Role of Mycoplasmas in Chronic Prostatitis

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In 17 out of 102 patients with clinically diagnosed chronic prostatitis the disease could be attributed to known urogenital tract pathogens. Of the remaining 85 patients, Ureaplasma urealyticum was isolated from 38, Chlamydia trachomatis from five, and both organisms together from two. The results of antimicrobial treatment of the patients suggest an etiological relationship between Ureaplasma urealyticum and certain cases of chronic prostatitis. In these cases urethritis seems to be an accompanying symptom (urethro-prostatitis). No relation could be demonstrated between a favorable outcome of therapy and particular serotypes of ureaplasma. Our study could not establish any pathogenic role for Mycoplasma hominis.

INTRODUCTION

The term “prostatitis” designates various inflammatory conditions affecting the prostate, including acute and chronic infections with specific bacteria and, more commonly, instances in which signs and symptoms of prostatic inflammation are present but no specific microorganisms can be detected.

Talking about prostatitis it is extremely important to use uniform terminology. At the moment no generally recognized, strictly defined criteria for the diagnosis of chronic prostatitis are available. Drach et al. [1] divide benign painful diseases of the prostate into four categories:

1. Acute bacterial prostatitis
2. Chronic bacterial prostatitis
3. Non-bacterial prostatitis
4. Prostatodynia

Acute prostatitis is usually caused by one of the common gram-negative urinary tract pathogens or Staphylococcus aureus. In the pre-antibiotic era N. gonorrhoeae was a common cause. The disease generally affects young male adults and is characterized by fever, chills, and dysuria. Acute prostatitis is nowadays a relatively rare condition.

Chronic bacterial prostatitis is caused by the same bacteria as acute prostatitis. Although chronic prostatitis may follow an attack of acute prostatitis, most patients

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give no history of this. Chronic bacterial prostatitis is one of the most common causes of relapsing urinary tract infection in men and is often secondary to structural disease; for instance, prostatic calculi.

Non-bacterial prostatitis (which is almost always chronic) and prostatodynia are the least well understood entities. Some authors combine the two categories and call it prostatosis. According to Drach et al. [1] non-bacterial prostatitis exists when significant numbers of bacteria cannot be cultured from prostatic fluid but the fluid consistently reveals 10–20 white blood cells per high-power field. In this category are those patients with rare conditions such as urethro-prostatic trichomoniasis or tubercular or fungal prostatitis.

This category may also include infections with chlamydia or mycoplasma.

In the fourth category, prostatodynia, remain those patients who have persistent complaints of urinary urgency, dysuria, poor urinary flow, and prostatic discomfort but who have no significant bacteria or purulence in the prostatic fluid. The prostate of these patients is often painful and congested. This condition is very probably not an infection. Many clinicians consider the symptoms of a substantial number of these patients to be psychological rather than somatic in origin.

When a urologist is talking about a patient with chronic prostatitis he usually means a patient from one of the categories 2, 3, or 4. Just on clinical examination it can be very difficult to decide in which category the patient belongs. Chronic prostatitis is a very common disease. It has been estimated that every year about 0.1 percent of the male population between 18 and 60 years will seek advice because of symptoms of prostatitis.

Whether or not a microorganism is the cause of the condition can only be proven by microbiological study of the prostatic fluid. The microbiological study of the prostatic fluid must be accompanied by careful study of the urethral flora and the bladder urine since microorganisms of non-prostatic origin can readily contaminate the prostatic secretion as it passes through the urethra during massage. Biopsy of the prostate by needle puncture seems to be the only way of avoiding contamination from urethra or urine. Needle biopsy is very unpleasant for the patient, and there is always the risk of causing septicemia. Apart from this the infection may be focal and the biopsy is difficult to quantitate microbiologically. Furthermore, it is difficult to diagnose prostatitis by histologic examination, because inflammatory changes in the prostate can be demonstrated in the absence of symptoms of prostatitis.

In our study the role of various microorganisms, including mycoplasmas and ureaplasmas, in the pathogenesis of chronic prostatitis was investigated.

MATERIALS AND METHODS

Study Population

The study included 102 patients with symptoms and signs of chronic prostatitis which had been present for at least three months. The patients varied in age from 18 to 69 years, and the mean age was 40.

Sampling and Culture

From each patient the following specimens were collected as described by Meares and Stamey [2]: urethral samples (taken with a sterile loop), the first 10 ml of voided urine, the midstream portion of urine, prostatic fluid (expressed by massage), and the first 10 ml of urine after prostatic massage. One week later seminal fluid obtained by masturbation was received. All specimens were inoculated onto blood agar plates and incubated under aerobic and anaerobic conditions.
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The specimens were further tested for the presence of *Neisseria gonorrhoeae*, yeasts, *Trichomonas vaginalis*, *Mycoplasma hominis*, *Ureaplasma urealyticum*, *Chlamydia trachomatis*, herpes simplex virus, and cytomegalovirus, as follows:

TM medium was used for cultivating *N. gonorrhoeae*, Sabouraud dextrose agar for yeasts, and a casein hydrolysate serum medium for *T. vaginalis*.

For cultivating and identification of *M. hominis* and *U. urealyticum*, we used trypticase soy broth urea U9 medium [3], differential agar medium A7 [4], and Herderscheé medium [5].

Because serotypes of ureaplasma may differ in pathogenicity [6], all isolated strains were serotyped by means of indirect immunofluorescence [7,8], using antiseras kindly provided by Dr. B. de Swaan (Rotterdam) and by Dr. J. Robertson (Edmonton, Canada).

For isolation of *C. trachomatis* diethylaminoethyl-dextran and cycloheximide-treated HeLa-229 cells were used [9,10].

Virus isolation tests were carried out by inoculating the specimens into human embryonic lung fibroblast tissue cultures. Before being discarded, the cultures were observed for six weeks for any cytopathic effect.

**Controls**

The results of the study of the patients were compared to those obtained from a group of 51 healthy men, varying in age from 27 to 52 years, whose mean age was 38 years. To collect specimens, these 51 men were subjected to the same procedures, except for prostatic massage. The reason for omitting the massage was that it was very difficult to find a volunteer for such a procedure, which is painful. The omission of tests of prostatic fluid in controls was probably not a serious shortcoming, because one of the results of the study of the patients was that seminal fluid was a good alternative for prostatic fluid in microbiological study.

**RESULTS**

**Culture**

In 15 out of the 102 patients aerobic bacteria were found to be the cause of the illness (11 *E. coli*, 2 *Staphylococcus aureus*, 1 *Klebsiella pneumoniae*, 1 *Neisseria gonorrhoeae*). The bacteria were present in prostatic fluid as well as in seminal fluid in quantities of approximately 100,000 per ml. In most cases there was a positive antibody coating. Thus, approximately 15 percent of the patients had chronic prostatitis due to bacteria. Similar figures have been mentioned in other studies.

In one of our patients *Trichomonas vaginalis* was discovered and in another a yeast (*Torulopsis glabrata*) was found to be the cause of the illness.

From one patient with bacterial prostatitis, herpes simplex virus was isolated; from two patients, cytomegalovirus. In the latter two cases the virus disappeared spontaneously without any change in the patient's condition.

Anaerobic bacteria were isolated from the urethral samples and the seminal fluid from more than half of the patients as well as from healthy controls (mostly peptococci, peptostreptococci, veillonellae, and bacteroides) but always in very low quantities. A pure culture of anaerobes in prostatic or seminal fluid was never found in quantities exceeding 10,000 per ml.

The overall results indicated that only 17 of the 102 patients had prostatitis due to known urogenital tract pathogens, whereas 85 had "non-specific" prostatitis. The term "non-specific" is used here in the sense of "not caused by known pathogens."
Approximately 30 of these 85 patients had in addition symptoms of prostatitis, and also symptoms of, in most cases, mild urethritis.

*Mycoplasma hominis* was found in two (3.9 percent) of the 51 healthy controls and in ten (11.8 percent) of the 85 patients with “non-specific” prostatitis. The difference between the two groups was not significant \( p = 0.26 \).

*Ureaplasma urealyticum* was isolated from 13 (25.5 percent) of the 51 healthy controls and from 40 (47.1 percent) of the 85 patients with “non-specific” prostatitis. The difference between the two groups was significant \( p = 0.02 \). However, it is well known that the rate of colonization with ureaplasma is closely associated with the number of sexual partners. We had no data to evaluate the possibility that the patients with prostatitis had more sexual partners than the control group. Therefore, it cannot definitely be concluded that there is an etiological relationship between *U. urealyticum* and chronic “non-specific” prostatitis.

*Chlamydia trachomatis* was isolated from seven (8.2 percent) of the 85 patients with “non-specific” prostatitis and from none of the 51 healthy controls \( p = 0.04 \).

No chlamydiae were isolated from the 17 patients with prostatitis caused by bacteria, yeasts, or *T. vaginalis*; *M. hominis* was additionally cultured from only one of them and *U. urealyticum* from two.

Table 1 shows the frequencies of isolation of mycoplasma, ureaplasma, and chlamydia alone and in combination from the 85 patients with “non-specific” prostatitis. From 38 patients we isolated only commensal flora.

All seven patients with chlamydia had symptoms of prostatitis (rectal palpation disclosed a swollen, painful prostate), and also of urethritis. Their main complaint was urethral discharge. The organism was isolated in all cases from the urethral samples and in six cases also from prostatic fluid, urine after prostatic massage, or seminal fluid.

*Antimicrobial Treatment*

All patients with mycoplasmas, ureaplasmas, or chlamydiae were treated with tetracycline, 1 gr a day, for at least three weeks. The sexual partners were also

| Organisms Isolated | Number of Patients | Number of Patients Free of Symptoms after Therapy |
|--------------------|--------------------|-----------------------------------------------|
| Mycoplasma         | 2                  | 0                                             |
| Ureaplasma         | 30                 | 10                                            |
| Mycoplasma + Ureaplasma | 8              | 2                                             |
| Chlamydia          | 5                  | 5                                             |
| Chlamydia + Mycoplasma | 0              |                                               |
| Chlamydia + Ureaplasma | 2              | 2                                             |
| Chlamydia + Mycoplasma + Ureaplasma | 0 | |
| Only “commensal” flora isolated  
(i.e. diphteroids, St. epidermidis, 
α-streptococci, micrococci, 
peptococcus, peptostreptococcus) | 38* | 3 |
| Total              | 85                 | 22                                            |

*Only 18 were treated in the same way as the other patients.*
treated. The organisms disappeared from all (two patients needed two cures). Twelve of the 38 patients with ureaplasma responded well to therapy, remaining free of symptoms during the follow-up of the study (12 months). The 12 patients had high leucocyte counts in the prostatic fluid, in the urine after prostatic massage, or in the seminal fluid, and 11 of the 12 patients also had symptoms and signs of urethritis. The seven patients with chlamydia were also cured.

Eighteen of the 38 patients from whom only commensal flora could be cultured were treated in the same way; that is, together with their partners, and three became free of complaints. The other 20 patients were treated with tetracycline for three weeks without any success. Their sexual partners were not treated. These were patients without significant numbers of leucocytes in the prostatic fluid and were therefore classified as having prostatodynia.

**Serotypes of Ureaplasma**

Several serotypes of ureaplasma were found to occur (Table 2). One strain was lost and typing of another strain has not yet been completed. The figures were too small for statistical analysis and allowed tentative conclusions only. There was no distinct difference in distribution of serotypes of ureaplasma between patients and healthy controls.

Furthermore, no relation could be demonstrated between a favorable outcome of tetracycline therapy and particular serotypes. In only one patient we found two serotypes of ureaplasma; this is less than expected. Perhaps there has been some cloning during culturing and subculturing.

**CONCLUSIONS**

The results of our study suggest that *Ureaplasma urealyticum* (and also *Chlamydia trachomatis*) plays a role in the pathogenesis of certain cases of prostatitis accompanied by urethritis (the so-called "urethro-prostatitis"). The urethritis seems to extend to the prostate gland. That the prostate can be infected during the course of a ureaplasma infection has already been indicated by studies of Taylor-Robinson and co-workers [11]. Other studies also have shown a relation between ureaplasma and prostatitis [12-14].

**TABLE 2**

Isolation of Various Serotypes of *U. urealyticum* from Patients with "Non-Specific" Prostatitis and from Healthy Controls

| Serotype | No. of Patients (n = 85) | No. of Healthy Controls (n = 51) |
|----------|-------------------------|----------------------------------|
| 1        | 6 (4)*                  | 4                                |
| 2        | 3 (2)                   | 1                                |
| 3        | 9 (3)                   | 1                                |
| 4        | 2 (2)                   | 2                                |
| 5        | 0                       | 0                                |
| 6        | 10                      | 3                                |
| 7        | 2                       | 0                                |
| 8        | 4                       | 1                                |
| 7 + 4    | 1 (1)                   | 0                                |
| Unknown  | 1                       | 1                                |
| Total    | 38 (12)                 | 13                               |

*Numbers of patients who became symptom-free after eradication of ureaplasma with tetracycline are given in parentheses.
We found, in only one patient, ureaplasma as a possible cause of chronic non-bacterial prostatitis, without contemporary urethritis. Our study could not establish any pathogenic role of Mycoplasma hominis.

The etiology of most cases of chronic non-bacterial prostatitis remains obscure.

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