Urinary symptoms and Micromotions of bladder wall in chronic pelvic pain (CPP)

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Urinary symptoms and Micromotions of bladder wall
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Urinewegverschijnselen en Microbewegingen van de blaaswand
bij
chronische pelviene pijn (CPP)

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You can learn a lot yet know nothing,
if you have never known love

to Ricardo
with whom
life is fun to live

CONTENTS

ABBREVIATIONS AND DEFINITIONS

CPP	Chronic Pelvic Pain.
MMD episode	Time period during MMD session.
MM	Micromotion(s).
MM in situ	Changes in the *transversal* (local) distance between two electrodes pressed onto the mucous membrane of bladder wall, not caused by mechanical transmission from the abdomen, not necessarily reflected in bladder pressure and observed under conditions standardised for this study.
MM^+	Episode(s) of MM observed for ≥ 0.1 minute, whether or not accompanied by variations in p_{det}.
$MM^+ \& p_{det}^+$	Episode(s) of simultaneous occurrence of MM and variations in p_{det}.
$MM^+ \& p_{det}^-$	Episode(s) of MM only.
MM^-	No MM observed ($MM^- \& p_{det}^+$ and/ or $MM^- \& p_{det}^-$).
$MM^- \& p_{det}^+$	Episode(s) of variations in p_{det} only.
$MM^- \& p_{det}^-$	MMD episode(s) without MM and/ or p_{det}.
MMD	Micromotion detection.
p_{abd}	Episode(s) of variations in abdominal pressure.
Pain density	Number of reports of pain per time unit.
Pain & urge	Lower abdominal pain and urinary urgency, occurring simultaneously.
Pain + urge	Sum of the number of reports of lower abdominal pain and urinary urgency, whether or not occurring simultaneously.
p_{det}	Variations in detrusor pressure with peaks reaching ≥ 5 cm H20, duration ≥ 0.1 minute. $p_{det} = p_{ves} - p_{abd}$.

p_{det}^{+}	Episode(s) of p_{det}, whether or not accompanied by MM.
p_{det}^{+} ***group***	A group of women whose MMD recordings show at least one episode of p_{det} (MM^{+} & p_{det}^{+} and/ or MM^{-} & p_{det}^{+}).
p_{det}^{-}	No p_{det} episodes (MM^{+} & p_{det}^{-} and/ or MM^{-} & p_{det}^{-}).
p_{det}^{-} ***group***	A group of women whose MMD recordings show no p_{det} (MM^{+} & p_{det}^{-} and/ or MM^{-} & p_{det}^{-}).
Persistent pain	Pain for more than one minute, reported during MMD and whether or not fluctuating in intensity.
Persistent urge	Urge for more than one minute, reported during MMD and whether or not fluctuating in intensity.
p_{ves}	An episode of phasic variation(s) in intravesical pressure, measured within MMD probe and observed under conditions standardised for this study.
Transient pain	Sudden onset of pain, reported during MMD and lasting up to one minute, in conformity with signals from pain marker.
Transient urge	Sudden onset of urge, reported during MMD and lasting up to one minute, in conformity with verbal reports by patients.
Urge density	Number of reports of urge per time unit.
Urinary urgency	Almost irresistible need to void, accompanied by fear of involuntary loss of urine or fear of pain.

SECTION I

GENERAL INTRODUCTION TO CHRONIC PELVIC PAIN (CPP)

Chronic lower abdominal pain of unknown origin in women has intrigued many investigators. It is the gynecologist in particular to whom patients with this syndrome address for relief. As a matter of fact not less than approximately 10% of patients visiting gynaecologists do so in connection with CPP (1). Chronic pelvic pain (CPP) is defined as a more or less continuous pain in the lower abdomen of unknown cause that has lasted for at least 6 months (2-5). Deep dyspareunia and radiation of pain to the lower back may also be present. Approximately 37% of women with CPP furthermore have urinary urgency although the results of urological examinations are normal (see section II) (6).

Although most studies on CPP have been carried out on women of fertile age, there are indications that this syndrome is not specifically restricted to patients in that age group. In a study involving 60 consecutive cases of CPP of all ages, 43% of the women turned out to be 50 years or older (mean: 48; median: 48; range: 23-79 years) (see section II) (6,7).

Different concepts about the origin of CPP have resulted in a wide variety of names given to this clinical feature (8), dependent on the diagnostic approach of the physician consulted by the patient (9). Although many authors have sought the cause of pelvic pain in disorders of the female genitalia and/ or their ligaments (8,10-13), others have attributed same to neuro-psychological (14-16) or gastro-enterological disorders (17-24). The possibility of urological causes of CPP has also been postulated (9,25-26), although this has so far not been supported by conventional cystometry. It has been postulated that due to the close developmental relationship of the lower urinary tract and the genital tract, urinary disorders may adversely affect the function of the genital tract and express themselves as CPP (9). The reproductive tract and the lower urinary

tract have the same embryological origin. The urogenital system develops from the primitive gut and cloaca respectively. The urogenital sinus is formed by the division of the cloaca by the urorectal septum. Further subdivision of the urogenital sinus eventually creates the urethra and bladder and the vestibule and lower vagina (27-28). The upper vagina, cervix, and uterus are formed from the müllerian ducts which are lying dorsal to the bladder. The close proximity of the upper reproductive tract to the bladder and urethra may result in bladder-located pain being mistaken for pain originating in the uterus or the adnexa (9).

Without exception gynaecologists examining the clinical features of CPP, report a varying measure of pain experienced by patients during gynecological examination. It has therefore been postulated that the tissue surrounding the uterus, namely the parametrium, is involved in the pathogenesis of this syndrome (8). However it has so far not been proven that the hyperalgia mentioned above, always finds its origin in the parametrium or other parts of the female genitalia. It is obvious that during coitus or gynecological examination pelvic organs and structures other than the genital organs and the parametrial tissue undergo spatial changes as well. This could result in the sensation of lower abdominal pain reported. One of these organs is the bladder, lying adjacent to the anterior wall of the uterus and the proximal vagina.

In the studies presented in this thesis, for the first time bladder symptoms in CPP are extensively evaluated; also spontaneous contractions of bladder wall in women with CPP are measured and analyzed in search of a relationship between spontaneous detrusor activity and complaints of lower abdominal pain and urinary urgency in these women.

Outline of the thesis

In this thesis two parallel studies are presented, carried out separately. The prevalence of urinary symptoms in CPP is presented in section II and is meant to highlight a group of symptoms of the CPP syndrome so far least investigated. Next follows the relationship between mechanical activity of the bladder wall and lower abdominal pain and urinary urgency in CPP, presented in section III.

In this section micromotion detection (MMD), a new method of measuring mechanical activity of the bladder wall, is introduced. The analytic approach in this section comprises, in the sequence indicated:

I. Recapitulation of specific features, encountered in the recordings, and the type and frequency of the occurrence of pain or urge and the sum of both.

II. Analysis of the presence of specific MMD features in relation to the number of reports of pain or urge, as well as the sum of both, established in:

   A. Entire group of women who underwent MMD examination. This analysis is mainly a fundamental study to investigate the significance of specific MMD features in relation to the number of reports of lower abdominal pain or urge and the sum of both.

   B. Two subgroups of CPP women, viz.

      1. women in whom at the time of MMD examination, conventional urodynamics would have been expected to show phasic variations in detrusor pressure and

      2. those who would not have shown variations in detrusor pressure.

The questionnaire (in Dutch), completed by CPP patients to register and evaluate a.o. voiding symptoms, is presented as an appendix.

SECTION II

URINARY SYMPTOMS IN CHRONIC PELVIC PAIN (CPP)[1]

II.1 INTRODUCTION

In the Netherlands prevalence of one or more voiding symptoms in women between 50 and 75 years of age has been found to be 36% (29). The prevalence of minor to serious urinary incontinence in the Netherlands, in women from 35 to 79 years of age, is about 27% (30) and in women, aged 50 years or older, about 25% (29,31). Serious incontinence has been defined as involuntary loss of urine, occurring at least once a week, and in amounts larger than a few drops, all other incontinence being "minor" (30).

Although the main complaint of CPP patients is lower abdominal pain, many of them upon close examination of their medical history also have irritative symptoms of the lower urinary tract such as recurrent non bacterial cystitis, urinary urgency and dysuria. It has been postulated that disorders of the lower urinary tract may present themselves as symptoms of CPP (25,26). So far however, the prevalence of these symptoms in CPP has not been evaluated.

The occurrence of urinary symptoms has been attributed to several syndromes, which are sometimes overlapping each other. Of these the urethral syndrome, with irritative symptoms such as dysuria and urinary urgency, is one of the most common conditions encountered in medical practice. Most authors define the

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1 Partly presented at the International Urogynaecological Association (22nd Annual Meeting, July 30-August 1, 1997).

urethral syndrome as a state of irritation of the urethra and the bladder, in which, without evident urinary tract pathology, voiding symptoms are predominant (32). The prevalence of the urethral syndrome is not known with certainty; the etiology thereof has been discussed by several authors (33-36). It has been postulated that irritation of the urethra, in particular in the area of the external urethral sphincter, is the cause of this syndrome (37). The symptoms are summarized by Bodner (38) as urinary urgency, dysuria, frequency and suprapubic discomfort. Hesitancy, incomplete bladder emptying, weak stream and symptoms unrelated to the urinary tract such as back discomfort may also be present. Although in a substantial subgroup bacterial infection in urethral syndrome has been suggested (39,40), there is no evidence of recurrent infection (33,41). Urodynamic studies have shown a relationship between elevations of urethral sphincter pressure and spasticity of urethral musculature with urge and suprapubic discomfort (42). The authors suggest that urethral spasticity may imply a predisposition to urinary tract infection.

Lower abdominal pain and voiding symptoms of unknown etiology occur also in interstitial cystitis (IC) (43). Both the urethral syndrome and IC are diagnosed by excluding physical disorders in the presence of voiding symptoms and both syndromes are overlapping each other in symptoms of an irritable bladder in the absence of infectious agents. In IC suprapubic pain constitutes the prominent feature; in the urethral syndrome voiding symptoms are predominant. Other somewhat vaguely defined disorders, found with voiding symptoms and "painful bladder" and sometimes with organic abnormalities, are detrusor myopathy, chronic non-specific cystitis and eosinophilic cystitis (43). It has been suggested that the urethral syndrome is a subclass of IC and in itself not severe enough to justify invasive diagnostic steps to ascertain the diagnosis IC (44).

It is believed that urgency and other sensations, caused by the irritation of the lower urinary tract, reach the central nervous system through the parasympathetic autonomic nerve fibers (45), which arise from the S2-4 spinal segments and reach the bladder through the pelvic splanchnic nerves.

As the main complaint of CPP women is lower abdominal pain and often one or

more IC exclusion criteria are present, many of these women eventually end up with the gynecologist, which led us to set up this study. In this investigation we evaluate the prevalence of voiding symptoms in a group of 60 CPP patients irrespective of age. Where the influence of age on the frequency of the occurrence of a symptom can be expected we repeat our analysis for women younger than 50 years and those of 50 years or older and where relevant data from population studies available, we compare these with our findings according to age groups. The CPP population of our study consists exclusively of women visiting our outpatient clinic. In order to make sure that the results of the prevalence study has not been influenced by this selection, we also investigate whether the prevalence of specific urinary symptoms in this group differs from a sample of non-CPP patients visiting our gynecological outpatient clinic.

II.2 METHODS

It is not known in which numbers CPP patients visit general practitioners, how severe their complaints are or to what extent these practitioners refer their patients to specialists. We are equally unaware of how many CPP patients turn to gynaecologists in hospitals other than our own. Our outpatient clinic is, especially in Rotterdam and surroundings, well known for it's CPP management and we may therefore expect that relatively many severe cases of CPP are being referred to us. This implies that the CPP population of our hospital generally consists of a select group of relatively severe cases.

In the orientation phase of this study we supplied "provisional" questionnaires to 25 women, complaining of chronic lower abdominal pain and voiding problems, whilst clear pathological evidence was lacking. The results of this pilot study were used a.o. to edit the definite lay-out and text of the questionnaire, we distributed later on. From our repeated interviews we gathered that specifically items in the questionnaire, demanding precision in counting and supplying data from memory, for example frequency of voiding, involuntary urine loss, etc. needed to be looked into. Asking patients to keep a diary of such items, did not appear practical in view of the large number of

questions (see Appendix) which would have had to be included. Moreover, keeping a diary of the voiding pattern by a patient herself could possibly have led to misinterpretation of data supplied and to other undesirable side-effects on the outcome. Throughout the final questionnaire we have therefore used terminology such as "never or hardly ever, sometimes, often, almost always and always" to establish the severity of symptoms. Although the effect of urinary symptoms on the quality of life must not be underestimated, this aspect falls beyond the scope of this study, reason why we abstained from including questions to this effect. The total number of questions we finally arrived at, amounts to 85, of which a.o. 14 on lower abdominal pain and 27 on voiding symptoms (see Appendix).

From January 1996 through March 1997 this questionnaire was given to 60 consecutive cases of women, who visited our outpatient clinic because of chronic lower abdominal pain of unknown origin. These women were referred to us either by general practitioners or were visiting us after first having consulted other specialists, such as urologists, general surgeons and gynaecologists.

We selected a control group of 31 consecutive cases of women, irrespective of age, visiting our outpatient clinic in connection with routine gynecological examination (14 women), menopausal complaints (6 women), menstrual disorders (6 women), and descensus uteri (5 women).

Practically all patients were living in or in the vicinity of Rotterdam; only a few came from places situated somewhat further away, up to say 100 kilometers as the crow flies. The majority of patients were middle class women of average education. No distinction in age was made and all were of white race and Dutch nationality.

At our outpatient clinic the diagnosis CPP was established by at least two physicians. To comply with the diagnosis CPP, patients had to have lower abdominal pain without showing evident urological-, genital-, or digestive tract pathology. Moreover lower abdominal pain would have to occur often, almost always or always, for six months or longer, accompanied by radiation of the

pain to the lower back and/or deep dyspareunia. Women who had undergone hysterectomy and who were not menstruating for this or other reasons and who were not sexually active, were included. In all patients, organic causes of pelvic pain were excluded by gynecological examination, echoscopic and -if necessary- laparoscopic examination, to make sure that the cause of the pain was not endometriosis, uterus myomatosus, pelvic adhesions or adnexa disorders. When urinary problems, occurring often or (almost) always, were reported, objective urological diseases were excluded by routine urological and urodynamic examinations. Patients with nocturia, known to have cardiovascular disorders and those with severe mental disorders in medical history were excluded.

All women were notified not to hesitate to mark the items in the questionnaire, which they wanted to discuss with us verbally. They were also asked to return the questionnaire within one week. Subsequently, within two weeks after return of the completed questionnaire, patients were invited to our outpatient clinic for an extensive interview to make certain that questions had not been misunderstood. This applied particularly to the item "urinary urgency", to ensure that if urge had been reported, this was in line with ICS criteria.

Symptoms occurring often or (almost) always were counted as being present and serious.

When analyzing the questions regarding urinary incontinence, an arbitrary division was made between " serious" and "minor" incontinence, more or less in line with the definition by Rekers e.a. (30). Serious incontinence was defined as incontinence occurring often, almost always or always, in amounts of more than a few drops of urine. Minor incontinence was defined as involuntary loss of a few drops of urine, occurring often, almost always or always or involuntary loss of a lot of urine, occurring sometimes only. All other incontinence was counted as not being present.

In this study only the occurrence of *serious* urinary symptoms has been analyzed. Some results have been compared with findings in epidemiological studies on samples of Dutch female population of comparable age (29-31).

Table II- 1. Selection of items from the questionnaire administered in this study. Patients were asked to tick off one of the following alternatives after each statement: ***Never or hardly ever, sometimes, often, almost always or always.***

- I have pain in my lower abdomen, not counting pain during menstruation.
- My lower abdominal pain radiates to the lower back.
- If I compare my present condition with the past, then there are days when I feel a frequent and almost irresistible need to void in daytime, even when I have not been drinking much.
- Within a few minutes after I have passed urine, I feel the need to void again.
- I have a burning pain during voiding.
- When I feel having to void, it takes sometimes before I can start passing urine.
- After voiding, I feel that I have emptied my bladder completely.
- Compared to the past, my urine stream is .....*
- When I feel I have to void, I am able to postpone voiding.
- Once I feel I have to void, I have leakage before I have reached the toilet
- I have to void at night time.
- When I get pain in my lower abdomen and/or when my pain becomes worse, I feel an almost irresistible need to void.
- When I have to void, I get more pain in my lower abdomen or my pain becomes worse.
- If I wanted, I could stop voiding halfway.
- I have to strain in order to be able to start voiding.
- I have to strain in order to be able to go on voiding.

*Alternative answers: *same, rather weak, weak, different, notably.....*(To be completed by patients).

Loss of urine associated with sneezing, laughing, coughing and/or physical exercise (at least two affirmative answers) was regarded as a positive stress incontinence symptom, loss in association with the need to void as symptomatic urge incontinence and both symptoms combined as mixed incontinence (31).

Some of the items from the questionnaire, selected for data analysis in this study, are summarized in Table II- 1 (see also appendix in Dutch).

Primary objective

The aim of this study was primarily to evaluate the prevalence of voiding symptoms in CPP to highlight one of the least investigated groups of symptoms in chronic pelvic pain syndrome.

II.3 RESULTS

All women responded. Mean age of the CPP patients was 48 years (median: 48; range: 23-79). Generally, the medical history of these women showed years of visits to different specialists, surgical treatments (mainly hysterectomy) and psychotherapy; all in connection with chronic lower abdominal pain. Although *all* women were certain that there was "something seriously wrong with their physical heath", those (having been) referred to psychotherapists, did not refuse to do so despite the fact that they generally said to experience this as irritating and as a sign that "nobody believed them" and that as long as it helped they did not care anymore to whom they were referred to.

Mean age of the controls was 49 years (median: 48; range: 18-77).

II.3.1 Prevalence of voiding symptoms in two groups of hospital-population: CPP and non-CPP women

In this series of analyses we first evaluate the prevalence of I. symptoms of urinary incontinence and dysfunction of the urethral sphincter (all types of incontinence, involuntary control of the urethral sphincter and inability to postpone) II. symptoms of irritation of the lower urinary tract (nocturia, dysuria, cystitis, urge-induced lower abdominal pain and pain-induced urge) and III. symptoms of pelvic floor spasticity (strain to initiate voiding, strain to continue voiding and incomplete voiding) in CPP patients. Thereafter we compare these finding with those of the control group to evaluate the influence of our selection of outpatients on the outcome. The frequency of the occurrence of these symptoms is for both groups summarized in Table II- 2. Only serious symptoms, i. e. symptoms occurring often, almost always or always, have been counted as being present.

Table II- 2. The frequency of the occurrence of urinary symptoms in CPP and non-CPP groups of gynecological outpatients. Some women reported two or more symptoms. Only symptoms reported to occur often, almost always or always have been counted as being present.

Urinary symptoms	*CPP (n = 60)*	*Controls (n = 31)*	*P-value**
I. Urinary incontinence and dysfunction of the urethral sphincter			
1. Incontinence (stress, urge and other types of incontinence)**	26 (43%)	8 (26%)	0.103
2. Inadequate voluntary control of the urethral sphincter	30 (50%)	7 (23%)	0.014
3. Inability to postpone	22 (37%)	9 (29%)	0.495
II. Irritative symptoms			
4. Urge	22 (37%)	3 (10%)	0.006
5. Nocturia ≥ 2x	11 (18%)	1 (3%)	0.053
6. Dysuria	7 (12%)	0 (0%)	0.091
7. Recurrent cystitis	22 (37%)	5 (16%)	0.054
8. Urge-induced lower abdominal pain	12 (20%)	0 (0%)	0.007
9. Pain-induced urinary urgency	11 (18%)	-	-
III.Pelvic floor spasticity			
10. Strain to initiate voiding	6 (10%)	0 (0%)	0.091
11. Strain to continue voiding	10 (17%)	0 (0%)	0.014
12. Incomplete voiding	22 (37%)	5 (16%)	0.002

*Fisher's exact test

**Only cases of involuntary urine loss, occurring often or (almost) always, in larger amounts than a few drops.

II.3.1.1 Prevalence of urinary symptoms in CPP

Serious urinary urgency was reported by 22 women. Of these, 50% were 50 years or younger. Nine of the women with urgency reported to experience urge also within a few minutes after having just emptied the bladder.

An interesting finding in this study is that in 11 (18%) of the CPP patients urge was triggered off or increased by lower abdominal pain (pain-induced urge), and in 12 (20%) lower abdominal pain was triggered off or increased by urge (urge-induced pain). Eight patients had pain-induced urge as well as urge-induced pain. In none of the 12 women with urge-induced pain, there was relief from pain after voiding.

Table II- 3. Nocturia, twice or more, in 60 CPP patients according to age group.

	Age (Years)	
Nocturia ≥ 2 x	< 50	≥ 50
Present	4 (12%)	7 (27%)
Absent	30 (88%)	19 (73%)
Total	34 (100%)	26 (100%)

P = 0.182; Fishers exact test

Of the 22 (37%) of the women with serious postponement problems, 10 also had urinary urgency. Nocturia, *once* or more, was reported by 42 (70%) of the women; nocturia, *twice* or more, was reported by 11 (18%) (Table II- 2.) (mean age: 54 years; median: 52; range: 31-79). Nocturia, twice or more, did not differ significantly between CPP women younger than 50 years and those of 50 years and older (Table II- 3).

In CPP women, aged 50 years or older, there is a trend to nocturia, twice or more, being related to urinary urgency (P = 0.080). This trend was not seen in those younger than 50 years.

Seven women (12%) had dysuria. Subjective inadequate function of the urethral sphincter was established in 35 (55%) individuals who reported never or only sometimes being able to interrupt voiding willfully. Serious urinary incontinence was reported by 26 (43%) CPP patients. There was no significant difference in the frequency of the occurrence of serious urinary incontinence, when comparing CPP women younger than 50 years, with CPP patients of 50 years or older (14/34 in age group < 50 vs. 12/26 in age group ≥ 50; P = 0.818).

II.3.1.2 Urinary symptoms in CPP as compared to non-CPP hospital patients

Comparison of the frequency of the occurrence of urinary symptoms between our outpatient CPP women and 31 non-CPP outpatients reveals that all symptoms of irritation of the lower urinary tract as well as all symptoms of pelvic floor spasticity are more often present in the CPP group than in the controls. This difference is in all cases significant with the exception of dysuria and strain to initiate voiding which show a trend (Table II- 2). Inability to voluntarily control the urethral sphincter, was also reported significantly more often by the CPP group. However there were no significant differences between the two groups as far as the inability to postpone was concerned and there was a trend to the frequency of urinary incontinence occurring more often in CPP than in controls. There were no urge incontinents in the controls group. Of the 8 controls who had urinary incontinence, six had positive symptoms of stress incontinence and in two the cause was unknown. No urge incontinence was reported by the control group. In all but one of the controls with stress incontinence no organic cause of these symptoms was found. The occurrence of stress incontinence did not differ significantly between our CPP patients and the control group (15/60 in CPP vs. 6/31 in controls; P = 0.798; Fisher's exact test).

II.3.1.3 Prevalence of one or more voiding symptoms in CPP

In this study the prevalence of one or more serious symptoms presented in Table II- 2, was 85%. Mean number of urinary symptoms was 3.5 (median: 3; range: 0-12). Approximately 63% (38/60) of the women had 2 or more and 35% (21/60) had 5 or more of these symptoms(Table II- 4).

As we expected an increase in the number of urinary symptoms with increasing age, we also analyzed the relation between these. The number of urinary symptoms present in our CPP patients, however, was not related to age (P = 0.119; Spearman's test; Figure II- 1).

Table II- 4. Frequency of the occurrence of one or more of the serious urinary symptoms presented in Table II- 2. , in 60 women with CPP.

Number of symptoms	*n (%)*
0	10 (17)
1	12 (20)
2	4 (7)
3	7 (12)
4	7 (12)
5	6 (10)
6	4 (7)
7	5 (8)
8	4 (7)
12	1 (2)

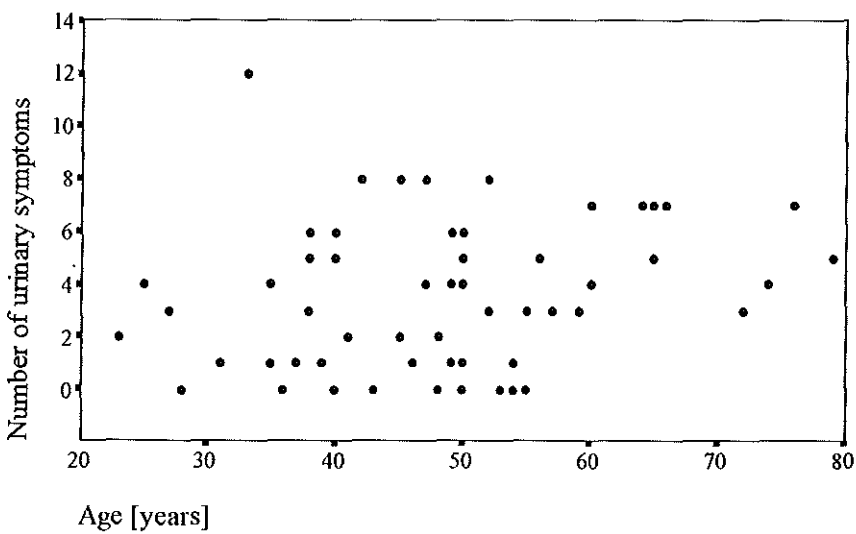

Figure II- 1. Number of urinary symptoms by age (n = 60).

II.3.1.4 Interrelation between urinary symptoms in CPP

Our study reveals that in one CPP patient one ore more elements from different symptom groups can be found and we decided therefore to also analyze the interrelation between different urinary symptoms in our CPP patients. This in line with the analytic model of Rekers e.a., who evaluated the interrelation between various urinary symptoms in a sample of Dutch menopausal women(31).

In the CPP patients participating in this study, urinary symptoms within each group of symptoms as presented in Table II- 2. were interrelated. Symptoms of urinary incontinence were not interrelated to other urinary symptoms with the exception of urinary urgency which was related to incontinence (Table II- 5).

Urge-induced pain and pain-induced urge were interrelated ($P < 0.001$; Fisher's exact test) and both were also related to all other irritative urinary symptoms as well as practically all symptoms of pelvic floor spasticity (Table II- 5)

There was also an interrelation between symptoms of pelvic floor spasticity, i.e. strain to initiate voiding, strain to continue voiding and incomplete emptying. Moreover, these symptoms were interrelated to most of the irritative urinary symptoms. Symptoms of urinary incontinence showed a within-group interrelation but were not interrelated to irritative symptoms or symptoms of pelvic floor spasticity.

II.3.2 Comparison of urinary incontinence between women with CPP and healthy female population

In this analysis we compare our findings on "urinary incontinence" with the results of an EPOZ[2] Dutch female population study on genito-urinary symptoms in menopausal women by Rekers e.a. (30). The study was conducted in the

[2] Epidemiologisch populatieonderzoek.

Table II- 5. Correlation between serious urinary symptoms of incontinence, irritation of lower urinary tract and pelvic floor spasticity in CPP (n = 60).

	Postp[x]	Sphinct[x]	Urge[xx]	Noct[xx]	Dys[xx]	Cyst[xx]	Urge→pain[xx]	Pain→urge[xx]	Strain1[xxx]	Strain2[xxx]	Incomp[xxx]
Incont[x]	*	*	**	NS	NS	NS	NS	NS	NS	NS	NS
	32/64	30/57	32/64	47/27	42/57	42/46	42/50	43/46	45/29	46/30	42/46
Postp[x]		***	NS	NS	NS	NS	NS	NS	NS	NS	NS
		13/60	32/46	35/46	34/57	34/41	38/33	37/36	38/29	36/40	32/46
Sphinct[x]			Tr	NS	NS	NS	NS	NS	NS	NS	NS
			40/68	49/55	53/29	47/55	48/58	49/55	51/43	48/60	42/64
Urge[xx]				Tr	**	NS	NT	NT	**	**	**
				31/64	30/86	30/50	-	-	30/86	28/80	24/59
Noct[xx]					NS	Tr	**	*	*	**	**
					15/43	11/32	10/50	12/46	13/57	10/60	5/41
Dys[xx]						Tr	*	*	NS	NS	Tr
						5/23	6/33	6/36	9/29	10/20	5/23
Cyst[xx]							**	***	*	NS	NS
							27/75	27/82	30/86	34/50	29/50
Urge→pain[xx]								***	***	**	*
								8/73	11/86	12/60	11/36
Pain→urge[xx]									**	*	Tr
									13/57	12/50	11/32
Strain1[xxx]										***	***
										2/60	0/32
Strain2[xxx]											**
											5/36

Tr = trend ($0.05 < P < 0.10$); *$P \leq 0.05$; **$P \leq 0.01$; ***$P \leq 0.001$; NS = not significant; NT = not tested.

Percentages were compared applying Fisher's exact test.
All associations were positive.

Values to the left of slashes are percentages of women *without* symptoms presented in columns, in whom symptoms in the rows are present.
Values to the right of slashes are percentages of women *with* symptoms presented in columns, in whom symptoms in the rows are present.

^{x} = Symptom of urinary incontinence;
^{xx} = Symptom of irritation of the lower urinary tract;
^{xxx} = Symptom of pelvic floor spasticity.

Incont= urinary incontinence (stress, urge and other types of incontinence);
Urge = urinary urgency;
Noct = nocturia, twice or more;
Dys = dysuria;
Cyst = cystitis;
Urge→pain = urge-induced lower abdominal pain;
Pain→urge = pain-induced urinary urgency;
Postp = inability to postpone;
Sphinct = inadequate voluntary control of urethral sphincter;
Strain1 = strain to initiate voiding;
Strain2 = strain to continue voiding;
Incomp = incomplete voiding.

Shaded area on the left part of the table, indicates the interrelation between various symptoms of urinary incontinence.
Shaded area in the center of the table, indicates the interrelation between various symptoms of the irritation of lower urinary tract.
Shaded area on the right part of the table, indicates the interrelation between various symptoms of pelvic floor spasticity.
Bordered area on the right indicates the interrelationship between symptoms of irritation of the lower urinary tract and symptoms of pelvic floor spasticity.

Table II- 6. Prevalence of mild to serious urinary incontinence in a sample of female population, 35-79 years of age [Rekers e.a., 1992], and serious incontinence in 60 women with CPP, aged 23-79 years.

Rekers e.a. (n = 1299)		*Current study (n = 60)*	
n	% of all women	n	% of all women
344	26.4	26	43.3

P = 0.004.; Fisher's exact test

town of Zoetermeer. The mixed population of this town can be considered a true representation of the Dutch population at large. The population studied by Rekers e.a. constituted a stratified sample of women between 35 and 80 years of age, drawn from the city register, two-thirds of these women being between 45 and 64 years of age. Data were obtained from postal questionnaires covering a.o. mild to serious urinary incontinence.

Table II- 7. Urinary incontinence in 60 CPP patients according to age group.

	Age (Years)	
Incontinence	< 50	≥ 50
Present	14 (41%)	12 (46%)
Absent	20 (59%)	14 (54%)
Total	34 (100%)	26 (100%)

P = 0.795; Fishers exact test

In our study 43% (26/60) of the CPP women had serious urinary incontinence, i.e. incontinence occurring often or (almost) always, in larger amounts than a few drops of urine, irrespective of the type. This percentage was significantly higher than the percentage of mild to serious urinary incontinence found by Rekers e.a. in a sample of female Dutch population of approximately the same age category (Table II- 6). The percentage of our incontinent CPP patients did not differ significantly between women of 50 years of age or older and those younger than 50 years (Table II- 7); in line with the Van Rekers e.a. study where no significant difference was found between urinary incontinence in pre- and post-menopausal women (30).

The percentage of women with positive symptoms of serious stress incontinence was extremely high in our study group (15 women; 25%), in agreement with the finding that the percentage of CPP patients with descensus uteri is significantly higher than that in CPP women with no organic disorders (8) and significantly higher than the percentage of women with stress incontinence (mild cases included) in the female Dutch population of approximately the same age group (Table II- 8). When adding the number of mixed incontinent women (4 patients) to those with stress incontinence, this percentage rises to about 32%. Also this percentage is significantly higher than the corresponding figure in the female population of comparable age group in whom mild to serious stress incontinence (women with mixed incontinence included), has been found to be 17% (P = 0.005; Fisher's exact test).

In line with above mentioned study, there was no significant difference in the

Table II- 8. Frequency of the occurrence of different types of mild to serious urinary incontinence in a sample of female population, 35-79 years of age [Rekers e.a., 1992] and serious urinary incontinence in 60 CPP patients, aged 23-79 years.

Urinary incontinence	*Rekers e.a. (n = 1213)*	*Current study (n = 60)*	*P-value**
Stress incontinence	64 (5%)	15 (25%)	< 0.001
Urge incontinence	53 (4%)	2 (3%)	1.000
Mixed incontinence	151 (12%)	4 (7%)	0.301
Unknown	47 (4%)	5 (8%)	0.076

*Fisher's exact test.

frequency of the occurrence of stress incontinence between CPP women of 50 years or older and those younger than 50 years (Table II- 9).

Table II- 9. Urinary stress incontinence in 60 CPP patients according to age group.		
Stress incontinence	*Age (Years)*	
	< 50	≥ 50
Present	11 (32%)	8 (31%)
Absent	23 (68%)	18 (69%)
Total	34 (100%)	26 (100%)

P = 1.000; Fisher's exact test

II.3.3 Some urinary symptoms in CPP and Dutch female population, aged 50 years and older.

In the following analysis three items from our questionnaire are compared with the results of a country-wide study, carried out by Van Geelen e.a. on a sample of Dutch female population of 50 years of age or older drawn from data of an independent board of registration. The population of Van Geelen e.a. study was a representative sample of the Dutch female population as far as age, education and menopausal age are concerned. Data were obtained from postal questionnaires covering a.o. the presence of some urinary symptoms and the degree of impediment (none, little, some, much) as a measure of the severity of a symptom.

For this analysis we selected women of 50 years and older from the 60 CPP patients participating in this study. In this age group the frequency of the occurrence of recurrent cystitis is in CPP significantly higher than in the female population (Table II- 10). The occurrence of dysuria does not differ significantly in the two groups. The frequency of urinary incontinence in CPP women, 50 years of age or older, was significantly higher than in the female population of the same age group (Table II- 10).

Table II- 10. Comparison of the prevalence of three urinary symptoms in Dutch female population, 50 years of age or older [Van Geelen e.a., 1992] and CPP women of the same age group [current study].

Urinary symptom (women ≥ 50 years)	*Van Geelen e.a. [1996]* (n=1761)*	*current study** (n=26)*	*P-value****
Dysuria	6%	8%	0.67
Recurrent cystitis	8%	31%	0.001
Incontinence	25%*	46%**	0.021

* Mild cases included
** Only serious cases
*** Fisher's exact test

II.4 DISCUSSION

The significant differences as well as the trend in the differences observed in the frequency of the occurrence of symptoms of the irritation of lower urinary tract and those of pelvic floor spasticity between CPP and non-CPP women, both groups selected from our gynecological outpatient clinic imply that the outcomes of this study has not been influenced by our choice of *hospital*-population as far as these symptoms are concerned..

Almost 37% of the CPP women completing the questionnaire in this study reported to have often or (almost) always urinary urgency. Routine urological and urodynamic examinations were in all cases normal except in three women who turned out to have bladder instability. The relatively high occurrence of serious urgency, i.e. urge experienced often or (almost) always in these women, can not be due to old age: 65% of the CPP women were 50 years or younger and about 87% were 60 years or younger.

Although 37% (22 women) of the CPP women had serious postponement problems, only 5 of these were urge-incontinent with the majority reaching the toilet dry. This suggests that in CPP we are dealing with a mainly afferent (sensory) phenomenon.

Although showing a trend, the number of urinary symptoms, present in this group of CPP patients, was not significantly related to age either, which would justify the suggestion that chronic lower abdominal pain and voiding symptoms in CPP might be related to the same cause or predisposing factor.

One of the interesting findings in the study is that three groups of urinary symptoms could be present in our CPP women: I. symptoms of incontinence; II. irritative symptoms and III. symptoms of pelvic floor spasticity. Most symptoms within each group were interrelated. However, whereas irritative symptoms and symptoms of pelvic floor spasticity were often seen to be interrelated, symptoms of incontinence showed no interrelationship with the other two categories of urinary symptoms with the exception of the interrelation between incontinence and urinary urgency. The above suggests a common, age-independent, cause or predisposing factor, underlying many of the urinary symptoms evaluated in this study as well as the lower abdominal pain in this group of CPP patients.

The interrelation between pain-induced urge and urge-induced pain suggests that there is an interaction between the lower abdominal pain and urinary urgency experienced in these patients, probably at the level of the central nervous system. Perhaps some patients find it hard to distinguish between pain and urgency due to lack in sensory possibilities to do so.

It is remarkable that 37% had (subjective) incomplete bladder emptying as in none of these women objective urethral obstruction was found. Spasm of the anterior pelvic floor is very likely to be the cause of this condition.

The percentage of patients with serious urinary incontinence did not differ significantly between CPP patients younger than 50 years and patients 50 years of age or older. This agrees with the findings of the study carried out by Rekers e.a. (30), where the rate of incontinence in post-menopausal women did not differ significantly from that in pre-menopausal women. However, the prevalence of incontinence was significantly higher in our CPP patients (23 to 79 years of age) than in the female population of comparable age group. This was also the case in women aged of 50 years or older. These differences would

have been strikingly impressive if as Van Geelen e.a. and Rekers e.a. did, mild cases of incontinence would have been included in our study.

When adding the number of mixed incontinent women (4 patients) to those with stress incontinence, this percentage rises to about 32%. Also this percentage is significantly higher than the corresponding figure in the female population of comparable age group in whom stress incontinence (including women with mixed incontinence) has been found to be 17% (31) ($P = 0.005$; Fisher's exact test). The high percentage of stress incontinence (32%) in our CPP patients is certainly a remarkable finding. Stress incontinence is due to some relaxation of the anterior pelvic floor, supporting the bladder neck. The high percentage of stress incontinence in this group of women is in line with the clinical experience that many CPP patients have uterine descencus as another expression of weakened supporting tissue within the pelvis (8). The strain exercised on the pelvic nerves running along the uterine supporting tissue, may explain the lower abdominal pain experienced by women with CPP (2,8). The age independence of stress incontinence in these women being in agreement with the findings of Rekers. e.a., suggests that the significant differences in the rate of the occurrence of stress incontinence in our CPP patients and the population of Van Rekers e.a. study may be mainly due to the difference in the state of health of these two groups of women. However, it is very well possible that the reason of the high percentage of stress incontinence found in these women, must be attributed to the fact that they were a select group of hospital patients, as there was no significant difference in the occurrence of stress incontinence between the CPP and the non-CPP patients.

The relatively low percentage of urge incontinence (10%; urge incontinence + mixed incontinence), found in the CPP patients in this study, is at least as impressive as the high rate of stress incontinence in these women, especially in the light of the high occurrence of the frequency of urinary urgency (37%) in these women. This supports the view that CPP is a mainly sensory disturbance (2).

Serious urinary incontinence, although interrelated to only a few other urinary symptoms in CPP, appears to be one of the main symptoms in CPP. To a lesser

extent this can also be said of the symptom recurrent cystitis.

The number of urinary symptoms present at the same time was in CPP patients participating in this study extremely high. In these women 63% have at least two symptoms and 35% have 5 symptoms or more. Although showing a trend the number of urinary symptoms in these women was age-independent. The presence of urinary symptoms in the female patient with chronic lower abdominal pain seems therefore indicative for the diagnosis CPP.

The foregoing suggests that at least in a subgroup of CPP patients we are dealing with a chronic painful bladder syndrome, resembling the urethral syndrome.

Because IC should be kept in mind when evaluating the female patient with chronic lower abdominal pain and urinary symptoms, special attention should be given to the exclusion criteria of this syndrome. One of these criteria is the absence of nocturia. Of the 50 CPP patients with at least one urinary symptom, in 24% (12 patients) IC can with certainty be excluded on the ground of the complete absence of nocturia. If the absence of serious nocturia (twice or more) would be maintained as an exclusion criterion in IC, the percentage of CPP women with urinary symptoms, in whom IC can be excluded, would rise to 78% (39/50 women).

Spontaneous phasic variations in detrusor pressure (p_{det}), another exclusion criterion of IC, have been observed in 40% (12/30) of women with CPP (see chapter 3). Thus, when evaluating the female patient with chronic lower abdominal pain, urological medical history and routine urodynamics must be the first step to exclude IC, certainly when the latter is suspected. At this point the question rises whether there are women with CPP who are mistaken for IC, on the basis of (also) having no spontaneous bladder contractions. After all not all spontaneous bladder contractions can be detected by conventional urodynamics (see chapter 3). Of the 30 women who underwent micromotion detection (MMD) examination and showed no variations in detrusor pressure, 47% (14 women) turned out to have micromotions of the bladder. This activity was detected during 30 minutes of measuring the distance between eight points

on the inner wall of the bladder. If spontaneous bladder activity, including micromotions, would be valid as an exclusion criterion of IC, the number of women diagnosed to have CPP might rise, with the number of IC patients decreasing by the same number.

Voiding symptoms such as urgency, incontinence, incomplete voiding, strain to initiate and/or continue voiding, etc., all in the absence of evident organic disorders, occur frequently in chronic pelvic pain without obvious cause. These symptoms, together with the relatively frequent occurrence of urge-induced pain and vice versa, suggest the existence of a painful bladder condition in (a subgroup of) CPP. A (functional) disturbance at the level of the central nervous system, with interaction between sensory messages, arriving from different structures within the pelvis, may be the cause of this condition.

II.4.1 Co-occurrence of pain and urge: A psychological approach

So far we have focused mainly on a "sensory" explanation of the occurrence of pain and urge. However, hypotheses involving central cognitive processes are also plausible[3].

According to the psychological theory of negative affectivity of Pennebaker (75), lower abdominal pain accompanied by a diversity of other symptoms such as low back pain, deep dyspareunia and urinary symptoms in CPP could be explained by a tendency to report physical complaints in general. This tendency is known to be enhanced in a state of high anxiety and patients visiting clinics repeatedly have been found to be generally more anxious than those who do not. This tendency manifests itself in greater attention to physical (and emotional) unpleasant sensations. When these sensations are interpreted by the patient as signs of an underlying disease this leads to an increase in the report

[3] Van Os-Bossagh P, Van Duyl WA, Passchier J, Vierhout ME, Drogendijk AC. Bladder control system: a hierarchical model. In preparation.

of many symptoms. Following this theory, the co-occurrence of pain and urinary symptoms such as urgency (see also section III) may be seen as the outcome of a central cognitive process rather than being merely a disorder of the afferent nerve fibers. However, several arguments, in relation to our data, plead against this view:

First of all our patients tend to report some symptoms more frequently than others, thus the frequency of the occurrence of voiding symptoms (Table II- 2) shows a wide range in diversity varying from 10 % (strain to initiate voiding) to 50 % (inadequate voluntary control of the urethral sphincter). This finding is contrary to the Pennebaker prediction of a general tendency to report all kinds of symptoms with no significant difference in the frequency of the occurrence of these symptoms. Secondly, in the CPP group, we found a higher prevalence of as well urgency as most of the other symptoms as presented in Table II- 2, than in the non-CPP gynecological patients, whereas comparable results would have been expected on the basis of Pennebaker's theory.

Like the psychosomatic model, the disability model proposes that health problems cause distress and dissatisfaction and it assumes that negative affectivity (NA) is related to individual differences in actual health problems. However, whereas a strong correlation exists between NA and somatic problems reported in normal adult and student populations, no consistent association has been found between NA and any major or chronic health difficulties. In other words, major or chronic health problems are not a significant cause of high NA levels in normal subjects. Moreover NA has been shown to be unrelated to health indicators such as fitness and lifestyle, dysfunction or pathology, health related visits or absence, frequency of illness and overall mortality. Whereas NA individuals report all kinds of physical problems, they do not show evidence of poorer health; e.g. they are not especially likely to visit their doctor or to miss work or school in general (75). Finally, although we cannot dismiss the psychological hypotheses in relation to CPP entirely, it is not our impression that the NA explanation is applicable here. Our CPP outpatient population did not only *complain* of pain (and urge), they also *did all they could*, to seek relief. Obviously further NA studies on

CPP (out-patients), measuring NA or other psychological traits are necessary to support or reject this view.

II.5 CONCLUSIONS

This study involving 60 relatively severe cases of CPP patients of 23 to 79 years of age has delivered the following results:

1. The prevalence of two or more voiding symptoms is 68%.
2. The occurrence of urinary stress incontinence is significantly higher than in the female population.
3. The occurrence of recurrent cystitis and urinary incontinence in a subgroup of these patients, aged 50 years or older, is significantly higher than in the healthy female population of the same age group.
4. A substantial subgroup of these women has voiding symptoms resembling the urethral syndrome.
5. Either the same source of afferent stimuli might be responsible for the experience of lower abdominal pain and urinary urgency, or there is an interaction between these sensations, at the level of the higher centers.
6. The presence of irritative urinary symptoms combined with symptoms of pelvic floor spasticity in the presence of chronic lower abdominal pain and in the absence of obvious organic disorders, supports the diagnosis CPP.
7. There are indications that negative affectivity theory of Pennebaker does not give a sufficient explanation of the coexistence of urinary urgency and lower abdominal pain in CPP.

SECTION III

MICROMOTIONS OF BLADDER WALL IN CHRONIC PELVIC PAIN (CPP)[1]

III.1 INTRODUCTION

Smooth muscle tissue exhibits spontaneous contractions in vitro (46-58). Micromotions (MM) in vitro are fine spontaneous contraction patterns observed in pig bladder strips by using the lighted glass fiber technique (46,49,54,56,57). Strips of the bladder wall obtained from all locations of the cat bladder exhibit spontaneous activity suggesting that the terrain of spontaneous activity covers the whole of the detrusor, from dome to the basis (55).

Micromotion Detection (MMD) equipment, introduced in 1995 (59), has made it possible for the first time to observe MM of bladder wall in human bladder in situ (60-62). The MMD equipment used in this study has in the meantime further developed and has the potential to register MM signals emitted from 16 locations in the wall of bladder (63-67). MM in situ is defined as fine (local) mechanical activity of bladder wall, not caused by mechanical transmission from the abdomen and not necessarily reflected in bladder pressure.

Frequency analysis has revealed that in pig bladder strips in vitro, most of the time two main frequencies of the spontaneous activity can be distinguished: one of about 2-4 per minute (low frequency MM) and the other about twice this frequency (high frequency MM) (49,53-57). Selective sensitivity of the low-

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[1] Partly presented at the 22nd Annual Meeting of International Urogynecological Association (IUGA), Amsterdam (The Netherlands), 1997.

and high frequency components to certain pharmacological agents and mechanical changes respectively, suggests that the two frequency components mentioned above are related to independent phenomena (52,54,56,57). Under isometric conditions, high frequency MM as well as low frequency MM tend to result in force pulses (overall contractions) across bladder strips if these motions are synchronized without shift in time. In case of a shift in time, a plateau in the overall force is seen or even no resulting force at all (46,54). This means that the absence of overall contractions does not imply the absence of local activity (54). It has therefore been postulated that micromotions may occur unnoticed when measuring variations in detrusor pressure (68). In an in vitro study the overall force measured across bladder strips was shown to be related to the frequency of micromotions (54,56,57).

During the orientation phase of this study, in search of a relationship between urinary urgency and micromotions of bladder wall, it was a chance finding to see that a woman with urge of unknown cause turned out to be a CPP patient, in whom reports of pain were accompanied by monophasic micromotions. The above, combined with own clinical findings that many women with CPP have also urinary urgency (see section II) (6), made us start this pilot study.

III.2 PRIMARY OBJECTIVE

This study was primarily set up to investigate the clinical feasibility of MMD and to establish the relationship between MM activity of bladder wall and reports of pain and/or urge by women with CPP.

III.3 METHODS

III.3.1 Patients

From the women visiting our outpatient clinic of Obstetrics and Gynaecology of the University Hospital Dijkzigt in connection with chronic lower abdominal pain, thirty consecutive cases who complied with the diagnosis CPP, were

consented to participate in the study. The age of these women varied from 25 to 76 years (mean: 46; median: 46).

The diagnosis CPP was based on the following criterion trias:

1. Lower abdominal pain of unknown cause, occurring often, almost always or always;
2. Radiation of pain to the lower back;
3. Deep dyspareunia.

Of these, the first was set as a prerequisite. At least one of the other two had to be present to comply with the selection criteria. Organic causes of low back pain were excluded. Deep dyspareunia was ascertained by gynecological examination.
Women with urinary symptoms as a result of organic disorders were excluded. Medical history of the CPP group showed that 82% had continuous pain in the lower abdomen. The others (18%) said to have had episodes of days with less pain or complete relief from pain during the past 6 months. The lower abdominal pain was dull in 7 women; the others had pain fluctuating in intensity with episodes of cramps or shooting pain.

Although lower abdominal pain was presented as the main complaint, the medical history of these women revealed that 15 of them (50%) had also often or (almost) always urge. Routine cystometry of these patients with urinary symptoms, performed at the Department of Urology of our hospital, showed no abnormalities in 13 women. Two women had bladder instability, but this did not explain their lower abdominal pain.

III.3.2 Control group

Seven healthy volunteers, women 19 to 50 years of age (mean: 38; median: 40), underwent MMD. Lower abdominal pain and/or urinary urgency were not excluded as long as the discomfort did not bother sufficiently to consult a physician.

None of the patients and controls had severe mental or physical disabilities during the last six months before MMD.

This experiment has been approved by the Committee of Medical Ethics EUR/AZR. The CPP patients as well as the healthy controls have been consented to participate in this study.

III.3.3 Materials and procedure

The MMD probe (Figure III- 1) (63-66), consists of an F14-catheter through which eight thin wires are led. Electrode discs on the inner wall of a high compliance latex balloon (condom) are connected to the bare ends of the wires.

On the outer wall of the balloon there are eight cylindrical latex knobs (2x2 mm), next to the discs and arranged in a circular configuration. This circular arrangement is, from a technical point of view, a necessity. Approximate angle of the circle, relative to the catheter is 60 degrees to facilitate easy introduction of the probe into the urethra. The catheter is long enough to protrude from the urethra after the insertion of the probe into the bladder and serves also to fill the balloon with saline.

When the balloon is filled, the knobs are pressed onto the mucous membrane of the inner wall of the bladder, thus following local motions of the wall during the measurement. Local displacements of the knobs are recorded at eight different locations in bladder wall as changes in electrical resistance between two neighboring electrodes, bathed in the saline content of the balloon. The electrodes have the double function of mediating alternating electrical current and measurement of the voltage. During the recording the wires are connected to the MMD interface and a 486-PC by an ADC-board (Figure III- 2). Signals are sampled at a rate of 5 per second. The pressure within the balloon is measured manometrically. Variations in this balloon pressure are a measure of variations in intravesical pressure (p_{ves}).

Before the introduction of the MMD probe the bladder was emptied with the help of an F14 catheter. During measurement, continuous drainage of bladder was carried out with an F6 catheter which was inserted into the bladder,

through the urethra and alongside the balloon. Another F6 catheter, placed for about 12 cm into the rectum was used to register intrarectal pressure as a measure of the abdominal pressure. Disposable hydrostatic transducers were connected to the intravesical and intrarectal catheters by standard intravenous extension tubes.

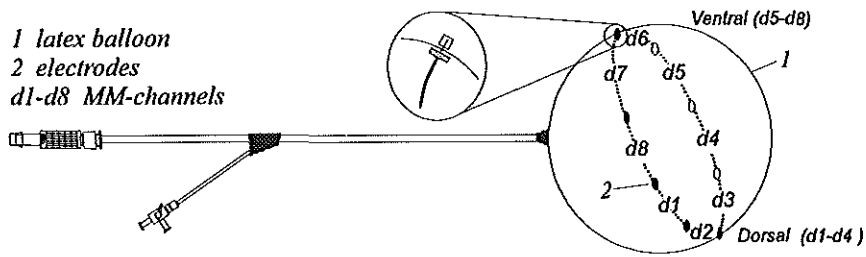

Figure III- 1. The MMD probe: A latex balloon provided with eight electrodes corresponding with 8 MM channels.
From: Kosterman LM, Op den Brouw LI, De Bakker JV, Van Os-Bossagh P, Drogendijk AC, Van Duyl WA. EMBS 1997 (67).

We used a modified version of the Visual analog Scale (VAS) (69), comparable to a modified VAS version introduced earlier (70), to obtain continuous information on the intensity of lower abdominal pain experienced by the patients during MMD. Our pain marker, containing a ten-leds level indicator is served by a manipulator which is placed in front of the patient. The leds are activated by the patient if and when pain is experienced. The number of leds lighted gives an indication of the level of pain experienced, ranging from 'no pain' (1 lighted led) to 'extreme pain' (10 lighted leds). Signals corresponding to the number of lighted leds were recorded continuously. Respiratory movements of the abdomen were transferred to the PC from a bellows fastened around the waist and were observed as changes in pressure within the bellows.

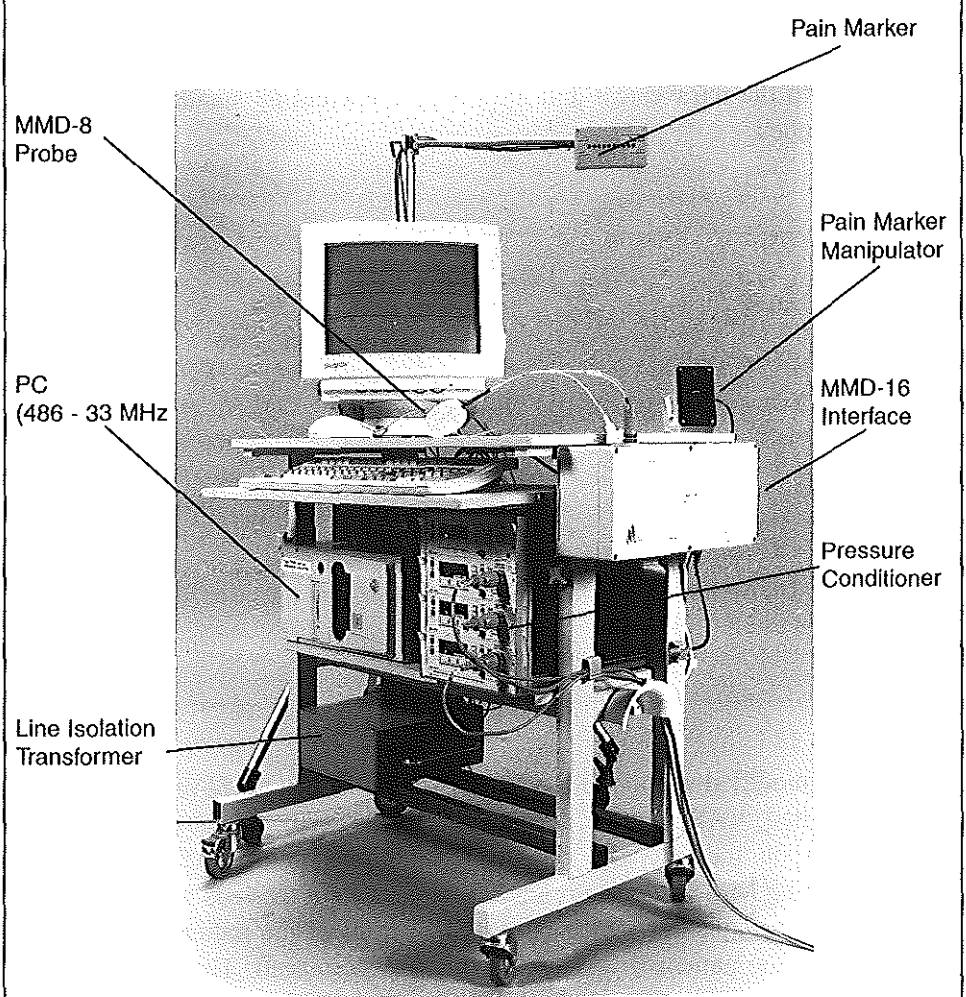

Figure III- 2. Equipment for micromotion detection (MMD).

Signals were registered and saved for further analysis, using a multichannel data acquisition computer program, the MKR (71).

All participants were requested not to drink two hours before measurement in order to reduce urine production. Just before the start of measurement they were furthermore asked to empty the bladder. Measurements took place with patients in lithotomy position.All equipment was tested before each session. The empty balloon of the MMD probe was then dipped in lubricating gel and was folded in a way, allowing easy introduction of the probe into the urethra. The locations of the knobs were roughly established with the help of markings on the protruding part of the probe (channels 1-4: dorsal; channels 5-8: ventral) (Figure III- 1). In this way we had aimed to pay special attention to possible preferential MM locations.

After the introduction of catheters for continuous measurement of abdominal pressure and drainage of bladder, a girdle made of a 30 cm bellows (diameter: ± 7 cm) and on both ends attached to a band, was put around the waist to allow the registration of respiratory excursions of the abdomen. Patients were instructed to report the degree of pain experienced during the measurement, by means of the pain marker. Any other sensation, e.g. urge, was to be reported verbally. The balloon was filled with 100 ml saline, approximately 1.5 ml/s, at body temperature. For the first 10 women this was done manually, later a pump was used. The recording then started with a cough test. Women were instructed to cough three times to ensure good transmission and to see whether the transducers were intact.

An MMD recording was obtained by simultaneous recordings of 12 signals: MM (eight channels) [mm], p_{ves} [cm H2O], p_{abd} [cm H2O], respiratory excursions of the abdomen (resp) and signals from the pain marker. The signals are recorded in such a way that each arbitrary episode of recording exhibits four vertically arranged windows. The upper two windows are reserved for MM signals. p_{ves} and p_{abd} signals are seen on the third window and respiration and pain signals are on the lowest window (Figure III- 3).

Table III- 1. Conversion factor of displacement by voltage as function of volume.
From: Kosterman LM, Op de Brouw LI, De Bakker JV, Van Os-Bossagh P, Drogendijk AC, Van Duyl WA. EMBS 1997 (67).

Volume (ml)	100	150	200
Estimated displacement (mm)/Voltage (V)	4	5.3	6.4

Changes in the distance between two electrodes are registered as changes in the voltage. The latter results from variations in resistance between two electrodes. The ratio between above mentioned displacements and measured voltages is used as a conversion factor to express voltages in displacements. This ratio, however, is volume-dependent (Table III- 1) (67). This volume-dependent ratio has been estimated for ideal conditions *in vitro*, where the balloon is spherical and at rest the distances between neighboring electrode discs are equal.

Fluctuations in the pain marker or urge reports following one another within 0.1 minutes (shortest duration of an MM wave observed), were counted as being one report.

Above mentioned signals were registered for about 10 minutes. This procedure was repeated at volumes of 150 and 200 ml. After the session the balloon was emptied and it's contents measured again to make sure that 1) the balloon was entirely empty and would not damage the urethra during withdrawal and 2) there had been no leakage during measurements. The catheters and the probe were then gently withdrawn. Hereafter the bladder was drained with the help of an F6 catheter to measure the volume of urine produced but not (properly) drained during recordings.

III.3.4 Data analysis

Because tonic variations in MM and p_{det} could have been artefacts, amongst others as a result of the difference between the temperature within the probe and that of bladder wall, the analysis of MM and p_{det} results were based on phasic variations thereof only.

MM episodes, recorded simultaneously from different channels, were counted as one observation in this study. This, in view of the fact that we can not yet with certainty eliminate the influence of the neighboring electrodes on the emitted signals from a certain channel. The *duration* of MM observed, not being affected by disturbances from the neighboring channels, plays an important part in our data analysis. When two or more channels showed MM activity, (partially) occurring at the same time, the channel with the longest MM duration was used to establish the duration of MM.

Although p_{ves} and p_{abd} channels were measured during all MMD sessions, detrusor pressure (p_{det}) was the parameter of utmost importance and was calculated by deducting the abdominal pressure from the intravesical pressure ($p_{det} = p_{ves} - p_{abd}$). When the occurrence of p_{det} in a recording was established, we measured the duration of p_{det} episodes in that recording, to allow comparison with MM episodes.

The aim of the study was to investigate:

1. The duration and the frequency of occurrence of *MM and* p_{det} in CPP and in healthy women and the relation between these outcomes and the instilled volume of the balloon within the bladder.
2. The frequency of occurrence of *pain and urge* in CPP and in healthy women and the relation between these outcomes and the instilled volume of the balloon within the bladder.
3. The relation between pain and/or urge and the presence of MM and/or p_{det} during MMD and evaluate the fundamental importance of these findings.
4. The clinical feasibility of MMD, by evaluating the relation between pain and/or urge during MMD and the presence of MM and/or p_{det}, in two groups of women:

   Group I. women *with* spontaneous bladder contractions, according to pressure criteria in conventional urodynamics.

   Group II. women *without* spontaneous bladder contractions, according to pressure criteria in conventional urodynamics.

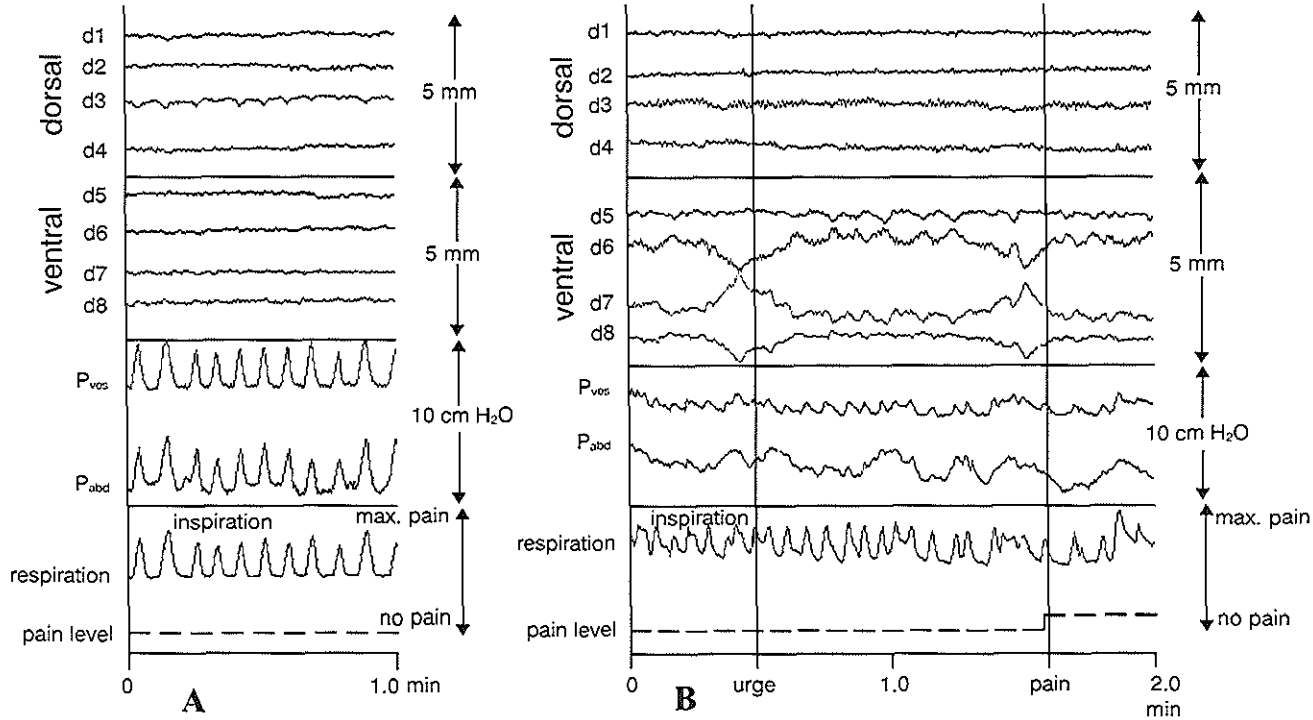

Figure III- 1. A) Example of an MMD recording of a healthy woman. The signals in the upper two windows represent 8 MM signals (d1-d8) [mm]. The third window is reserved for intravesical pressure (p_{ves}) and abdominal pressure (p_{abd}) [cm H20]. Respiratory excursions of the abdomen and signals from the pain marker are seen in the lowest window. Pain signals remain at level 1 in this recording in conformity with no pain during MMD. The rhythmic phasic activities observed in some MM channels of this recording, are all reflections of respiratory excursions of the abdomen. B) Example of an MMD recording of a CPP patient with urinary urgency and sudden start of pain in the lower abdomen during measurements. Both sensations are associated with the same MM feature, here a single monophasic MM with no change in the pattern of p_{ves}.

Percentages were compared between groups, using Fisher's Exact test. Between group comparisons of continuous outcomes were done, using Mann-Whitney's test. Within group comparisons were carried out, applying Wilcoxon's signed rank test or Friedman's test. To assess correlations between variables, Spearman's correlation coefficients were calculated. Data analysis was done, using the statistical package SPSS. The limit for statistical significance was set at $P = 0.05$ (two sided).

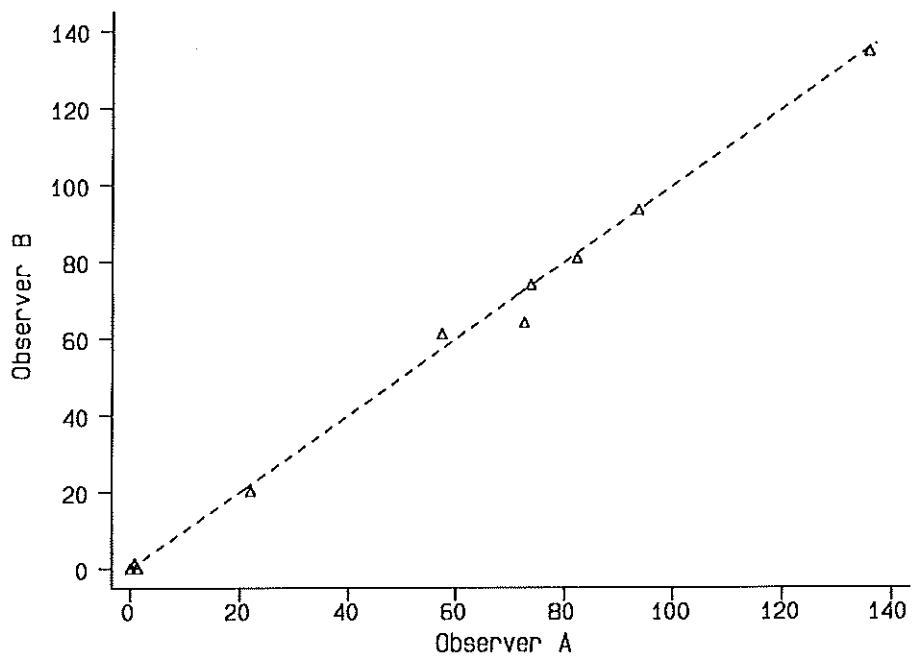

Figure III- 4. Inter-observer variation between two observers (A and B) when measuring the total length (in mm) of MM episodes, occurring during a three minute recording. Each point represents the mean of three independent readings and the dotted line is the line of identity.

III.3.5 Inter- and intra-observer variations

As MM had to be detected visually from the recordings, some subjectivity might be affecting the result in the outcomes. For this reason we investigated the inter- and intra-observers variations performed by two investigators. Ten representative 3-minutes recordings were selected from all recordings (CPP patients and healthy controls) by a third person. Independent analyses of each of the readings were performed three times by both investigators. The total duration of MM activity in each of the readings was determined. The results of both observers showed an excellent agreement (Intra-class correlation = 0.99) as shown in Figure III- 4. There was a minor difference between both observers regarding the within recording variability of readings. The standard deviation of the repeated measurements of observer A was on an average 0.12. The corresponding figure for observer B was somewhat greater, 2.0 ($P = 0.03$; Wilcoxon's test), but could nevertheless be considered small.

III.4 RESULTS

III.4.1 Obstacles and adverse events during and after measurements

The establishment of the location of MM activity falls beyond the scope of this study. Displacement signals are not a direct measure of the distance between two electrodes, as variations in the distance between neighboring electrodes contribute to the displacement signals. One true contraction could affect the outcomes of the neighboring displacement signals to such an extent that electrodes at non-contracting locations can emit displacement signals. We call this the 'cross talk phenomenon'. On the other hand, displacement signals recorded from any channel during a certain period are with certainty an indication that MM has occurred during at least the same period in a location in bladder wall which does not necessarily have to be the same as the spot where the relevant electrode is situated. Due to this technical restriction we have not yet been able to designate the MM recorded to specific locations in the wall of

the bladder. Rough estimations indicate that there are no preferential activity sites.

During measurements in four patients hampered drainage of bladder occurred for 10-15 minutes, mainly at 200 ml volume. Judging by the ongoing MMD feature, this did not seem to have an effect on the recordings.

The healthy controls said to have experienced an unpleasant sensation during the insertion and withdrawal of the probe. Once the balloon was filled and recordings had begun, the MMD was experienced by these women as being unpleasant or 'boring' only.

Post-examination interviews of the CPP women revealed that the insertion of the probe in the majority of cases was experienced as unpleasant, painful or even very painful. The pain experienced during measurements had been recognized by these women as 'the well known own lower abdominal pain'.

In two cases spasms of the urethra did not allow the insertion of the probe or even the thin drainage catheter. In both cases we have overcome the obstacle by first inserting an (F14) catheter which almost instantly resulted in the relaxation of the urethra. We then pushed the drainage catheter and the probe, one after the other, gently into the bladder alongside the first catheter which was then withdrawn.

In three women, although the insertion of the probe met with no difficulties, there were traces of blood on the balloon after withdrawal. Of these, two women said to have had traces of blood for about 24 hours after examination. Worsening of pain during 2-3 days after examination was reported by 2 patients. One patient had to be treated for urinary infection two days after MMD.

All healthy controls expressed that they would not object to repeat the examination. The experiences of 10 CPP women during MMD were comparable to those of the control group. Six women said to never want to repeat the MMD unless they absolutely had to. Fourteen patients were willing to repeat the examination although having experienced the examination as being uncomfortable or even painful.

III.4.2 Observational statistics

III.4.2.1 Occurrence and duration of MM and pdet episodes at different bladder volumes

Phasic variations in MM, whether or not accompanied by variations in detrusor pressure (p_{det}), with a total duration of 0.4-29.8 (mean: 12.5; median: 7.9) minutes were observed in the recordings of 26 women with CPP. The

Table III- 2. Significance of the differences in the sum of the duration of various MMD episodes, observed in the recordings of 30 women with CPP, at different bladder volumes.

	Duration [minutes]			*P-*
Observation	100 ml	150 ml	200 ml	*value**
MM^+ & p_{det}^-	2.3; 0.5; 0.0-10.0	1.9; 0.1; 0.0-10.0	2.2; 0.0; 0.0-10.0	0.564
MM^- & p_{det}^+	0.1; 0.0; 0.0-2.0	0.0; 0.0; 0.0-0.0	0.5; 0.0; 0.0-10.0	0.061
MM^+ & p_{det}^+	1.4; 0.0; 0.0-10.0	1.7; 0.0; 0.0-10.0	1.3; 0.0; 0.0-10.0	0.614
MM^- & p_{det}^-	6.3; 7.8; 0.0-10.0	6.3; 9.1; 0.0-10.0	6.0; 8.8; 0.0-10.0	0.988
MM^+	3.7; 2.3; 0.0-10.0	3.7; 0.9; 0.0-10.0	3.5; 0.6; 0.0-10.0	0.796
p_{det}^+	1.5; 0.0; 0.0-10.0	1.7; 0.0; 0.0-10.0	1.9; 0.0; 0.0-10.0	0.325

*Friedman's test
Values are means, medians and ranges.

recordings of two of the healthy controls showed MM activity. One woman had one episode of three minutes; in the other, MM activity was present during 10 minutes. None of the MMD recordings of the controls showed p_{det} whereas 22 of the CPP patients were p_{det} positive.

The appearance of MM and/or p_{det} was episodic. At least one of the following basic (episodic) observations was encountered in an MMD recording:

1. MM^+ & p_{det}^- = MM only

2. MM^+ & p_{det}^+ = Simultaneously occurring MM and p_{det}.

3. MM^- & p_{det}^+ = p_{det} only.

4. MM^- & p_{det}^- = No MM or p_{det} activity

It is also useful to define MM^+ and p_{det}^+. Here, MM^+ denotes MM activity, irrespective of p_{det}, and p_{det}^+ denotes variations in detrusor pressure, irrespective of MM. Analysis of the results, carried out on *all* recordings of CPP women (Table III- 2) and healthy controls, separately at 100, 150 and 200 ml (10 minutes at each volume), reveals that the *total* duration of none of above mentioned episodes was related to the bladder volume. The number of MM episodes in CPP, as well as in the control group, was not dependent on the volume of bladder either (P = 0.602 and 0.368 respectively; Friedman's test).

III.4.2.2 Distribution of MM episodes

One of the two MM-positive controls had one MM episode of 3 minutes. In the other control, MM activity was present during 10 minutes. In total 109 MM^+ episodes were observed in the CPP group. The mean number of MM^+ episodes was 4.2 (range: 1-13; median: 3). The mean duration of MM episodes observed in CPP women was 3.0 minutes (median: 0.8; range: 0.1-10 minutes) (Figure III- 5).

So far, the choice of 3 times 10 minutes measurement time per woman, has been based on the fact that our isovolumetric recordings have been interrupted by the filling of the probe. About 37% (40/109) of the MM episodes (mean duration: 6.9 minutes; median: 9.5; range: 0.3-10) were bordering on these interruptions, occurred at the beginning or at the end of the recording. The true durations of such episodes therefore, cannot be assessed. If measurements would have begun earlier, would have been continued for a longer period or would not have been interrupted, it is likely that some MM episodes would have had longer duration.

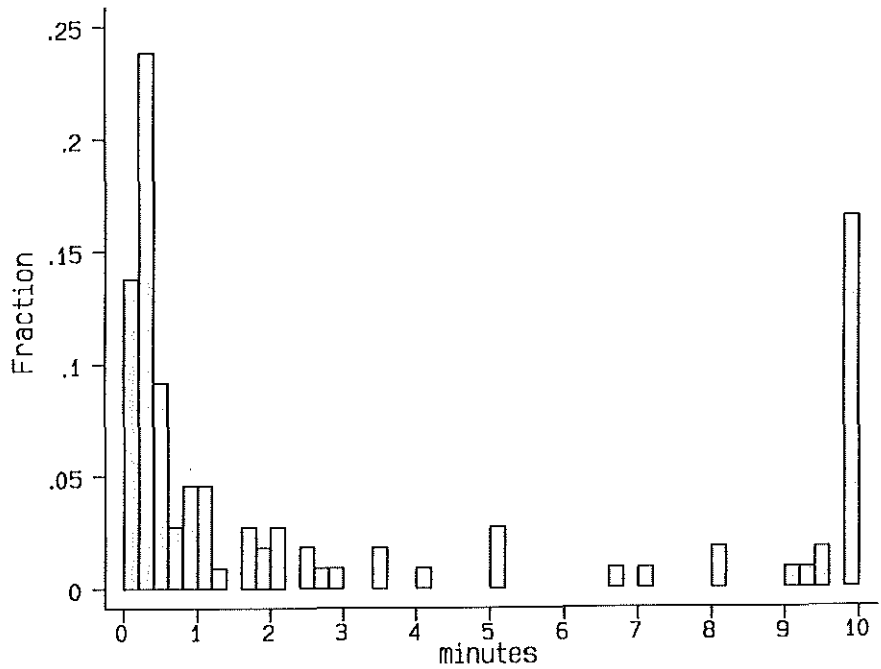

Figure III- 5. Distribution of the duration of 109 MM episodes observed during MMD measurements of 26 women with CPP whose recordings showed at least one episode of MM. Each measurement of 30 minutes consists of 3 consecutive sessions of 10 minutes, with bladder volumes of 100, 150 and 200 ml respectively. The maximum duration of episodes (10 minutes) is based on the maximum duration of recordings at each volume mentioned above.

III.4.2.3 Micromotion patterns of bladder wall

Phasic variations in MM, just as in p_{det}, generally do not cross the extrapolation line of the MM signals in rest (zero line), thus are not multiphasic. MM tends to appear in single monophasic (Figure III- 3.B) or multiple monophasic episodes

(Figure III- 6). MM is denoted multiple monophasic if 2 or more monophasic signals follow one another within an interval which is equal to, or less than the average of the duration of all monophasic signals in the same recording. MM episodes of less than 0.4 minutes are all monophasic. In the CPP group, about 40% (44/109 MM episodes) were monophasic with a duration ranging from 0.1 to 0.4 minutes (mean: 0.2; sd: 0.1). None of the healthy controls had single monophasic MM.

Multiple monophasic MM episodes observed in this study were more or less rhythmic (Figure III- 6). In 10 CPP patients, the MM pattern observed was predominantly rhythmic phasic (0.5-8 per minute) (Figure III- 6 and Figure III-7). This MM feature was seen also in the recordings of two women of the control group, be it of relatively low amplitude. Five patients had mainly arhythmic phasic MM. Rhythmic appearance of MM bursts were seen in one patient (Figure III- 8). Two or more of above mentioned MM features sometimes appear in one and the same recording.

The distribution of various frequencies of 37 rhythmic phasic MM episodes, observed in 11 patients is illustrated in Figure III- 9-A & B and shows a peak at 2-3 per minute. The peak at 7-8 per minute can not be considered to be representative, as the MM episodes causing this peak, originate mainly from the recording of one patient with bursts of MM activity.

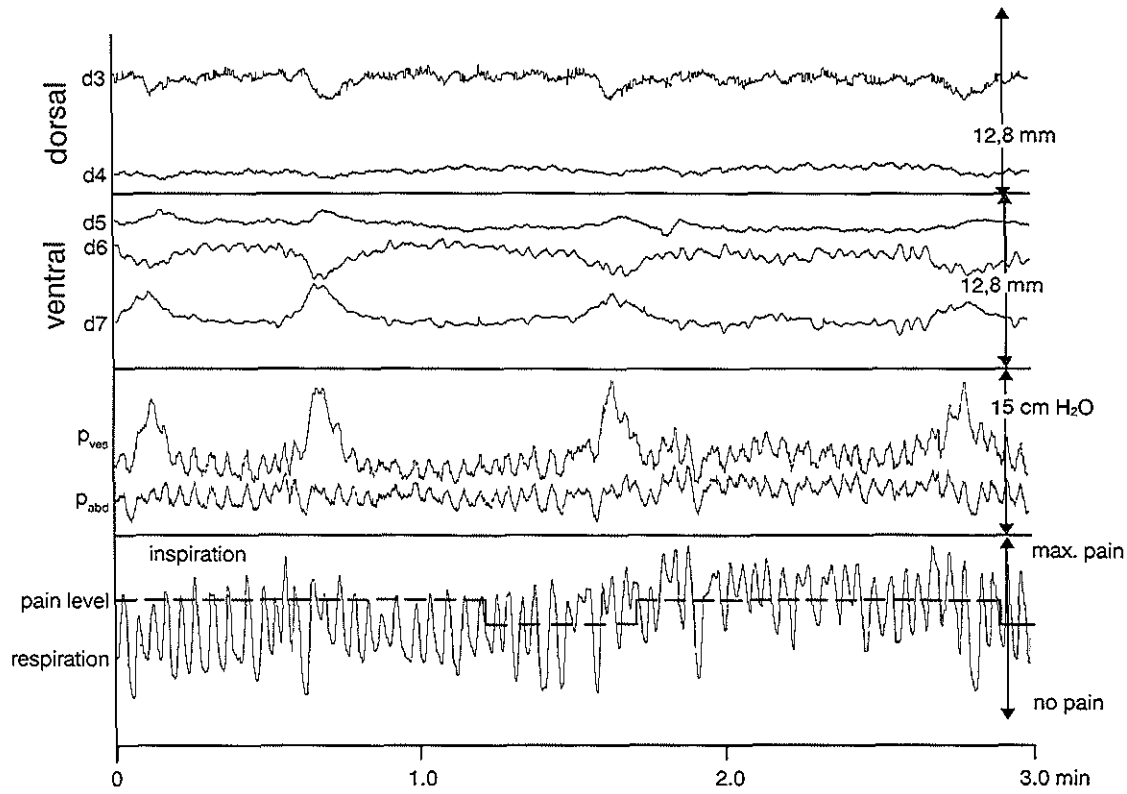

Figure III- 6. A three minutes recording of a CPP patient with persistent pain and urge, fluctuating in intensity and accompanied by multiple monophasic MM synchronous with variations in intravesical pressure (p_{ves}).

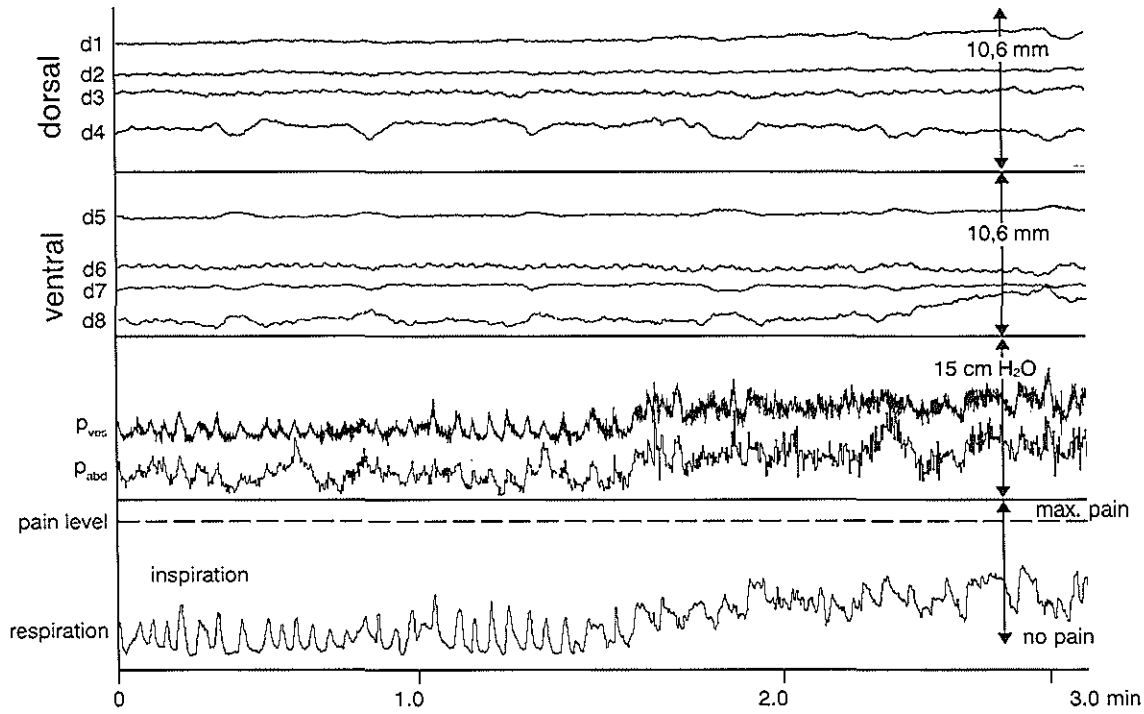

Figure III- 7. A three minutes MMD recording of a woman with CPP. Rhythmic phasic MM (2-3 per minute), not reflected in p_{det}, was recorded practically throughout the session and was accompanied by persistent pain. Pain signals indicate the level of (increase in) lower abdominal pain.

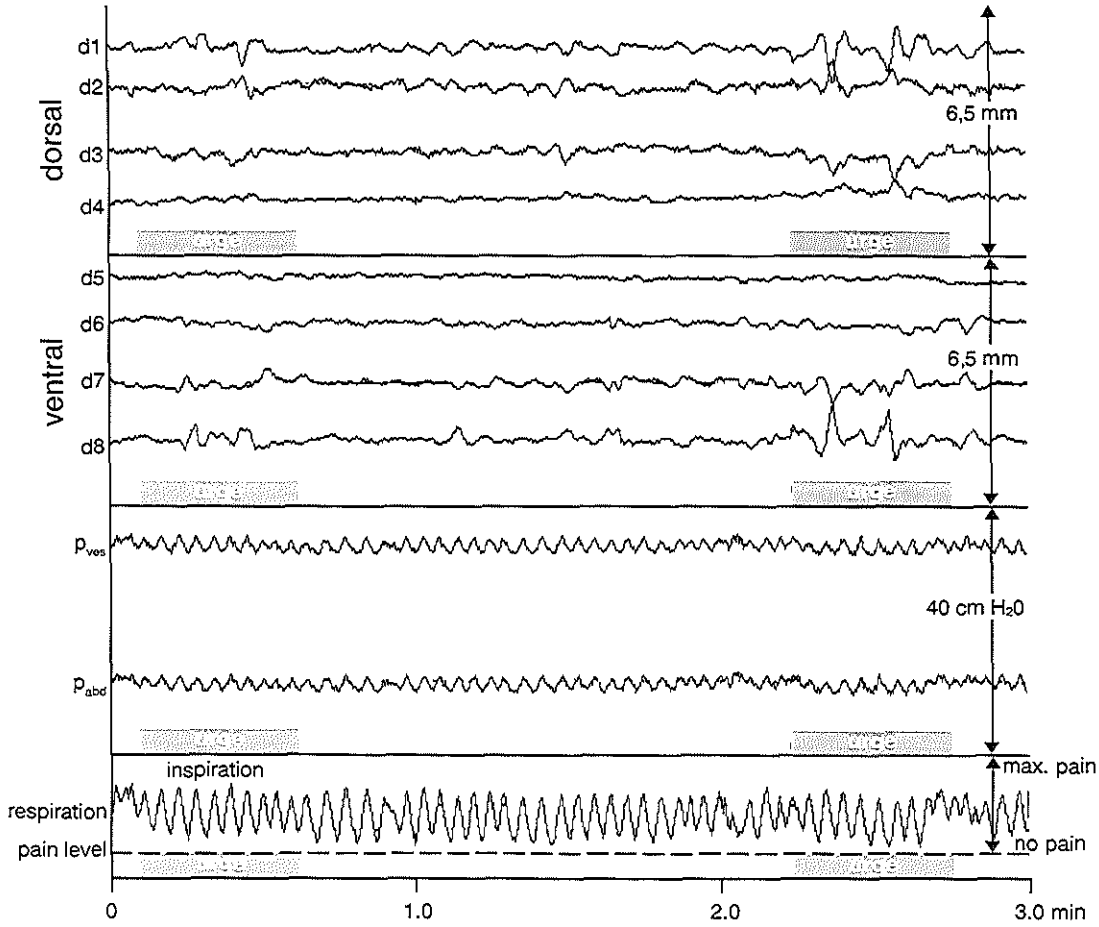

Figure III- 8. Bursts of MM accompanying reports of transient urinary urgency.

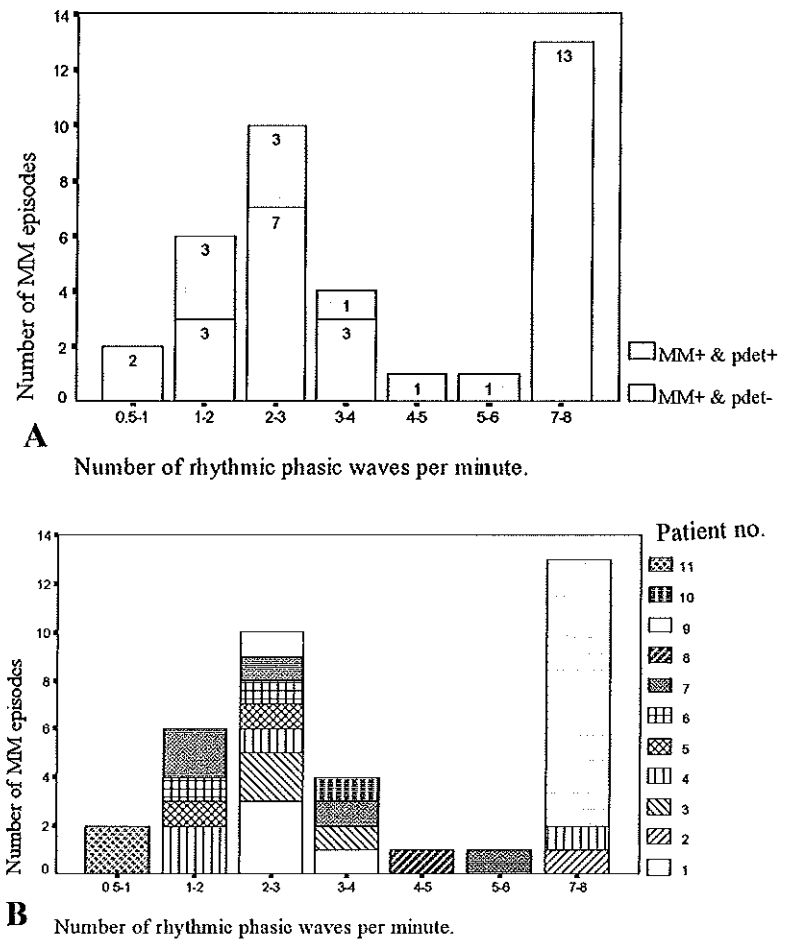

Figure III- 9. Stacked bar charts of 37 rhythmic phasic MM episodes observed in MMD recordings of 11 women with CPP.

A. Grated stacks in the upper chart represent MM episodes accompanied by variations in detrusor pressure (MM^{+} & p_{det}^{-}). Clear stacks correspond with MM episodes not accompanied by variations in detrusor pressure(MM^{+} & p_{det}^{-}).

B. The relatively high number of rhythmic MM episodes at 7-8 waves per minute is mainly due to observations in the recording of one patient. Stacks represent episodes of rhythmic phasic MM observed in 11 patients (no. 1-11).

III.4.2.4 Lower abdominal pain and urinary urgency during MMD

During measurements 20 women with CPP (67%) expressed *lower abdominal pain* at least once, and 18 (60%) expressed *urinary urgency* at least once. Of these, 6 women had at least one episode of pain and urge occurring simultaneously. None of the healthy controls expressed pain or urge during the session. The occurrence of pain during MMD was in CPP significantly higher than in controls ($P < 0.001$; Fisher's exact test). Also the occurrence of urinary urgency was in CPP significantly higher than in controls ($P = 0.008$; Fisher's exact test).

The sensations reported during measurements could be classified as follows:

1. Persistent lower abdominal pain and/or persistent urge, whether or not fluctuating in intensity; duration: 15-30 minutes.
2. Transient lower abdominal pain and/or transient urge with a sudden onset and in the absence of simultaneously occurring background persistent pain or urge; maximum duration: 1 minute.

III.4.2.4.1 Persistent lower abdominal pain and persistent urge during MMD

Persistent *pain and/or urge* was reported by 22 (73%) of the CPP group. Of these, 14 had pain only , 5 had urge only and 3 had persistent pain and persistent urge at the same time (Table III- 3). In 4 women the persistent pain and/or urge was dull with no change in the intensity throughout the session. The remainder 18 had episodic increase in the intensity of their pain and/or urge. In total 193 of such reports were registered. Mean number of reports of increase in the intensity of pain and/or urge per patient was 10.7 (median: 4.5; range: 1-41). When counting the number of reports of increase in pain or urge, reports following one another within a more or less arbitrary period of 0.1 minute, conform the minimum duration of single monophasic MM, were counted as being one.

Table III- 3. Summary of the frequency analysis of the duration of persistent pain and/or urge (middle column) and the number of reports of increase in the intensity thereof (n = 30).

Persistent		*Duration [minutes]*			*Number of reports of increase in intensity*		
sensation	n (%)	Mean	Range	n (%)	Mean	Median	range
Pain	14 (47%)	27.4	15-30	13 (43%)	9.6	4.0	1-39
Urge	5 (17%)	30.0	30-30	4 (13%)	16.5	11.5	2-41
Pain & urge	3 (10%)	29.7	29-30	1 (3%)	-	-	-

The average persistent urge, whether or not combined with pain, lasted practically throughout the session (Table III- 3).

III.4.2.4.2 Transient lower abdominal pain and transient urge during MMD

Transient pain and/or transient urge were reported by 15 women in total 160 times (mean: 10.7; median: 6.0; range: 1-32). Episodes of transient pain as well as episodes of transient urge or combined pain and urge were sometimes reported by one and the same woman in different episodes during the same recording session.

III.4.2.4.3 Number of reports of pain or urge during MMD

To obtain an indication of the total number of pain and/or urge reports, we added the number of reports of transient pain or urge to that of increase in the intensity of persistent pain or urge:

Number of reports of lower abdominal pain

= Number of reports of transient pain whether or not accompanied by urge plus the number of reports of increase in persistent pain whether or not accompanied by urge.

Number of reports of urge

= Number of reports of transient urge whether or not accompanied by pain plus the number of reports of increase in persistent urge whether or not accompanied by pain.

Total number of pain and/or urge reports

= Total number of reports of pain plus total number of reports of urge.

No relation was found between the number of pain and/or urge reports and the volume of bladder (Table III- 4).

Table III- 4. Significance of the differences in the number of pain and/or urge reports during MMD, at different bladder volumes.

	Duration [minutes]			*P-*
Sensation	100 ml	150 ml	200 ml	*value**
Pain	2.5; 1.0; 0-14	2.0; 1.5; 0-15	2.0; 0.0; 0-13	0.720
Urge	2.1; 0.0; 0-22	1.6; 0.5; 0-12	1.7; 0.0; 0-13	0.701
Pain + urge	4.5; 3.0; 0-29	3.6; 2.0; 0-15	3.7; 1.0; 0-22	0.360

*Friedman's test

Values are means, medians and ranges.

III.4.2.5 Occurrence and duration of MM and/or variations in detrusor pressure in CPP and healthy controls

Because the occurrence and the duration of MM and/or p_{det}, as well as the number of reports of pain and/or urge, were not dependent on the volume of the bladder, our data analyses are, as from now, based on observations during the total recording time, i.e. 30 minutes for each woman.

As mentioned before, the duration of MMD episodes plays an important part in our data analyses where the presence of different MMD episodes in relation to the occurrence of pain and/or urge is evaluated. For each we woman have

therefore established the total time for each of the four basic types of episodes (1. MM^+ & p_{det}^-; 2. MM^+ & p_{det}^+; 3. MM^- & p_{det}^+ and 4. MM^- & p_{det}^- in Figure III- 10), occurring during 30 minutes recording time.

The MM portion [MM^+ in Table III- 5; (MM^+ & p_{det}^-) + (MM^+ & p_{det}^+) in Figure III- 10] of the total recording time is in CPP larger than that in the control group. The difference is significant (P = 0.015; Mann-Whitney's test). This was not the case with the total p_{det} time [p_{det}^+ in Table III- 5; (MM^+ & p_{det}^+) + (MM^- & p_{det}^+) in Figure III- 10], despite the fact that no change in the pattern of p_{det} was observed in the control group.

Table III- 5. Occurrence and duration of MM and p_{det} in 30 women with CPP and 7 healthy women. Different types of MM and p_{det} observations are often observed in one and the same recording.

	Number of women			*Total duration of MMD episodes [minutes]*		
Observation	CPP n (%)	Controls n (%)	P-value*	CPP mean; median (range)	Controls mean; median (range)	P-value**
MM^+	26 (87%)	2 (29%)	0.005	10.8; 3.8 (0.0 - 29.8)	1.9; 0.0 (0.0 - 10.0)	0.015
p_{det}^+	12 (40%)	0 (0%)	0.072	5.1; 0.0 (0.0 - 30.0)	-	-
MM^+ & p_{det}^-	21 (70%)	2 (29%)	0.080	6.4; 1.5 (0.0 - 29.0)	1.9; 0.0 (0.0 - 10.0)	0.128
MM^+ & p_{det}^+	12 (40%)	0 (0%)	0.073	4.5; 0.0 (0.0 - 29.8)	-	-
MM^- & p_{det}^+	3 (10%)	0 (0%)	1.000	0.6; 00 (0.0 - 12.0)	-	-
MM^- & p_{det}^-	28 (93%)	7 (100)	1.000	18.6; 26.3 (0.0 - 30.0)	28,1; 30 (10.0 - 30.0)	0.015

*Fisher's Exact Test
**Mann Whitney's Test

It must be emphasized that more than one of the different (episodic) observations, as seen in Table III- 2, may occur in one and the same recording. Collective duration of various (episodic) observations is summarized in Figure III- 10.

MMD recordings with at least 1 episode of MM activity (MM^+), whether or not accompanied by variations in p_{det}, were seen in women with CPP more frequently than in the healthy (P = 0.005; Table III- 5). The same test shows a trend to the occurrence of p_{det} (p_{det}^+ in Table III- 5; P = 0.072).

In conventional urodynamics special attention is given to the phasic variations in detrusor pressure (p_{det}), the presence of which justifies the diagnosis bladder instability.
In order to establish the clinical feasibility of MMD, as compared to conventional urodynamics, we next divided our CPP patients into two groups: Women whose recordings showed no phasic variations in detrusor pressure (p_{det}), irrespective of MM, and patients in whose recordings at least one episode of p_{det}, irrespective of MM was observed.

The recordings of 18 patients and all recordings of the healthy showed no phasic variations in p_{det} (p_{det}^- group) throughout the session (Table III- 6). These recordings however, were not free from events. In this group 14 CPP women and 2 healthy controls had at least one episode of MM activity. The recordings of the remaining controls (5 women) showed neither MM nor p_{det}. The remaining 12 CPP women had recordings with at least one episode of p_{det}^+.

In all recordings of the p_{det}^+ group MM was observed accompanying variations in p_{det} (Table III- 6). However, in 3 of these recordings, also episodes of increase in p_{det} were observed without MM occurring simultaneously.

There is a trend that in all p_{det}^- women MM is more likely to be observed in the recordings of women with CPP than in those of the healthy (Table III- 6; P = 0.058). There is also a trend that women with CPP are, as compared to the healthy, more likely to have (a) p_{det}^+ episode(s) (Table III- 5; 12/30 *vs.* 0/7; P = 0.072).

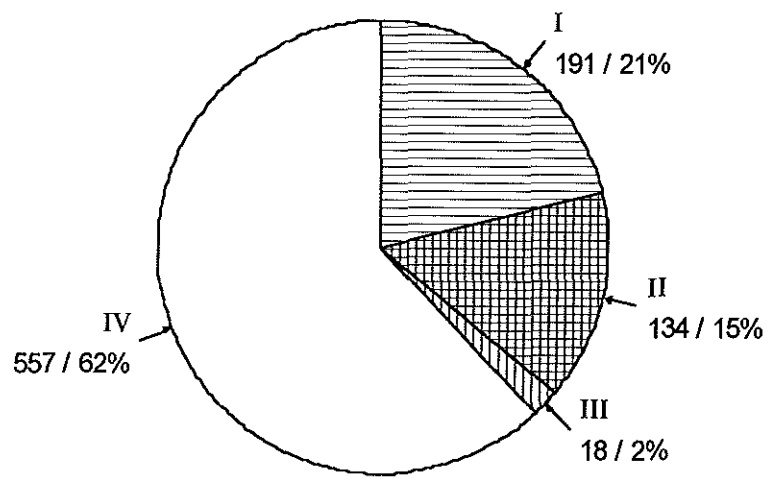

Figure III- 10. Summary of the collective duration (in minutes) of four basic types of MMD episodes in the recordings of 30 women with CPP, observed in *all cases*. The total surface of the pie chart represents 900 minutes of recordings (30 x 30 = 900 minutes; total recording time of the CPP group). Call outs refer to various types of MMD episodes, sum of the duration thereof and the percentages of each sum relative to the total recording time of 900 minutes.

I = MM^+ & p_{det}^- II = MM^+ & p_{det}^+ III = MM^- & p_{det}^+ IV = MM^- & p_{det}^-

As mentioned before, the recordings of one subject may exhibit various types of MMD episodes. Episodes of MM only (MM^+ & p_{det}^-), p_{det} only (MM^- & p_{det}^+) simultaneously occurring MM and p_{det} (MM^+ & p_{det}^+), and periods of no events at all (MM^- & p_{det}^-) can exist side by side in one and the same recording (Table III- 5). This is particularly the case in recordings with episodes of p_{det}^+ (Table III- 6). In this group 82% of the total time, during which MM was recorded, p_{det}^+ was observed simultaneously (Figure III- 11).

Table III- 6. Presence or absence of MM and p_{det} in MMD recordings of 30 women with CPP. In p_{det}^{+} group, at least one episode of increase in p_{det} (≥ 5 cm H2O, duration ≥ 0.1 minutes) is registered during 30 minutes of measurement.

	p_{det}^{-}		p_{det}^{+}	
	CPP (n=18)	Controls (n=7)	CPP (n=12)	Controls (n=0)
MM^{+}	14 (47%)	2 (29%)	12 (40%)	-
MM^{-}	4 (13%)	5 (71%)	0 (0%)	-
Total	18 (60%)	7 (100%)	12 (40%)	-
	P = 0.058 (Fisher's Exact Test)		-	

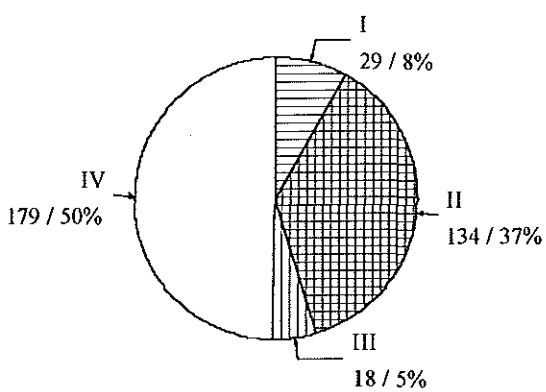

Figure III- 11. Time segments of the total duration of measurements (12 x 30 minutes = 360 minutes) carried out on 12 women with CPP, whose MMD recordings showed at least 0.1 minutes of variations in p_{det}. Call outs refer to various types of MMD episodes observed, total duration of the episodes and the percentages thereof relative to the total recording time of 360 minutes.

I = MM^{+} & p_{det}^{-} II = MM^{+} & p_{det}^{+} III = MM^{-} & p_{det}^{+} IV = MM^{-} & p_{det}^{-}

III.4.3 Density of pain and urge during different MMD episodes

The density of reports (pain, urge or pain + urge) is defined as the number of reports of these complaints per minute, during the total time of each of the four basic types of MMD episodes (MM^+ & p_{det}^-, MM^+ & p_{det}^+, MM^- & p_{det}^+ and MM^- & p_{det}^-), but also during MM^+ episodes as well as during p_{det}^+ episodes.

For each woman the density of a particular sensation (x) was calculated as follows:

$$D_{x/y} = n_x / t_y$$

where $D_{x/y}$ = Density of the number of reports of a specific sensation (x) per minute;
t_y = Total duration of a specific MMD episode (y);
n_x = Total number of reports of x during t_y.

The densities of urge or pain and those of pain plus urge are determined for each of the six types of MMD episodes (Figure III- 12).

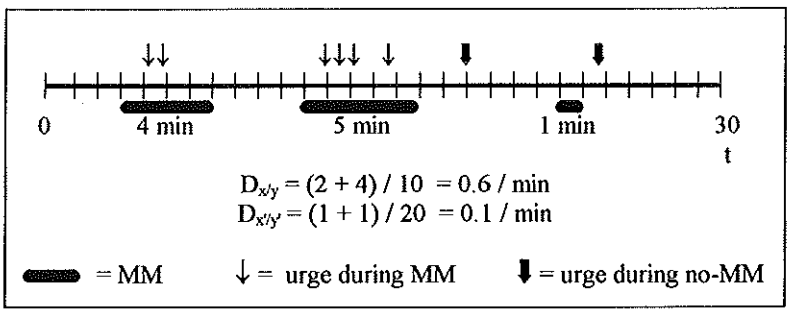

Figure III- 12. Schematic drawing of an arbitrary MMD session of 30 minutes. Urge densities during MM ($D_{x/y}$) and those during the periods when no MM is observed ($D_{x'/y'}$) are calculated.

III.4.3.1 Collective densities of pain and urge reports

In the following series of analyses, we look at MM and/or p_{det} episodes as separate phenomena and calculate the densities of urge, pain and that of pain plus urge for each type of MMD observation in *all* recordings of *all* CPP patients. These analyses are primarily meant as a fundamental study to evaluate the relationship between the presence of MM and/or p_{det} and the number of reports of lower abdominal pain and/or urge

III.4.3.1.1 Density of reports during MM *vs.* no-MM

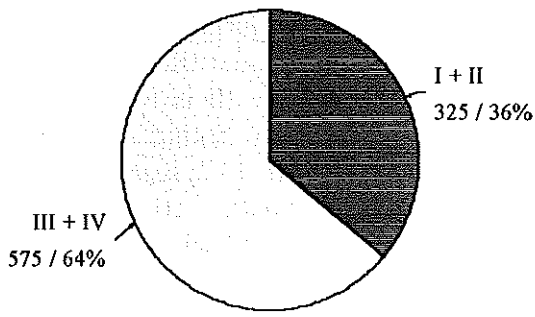

Figure III- 13.1. Collective duration of MM^+ episodes *vs.* MM^- episodes in 30 women with CPP.
$I + II = MM^+ = (MM^+ \& p_{det}^-) + (MM^+ \& p_{det}^+)$;
$III + IV = MM^- = (MM^- \& p_{det}^+) + (MM^- \& p_{det}^-)$.

In this analysis mean densities of reports during MM, whether or not accompanied by p_{det} (Figure III- 13.1; segment I + II in Figure III- 10), were compared with those during the periods when no MM were observed (Figure III- 13.1; segment III + IV in Figure III- 10) (Table III- 7.1).

Per minute, both lower abdominal pain and urge were significantly more often reported during MM episodes than during periods when no MM were registered. The densities of pain, urge and those of the sum of pain and urge reports were on average 5, 10 and 6 times higher during MM than during no-MM.

Table III- 7.1. Mean densities of pain and/or urge reports during the time MM were observed *vs.* the time when no MM were registered in 30 women with CPP. Twenty six women had at least one episode of MM^+. All thirty women had at least one episode when no MM were observed.

Report	*Density of reports*		*P- value**
	MM^+ (n = 26)	MM^- (n = 30)	
Pain	0.58 (0.22; 0.0-5.0)	0.13 (0.00; 0.0-0.8)	0.008
Urge	0.50 (0.06; 0.0-4.0)	0.05 (0.00; 0.0-0.5)	0.002
Pain + urge	1.08 (0.79; 0.0-5.0)	0.18 (0.06; 0.0-1.1)	<0.001

Values are means with medians and ranges in brackets.
* Wilcoxon's test

III.4.3.1.2 Density of reports during p_{det} *vs.* no-p_{det}

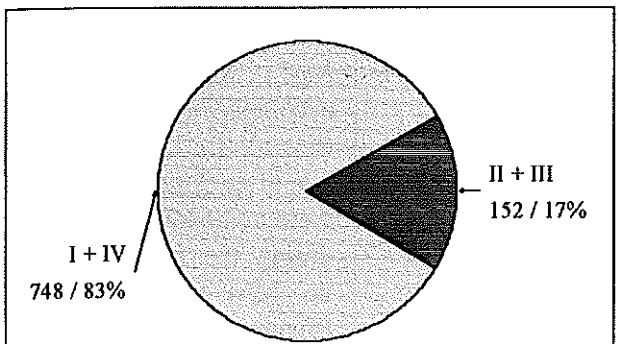

Figure III- 13.2. Collective duration of p_{det}^{+} episodes *vs.* p_{det}^{-} episodes in 30 women with CPP.
II + III = p_{det}^{+} = (MM^{+} & p_{det}^{+}) + (MM^{-} & p_{det}^{+});
I + IV = p_{det}^{-} = (MM^{+} & p_{det}^{-}) + (MM^{-} & p_{det}^{-}).

Although lower abdominal pain was reported on average 4 times more frequently during p_{det}^{+} (Figure III- 13.2; segment II + III in Figure III- 10) than during p_{det}^{-} (Figure III- 13.2; segment I + IV in Figure III- 10), this difference was not significant. Urge however was reported significantly more often during p_{det}^{+} than during p_{det}^{-} (on average about ten times as frequently; P = 0.017). This was also the case for the total of the reports, i.e. pain plus urge (on average seven times as often; P = 0.037) (Table III- 7.2).

Table III- 7.2. Mean densities of pain and/or urge during the time p_{det} were observed *vs.* the time when p_{det}^{-} were registered, in 30 women with CPP. Twelve women had at least one episode of p_{det}^{+} and 28 had at least one episode of p_{det}^{-}.

	Density of reports		
Report	p_{det}^{+} (n = 12)	p_{det}^{-} (n = 28)	*P- value**
Pain	0.70 (0.17; 0.0-5.0)	0.17 (0.05; 0.0-1.1)	0.311
Urge	1.07 (0.27; 0.0-5.0)	0.10 (0.00; 0.0-0.6)	0.017
Pain + urge	1.77 (0.90; 0.0-10.0)	0.27 (0.12; 0.0-1.1)	0.037

Values are means with medians and ranges in brackets.
* Wilcoxon's test

III.4.3.1.3 Density of reports during MM only *vs.* during no-MM and no-pdet

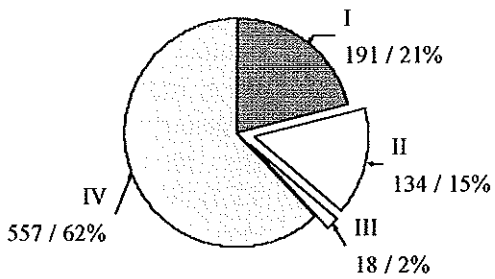

Figure III- 13.3. Collective duration of MM^+ & p_{det}^- (I) episodes *vs.* MM^- & p_{det}^+ (IV) episodes in 30 women with CPP. Segments II (MM^+ & p_{det}^+) and III (MM^- & p_{det}^+) have been excluded.

This analysis is meant to test the significance of the density of urge and/or pain reports during MM, in the absence of p_{det} (segment I in Figure III-10; Figure III- 13.3), as compared to the periods when no MM or p_{det} episodes were observed (segment IV in Figure III-10). In all recordings therefore, we omitted the time span of all episodes, where variations in p_{det} were observed (segment II + III in Figure III- 10; Figure III- 13.3). Reports during these episodes were not counted either. Pain and urge densities during MM only were significantly higher than during the periods when neither MM nor p_{det} were recorded (P = 0.006 and 0.038 respectively) (Table III- 7.3).

Table III- 7. 3. Mean densities of pain and/or urge during the time when only MM were observed *vs.* the time when neither MM nor p_{det} were registered in 30 women with CPP. Twenty one women had at least one episode of MM only and 28 had at least one episode of no MM or p_{det} episode.

	Density of reports		
Report	MM^+ & p_{det}^- (n = 21)	MM^- & p_{det}^- (n = 28)	*P-value**
Pain	068 (0.18; 0.0-5.0)	0.10 (0.0; 0.0-0.6)	0.006
Urge	0.56 (0.00; 0.0-5.0)	0.04 (0.00; 0.0-0.5)	0.038
Pain + urge	1.24 (1.49; 0-5.0)	0.15 (0.06; 0.0-1.0)	0.002

Values are means with medians and ranges in brackets.
* Wilcoxon's test

III.4.3.1.4 Density of reports during p_{det} only *vs.* during no-MM and no-p_{det}

Above mentioned analysis was repeated for p_{det} only (segment III in Figure III-10 and Figure III- 13.4). This time however, we omitted the time span, when MM were observed (segment I + II in Figure III- 10 and Figure III- 13.4). Reports during these episodes were not counted either. The densities of reports during p_{det} only *vs.* those during the time when no p_{det} were observed, were compared. Due to the small number of CPP women who had MMD episodes when only variations in p_{det} were registered, no reliable statistical comparison could be made. The data however, do not suggest great differences (Table III- 7.4).

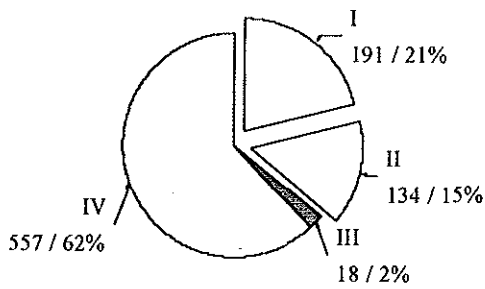

Figure III- 13.4. Collective duration of MM^- & p_{det}^+ (III) episodes *vs.* MM^- & p_{det}^- (IV) episodes in 30 women with CPP. MM^+ & p_{det}^- (I) and MM^+ & p_{det}^+ episodes have been excluded.

Table III- 7.4. Mean densities of pain and/or urge during the time when p_{det} only were observed *vs.* the time when no p_{det} were registered in 30 women with CPP. Only three women had episode(s) of p_{det} in the absence of simultaneously occurring MM whereas 28 had at least one episode of no MM or p_{det} episode.

	Density of reports	
Report	MM^- & p_{det}^+ (n = 3)	MM^- & p_{det}^- (n = 28)
Pain	0.30 (0.08; 0.0-0.8)	0.10 (0.0; 0.0-0.6)
Urge	0.07 (0.00; 0.0-0.2)	0.04 (0.00; 0.0-0.5)
Pain + urge	0.36 (0.08; 0.0-1.0)	0.15 (0.06; 0.0-1.0)

Values are means with medians and ranges in brackets.

III.4.3.1.5 Density of reports during MM only *vs.* MM and p_{det} combined

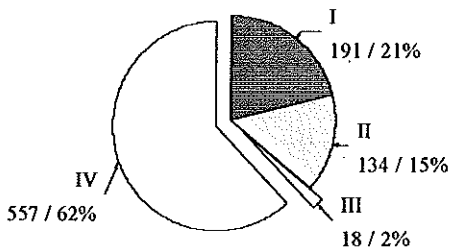

Figure III- 13.5. Collective duration of MM^+ & p_{det}^- (I) episodes *vs.* MM^+ & p_{det}^+ (II) episodes, in 30 women with CPP. MM^- & p_{det}^+ (III) and MM^- & p_{det}^- (IV) episodes have been excluded.

Mean densities of urge and/or pain during episodes when MM only is observed (segment I in Figure III- 10 and Figure III- 13.5) do not differ significantly from those when MM and p_{det} are recorded at the same time (Table III- 7.5) (segment II in Figure III- 10; Figure III- 13.5).

Table III- 7.5. Mean densities of pain and/or urge during the time when only MM were registered *vs.* the time when MM and p_{det} were observed simultaneously, in 30 women with CPP. Twenty one women had at least one episode of MM only and 12 had at least one episode of simultaneously occurring MM and p_{det}.

	Density of reports		
Report	MM^+ & p_{det}^- (n = 21)	MM^+ & p_{det}^+ (n = 12)	*P-value**
Pain	0.68 (0.18; 0.0-5.0)	0.29 (0.08; 0.0-1.9)	0.375
Urge	0.56 (0.00; 0.0-5.0)	1.09 (0.27; 0.0-5.0)	0.813
Pain + urge	1.24 (1.49; 0-5.0)	1.38 (1.0; 0.0-5.0)	0.688

Values are means with medians and ranges in brackets.
* Wilcoxon's test

III.4.3.1.6 Density of reports during p_{det} only *vs.* MM and p_{det} combined

As compared to the 12 CPP patients with simultaneously occurring MM and p_{det} (segment II in Figure III-10; Figure III- 13.6), only 3 women had episodes of MM^- & p_{det}^+ (segment III in Figure III- 10; Figure III- 13.6) (Table III- 7.6). Therefore no reliable statistical comparison is possible.

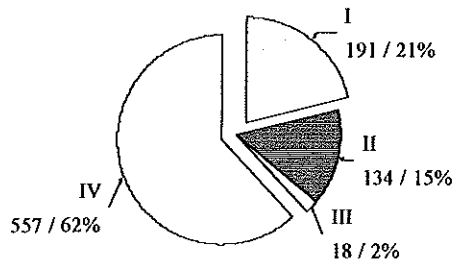

Figure III- 13.6. Collective duration of MM^- & p_{det}^+ (III) episodes *vs.* MM^+ & p_{det}^+ (II) episodes, in 30 women with CPP. MM^+ & p_{det}^- (I) and MM^- & p_{det}^- (IV) episodes have been excluded.

Table III- 7.6. Mean densities of pain and/or urge during the time when only p_{det} were registered *vs.* the time when MM and p_{det} were observed simultaneously in 30 women with CPP. Only three women had at least one episode of p_{det} in the absence of MM whereas 12 women had at least one episode of simultaneously occurring MM and p_{det}.

	Density of reports	
Report	MM^- & p_{det}^+ (n = 3)	MM^+ & p_{det}^+ (n = 12)
Pain	0.30 (0.08; 0.0-0.8)	0.29 (0.08; 0.0-1.9)
Urge	0.07 (0.00; 0.0-0.2)	1.09 (0.27; 0.0-5.0)
Pain + urge	0.36 (0.08; 0.0-1.0)	1.38 (1.0; 0.0-5.0)

Values are means with medians and ranges in brackets.

III.4.3.1.7 Density of reports during MM only *vs.* p_{det} only

Only 3 women had episodes of variations in only p_{det} in their MMD recordings (Table III- 7.7). This number is too small to allow a reliable comparison between densities of reports during MM only (segment I in Figure III- 10 and Figure III- 13.7) and those during p_{det} only (segment III in Figure III- 10 and Figure III- 13.7).

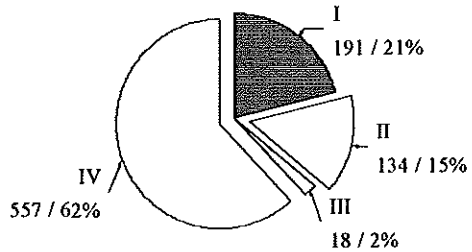

Figure III- 13.7. Collective duration of MM^+ & p_{det}^- (I) episodes *vs.* MM^- & p_{det}^+ (III) episodes, in 30 women with CPP. MM^+ & p_{det}^+ (II) and MM^- & p_{det}^- episodes have been excluded.

Table III- 7.7. Mean densities of pain and/or urge during the time when only MM were registered versus the time when only p_{det} were observed in 30 women with CPP. Twenty six women had at least one episode of MM only whereas only 3 had at episode(s) of p_{det} in the absence of simultaneously occurring MM.

	Density of reports	
Report	MM^+ & p_{det}^- (n = 26)	MM^- & p_{det}^+ (n = 3)
Pain	0.68 (0.18; 0.0-5.0)	0.30 (0.08; 0.0-0.8)
Urge	0.56 (0.00; 0.0-5.0)	0.07 (0.00; 0.0-0.2)
Pain + urge	1.24 (1.49; 0-5.0)	0.36 (0.08; 0.0-1.0)

Values are means with medians and ranges in brackets.

III.4.3.1.8 Density of reports during p_{det} *vs.* MM

The mean densities of reports during episodes, when variations in p_{det}, whether or not simultaneously with MM, were observed (segment II + III in Figure III-10), were higher than when MM, whether or not accompanied by p_{det}, were recorded (segment I + II in Figure III- 10) (Table III- 7-8). The differences, however, are not significant.

Table III- 7.8. Mean densities of pain and/or urge during the time when MM, whether or not accompanied by p_{det} were registered vs. the time when p_{det}, whether or not accompanied by MM were observed in 30 women with CPP. Twenty six women had at least one episode of MM^+ and 12 had at least one episode of p_{det}^+.

	Density of reports		
Report	MM^+ (n = 26)	p_{det}^+ (n = 12)	*P-value**
Pain	0.58 (0.22; 0.0-5.0)	0.70 (0.17; 0.0-5.0)	0.735
Urge	0.50 (0.06; 0.0-4.0)	1.07 (0.27; 0.0-5.0)	0.612
Pain + urge	1.08 (0.79; 0.0-5.0)	1.77 (0.90; 0.0-10.0)	0.441

Values are means with medians and ranges in brackets.
* Wilcoxon's test

III.4.3.1.9 Summary of collective MMD results of CPP patients

Evaluation of the collective MMD results, primarily meant as a fundamental study, reveals that:

1. The density of pain and/or urge reports in the presence of MM (whether or not accompanied by p_{det}) is significantly higher than that in the absence of MM.

2. The density of pain and/or urge reports does not differ significantly in the presence of p_{det} (whether or not accompanied by MM) or the absence thereof.
3. The density of pain and/or urge reports in the presence of MM (whether or not accompanied by p_{det}) and that in the presence of p_{det} (whether or not accompanied by MM) do not differ significantly.
4. The density of pain and/or urge reports in the presence of MM episodes, which are not reflected in p_{det}, is significantly higher than that in the absence of MM and p_{det}.
5. p_{det} episodes in the absence of MM are very scarce.
6. In CPP patients approximately half of the time, when MM and or variations in detrusor pressure are observed, both are present at the same time.
7. There is no significant difference between the density of pain and/or urge reports in the presence of MM episodes, which *are* reflected in p_{det}, and that in the presence of MM episodes, which *are not* reflected in p_{det}.

III.4.3.2 Densities of reports in CPP patients subdivided according to urodynamic behavior of the bladder.

This series of analyses is meant to evaluate the clinical feasibility of MMD as compared to conventional urodynamics, where phasic variations in detrusor pressure are seen as an expression of bladder instability. It can be assumed that in the women with variations in detrusor pressure during MMD the mechanical activity of bladder wall could have been detected by conventional urodynamics as well. The occurrence of fine mechanical activity of the detrusor in the p_{det}^- group, not detectable by urodynamics but observed during MMD, is particularly important. For this reason we divided our population of CPP patients into two groups according to whether or not variations in detrusor pressure were present in their MMD recordings. Various densities were determined for two groups of CPP patients:

Group I. Women whose MMD recording showed no p_{det} (p_{det}^- group; n = 18; Table III- 6). According to conventional urodynamics the recordings of these women would be labeled normal.

Group II. Women with at least one episode of p_{det} in their MMD recording (p_{det}^+ group; n = 12; Table III- 6). Conventional urodynamics at the time of MMD examination would probably show bladder instability.

In both groups we compared the density of reports during the time when MM were observed and during the time when no-MM were recorded. In group II we also compared the density of reports of pain and/or urge during p_{det}^+ and p_{det}^- episodes.

III.4.3.2.1 Densities of reports in CPP patients with no variations in detrusor pressure

In the 18 CPP women who had recordings with no p_{det}, the MM portion of the *total* recording time (18 x 30 = 540 minutes) was 30%. The mean density of pain in this group, was significantly higher during the time when MM were observed than during no-MM episodes (about 10 times as high; Table III- 8). The same analysis shows a trend in the case of urge (P = 0.08) (Table III- 8). The mean density of the sum of all reports (pain + urge) was also significantly higher during MM episodes.

Table III- 8. Comparison of the mean densities (number of reports per minute) of pain and/or urge during the time MM were recorded (MM^+) and the time when no MM were recorded (MM^-), in 18 CPP patients whose recordings showed no variations in p_{det}. Fourteen of these women had at least one episode of MM^+. All had at least one episode MM^-.

	Density of reports [per minute]		
Report	MM^+ (n = 14)	MM^- (n = 18)	*P-value**
Pain	0.71 (0.91; 0-5.0)	0.06 (0.00; 0-0.6)	0.018
Urge	0.18 (0.00; 0-0.1)	0.03 (0.00; 0-0.2)	0.080
Pain + urge	0.88 (0.45; 0.0-5.0	0.09 (0.00; 0-0.6)	0.008

Values are means with medians and ranges in brackets.
* Wilcoxon's test

III.4.3.2.2 Densities of reports in CPP patients with variations in detrusor pressure

In MMD recordings of the p_{det}^{+} group of CPP patients (n = 12), 50% of the *total* measurement time (12 x 30 = 360 minutes) was occupied by MMD events (segment I + II + III in Figure III- 11). MM were observed during 45% (segment I + II in) and p_{det} during 42% (segment II + III in Figure III- 11) of the *total* measurement time of the whole group. The time span of the overlap of MM and p_{det} (segment II in Figure III- 11) was 37%.

Tables III- 9,1-3 show the comparisons of the mean of pain and/or urge during various MMD episodes in the p_{det}^{+} CPP patients.

The mean density of pain reports in this group does not differ significantly during the time when MM is observed (segment I + II in Figure III- 11) and the time when no MM is present (segment III + IV in Figure III- 11) (Table III- 9.1). Nor is there a significant difference in the density of pain during the time when p_{det} is observed (segment III + IV in Figure III- 11) and when no variations in p_{det} are present (segment I + II in Figure III- 11) (Table III- 9.2). The same test shows that per time unit urge was reported significantly more often (about 10 times as often) during MM than during no-MM and that the number of urge reports during the time, when variations in p_{det} were seen, was significantly higher than during the periods, when no variations in p_{det} were registered (P = 0.017). The densities of reports during the time when MM, whether or not accompanied by p_{det}, were observed (segments I + II in Figure III- 11), did not differ significantly from those during the time, when p_{det}, whether or not simultaneously with MM, were recorded (segments II + III in Figure III- 11) (Table III- 9.3).

Table III- 9.1. Mean densities of pain and/or urge during the time when MM were registered vs. the time when no MM were observed in 12 p_{det} CPP women. All 12, had at least one episode of MM^{+} and one episode when no MM was observed.

	Density of reports		
Report	MM^{+} (n = 12)	MM^{-} (n = 12)	*P-value**
Pain	0.44 (0.26; 0.-1.7)	0.22 (0.13; 0.0-0.8)	0.285
Urge	0.87 (0.22; 0.0-4.0)	0.09 (0.02; 0.0-0.5)	0.009
Pain + urge	1.30 (1.34; 0.0-4.0)	0.30 (0.20; 0.0-1.0)	0.008

Values are means with medians and ranges in brackets.
* Wilcoxon's test

Table III- 9.2. Mean densities of pain and/or urge during the time when p_{det} were registered vs. the time when no p_{det} were observed in 12 p_{det} CPP women. All 12, had at least one episode of p_{det} and 10 women had at least one episode of p_{det}^{-}.

	Density of reports		
Report	p_{det}^{+} (n = 12)	p_{det}^{-} (n = 10)	*P-value**
Pain	0.70 (1.17; 0.-5.0)	0.26 (1.14; 0.0-1.1)	0.311
Urge	1.07 (0.27; 0.0-5.0)	1.16 (0.03; 0.0-0.6)	0.017
Pain + urge	1.77 (0.90; 0.0-10.1)	0.43 (0.41; 0.0-1.1)	0.028

Values are means with medians and ranges in brackets.
* Wilcoxon's test

Table III- 9.3. Mean densities of pain and/or urge during the time MM were registered *vs.* the time when p_{det} were observed in 12 p_{det} CPP women. All 12, had at least one episode of MM^{+} and one episode of p_{det}^{+}.

	Density of reports		
Report	MM^{+} (n = 12)	p_{det}^{+} (n = 12)	*P-value**
Pain	0.44 (0.26; 0.0-1.7)	0.70 (1.17; 0.-5.0)	0.612
Urge	0.87 (0.22; 0.0-4.0)	1.07 (0.27; 0.0-5.0)	0.735
Pain + urge	1.30 (1.34; 0.0-4.0)	1.77 (0.90; 0.0-10.1)	0.441

Values are means with medians and ranges in brackets.
* Wilcoxon's test

III.4.3.2.3 Summary of MMD results of two groups of CPP patients

The foregoing data analysis was primarily meant to evaluate the clinical feasibility of MMD as compared to conventional urodynamics, in which spontaneous bladder contractions are recorded indirectly by measuring variations in detrusor pressure. We therefore have divided our patients into I. p_{det}^{+} (patients with variations in detrusor pressure) and II. p_{det}^{-} (those without variations in detrusor pressure). Data analysis carried out for each group reveals that:

1. In CPP patients *without* variations in detrusor pressure spontaneous bladder activity can be detected directly by measuring the variations between two points on the inner wall of the bladder. MMD offers the means to detect such variations (MM) of even less than one millimeter.
2. In CPP patients *without* variations in detrusor pressure, the presence of *MM* is related to the density of reports of pain and shows a trend in relation to the density of urge reports.
3. In CPP patients *with* variations in detrusor pressure the presence of *MM* is related to the density of reports of urge, but not to that of pain reports.
4. In CPP patients *with* variations in detrusor pressure the presence of p_{det} is related to the density of reports of urge, but not to that of pain reports.
5. In CPP patients *with* variations in detrusor pressure most of the time, when MM and/or variations in detrusor pressure are observed, both are present at the same time; probably therefore:
6. In CPP patients *with* variations in detrusor pressure the density of pain and/or urge reports does not differ significantly in the presence of MM (whether or not accompanied by p_{det}) and in the presence of p_{det} (whether or not accompanied by MM).

III.4.4 Classification of women according to state of health and presence or absence of variations in detrusor pressure

When evaluating patients with urinary urgency it is customary to subject patients to (amongst others) urodynamic examination.

Urge patients, in whom variations in detrusor pressure are observed, are diagnosed to have motor urge; urgency in the absence of detrusor pressure variations is denoted sensory urge.

This analysis is primarily meant to find out whether there are enough differences between CPP women *with* and *without* p_{det}, to justify the subdivision of patients into p_{det}^+ and p_{det}^- groups.

In view of the foregoing and keeping in mind the MMD results of the healthy control group, in whom MM but not p_{det} were observed, we could classify the women who underwent MMD examination for this study, as follows:

A. Healthy control group (n = 7; all p_{det}^-).

B. CPP women (n = 30):

I. p_{det}^- group (n = 18; Table III- 6 and Table III- 10).

II. p_{det}^+ group (n = 12; Table III- 6 and Table III- 10).

Some of the results found in this study were already used to compare between group A (healthy controls) and group B (CPP patients).

In the following we shall compare subgroups I (CPP patients without p_{det} in their recordings) and II (CPP patients with at least one episode of p_{det}^+), in as much as the outcome of measurements was not affected by the aforementioned division of the CPP group into subgroups (Table III- 10). Densities of reports during p_{det} were thus not compared.

Total duration of MM does not differ significantly in the two groups. Most of the reports of pain and urge during measurements came from the p_{det}^+ group (P = 0.02 and P = 0.005 respectively). The differences in the densities of pain reports during MM were not significant between the two groups.

However, the density of urge reports during MM, whether or not accompanied by p_{det}, , was highest in the p_{det}^{+} group (P = 0.024). Densities of pain and/or urge during the time, when no MM or p_{det} episodes were observed, did not differ significantly when comparing p_{det}^{+} and p_{det}^{-} groups of women with CPP.

III.4.4.1.1 Summary of the comparison of the MMD results between different groups of women

This analysis was primarily meant to seek justification for the classical subdivision of patients with urinary symptoms according to urodynamic behavior of the detrusor i.e. patients *with* and patients *without* variations in detrusor pressure.

Our results reveal that:

1. Although only in the p_{det}^{-} group the density of *pain* reports is related to the presence of MM, this density does not differ significantly between patients *with* and patients *without* variations in detrusor pressure.
2. Although only in the p_{det}^{+} group the density of *urge* reports is related to the presence of MM, this density does not differ significantly between patients *with* and patients *without* variations in detrusor pressure.
3. The density of pain and/or urge reports in the absence of both MM and variations in detrusor pressure does not differ significantly between CPP patients *with* and those *without* variations in detrusor pressure.
4. The density of the total number of pain and/or urge reports does not differ significantly between CPP patients *with* and those *without* variations in detrusor pressure.

CPP patients *with* variations in detrusor pressure report significantly more often pain and/or urge during MMD than the p_{det}^{-} group, with a relationship

1. between the density of urge reports and the presence of MM, which is most of the time accompanied by variations in detrusor pressure.

Table III- 10. Collective duration of comparable MMD episodes and the density of pain and/or urge during these episodes, in p_{det}^{+} (n = 12) and p_{det}^{-} (n = 18) groups of women with CPP. Collective number of pain and/or urge reports is also compared.

Variable	Group I (p_{det}^{-})*	Group II (p_{det}^{+})**	P-value**
Duration [minutes]			
MM^{+}	18 (9.0; 1.8; 0.0-29.0)	12 (13.6; 13.5; 0.4-29.8)	0.182
MM^{-} & p_{det}^{-}	18 (21.0; 28.2; 1.0-30-0)	12 (14.9; 16.1; 0.0-29.6)	0.086
Number of reports:			
Pain	18 (3.8; 1.0; 0.0-22.2)	12 (10.5; 8.0; 0.0-39.0)	0.020
Urge	18 (1.8; 0.0; 0.0-12.0)	12 (10.6; 5.5; 0.0-46)	0.005
Pain + urge	18 (5.6; 3.0; 0.0-22.0)	12 (21.1; 17.5; 3.0-55.0)	0.001
Density during			
MM^{+}			
Pain	14 (0.71; 0.1; 0.0-5.0)	12 (0.4; 0.3; 0.0-1,7)	0.831
Urge	14 (0.18; 0.0; 0.0-0.9)	12 (0.9; 0.2; 0.0-4.0)	0.024
Pain + urge	14 (0.9; 0.5; 0.0-5.0)	12 (1.3; 1.3; 0.0-4.0)	0.115
MM^{-} & p_{det}^{-}			
Pain	18 (0.07; 0.0; 0.0-0.6)	10 (0.2; 01; 0.0-0.5)	0.232
Urge	18 (0.03; 0.0; 0.0-0.2)	10 (0.1; 0.0; 0.0-0.5)	0.200
Pain + urge	18 (0.1; 0.0; 0.0-0.6)	10 (0.3; 0.2; 0.0-1.0)	0.128

Values are number of patients with means, medians and ranges in brackets.

* CPP patients without phasic variations in detrusor pressure.

** CPP patients with at least one episode of phasic variations in detrusor pressure.

*** Mann-Whitney's test.

III.4.5 MM and p_{det} features during lower abdominal pain and/or urge

Single monophasic and multiple monophasic MM and/or p_{det}, observed during lower abdominal pain, urinary urgency and combined pain and urge, had generally the same wave length or shape and often also the same amplitude. This similarity of features was most striking in patients reporting pain, urge and combined pain and urge during different episodes of recording. In all women, who had monophasic MM accompanied by pain and/or urge, reports of these sensations were always lagging somewhat behind the peak in MM or p_{det} waves (Figure III- 3-B). To a lesser extent this was also observed in women, who had multiple monophasic MM, accompanied by persistent pain and/or urge fluctuating in intensity.

III.4.6 Location of MM activity

As mentioned before (see page 42), due to the 'cross talk phenomenon' we have not yet been able to designate MM recordings to specific locations in the wall of the bladder. Rough estimates, however, indicate that there are no preferential activity sites.

III.4.7 Variations in abdominal pressure

In 15 CPP women and 5 of the control group rhythmic multiphasic variations in abdominal pressure, measured intrarectally, 2-4 per minutes, were observed. The occurrence as well as the duration of p_{abd} did not differ significantly between the two groups.

III.5 DISCUSSION

III.5.1 Micromotions as source generation of afferent stimuli

An interesting finding in this study is that the occurrence and the duration of MM and/or p_{det}, are not dependent on bladder volume; further that urinary urgency during MMD is also independent of the volume of the bladder, but is related to both MM and p_{det}.

It goes without saying that the 'normal' desire to void is volume-dependent with expulsion phase of the bladder being the eventual motor response. We speculate that spontaneous contractions are premature efforts of the bladder control system to empty the bladder, which in turn would stimulate afferents, specifically involved in the conduction of noxious and other stimuli. Lower abdominal pain and/or urge reported during MMD were, just as MM, not dependent on the volume of the bladder. This is in line with findings that although 15% of women with CPP have urge-induced lower abdominal pain, in none of these women voiding relieves pain (6) (see also section II).

With the exception of occasional Paccinian and Pacciniform corpuscles, in the human bladder no receptors have been identified which could with certainty be denoted stretch-, pressure- or tension receptors. We postulate that (local) phasic motions stimulate volume-independent afferents in the detrusor muscle coat. This view is in accordance with the receptor model introduced by Iggo (72), where the receptors in bladder wall are stimulated by phasic contractions. The results of this study make the concept 'MM as source of pathological afferent stimuli, not dependent on bladder volume and resulting in unpleasant sensations such as lower abdominal pain and urge', an interesting one. Suppression of MM and it's after-effect on patients with lower abdominal pain and/or urge of unknown cause, would be a useful step to find out whether this view can be supported.

The fact that MM in the healthy controls was not accompanied by pain or urge and that the healthy controls, compared with the CPP patients, showed significantly shorter MM duration and relatively low amplitude MM, suggest that lower abdominal pain and urge are not only related to the duration of MM, but probably also to the amplitude thereof.

The independence of the results of MMD of the filling state of the bladder would make measurements at different volumes superfluous. Recordings could be carried out at a low bladder filling at for example 100 ml or even less. In this way problems, faced as a result of the stiffness of the balloon at higher volumes, will no longer exist. Estimation of the amplitude of MM for example would be greatly simplified if not only the cross talk phenomenon but also the stiffness of the balloon could be eliminated.

III.5.2 Frequency of rhythmic phasic micromotions in animal bladder strips *in vitro* and in human bladder *in situ*.

Contrary to *in vitro* studies on animal bladder strips, which show two frequency components of MM, we have found only one clearly recognizable frequency in the MM of human bladder *in situ*, notably at 2-3 per minute, which falls within the low frequency range of MM *in vitro*.

Although measurements have been carried out under isovolumetric conditions, the relatively fast filling of the bladder, carried out in 3 stages, may have acted as fast strain rate stimulus *in situ*. Contrary to *in vitro* studies on bladder strips, where MM frequency has been shown to be related to the state of strain, MM frequency *in situ* appeared to be independent of bladder volume (read state of strain).

III.5.3 Lower abdominal pain in medical history and during MMD

The fact that there was no relationship between urge in medical history and urge during MMD, suggests the possibility of the induction of urge by MMD,

in particular by the knobs on the outer surface of the balloon. However, it is interesting to observe that urge during (and probably triggered by) MMD is reported only by women with CPP and is totally absent in the control group and that the MM, even if it would have been triggered by MMD, had a significantly longer duration and a relatively higher amplitude in CPP than in the the healthy controls. This could be due to a heightened bladder sensitivity to mechanical stimulation in these pelvic neuralgic patients. This is of fundamental importance. Assuming that urge reported was indeed induced by MMD we have been able to provoke sensory urge, i.e. reports of urge not reflected in p_{det} and to show a relationship between these reports on the one hand and MM and/or p_{det} on the other in women with CPP. The MMD probe has in the mean time been improved and the size of the knobs on the outer surface of the balloon has been reduced considerably. Perhaps the knobs are not required for the local adhesion of the balloon onto the mucous membrane of bladder.

An important finding during this study was the pluriformity of the duration and quality of urge reported during MMD. Just like pain, urinary urgency seems to be continuous (persistent) whether or not fluctuating in intensity or of short duration (transient). Unfortunately, not suspecting these variations in the duration and quality of urge experienced, we paid no attention to this in our questionnaire, nor in our interviews. As yet, we do not know whether or not differentiation between persistent and transient urge is justified in normal every day life. The same applies to dull and fluctuating urge.

Obviously, it has been impossible for us to determine whether urge reported during MMD was always in conformity with ICS definition. Subjects were instructed to move and speak as little as possible in order to minimize artefacts. It was therefore not practicable to check the 'fear for pain' element during the 'almost irresistible need to void' with each report of urge. The 'almost irresistible need to void' was established by watching the facial muscles, notably the m. frontalis, and by post examination interviews. The statistical analysis in this study indicates that the need to void, reported by the CPP group during measurements, was most probably pathological as such reports were absent in the healthy control group.

There are no indications that the occurrence of pain during MMD was also induced by the method of investigation, since all women in our CPP group had been selected on the basis of having often, almost always or always lower abdominal pain in medical history.

In contrast to urge, the duration of pain episodes and whether or not the pain was fluctuating in intensity, had been extensively discussed with patients prior to MMD. It turned out that *fluctuating* pain during MMD, i.e. relatively high number of pain reports, was not significantly related to *fluctuating* pain in medical history. The attention focused on the quality of pain during measurements could in itself have made a patient realize that her pain after all was not as 'dull' as she thought. Nonetheless, the possibility that *fluctuations* in pain have been induced by MMD cannot be discarded altogether.

III.5.4 MMD versus conventional urodynamics

Although the methods and procedures in this study, including the measurements of p_{det}, differ from those of conventional urodynamics, we have found it justified to give special attention to reports of urge but also pain accompanied by p_{det} and those in the absence thereof. Worst case scenario for micromotions as compared to intravesical pressure has been maintained by the inclusion of p_{det} variations $\geq$ 5 cm H20. The minimum duration accepted for MM, 0.1 minutes, has also been applied to p_{det} variations. In this way we have been able to divide our population into two groups: women with p_{det} (p_{det}^{+} group), and those without (p_{det}^{-} group). The MMD results in the p_{det}^{-} group are in particular important when testing the significance of MM as diagnostic criterion for CPP. As it happens, spontaneous bladder activity of the p_{det}^{+} group could have been detected by urodynamics anyhow. The trend ($P = 0.058$) that in women with no variations in p_{det}, MM is more likely to be seen in CPP than in the healthy controls, makes it worth while to extend this investigation, now to a larger group of women with CPP. However, looking at the total time when in the p_{det}^{+} group of CPP women MM is recorded, we find that reflections of MM in p_{det} are observed during 82% of the total measurement time. If these results are confirmed in a larger group of p_{det}^{+} CPP patients, these patients should

thereafter be excluded by conventional urodynamics to minimize unnecessary investigations and costs.

When looking at MM and p_{det} episodes as phenomena which can occur side by side in each and every recording of women with CPP, collective densities of pain and/or urge reports of these women remain significantly higher during MM episodes than during the time when no MM is observed, irrespective of whether we are dealing with episodes of MM only (MM^+ & p_{det}^-) or episodes of simultaneously occurring MM and p_{det} (MM^+ & p_{det}^+). This means that the appearance of p_{det} at a given time span during an arbitrary episode of MM, does not mean that more (or less) pain or urge is experienced by a CPP patient. Remarkably enough, however, when we divide the CPP women into p_{det}^+ and p_{det}^- groups, in the p_{det}^- group pain is related to MM whereas the relationship between urge and pain shows a trend ($P = 0.08$). On the other hand, in the p_{det}^+ group pain is not related to MM, whereas urge is significantly related to MM as well as to p_{det}. The mean number of the sum of urge and pain reports is in the p_{de}^+ group significantly higher than in the p_{det}^- group, mainly due to the higher number of urge reports. The fact that the duration of MM does not significantly differ between the two groups and that MM features during urinary urgency do not differ from same during lower abdominal pain, is suggestive of a transition of lower abdominal pain to urge or the latter overriding lower abdominal pain, as soon as micromotions are large or synchronized enough to be observed accompanied by p_{det}.

We summarize our findings as follows:

1. For the first time, an objective and measurable somatic phenomenon, notably MM, has been demonstrated in chronic lower abdominal pain without obvious cause.
2. Chronic lower abdominal pain during MMD is related mainly to small, probably poorly synchronized, mechanical activity of bladder wall; too small or too chaotic in behavior to be detected by (current) methods for the measurement of detrusor pressure.

3. Urinary urgency during MMD is related mainly to large spontaneous, probably well synchronized mechanical activity of bladder wall; large enough to be detected also by current methods for the measurement of detrusor pressure.
4. Spontaneous mechanical activity of bladder wall is either the same cause of, or the same motor response to, two different unpleasant sensations in CPP: Lower abdominal pain and urinary urgency. In CPP, the sensation of urge may override or masque the sensation of lower abdominal pain. Perhaps urologic patients with sensory urge represent CPP patients who do not mention their lower abdominal pain when visiting their urologist, or whose lower abdominal pain is (most of the time) masqued by urinary urgency.

This study shows that the border between 'sensory' and 'motor' bladder symptom, at least in CPP patients, is a vague one. Motor urge, i.e. urge accompanied by p_{det} and sensory urge, not accompanied by p_{det}, can be registered side by side during one and the same MMD session. We have shown that there are no significant differences between the mean densities of pain and/or urge during episodes of MM only and episodes of MM combined with p_{det}. A patient can have (sensory) urge during an MM^+ & p_{det}^- episode and (motor) urge during an immediately following MM^+ & p_{det}^+ episode. Practically speaking, however, the division of patients with bladder symptoms, according to urodynamic behavior of the detrusor, i.e. the division into MM^+ & p_{det}^- groups, is useful: The relation between urgency and p_{det}, at least under conditions comparable with the methods maintained in this study, justifies conventional urodynamics to be the first step when evaluating urinary urgency in (CPP) patients. However, as far as the lower abdominal pain in CPP is concerned, conventional urodynamics fails in detecting a relation between the pain reported and the mechanical activity of bladder wall. As the presence of MM only (MM^+ & p_{det}^-) in the whole group of CPP patients (n = 30), was proven to be related to the number of urge reports, we may assume that the trend seen in the *small* p_{det}^- group (n = 18) is not valid and that the presence of MM in women with no variations in p_{det} is significantly related to MM.

III.5.5 Technical imperfections

MM recordings *in situ* are the result of displacements in bladder wall, presumably due to (local) contractions as seen in bladder strips *in vitro*. Displacements in one location however, can also affect the outcome of signals emitted from the neighboring channels in such a way that changes in the direction of the electrical displacement signals, i.e. information about lengthening or shortening of the distance between two electrodes, may differ from the true variations in the distance between the two points in the wall of bladder. As yet therefore we prefer to abstain from passing judgment about whether a recorded phasic change in an MM pattern represents contraction or relaxation.

Prior to recordings, the location of electrodes relative to specific locations of the wall of bladder were (roughly) established in order to obtain information about possible preferential locations of MM. However, also here the influence of cross talk cannot be neglected. Because of this, we have for the time being postponed our data analysis concerned with the exact locations of MM. Rough estimations indicate that, conform *in vitro* studies (55), the occurrence of spontaneous bladder activity does not have preferential locations.

Again, mainly due to the intervention of 'cross talk', it is not yet possible to make, with certainty, statements concerning the relationship between the amplitude of MM and that of possible, simultaneously occurring variations in p_{det}. Rough estimations of the collective outcome of all patients, however, indicate no relationship, whereas individual recordings of patients with both MM^+ & p_{det}^- and MM^+ & p_{det}^+ episodes suggests the existence of a threshold, probably related to the amplitude of MM, and different for each individual and above which, MM is reflected in p_{det}. Nonetheless, the occurrence of identical MM features with seemingly the same amplitude, only sometimes reflected in p_{det} has also been observed in one and the same recording. In case of negligible effect of cross talk on the amplitude of MM measured, this would mean that MM in human bladder *in situ*, just as in porcine bladder strips *in vitro* (46,48,49,57), is local by nature. We speculate that MM might behave in a

chaotic asynchronous manner resulting in no- or little change in detrusor pressure and that the latter is affected only when certain conditions are satisfied. Transient total synchronization would for example, result in a phasic increase in p_{det}, provided it would occur rapidly enough to occur before the compliant response of the bladder would have the opportunity to prevent the increase in detrusor pressure.

Although only 2% of the total recording time of all CPP patients was occupied with p_{det} in the absence of MM, this is an important finding for fundamental studies. With the 8 bladder locations measured in this study, it is probable that some local MM activity, falling beyond the reach of the electrodes, would be missed. Local strong contractions, located outside the reach of the electrodes could explain the phenomenon 'MM^- & p_{det}^+'. Another explanation would be the total contraction of a *spherical* bladder, under isovolumetric conditions, where increase in detrusor pressure can be expected with no change in the total surface of the wall of bladder. A perfect spherical shape of the bladder *in situ* is very unlikely to occur. On the other hand, episodes of p_{det} only, as encountered in this study, were very scarce indeed.

In the absence of MM in a recording, the existence thereof in a location beyond the reach of the electrodes can not be excluded. On the other hand it can with certainty be stated that MM in a recording is always associated with phasic changes in the surface of bladder wall, not necessarily at the location of the electrode emitting the signal but also not necessarily local by nature. Under isovolumetric measurement conditions it can be expected that contractions involving large areas of the detrusor would result in non-contracting areas to bulge out. In other words, the isovolumetric measurement condition, as maintained in this study, does not mean that displacement signals necessarily have to telltale the local nature of the ongoing activity.

Corrections for 'cross-talk', falling beyond the scope of this study, are necessary to define the quality of displacements measured as MM and to establish with certainty, the amplitude of MM as well as the location thereof. In our institute we have in the mean time been able to make partial corrections for this cross talk phenomenon in vitro (67).

In this study, with the choice of reliable parameters, for example the duration, rather than the amplitude of micromotions, we have been able to carry out our data analysis without disturbances from 'cross talk'.

The delay between the sensation felt and the manual or verbal reports of pain or urge respectively, and in case of urge, the manual insertion of the marker in the recordings by the investigator might explain why markers generally were found to lag behind the peaks in MM and p_{det}. Variations in pain marker signals do not always follow variations in MM in patients with fluctuating lower abdominal pain. Perhaps better instruction or a short training program for patients, before the MMD measurements, would improve the synchrony of fluctuations in pain marker and that of MM variations. With the version of pain marker used in this study, only qualitative variations in the intensity of pain can be established. Correction for *subjective* pain experience and calibration of pain marker before each measurement would improve the establishment of the intensity of pain during MMD.

In patients with high transmission of abdominal pressure to the bladder, using the pain marker to mark fluctuations in urge instead of verbal reports, might lessen the artefacts caused by speaking. However, as far as pain is concerned, it is our experience that the very opportunity to report 'exactly' each and every variation in the intensity of pain, can cloud the outcomes. For example seven or more fluctuations in the level of pain marker have sometimes been observed within 0.2 minutes of recording. We have experienced these clusters of reports as a hindrance when counting the number of pain reports. By maintaining the same criteria for counts within- and between recordings, we have restricted incorrect outcomes when comparing pain densities during various episodes of MM and p_{det} as well as during episodes when no MM or p_{det} were recorded. Looking back, a 3-level pain marker button would have been preferable: Level 0 = no pain; level 1= persistent pain; level 2 = transient pain or sudden increase in persistent pain. Obviously, such a marker could not be used to establish the intensity of pain or urge. On the other hand, without extensive training of patients and calibration of pain marker before each recording, the value of markers for the intensity of pain or urge remains questionable.

Further research and computerized feature detection are necessary to answer many questions brought up by this pilot study. It is for example not yet clear why -compared to *in vitro* studies, where strips from all regions of cat bladder show spontaneous activity- in about half of patients the dorsal channels and in the other half, the ventral channels exhibit more activity. In a hierarchical model of bladder control system[2], it is postulated that locally synchronized MM waves can be seen as premature autonomous attempts to empty bladder, occurring at the most primitive level of an hierarchical bladder control system. The authors speculate that a premature expulsion phase, i.e. a spontaneous, volume-independent bladder contraction, is in the healthy adult usually prevented by descending inhibitory forces. The total isolation of the detrusor muscle tissue from the central nervous system might account for the totally uninhibited spontaneous contractions observed in the detrusor tissue of cat, obtained from all regions of bladder wall as reported in literature (55). Partial, (functional) isolation of the detrusor in human bladder, with no preference for specific areas of the wall of the detrusor, might account for the observations in this study that not all MM channels exhibit activity and that there seem to be no preferential MM locations.

It is remarkable that MM, displacements of a matter of millimeters, accompany pain and urinary urgency. The sequence of pain/urge reports following within a short delay, peaks in MM^{+} & p_{det}^{-} or MM^{+} & p_{det}^{+}, suggest that pain and urge are sensory responses to mechanical activity of bladder wall. MM, as an autonomic motor response to pain and urge, however, is also an option.

In the absence of computerized data analysis, experienced eyes for the detection of MM are much more a 'must' than when interpreting p_{det}. Where the latter can be clearly identified as an eye-catching spontaneous pressure wave, a monophasic MM may be a modest low amplitude event, in the middle of a

[2] Van Os-Bossagh P, Van Duyl WA, Passchier J, Vierhout ME, Drogendijk A.C. Bladder control system: a hierarchical model. In preparation.

cloud of noise; the latter as the result of -amongst others- the respiratory excursions of the abdomen. Making sure that the MM observed was not merely a reflection of respiratory excursions by comparing the wave length of each and every (potential) MM and that of the simultaneously occurring respiration, has been experienced by us as a very arduous and time consuming job. Automation of signal analysis would not only improve the economical feasibility in a great extent, but also would eliminate inter- and intra-observer's variations.

III.5.6 Diagnostic value of MMD

Although MM was also recorded from the bladder of the healthy control group, the duration thereof was significantly less than in the CPP group. Therefore, long duration mechanical activity of bladder wall can be seen as an important diagnostic criterion when evaluating chronic pelvic pain of unknown origin in women. The existence of MM^+ & p_{det}^- episodes shows that variations in detrusor pressure as means to detect spontaneous bladder contractions, cannot always be counted on. The number and the total duration of MM^+ & p_{det}^- episodes exceed those of MM^- & p_{det}^+ episodes overwhelmingly. A follow-up study of MM^+ healthy individuals would be useful to find out whether these women run a greater risk to develop CPP.

Current concepts in respect of bladder function and inherent urological problems still leave many questions unanswered. Micromotion activity as means of communication between bladder and central nervous system may constitute a key factor in achieving further progression in comprehending some pathological bladder behavior. Although psychological influences on the experience of pain and/or urge in CPP can not be discarded, it may well be possible that a derailed neural regulation system is the main underlying mechanism in the occurrence of MM as well as in the experienced pain and urge.

The diagnostic value of MMD in CPP is proven by the significant coincidence of MM and reports of pain and/or urge; in the case of pain, also in the p_{det}^- group. The duration of p_{det} on the other hand, is significantly related to the

number of urge reports only. MMD as diagnostic tool in CPP seems therefore valuable, certainly as far as lower abdominal pain is concerned. MMD should be seen as a diagnostic tool, complimentary to the conventional urodynamics. It must be emphasized that in women with lower abdominal pain with unknown cause, for the first time a relationship has been found between their pain and objective patho-physiological findings. Although not lethal, CPP has a considerable effect on the quality of life. The female patient with chronic pelvic pain is often 'accused' of medical shopping and in constant search of a 'legitimate' diagnosis. The very assurance that 'it's not all in your head' (73,74) and that 'when you have pain, there are these little innocent movements in your belly, which we do not yet know how to get rid of', makes patients with chronic pain feel understood and therefore somewhat better.

We end this section with a citation from the diary of a woman with CPP who participated in this study (translated from Dutch):

"It's not only this ever present pain which makes me suffer, but also the knowledge that nobody believes me. My husband thinks I am hysterical and my family doctor keeps referring me to psychotherapists. I am no longer the one I used to be and I seem to be the only one who knows there is something seriously wrong with my physical health".

III.6 CONCLUSIONS

1. For the first time, an objective and measurable somatic phenomenon, notably MM, has been demonstrated in chronic lower abdominal pain without obvious cause.

   Based on the findings in this study, there are indications that:

2. The occurrence and duration of micromotions and/or phasic variations in detrusor pressure are volume-independent.
3. The number of reports of lower abdominal pain, urge and sum of both, is not dependent on the volume of the bladder.
4. Micromotions occur more frequently in CPP than in the healthy.

5. In CPP, the presence of micromotions is related to the number of pain and/or urge reports during MMD.
6. In CPP, the presence of variations in detrusor pressure, is related to the number of urge reports but not to the number of pain reports.
7. Lower abdominal pain during MMD is related mainly to the presence of small, probably poorly synchronized, mechanical activity of bladder wall; too small or too chaotic in behavior to be detected by (conventional) methods for the measurement of detrusor pressure but detectable as micromotions.
8. Urinary urgency during MMD is related mainly to the presence of large spontaneous, probably well synchronized mechanical activity of bladder wall; large enough to be detected also by (conventional) methods for the measurement of detrusor pressure.
9. Spontaneous mechanical activity of bladder wall is either the same cause of, or the same motor response to, two different unpleasant sensations in CPP: Lower abdominal pain and urinary urgency. In CPP, the sensation of urge may override or masque the sensation of lower abdominal pain. Perhaps urologic patients with sensory urge represent CPP patients who do not mention their lower abdominal pain when visiting their urologist, or whose lower abdominal pain is (most of the time) masqued by urinary urgency.
10. Micromotion features observed in association with lower abdominal pain, are of approximately the same shape and duration as micromotions accompanied by urinary urgency, although micromotions in the presence of urge have somewhat higher amplitude and are most of the time accompanied by variations in detrusor pressure.
11. Mean densities of pain and/or urge reports during episodes when micromotions are observed and during the time when episodes of variations in detrusor pressure are registered, do not differ significantly.
12. A subgroup of CPP patients partaking in this study, had no variations in detrusor pressure. In this small group:

    - lower abdominal pain during MMD is related to the presence of MM.

- The relation between (sensory) urge and the presence of MM, contrary to the results in the total group, shows a trend presumably because of smaller population. It can be assumed that sensory urge is related to MM.

SUMMARY

Section I
General introduction to chronic pelvic pain (CPP)

Chronic pelvic pain (CPP) is defined as pain in the lower abdomen of unknown origin that has lasted for at least 6 months. Deep dyspareunia, radiation of the pain to the lower back and voiding symptoms may accompany this syndrome. Diagnosis of the female patient with chronic lower abdominal pain without showing apparent organic abnormalities may vary from irritable bowel syndrome, urethral syndrome, pelvic neuralgia, parametrial hyperalgia and chronic pelvic pain (CPP), largely caused by the fact that the illness is not properly understood yet. As many as 10% of patients visiting gynaecologists do so in connection with this syndrome and amongst them we find women of all ages. It has been postulated that due to the close developmental relationship of the lower urinary tract and the genital tract, disorders of the first may adversely affect the function of the second and present themselves as CPP.

In the studies presented in this thesis, for the first time bladder symptoms in CPP are extensively evaluated (Section II). Also spontaneous contractions of bladder wall in women with CPP are measured and analyzed in search of a possible relationship between spontaneous detrusor activity and lower abdominal pain and urinary urgency (section III). A questionnaire, partially used to obtain data for the evaluation of urinary symptoms in CPP (Section II), is presented as appendix. It contains statements concerning medical history, the degree and the quality of the lower abdominal pain, pelveo-perineal dysaesthesia, voiding symptoms, gastro-intestinal complaints, symptoms of the reproductive organs, etc.

Section II
Urinary symptoms in chronic pelvic pain (CPP)

In the Netherlands the prevalence of one or more voiding symptoms in women between 50 and 75 years of age, is 36%. Although the main complaint of CPP

patients is lower abdominal pain, many of them also report lower urinary tract problems such as recurrent cystitis, urgency, incontinence and dysuria.

Painful bladder conditions and voiding symptoms of unknown etiology occur also in the urethral syndrome, in interstitial cystitis (IC), in detrusor myopathy, in chronic nonspecific cystitis and in eosinophilic cystitis. It has been suggested that the urethral syndrome is a subclass of IC whilst the urethral syndrome being mistaken for CPP has also been reported. The symptoms of the urethral syndrome are urinary urgency, dysuria, frequency and suprapubic discomfort. Also hesitancy, incomplete bladder emptying and weak stream may be present as well as symptoms not related to the urinary tract, such as back discomfort.

Sixty CPP patients completed a questionnaire covering amongst others urinary symptoms. The items selected from the questionnaire for this study, cover I. symptoms of urinary incontinence; II. symptoms of irritation of lower urinary tract and III. symptoms of pelvic floor spasticity. Those answers confirming symptoms occurring often or (almost) always, were taken into account as being serious symptoms. In case of urinary incontinence, also involuntary loss of urine, irrespective of type (stress, urge, mixed or unknown), in amounts larger than a few drops had to be present. The frequency of these symptoms and their interrelationship were both analyzed. Also in a group of non-CPP hospital patients the frequency of the occurrence of these symptoms was established in order to make sure that the outcome was not affected by the CPP women being a hospital population. Where available, data from studies on samples of the female population were compared with our own findings. A psychological approach to the co-occurrence of lower abdominal pain and voiding symptoms in CPP is also discussed.

Results: There was a wide range in the frequency of the occurence of various voiding symptoms in CPP and the majority of symptoms were significantly more often reported by CPP than by non-CPP patients.

I. Symptoms of urinary incontinence: incontinence 43%; inadequate voluntary control of the urethral sphincter 50%; inability to postpone 37%.

II. Symptoms of irritation of lower urinary tract: urinary urgency 37%;

nocturia, twice or more 18%; dysuria 12%; recurrent cystitis 37%; urge-induced lower abdominal pain 20%; pain-induced urge 18%.

III. Symptoms of pelvic floor spasticity: strain to initiate voiding 10%; strain to continue voiding 17% and incomplete voiding 37%. Also these symptoms were more often reported by CPP patients than the non-CPP controls.

Interrelation between urinary symptoms: Symptoms within each of the three symptom groups were interrelated. Moreover, many irritative symptoms and symptoms of pelvic floor spasticity were interrelated.

Prevalence of one or more voiding symptoms in CPP: 63% had two or more symptoms and 33% had five symptoms or more.

Comparison of some urinary symptoms between CPP patients and healthy women: Serious urinary incontinence prevailed in 43% of these patients. This is significantly higher than urinary incontinence prevailing in a sample of Dutch female population of comparable age group [Rekers e.a., 1992] ($P = 0.004$). We found the prevalence of stress incontinence in CPP to be extremely high (25%) as compared to the findings of above mentioned authors (5%). This difference is strongly significant ($P < 0.001$). Urinary incontinence as well as recurrent cystitis in CPP women 50 years of age or older, was significantly higher than the prevalence of these symptoms found by Van Geelen e.a., [1996] in a study on a sample of Dutch female population of comparable age group.

Conclusions: The results of this study indicates that:

1. The prevalence of two or more serious urinary symptoms in the CPP patients participating in this study is extremely high.
2. Chronic lower abdominal pain accompanied by irritative urinary symptoms and pelvic floor spasticity, all in the absence of organic disorders, supports the diagnosis CPP.
3. At least a subgroup of CPP patients has voiding symptoms resembling the urethra syndrome.

4. The negative affectivity theory of Pennebaker does not give a sufficient explanation of the coexistence of lower abdominal pain and urinary urgency in CPP.

Section III
Micromotions of bladder wall in chronic pelvic pain (CPP)

In conventional urodynamics, spontaneous bladder contractions are detected as spontaneous phasic variations in the detrusor pressure. With micromotion detection (MMD), detrusor pressure and fine (local) contractions (micromotions; MM) are recorded simultaneously. This study reveals a relationship between lower abdominal pain as well as urinary urgency in CPP and spontaneous mechanical activity of bladder wall.

Thirty CPP patients and 7 healthy women underwent MMD examination. A latex balloon (condom), provided with eight electrodes attached to it's inner wall, was placed within the bladder through the urethra. The signals emitted by these electrodes enabled us to establish variations in the distance between neighboring electrodes, observed as MM. The pressure within the balloon, abdominal pressure and respiratory excursions of the abdomen were registered simultaneously. The detrusor pressure was calculated by deducting the abdominal pressure from the pressure within the balloon. Signals from a hand held device, operated by patients and controls, were registered as a means to inform us about the presence of pain and possible fluctuations in the intensity thereof. Urinary urgency was reported verbally. Each session lasted three times 10 minutes with the instilled volume of the balloon being raised from 100 to 150 and 200 ml respectively. The duration of MM and/ or variations in detrusor pressure were established for each woman. The density of pain, urge and sum of both was obtained by dividing the number of these reports by the total time MM and/ or variations in detrusor pressure were observed as well as the time when no bladder activity was registered.

Results: Like lower abdominal pain, urinary urgency was either persistent or transient with complete relief between two reports. Pain and urge were sometimes present at the same time. MM and/ or variations in detrusor pressure

were not dependent on the volume of the balloon. The same applies for lower abdominal pain as well as urge. Therefore all statistics were performed for the entire session of 30 minutes, irrespective of the volume of the bladder. Two of the healthy controls had low amplitude MM. None of the controls had variations in detrusor pressure, pain or urge during MMD.

Collective densities of pain/ urge reports: These series of analyses were primarily meant as a fundamental study to evaluate the relationship between the presence of MM and/ or variations in detrusor pressure and the number of reports of pain and/ or urge.

In CPP, significantly more often pain/ urge was reported per time unit in the presence of MM than in the absence thereof. The presence of variations in detrusor pressure, moreover, was related to the number of urge reports. The number of reports in the presence of MM only, did not differ significantly from that during simultaneous presence of MM and variations in detrusor pressure.

Densities of pain/ urge in CPP patients subdivided according to the presence or absence of variations in detrusor pressure: This analysis was meant to evaluate the clinical feasibility of MMD, as compared to conventional urodynamics. It can be assumed that women with variations in detrusor pressure during MMD, would show the same variations also during conventional urodynamics. In patients *with* at least one episode of phasic variations in detrusor pressure, the presence of MM and/or variations in detrusor pressure was related to the number of urge reports but not to that of pain reports. In patients *without* variations in detrusor pressure, the presence of MM was related to the number of pain reports and showed a trend in relation to the number of urge reports. It can be assumed that this 'trend' is the result of the subdivision of the CPP patients into groups of smaller numbers. We had shown earlier that the presence of MM only is related to the number of pain as well as that of urge reports.

Comparison of the results between patients with- and without variations in detrusor pressure: This analysis was primarily meant to seek justification for the classical subdivision of patients with urinary symptoms, according to the

urodynamic behavior of the detrusor as mentioned above. Per time unit of the total MMD session, CPP patients *with* variations in detrusor pressure, reported more pain/ urge than those *without*.

Conclusions: This study indicates that in CPP:

1. Lower abdominal pain, urinary urgency as well as the presence of MM and/ or variations in detrusor pressure, are not related to the volume of the bladder.
2. Lower abdominal pain as well as urinary urgency during MMD are related to the presence of micromotions of bladder wall. Urinary urgency is moreover related to the presence of phasic variations in detrusor pressure.
3. The classical subdivision of urge patients into sensory and motor urge patients is, at least in CPP women, justified as far as the frequency of urge reports is concerned: Patients *with* variations in detrusor pressure, report significantly more often urge during the measurements than those *without*. However, the border between sensory and motor urge is a vague one. Mechanical activity of bladder wall can exist without being detected as variations in detrusor pressure. These micromotions, not reflected detrusor pressure, are related to lower abdominal pain as well as to urinary urgency. In other words, 'sensory urge' in CPP is related to micromotions of bladder wall.
4. It can be expected that not only in CPP patients, but also in other patients with urinary urgency, 'sensory urge' is related to micromotions of bladder wall.

General conclusions: The results of this study indicate that a substantial subgroup of severe cases of CPP patients has serious urinary symptoms besides lower abdominal pain and that this co-occurrence cannot sufficiently be explained by the negative affectivity theory of Pennebaker. In CPP patients, pain as well as urinary urgency during MMD are related to micromotions of bladder wall. Urinary urgency, moreover, is related to variations in detrusor pressure. In CPP, sensory urge is related to micromotions of bladder wall.

SAMENVATTING

Deel I
Chronische pelviene pijn (CPP): algemene introductie

Chronische pelviene pijn (CPP) wordt gedefinieerd als pijn in de onderbuik zonder bekende oorzaak, gedurende minstens zes maanden. Diepe dyspareunie, uitstraling van de pijn naar de lage rug en urinewegverschijnselen kunnen de pijn in de onderbuik vergezellen. De diagnose van een vrouwelijke patiënt met chronische onderbuikpijn zonder duidelijke organische aandoeningen kan variëren van spastische colon, urethra syndroom, pelviene neuralgie en parametrium hyperalgesie tot chronische pelviene pijn (CPP), voornamelijk omdat de kennis omtrent deze aandoening nog steeds beperkt is gebleven. Ongeveer 10% van de vrouwen bezoeken de gynaecoloog i.v.m. dit syndroom. Het syndroom betreft vrouwen van elke leeftijd. In de literatuur is reeds gemeld dat de nauwe relatie tussen de lagere urinewegen en de genitale organen tijdens de intra-uteriene ontwikkeling als gevolg zou kunnen hebben dat de aandoeningen van de eerste de functie van de tweede zouden kunnen beïnvloeden en zich zo zouden kunnen voordoen als CPP.

In de studies, gepresenteerd in dit proefschrift, werden voor het eerst urinewegverschijnselen uitgebreid geëvalueerd in een groep van CPP patiënten(Deel II). Ook werd het optreden van lokale spontane contracties in de blaaswand bij CPP patiënten voor het eerst vastgesteld en gemeten, en vervolgens geanalyseerd met als doel een mogelijke relatie te vinden tussen enerzijds deze contracties en anderzijds de klachten van onderbuikpijn en aandrang tot urinelozing bij deze vrouwen (Deel III). Een vragenlijst, ingevuld door zestig vrouwen met CPP, werd gebruikt om de urinewegverschijnselen bij deze vrouwen te evalueren (Deel II). Deze lijst, die is toegevoegd aan dit proefschrift als appendix, omvat o.a. de volgende onderwerpen: medische voorgeschiedenis, de ernst en de kwaliteit van de pijn in de onderbuik, pelveoperineale dysaesthesie klachten, gastrointestinale klachten, urineweg-verschijnselen en gynaecologische klachten.

Deel II
Urinewegverschijnselen bij chronische pelviene pijn (CPP)

De prevalentie van één of meer urinewegverschijnselen bij Nederlandse vrouwen tussen 50 en 75 jaar, is 36%. Alhoewel onderbuikpijn de voornaamste klacht van de CPP patiënten is, hebben veel van deze vrouwen tevens urinewegverschijnselen zoals recidiverende cystitis, frequent aandrangsgevoel, urine-incontinentie and dysurie. Urinewegverschijnselen en blaaspijn zonder bekende etiologie worden ook gezien bij het urethra-syndroom, interstitiële cystitis (IC), detrusormyopathie, chronische niet-specifieke cystitis en eosinofiele cystitis. Men heeft wel gesuggereerd dat het urethra-syndroom een subgroep zou (kunnen) zijn van het IC syndroom. In de literatuur wordt tevens gewaarschuwd dat het urethra-syndroom ten onrechte als CPP gediagnostiseerd zou kunnen worden.

De symptomen van het urethra-syndroom zijn sterke aandrang tot urinelozing, dysurie, frequente mictie en suprapubische pijn. Ook moeite met het op gang komen van de urinelozing, het gevoel niet volledig te kunnen plassen en het produceren van slechts een dunne urinestraal kunnen aanwezig zijn evenals symptomen niet gerelateerd aan de urinewegen zoals lage rugpijn.

Voor dit onderzoek vroegen wij zestig vrouwen met CPP om een vragenlijst, o.a. betrekking hebbend op urinewegverschijnselen (zie appendix) in te vullen. De vragen die wij uit deze lijst hebben geselecteerd, hebben betrekking op I. verschijnselen van urine-incontinentie, II. verschijnselen van irritatie van de lage urinewegen en III. verschijnselen van bekkenbodemspasticiteit. Alleen die antwoorden die weergaven dat een probleem vaak, bijna altijd of altijd optrad, werden in acht genomen als "ernstige problemen". Wat de urine-incontinentie betreft hebben wij als criterium genomen dat de ongewilde urinelozing, ongeacht het type (stress, urge, gemengd of onbekend), meer moest zijn dan enkele druppels. De frequentie van deze verschijnselen zowel als hun onderlinge relatie werden geanalyseerd. Ook bij 31 patiënten, die onze gynaecologische kliniek bezochten, werd de frequentie van deze symptomen vastgesteld om na te gaan of de uitkomsten niet waren beïnvloed door het feit dat de CPP patiënten tot een ziekenhuis-populatie behoorden. Waar gegevens

uit bevolkingsonderzoek beschikbaar waren, hebben wij deze vergeleken met onze uitkomsten. Een psychologische benadering van het gelijktijdig optreden van onderbuikpijn en urinewegverschijnselen komt eveneens ter sprake.

Resultaten: Er werd een brede spreiding gevonden in de frequenties van verschillende urinewegverschijnselen en de meeste klachten werden significant vaker gemeld door CPP patiënten dan door de niet-CPP controle-patiënten.

Prevalentie van urinewegverschijnselen bij 60 CPP patiënten die deel hebben genomen aan dit onderzoek:

I. Verschijnselen van urine-incontinentie: incontinentie: 43%; gestoorde funktie van de urethrale sphincter 50%; urinelozing niet kunnen uitstellen 37%.

II. Verschijnselen van irritatie van de lage urinewegen: sterke aandrang 37%; nocturie, tweemaal of meer 18%; dysurie 12%; recidiverende cystitis 37%; onderbuikpijn bij aandrang 20%; aandrang bij onderbuikpijn 18%.

III. Verschijnselen van bekkenbodemspasticiteit: persen om de urinelozing te kunnen starten 10%; persen om met de urinelozing door te kunnen gaan 17% en onvolledige urinelozing 37%.

Onderlinge relatie tussen de urinewegverschijnselen: Er werd een onderlinge relatie geconstateerd van de symptomen binnen ieder van de drie bovengenoemde symptoomgroepen. Bovendien waren de verschijnselen van irritatie van de urinewegen gerelateerd aan verschijnselen van bekkenbodemspasticiteit.

Prevalentie van één of meer urinewegverschijnselen: 63% had twee of meer verschijnselen en 33% had vijf of meer verschijnselen.

Vergelijking van het vóórkomen van urineverschijnselen bij CPP patiënten en gezonde vrouwen: De prevalentie van urine-incontinentie bij de CPP patiënten die aan deze studie deelnamen, was 43%. Dit percentage is significant hoger dan het overeenkomstige percentage in een onderzoek bij een steekproef uit de Nederlandse vrouwelijke bevolking van vergelijkbare leeftijd [Rekers e.a., 1992] ($P = 0.004$). Wij vonden de prevalentie van stressincontinentie bij onze

CPP patiënten extreem hoog (25%) vergeleken met de bevindingen van bovengenoemde auteurs (5%). Dit verschil is sterk significant ($P < 0.001$).

Urine-incontinentie, maar ook recidiverende cystitis bij CPP patiënten in de leeftijd van 50 jaar of ouder, was significant hoger dan de prevalentie van deze verschijnselen in een steekproef uit de Nederlandse vrouwelijke populatie [Van Geelen e.a., 1996].

Conclusies: De resultaten van deze studie tonen aan dat:

1. De prevalentie van twee of meer urinewegverschijnselen in deze groep CPP patiënten is extreem hoog.
2. Chronische onderbuikpijn gepaard met symptomen van irritatie van lage urinewegen en bekkenbodemspasticiteit is ondersteunt de diagnose CPP.
3. Een belangrijke subgroep van deze CPP patiënten heeft urineweg-verschijnselen, die lijken op het urethra-syndroom.
4. De negatieve affectiviteitstheorie van Pennebaker geeft onvoldoende verklaring voor klachten over het gelijktijdig optreden van onderbuikpijn en frequente aandrang tot urinelozing in CPP.

Deel III
Spontane microcontracties van de blaaswand in chronisch pelviene pijn (CPP)

In het conventioneel urodynamisch onderzoek (UDO), worden de spontane blaascontracties indirect waargenomen door de drukvariaties binnen de blaas te meten. Met de MMD (micromotion detection), worden de blaasdruk en fijne (lokale) contracties van de blaaswand (micromotions, MM), simultaan gemeten. Dit onderzoek laat een relatie zien tussen spontane activiteit van de blaaswand (MM en/of blaasdruk) enerzijds en meldingen van onderbuikpijn en/of aandrang anderzijds.

Dertig vrouwen met CPP en zeven gezonde vrijwillige vrouwen ondergingen MMD. Een latex ballon, voorzien van acht elektroden aan de binnenwand daarvan, werd via de urethra binnen de blaas gebracht. De signalen uitgezonden door deze electrodes, maakten het ons mogelijk om de veranderingen in de

afstand tussen aan elkaar grenzende electrodes waar te nemen in de vorm van MM. Tevens werden de druk binnen de ballon, de abdominale druk en de ademhalingsexcursies van het abdomen geregistreerd. De detrusordruk werd berekend door de waarde van druk binnen de blaas te verminderen met die van de abdominale druk. De signalen van een pijnindicator, bediend door de patiënt zelf, zorgden voor een continue informatie omtrent de aanwezigheid van onderbuikpijn en de mogelijke fluctuaties daarin. Aandrang tot urinelozing werd verbaal aangegeven. Elke sessie duurde driemaal tien minuten bij respectievelijk 100, 150 en 200 ml geïnstilleerde volume van de ballon. De tijdsduur van de MM en/of detrusordruk werd vastgesteld voor alle deelnemers. De "dichtheid" van pijn, aandrang of die van beide werd berekend door het aantal van deze meldingen te delen door de totale tijd van MM en/of detrusordruk zowel als die van de perioden zonder blaasactiviteit waarbinnen deze meldingen plaats vonden.

Resultaten: Tijdens de metingen, was de aandrang tot urinelozing net als de onderbuikpijn, continu of voorbijgaand met volledig pijnvrije episoden tussen twee meldingen. Pijn en aandrang waren soms simultaan aanwezig. MM en/of detrusordruk waren onafhankelijk van de volume van de blaas (lees: binnen de ballon). Hetzelfde geldt voor onderbuikpijn en aandrang tot urinelozing. Daarom werden alle statistische bewerkingen uitgevoerd voor de totale sessie van dertig minuten, ongeacht het volume van de blaas.

Twee van de gezonde vrouwen had MM, wellicht van een lage amplitude. Geen van deze controle groep had variaties in de detrusordruk.

Collectieve dichtheid van meldingen van pijn en of aandrang: Deze serie analyses was primair bedoeld als fundamentele studie om de relatie tussen de aanwezigheid van MM en/of detrusordruk enerzijds en pijn en/of aandrang anderzijds te evalueren. Onze CPP patiënten meldden per tijdeenheid bij aanwezigheid van MM, significant vaker pijn en/of urge dan bij afwezigheid van MM. De aanwezigheid van fasische variaties in de detrusordruk was bovendien gerelateerd aan de frequentie van aandrangmeldingen. De frequentie van bovengenoemde meldingen in de aanwezigheid van uitsluitend MM,

verschilde niet significant van die bij simultane aanwezigheid van MM en verhoogde detrusordruk.

Dichtheid van pijn/aandrang bij CPP patiënten naar het urodynamisch gedrag van de blaaswand. Deze analyse was bedoeld om de klinische relevantie van de MMD vergeleken met conventioneel urodynamisch onderzoek te toetsen. Men mag aannemen dat vrouwen met variaties in detrusordruk tijdens MMD dezelfde variaties zouden laten zien tijdens het urodynamisch onderzoek. In patiënten *met* minstens één episode van fasische variaties in detrusordruk, was de aanwezigheid van MM en/of detrusordruk gerelateerd aan het aantal meldingen van aandrang maar niet met het aantal pijnmeldingen. Bij patiënten *zonder* fasische variaties in de detrusordruk, was de aanwezigheid van MM gerelateerd aan het aantal meldingen van onderbuikpijn en vertoonde deze een trend t.a.v. de relatie tot aandrangmeldingen. Eerder hadden wij al aangetoond dat de aanwezigheid van uitsluitend MM, significant gerelateerd is met het aantal meldingen van pijn zowel als aandrang.

Vergelijken van de resultaten tussen patiënten met- en patiënten zonder variaties in detrusordruk: Deze analyse is primair bedoeld om te zien of de klassieke verdeling van patiënten met aandrang, in sensorische- en motorische urge-groep, afhankelijk van het urodynamisch gedrag van de blaaswand, gerechtvaardigd is.

Per tijdseenheid van de totale MMD sessie, meldden CPP patiënten *met* variaties in detrusordruk significant vaker pijn en/of aandrang dan CPP patiënten *zonder* variaties in detrusordruk.

Conclusies: De resultaten van deze studie laten het volgende zien:

1. Onderbuikpijn, aandrang tot urinelozing zowel als MM en/of variaties in detrusordruk, zijn onafhankelijk van het volume van de blaas.
2. Onderbuikpijn zowel als aandrang tot de urinelozing tijdens de MMD, zijn gerelateerd aan de aanwezigheid van MM. Aandrang is bovendien gerelateerd aan de aanwezigheid van fasische variaties in de detrusordruk.

3. De klassieke verdeling van patiënten met aandrang volgens het urodynamisch gedrag van de blaaswand lijkt althans bij CPP, slechts in zoverre gerechtvaardigd dat vrouwen *met* variaties in detrusordruk significant *vaker* pijn en/of aandrang tot urinelozing melden dan die *zonder*. Deze verdeling echter, is vrij kunstmatig. Mechanische activiteit van de blaaswand kan aanwezig zijn zonder variaties in de detrusor druk. Microbewegingen van de blaaswand niet gereflecteerd in de blaasdruk blijken te zijn gerelateerd zowel met onderbuikpijn als met aandrang tot urinelozing. Met andere woorden "sensory urge" bij CPP patiënten is gerelateerd aan microbewegingen van de blaaswand.
4. Het is te verwachten dat niet alleen bij CPP patiënten, maar ook bij andere patiënten met abnormale aandrang to urinelozing, "sensory urge" gerelateerd is aan microbewegingen van de blaaswand.

Algemene conclusies:

De resultaten van deze studie laten zien dat een belangrijke subgroep van patiënten met ernstige CPP naast onderbuikpijn ook ernstige urineweg-verschijnselen heeft en dat deze gelijktijdig optredende klachten onvoldoende te verklaren zijn vanuit de negatieve affectiviteitstheorie van Pennebaker. Bij CPP patiënten zijn pijn zowel als aandrang gerelateerd aan microbewegingen van de blaaswand. Aandrang is bovendien gerelateerd aan de aanwezigheid van fasische variaties in de detrusordruk. Bij CPP is "sensory urge" gerelateerd aan micro-bewegingen van de blaaswand. Microbeweginen van de blaas zowel als onderbuikpijn en aandrang zijn bovendien onafhankelijk van de volume van de blaas.

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APPENDIX

LICHAMELIJKE KLACHTEN BIJ VROUWEN

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INLEIDING

Deze vragenlijst maakt deel uit van een onderzoek dat wordt uitgevoerd door de afdeling Gynaecologie en Verloskunde van het Academisch Ziekenhuis Rotterdam Dijkzigt in samenwerking met de Erasmus Universiteit Rotterdam. Met behulp van deze vragen wordt een onderzoek gedaan naar verschillende klachten van onderbuik en onderlichaam bij vrouwen.

Wij zijn blij dat u aan dit onderzoek wilt meewerken.

Vult u de vragenlijst op uw gemak in. Het invullen zal u ongeveer drie kwartier kosten.

Omcirkel steeds het cijfer links van een antwoord dat volgens u het meest bij *uw* situatie past. U mag meer dan één antwoord op een vraag geven. Op een aantal plaatsen wordt een korte toelichting gevraagd. In zo'n geval svp de toelichting op de stippellijn schrijven. Tevens kunnen er vragen voorkomen die voor uw situatie (pijn in de onderbuik en/of in het onderlichaam) overbodig lijken. Verder zijn er vragen die erg intiem lijken. Wilt u proberen die vragen toch te beantwoorden?
Als het beantwoorden van een vraag moeilijk is, zet u dan een kruisje in de marge, links van de vraag. Tijdens het spreekuur kan de arts deze vraag dan duidelijk maken.

Er zijn geen "goede" of "foute" antwoorden. Het gaat erom hoe *uw* situatie is.

Uiteraard is bij al uw antwoorden op deze vragenlijst strikte geheimhouding verzekerd.

Wilt u als u begint met invullen de ***datum*** en de ***tijd*** noteren op de stippellijnen hieronder?

Datum: Het is vandaag 199

Tijd: Het is nu .....uur

(Aan het eind van de vragenlijst zal u weer worden gevraagd de tijd te noteren).

A. ALGEMENE VRAGEN

De vragenlijst begint met enkele *algemene* vragen:

A01. Naam ..... **A02. Meisjesnaam** .....

A03. Voorletters ..... **A04. Geboortedatum** .....19.....

A05. Adres .....

.....

..... **A06. tel. nr.** .....

A07 Persoonlijke omstandigheden (omcirkel de letter links van een antwoord die bij *uw* situatie past):

0. gehuwd / samenwonend
1. alleen wonend ongehuwd
2. alleen wonend gescheiden
3. alleen wonend weduwe

A08. Heeft u kinderen? ja / nee (doorhalen wat niet van toepassing is)

A09. Zoja; hoeveel kinderen heeft u? .....
Vul svp de volgende schema in. Kies bij het invullen van de schema steed uit de volgende alternatieven:
Verloop va zwangerschap: normaal, gecompliceerd
Verloop van bevalling: normaal, gecompliceerd
gezondheid: gezond, ziek, gehandicapped.

	leeftijd (jaren)	verloop zwangerschap (normaal/gecompliceerd)	verloop bevalling (normaal/gecompliceerd)	gezondheidstoestand (gezond/ziek/gehandicapped)
1e kind				
2e kind				
3e kind				
4e kind				
5e kind				
6e kind				

A10. Heeft u één of meerdere miskramen gehad? .....

Hieronder volgen een serie vragen die met *ja* of *nee* dienen te worden beantwoord. Svp doorhalen wat niet van toepassing is. Waar een toelichting wordt gevraagd, wilt u die dan op de stippellijnen schrijven?

A11. Is uw baarmoeder verwijderd? ja / nee

Zoja; **A12. wanneer?** .....

A13. waarom? .....

A14. Hoe? (vaginaal?, Via de buik?) .....

A15. Gebruikt u de pil? ja / nee (doorhalen wat niet van toepassing is)

zo ja; **A16. naam van de pil** .....

A17. sinds wanneer? .....

A18. gebruik u de pil omdat u niet zwanger wil worden? ja / nee

zo nee; **A19. waarom neemt u de pil?** .....

A20. Heeft u een hormoonkuur in verband met overgangsklachten? ja / nee

zo ja; **A21. naam van de geneesmiddel** .....

A22. sinds wanneer? .....

A23. Gebruikt u een vaginaal zalf? ja / nee

zo ja; **A24. naam van de zalf** .....

A25. sinds wanneer? .....

A26. Bent u overgevoelig voor penicilline? ja / nee

A27. Bent u overgevoelig voor rubber? ja / nee

A28. Heeft u een verzakkingsoperatie gehad? ja / nee

A29. Heeft u spataderen (gehad)? ja / nee

A30. Heeft u aambeien (gehad)? ja / nee

A31. Heeft u schildklierziekte (gehad)? ja / nee

A31. Komt schild klierziekte in de familie voor? ja / nee

A32. In verband met welke klacht of klachten bezoekt u uw gynaecoloog?

B. ONDERBUIKPIJN BIJ VROUWEN

Hieronder volgt een aantal vragen over ***pijn in de onderbuik*** bij vrouwen.

Omcirkel bij vraag **B1** en **B2** wat ***voor u*** in de **laatste *twee maanden*** van toepassing is of was.

B1. Ik heb pijn in de *onderbuik*:

a. zelden of nooit
b. soms
c. meestal
d. bijna altijd
e. altijd

B2. De pijn in de onderbuik trekt naar lage rug:

a. zelden of nooit
b. soms
c. meestal
d. bijna altijd
e. altijd
f. niet van toepassing, ik heb geen pijn in onderbuik

Denk bij vraag **B3** aan het ***afgelopen jaar***. Omcirkel de letter links van een antwoord dat volgens u het meest bij ***uw*** situatie past. Schrijf dan op de stippellijn een cijfer dat volgens u het meest bij ***uw*** situatie past.

B3. De onderbuikpijn komt in aanvallen opzetten:

a. ja; ik heb ongeveer .....dagen per ***week*** onderbuikpijn; doch zijn er soms ***weken*** achtereen dat ik geen pijn in de onderbuik voel
b. ja; ik heb ..... dagen per ***week*** onderbuikpijn; doch zijn er soms ***maanden*** achtereen dat ik geen pijn voel
c. nee; ik heb ***bijna altijd*** pijn in de onderbuik
d. niet van toepassing; ik heb zelden of nooit pijn in de onderbuik
e. anders dan bovengenoemde, nl. .....
.....

Denk bij het beantwoorde van vraag **B4** aan de ***laatste twee maanden.*** Bij deze vraag mag u meer dan één antwoord kiezen.

B4. Als ik onderbuikpijn heb dan is die overwegend:

a. steeds aanwezig en verandert nauwelijks in hevigheid (zeurend)
b. steeds aanwezig en verandert nauwelijks in hevigheid (zeurend); af en toe zijn er echter kortdurende steken of krampen
c. steeds aanwezig maar verandert steeds van hevigheid binnen één tot enkele minuten
d. steeds aanwezig maar verandert steeds van hevigheid binnen één tot enkele minuten; af en toe zijn er ook kortdurende steken of krampen
e. stekend / schietend / krampend (doorhalen wat niet van toepassing is); tussen deze kortdurende aanvallen heb ik geen pijn
f. niet van toepassing; ik heb zelden of nooit pijn in de onderbuik
g. anders dan bovengenoemde, nl. .....
.....

Bij het beantwoorden van vraag **B5,** omcirkel de letter links van een antwoord dat volgens u het meest bij *uw* situatie past. Schrijf dan op de stippellijn een cijfer dat volgens u het meest bij *uw* situatie past.

B5. De *onderbuikpijn* heb ik sinds:

a. ongeveer ..... weken
b. ongeveer ..... maanden
c. ongeveer ..... jaren
d. niet van toepassing; ik heb zelden of nooit onderbuikpijn

Bij het beantwoorden van vraag **B6,** mcirkel de letter links van een antwoord dat volgens u het meest bij *uw* situatie past. Schrijf dan op de stippellijnen een korte toelichting.

B6. De *onderbuikpijn* heb ik sinds:

a. een operatie, namelijk .....
in verband met .....
b. ik begon met een medicijn (b.v. de pil, hormoontherapie, enz), namelijk
.....
in verband met .....
c. een andere gebeurtenis, namelijk .....
d. niet van toepassing; ik heb zelden of nooit onderbuikpijn
e. Ik weet het niet

Denk bij de volgende vragen aan de laatste *twee maanden.*

B7. De pijn in onderbuik ontstaat en/of wordt erger *tijdens* geslachtsgemeenschap:

a. zelden of nooit
b. soms
c. meestal
d. bijna altijd
e. niet van toepassing; ik heb geen geslachtsgemeenschap
f. niet van toepassing; ik heb geen pijn in de onderbuik

B8. De pijn in onderbuik ontstaat en/of wordt erger *na* geslachtsgemeenschap:

a. zelden of nooit
b. soms
c. meestal
d. bijna altijd
e. altijd
f. niet van toepassing; ik heb geen geslachtsgemeenschap
g. niet van toepassing; ik heb geen pijn in de onderbuik

B9. 's Nachts word ik wakker van pijn in de onderbuik:

a. zelden of nooit
b. soms
c. meestal
d. bijna altijd
e. altijd

B10. De pijn houdt verband met de menstruatiecyclus:

a. ja, ik heb uitsluitend pijn in onderbuik rondom menstruatie
b. ja, de onderbuikpijn verergert rondom menstruatie
c. niet van toepassing, ik heb geen menstruatie meer
d. niet van toepassing, ik heb geen pijn in de onderbuik
e. nee

B11. De pijn gaat gepaard met aandrang tot plassen:

a. zelden of nooit
b. soms
c. meestal
d. bijna altijd
e. altijd
f. niet van toepassing, ik heb zelden of nooit pijn in onderbuik

B12. De pijn verdwijnt na het plassen:

a. zelden of nooit
b. soms
c. meestal
d. bijna altijd
e. altijd
f.. niet van toepassing, ik heb zelden of nooit pijn in onderbuik

Heeft u bij het invullen van de vragen aan de ***laatste twee maanden*** gedacht?

B13. De pijn verdwijnt na het krijgen van ontlasting:

a. zelden of nooit
b. soms
c. meestal
d. bijna altijd
e. altijd
f. niet van toepassing, ik heb zelden of nooit pijn in onderbuik

Bij het beantwoorden van vraag **B14** omcirkel de letter links van een antwoord dat volgens u het meest bij *uw* situatie past in de afgelopen twee maanden. schrijf dan op de stippel lijn een korte toelichting; bijvoorbeeld: vóór het eten, na het eten, bij het eten van bepaalde voedingsmiddelen, enz).

B14. De pijn heeft verband met het eten:

a. zelden of nooit
b. soms, namelijk .....
c. meestal, namelijk .....
d. bijna altijd, namelijk .....
e. altijd, namelijk .....
f. niet van toepassing, ik heb zelden of nooit pijn in onderbuik

C. PIJN IN HET ONDERLICHAAM BIJ VROUWEN

Hieronder volgt een aantal vragen over ***pijn in het onderlichaam*** (dat is pijn in de vagina, anus, het zitvlak en het stuitje) bij vrouwen.

Omcirkel bij vraag **C1** wat ***voor u*** in de laatste ***twee maanden*** van toepassing is of was.

C1. Ik heb pijn in het *onderlichaam*:

a. zelden of nooit
b. soms
c. meestal
d. bijna altijd
e. altijd

Denk bij vraag **C2** aan de ***afgelopen jaar***. Omcirkel de letter links van een antwoord dat volgens u het meest bij ***uw*** situatie past. Schrijf dan op de stippellijn een cijfer dat volgens u het meest bij ***uw*** situatie past

C2. De pijn in het onderlichaam komt in aanvallen opzetten:

a. ja; ik heb ongeveer .....dagen per ***week*** pijn in het onderlichaam; doch zijn er soms ***weken*** achtereen dat ik geen pijn in het onderlichaam voel
b. ja; ik heb ..... dagen per ***week*** pijn in het onderlichaam; doch zijn er soms ***maanden*** achtereen dat ik geen pijn in het onderlichaam voel
c. nee; ik heb ***bijna altijd*** pijn in de onderlichaam
d. niet van toepassing; ik heb zelden of nooit pijn in het onderlichaam.
e. anders dan bovengenoemde, nl. .....
.....

Denk bij het beantwoorde van vraag **C3** aan de ***laatste twee maanden.*** Bij deze vraag mag u meer dan één antwoord kiezen.

C3. Als ik pijn in het onderlichaam heb dan is die overwegend:

a. zeurend
b. brandend
c. stekend /schietend / krampend (doorhalen wat niet van toepassing is)
d. anders dan bovengenoemde; namelijk .....
e. niet van toepassing; ik heb zelden of nooit pijn in het onderlichaam

C4 Er zijn (ook andere) onaangename gevoelens; namelijk:

a. gevoel van druk op of naar onderen
b. balgevoel
c. gevoel dat iets van binnen beweegt
d. anders dan bovengenoemde; namelijk .....
e. niet van toepassing; ik heb zelden of nooit (andere) onaangename gevoelens in het onderlichaam

Denk bij het beantwoorden van vraag **C5** aan de ***afgelopen één tot vijf jaar***. Omcirkel de letter links van een antwoord dat volgens u het meest bij ***uw*** situatie past. Schrijf dan op de stippellijn een cijfer dat wederom het meest bij ***uw*** situatie past.

C5. De *pijn in het onderlichaam* heb ik sinds:

a. ongeveer ..... weken
b. ongeveer ..... maanden
c. ongeveer ..... jaren
d. niet van toepassing; ik heb zelden of nooit pijn in het onderlichaam

Denk bij het beantwoorden van vraag C6 aan de *afgelopen één tot dertig jaar*. Omcirkel de letter links van een antwoord dat volgens u het meest bij *uw* situatie past. Schrijf dan op de stippellijnen een korte toelichting.

C6. De *pijn in het onderlichaam* heb ik sinds:

a. een operatie, namelijk .....
de operatie was in verband met .....
b. ik begon met een medicijn (b.v. de pil, hormoontherapie, enz), namelijk (naam medicijn) .....
de medicijn kreeg ik in verband met .....
c. een andere gebeurtenis, namelijk .....
d. niet van toepassing; ik heb zelden of nooit pijn in het onderlichaam
e. ik weet het niet

Denk bij de volgende vragen aan de laatste *twee maanden*.

C7. De pijn in het onderlichaam ontstaat en/of wordt erger *tijdens* geslachtsgemeenschap:

a. zelden of nooit
b. soms
c. meestal
d. bijna altijd
e. altijd
f. niet van toepassing; ik heb geen geslachtsgemeenschap
g. niet van toepassing; ik heb geen pijn in het onderlichaam

C8. De pijn in in het onderlichaam ontstaat en/of wordt erger *na* geslachtsgemeenschap:

a. zelden of nooit
b. soms
c. meestal
d. bijna altijd
e. altijd
f. niet van toepassing; ik heb geen geslachtsgemeenschap
g. niet van toepassing; ik heb geen pijn in het onderlichaam

C9. 's Nachts word ik wakker van pijn in het onderlichaam:

a. zelden of nooit
b. soms
c. meestal
d. bijna altijd
e. altijd

C10. De pijn houdt verband met de menstruatiecyclus:

a. ja, ik heb uitsluitend pijn in het onderlichaam rondom menstruatie
b. ja, de pijn in het onderlichaam verergert rondom menstruatie
c. niet van toepassing, ik heb geen menstruatie meer
d. niet van toepassing, ik heb geen pijn in het onderlichaam
e. nee

Heeft u bij het invullen van de vragen aan de ***laatste twee maanden*** gedacht?

D. PIJN IN LAGE RUG

Hieronder volgt een aantal vragen over pijn *laag in de rug*. Omcirkel wat *voor u* in de laatste *twee maanden* van toepassing is of was.

D1. Ik heb pijn in de *lage rug*:

a. zelden of nooit
b. soms
c. meestal
d. bijna altijd
e. altijd

D2. De pijn in *lage rug* straalt uit naar:

a. één of beide benen
b. naar elders, namelijk naar .....
c. niet van toepassing; de pijn in lage rug straalt niet uit
d. niet van toepassing; ik heb geen pijn in lage rug

Denk bij het beantwoorden van vraag **D3** aan de *afgelopen één tot vijf jaar*. Omcirkel de letter links van een antwoord dat volgens u het meest bij *uw* situatie past. Schrijf dan op de stippellijn een cijfer dat wederom het meest bij *uw* situatie past.

D3. De *pijn in lage rug* heb ik sinds:

a. ..... weken
b. ..... maanden
c. ..... jaren
d. ..... niet van toepassing; ik heb geen pijn in lage rug

E. PROBLEMEN BIJ HET PLASSEN

De volgende serie vragen gaat over ***problemen bij het plassen***. Omcirkel wat ***voor u*** in de ***afgelopen maand*** van toepassing is of was.

E1. Ik heb overdag het bijna onweerstaanbare gevoel te moeten plassen; zelfs wanneer ik weinig heb gedronken:

a. zelden of nooit
b. soms
c. meestal
d. bijna altijd
e. altijd

E2. Ik moet de meeste nachten mijn bed uit om te plassen:

a. ja; 1-2 maal per nacht
b. ja; 2-3 maal per nacht
c. ja; meer dan 3 maal per nacht
d. nee; vrijwel nooit

E3. De aandrang om te plassen gaat gepaard met pijn in de onderbuik:

a. zelden of nooit
b. soms
c. meestal
d. bijna altijd
e. altijd

E4. Ik heb een brandend gevoel tijdens het plassen:

a. zelden of nooit
b. soms
c. meestal
d. bijna altijd
e. altijd

E5. Bij aandrang kan ik de plas nog een tijdje ophouden:

a. zelden of nooit
b. soms
c. meestal
d. bijna altijd
e. altijd

E6. Als ik het gevoel krijg te moeten plassen, verlies ik urine voordat ik de w.c. heb bereikt:

a. zelden of nooit
b. soms
c. meestal
d. bijna altijd
e. altijd

Heeft u bij het invullen van de vragen aan de ***afgelopen maand*** gedacht?

E7. Als ik plas kan ik, als ik dat wil, halverwege stoppen:

a. zelden of nooit
b. soms
c. meestal
d. bijna altijd
e. altijd

E8. Als ik het water uit een kraan hoor lopen, verlies ik wat urine:

a. zelden of nooit
b. soms
c. meestal
d. bijna altijd
e. altijd

E9. Ik heb urineverlies bij het lachen:

a. zelden of nooit
b. soms
c. meestal
d. bijna altijd
e. altijd

Heeft u bij het invullen van de vragen aan de ***afgelopen maand*** gedacht?

E10. Ik heb urineverlies bij hoesten, niezen, traplopen:

a. zelden of nooit
b. soms
c. meestal
d. bijna altijd
e. altijd

E11. Ik heb urineverlies bij springen, tillen, sporten:

a. zelden of nooit
b. soms
c. meestal
d. bijna altijd
e. altijd

E12. Ik heb urineverlies bij geslachtsgemeenschap:

a. zelden of nooit
b. soms
c. meestal
d. bijna altijd
e. altijd
f. niet van toepassing, ik heb geen geslachtsgemeenschap

Heeft u bij het invullen van de volgende twee vragen aan de *afgelopen drie jaar*:

E13. Als ik ongewild urine verlies, dan is het ook een hele plas:

a. nee; ik verlies alleen kleine hoeveelheden urine
b. soms
c. meestal
d. bijna altijd
e. altijd
f. niet van toepassing; ik heb geen ongewild urineverlies

E14. 's Nachts verlies ik ongemerkt urine:

a. zelden of nooit
b. soms
c. meestal
d. bijna altijd
e. altijd

E15. Ik moet meestal maatregelen nemen om het ongewild urineverlies te verbergen:

a. ja; ik verwissel vaker van onderbroek
b. ja; ik gebruik een inlegkruisje
c. ja; ik draag een verband of luier
d. ja; ik neem andere maarteelen , namelijk .....
..... (s.v.p. invullen)
e. niet van toepassing; ik heb geen ongewild urineverlies

Heeft u bij het invullen van de vragen aan de ***afgelopen maand*** gedacht?

E16. Als ik op het toilet zit duurt het even voordat de plas komt:

a. zelden of nooit
b. soms
c. meestal
d. bijna altijd
e. altijd

E17. Om te kunnen plassen heb ik een speciale houding nodig:

a. zelden of nooit
b. soms
c. meestal
d. bijna altijd
e. altijd

E18. Ik moet persen om te kunnen starten met plassen:

a. zelden of nooit
b. soms
c. meestal
d. bijna altijd
e. altijd

Heeft u bij het invullen van de volgende twee vragen aan de *afgelopen drie jaar*.

E19. Ik moet persen om met plassen te kunnen doorgaan:

a. zelden of nooit
b. soms
c. meestal
d. bijna altijd
e. altijd

E20. Vergeleken met vroeger is de straal van mijn urine:

a. hetzelfde
b. tamelijk dun
c. dun
d. zeer dun
e. anders, namelijk .....

E21. Tijdens het plassen, stop en start ik meer dan één maal, zonder dat ik dat wil:

a. zelden of nooit
b. soms
c. meestal
d. bijna altijd
e. altijd

Heeft u bij het invullen van de volgende twee vragen aan de *afgelopen drie jaar*.

E22. Ik kan volledig uitplassen:

a. zelden of nooit
b. soms
c. meestal
d. bijna altijd
e. altijd

E23. Als ik na het plassen opsta druppelt het nog na:

a. zelden of nooit
b. soms
c. meestal
d. bijna altijd
e. altijd

E24. Enkele minuten na het plassen, wordt mijn onderbroek enigszins nat:

a. zelden of nooit
b. soms
c. meestal
d. bijna altijd
e. altijd

Heeft u bij het invullen van de volgende twee vragen aan de ***afgelopen drie jaar***:

E25. Binnen enkele minuten nadat ik dacht klaar te zijn met het plassen moet ik alweer plassen:

a. zelden of nooit
b. soms
c. meestal
d. bijna altijd
e. altijd

E26. Ik heb het meegemaakt dat ik niet kon plassen, en dat er een catheter aan te pas moest komen:

a. ja; ..... maal volgend op een operatie; namelijk .....
b. ja; ..... maal in verband met .....
c. ja; ..... maal zonder bekend oorzaak
d. nee; dit is mij nooit overkomen

E27. Ik heb regelmatig een blaasontsteking:

a. ja; meer dan zes maal per jaar
b. ja; drie tot vijf maal per jaar
c. ja; één tot twee maal per jaar
d. nee

Heeft u bij het invullen van de volgende twee vragen aan de ***afgelopen drie jaar***:

F. PROBLEMEN BIJ DE STOELGANG

Hieronder volgt een aantal vragen over ***problemen bij de stoelgang***. Omcirkel wat ***voor u*** in de ***afgelopen maand*** van toepassing is of was:

F1. Ik heb dunne waterige ontlasting:

a. zelden of nooit
b. soms
c. meestal
d. bijna altijd
e. altijd

F2. Ik heb harde ontlasting:

a. zelden of nooit
b. soms
c. meestal
d. bijna altijd
e. altijd

F3. Ik heb keutelontlasting:

a. zelden of nooit
b. soms
c. meestal
d. bijna altijd
e. altijd

F4. Ik heb slijm bij de ontlasting:

a. zelden of nooit
b. soms
c. meestal
d. bijna altijd
e. altijd

F5. Ik heb bloed bij de ontlasting:

a. zelden of nooit
b. soms
c. meestal
d. bijna altijd
e. altijd

F6. Ik heb krampen bij of in de richting van anus:

a. zelden of nooit
b. soms
c. meestal
d. bijna altijd
e. altijd

Heeft u bij het invullen van de vragen aan de *afgelopen maand* gedacht?

F7. Ik voel de aandrang tot ontlasting, maar op de wc komt er niets of weinig uit:

a. zelden of nooit
b. soms
c. meestal
d. bijna altijd
e. altijd

F8. Ik moet hard persen om de ontlasting eruit te krijgen:

a. zelden of nooit
b. soms
c. meestal
d. bijna altijd
e. altijd

F9. Ik heb het gevoel dat na stoelgang nog ontlasting is achtergebleven:

a. zelden of nooit
b. soms
c. meestal
d. bijna altijd
e. altijd

Heeft u bij het invullen van de vragen aan de ***afgelopen maand*** gedacht?

F10. Ik help de ontlasting naar buiten te komen door vingerdruk van buiten:

a. zelden of nooit
b. soms
c. meestal
d. bijna altijd
e. altijd

F11. Ik help de ontlasting naar buiten te komen door vingerdruk in de vagina:

a. zelden of nooit
b. soms
c. meestal
d. bijna altijd
e. altijd

F12. Ik help de ontlasting naar buiten komen met een vinger in de anus:

a. zelden of nooit
b. soms
c. meestal
d. bijna altijd
e. altijd

Heeft u bij het invullen van de vragen aan de *afgelopen maand* gedacht?

F13. Ik kan de anus goed dichtknijpen:

a. zelden of nooit
b. soms
c. meestal
d. bijna altijd
e. altijd

F14. Ik verlies ontlasting zonder dat ik het wil:

a. zelden of nooit
b. soms
c. meestal
d. bijna altijd
e. altijd

F15. Ik heb een wat vochtige anus:

a. zelden of nooit
b. soms
c. meestal
d. bijna altijd
e. altijd

Heeft u bij het invullen van de vragen aan de ***afgelopen maand*** gedacht?

F16. Ik gebruik voor de stoelgang (tarwe)zemelen:

a. zelden of nooit
b. soms
c. meestal
d. bijna altijd
e. altijd

F17. Ik gebruik voor de stoelgang een dieet:

a. zelden of nooit
b. soms
c. meestal
d. bijna altijd
e. altijd

F18. Ik gebruik voor de stoelgang een laxeermiddel:

a. zelden of nooit
b. soms
c. meestal
d. bijna altijd
e. altijd

Heeft u bij het invullen van de vragen aan de ***afgelopen maand*** gedacht?

F19. Ik moet meestal maatregelen nemen om ontlastingverlies te verbergen:

a. ja; ik verwissel van onderbroek
b. ja; ik gebruik een damesverband
c. ja; ik draag een luier
d. ja; ik neem andere maarteelen , namelijk .....
..... (s.v.p. invullen)
e. niet van toepassing; ik heb geen ongewild ontlastingverlies

G. ALGEMENE GYNAECOLOGISCHE PROBLEMEN

Hieronder volgt een aantal vragen over ***algemene gynaecologische problemen***. Omcirkel wat ***voor u*** van toepassing is.

Denk bij de volgende vragen aan de afgelopen ***twee maanden***

G1. Ik heb bloedverlies bij geslachtsgemeenschap:

a. zelden of nooit
b. soms
c. meestal
d. bijna altijd
e. altijd
f. niet van toepassing; ik heb geen geslachtsgemeenschap

G2. Ik heb bruine afscheiding:

a. zelden of nooit
b. soms
c. meestal
d. bijna altijd
e. altijd

G3. Ik heb opvliegers:

a. zelden of nooit
b. soms
c. meestal
d. bijna altijd
e. altijd

G4. Ik heb last van zweten:

a. zelden of nooit
b. soms
c. meestal
d. bijna altijd
e. altijd

G5. Ik heb een droge vagina:

a. zelden of nooit
b. soms
c. meestal
d. bijna altijd
e. altijd

G6. Mijn menstruatiecyclus is regelmatig:

a. niet van toepassing; ik heb geen menstruatie meer
b. ja en ik gebruik 'de pil'
c. ja en ik gebruik 'de pil' niet
d. nee en ik gebruik 'de pil' niet

Heeft u bij het invullen van de vragen aan de *afgelopen twee maanden* gedacht?

G7. Mijn menstruatie duurt:

a. niet van toepassing; ik heb geen menstruatie meer
b. 1-2 dagen
c. 3-5 dagen
d. 6-7 dagen
e. 8 dagen of meer

G8. Om het menstruele bloedverlies op te vangen gebruik ik:

a. niet van toepassing; ik heb geen menstruatie meer
b. uitsluitend inlegkruisjes
c. normaal damesverband
d. minstens 1-2 dagen extra dik verband
e. minstens 1-2 dagen luiers

G9. Ik heb tussentijds bloedverlies:

a. zelden of nooit
b. soms
c. meestal
d. bijna altijd
e. altijd

Heeft u bij het invullen van de vragen aan de ***afgelopen twee maanden*** gedacht?

G10. Ik moet maatregelen nemen om tussentijds bloedverlies op te vangen:

a. ja; ik moet een damesverband dragen
b. ja; ik moet een inlegkruisje gebruiken
c. het verwisselen van onderbroek is voldoende
d. ja; ik neem andere maarteelen , namelijk .....
..... (s.v.p. invullen)
e. niet van toepassing; ik heb geen tussentijds bloedverlies

G11. Vóór de menstruatie heb ik :

a. niet van toepassing; ik menstrueer niet meer
b. hoofdpijn
c. misselijkheid
d. pijn in de onderbuik
e. andere klachten, namelijk .....
.....
.....(s.v.p. invullen)
f. geen klachten

G12. Tijdens de menstruatie heb ik :

a. niet van toepassing; ik menstrueer niet meer
b. hoofdpijn
c. misselijkheid
d. pijn in de onderbuik
e. andere klachten, namelijk .....
.....
.....(s.v.p. invullen)
f. geen klachten

Heeft u bij het invullen van de vragen aan de ***afgelopen twee maanden*** gedacht?

H. MEDISCHE GESCHIEDENIS

Bent u ***in het afgelopen jaar*** onder behandeling van andere artsen (specialisten) geweest? Ja/nee*
Zo ja, gaarne het volgende schema invullen:

In verband waarmee?	Soort specialisme?	Naam arts/specialist?	Naam ziekenhuis/instelling?
1.			
2.			
3.			
4.			
5.			

*Doorhalen wat niet van toepassing is.

Bent u ***vóór het afgelopen jaar*** onder behandeling van een arts (specialist) geweest? Ja / nee*
Zo ja, gaarne het volgende schema invullen:

In verband waarmee?	Welk jaar?	Soort specialisme?	Soort behandeling (bijvoorbeeld geneesmiddelen, bestraling, operatie)
1.			
2.			
3.			
4.			
5.			
6.			

Gaat u verder met de volgende pagina indien u ***vóór het afgelopen jaar*** meerdere malen een arts/specialisten heeft geraagpleegd.

*Doorhalen wat niet van toepassing is.

I. GENEESMIDDELENGEBRUIK

Gebruikt u medicijnen? Ja / nee*
Zo ja, gaarne het volgende schema invullen:

*Doorhalen wat niet van toepassing is.

Naam van geneesmiddel?	In verband waarmee?
1.	
2.	
3.	
4.	
5.	
6.	
7.	
8.	

J. SLOT

Wilt u als u klaar bent de ***tijd*** noteren op de stippellijn hieronder?

Tijd: Het is nu ..... uur.

Hartelijk dank voor uw medewerking.
Als u opmerkingen over de bovenstaande vragenlijst of uw klachten hebt, gebruikt u dan de volgende twee bladzijden a.u.b.

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