

Preliminary study on the diagnostic and therapeutic value of prostate massage in apparently abacterial chronic or sub-acute prostatitis. About 166 observations

Patrick CONSTANCIS^{a1}, Patrick SAADA^b, Francis TOBOLSKI^c, Michelle JOURDAIN^{a2}. Jonathan CONSTANCIS^{a3*}

Abstract

Endpoint : 166 patients with signs of chronic or sub-acute prostatitis received prostate massages to enhance microbiological diagnosis.

A suitable anti-infection protocol, together with prostate massages, was then proposed to drain the prostatic acini and fragment and eliminate the biofilms responsible for persisting lesions.

Stamey was one of the first urologists to promote prostate massage (PM) in the '60s in order to find the infectious agents not detected by urine cytobacteriological examination (CBEU) and a standard urethral sample (US) : whence the unwarranted name of « nonbacterial prostatitis ».

Results : The additional diagnostic value of these massages is clear (moving from 85% false negatives for standard samples to under 15% for urethral samples with prostate massage).

In terms of treatment : prostate massages fully comply with guide-lines for other infectious disorders involving biofilms : eliminate them as actively as possible. The long-term cure rate of these prostatitis syndromes is 90%. Complications are benign and rare.

Conclusion : These results are predicated on scrupulous respect for contraindications, a demanding therapeutic protocol and strict criteria for cure.

Key words : prostatitis, chronic prostatitis, sub-acute prostatitis, abacterial prostatitis, prostate massage

* Correspondence : constancis@gmail.com

a Cabinet d'Uro-Andrologie, de Sexologie et de Naturopathie, 3 rue Auguste Comte 75006-Paris

a1 Urologist-Andrologist

a2 Sexologist

a3 Naturopath

b Laboratoire d'analyses microbiologiques, 32 Bd du Temple, 75011- Paris

c Centre Radiologique Daumesnil, 31 Bd Diderot, 75012- Paris

Introduction

We have tried to answer 2 tricky questions in terms of chronic and subacute prostatitis :

1) Why do so many standard urine and urethral sample readings yield no infectious agents in a large majority of chronic and subacute prostatitis syndromes ?

2) Why is the standard treatment combining antibiotics, anti-inflammatories and alpha-blockers so often disappointing ?

Materiel and Methods

Patients

N=166 (Age : 19-72 ; average : 35)

Our study concerns 166 patients with incapacitating urinary signs combining, in a variable degree, urinary burning sensations, perineal pain heightened by pressure on the buttocks, cystalgias, painful ejaculation, and, secondarily, hemospermia, atypical pelvic pain, severe psychological and sexual impacts.

In typical cases, a clinical examination highlights gland pinching or pain evocative of distal urethritis and a sensitive, even painful, inflammatory prostate in precise areas when pressure is applied by the finger, bearing witness to more or less actively evolving scar foci. There is no fever.

Standard urinary samples without prostate massage

A cytobiological examination of the first urine passed before cleansing the meatus, using PCR to detect the presence of Chlamydiae, and a PCR analysis of a urethral swab more often than not highlight germ-free hyperleucocytosis, whence the name « abacterial prostatitis ». [1-4].

Samples with prostate massages

They sensitize both the urine cytobiological examination (urine after prostate massage) and the urethral swab and use PCR to identify the presence of chlamydiae [4]. Urinary samples with prostate massage were taken in almost all the patients (153), and urethral samples with prostate massage in all the patients (166). Urethral swabbing is performed after administration of paracetamol (2 gr) or opioid suppository ½ hour before the sample is taken

The therapeutic protocol

It draws inspiration from the Manila protocol, available at :
<https://www.sexualhealthclinics.org/asia-infertility-treatment-clinics/the-manila-protocol-philippines.html>
<https://www.cureprostatitis.org/management-of-prostatitis/prostatitis-massage>

Table 1 Therapeutic protocol

Medical treatment
<ul style="list-style-type: none">- Suitable anti-infection treatment :<ul style="list-style-type: none">* 1 month for chlamydiae (azithromycin 500 mg/2 days, or doxycycline 200 mg/day)* 3 weeks for mycoplasma (Doxycycline 200 mg/day)* treatment every 5 days for parasites (metronidazol 1 gr/day)- Non-steroid anti-inflammatories: throughout the course of antibiotics (ketoprofen 100 mg/day).
Prostate and anterior urethral massages
<p>To get rid of biofilms and drain the prostate during the course of antibiotics.</p> <ul style="list-style-type: none">- Prostate massages for therapeutic purposes only begin after antibiotic treatment. They are performed by the microbiologist, who can analyse and count the number of leukocytes, epithelial cells and biofilms per field immediately after placing prostate secretions on a slide (without swabbing) to ascertain with accuracy the evolution of the prostatitis.- Anterior urethral massages are performed, daily, by the

patient himself some time after the prostate massages.

Life-style advice

Designed to reduce inflammation of the prostate

- * Total sexual rest
- * No alcohol
- * No spicy or acid food (chili, pepper, curry, cayenne pepper,...)
- * avoid urinary cristals (oxalates in particular : chocolate, black tea, asparagus...)
- * Sports, drink large amounts of mineral-poor water (to avoid biofilm calcification), healthy life-style.

This therapeutic protocol was proposed to all our patients. We selected the following criteria corresponding to cure.

Table 2 Criteria corresponding to cure

Subjective criteria
Disappearance or major reduction in pelvic pain, pain when passing water, urinary discomfort.
Objective clinical criteria
Clear improviement in prostatitis: smaller, firmer prostate, less and less painful during massage. Prostate secretion far less abundant, if at all ; absence of prostate scar tissue zone during rectal examination.
Healing of distal urethritis : disappearance of pain during pinching of gland.
Microbiological criteria
After prostate massage, direct examination of prostate secretions : strong drop in leukocytes (less than 3 per field with 40mm lens) and number of epithelial cells, almost complete disappearance of biofilms, total disappearance of parasites and/or pathogenic bacteria in culture, and negative PCR for Chlamydiae Trachomatis.
Biological criteria
PSA return to normal.

Microbiological analysis after each prostate

massage for therapeutic purposes

This is the key component in patient treatment monitoring. It makes it possible to assess the status of the prostatitis by counting its three fundamental elements : leucocytes, biofilms and epithelial cells.

Figure 1. Counting of leucocytes, biofilms and epithelial cells after each therapeutic prostate massage.

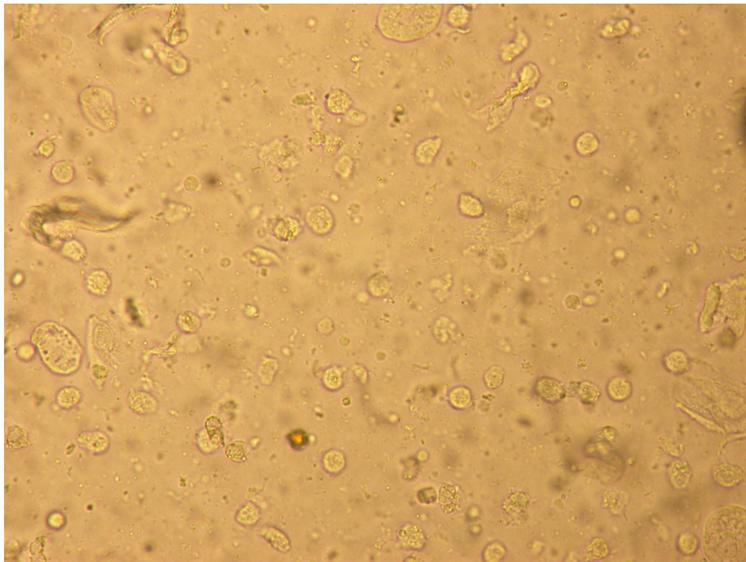


Figure 1A: numerous altered leucocytes, a small number of normal leucocytes

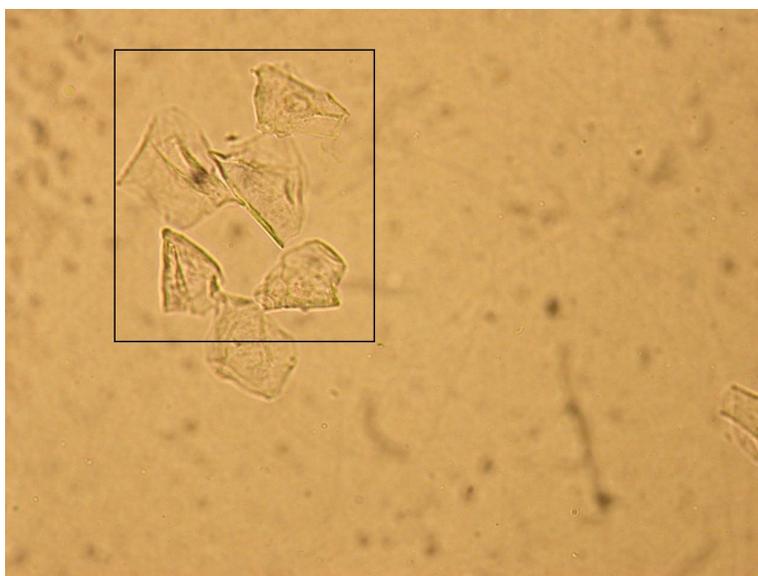


Figure 1B: Separate, free epithelial cells

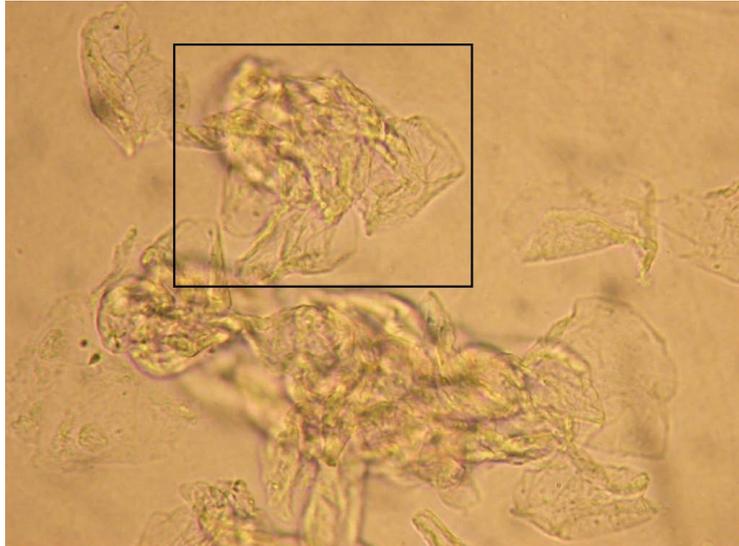


Figure 1C: Biofilms (intertwined cells that adhere to each other)
Source : Personal data

Results

Diagnostic value of the various initial samples

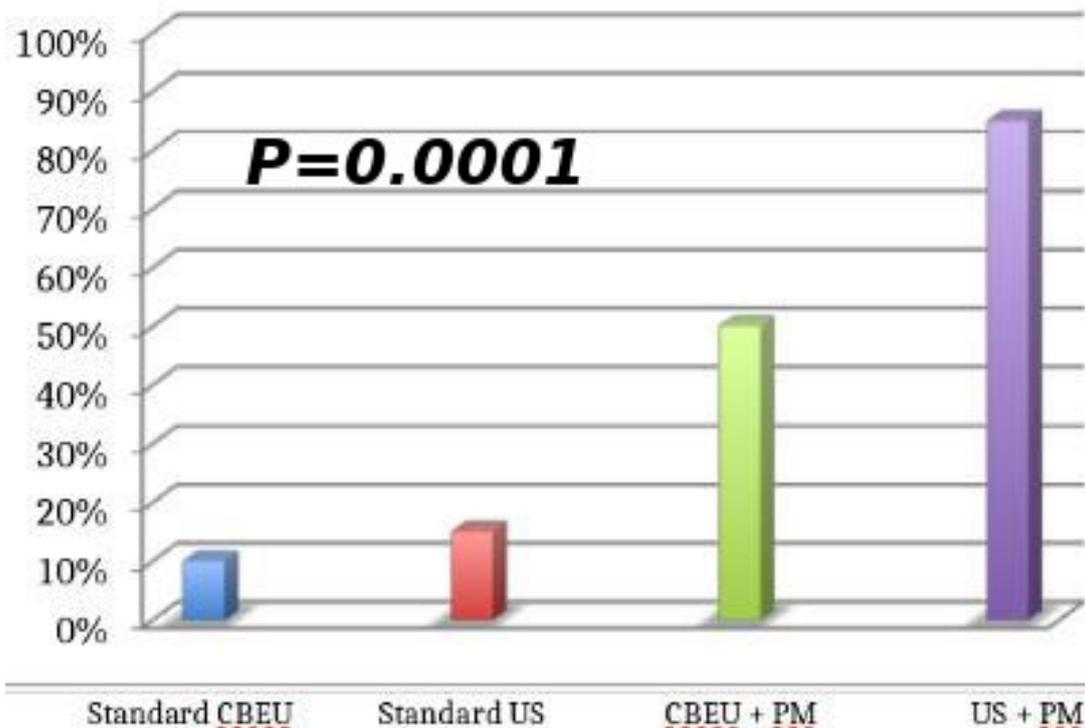


Figure 2 : Diagnostic value of the different samples
Respective percentage of positive results

A « false negative » is a microbiological examination in which no infectious agent is found, whereas another, more sensitive

test, or an examination made later in more favourable conditions, find an infectious agent.

- Standard CBEU : Urine cytobacteriological examination (with PCR and without prostate massage) : 90% false negatives (52/58 patients).
- Standard US : urethral swab (with PCR and without prostate massage): 85% false negatives (33/39 patients).
- CBEU + PM : Urine cytobacteriological examination with prostate massage (with PCR): 50% false negatives (75/153 patients).
- US + PM : Urethral swab with prostate massage (with PCR): 15% false negatives (25/166 patients at time of first swab).

Diagnostic and prognostic value of prostate secretion sample after each therapeutic prostate massage :

Table 3 Diagnostic and prognostic value of microbiological analysis of prostate secretion after each therapeutic prostate massage.

Massage-drained prostate secretion (simply placed on a slide without swabbing) is studied microscopically after each massage to monitor the gradual elimination of the prostate infection (reduction in leucocytes (fewer than 3/field), epithelial cells and biofilms).

Figure 3 : Evolution of post massage prostate secretions during the therapeutic protocol.

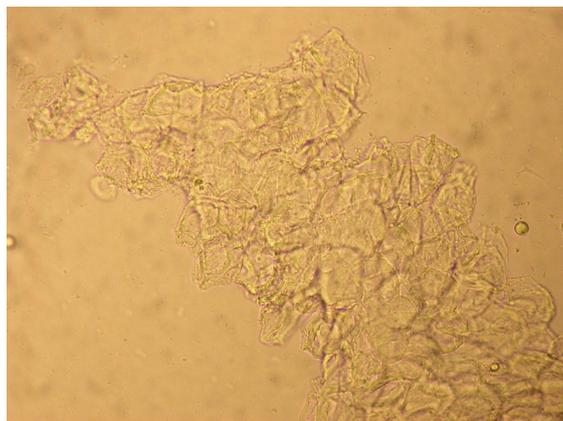


Figure 3A: Numerous biofilms

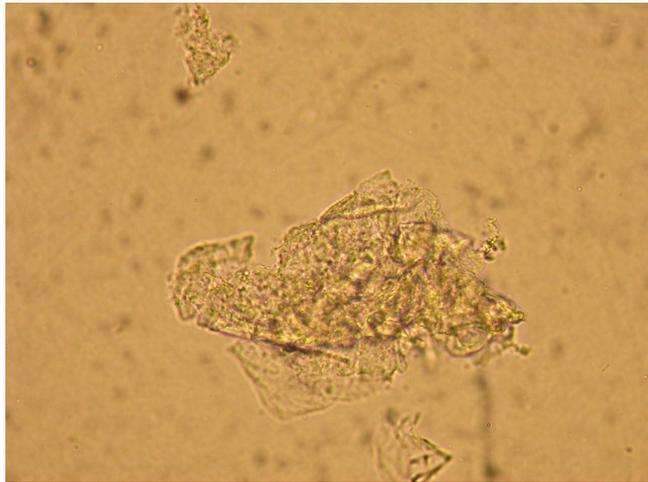


Figure 3B: Clear reduction in biofilms

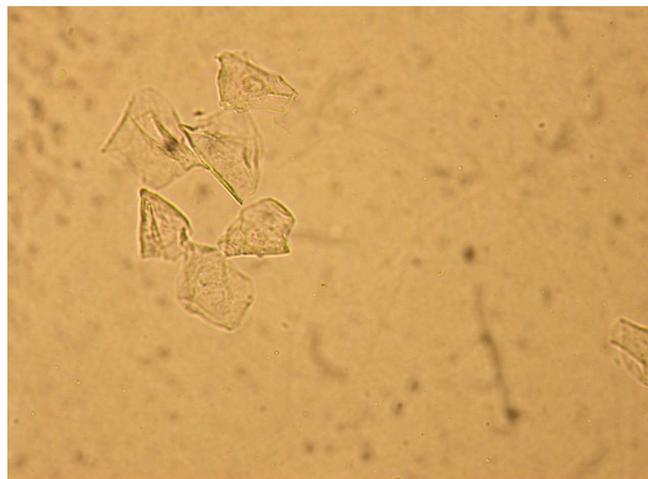


Figure 3C: Very few separate epithelial cells, disappearance of biofilms
Source : Personal data

Figure 3 shows the precise monitoring of the prostatitis, with a reduction in inflammation and the gradual disappearance of biofilms in figures 3A, 3B and 3C.

In addition, these samples, in the course of treatment, make it possible in a non-negligible number of cases (26/166, that is 16%) to find other infectious agents not initially diagnosed: round forms of *Trichomonas* (90% of cases), *mobilincus* (5% of cases). Their discovery often coincides with a sudden upswing in the number of leucocytes in the sample. This secondary discovery may be explained by the progressive improvement in inflammatory phenomena and the repermeation of the prostatic

ducts, draining the prostatic acini that were initially totally blocked. Treatment of these infectious agents is indispensable per se, and also owing the risk of colonisation by parasitic chlamydiae.

Therapeutic results

We began this protocol in early 2013 and the long-term results are encouraging. Out of the 166 cases treated, 150 have met the criteria corresponding to cure (Table 2), that is nearly 90%.

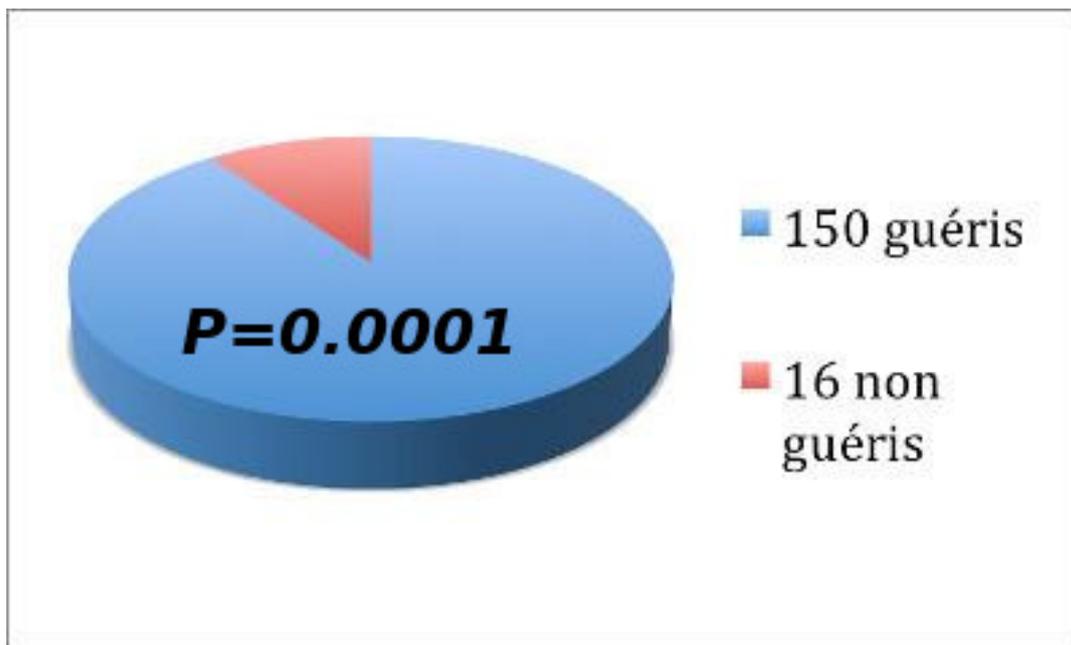


FIGURE 4

The 16 patients who failed to respond to the therapeutic protocol proposed did not meet all the criteria for cure at the end of treatment, owing to lack of rigorous compliance with the protocol (7 cases), reinfestation (3 cases), weak immune defenses (1 case), or a combination of these factors (5 cases). This is why we insist so heavily on rigorous life-style measures.

Complications

We did not note any major complications in any of the 166 cases:

- 1 case of Doxycycline photosensitization that regressed when treatment was stopped.

- 5 cases (<3% of cases) of hemorrhoid exacerbation during the period of therapeutic massage, which also regressed with the prescription of ointments and local decongestant suppositories, which hardly upset the frequency of massages.

- No case of post-swab urethral stenosis was noted in our series. Scrupulous compliance with prostate massage contraindications (see Table 4 below) is the best guarantee of trouble-free treatment.

Discussion

Why do these prostatitis syndromes initially seem abacterial ?

The infectious agents are in fact locked into the prostatic acini, which no longer communicate with the urethra owing to the inflammatory lesions that obstruct the drainage channels.

How can these infectious agents be brought into the urethra for the purposes of diagnosis ?

Back in 1936, O'Connor described the benefits of prostate massages [5].

But it is above all in the '60s that Stamey advocated prostate massage for diagnostic purposes in order to propell the germs into the urethral lumen and then take a swab [6].

Later, other schools proposed this protocol in order to improve the diagnosis of these « inexplicable » but incapacitating prostate pains and burning sensations which are often unfelicitously called « psychosomatic »:

- Dr Feliciano's team in Manila in the Phillipines [7-16].
- The team led by Dr Hennenfent [7-12, 15, 17] in Chicago, the team of Dr Shoskes [18, 19] (California) in the United States
- Dr Zhongming's team in China [20]

- a review of the literature by Mishra [21] in 2008 confirms the value of repeated prostate massages in chronic prostatitis.

A urethral sample with prostate massage thus makes it possible to highlight germs not found in a urine cytobacteriological examination and simple urethral sample without massage (false negatives). More often than not, they are : Chlamydiae Trachomatis, T- or H- Mycoplasma, round forms of Trichomonas, Mobilincus, Gonococci (chronic form)...

It also makes it possible to quantify the number of altered leukocytes, indicating the magnitude of the infection, and the quantity of biofilms, indicating how chronic the condition is (see chapter on biofilms).

This massage must be a true prostate drainage, with an immediate analysis of all the urethral secretions, and not just a rectal examination, if the aim is truly to highlight the pathogenic infectious agent(s), and the quality of the massage conditions the quality of the results.

Importance of the quality of the prostate massages

The need to perform effective prostate massages is based on microbiological findings. When the massages are diffuse and fail to target the collected, productive areas, the microbiological analysis of the prostate secretions is not very enlightening (see Figure 4A below).

Figure 5: Quality of therapeutic prostate massage.



Figure 5A : prostate secretions with a subnormal appearance without biofilm after poorly targeted massage.

Conversely, when the massage focuses on the softest, most painful, depressible areas, drainage of these inflammatory foci makes it possible to identify numerous biofilms in the prostate secretions. (See Figure 4B below).

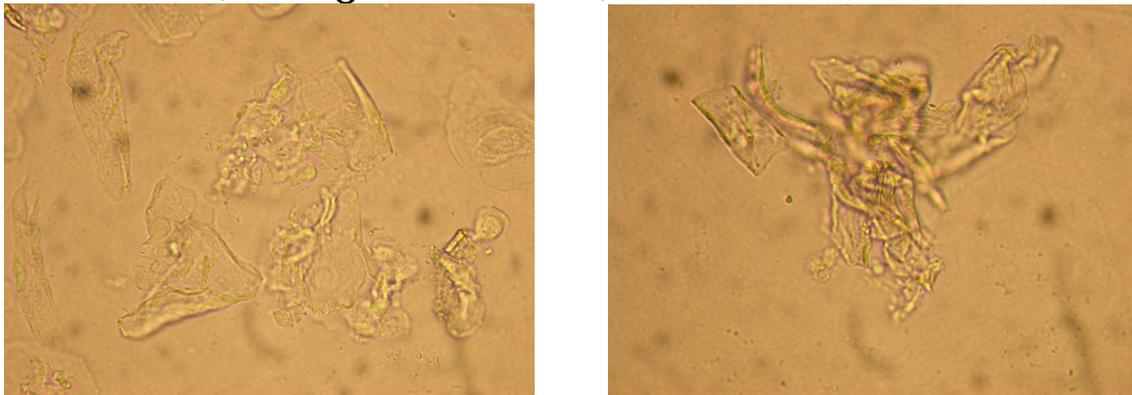


Figure 5B: Prostate secretions after massages of the depressible area (multiple abscessed foci) with drainage of numerous biofilms.

Source: personal data

This massage is only performed in the absence of the usual contraindications

Table 4 Contraindications to prostate massage

Fever, acute evolving prostatitis with exquisite pain in the entire prostate during rectal examination.

Prostate massage for diagnostic purposes is set aside for chronic prostatitis and subacute prostatitis that do not appear to be worsening, in the absence of coagulation disorders and any suspicion of prostate cancer.

What to do with false negatives despite samples with prostate massages in the event of a strong suspicion of chronic prostatitis ?

In these evocative clinical cases (germ-free significant leucocyturia : corresponding to the 15% false negatives in figure 2) where, despite prostate massage, samples remain negative with a first microbiological examination, but the altered leucocytes, epithelial cells and biofilms are numerous, PSA, ultrasound, even prostate MRI are useful to confirm the prostatitis [11, 22]. It is worth noting that these initial false negatives were more frequent at the beginning of our experience than now.

In certain circumstances, where diagnosis is difficult, a perineal electromyography may be considered to eliminate an Alcock canal syndrome [20, 23].

In typical clinical cases where prostate massage reveals a few altered leukocytes, some biofilms, but no micro-organisms, even with PCR, it may sometimes be necessary to reactivate the prostatitis (sex, beer, spicy food) some time after the initial examination and antibiotic treatment in order to highlight the infectious agents [10, 14, 24].

Pathophysiology of chronic prostatitis:

These tricky, lingering, hard to treat, worrying disorders with few symptoms are linked mainly to prostate lesions (intra-prostatic micro-abscesses surrounded by often calcified scar tissue (Biofilms)) hard to treat with antibiotics (A-B). Indeed,

the Chlamydiae are enveloped in biofilm (polysaccharide envelope) which makes A-B dissemination even more random.

In these chronic infections, particularly due to Chlamydiae (by far the most frequent), the pathogenic agents are mainly located in the prostate cells and epithelial cells of the anterior urethra (typical pain resulting from pressure on the gland) This is why so many urine cytobacteriological examinations (simple urine examination using PCR to detect Chlamydiae, but without prostate massage) end up being falsely negative. A very large bacterial load is required for the Chlamydiae to be found in the urethra lumen.

The same is true to a lesser degree for urethral swabs with PCR search for Chlamydiae, as they do not entail prostate massage. Thus, the absence of Chlamydiae in the urine cytobacteriological examination and urethral sample without prostate massage is very frequent (figure 2) and does not eliminate the diagnosis ; the same applies to a normal ultrasound of the prostate.

In fact, it is only by expelling them from their intra-cellular prostate hiding places in the prostate (by « effective prostate massages ») that they can be identified, as advocated by Stamey [6]. Furthermore, other pathogenic agents are often associated (Gonococci, Trichomonas, Mycoplasma, Staphylococci...), micro-organisms that are also colonised by Chlamydiae, and which may constitute secondary vectors if they are not eradicated at the same time.

Thus, a urethral swab after prolonged prostate massage is key to diagnosing these urethro-prostatitis syndromes. The number of false negatives then falls significantly (this is the only examination with a tolerable false negative rate under 20%). In the absence of massage, false negatives number over 50%, and patient symptoms are considered psychogenic !

Sibert and Grise, in '96 [24], had already noted the benefit of prostate massage and the technical difficulties with the Stamey test

Most foreign schools confirm the difficulties interpreting simple urine cytobacteriological examinations and urethral samples without prostate massage [1-4, 6, 10, 16, 18, 20, 21].

Let us not forget that some of these patients have undergone a real psychological and sexological ordeal for many years for lack of proper diagnosis, and some have even become addicted to opioids (3 in our case) owing to the incapacitating nature of this disorder.

The same rigorous reasoning applies to samples in women, which must specifically be taken in the endocervix in order truly to highlight Chlamydiae and other associated germs (difficulties with a retroverted uterus). Thus, vaginal samples collected by the patient herself have the same drawbacks as CBEUs and urethral samples in men in the absence of prostate massage. A complete diagnosis of all the partners is obviously indispensable in order truly to stem dissemination of Chlamydiae, and other associated germs.

What are the therapeutic obstacles in chronic or subacute prostatitis ?

There are basically three:

- Prostatic barrier
- Biofilms
- Immune defenses

1) The prostatic barrier:

Concerning the relative penetration of antibiotics in the prostate, which may or may not be easy, we always add non-steroid anti-inflammatories (NSAIDs) to the antibiotics prescribed to foster their penetration in the prostate. These NSAIDs are prescribed with gastric protectors and in the absence of the usual contraindications.

2) Biofilms :

What is biofilm ?

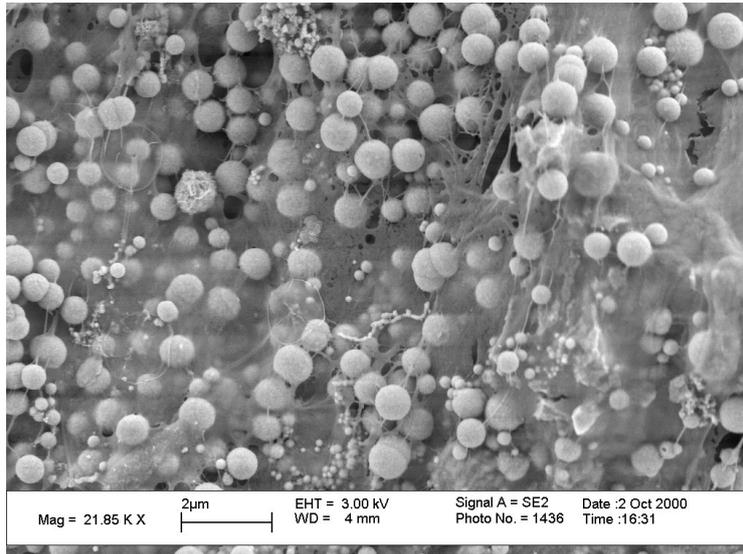


Figure 6: Electron scanning microscope photo. Numerous biofilms

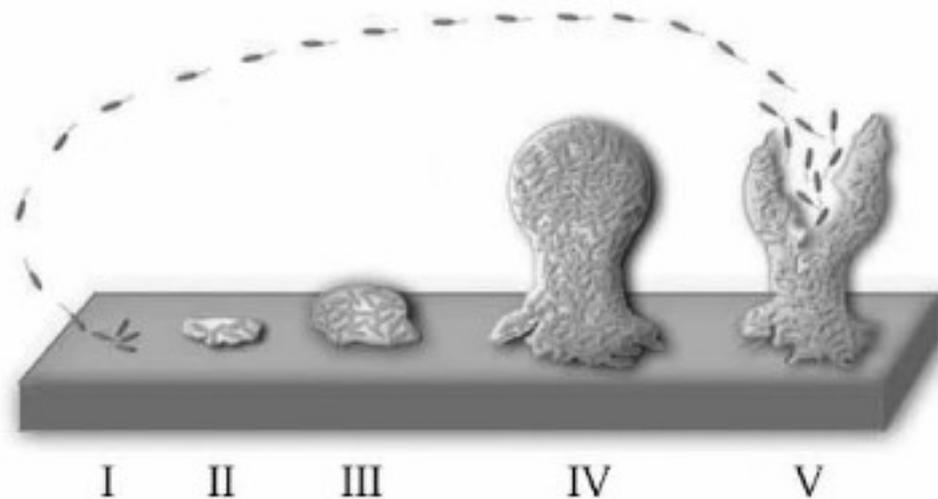
Source : Biofilm Wikipedia

Biofilm is a special way in which infectious agents evolve ; they go into hibernation in order to protect themselves better from outside aggression [25, 26] (Antibodies, immune system cells (macrophages, polynuclears,...), various anti-infectious agents).

Biofilm builds up in a few hours in the following manner:

- 1) Adhesion of infectious agents among themselves and on a surface (skin, mucosa, wall of prostatic acini,...), initially in a reversible, and then in an irreversible way.
- 2) Secretion by the micro-organisms of extra-cellular polymeric substances (EPS), which cement the set of germs among themselves and on the adhesion surface, creating a viscous, protective matrix. (This matrix is made up of polysaccharides, proteins, glycolipids and bacterial DNA). These biofilms thus constitute colonies of bacteria in hibernation, ready to wake up if local conditions are favourable (inflammation,...) and become « planctonic » again, that is, free and active. It is worth noting that biofilms constantly secrete planctonic infectious agents and micro-colonies of bacteria in the form of micro-biofilms, which will proliferate and adhere solidly in turn to the walls of the prostatic acini.

Figure 7 «Biofilmisation - planctonisation» cycle



Temporal evolution of biofilm. Schematization of the four stage universal growth cycle of a biofilm with common characteristics (that includes initiation (I), maturation (I) and (II), maintenance (IV) and dissolution (V)).

Source : Bernard C.S., Giraud C., Spagnolo J., De Bentzmann S. *Biofilms : The secret story of microbial communities* In: Locht C., Simonet M. editor. *Bacterial Pathogenesis. Molecular and Cellular Mechanisms*, Caister Academic Press. 2012, 6. 128-168. [27].

In the prostate, the epithelial cells (figure 1B) are colonised by the infectious agents, which secrete extra-cellular polymeric substances (EPS) and cement the epithelial cells together, creating a characteristic intertwining (figures 1C, 3A, 3B, 4B).

Infectious agents may thus take two forms : active, free and circulating (planctonic sensitive to antibiotics), or biofilms (in hibernation), totally impervious to anti-infectious agents [28]. Whence the need to get rid of them, as advised by major burn departments and departments that treat extensive skin damage [29] : daily cleansing and wide resection of tissue covered by biofilm, responsible for delays in healing.

These biofilms are also responsible for prosthetic infections, and require removal of the prosthesis to eliminate the septic foci.

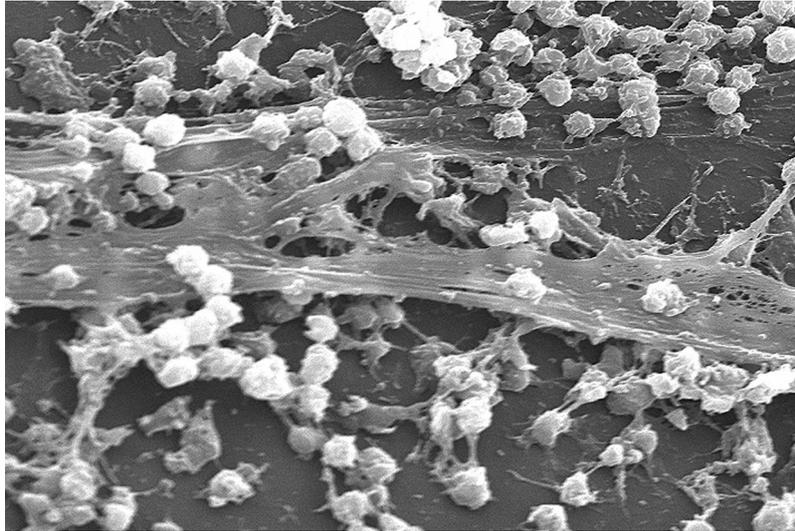


Figure 8 : staphylococcus aureus biofilm on indwelling catheter
Source : Biofilm Wikipedia

In odontology, dental plaque is a cluster of biofilm responsible for dental caries, and must systematically be eliminated.

We are thus simply applying to the prostate the active attitude of all biofilm specialists : get rid of it as quickly as possible.

The Manila team, for over 15 years, has treated thousands of chronic and subacute prostatitis syndromes using massage [9, 13, 14, 16], providing experimental confirmation of this protocol.

Indeed, we do not currently have a truly effective chemical treatment that provides for specific lysis of the extra cellular polymeric substances (EPS) that protect the micro-organism.

For this reason, following several foreign schools, we propose fragmenting this biofilm mechanically through effective prostate massages and anterior urethral massage (2 to 3 a week for 4 weeks by the microbiologist) and anterior urethral massages (by the patient himself) combined with antibiotics effective against the various infectious agents found among all the partners.

These massages (in addition to fragmenting the biofilm) have the advantage of draining the prostatic infectious foci, « flushing the micro-abscesses », and reducing the bacterial load.

3) Immune defences :

We have noted that immune defences play a key role in the development of these prostatic syndromes. Patients with healthy life-styles (healthy diets, non-smokers, regular exercise, good stress management,...) have prostatitis that evolves much less than others, and are cured much more quickly thanks to the protocol (improvement in clinical signs and post massage secretion microbiological criteria twice as quick).

It is worth noting that these life-style measures have been known for millenia in Indian medicine (Ayur-Veda) and are used to reduce inflammation of the pelvic organs.

Patients who best follow this life-style advice have post massage prostate secretions that return most quickly to normal (quick reduction in biofilms, leukocytes and epithelial cells).

150 of the 166 patients treated met these criteria for cure, that is 90%, based on demanding, stringent measures ; this is encouraging in particular for longstanding, incapacitating chronic forms that are often not diagnosed ; patients were thus able to recover an unexpected degree of comfort, after many years of « false negatives ».

Rigorous compliance with protocol

We have noted that whenever patients fail to respect one of these constraints, the next day during the prostate massage and the microscopic examination of prostate secretions, the number of leukocytes, epithelial cells and/or biofilms has gone back up.

Conclusion

Such a high cure rate for these chronic and subacute prostatitis syndromes is linked to a rigorous, demanding therapeutic

protocol, and above all to microbiological controls after each prostate massage. This systematic control makes it possible better to monitor the evolution of the prostatitis and to guide and support the patient in his therapeutic pathway.

A multicentre, randomised, double-blind study with a large number of patients using the NIH-CPSI questionnaire is indispensable for a statistically significant, reliable, definitive evaluation. We propose adding the immediate microbiological count of leucocytes, epithelial cells and biofilms in urethro-prostatic secretions sampled after therapeutic prostate massage to the NIH-CPSI to make an accurate evaluation of prostate inflammation.

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