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PROSTATE BIOPSY CULTURE FINDINGS OF MEN WITH CHRONIC PELVIC PAIN SYNDROME DO NOT DIFFER FROM THOSE OF HEALTHY CONTROLS

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ABSTRACT

Purpose: Previous reports have identified bacteria in the prostate of men with chronic pelvic pain syndrome. To examine whether prostatic bacteria are more prevalent among patients with chronic pelvic pain syndrome than among those without pelvic pain, we compared 4-glass urine test and prostate biopsy results.

Materials and Methods: A total of 120 patients with types IIIa and IIIb chronic pelvic pain syndrome and 60 asymptomatic controls underwent a standard 4-glass urine test, examination of expressed prostatic secretion leukocytes by hemocytometer and transperineal, digitally guided prostate biopsies. Tissue was cultured for aerobes, anaerobes, Trichomonas vaginalis, Chlamydia trachomatis and herpes simplex virus. Skin cultures were performed on a subset of patients and controls.

Results: Positive prostate biopsy cultures were obtained from patients and controls. Bacteria were found in 45 of 118 pain patients (38%) and in 21 of 59 controls (36%) ($p = 0.74$). Older men were more likely to have positive cultures. Men with type IIIa chronic pelvic pain syndrome were more likely than those with type IIIb to have positive prostate biopsy cultures.

Conclusions: Bacteria cultured from transperineal prostatic biopsies do not differ between men with and without chronic pelvic pain syndrome. Prostatic bacteria obtained by biopsy are probably not etiologically related to the symptoms in the majority of men with chronic pelvic pain syndrome.

KEY WORDS: prostatitis, case-control studies, biopsy, pelvic pain, bacteria

In 1997 there were 2 million health care visits associated with the diagnosis of prostatitis in the United States.[1] Of these men 45% received antibiotics, contrasting sharply to the estimates that fewer than 10% of cases of prostatitis are bacterial in origin.[2] In an attempt to better delineate the syndromes diagnosed as prostatitis the National Institutes of Health (NIH) adopted a new classification system.[3] Men with acute (type I) and chronic (type II) bacterial prostatitis consistently have evidence of microbial involvement and bacteriuria. Men with type II chronic prostatitis have relapsing bacteriuria, and bacteria are localized to the prostate from 4-glass urine cultures.[4] Routine 4-glass urine cultures usually fail to identify pathogenic organisms in type III chronic pelvic pain syndrome but some still believe that the etiology of the syndrome is infectious. Type III chronic pelvic pain syndrome is subdivided into type IIIa, which associated with leukocytes in prostatic fluid and type IIIb, which is not.

To identify bacteria in patients with chronic pelvic pain syndrome we and others have biopsied the prostate.[5–7] We were able to isolate various bacteria from these biopsy samples but the etiological significance is unclear because of the lack of comparison to healthy men without chronic pelvic pain syndrome and the possibility of contamination. In this study we compare bacterial growth from prostate biopsies from healthy controls without urological disease to that from patients with type III chronic pelvic pain syndrome. We also examine the relationship of positive biopsy cultures to expressed prostatic secretion leukocytes and status as either type IIIa or IIIb chronic pelvic pain syndrome.

MATERIALS AND METHODS

Study was approved by the University of Washington institutional review board and the subjects provided written consent. Patients with chronic pelvic pain syndrome were identified from the University of Washington Prostatitis Clinic. All patients had negative prostatic localization cultures for pathogens, pelvic pain of at least 3 months in duration and no identified pathology to account for symptoms. For study inclusion patients had to have suprapubic, perineal or penile pain. Many men had several locations of pain but none had only rectal, back or testicular pain. Controls were healthy volunteers without pelvic pain or history of urological disease, who were recruited from advertisements and paid $250.00 for study participation.

All subjects were accrued from June 1991 to January 2001. Study exclusion criteria were active urinary tract infection or infection localized to the prostate from a 4-glass urine sample, positive cultures for C. trachomatis or Neisseria gonorrhea, genitourinary malignancy, suicidal ideation or overtly psychotic behavior, postoperative or genitourinary pain, or history of radiation therapy, genitourinary tuberculosis and/or cancer. Men with urethral white cells were not excluded from study. No subject had urethral discharge on physical examination.

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Subjects were not allowed to have taken antimicrobial agents within 6 weeks of the biopsy and were instructed to abstain from ejaculation for 48 hours before assessment. Following a standardized history and physical examination, the men underwent 4-glass urine localization and urethral cultures for C. trachomatis, Ureaplasma urealyticum, Mycoplasma hominis and T. vaginalis. We defined a positive prostatic localization culture as 1-log greater bacteria in the post-massage urine than in the first void urine. Patients with nonpathogens localized to the prostate were not excluded from study. Expressed prostatic secretion was assessed for leukocyte concentration by hemocytometer counts using a phase contrast microscope.[8]

We performed transperineal prostatic biopsies (3 on the left and 3 on the right side) 1 to 3 weeks later using a transperineal approach to prevent contamination by rectal flora as described previously.[5] Different cores of tissue were cultured for herpes simplex virus, C. trachomatis, aerobic and anaerobic bacteria, U. urealyticum and M. hominis, and T. vaginalis.[5] Skin biopsy cultures were implemented midway through the study to evaluate possible skin contamination of prostate cultures.

One core of tissue was placed in 1.5 ml. of phosphate buffered saline and processed in a tissue grinder. We reported number of bacteria per ml. of this fluid. Microbiological cultures, expressed prostatic secretion leukocyte counts and clinical evaluations were performed independently by different personnel/laboratories. Of the 120 patients 48 (40%) and of the 60 controls 30 (50%) had 4-glass urine cultures performed with special media and prolonged incubations in an identical fashion to the prostate biopsy specimens. The remaining men had 4-glass urine cultures performed by our clinical laboratory. No cultures were performed on expressed prostatic secretion specimens because all of this fluid was used for other laboratory purposes.

Wilcoxon rank sum or t tests were used to compare patients and controls on continuous measures, and chi-square or Fisher's exact test was used for comparison on categorical measures. Logistic regression analysis was performed to determine if there were factors associated with positive biopsies. Models were created using a stepwise method, keeping only the variables and interactions with $p < 0.10$ (to be conservative by keeping potentially important factors in the model). All statistics were generated using Splus® (Insightful Inc., Seattle, Washington).

RESULTS

All 120 patients and 60 controls completed the biopsy study. Demographics for all subjects are shown in table 1. Mean age ± SD was 39.7 ± 11.6 years for patients (range 18 to 66) and 33.1 ± 10.3 years for controls (range 19–71) (t test $p = 0.001$). There was no difference in sexual orientation of the two groups, and data were not collected on sexual activity. Prostatic tissue culture yielded T. vaginalis in 1 patient, herpes simplex virus in 1 patient and C. trachomatis in 1 control. These subjects were excluded from study, leaving 118 patients and 59 controls. Prostatic tissue culture yielded no U. urealyticum or M. hominis.

TABLE 1. *Demographics and leukocyte categories of men with type III chronic pelvic pain syndrome and controls*

	Pts.	Controls	p Value*
No.	118	59	
Mean ± SD (range)	39.9 ± 11.6 (18–66)	32.2 ± 10.0 (19–71)	<0.001
% Race:†			0.55
White	88.7	83.1	
Black	6.1	10.2	
Other	5.2	6.8	
% Leukocyte/mm.^{3}:			0.30
500 or Greater	63	53	
Less than 500	37	47	

* T test for age and chi-square test for race and leukocyte category.
† Information was not available for 2 patients.

Expressed prostatic secretion was obtained from 70 of the 118 patients (59%) and 45 of the 59 controls (76%). The patients and controls did not differ significantly in the proportion of individuals with leukocyte concentrations 500 or greater than versus less than 500 leukocytes per mm.^{3} (table 1, chi-square test $p = 0.3$). Of the 78 men who had prostatic localization cultures taken 3 of 30 controls and 11 of 48 patients had a nonpathogen localized to the prostate (chi-square $p = 0.15$). There was no relationship in patients between number of leukocytes in the expressed prostatic secretion and localization of bacteria to the prostate on 4-glass localization cultures (chi-square $p > 0.05$).

Of controls 0 of 16 men with less than 500 leukocytes per mm.^{3} and 3 of 7 men with 500 or greater leukocytes per mm.^{3} had bacteria localized to the prostate on the 4-glass test (Fisher's exact test $p = 0.02$). There was no relationship between bacteria localization to the prostate on localization cultures and finding the same bacteria on prostate biopsy cultures in either control group (chi-square $p > 0.05$). Of the 48 patients 8 (Porphyromonas asaccharolytica 1, diptheroids 2, coagulase negative staphylococcus 5) and of the 30 controls 5 (diptheroids 2, coagulase negative staphylococcus 1, Prevotella 1) had the same bacteria in post-massage urine as prostate biopsies (chi-square $p = 0.5$). Controls (53%) were more likely than patients (29%) to have an anaerobic isolate from the post-massage urine (chi-square $p = 0.03$). Patients and controls did not differ in the rate of isolation of diptheroids or coagulase negative staphylococcus in the post-massage urine.

Positive prostate biopsy cultures were obtained from patients and controls. Bacteria were found in 45 of 118 patients (38%) and 21 of 59 controls (36%) (chi-square $p = 0.74$). Age was not related to the log concentration of bacteria in post-massage urine or prostate biopsy, regardless of whether expressed prostatic secretion was obtained, the concentration of leukocytes in post-massage urine, whether bacteria were found in the post-massage urine and the presence of coagulase negative staphylococcus, diptheroids or anaerobes in the biopsy or post-massage urine. The logarithm of total bacteria in prostatic biopsy cultures was not significantly associated with finding the same bacteria in the expressed prostatic secretion (Student's t test $p = 0.54$) or with the number of leukocytes in expressed prostatic secretion (chi-square $p = 0.55$). The number of positive prostate cultures in men with 500 or greater or less than 500 leukocytes per mm.^{3} and no expressed prostatic secretion obtained did not differ significantly (31%, 44% and 50%, respectively) (chi-square $p = 0.1$). The log of total bacteria in post-massage urine was not significantly associated with the log of total bacteria in prostatic biopsies ($p = 0.57$, simple regression $R^2 = 0.004$).

Logistic regression analysis was performed to examine whether a positive culture was associated with age, subject status (control versus patient), leukocyte concentration category (500 or greater than versus less than 500 leukocytes per mm.^{3}) or the interaction between subject status and leukocyte category (table 2). Race and sexual preference were not included in the model due to the small number of observations in these categories. When those cases that did not have expressed prostatic secretion obtained were included in the model, the only statistically significant variable was age ($p = 0.04$), which indicates possible relationships among biopsy culture results, age and whether expressed prostatic secretion was obtained. Among controls younger individuals were less likely to have expressed prostatic secretion obtained, whereas among patients the age range was similar in subjects with and without expressed prostatic secretion obtained. We repeated the logistic regression separately for patients and controls (table 3). Age was not significantly associated with the probability of a positive culture among

TABLE 2. *Positive versus negative results of logistic regression predicting prostate biopsy culture results*

Explanatory Variable	p Value*
Model restricted to obtained expressed prostatic secretion leukocyte counts:	
Age	0.09
Expressed prostatic secretion leukocyte count (reference 500 or less)	0.16
Pt. status (reference healthy control)	0.78
Interaction subject status and expressed prostatic secretion leukocyte count category	0.09
Model for all subjects: age	0.04

* Specific variable after adjusting for all previous variables in the model.

TABLE 3. *Positive versus negative results of logistic regression predicting culture results by subject status*

	OR (90% CI)	p Value*
Model for controls:		
Age	1.01 (0.96, 1.07)	0.72
Leukocyte count (reference 500 or less)	0.89 (0.52, 1.53)	0.73
Model for pts.:		
Age	1.02 (0.98, 1.07)	0.13
Leukocyte count (reference 500 or less)	1.73 (1.08, 2.76)	0.05

* Specific variable after adjusting for all previous variables in the model.

controls or patients. Leukocyte concentration category was statistically significant for the patients (likelihood ration test $p = 0.05$) but not the controls. No statistically significant difference was found between the 2 groups for any type of bacteria (table 4).

Cultures of skin biopsies obtained after the skin was cleaned with povidone iodine were performed in 19 patients and 29 controls in the latter part of the study to evaluate the role of skin contamination in obtaining cultures. 19 Skin cultures (58.0%) were positive in 11 (58%) patients and 9 (31%) controls (chi square $p = 0.12$). We compared the species of bacteria grown from the prostate to those isolated from the skin, and 2 patients (11%) and 4 controls (14%) had the same species in prostate and skin samples.

DISCUSSION

We found no differences between patients and healthy controls in the rates of positive biopsy cultures or types of bacteria isolated from prostate biopsy. Our findings do not support a predominantly infectious etiology of type III chronic pelvic pain syndrome. It has generally been assumed that the prostate is a sterile organ and that positive bacterial cultures are pathological. However, we found a high incidence of bacteria isolated from the prostatic parenchyma in symptomatic and asymptomatic men. Thus, it appears that the prostate may not be a sterile organ but may be intermittently or continuously colonized by commensal urethral bacteria. All bacteria isolated from the prostate in our study have been previously noted to be present in the normal urethra.[9] These bacteria may also colonize the prostate. Our study has shown that the presence of bacteria is not necessarily related to symptoms or inflammation. It is possible that prostatic secretion leukocytosis and prostatic bacteria are unrelated to the symptoms of chronic pelvic pain syndrome.

Our results showed a positive relationship of leukocytes in prostatic fluid to positive prostate biopsy cultures in the controls. Although our controls the leukocyte concentrations did not differ between our controls and patients, we found no relationship of leukocyte concentration to positive cultures in patients. The proportion of positive cultures was similar in patients (38%) and controls (36%), which suggests that for the majority of patients in a tertiary care prostatitis clinic no bacterial etiology of symptoms can be identified.

Hochreiter et al did not find bacterial 16s RNA in surgically obtained prostates from transplant donors.[10] The lack of association between our perineal skin and prostate biopsy cultures strongly suggests that contamination did not occur from the skin in most men. We also noted little correlation between urine cultures and prostate biopsy cultures and would have expected a higher correlation if the urethra were entered during biopsy. Of the 78 subjects only 9 had the same bacteria in the first void urine and only 13 had the same bacteria in the post-massage urine as in the biopsy. Furthermore, the fact that we found so little correlation between prostate biopsy and post-massage urine cultures suggests that bacteria expressed from the prostate during prostate massage are not those grown from prostate biopsies. An explanation of this finding may be because the needle biopsies of most of these relatively young men contain mostly parenchyma and not glands[11] or that the glands sampled by perineal biopsy are different from those sampled by 4-glass urine cultures.

As with any biopsy study, there is a risk of sampling error. With prostatic inflammation the areas of leukocyte infiltrate can be focal or diffuse.[11,12] Therefore, it is possible that infected areas could easily be missed by needle biopsy and actual colonization is more frequent than we have determined by needle biopsy. We performed skin biopsies at the site of needle insertion to determine whether the prostate biopsy was a result of contamination from cutaneous flora. Only 10% of the skin biopsies isolated bacteria that were similar to the microbes identified from the prostate. We cannot conclude that a significant number of the prostate biopsies were contaminated with skin flora, which would leave the perineum, muscle or lymphatics as a possible candidate for contamination. Whether viable bacteria transit the abundant lymphatic channels in this area is not known. At this time we do not have an adequate explantation for the discrepancy between our data and those of Hochreiter et al.[10]

We deliberately did not report data on histology because they may be misleading. Biopsies were obtained from different prostatic areas. The core biopsy used for culture was not used for histology. Because inflammation is unevenly distributed in the prostate, the area of biopsy for histology may not be representative of the area used for culture. Furthermore, we have previously reported that the amount of prostatic

TABLE 4. *Bacteria isolated from prostate biopsies of patients and controls*

Bacteria Type	No. Pts. (%)*	No. Controls (%)*	p Value†
Anaerobic growth	19 (16.2)	12 (20.3)	0.50 (chi-square test)
Diptheroids	24 (20.5)	12 (20.3)	0.97 (chi-square test)
Coagulase neg. Staphylococcus	15 (12.8)	9 (15.3)	0.66 (chi-square test)
Anaerobic gram-neg.	19 (16.2)	12 (20.3)	0.50 (chi-square test)
Gram-neg. aerobic rods and anaerobes	23 (19.7)	12 (22.0)	0.71 (chi-square test)
Gram-neg. aerobic rods	4 (3.4)	5 (8.6)	0.16 (Fisher's exact test)
P. asaccharolytica	6 (5.1)	0 (0.0)	0.18 (Fisher's exact test)
Propionibacterium	7 (6.0)	1 (1.7)	0.27 (Fisher's exact test)
Prevotella	5 (4.2)	2 (3.4)	1.00 (Fisher's exact test)

* Percentages are calculated over the number of observations for specific bacteria (59 controls and 117 patients, except for Gram-neg. aerobic rods [58 controls] and Prevotella [118 patients]).

† Some expected values were smaller than 5.

inflammation in these men is generally scant and often not seen on needle biopsy.[11]

Age and presence of other urological disease may have confounded previous controlled studies.[5,7,13,14] However, when we controlled for age we still did not find differences in prostate biopsy cultures between patients and controls. One caveat is that controls were recruited through advertisement, and there is a possibility that self-selection bias was present. All controls confirmed verbally and in writing on several occasions that they had no symptoms. In our study younger controls but not patients were less likely to have expressed prostatic secretion obtained after prostate massage. It is possible that the investigators performed a less vigorous massage in younger controls or that the prostate contained more fluid in older patients.

Szoke et al have criticized previous biopsy studies, stating that fastidious organisms cannot be cultured by standard means.[15] They performed specialized cultures on expressed prostatic secretion from 30 patients with chronic prostatitis. Gram-positive aerobes, such as coagulase negative staphylococcus, as well as anaerobic bacteria were isolated. Nickel and Costerton performed transperineal biopsy cultures and identified coagulase negative staphylococcus.[14] In a previous biopsy study of patients with pain we identified anaerobes and coagulase negative staphylococcus after extended incubation.[5] In the present study coagulase negative staphylococcus was also isolated in patients. However, this organism was also found in a similar number of biopsies of controls. Thus, it cannot be concluded that these microbes are associated with chronic pelvic pain syndrome. It is certainly possible that fastidious organisms that cannot currently be isolated are responsible for some cases of chronic pelvic pain syndrome. However, we would expect that some alteration in the normal flora would occur if the prostate were infected with another single pathogenic organism.[9]

CONCLUSIONS

In this study we found no differences in expressed prostatic secretion leukocyte concentration or in positive prostate biopsy cultures between men with and without chronic pelvic pain syndrome. Our results suggest that prostate colonization by bacteria is not related etiologically to chronic pelvic pain syndrome and that the prostate is often colonized with urethral bacteria in men with and without chronic pelvic pain syndrome.

REFERENCES

1. McNaughton Collins, M., Stafford, R. S., O'Leary, M. P. and Barry, M. J.: How common is prostatitis? A national survey of physician visits. J Urol, **159:** 1224, 1998
2. de la Rosette, J. J., Hubregtse, M. R., Meuleman, E. J., Stolk-Engelaar, M. V. and Debruyne, F. M.: Diagnosis and treatment of 409 patients with prostatitis syndromes. Urology, **41:** 301, 1993
3. Nickel, J. C., Nyberg, L. M. and Hennenfent, M.: Research guidelines for chronic prostatitis: consensus report from the first National Institutes of Health International Prostatitis Collaborative Network. Urology, **54:** 229, 1999
4. Meares, E. M. and Stamey, T. A.: Bacteriologic localization patterns in bacterial prostatitis and urethritis. Invest Urol, **5:** 492, 1968
5. Berger, R. E., Krieger, J. N., Rothman, I., Muller, C. H. and Hillier, S. L.: Bacteria in the prostate tissue of men with idiopathic prostatic inflammation. J Urol, **157:** 863, 1997
6. Doble, A., Thomas, B. J., Furr, P. M., Walker, M. M., Harris, J. R., Witherow, R. O. et al: A search for infectious agents in chronic abacterial prostatitis using ultrasound guided biopsy. Br J Urol, **64:** 297, 1989
7. Weidner, W., Schiefer, H. G., Krauss, H., Jantos, C., Friedrich, H. J. and Altmannsberger, M.: Chronic prostatitis: a thorough search for etiologically involved microorganisms in 1,461 patients. Infection, **19:** S119, 1991
8. Muller, C. H., Berger, R. E., Mohr, L. E. and Krieger, J. N.: Comparison of microscopic methods for detecting inflammation in expressed prostatic secretions. J Urol, **166:** 2518, 2001
9. Bowie, W. R., Pollock, H. M., Forsyth, P. S., Floyd, J. F., Alexander, E. R., Wang, S. P. et al: Bacteriology of the urethra in normal men and men with nongonococcal urethritis. J Clin Microbiol, **6:** 482, 1977
10. Hochreiter, W. W., Duncan, J. L. and Schaeffer, A. J.: Evaluation of the bacterial flora of the prostate using a 16S rRNA gene based polymerase chain reaction. J Urol, **163:** 127, 2000
11. True, L. D., Berger, R. E., Rothman, I., Ross, S. O. and Krieger, J. N.: Prostate histopathology and the chronic prostatitis/chronic pelvic pain syndrome: a prospective biopsy study. J Urol, **162:** 2014, 1999
12. Kohnen, P. W. and Drach, G. W.: Patterns of inflammation in prostatic hyperplasia: a histologic and bacteriologic study. J Urol, **121:** 755, 1979
13. Gorelick, J. I., Senterfit, L. B. and Vaughan, E. D., Jr.: Quantitative bacterial tissue cultures from 209 prostatectomy specimens: findings and implications. J Urol, **139:** 57, 1988
14. Nickel, J. C. and Costerton, J. W.: Coagulase-negative staphylococcus in chronic prostatitis. J Urol, **147:** 398, 1992
15. Szoke, I., Torok, L., Dosa, E., Nagy, E. and Scultety, S.: The possible role of anaerobic bacteria in chronic prostatitis. Int J Androl, **21:** 163, 1998

EDITORIAL COMMENTS

The authors compared transperineal prostate biopsy cultures in men with chronic pelvic pain syndrome with and without inflammation, and controls. The results indicate that the prevalence of bacteria, predominantly of urethral origin, was similar in all of the categories. A urine culture was considered positive if the post-massage urine showed a log or greater number of bacteria than found in the first void urine. No cultures were performed on expressed prostatic secretions. The number of bacteria in the tissue required for a positive result is not stated, and so presumably 1 or more bacteria in a culture would render the biopsy positive.

All bacteria identified have been previously identified in a normal urethra. In addition, approximately 10% of the patients had the same bacteria on the perineal skin biopsy as they did on the prostate tissue biopsy. Thus contamination of the specimens from urethral or perineal flora probably contributed to the positive results identified in the many patients. The clinical relevance of the findings is unclear. The absolute numbers of bacteria cultured are not presented but it is unlikely that low numbers of nonpathogenic bacteria would contribute to any disease state, much less chronic pelvic pain syndrome.

Using a more sensitive reverse transcriptase polymerase chain reaction assay, Hochreiter et al demonstrated that no bacteria were present in tissue samples obtained from prostates surgically removed from organ donors (reference 10 in article). Furthermore, even when bacteria are present in the prostate, such as in men with chronic bacterial prostatitis, individuals invariably are asymptomatic unless they have an acute urinary tract infection.

Taken together, these studies suggest that no significant pathogenic bacteria are present in the prostate of most healthy men, as well as those with chronic pelvic pain syndrome, and that other factors should be suspected in the etiology of chronic pelvic pain syndrome.

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The last few years have been exciting and fruitful for chronic prostatitis research, and in particular for NIH category III prostatitis or chronic pelvic pain syndrome, the most common category. There are many competing etiologies proposed, including infection, inflammation/autoimmunity and neuromuscular spasm. Most urologists "vote with their feet" in favor of infection since antibiotics are the most commonly prescribed therapy even though cultures are seldom done.[1] While antibiotics frequently are effective in the face of negative cultures,[2] the commonly used antibiotics have direct anti-inflammatory effects independent of their antimicrobial effects.[3] Indeed, the NIH chronic prostatitis cohort study recently published that expressed prostatic secretion cultures had no correlation with patient symptoms[4] and reported at the American Urological

Association that there were no differences in expressed prostatic secretion culture results between patients and controls.

In the present study carefully obtained prostate biopsies were compared between patients with chronic pelvic pain syndrome and healthy controls. The incidence of positive cultures for any category of bacteria was no different between the groups. Patients were more likely to have positive cultures if they were older or they had inflammation in the expressed prostatic secretion. A valid criticism of expressed prostatic secretion studies is the concern that expressed prostatic secretion only samples urethral and ductal fluid, while bacteria may remain undetected within the prostatic stroma, particularly within biofilms. Indeed, the fact that biopsy and post-massage urine cultures differed suggests this to be true. Nevertheless, these bacteria were not different than those found in normal men.

Do these findings prove that bacteria are not etiologically related to chronic pelvic pain syndrome? Not entirely. Culture studies such as these do not address issues of virulence factors or host resistance. The same bacteria which live happily within the prostate of controls may produce prostatic injury and elicit an inflammatory response in patients. Studies of bacterial 16S rRNA in expressed prostatic secretion and prostate biopsies typically show higher prevalence in patients than controls, although no etiological role has been proven. Furthermore, while the cause of symptoms in chronic pelvic pain syndrome may not be due to the current microbiological environment, previous infection may have instigated an inflammatory or autoimmune response through direct T cell stimulation or antigenic mimicry. Further insight into the role of bacteria and antibiotic therapy will come from the recent NIH placebo controlled clinical trial, which recently closed to enrollment. In the meantime however, data such as these should give us pause before subjecting patients with prostatitis to endless courses of empiric antibiotics with no clinical benefit and the potential for harm.

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1. McNaughton Collins, M., Fowler, F. J., Jr., Elliott, D. B. et al: Diagnosing and treating chronic prostatitis: do urologists use the four-glass test? Urology, **55:** 403, 2000
2. Nickel, J. C., Downey, J., Johnston, B. et al: Predictors of patient response to antibiotic therapy for the chronic prostatitis/chronic pelvic pain syndrome: a prospective multicenter clinical trial. J Urol, **165:** 1539, 2001
3. Yoshimura, T., Kurita, C., Usami, E. et al: Immunomodulatory action of levofloxacin on cytokine production by human peripheral blood mononuclear cells. Chemotherapy, **42:** 459, 1996
4. Schaeffer, A. J., Knauss, J. S., Landis, J. R. et al: Leukocyte and bacterial counts do not correlate with severity of symptoms in men with chronic prostatitis: the National Institutes of Health chronic prostatitis cohort study. J Urol, **168:** 1048, 2002