmes to IBM compatible microprocessors but this was subsequent to the data collection for this thesis. Discussions with other workers (person~~ne~~l communications; van Mastrigt 1987, Schafer 1988, Griffiths 1990) lead me to believe that an optimum sampling rate during the urodynamic study would be 10 Hertz. An additional point is that the mathematical treatment of the voiding study assumes laminar flow (Griffiths 1980). In a certain circumstances, especially where there is a marked urethral obstruction, this assumption will not hold and we will find ourselves observing the more chaotic turbulent flow which is very difficult to treat mathematically. This in part explains why the interpretation of obstructive patterns is more difficult and why I disagree with Spangberg et al (1989) over the view that it is possible to identify different types of obstruction by fitting curves to the voiding pressure flow plot and calculating the urethral elasticity constants (Schafer 1989). Having said that, I am impressed by the very large number of voiding pressure/flow plots which are in concert with the mathematical models which have been proposed.

The description of the unstable bladder activity during filling by means of the principal components analysis variables PC1 and PC2 should be viewed with some caution and ought to be subject to further investigation. I have used mathematical tools to describe what I believe I am seeing by means of a small set of numbers. I do not claim to have discovered a new urodynamic measure which necessarily has clinical significance. As it happened PC1 was associated with symptom differences but I would wish to remain guarded about this point while awaiting the results of further research. What is important is this approach has allowed me to classify my data in an ordered manner whereas previously there was no suitable technique.

A striking aspect of my data is the difference between elderly women and elderly men. Men showed no evidence of age related changes in detrusor contractility. Older men certainly had lower flow rates and higher residual urine volumes as well as lower bladder capacities but it was not possible to explain their voiding difficulties by reduced isotonic or isometric activity. I appreciate that I had far smaller numbers of men in this study, but nevertheless achieved higher numbers of elderly males than others have studied elderly women (Hilton & Stanton 1981 and Castleden et al 1981). I suspect that the prostate gland has much to do with this. Prostate enlargement starts in the forties (McNeal 1983) and the bladder will alter in response to this, these changes are likely to be so important that they will overshadow age associated changes in late life such that my methods are unable to detect them. Unfortunately at the moment, data on the morphological changes in the bladder in late life do not take account of sex differences nor is there much data collected according to the decades of old age.

There are a number of findings which deserve emphasis. There was a very marked difference in detrusor behaviour between the filling phase and the voiding phase. I believe that I have been able to refute the belief that older people are unable to generate adequate detrusor pressures. I have shown that pure isometric detrusor activity amongst the elderly is as effective as in the young. The problems with detrusor contractility occur during voiding where there is a simultaneous breakdown in a number of components. Isotonic detrusor activity is markedly reduced and in addition, during voiding, isometric detrusor activity also seems to be reduced. In many cases, elderly people fail to sustain the detrusor contraction adequately until the bladder is emptied. The increased energy requirements for an isotonic muscle contraction (the Fenn effect) may explain the low speeds of contraction shown by the elderly but we still have to account for the problems in sustaining micturition. I think that there are three possible explanations of the latter difficulty. Firstly, the relative slowness of shortening may prevent the detrusor from keeping up with the momentum of voiding with the result that the pressure in the bladder falls and voiding is interrupted as the pressure drops below the pressure of meatal opening (p_{mo}). Secondly, it may be that changes in the lateral reticulo-spinal tract (Fletcher & Bradley 1978) result in a neural failure to sustain micturition once it has commenced. Thirdly, changes in the medial reticulo-spinal tract (Fletcher & Bradley 1978) may result in a failure to coordinate sphincter relaxation with a detrusor contraction, this being termed "detrusor sphincter dyssynergia" (Griffiths 1983). This situation results in a contracting sphincter at the beginning of voiding causing obstruction. I have found that 80% of patients with obstructive voiding patterns, whatever the cause, showed a failure to sustain the detrusor contraction, and this is in agreement with the osbervations of other workers (Griffiths 1983).

Evidence for a strong neurological role in the age associated changes is shown by the way neurological diseases reproduced all of the changes that I noted in my elderly patients; higher rates of instability, similar values for PC1 and PC2, small bladder capacities in Parkinson's disease and cerebrovascular disease, high residual urine volumes in multiple sclerosis and dementia, reduced bladder speeds in Parkinson's disease. The fact that elderly experience degenerative changes in the central nervous system is well recognised and we should expect secondary effects on the lower urinary tract (Brocklehurst and Dillane 1966a, 1966b).

The menopausal changes which occur in the lower urinary tract seem to be affecting elderly women. Oestrogen withdrawal results in a reduction in the elastin in the urethra in favour of collagen (Hilton & Varam 1984). I noted a marked absence of urethral pressure/flow plots compatible with good urethral elasticity in my elderly patients. In addition I noted a tendency for elderly women to produce greater numbers of studies classed as equivocal rather than unobstructed. These observations indicate an increased urethral resistance to flow during voiding in elderly women. Certainly, Brocklehurst (1972) was able to demonstrate obstructive fibrosis of the bladder neck in elderly women. The lower incidence of anterior vaginal wall prolapse amongst my elderly women, which complements an observation by Hilton and Stanton (1981) may be due to a reduction in pelvic elasticity leading to a better fixation of the anterior pelvic organs. Whatever the cause of the voiding difficulties amongst elderly women, it may be that are to their advantage, especially if they suffer from detrusor instability.

Although the symptom of stress incontinence was common amongst women of all age groups, the demonstration of genuine stress incontinence was less common and showed no age-related differences. Elderly women with genuine stress incontinence had a higher incidence of detrusor instability as would be expected. It would seem therefore, that the postmenopausal changes affecting elderly women do not result in an increased incidence of sphincter incompetence but more the opposite phenomenon of an increased urethral resistance.

My findings make it difficult to agree with other workers (Brocklehurst & Dillane 1966b, Hilton & Stanton 1981, Castleden et al 1981, Resnick a/ & Yall/1987) that it is possible to classify elderly patients, with incontinence into distinct groups. I have found that the overwhelming majority have unstable bladders and that this diagnosis must be qualified by descriptions of voiding contractility and completeness of emptying. These qualifications are not clearly separated and form a continuous spectrum.

I was surprised but nevertheless pleased to note that age, bladder capacity and the vigour of detrusor activity did not seem to affect the outcome as far as treatment was concerned. These observations are at variance with those made by other workers (Frewen 1982, Castleden et al 1981). My interpretation should be qualified as I studied the treatment in patients who were relatively ambulant and able to cooperate with bladder retraining and medication.

Although the mathematical treatment of urodynamic data is quite difficult to understand I do not think that should necessarily stop these principles being adopted more widely. The software which was developed for this project will calculate the variables automatically at the end of a standard urodynamic test. This means that an investigator will be able to describe the data more fully without necessarily understanding the mathematical processes. In my teaching, I have noted that people have great difficulties over the interpretation of voiding pressure/flow plots. My own experience is that the computerised mathematical model which I have created is of enormous help in coming to an understanding and I would hope will be used widely as a teaching aid.

I would summarise my thesis with the following statement. A purely mechanical analysis of bladder function shows that there are urodynamic changes associated with aging in patients of both sexes with lower urinary tract symptoms. Women show more obvious age related changes than men. The elderly have lower bladder capacities and many of them empty incompletely. The incidence of detrusor instability is high in the elderly of both sexes, but this often coincides with a more complicated voiding difficulty. The problems in emptying are caused by relative mixtures of the following elements, urethral obstruction, a marked reduction in detrusor isotonic activity and a failure in sustaining a voiding detrusor contraction. Although pure isometric activity does not appear to be reduced in the elderly there is an age-related reduction in this component during voiding. Despite the very much more complex nature of the urodynamics of late life, these do not seem to alter the prognosis for the treatment of detrusor instability. Many of the changes in bladder behaviour in late life are comparable to changes observed in patients with cerebrovascular disease, Parkinson's disease, multiple sclerosis and dementia. *

My findings inevitably precipitate a wide variety of questions. The sex differences suggest that we ought to be able to i~~n~~dentify different morphologies in the lower urinary tracts of old men and women. The differences in isotonic and isometric activity cause one to wonder whether there are pharmacological implications of therapeutic significance. Are the contraction velocity changes of neurological orig~~e~~n or are there specific changes in the detrusor muscle? It will only be possible to attempt to answer these enigmas when we have collected relevant data on individuals whose urodynamics have been analysed in the way that I have described. Before that occurs the approaches used in this thesis will need to attain wider acceptance.

Appendix A

Table 9

Patients from groups A & B with no key illness

Age group (decade)	Females	Males
20	73	15
30	174	21
40	311	25
50	249	49
60	196	80
70	208	73
80	159	54
90	21	7

Table 10

Patients from groups A & B with none or only one key illness

Disease group	Females	Males
No key illness	1391	324
Diabetes	69	19
Dementia	41	16
Parkinson's	28	36
Cerebrovascular	67	58
Multiple sclerosis	107	35
Spinal injury	26	17
Other neurological	48	25

Table 11

Patients from groups A & B with unstable bladders and no key illness

Age group (decade)	**Females**	**Males**
20	39	13
30	98	12
40	162	17
50	150	37
60	128	63
70	168	69
80	123	51
90	19	7

Table 12

Patients from groups A & B with stable bladders and no key illness

Age group (decade)	Females	Males
20	34	2
30	76	9
40	149	8
50	99	12
60	68	17
70	40	4
80	36	3
90	2	0

Table 13

Patients from groups A & B with unstable bladders, none or one key illness

Disease group	Females	Males
No key illness	887	269
Diabetes	46	16
Dementia	36	16
Parkinson's	22	32
Cerebrovascular disease	57	54
Multiple sclerosis	85	33
Spinal injury	25	16
Other neurological	35	23

Table 14

Patients from groups A & Bwith data on the first sensation of bladder fullness and no key illness

Age group (decade)	**Females**	**Males**
20	60	10
30	137	10
40	271	14
50	197	19
60	150	37
70	151	38
80	107	29
90	12	2

Table 15

Patients from groups A & B with data on the first sensation of bladder fullness and none or one key illness

Disease group	Females	Males
No key illness	1085	159
Diabetes	52	12
Dementia	4	3
Parkinson's	15	13
Cerebrovascular disease	41	24
Multiple sclerosis	100	28
Spinal injury	14	10
Other neurological	35	17

Table 16

Patients from group B with unstable bladders and digitised analogue data and no key illness

Age group (decade)	Females	Males
20	35	10
30	77	6
40	143	10
50	122	14
60	98	26
70	119	37
80	79	26
90	10	2

Table 17

Patients from group Bwith unstable bladders and digitised analogue data and none or one key illness

Disease group	Females	Males
No key illness	683	131
Diabetes	32	11
Dementia	4	3
Parkinson's	10	12
Cerebrovascular disease	34	22
Multiple sclerosis	79	27
Spinal injury	14	9
Other neurological	26	15

Table 21

Patients from groups Ai & Bi with no key illness

Age group (decade)	Females	Males
20	55	11
30	143	17
40	261	19
50	199	39
60	148	55
70	147	52
80	111	33
90	10	1

Table 22

Patients from groups Ai & Bi with none or only one key illness

Disease group	Females	Males
No key illness	1074	227
Diabetes	54	14
Dementia	22	11
Parkinson's	16	23
Cerebrovascular disease	47	37
Multiple sclerosis	68	23
Spinal injury	16	8
Other neurological	33	12

Table 26

Patients from groups Bi with no key illness and data sufficient to calculate additional voiding parameters.

Age group (decade)	**Females**	**Males**
20	45	7
30	112	8
40	226	12
50	159	14
60	115	27
70	118	28
80	80	21
90	6	0

Table 27

Patients from groups Bi with none or only one key illness and data sufficient to calculate additional voiding parameters.

Disease group	Females	Males
No key illness	861	117
Diabetes	36	8
Dementia	2	2
Parkinson's	8	9
Cerebrovascular disease	28	15
Multiple sclerosis	65	19
Spinal injury	11	7
Other neurological	22	6

Table 28

Patients from groups Ai & Bi with no key illness and data sufficient to calculate standardised Q^*.

Age group (decade)	Females	Males
20	42	6
30	112	13
40	204	13
50	155	23
60	124	40
70	121	47
80	99	24
90	9	1

Table 29

Patients from groups Ai & Bi with none or only one key illness and data sufficient to calculate standardised Q^*.

Disease group	Females	Males
No key illness	866	167
Diabetes	35	12
Dementia	11	9
Parkinson's	11	14
Cerebrovascular disease	37	24
Multiple sclerosis	63	21
Spinal injury	14	6
Other neurological	25	10

Table 31

Patients from groups Bi with no key illness whose voiding pressure/flow plots were sampled.

Age group (decade)	Females	Males
20	41	10
30	113	17
40	214	15
50	160	21
60	126	29
70	131	38
80	90	26
90	5	0

Table 32

Patients from groups Bi with none or only one key illness whose voiding pressure/flow plots were sampled.

Disease group	**Females**	**Males**
No key illness	720	99
Diabetes	29	6
Dementia	1	0
Parkinson's	6	7
Cerebrovascular disease	27	13
Multiple sclerosis	55	16
Spinal injury	9	5
Other neurological	19	6

Appendix B

The definition of the basic filling urodynamic variables

The first residual vloume is the measure of the volume of urine drained by means of a catheter from the patient's bladder after it has been emptied just prior to the urodynamic study.

The bladder volume at first sensation is the volume of saline infused at the point where the patient declares that he or she is experiencing the sensations whihc would normally cause him or her to seek a lavatory in order to urinate. I express it as the proportion (%) of the bladder capacity

The bladder capacity is the total volume of saline infused into the patient's bladder at a rate of 60 ml/min before an endpoint is reached. The endpoint may be: the point at which a patient is unable to tolerate any more filling; the point at which an uninhibited contraction of the detrusor precludes further filling; the point at which 500 ml has been infused into the bladder. The last point, very occasionally was exceeded as a result of operator error.

The maximum filling detrusor pressure is the maximum value of the equation (Bladder pressure - Rectal pressure = Detrusor pressure) recorded during the filling study. This pressure is used to diagnose detrusor instability according to the International Continence Society criteria described earlier.

The end filling pressure is the value of the equation (Bladder pressure - Rectal pressure = Detrusor pressure) recorded at the end of filling.

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