W. Weidner, H. G. Schiefer, H. Krauss, Ch. Jantos, H. J. Friedrich, M. Altmannsberger

Chronic Prostatitis: A Thorough Search for Etiologically Involved Microorganisms in 1,461 Patients

Summary: The paper summarizes the results of a thorough search for involved microorganisms in 1,461 patients suffering from chronic prostatitis and 202 controls from 1976 to 1988 following a standardized diagnostic program.

Zusammenfassung: *Chronische Prostatitis: Erregersuche bei 1461 Patienten.* Die Untersuchung faßt die Ergebnisse einer kompletten Durchuntersuchung nach ätiologischen Mikroorganismen bei 1461 Patienten mit der Symptomatik einer chronischen Prostatitis und 202 gesunden Kontrollen in den Jahren 1976 bis 1988 zusammen.

Introduction

At present the etiology and pathogenesis of chronic prostatitis are only partially understood. In chronic bacterial prostatitis (CBP) enterobacteriaceae, such as *Escherichia coli,* are generally accepted pathogens whereas the role of gram-positive bacteria is still debatable [1]. In the case of "nonbacterial" prostatitis (NBP) pathogens which cannot be grown on conventional media have been assumed to be involved. Since *Ureaplasma urealyticum* and *Chlamydia trachomatis* are known to be the main pathogens causing non- and postgonococcal urethritis, the assumption appears plausible that via urethral ascension they might subsequently infect the prostate [2]. This paper summarizes our experience in the search for a microbiological origin of chronic prostatitis with special reference to these microorganisms.

Patients and Methods

Patients: All the patients (n = 1,461) attended our special outpatient department for prostatitis (Prostatitis-Sprechstunde Giessen) with the typical complaints [2] of chronic prostatitis. Four groups of patients were analyzed from 1976 through 1988 (Table 1) following the same diagnostic procedure in every group. Furthermore, healthy controls were examined in the same way. There were no differences in age distribution between the four groups and the controls: the range was between 17 and 67 years, with most persons aged between 30 and 50 years and median age of 40.3 years. The clinical selection of patients excluded men with known complicated urinary tract infection and spontaneous urethral discharge (urethritis).

For enrollment a medical history of chronic prostatitis of at least six months was mandatory. Each patient was referred to our department by the General Urologic Outpatient Department, the Department of Andrology or other urologists for further prostatitis investigations.

Table 1: Groups of patients and controls (Group I: including isolation of *Chlamydia trachomatis* only when "ureaplasma-associated" prostatitis was suspected. Groups II and III: including quantitative analysis of granulocytes in VB 1; additional investigation of chlamydial serology in group II. Group IV: including sonographic study of the prostate gland, but no analysis of granulocytes in VB 1).

	Patients No.	Controls No.
1976–1979 (I)	698	48
1980–1982 (II)	233	65
1983–1986 (III)	295	69
1986–1988 (IV)	235	20

The healthy controls were volunteers or outpatients without prostatic complaints.

Localization studies: Patients and controls underwent our standardized investigation program based on the "four-specimen-technique" [3] including the quantitative determination of common bacteria, fungi, and mycoplasmas [4, 5]. Material obtained by urethral swabs after prostatic massage was cultivated for *C. trachomatis* and *Neisseria gonorrhoeae. Trichomonas vaginalis* was looked for in urine after prostatic massage [5, 6]. In cases of clinical suspicion *Mycobacterium tuberculosis* was cultivated from three morning urine, and urine specimens after prostatic massage.

Leucocyte analysis in prostatic secretions: Leucocyte analysis of prostatic secretions was performed on a fresh smear of expressed prostatic secretions (1,000 x) and also, for a comparative analysis of granulocytes, on 3 ml of cytocentrifuged urine specimens obtained before and after prostatic massage [7] using Papanicolaou staining. In the patients of groups II and III granulocytes were also counted using a counting chamber in the urine specimens including first voided urine [8] thus hinting at additional urethral inflammation in the case of equally high numbers of granulocytes in both samples after the exclusion of urinary tract infection.

Prof. Dr. med. *W. Weidner,* Urologische Klinik der Georg-August-Universität Göttingen, Robert-Koch-Strasse 40, W-3400 Göttingen; *Prof. Dr. med. H. G. Schiefer,* Dr. med. *Ch. Jantos,* Institut für Medizinische Mikrobiologie, Schubertstr. 1, W-6300 Giessen; Prof. Dr. med. vet. *H. Krauss,* Institut für Infektionskrankheiten der Tiere, Abteilung Zoonosen, Frankfurter Str. 91, W-6300 Giessen; Dr. med. *H. J. Friedrich,* Institut für Medizinische Statistik und Dokumentation, Medizinische Universität, Ratzeburger Allee 160, W-2400 Lübeck 1; Prof. Dr. med. *M. Altmannsberger,* Zentrum für Pathologie, Langhansstr. 10, W-6300 Giessen, Germany.

Dedicated to Prof. *C. F. Rothauge* on the occasion of his 65th birthday.

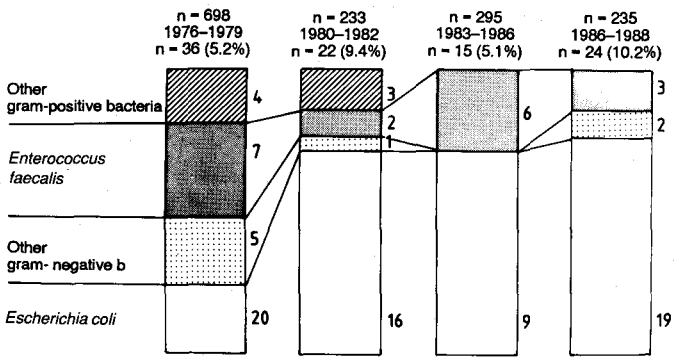

Figure 1: Evidence of chronic bacterial prostatitis.

Classification of prostatitis: For common bacteria, yeasts and mycoplasmas a typical pattern of microorganisms was mandatory: i. e. $< 10^3$ cfu/ml in VB1 and VB2; $\geq 10^4$ cfu/ml in expressed prostatic secretions, and $\geq 10^3$ cfu/ml in VB3, but at least a ten-fold increase of numbers of microorganisms in VB3 compared to VB1 [2, 3, 5]. *C. trachomatis, N. gonorrhoeae* and *Trichomonas vaginalis* detected in the urethral swabs after prostatic massage and/or in VB3 were considered the etiologic agents in lower urogenital tract infection without localization.

Leucocyte counts in prostatic secretions were considered significant when ≥ 10 leucocytes in a smear of expressed prostatic secretion (1,000 x), and ≥ 10 granulocytes in the sediment of centrifuged VB3 (400 x) were detected in the case of leucocyte-free midstream urine [7].

Classifications were based on duplicate investigations.

Sampling and special microbiology: Standard sampling was done using a bacteriologic loop (0.01 ml). The microbiologic techniques and quantitative determinations have been described in detail [2, 4–6].

Other diagnostic procedures: Depending upon varying scientific intentions and available diagnostic procedures, examinations differed in the four patient groups (Table 1).

Routine urethral swabbing for *C. trachomatis* was started with group II.

In some group II patients chlamydial serology using a modified microimmunofluorescent test [6] completed our search for chlamydial prostatic infections. This test used 16 antigen dots including all known 15 serotypes of *C. trachomatis* plus a pool of four strains of *Chlamydia psittaci.* Titers of > 1 : 8 were regarded as positive [6].

Furthermore, some patients from group IV with recurrent non-bacterial prostatitis without positive microbiologic findings were studied by transrectal sonography. In cases of abnormal echogenicity these areas were biopsied under sonographic guide and under sterile conditions by the perineal route [9]. Additional biopsy was taken endoscopically from the urethra posterior. All specimens were cultivated for bacteria, mycoplasmas, and *C. trachomatis* as well as histologically examined.

Statistical procedures: Data were documented and computerized using a PDP calculator (DEC^R). Analysis included distribution range, calculation of median values, percentiles and differences when performing the Mann-Whitney U-Test.

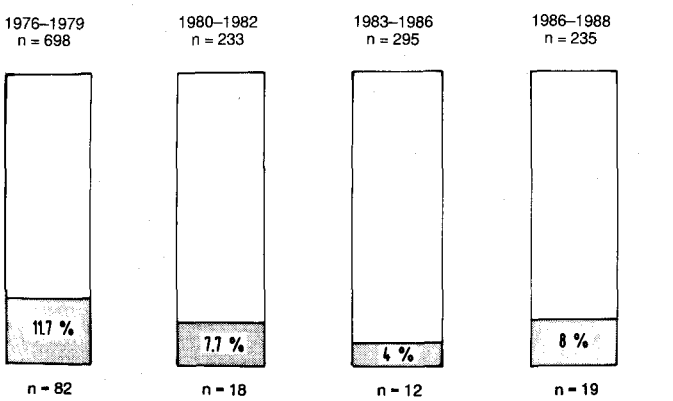

Figure 2: Evidence of "ureaplasma-associated" prostatitis. ($< 10^3$ cfu/ml in VB1 and VB2; $\geq 10^4$ cfu/ml in expressed prostatic secretions and/or $\geq 10^3$ cfu/ml in VB3)

Results

Evidence of Chronic Bacterial Prostatitis (Figure 1)

Chronic bacterial prostatitis was diagnosed in 5.1–10.2% of our patients. *E. coli* was the most prevalent microorganism. In eight cases other gram-negative bacteria, e. g. *Enterobacter aerogenes* (3x), *Pseudomonas aeruginosa* (3x) and *Klebsiella pneumoniae* (2x), were found. Gram-positive microorganisms were rare even if enterococcal infections were involved. *Staphylococcus saprophyticus* (2x), hemolytic streptococci group A (4x) and B (1x) were detected in seven patients in a typical distribution pattern indicating prostatitis.

Increased numbers of leucocytes in prostatic secretions were found in all cases considered as having chronic bacterial prostatitis.

Chronic bacterial prostatitis was detected in none of the controls.

Evidence of "Ureaplasma-associated" Prostatitis (Figure 2)

"Ureaplasma-associated" prostatitis was detected in 4–11.7% of our patients. In 102/131 cases (77.8%) a mono-infection by *U. urealyticum,* and in 29/131 men a mixed infection with *Mycoplasma hominis* were found. Starting in 1980 it became possible to exclude chlamydial infection beginning with group II.

In 16/18 men in group II, 11/12 men in group III, and 14/19 men in group IV with "ureaplasma-associated" prostatitis increased numbers of leucocytes in prostatic secretions were detected.

In none of the controls was "ureaplasma-associated" prostatitis detected. In one case high numbers of *M. hominis* were cultivated from prostatic secretions but without cytologic signs of prostatitis.

Long-term Follow-up Studies

In some patients we were able to follow the infectious situation of men with "ureaplasma-associated" prostatitis over a period of several years. Table 2 gives an example demonstrating the clinical follow-up of one man with recurrent attacks of urethritis or prostatitis associated with high numbers of ureaplasmas either classified as non-bacterial prostatitis or mere urethritis.

Table 2: Long-term follow-up study of a man with recurrent urogenital infections due to *Ureaplasma urealyticum* (NBP: nonbacterial prostatitis, C+: positive urethral chlamydia culture).

	Isolation studies (cfu/ml)				Comment
	VB 1	VB 2	EPS	VB 3	
12/1978	10^2 Therapy	–	$2x10^4$	$3x10^3$	NBP
1/1979	$3x10^2$	–	–	–	No symptoms
4/1981	10^4 Therapy	10^3	–	–	Urethral discharge
4/1981	10^2	10^3	–	–	No symptoms
5/1981	10^2 Therapy	$2x10^2$	$9x10^3$	$2x10^3$	NBP
6/1981	–	–	–	–	No symptoms
7/1986	10^4 Therapy	10^3	10^3	10^3	Urethral discharge, C+
9/1986	–	–	–	–	No symptoms
12/1988	10^3	–	–	–	No symptoms

Isolation of Chlamydia trachomatis (Figure 3)

Detection of *C. trachomatis* was analyzed separately for groups II and III (n = 528) and the controls (n = 134). In these patients a urethral inflammation was routinely excluded using leucocyte counts in VB1 and VB2. Chlamydial culture from urethral swabs was positive in 79/528 patients (14.9%) compared to 7/134 controls (5%). Correlating these findings to leucocyte reaction, chlamydiae were found in 36/79 men (45%) without cytologic signs of inflammation (these men were therefore classified as having prostatodynia), in 33/79 men (42%) with typically increased numbers of leucocytes in prostatic secretions (these men were classified as having chronic prostatitis) and in 10/79 men (13%) with the additional findings of increased numbers of leucocytes in VB1 (these men were classified as having prostatitis plus urethritis [prostato-urethritis]).
C. trachomatis could be isolated from seven controls without increased leucocyte numbers.

Chlamydia Serology

In some of the chlamydia positive men with prostato-urethritis, chronic prostatitis and prostatodynia, the serologic reaction against *C. trachomatis* was analyzed using the MIF-test. Significant differences ($p < 0.05$) in the prevalence of negative and positive MIF-titers were found in patients with chronic prostatitis, prostato-urethritis and

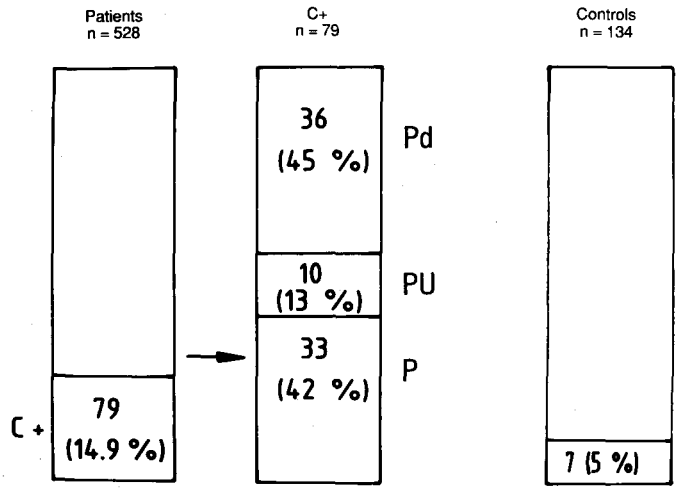

Figure 3: Isolation of *Chlamydia trachomatis* in 528 patients from groups II and III and 134 controls (P: prostatitis; PU: prostato-urethritis; Pd: prostatodynia).

prostatodynia (Table 3), when titers of > 1 : 8 were regarded as positive; no significant differences were detected in the reciprocal geometric median titers and in the predominantly reacting antigen types.

Biopsy Studies

Biopsy studies in 22 men with persistent non-bacterial prostatitis, negative microbiologic findings and abnormal sonographic features of the prostate were conducted with special reference to chlamydial findings in the specimens from the posterior urethra and the prostate (Table 4). Chlamydia could only be isolated in four cases from the urethral biopsies of the prostatic urethra, but in no case from the prostate. Other microorganisms could be detected in a further two men: small numbers of *E. coli* in perineal biopsies taken under aseptic conditions from sonographically suspicious areas hinted at silent bacterial infection in both men. Histology demonstrated round cell infiltrates in the urethra in six men, granulocytic periacinar infiltration of the prostate in two, and granulomatous prostatitis in one.

Table 3: Chlamydia serological findings.

Diagnosis	No.	Age (Years)	MIF-T positive (≥ 1 : 8)	MIF-T negative	Titer-value (rec. geom. med.)	Antigens
PU	15		14			
P	15	37	11	4	21.7	D, E, G, H, I, J
Pd	36	38	4	32	18.8	D, G, J

Table 4: Biopsy findings in 22 men with persistent NBP (CU: Chronic urethritis; Ep: epididymitis; BP: bacterial prostatitis; C+: positive urethral chlamydia culture).

N	History	Urethral swab after P. M.	Urethra			Transrectal sonography	Prostate	
			Urethritis posterior	Infiltration (Round cells)	Bacteria		Infiltration (Granulocytic)	Bacteria
16	CU 3x Ep 2x	C ∅	7	2	–	8 normal 4 pathological	2 1 (granulomatous)	–
2	CU 1x BP 1x	C ∅	normal	normal	–	2 pathological	–	*E. coli* 2900/ml *E. coli* 100/ml
4	CU 4x (Reiter 3x)	C+ 2x	4	4	C+ 4x	4 normal	–	–

Microbiologic and Cytologic Findings and Distribution of Types of Prostatic Infection (Figure 4)

The data demonstrate that in 255/528 patients with symptoms and history of recurrent prostatitis the examined specimens were free of bacteria and leucocytes, i. e. these men suffered from prostatodynia. Specific prostatitis (1 x *M. tuberculosis,* 3 x *T. vaginalis)* (0.8%) and chronic bacterial prostatitis (7%) were rare; non-bacterial prostatitis, however, was the most common type of prostatitis (28%). "Ureaplasma-associated" prostatitis could be verified in 25 men, i. e. in 16.9% of the "non-bacterial" group; in a further six cases the ureaplasmas might have originated from the urethra. *C. trachomatis* could be isolated from 33 men, i. e. in 22.2% of the "nonbacterial" group. Chlamydia could also be isolated in 16% of patients with prostato-urethritis, and in 14.1% of patients with prostatodynia. Gonococci and fungi were not found.

In the healthy controls evidence for specific, bacterial and "ureaplasma-associated" prostatitis was not found. In three men (2.2%) increased leucocyte numbers revealed nonbacterial prostatitis, and in a further seven men (5.2%) positive chlamydial findings became obvious without leucocyte reaction in prostatic secretions.

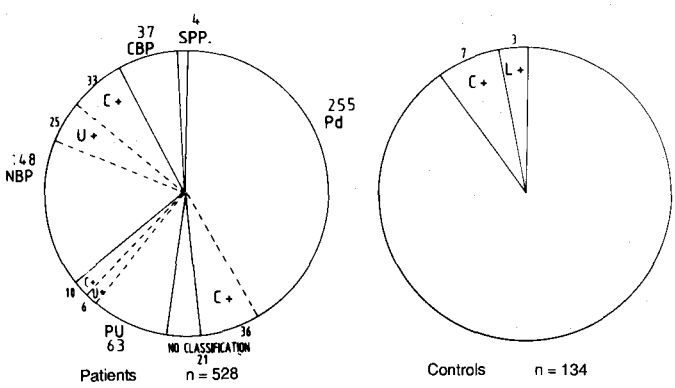

Figure 4: Microbiologic and cytologic findings as well as distribution of the type of prostatic infection in 528 patients from groups II and III and 134 controls (SPP.: specific prostatitis; CBP: chronic bacterial prostatitis; NBP: non-bacterial prostatitis; PU: prostato-urethritis; C+: positive urethral chlamydial culture; U+: "ureaplasma-associated" infection).

Discussion

Our data confirm earlier studies demonstrating chronic bacterial prostatitis as an important but uncommon disease [1]. Between 5–10% of patients with chronic prostatitis suffer from chronic bacterial prostatitis primarily due to *E. coli* [1, 10, 11].

The role of gram-positive bacteria is debatable. Some authors [12–14] assume gram-positive bacteria have an important role, e. g., enterococci, *Staphylococcus aureus* and *S. saprophyticus* in chronic bacterial prostatitis; others [1, 10] do not. According to our data only a few patients have a typical "prostatitis" pattern of gram-positive bacteria and a concomitant leucocyte reaction; nevertheless, we believe that these bacteria are important etiologic agents in some cases of prostatitis.

Until today the role of *U. urealyticum* in "non-bacterial" prostatitis has been uncertain [2]. These microorganisms are part of the normal male urethral flora [20]. Therefore, quantification of *U. urealyticum* is obligatory thus allowing comparison of the numbers of these microorganisms in first voided urine and in specimens after prostatic massage. Numbers of $< 10^3$ cfu/ml in first urine samples are considered normal urethral colonization [5, 15–17] (Table 5). There has, however, been a recent report [18] of higher numbers in the first urine sample of healthy men which is contradictory to all other studies.

Three relevant studies (Table 5) were done on patients with prostatitis following our first examinations dealing with high numbers of ureaplasmas in prostatic secretions in 1980 [4]. Our previous data were confirmed by *Brunner* et al. [5] and *Meseguer* et al. [19] whereas *Berger* et al. [18] did not find any indication of localization of ureaplasmas in the prostatic secretions of men with non-bacterial prostatitis. These conflicting data need comment. The studies confirming the pathogenic role of ureaplasmas in non-bac-

Table 5: Evidence of "ureaplasma-associated" urogenital infection in healthy controls and patients with prostatitis.

Authors	No.	No. (U+) (%) (VB1)	Titer (cfu/ml) (VB1)	No. (U+) (%) (EPS/VB 3)	Titer (cfu/ml) (EPS/VB 3)
			Healthy Controls		
Hofstetter (1973) [15]	60	5 (8.3%)	$< 10^3$	0	–
Bowie et al. (1977) [16]	37	21 (56.8%)	3 ($> 10^3$)	–	–
Weidner et al. (1978) [17]	65	9 (13.9%)	$10^{1.8}$	0	–
Brunner et al. (1983) [5]	48	8 (16.7%)	$10^{1.6}$	3 (6.3%)	$10^{2.8}$
Berger et al. (1989) [18]	50	21 (42%)	3.7×10^3	13 (26%)	?
			Prostatitis		
Brunner et al. (1983) [5]	597	51 (8,5%) (49) (2)	$< 10^3$ $> 10^3$	82 (13.7%) (49) (31)	$> 10^3$ $> 10^4$
Meseguer et al. (1986) [19]	131	?	?	8 (6.1%)	5×10^4
Berger et al. (1989) [18]	30	2 (7%)	1×10^3	0	–

Table 6: Results of chlamydia isolation studies in non-bacterial urethritis (IFT: immunofluorescent test).

Author	Patient No.	Culture		Serology	Comment
		Urethra	a. P. M. Urethra or EPS		
Mårdh et al. (1978) [25]	53	1	∅	6 (IFT)	Cases with history of NGU
Hellein et al. (1979) [26]	293		31	–	NBP without other findings
Bruce et al. (1981) [27]	70		39	–	NBP not always diagnosed by microscopic evidence of leucocytes in EPS
Nilsson et al. (1981) [28]	275		26	–	NBP without signs of urethral infection
Weidner et al. (1983) [6]	233		43	37/43 (IFT)	NBP with chlamydia findings correlated to serological response
Peeters et al. (1985) [22]	102		7	50 (IFT)	Considered as etiologic agents
Grant et al. (1985) [29]	9		3	9 (IFT)	Considered as etiologic agents
Berger et al. (1989) [18]	34		0	Not done	No cause for idiopathic prostatitis

Table 7: Biopsy studies in non-bacterial prostatitis and evidence of *Chlamydia trachomatis*.

Author	Patients	Biopsy		Comment
	No.	Urethra	Prostate	
Poletti et al. (1985) [32]	30	–	10	Transrectal biopsy • culture
Pust et al. (1986) [33]	32	6	1	Urethral and perineal biopsy • IFT
Shurbaji et al. (1988) [34]	16	–	5	TUR, needle biopsy, operation • immunohistochemistry
Doble et al. (1989) [9]	50	–	None	Perineal biopsy, ultrasonically guided • culture, IFT

terial prostatitis [5, 19] analyzed patients with significantly increased leucocyte numbers in prostatic secretions whereas in *Berger's* study [18] the majority of his patients had no cytologic signs of prostatitis. Our results have been confirmed by *Hofstetter* [21] who found a correlation between excessive numbers of ureaplasmas and increased numbers of leucocytes in expressed prostatic secretions; in 15 cases a perineal biopsy from the prostate was cultivated and in 12/15 cases ureaplasmas were detected.

Results of tetracycline therapy also indicate that *U. urealyticum* is involved in the disease: eradication of ureaplasmas was accompanied by the relieving of symptoms [17, 22]. This experience is similar to therapeutic findings after tetracycline therapy in non-gonococcal urethritis [20].

However, data concerning the possible role of ureaplasmas in chronic prostatitis are still confusing. One way out of this dilemma may be to consider the ureaplasma infection of the prostate as an end stage of the ascension of this microorganism through the urethra presenting the clinical symptoms of urethritis, prostato-urethritis or even prostatitis. Finally, in this context one remark seems to be necessary: after intraurethral self-inoculation of ureaplasmas, *Taylor-Robinson* developed infection of the prostate finding the largest portion of the microorganisms in the prostatic portion of his split ejaculate [23].

The etiologic role of *C. trachomatis* in "non-bacterial" prostatitis remains debatable [18, 25]. These microorganisms can be isolated by urethral swabbing more frequently from patients than from controls [22, 26–28]. In some studies [6, 22, 29] the pathogenic role was confirmed by serology (Table 6). Nevertheless, the design of all these studies did not allow strict discrimination between urethral colonization and prostatic infection [24]. Recently *Bruce* and *Reid* [30] reported on a new attempt to exclude urethral contamination. Chlamydial elementary bodies were stained by direct immunofluorescence in prostatic secretions, and chlamydial infection of the prostate was diagnosed in cases of chlamydia-free urethral specimens. A further promising approach to correct classification is provided by directly measuring IgG and IgA response in prostatic secretions combined with direct immunofluorescence [31].

In fulfilling one of *Koch's* postulates, some authors have tried to establish chlamydial infection of prostatic epithelial cells directly in prostatic tissue taken under sterile conditions (Table 7). Our data presented in Table 4 confirm that in some cases of non-bacterial prostatitis chlamydiae can be isolated from the urethra posterior [33] whereas positive isolates from the prostate were not available. So far our data agree with those of other investigators [9] who performed the same technique of sonographically guided biopsy of the prostate. One cause for the results which are in contrast to those of other studies [32, 34] may be the different techniques used for gaining prostatic material. Via transrectal aspiration biopsy and transurethral resection of the prostate, tissue is available from the whole prostate and also from the urethra [35]; the perineal biopsy done in our study and by *Doble* et al. [9] only gains tissue from the peripheral prostatic lobe. In other words, tissue from transrectal biopsy or transurethral resection of the prostate also contains urethral epithelia. Accordingly the data mentioned [32, 34] seem to be in accordance with the positive biopsy findings from the urethra posterior.

According to our data high numbers of gram-negative and gram-positive bacteria, and also in most cases *U. urealyticum* in a typical prostatitis pattern are correlated to increased numbers of leucocytes in prostatic secretions. For *C. trachomatis* the isolation rates do not clearly differ between patients with and without increased leucocyte numbers in prostatic secretions. Nevertheless, there is an important difference in classification [36] between patients with increased numbers of leucocytes in prostatic secretions as having prostatitis, and patients without leucocytes as having prostatodynia [37, 38]. In our opinion, all efforts must be concentrated on the first type of prostatic inflammation mentioned following a distinct classification as "non-bacterial". Studies in idiopathic forms [18] based on recurrent symptoms attributed to prostatitis but without evidence of increased numbers of leucocytes in prostatic secretions do not deal with prostatitis but prostatodynia. However, we agree with others [18] that in many cases routinely done localization studies do not provide useful information; therefore, we limited these investigations to patients with repeated evidence of increased leucocyte numbers in prostatic secretions or urine after prostatic massage.

For discussion of this topic see page S 178

References

1. **Meares, E. M.:** Prostatitis syndromes: new perspectives about old woes. J. Urol. 123 (1980) 141–147.
2. **Weidner, W., Schiefer, H. G.:** Urethro-Adnexitis des Mannes und sexuell übertragbare Erreger. Urologe A 27 (1988) 123–131.
3. **Meares, E. M., Stamey, T. A.:** Bacteriologic localisation patterns in bacterial prostatitis and urethritis. Invest. Urol. 5 (1968) 492–518.
4. **Weidner, W., Brunner, H., Krause, W.:** Quantitative culture of *Ureaplasma urealyticum* in patients with chronic prostatitis or prostatosis. J. Urol. 124 (1980) 622–625.
5. **Brunner, H., Weidner, W., Schiefer, H. G.:** Studies on the role of *Ureaplasma urealyticum* and *Mycoplasma hominis* in prostatitis. J. Infect. Dis. 147 (1983) 87–113.
6. **Weidner, W., Arens, M., Krauss, H., Schiefer, H. G., Ebner, H.:** *Chlamydia trachomatis* in "abacterial" prostatitis: microbiological, cytological and serological studies. Urol. Int. 38 (1983) 146–149.
7. **Weidner, W., Ebner, H.:** Cytological diagnosis of urine after prostatic massage – a new technique for a discriminating diagnosis of prostatitis. In: *Brunner, H., Krause, W., Rothauge, C. F., Weidner, W.* (eds): Chronic prostatitis. Schattauer, Stuttgart 1985, pp. 141–145.
8. **Weidner, W., Schiefer, H. G., Ebner, H., Brunner, H.:** Nongonococcal urethritis: leucocyte counts in urethral secretions correlated to chlamydial and ureaplasmal infections. Europ. J. Sex. Transm. Dis. 3 (1986) 207–211.
9. **Doble, A., Thomas, B. J., Walker, M. M., Harris, J. R. W., O'N Witherow, R., Taylor-Robinson, D.:** The role of *Chlamydia trachomatis* in chronic abacterial prostatitis: a study using ultrasound guided biopsy. J. Urol. 141 (1989) 332–333.
10. **Pfau, A.:** Therapie der unteren Harnwegsinfektionen beim Mann unter besonderer Berücksichtigung der chronischen bakteriellen Prostatitis. Akt. Urol. 18 (Suppl.) (1987) 31–33.
11. **Fair, W. R.:** Comment. J. Urol. 120 (1978) 184–185.
12. **Drach, G. W.:** Problems in diagnosis of bacterial prostatitis: gram-negative, gram-positive and mixed infections. J. Urol. 111 (1974) 630–636.
13. **Carson, C. C., Mc Graw, V. D., Zwadyk, P.:** Bacterial prostatitis caused by *Staphylococcus saprophyticus*. Urology 19 (1982) 576–578.
14. **Bergman, B., Wedrén, H., Holm, St. E.:** *Staphylococcus saprophyticus* in males with symptoms of chronic prostatitis. Urology 34 (1989) 241–245.
15. **Hofstetter, A.:** Mykoplasmen bei entzündlichen Erkrankungen des Urogenitaltraktes. Infection 1 (1973) 247–249.
16. **Bowie, W. R., Wang, S.-P., Alexander, E. R., Floyd, J., Forsyth, P., Pollock, H. M., Lin, J.-S. L., Buchanan, Th. M., Holmes, K. K.:** Etiology of nongonoccal urethritis. J. Clin. Invest. 59 (1977) 735–742.
17. **Weidner, W., Brunner, H., Krause, W., Rothauge, C. F.:** Zur Bedeutung von *Ureaplasma urealyticum* bei unspezifischer Prostato-Urethritis. Dtsch. Med. Wochenschr. 103 (1978) 465–470.
18. **Berger, R. E., Krieger, J. N., Kessler, D., Ireton, R. C., Cose, C., Holmes, K. K., Roberts, P. L.:** Case control study of men with suspected chronic idiopathic prostatitis. J. Urol. 141 (1989) 328–331.
19. **Meseguer, M. A., de Rafael, L., Ferrer, M. M., Allona, A., Baquero, F., Sanz, I.:** *Ureaplasma urealyticum* counts and other laboratory findings in male urologic disorders. In: *Weidner, W., Brunner, H., Krause, W., Rothauge, C. F.* (eds.): Therapy of prostatitis. Zuckschwerdt, München 1986, pp. 110–113.
20. **Shepard, M. C.:** Quantitative relationship of *U. urealyticum* to the clinical course of nongonococcal urethritis in the human male. INSERM (Bordeaux) 33 (1974) 375–380.
21. **Hofstetter, A.:** Mycoplasmeninfektion des Urogenitaltraktes. Hautarzt 28 (1977) 295–298.
22. **Peeters, M., Polak-Vogelzang, A., Debruyne, F., van der Veen, J.:** Abacterial prostatitis: microbiological data. In: *Brunner, H., Krause, W., Rothauge, C. F., Weidner, W.* (eds.): Chronic prostatitis. Schattauer, Stuttgart 1985, pp. 55–62.
23. **Taylor-Robinson, D., Csonka, G. W., Prentice, M. J.:** Human intraurethral inoculation of ureaplasmas. Quart. J. Med. 46 (1977) 309–326.
24. **Uehling, D. T.:** Abacterial prostatitis: more about what isn't but what is it? J. Urol. 141 (1989) 367–368.
25. **Mårdh, P. A., Ripa, K. T., Colleen, S., Treharne, J. D., Darougar, S.:** Role of *Chlamydia trachomatis* in nonacute prostatitis. Br. J. Ven. Dis. 54 (1978) 330–334.
26. **Hellein, G., Metz, H., Hofstetter, A.:** Nachweis von *C. trachomatis* bei unspezifischer Prostato-Urethritis. Fortschr. Med. 97 (1979) 531–538.
27. **Bruce, A. W., Chadwick, P., Willett, W. S., O'Shaughnessy, M.:** The role of chlamydia in genito-urinary disease. J. Urol. 126 (1981) 625–629.
28. **Nilsson, St., Johannisson, G., Lycke, E.:** Isolation of *C. trachomatis* from the urethra and from prostatic fluid in men with signs and symptoms of acute urethritis. Acta Derm. Venerol. 61 (1981) 456–459.
29. **Grant, J. B. F., Brooman, P. J. C., Chowdhury, S. D., Sequeira, P., Blacklock, N. J.:** The clinical presentation of *C. trachomatis* in a urological practice. Br. J. Urol. 57 (1985) 218–221.
30. **Bruce, A. W., Reid, G.:** Prostatitis associated with *C. trachomatis* in six patients. J. Urol. 142 (1989) 1006–1007.
31. **Tsunekawa, T., Kumanoto, Y.:** *Chlamydia trachomatis* Ig-A. J. Japanese Ass. Infect. Dis. 63 (1989) 130–137.
32. **Poletti, F., Medici, M. C., Alinovi, A., Menozzi, M. G., Sacchini, P., Stagni, G., Toni, M., Benoldi, D.:** Isolation of *C. trachomatis* from the prostatic cells in patients affected by nonacute abacterial prostatitis. J. Urol. 134 (1985) 691–692.
33. **Pust, R., Schäfer, R., Stumpf, Ch., Leitenberger, A., Engstfeld, J. E., Meier-Ewert, H.:** Urethritis posterior. In: *Weidner, W., Brunner, H., Krause, W., Rothauge, C. F.* (eds.): Therapy of prostatitis. Zuckschwerdt, München 1986, pp. 102–109.
34. **Shurbaji, M. S., Gupta, P. K., Myers, J.:** Immunohistochemical demonstration of chlamydial antigens in association with prostatitis. Modern Pathol. 1 (1988) 348–351.
35. **Weidner, W., Schiefer, H. G.:** Letter to the editor. J. Urol. 136 (1986) 690.
36. **Drach, G. W., Meares, E. M., Fair, W. R., Stamey, T. A.:** Classification of benign diseases associated with prostatic pain: prostatitis or prostatodynia? J. Urol. 120 (1978) 266.
37. **Anderson, R. U., Weller, Ch.:** Prostatic secretion leucocyte studies in non-bacterial prostatitis (prostatosis). J. Urol. 121 (1979) 292–294.
38. **Schaeffer, A. J., Wendel, E. F., Dunn, J. K., Grayhack, J. T.:** Prevalence and significance of prostatic inflammation. J. Urol. 125 (1981) 215–219.