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# PROSTATITIS INFORMATION

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## CHRONIC PROSTATITIS AT AUA 2013

This past May, as in 2012, there wasn't a lot of research on chronic prostatitis presented at the 2013 American Urological Association Meeting. Federal research dollars for this research have gone mainly into the Multidisciplinary Approach to Pelvic Pain (MAPP) program, which is aimed at looking for the cause or causes of chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS) and interstitial cystitis (IC, also known as IC/PBS or IC/BPS). MAPP has only begun to produce some results, and the numbers of patients in the studies reported so far are low. Today, treatment trials are up to industry, where the potential therapies include a new type of anti-inflammatory drug, a cannabinoid (a marijuana-like compound), benign prostatic hyperplasia (BPH or prostate enlargement) medications, Botox injections, a pollen extract, and saw palmetto.

## TREATMENT

### *ED Drug Improves More than ED for Men with CP/CPPS*

The Efficacy of Mirodenafil for Chronic Prostatitis/ Chronic Pelvic Pain Syndrome in Middle Aged Patients
*Hyun Jun Park; Nam Cheol Park; Tae Nam Kim; Jong Kil Nam*

A PDE5 inhibitor helped men with CP/CPPS, not just with erectile function, but also with their other CP/CPPS symptoms, especially voiding symptoms, and improved their quality of life. In this study, which was only single-blinded (that is, the patients did not know what treatments they received but their doctors did), 40 middle-aged men with CP/CPPS were treated with the antibiotic levofloxacin alone and 48 men with levofloxacin and the PDE5 inhibitor mirodenafil for six weeks. The men who got mirodenafil had significantly greater improvements in their International Prostate Symptom Score (IPSS) and its voiding subscore, their NIH Chronic Prostatitis Symptom Index (NIH-CPSI) scores, and erectile function scores at six weeks. At four weeks, the men who got mirodenafil also had larger improvements in the voiding and quality-of-life subscores of the NIH-CPSI. Some of the men who took mirodenafil had side effects, such as frequent erections, dyspepsia, and headache, but none of them stopped their treatment because of side effects. Mirodenafil is not approved for use in the United States. The PDE5 inhibitors that are approved in the United States include sildenafil (Viagra), tadalafil (Cialis), and vardenafil (Levitra).

### *Attack Symptoms on More than One Front*

The efficacy and safety of a multimodal therapy for chronic prostatitis/chronic pelvic pain: a prospective randomized study
*Antonella Giannantoni; Silvia Proietti; Marilena Gubbiotti; Jacopo Adolfo Rossi de Vermandois; Massimo Porena*

Attacking CP/CPPS on a number of fronts at once (called "multimodal therapy") works better than a one-treatment-at-a time approach, at least with the treatments used in this study of 38 men with CP/CPPS. For 16 weeks, the men in one group received an alpha blocker (tamsulosin or Flomax) as well as duloxetine (Cymbalta, an antidepressant also used for pain), and the herbal remedy saw palmetto. The other group got tamsulosin alone over the 16 weeks. The men in both groups had significant reductions in their NIH Chronic Prostatitis Symptom Index (NIH-CPSI) scores and in their anxiety scores. The patients who got tamusulosin alone also had significant reductions in their urinary symptoms and anxiety, but the patients who got multimodal therapy had improvements in anxiety and depression as well as in pain and quality of life. One caveat the authors noted was that four of the men who got multimodal therapy stopped taking duloxetine because of side effects.

## EPIDEMIOLOGY AND NATURAL HISTORY

### *Longer Flares Equal Worse Symptoms*

Symptoms, health care utilization, and bother associated with urologic chronic pelvic pain symptom flares of varying duration: results from the MAPP study
*Siobhan Sutcliffe; Graham Colditz; Ratna Pakpahan; Melody Goodman; Gerald Andriole; Henry Lai*

Symptoms are worse with longer flares, showed this MAPP study, which analyzed flare surveys from a small group of patients (49) with either IC or CP/CPPS. Previously, this team found that flares varied much more than they expected in terms of duration (which ranged from minutes to months) and frequency. Now they have found that symptoms were more severe as the length of flares increases. Patients with longer flares were more likely to contact a healthcare provider, increase or change their medication, not engage in their usual activities, think about their symptoms, and be bothered by their symptoms. Even short flares (lasting less than an hour) disrupted usual activities for most of these patients.

### *"Gotta Go" in CP/CPPS May Result from Prostate-to-Bladder Nerve Crosstalk*

Prostate-to-bladder afferent cross-sensitization as a mechanism inducing bladder overactivity in prostatic inflammation
*Yasuhito Funahashi; Ryosuke Takahashi; Pradeep Tyagi; Momokazu Gotoh; Naoki Yoshimura*

This possibility that nerve crosstalk between pelvic organs may be responsible for multiple pelvic problems has been researched for some time in interstitial cystitis (IC), and now researchers are looking at the possibility in CP/CPPS. This research team's experiments showed that nerve crosstalk between the prostate and bladder is a real possibility as a cause of bladder symptoms in CP/CPPS. Rats whose prostates were irritated chemically showed overactive bladder-type symptoms a week later, despite inflammation showing up in the prostate but not in the bladder. That's similar to men with CP/CPPS who show overactive bladder symptoms but don't show evidence of bladder inflammation. The rats' bladders had increased numbers of activated mast cells (an allergic-type reaction) and expression of nerve growth factor. Nerves coming from the blader as well as those communicating between the prostate and bladder, had ramped up activity.

### *But Is the Bladder the Bad Actor in CP/CPPS?*

Urine chemokines reflect contribution of bladder in the symptoms of chronic prostatitis
*Pradeep Tyagi; Kim Killinger; Gregory McLennan; Jayabalan Nirmal; Naoki Yoshimura; Michael Chancellor; Kenneth Peters*

Maybe CP/CPPS symptoms don't come from the prostate at all, but from the bladder. The team compared the levels of inflammatory chemicals in the urine of 21 men with CP/CPPS and 10 healthy men. The men with CP/CPPS underwent 12 weeks of therapy with a PDE4 inhibitor, a type of drug that reduces inflammation. The men with CP/CPPS had high levels of the inflammatory chemicals and lower levels of an inflammation dampener than healthy men. The improvements the men felt with treatment tracked with reduced levels of inflammatory chemicals in urine. Measuring these chemicals might be a way to monitor the response to treatment of CP/CPPS.

### *Cutting the Fat Might Help Your Prostate*

High-fat Diet Induced Inflammation in the Prostate: Role of Stat-3, ER-alpha and Aromatase
*Natarajan Bhaskaran; Sanjeev Shukla; Vijay Thakur; Melissa Babcook; Gregory MacLennan; Guiming Liu; Firouz Daneshgari; Sanjay Gupta*

Feeding mice a high fat diet increased estrogen levels in the prostate and belly fat by increasing the binding of certain signaling molecules involved in inflammation to the promoter of aromatase, an

enzyme involved in the synthesis of estrogens. That interaction is associated with increased inflammation in the prostate. These results hint that loading up on the burgers and fries is a particularly bad idea for men with CP/CPPS.

### *ED in CP/CPPS Said To Be Mostly Psychogenic, But Sometimes Related to Blood Flow*

Etiologic Evaluation of Erectile Dysfunction in Men with Chronic Prostatitis/Chronic Pelvic Pain Syndrome
*Gregory Lieser; Daniel Shoskes*

These researchers looked at potential causes of erectile dysfunction (ED) in 10 young men (average age 33) with CP/CPPS. Most of them had normal hormone levels and normal blood flow, which suggested a psychogenic cause of ED related to pain or stress, said the authors. But a few of the men showed abnormal blood flow characteristics. Three had abnormal tone in their peripheral arteries and four had abnormal blood flow in the penis itself. These men might have higher cardiac risks than other men their age. In addition, some of the men with abnormal blood flow had pelvic floor tenderness, implying that these might have a common cause and might be helped with pelvic floor physical therapy.

## ETIOLOGY (CAUSES AND ORIGINS)

### *CP/CPPS May Be a Vascular Problem*

"Chronic Prostatic Ischemia": Myth or Reality?
*Mikhail Kogan; Igor Belousov; Alexander Shangichev*

In the 10 young men (average age 27) with CP/CPPS in this study, nearly all had dyslipidemia, that is, high cholesterol or unfavorable cholesterol ratios. The decreased arterial blood supply in the prostate also correlated with CP/CPPS symptoms. Under the microscope, prostate tissue showed restricted blood supply typical of blood vessel disease. That led these authors to suspect that chronic poor blood flow in the prostate may play an important role in the development of CP/CPPS.

### *Smoking May Contribute to Prostate Symptoms*

Smoking is associated with acute prostatic inflammation in men with a negative prostate biopsy: Results from the REDUCE study
*Daniel Moreira; J. Curtis Nickel; Leah Gerber; Roberto Muller; Gerald Andriole; Ramiro Castro-Santamaria; Stephen Freedland*

Smoking is known to increase inflammation in general, but now this study makes clear that smoking plays a role in prostate inflammation. Current smokers were much more likely to have acute prostate inflammation than former smokers or nonsmokers. The study was an analysis of information from a trial of a drug used in BPH, but because inflammation has also been implicated in CP/CPPS, it's a good idea to quit or never take up smoking if you have CP/CPPS.

### *Biomarkers Point to Treatment Targets for Urinary Symptoms in CP/CPPS*

Significant biomarker for lower urinary tract symptoms or pain from chronic prostatitis
*Fukashi Yamamichi; Minori Matsumoto; Katsumi Shigemura; Toshiro Shirakawa; Hideaki Miyake; Soichi Arakawa; Kazushi Tanaka; Masato Fujisawa*

This team, which previously looked at inflammatory and immune biomarkers in prostate tissue from CP/CPPS patients, expanded their study with a greater number of patients. This expanded study showed that three markers—interleukin-6 (a cytokine that plays roles in both promoting and quelling inflammation), CD-3 (a marker of the T cells, which play a role in immunity), and CD-163 (a marker for macrophages, which also plays a role in immunity)—correlated well with urinary symptoms, pain, or impact of symptoms. CD-3 correlated especially well with urinary frequency and correlated significantly with urinary frequency and other lower urinary tract symptoms. The team hopes the research will help

point to a new molecular target for therapy for these symptoms in men with CP/CPPS.

## SOCIAL ISSUES

***Poor Coping Said to Make Symptoms Disabling***

Understanding the Mechanistic Role of Pain Appraisals and Behavioural Coping Strategies between Pain and Quality of Life in Chronic Prostatitis/Chronic Pelvic Pain Syndrome (CP/CPPS)
*Dean A. Tripp; J. Curtis Nickel; Adrijana Koljuskov; Daniel Shoskes; Michel Pontari; Mark S. Litwin; Mary F. McNaughton-Collins*

These researchers looked at the relationship between coping strategies and pain and quality of life in men with CP/CPPS. The analysis implicated the "illness focused coping" mechanism of "guarding," that is, restricting the use or movement of a body part as a way of coping with pain in the relationship between pain and physical quality of life and social support, especially friends, and "catastrophizing," especially feeling helpless, in the relationship between pain and mental quality of life. The authors concluded that these elements both drive and buffer the negative relationship between pain and quality of life. They concluded that CP/CPPS symptoms can be physically and mentally disabling because of behavior, cognition, and environmental mechanisms. The research did not look at changes in coping over time or with successful treatment. This research was supported through cooperative agreements from the National Institute of Diabetes and Digestive and Kidney Diseases.

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The above research is not all that is being done nationwide and worldwide.
These above are only the research papers accepted at the AAUA Annual Meeting and presented there. There is a European research plan that has been underway for some time and has some time to go. There are a lot of good doctors involved and we will be following it for what we hope will be interesting results We will try to bring information to our readers as soon as it becomes available to us. The Society for Infection and Inflammation also accept related research papers at a meeting that coinsides with the AUA Annual Meeting and were not accepted there for presentation.

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We have tried to leave the field of Prostate Cancer to those who specialize in cancer information. Many advocacy groups concentrate on cancer information and do it well. It is hard not to have an overlap between prostate cancer and prostatitis because a lot of the symptoms and treatments overlap. The recent issue of the US TOO Prostate Cancer HOT Sheet had this headline for one article they printed: PSA Screening Does More Harm Than Good. It was reported by lead author Mathieu Boniol MD in a paper presented at the European Cancer Conference in 2013. The doctors themselves would debate that and not reach an agreement, probably.

Everyone agrees I believe that prostatitis can cause a rise in PSA numbers. There is debate about excessive use of biopsies to determine if cancer is present or if the rise is caused by prostatitis. With the acknowledgement that biopsies themselves can cause infections it leaves many wondering what to do. At this time your own doctor is probably your best source of information until there are more positive research results to rely on. In an article on page 7 of the same newsletter Dr. Chodak says, "Until better tools to gauge cancer aggressiveness are developed, the overall harms of widespread screening appears to outweight the benefits, though some lives are saved."

For the Prostate Cancer Helpline at US TOO--call 1 800-808-7866 or see www.ustoo.org

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In response to inquiries we have had, and inquiries we have made, we can report that Doctor Antonio

Feliciano was in the States when the hurricane devastated parts of the Philippines so his family escaped injury.

Doctor Polacheck, from Tucson, AZ, has reported that he is retired.

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This post below is from the Prostatitis.org Webpage Forum. Re: Constant Feeling of Having to Urinate - Suggestions?

One patients answer as abbreviated: I have had chronic non-bacterial prostatitis for 15 years, starting at age 16, and also have frequent urination which is my most annoying symptom.

One I've figured out for myself: baking soda. Take a spoonful of baking soda every several hours (2-3 times per day, especially before bed) as it raises the alkalinity of your urine which makes it irritate the urinary tract less, which reduces urinary frequency.

The single most important thing I've discovered is to internally massage the prostate daily after a hot shower. I've found the best reach and leverage through squatting in the shower and using my middle finger. You need to do that to pop the "zits" in your prostate so that the swelling can go down, which is what I suspect your cystoscopy did. In case you didn't know, it's the enlarged size of your prostate that is causing your urgency to pee because it is pushing unnaturally on your bladder. After the shower and the following massage, I've found that an ejaculation really completes the clearing of the prostate.

Lastly, keep avoiding caffeine and alcohol (at least for the second half of the day) and stop drinking fluids several hours before bed.

Try these and any idea in consultation with your doctor. The prostatitis foundation cannot be responsible for any doctor, medicine, or treatment protocol.

The Prostatitis Foundation thanks Farr Labs LLC. for their support of this newsletter and our webpage. They are the makers of ProstaQ for Chronic Prostatitis. For more information visit ProstaQ.com or call 877-284-3976.

(please clip and mail)

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