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ABSTRACTS

ORAL / POSTER

Diagnostic Studies

Could a pelvic pain score be useful in an assessment of men with chronic pelvic pain?

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MATERIALS & METHODS

This is a prospective, descriptive, controlled study of a pelvic pain score in 3 groups of patients:
A) symptomatic types IIIa and IIIb prostatitis;
B) patients presenting to our Chronic Pelvic Pain Syndrome (CPPS) clinic with unilateral testicular pain n=4 or asymptomatic (CPSI <13) patients previously diagnosed with types IIIa or IIIb prostatitis n=2;
C) controls (general urology clinic patients undergoing DRE for other reasons). From July 2000 to September 2000, 11 patient in group A and 6 patients in group B were assessed in our CPPS clinic. Group C included 10 men who completed a CPSI before their digital rectal examination (DRE). Instructions were given to the patients to complete a 10 cm visual analogue pain scale (VAS) during digital palpation with equal pressure for about 5 seconds in each of 4 areas a) posterior rectum, b) right lateral rectum, c) left lateral rectum, and d) prostate. These areas are all in the same plane as the prostate. The patient was positioned in the left lateral position and asked to mark a line through the VAS for each of the 4 areas referred to as position 1-4 by the examining surgeon. The scores were measured in cm using a ruler. The VAS prostate (VASP) and the highest other VAS (VASH) were used, and the difference between the 2 calculated. A power calculation has been performed Dr. B. Toms (Institute of Public Medicine, Cambridge University) and the study has an 80% power to detect a 2cm difference in the (VAS prostate-VAS highest) (VASP-H) with 9 patients in each group. Final statistical analysis was performed by Dr. B. Toms using a Bonferroni correction for multiple variables.

RESULTS *(See table below)*

There is a statistically significant difference in the VASP-H between group A and group B p<0.0001, and between group A and group C p<0.0001. Interestingly only 2 patients in group A had a VASP-H of less than 2cm and both these had VASH of greater than 8cm which might indicate a generalized pelvic neuralgia. Only 1 patient in group C had a VASP-H greater than 2cm.

CONCLUSIONS

The prostate-pelvic tenderness test may prove to be useful in distinguishing pain caused by the prostate, from other causes of pelvic pain. The difficulty of this test is standardizing palpation pressure in all 4 areas.

	GroupA n=11 IIIa n=1, IIIb n=10			**Group B n=6**			**Group C n=10**			p value between grpA and grp C
	Mean	*SD*	*Range*	*Mean*	*SD*	*Range*	*Mean*	*SD*	*Range*	
Age	50	11.2	(33-74)	51	13.4	(33-65)	57	12.5	(35-77)	p=0.493 (1 way analysis of variance)
Symp/mo	46	87	(6-300)	50	58	(9-156)	not applicable			
CPSI total	22	6	(15-32)	16	9	(3-30)	6	5	(1-13)	*p<0.0001
VASP/cm	6.4	2.0	(3.0-10)	3.5	1.9	(1.3-7.0)	2.8	1.7	(0-5.1)	*p=0.001
VASH/cm	3.0	2.9	(0-8.5)	3.9	2.4	(1.8-8.0)	2.2	1.4	(0-4.0)	p=0.394
VASP-H/cm	3.4	1.8	(-0.7-5.5)	-0.3	1.0	(-1.5-1.0)	0.6	0.8	(-.3-2.2)	*p<0.0001

**Indicates significant result*

Pelvic muscle evaluation in men with chronic pelvic pain and controls

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INTRODUCTION

Men with chronic pelvic pain syndrome (CPPS) experience pelvic pain that may be related to muscle dysfunction. Since few studies have attempted to document pelvic floor muscle function in men with CPPS we performed a comparative study of the pelvic floor muscles in men with CPPS and men without pain.

METHODS

To date, 30 men with CPPS and 51 controls underwent a standardized physical therapy evaluation. The evaluation was done in an unblinded manner by a licensed physical therapist (D.H.) specializing in pelvic floor dysfunction.

RESULTS

Pelvic floor muscle tone increase was found in 16/30 (53%) of patients and 5/50 (10%) of controls (p-value<0.001). Increased pain with palpation of pelvic floor muscles was found in 21/30 (70%) of patients and 2/51 (4%) of controls (p-value<0.001). Pelvic floor muscle spasms were detected in 7/29 (24%) of patients and 0/51 (0%) of controls (p-value=0.004). Abdominal myofascial tension with palpation was found in 7/30 (23%) of patients, and 9/51 (18%) of controls (p-value=0.01). Abdominal myofascial pain with palpation was found in 7/30 (23%) of patients and 2/51 (4%) of controls. (p-value=0.01). Pelvic floor quick contractions were found to be of normal strength in 8/29 (28%) of patients and 23/51 (45%) of controls (p-value=0.036). Ten second contractions of the pelvic floor muscle showed the same results as for the quick contraction.

CONCLUSIONS

Men with CPPS have more abnormal pelvic floor and abdominal muscular pathologic findings as compared with a group of men without pain.

ADDENDUM

It was decided that blinding the PT during evaluations would be useful to further validate the data. Starting in July 2000, the Physical Therapist was blinded for evaluations. A preliminary look at that data indicates that many of the findings continue to follow the trends described above.

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Comparison of urodynamic findings in patients with Chronic Pelvic Pain Syndrome IIIa and IIIb

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INTRODUCTION & OBJECTIVES

Medical therapy of Chronic Pelvic Pain Syndrome (CPPS) with α-blockers has been recommended for both categories IIIa and IIIb. The rational for this treatment strategy is based on clinical observations and urodynamic findings. The aim of this study was to look for urodynamic differences between IIIa and IIIb in order to distinguish further between these 2 forms of CPPS.

MATERIAL & METHODS

Ninety-eight patients were included in this study. Based on symptoms and number of white blood cells (WBC) in the expressed prostatic secretions (<10 or ≥ 10 WBC/hpf) they were diagnosed to have CPPS IIIa (n=48) or IIIb (n=50). Infection has been excluded by standard microbiological methods. Urethrocystoscopy was normal in all patients. At the time of urodynamic evaluation any medical treatment with antibiotics or α-blockers has been discontinued for at least 6 weeks

RESULTS

The urodynamic parameters included detrusor opening pressure (DOP), maximal urinary flow (Qmax), maximal detrusor pressure (Pdetmax), detrusor pressure at maximal flow (PdetQmax), minimal urethral opening pressure (Pmuo) and micturition volume (Micvol). Both groups (IIIa vs. IIIb) showed similar values of DOP (39 vs. 38 cm H2O), Qmax (12 vs. 13 ml/sec), Pdetmax (51 vs. 55 cm H_2O), PdetQmax (39 vs. 44 cm H2O) and Pmuo (26 vs. 26 cm H_2O). There was no statistically significant difference between the 2 groups. Only the micturition volume was different between IIIa and IIIb (275 vs. 362 ml, $p<0.05$). The assessment of symptoms with the International Prostate Symptom Score (IPSS) was identical for both groups (13 vs. 13).

CONCLUSIONS

Patients with CPPS either IIIa or IIIb show a very similar spectrum of urodynamic findings. It is possible that the lower micturition volume in category IIIa is caused by a certain frequency due to the presence of prostatic inflammation. Although urodynamic investigation is an important instrument in the evaluation of CPPS it does not seem to be of value to distinguish category IIIa from IIIb.

One year experience of using the National Institutes of Health Chronic Prostatitis Symptom Index (NIH-CPSI) for diagnosis and survey of Chronic Prostatitis/ Chronic Pelvic Pain Syndrome (CP/CPPS)

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INTRODUCTION & OBJECTIVE

The NIH-CPSI was introduced and recommended for clinical use in 1999. The aim of the present study was to analyse the experience of using this questionnaire in the daily work at 2 different urology outpatient departments.

METHODS

The translation and validation of the NIH-CPSI in Finnish was done between June- August 1999. The survey was carried out between September 1999 and August 2000 when all consecutive patients with CP/CPPS filled the questionnaire. The patients also gave a subjective assessment of the accuracy and feasibility of the questionnaire in a scale from 5 (excellent) to 1 (poor). An independent doctor checked the patients' medical records and the questionnaires and gave the same assessment. The material includes altogether 155 consecutive patients with CP/CPPS (categories IIIA and IIIB). Age distribution was as follows: 16 (10%) between 20-34, 37 (24%) between 35-49, 73 (47%) between 50-64 and 29 (19%) between 65-79 years. 118 patients (76%) had an outdoor work.

RESULTS

The mean sum of the NIH-CPSI scores was 20 (range 0-38), the mean pain score 10 (range 0-18), the mean score of voiding disturbances 4 (range 0-10) and the mean score for quality of life 5 (range 0-18). 114 patients (74%) localized one maximum pain area, 31 (20%) 2 areas and 9 (6%) had pain in 3 different areas. Pain was localized mainly in the lower abdomen, perineal area and groins. 91 patients (58.7%) visited outpatient department in wintertime (November-March), 26 (16.8%) in spring, 34 (21.9%) in summer and only 4 (2.6%) in autumn. Duration of CP/CPPS: 0-4 years 32%, 5-9 years 15%, 10-14 years 23% and over 15 years 30%. The patients´ subjective assessment about the questionnaire was 5 points in 40% and 4 points in 41% cases (the physician's figures were respectively 36 and 54%).

CONCLUSIONS

This one year survey showed good correlation between patients' symptoms and signs and the NIH-CPSI. During wintertime there is in Finland a peak for exacerbation and recurrences of CP/CPPS.

PSA elevation with Chronic Pelvic Pain Syndrome — A Case Study

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Symptomatic and asymptomatic prostatitis (CPPS) may be the cause of more than one half of PSA elevations. Therefore, prostate trauma could be the cause of the prostate inflammation and causes elevated PSAs. Pathologists now think that disruption of the prostatic epithelium causes noncancerous PSA elevations.

This case report suggests a causal relationship between prostatic trauma and noncancerous PSA elevations. Prevention of prostatic trauma with aninflatable donut cushion while riding and sitting could reduce noncancerous PSA elevations and reduce the number of prostatic biopsies. A double blindrandom multi-center study is needed to prove or disprove this theory.

The Stamey localisation procedure is painful

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MATERIALS & METHODS

This is a prospective descriptive study of the pain associated with a Stamey localisation procedure. The Stamey localisation procedure is widely recognized by Urologists as being an uncomfortable test but objective data to confirm this impression has not been published. From July 2000 to September 2000, men attending our Chronic Pelvic Pain Syndrome clinic who underwent a Stamey localisation participated in this study. The patient's age, duration of symptoms, NIH CPSI score, the surgeon who performed the localisation procedure, patient position, duration of massage, number of drops of EPS obtained and the final Stamey result were recorded. Within 5 minutes all men were asked to complete a 10 cm visual analogue scale (VAS) documenting the pain of the prostatic massage.

0 _____ 10
no pain *worst pain*

The pain scores were measured using a ruler and documented in cm.

RESULTS *(See table below)*

20 men participated in this study, all were performed in the lean over position, and EPS was obtained in 6 patients.

CONCLUSIONS

With a median pain score of 6.9, only 2/20 patients recording no pain with the procedure <1cm on VAS, 14/20 (70%) scoring more than 6cm, and 3/20 scoring >9cm it is noted that this procedure is extremely uncomfortable for the majority of men. We recommend analgesia prior to a Stamey localisation and shall be commencing a randomised controlled trial. Given the high levels of pain associated with the procedure, the Stamey localisation could prove to be a useful model for studying prostatic pain relief.

	Mean	Median	S.D.	Range
Age	48	46	13	33-74
Duration of symptoms/months	39	18	70	5-300
NIH CPSI total score	19	20	8.5	1-31
Duration of massage/min	3	3	1.2	1-5
Pain score/ cm	6.3	6.9	2.6	0.2-10

High PSA prostatic inflammation

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PURPOSE

To report an unusual form of chronic prostatitis simulating adenocarcinoma because of an extremely high serum prostate specific antigen (PSA) level.

MATERIALS & METHODS

From a referral cohort of 3200 urology patients for transrectal ultrasound (TRUS) and biopsy, there were 10 with serum PSA greater than 20 ng/ML. One had an abnormal digital rectal examination, 1 had previous history of urinary tract infection, but none had a history of clinical prostatitis or urinary tract infection. Baseline data included the following mean, range, median values: Age 71.6 (59-77), 74, Total Prostate Volume 82.5 (19.9-199), 72.2, PSA 33.1 (21.9-51.5), 31.9, PSAD 0.61 (0.16-1.61), 0.45, PSA-TZ 1.28 (0.21-4.45), 0.69. TRUS volume measurements were made using the prolate ellipsoid model. Two to three biopsies were taken from suspicious foci plus six to twelve bilateral random cores including transition zone and anterior peripheral zone.

RESULTS

Biopsies were negative for carcinoma and positive for acute and/or chronic inflammation in all patients. One patient later underwent suprapubic prostatectomy pathologically showing prostatic intraepithelial neoplasia, infarction , and acute and chronic inflammation. Mean, range and median follow-up was 34.7 months (15-65), 31.5. No follow-up PSA is available for 2 patients. PSA increased in 2 patients who have not been referred for repeat biopsy, and decreased by a mean of 21.1 ng/ML in the remaining 6 patients.

CONCLUSIONS

Subclinical histologic prostatitis may be the only etiology for some patients with with PSA > 20 ng/ML. Our follow-up in some patients does not allow us to rule out occult cancer. If initial repeat biopsies are negative for malignancy, these patients should be followed to assure stable or falling PSA values to determine the need for subsequent biopsies.

ABSTRACTS

ORAL / POSTER

Antibiotic Therapy

A prospective, randomized, double-blind, placebo-controlled study of antibiotics for the treatment of Category IIIb Chronic Pelvic Pain Syndrome in men

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BACKGROUND

Chronic pelvic pain (category IIIB) is a frustrating clinical entity to both patients and clinicians alike. As recently detailed by an expert in the field, many researchers feel that the majority of patients do, in fact, have a microbial etiology for their disease, but that urologists are just not culturing the correct organism. Others feel that the majority of cases, especially those in patients with no demonstrable inflammation, do not have a microbial etiology. To complicate things further, many asymptomatic patients in whom a diagnosis of chronic prostatitis has not been made have had both inflammation and microorganisms identified in prostate-specific specimens.

PRIMARY END-POINT

Evaluation of long-term (six- and eighteen-month) antibiotic safety and efficacy.

SECONDARY END-POINTS

Evidence for improvement in EPS and PPMU of inflammatory (cytokine profile-based) parameters.

MATERIAL & METHODS

One hundred male patients (median age 21, range 18-45) who met the criteria for category IIIB were enrolled in the study. Patients were randomized to receive either Ciprofloxacin 500 mg bid (or placebo) for 6 weeks in combination with prostatic massage. None of the patients had received antibiotics during the preceding 8 weeks. Patients were meticulously evaluated using the Meares and Stamey four-glass technique plus a urethral swab. Samples were cultured for bacteria aerobically on blood sheep and McConkey agar for 1 week and on Sabouraud's media for detection of fungal growth for 30 days. Thereafter, frozen samples were evaluated for presence of bacterial signal using the 16S rRNA detection kit (Qiagen, Valencia, CA), the Roche CT/NG Amplicor Assay (Roche Molecular Systems, Branchburg, NJ) and LCR (Abbott Laboratories, Abbott Park, Chicago, IL) and nested Mycoplasma-specific as well as Mycoplasma genitalium-specific protocols. Inflammatory activity was evaluated using commercial ELISA kits.

RESULTS *(See table below)*

By definition, all patients had negative microbiological results.

CONCLUSIONS

The results of our study show that antibiotics have an unacceptably high rate of adverse side effects as well as a statistically insignificant improvement over placebo and should be avoided in Category IIIB CPPS patients with negative PCR findings for the presence of bacteria.

Supported by Commercial League-National Pharma Center, Bulgaria and Bayer Ltd., Bulgaria

Group/Cure Rate	6 Weeks	6 Months	18 Months	Adverse Reactions
Cipro	53%	21%	3%	65%
Placebo	69%	18%	5%	9%

Symptom improvement and TRUS-documented reduction of prostate size after repetitive prostatic massage and antimicrobial therapy

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INTRODUCTION

We describe the treatment of urinary symptoms in a 78-year-old man with an enlarged prostate (63 g). The treatment consisted of 10 prostatic massages combined with antibiotics.

METHODS

Symptom severity was monitored by the patient, who was asked to assign a global symptom score to his symptoms throughout the treatment period. A 10-point scoring system was used, with 10 representing the most severe symptoms. Prostate volume was measured before and after treatment by transrectal ultrasound (TRUS).

RESULTS

The global symptom score fell from 5 before treatment to <1 at the end of the treatment period. His prostate volume decreased by 52% from 63 g to 30 g.

CONCLUSION

This case reports suggests that prostatic massage plus antibiotic therapy is effective in decreasing the size of the prostate in BPH, and that TRUS can beused to objectively monitor the change in prostate size.

KEYWORDS

prostate, prostatitis, prostatic hyperplasia, prostatism, benign prostatic hyperplasia, prostatic hypertrophy, prostatic massage, infection, transrectal ultrasound, transurethral resection of the prostate, transurethralprostatectomy

Transrectal thermotherapy of chronic prostatitis

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Transrectal thermotherapy (TRT) is an effective way to improve prostatitis of a chronic nature. Its mode of action is not clear but probably works to increase the local blood flow through the prostatic gland and pelvic muscle area.

During Jan. 1990 to Dec. 1999, 2685 men (age 16-61 years) were treated at least two times (range 3-119 treatments). 485 men had to be treated more than two times.

The equipment was manufactured by DELWA (Thermo H).

Each treatment interval was 12 minutes at a temperature of +41°C (+106°F) and the interval periods varied between one week to four weeks.

The treatment was performed without any sedation/ anaesthesic. Prior to the treatment antibiotic Norfloxacin 500 mg x2 was orally given during 10 days. Transrectal prostatic massage was performed.

Carcinoma of the prostatic gland was excluded testing PSA.

RESULTS

95% of the material were satisfied/cured by this treatment.

CONCLUSION

TRT is an effective and safe alternative way to treat chronical prostatitis and furthermore, to prevent recurrency of this disease when used as a prophylactic manner. And most of the patients did not have the need of any more antibiotic treatment.

Rofecoxib *in the treatment of chronic nonbacterial prostatitis: A Phase II randomized placebo controlled study*

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PURPOSE

To determine the effects of treatment with rofecoxib for six weeks compared to placebo on pain, voiding symptoms and quality of life associated with chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS category III) as measured by the NIH chronic prostatitis symptom index (NIH-CPI) and patient global assessment questions. None of these tools had been previously used in multicenter placebo-controlled trials; therefore, an additional goal was to assess the responsiveness of these instruments in this setting.

STUDY DESIGN

The study was a randomized, double-blind, placebo controlled parallel group, multicenter study. Following a one week placebo run in, patients were randomized to 6 weeks treatment with placebo, rofecoxib 25 mg/day or rofecoxib 50 mg/day. Male patients older than 18 years of age who met the NIH definition of Category III CP/CPPS, with a minimum NIH-CPSI average pain score (question 4) of greater than or equal to 4 were eligible for enrollment. The evaluation of symptoms was determined by the following patient questionnaires: NIH-CPSI, patient global assessment questions, symptom frequency questionnaire (SFQ), symptom severity index (SSI), and the short form health survey (SF-12). Safety measurements included clinical evaluation and laboratory safety tests.

RESULTS

A total of 161 eligible patients were randomized to placebo (n=59), 25 mg/day of rofecoxib (n=53) or 50 mg/day of rofecoxib (n=49). The baseline patient characteristics (age, height, body weight and race) were similar between treatment groups. Twenty-seven percent of the patients were classified as Category IIIA CPPS while 73% were classified as Category IIIB CPPS. Preliminary data analysis demonstrated improvement on rofecoxib, especially in category IIIB patients. Subjective global assessment questions appeared to provide a more sensitive indication of response to therapy than the change in NIH-CPSI score (either total score or specific domain score). Rofecoxib was generally well tolerated.

CONCLUSION

This phase II pilot study suggests that patients with Category IIIB CPPS may benefit from treatment with rofecoxib; however, further study is needed.

This study was funded by Merck Research Laboratories

ABSTRACTS

ORAL / POSTER

Other Therapies

Ultrasound-guided infiltration in chronic prostatitis

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VIDEO ABSTRACT

When treating chronic prostatitis the urologist is faced with an obstacle which cannot apparently be overcome: the gap between the therapeutic efficacy of what can be prescribed and effective disease eradication. Failure to achieve a complete cure is due fibrous calcifications of pathogens in the prostate parenchyma which remain indestructible as they cannot be reached by pharmaceutical agents. This video film shows how to breach and explode these fibrous calcifications by using a transperineal puncture and ultrasound guidance to deliver an appropriate cocktail of drugs and cortisone.

Epidemiological data on the prevalent diagnostic and treatment procedures for chronic prostatitis in the ambulatory care setting

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INTRODUCTION & OBJECTIVES

Chronic prostatitis has remained an enigmatic clinical condition for a number of years. In the past several years substantial progress has been made in the area of understanding clinical aspects of chronic prostatitis. Recently developed NIH chronic prostatitis classification and symptom index create a foundation for a more uniform assessment of this condition. Rapidly increasing interest to this disease entity confronts by a relative last of the sufficient epidemiological data on the principal methods of the chronic prostatitis diagnosis and clinical management.

METHODS

For the analysis we have utilized data from the National Survey of Ambulatory Surgery (NSAS) for the years 1994-1996. The weighted distribution data were obtained to identify the ten most common procedures for ambulatory visits associated with chronic prostatitis (ICD code 601.1) in adult males (age 25+). Chronic prostatitis was listed as a first and any diagnosis.

RESULTS *(See table below)*

Weighted numbers for the procedures associated with a chronic prostatitis as a first listed diagnosis during ambulatory visits for the years 1994, 1995 and 1996 have shown in the table below.

CONCLUSION

Data from the NSAS represent the number of procedures for chronic prostatitis in ambulatory care setting and show consistent decline in the volume of both diagnostic and treatment modalities. The most dramatic decrease (-65.6%) was found for the number of cystoscopies. The number of office visits for chronic prostatitis has been increasing during the years 1994-1996. Analysis of the data for the most recent years will be valuable in proving that newly developed various symptom indexes and especially NIH-CPSI are instrumental in the decline of the number of diagnostic procedures done for chronic prostatitis.

Diagnostic/treatment procedures	1994	1995	1996
Cystoscopy	3,986	3,132	1,372
Prostate biopsy	1,713	1,398	1,308
IVP	338	NA	304
Prostate massage	1,223	723	414
Antibiotic injection into prostate	NA	328	NA
Number of visits	6,661,857	7,223,285	7,789,773

Prostatitis in France, a very common disease — A 15 years experience

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Prostatitis is a very common disease in the south of France.

The authors think:

- It is a couple-related disease
- There is frequently a corrolation with a urethral problem in the male partner.

The authors give their experience of treating Prostatitis for the last 15 years with successful results.

A beneficial effect of prostate massage for patients with chronic prostatitis: The expression of intraglandular prostatic inflammatory aggregates

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We decided to obtain objective evidence that digital-rectal massage of the prostate has a beneficial effect. The following study has been initiated: In patients with signs and symptoms of chronic prostatitis, we compared the cytopathology of their expressed prostatic secretions (EPS) obtained by prostatic massage to that of their semen obtained by ejaculation. We would like to report our preliminary findings from a small sample (N=10) of patients (mean age 42 years, range 29-66).

Semen was collected shortly after patients woke-up in the morning, and in each case they were instructed to void before collecting their sample. Immediately after obtaining the sample, 35 ml of preservative (50 percent isopropyl alcohol) was added, and the mixture was kept cool. Smears and cell blocks were prepared and staining was done with a modified Wright's, PAS, H & E and Papanicolau stains. For the EPS, two slides were made and stained with a modified Wright's stain and PAS.

In 8 cases (80%), the EPS showed signs of acute inflammation, containing both individual polymorphonuclear leukocytes (PMNs) and cohesive aggregates of PMNs. We call these aggregates "PIAs," prostatic inflammatory aggregates.

By sharp contrast, the semen from all the patients showed either no findings of inflammation (no PMNs nor PIAs) or only very mild changes (rare PMNs). In this small series, we did not observe PIAs in semen.

Our observations suggest that the muscular force of ejaculation is not sufficiently strong to express PIAs from the prostate, at least in the majority of patients with chronic prostatitis. PIAs can, however, beexpressed by digital-rectal prostate massage. Furthermore, we see scanty amounts of PAS positive protein in the total ejaculate specimens whereas it is prominent in EPS specimens. This suggests the total ejaculate of prostatitis patients contains only a minimal amount of prostate secretions.

Additional studies are in progress.

Details of treatment of prostatitis understood as a tension disorder: Intrapelvic myofascial release and progressive relaxation of the pelvic floor

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The Rationale of the viewpoint of chronic prostatitis understood as a tension disorder will be presented. The details of treating prostatitis as a tension disorder including the methods of myofascial release inside thepelvic floor and progressive relaxation of the pelvic floor will comprise the bulk of the presentation.

ABSTRACTS

ORAL / POSTER

Basic Science

The results of an auto-immune screen in patients with types IIIa and IIIb prostatitis

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MATERIALS & METHODS

This is a prospective, descriptive, controlled study of an auto-immune screen measuring: anti-nuclear antibodies (ANA); rheumatoid factor (RhF); anti-thyroid antibody (ATA); as well as inflammatory markers ESR and CRP in patients with types IIIa and IIIb prostatitis. This is the first report of the incidence of these auto-antibodies in types IIIa and IIIb prostatitis, as far as we are aware. From March 2000 to September 2000, 23 patients with types IIIa and IIIb prostatitis were assessed in our Chronic Pelvic Pain clinic. Their age, duration of symptoms, CPSI score, auto-immune screen and Stamey localisation results were recorded. 17 age matched male controls either volunteers n=7 or urology clinic patients (patients with a single stone episode and currently stone free) n=10 with no history of auto-immune disorders completed a CPSI and had blood taken for the auto-immune screen. A power calculation has been performed by Dr. B. Toms (Institute of Public Medicine, Cambridge University) and 26 patients are required for the study to have an 80% power for detecting a 40% difference in the overall incidence of abnormalities between the two groups. The final statistical analysis is by Dr. B. Toms.

CONCLUSIONS

From this study we conclude that there is no association between these auto-antibodies and types IIIa or IIIb prostatitis.The limitations of the study are the small number of type IIIa patients included. This study is also insufficiently powered to detect a smaller difference than 40% in abnormalities in these patients, compared with controls. It is also possible that the choice of volunteers altered the incidence of abnormalities in the control group.

RESULTS

	Patients n=23 (IIIa n=3, IIIb n=20)			Volunteers n=17				
	Mean	**S.D.**	**Range**	**Mean**	**S.D.**	**Range**	**p Value**	
Age	48.3	12.3	21-74	41.4	13.7	22-68	p=0.071	(2 sample T test)
Duration of symptoms/mo	75	93	5-300		NA			
NIH CPSI total score	24	8	11-42	4	5	0-18	p<0.0001	(Mann Whitney U-test)
ANA positive		n=4		n=2	p=1			
RhF positive		n=1		n=1	p=1			
ATA positive		n=1		n=1	p=1			
CRP elevated		n=0		n=0	p=1			(All fisher exact test)
ESR elevated		n=4		n=4	p=0.69			
Men w/1 abnormality		n=9		n=6	p=1			
Men w/2 abnormalities		n=1		n=2	p=0.556			

Single nucleotide polymorphism studies in patients with CPPS: Preliminary Results

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BACKGROUND

Information about the genome of our species is accumulating along two dimensions: While the latitudes of our chromosomes are being charted, crudely at first, but with the expectation of a complete nucleotide sequence of one reference human genome early this millennium, the longitudes of sequence variation at specific locations in the genome are also explored, revealing how different we all are. This variation consists mostly of sequence differences in single nucleotide positions, referred to as single nucleotide polymorphisms or SNPs. An expanding panel of known sequence variants, along with greatly improved methods to monitor them, now promise to offer fresh insights into human biology and pathophysiology.

MATERIAL & METHODS

Expanding on our previous experience with linkage analysis in patients with autosomal dominant polycystic kidney disease (ADPKD), we performed linkage analysis on a total of 228 male patients affected with CPPS and used as controls in a previously published linkage analysis study and 59 unaffected individuals, and 54 spouses using eight polymorphic markers linked to PKD1 which has been mapped to chromosome 16. Since the interleukin(IL)-4 receptor gene (IL4R) shown to be abnormal in inflammatory diseases, is also located on chromosome 16 it is thus both a positional and functional candidate for a susceptibility gene for CPPS. We screened this gene for single-nucleotide polymorphisms (SNPs) by fluorescent chemical cleavage analysis, and tested a subset of known and novel SNPs for allelic association with CPPS.

RESULTS

Associations were observed between a haplotype of four SNPs (val50ile, gln576arg, A3044G, G3289A) with a lod score of 5.8. Evidence for association was found even when the four markers were analyzed individually. The results indicate that these variants are important in determining genetic predisposition to CPPS and that the IL4R gene is a likely candidate for a target gene in CPPS. Linkage disequilibrium analyses showed that the val50ile and gln576arg variants were in linkage disequilibrium with each other which is underscored by the fact that they are separated by only about 21 kilobases of genomic DNA.

CONCLUSIONS

For the majority of human diseases, there is no single, highly penetrant mutation that is responsible for disease. Instead it is likely that common polymorphisms (> 1 % frequency) within one or more pathways directly influence the expression of disease, Often, the phenotype is subtle or not apparent at all. Yet, in combination with and against a vulnerable background, the wrong set of variable could cumulatively undermine one or more biological functions and lead to disease. Our findings underscore the importance of further studies into the SNPs in a large cohort of CPPS patients.

Dr. Dimitrakov was supported by the European Consortium for Concerted Action Against Polycystic Kidney Disease

Application of universal academic principles to diagnosis and management of Pelvic Disorders (PD), Prostatitis in particular

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Present day lab procedures for diagnosis of PD are a spin-off from an article by Kass in1956 entitled "Asymptomatic Infections of the Urinary Tracts." According to a universal rule handed down to medical schools, there can be no such event as "asymptomatic infection." All infections are symptomatic based on the proven authenticated trilogy rule of about 1500+ years ago. Reliance on the Kass report is absolutely irresponsible, also proven by another authentic universal rule: Cause and Effect. Every PD has a cause (100%) which must be found by proven authentic procedures for isolation of a specific PD etiologic agent. This does not emerge as promoted by the Kass report, to simple colony counts of normal non-pathogenic human strains of E-coli Saprophytes; UA, pus cell microscopic, or any other cost sparing device. Such approach actually serves to overrule the clinician's prior diagnosis of infection. The authentic obligation of the laboratory is to find the cause, not to make a clinical judgment of the patient's condition.

In the case of prostatitis, we at CRC have found, as have other workers, that the insulting agent is a staphylococcus: specifically Staphylococcus albus (or epidermidis). This organism has long been recognized as a saprophyte—non pathogenic. Its adverse effect, as confined to the prostate area, is due to the First Law of Nature: Self Preservation. As such, this organism is unique in fostering pustule formation. These pustules block the normal functions of the prostate, causing discomfort due to blockage or obstruction from colonial buildup. This is not infection. It requires expression of pustules, as well as appropriate antibiotic treatment for proper management.

Chlamydia pneumoniae *as an impacting emerging pathogen in prostate pathologies*

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Chlamydia pneumoniae (C.p.) is one of the newest pathogens of the respiratory tract in humans. Every year almost 10% communicable pneumonitis are caused by this microorganism. The seroprevalence of C.p. in normal populations is high, estimated to be 50% at the age of fifthly, confirming its wide diffusion. Recently, C.p. has been connected with coronary chronic disease and myocardial infarction. Very recently C.p. has been found in patients with interstitial cystitis, a condition related to prostatitis.

We have analyzed for the presence of C.p.DNA, by nested PCR, prostatic biopsies, EPS, post EPS urine, total ejaculate and first void early morning urine from patients affected by different prostatic pathologies: chronic abacterial prostatitis, benign prostatic hyperplasia (BPH) and prostate cancer.

40 patients were included in the study and 87% resulted positive for Chlamydia pneumoniae DNA.

100% of the prostate biopsies (N. 10 patients) were positive, demonstrating the presence of the microorganism inside the prostate gland both in prostatitis, BPH and prostate cancer patients.

Chlamydia pneumoniae, a microorganism inducing chronic body damages, has to be better studied in relation to chronic prostatic pathologies and prostate cancer. Several interrogatives remain also open: the role of machrophages and other immunologically related cells in transporting the microrganism inside the prostate gland and in modulating the infection; its persistence in relation to the various stages of prostate damage.

C.p. positivity in these chronic prostatitis, resistant to several therapeutic regimens of antibiotics, open new pharmacological approaches.

The constant presence of Chlamydia pneumoniae in all the prostate pathologies examined open a discussion about the role of this microrganism in their development during the time: we postulate that the three conditions — prostatitis, BPH, prostate cancer — may represent different moment of the same process in which external conditions due to the host, especially immunological conditions, can induce the determinism of the one instead of the other pathology.

ABSTRACTS

ORAL / POSTER

Pathophysiology

Category III Prostatitis: Changing the paradigm— The role of pudendal nerve entrapment

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Ninety percent of men with prostatitis are considered to have Category III, non-bacterial prostatitis. Patient symptoms are relatively consistent namely, perineal, scrotal and/or penile pain after sitting, relieved when standing or supine. An effect on continence, impotence and autonomic dysfunction is common. Symptoms are often aggravated by ejaculation. Since no evidence of infection can be found in prostate secretions or seminal fluid, evaluation for other pathology is undertaken. Pudendal nerve entrapment (PNE) is frequently identified as the basis for the symptoms of "prostatitis." A review of the pathophysiology, evaluation and treatment is discussed.

Urologists are most aware of the effect of distal pressure on the dorsal nerve of the penis associated with cycling. The pudendal nerve traverses the pelvis between the sacrotuberous and the sacrospinous ligaments prior to entering the pudendal (Alcock's) canal. Compression between the ligaments may occur. A firm, sharp edge of the sacrospinous ligament may engage and irritate the nerve in the sitting position. Lastly fibrosis within Alcock's canal may trap the nerve limiting movement during body motion.

Elimination of infection as a basis for symptoms is necessary. Prostate ultrasound occasionally reveals a small Müllerian duct cyst. Ischiocavernosus EMG may show abnormal motor unit potentials characteristic of neuropathy. Pudendal terminal motor latency testing is confirmatory. Neurophysiological testing results vary mainly with the duration of pudendal nerve compression.

Treatment consists, foremost, of perineal hyperprotection. Punctilious avoidance of sitting and cycling and use of special seating pads which spare the perineum from pressure is often curative. Perineural injections of lidocaine/steroid mixture can be diagnostic and therapeutic. Neurolysis and transposition of the pudendal nerve is performed after failure of other treatment programs.

Comparison of a mollicute-specific PCR, a ureaplasma-specific PCR, and a RAPD protocol for detection of ureaplasma urealyticum *in men with chronic prostatitis*

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BACKGROUND

The results from human and animal inoculation studies and observations on immunocompromised patients provide substantial evidence that ureaplasmas are a cause of non-chlamydial non-gonococcal urethritis and prostatitis in men and controlled antibiotic and serological studies lend some support to this contention. However, the proportion of patients with ureaplasma-induced prostatitis is unknown; the occurrence of urethral ureaplasmas in healthy men suggest that the organism may persist after causing asymptomatic untreated disease and/or that only certain serovars are pathogenic or that predisposing factors such as lack of mucosal immunity exist in those who develop the disease.

MATERIAL & METHODS

We evaluated one hundred category IIIA chronic abacterial prostatitis patients (median age 25, range 18-40) and one hundred asymptomatic age-matched controls. Patients were assigned to category III A if they met the diagnostic criteria for isolation, quantitative determination, and localization of Ureaplasma urealyticum to the prostate as detailed by Weidner et al (1988). Urethral and expressed prostatic secretion (EPS) and/or post-prostatic massage urine (PPMU) samples were evaluated using *Mollicute*-specific PCR, *Ureaplasma*-specific PCR and the recently proposed PCR protocol for species identification and subtyping of *Ureaplasma parvum* and *Ureaplasma urealyticum* (Gilbert GL et al, 2000) and published RAPD protocols.

CONCLUSIONS

The results from our study show that *Ureaplasma parvum* is instrumental in the pathogenesis of a subgroup of category IIIA chronic prostatitis patients. RAPD results show that **mba** serovars 3/14 and 1 are most frequently implicated in prostatic inflammation and they are different from the urethral serovars. We therefore propose an algorithm for the diagnosis of *Ureaplasma*-associated prostatitis.

Supported by a grant to Dr. J. Dimitrakov from the Prostatitis Foundation of America

RESULTS

Patients/ Methods	Sample site	Mollicute-specific PCR	*Ureaplasma*-specific PCR	*Ureaplasma-parvum*	*Ureaplasma-urealyticum*
Patients	Urethra	25	22	10	12
	EPS/PPMU	32	35	29	6
Controls	Urethra	21	17	7	10
	EPS/PPMU	25	20	3	17

The immunopathology of Chronic Pelvic Pain Syndrome — Type IIIa

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INTRODUCTION & OBJECTIVES

Chronic Pelvic Pain Syndrome (CPPS) Type IIIa is a poorly understood condition with little data on the underlying immunopathology. Ultrasound guided biopsy and the use of panels of monoclonal antibodies have enabled characterisation of the phenotype of the inflammatory population and postulation of the immunopathological mechanisms.

METHODS

Prostatic biopsy material obtained under ultrasound guidance from 24 patients with CPPS Type IIIa and 10 controls was subjected to immunohistochemical analysis. A panel of monoclonal antibodies (RFDR-HLA DR, RFT mix–pan leucocyte, CD4–helper T lymphocytes, CD8–suppressor/cytotoxic T lymphocytes, RFB mix–B lymphocytes, RFD1–antigen presenting cells, RFD7–tissue macrophages, CD7–activated T lymphocytes) was used to define the inflammatory cell phenotype.

RESULTS

In controls faint HLA DR expression (MHC class II antigen) was observed in basal epithelial cells and a scanty T cell distribution with equal numbers of CD4 and CD 8 lymphocytes. There were no B cells and only scanty members of the monocyte/macrophage series. In type IIIa patients HLA DR expression was most marked in glandular structures increasing in intensity with inflammatory grade severity. T cell numbers increased with the degree of inflammation, with CD8 cells becoming increasingly prominent. With advancing inflammatory grade the number of antigen-presenting cells and mature tissue macrophages increased as did the proportion of activated CD8 lymphocytes. The same pattern was not observed with the CD4 subset.

CONCLUSION

The inflammatory cell phenotype can be compared with inflammatory conditions whose immunopathology is defined. The pattern observed in type IIIa prostatitis is cell mediated. The antigen-presenting cell distribution and CD4/CD8 lymphocyte ratio is more in keeping with a persistent antigenic presence rather than immunoregulatory dysfunction, as seen in rheumatoid arthritis.

A histopathological framework for prostatitis

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Since prostate tissue from patients with prostatitis is rarely available for histopathologic examination, we decided to study surgically removed tissue, total prostatectomy specimens, as a model to study prostatitis. In all cases, the prostate gland was removed for carcinoma. We also have studied tissue derived from transurethral resections of the prostate (TURPs) from patients with benign prostatic hypertrophy/hyperplasia (BPH). However, in general, that tissue was less satisfactory because of the small amount of prostate tissue available. Also, tissue samples obtained from TURPs are generally periurethral, and only rarely is more peripheral tissue obtained, and the anatomical relationships can not be easily reconstructed.

In our study of total prostatectomies, we found areas of prostatitis in the great majority of cases. The relationship between the prostatitis and the carcinoma needs to be studied further. We observe two distinct patterns:

1. **Chronic inflammation** of the interstitium/stroma, consisting of small foci of inflammatory cells, predominately lymphocytes. This chronic interstitial inflammation is common and appears to be diffusely distributed.

2. **Acute inflammation** within glands and ducts, consisting predominately of polymorphonuclear leukocytes (PMNs). This acute inflammation is less common than the chronic interstitial inflammation. It is focal, and usually found in the peripheral regions of the prostate gland. Frequently, acute inflammatory changes are also seen within the epithelium of glands. Only rarely is acute inflammation seen within the interstitium. Then, it is always associated with inflamed glands. We note that the PMNs within glands appear to be "organized": cohesive aggregates of PMNs with a protein matrix, at times admixed with corpora amylacea. The glands may be dilated and the aggregates of PMNs are generally larger in size than the diameter of the ducts which lead to the urethra. As we have previously reported, we find remarkably similar cohesive aggregates of PMNsin expressed prostatic secretions (EPS) from patients with prostatitis. We call these "prostatic inflammatory aggregates" (PIAs). At times PIAs are admixed with corpora amylacea supporting our premise that they are derived from inflamed glands within the prostate.

Further studies are needed to study the etiology of the inflammation, the interaction between the chronic and acute inflammation, and also the relationship to patients' symptoms.

Strategies for identifying prostatitis—Predisposing genetic loci

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BACKGROUND

Genetic background is important in urological disorders such as prostate cancer, hypospadias, and androgen insensitivity. In women, the risk of recurrent urinary tract infection clearly reflects genetic background, e.g., blood group antigen and secretor status. Previous investigators have used weakly polymorphic sites to find associations of genetic loci with prostate diseases such as prostate cancer.

METHODS

Newly available human genome sequencing data was searched for highly polymorphic short tandem repeats (STRs) near loci previously implicated in prostate diseases. The international human gene mapping consortium, Genemap, was used to locate, with high resolution, prostate disease-predisposing sites. Sequence data from the Human Genome Sequencing Project were searched for STRs near predisposing loci. PCR primers were then designed to test the STRs for polymorphism in a panel of DNA samples from clinical populations.

RESULTS

We identified two promising STRs. One STR, located 3 inches to the human phosphoglycerate kinase (PGK1) gene, is hemizygous, and exhibited 9 distinct alleles. This represents the most pleomorphic site identified to date in this region. The second STR, in the region of the glutamate receptor gene (GLU1), is located near the terminus of the long arm of the X chromosome, a region implicated in familial prostate cancer.

CONCLUSIONS

Newly available genetic techniques should allow us to determine the relative importance of genetic and environmental factors in chronic prostatitis/chronic pelvic pain syndrome.

Correlation of β-endorphin and PGE2 levels in prostatic fluid of men with Chronic Prostatitis/CPPS

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INTRODUCTION

Chronic pelvic pain syndrome is a clinically defined symptom complex which may have infective, inflammatory or neuromuscular components. The inability to differentiate the chronic prostatitis syndromes by symptoms alone suggests a common final pathways in symptom pathogenesis. We have shown that increased oxidative stress is present in prostatic fluid of men with categories II, IIIa and IIIb prostatitis. Since inflammation and increased oxidative stress represent injury, and immune cells have been shown to produce the natural opiod β-endorphin (END) at the site of injury we wished to measure the levels of END and PGE_2 (COX-2 product) in the EPS of prostatitis patients.

METHODS

EPS was collected from 35 patients and frozen until use. EPS was centrifuged and a 5-10 μl sample was used to measure END (Peninsula Labs) and PEG2 (Caymen Chemicals) by EIA and data presented as ng/ml EPS. Samples were stratified according to prostatitis category and samples from patients who had samples before and after successful therapy were compared.

RESULTS

In symptomatic patients, levels of END and PGE-2 were similar regardless of diagnosis. Comparing category II vs IIIa vs IIIb in symptomatic patients yielded similar results for END (12.2 vs 9.7 vs 9.1, p=NS) and PGE-2 (6.4 vs 4.9 vs 5.2, p=NS). In aggregate however, successful treatment with antibiotics, phytotherapy (Prosta-Q) or neuromuscular treatments increased END levels (23.8 ± 11 vs 8.7 ± 4.7 p=0.0001) and reduced PGE_2 levels (6.01 ± 2.9 vs 3.01 ± 2.9 p=0.001).

DISCUSSION

Regardless of etiology, patients with chronic pelvic pain syndrome have high levels of a COX-2 mediated inflammatory marker and low levels of the natural opiod β-endorphin. Successful treatment of the pain syndrome increases β-endorphin levels and reduces PGE-2 in the EPS. These findings suggest that agents which inhibit oxidative stress (eg COX-2 inhibitors, Prosta-Q) may reduce pain by increasing local opiod levels.

Identification of high-titer autoantibodies to prostate-associated antigens in some patients with chronic abacterial prostatitis

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OBJECTIVE

Based on studies suggesting that the inflammation observed in some patients with chronic abacterial prostatitis may be due to autoimmune prostatitis, the goal of these studies was to determine if a subgroup of these patients had high-titered IgG autoantibodies to prostate-associated proteins.

METHODS

Using the recently developed strategy, SEREX (serological analysis of antigens by recombinant expression cloning), we constructed a cDNA expression library from normal prostate tissue. Recombinant proteins were immunoscreened with patient and control sera. Clones reactive with high-titer IgG antibodies were subcloned and the nucleotide sequence of the insert cDNA determined.

RESULTS

We have currently immunoscreened the normal prostate cDNA expression library with the sera from four patients with chronic abacterial prostatitis. Twenty-seven positive clones, representing 5 different antigens, were identified with serum from a single chronic abacterial prostatitis patient, while two positive clones encoding a single antigen were identified with serum obtained from a second patient. Sera from the other two patients did not react with any of the expressed proteins. Four of these clones encoded sequences identical to previously characterized molecules. Clone 1 encoded a protein originally isolated from a 10-week whole embryo. The function and tissue expression of clone 1 is currently unknown. Three of the clones (clones 2-4) encoded ubiquitously expressed proteins. Interestingly, clone 5 encoded a protein known to be associated with other autoimmune states including Hashimoto's thyroiditis, Graves' disease, and idiopathic myxedema (J Clin Endo Metab, 72, 1375 [1991]). All other sera, including that from normal individuals, were negative for reactivity to the protein encoded by clone 5. The protein was found to be highly expressed in normal human thyroid and extraocular muscle, but not skeletal muscle.

CONCLUSIONS

Our results demonstrate that high-titer IgG autoantibodies to several prostate-associated antigens can be identified in some patients with chronic abacterial prostatitis. The identity of the protein encoded by clone 5 with a protein expressed in other autoimmune states suggests a possible autoimmune etiology for some cases of chronic abacterial prostatitis.