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We want to let all patients and their families know about Research America. They are an organization that understands the value of research for all diseases and the crisis we have with chronic diseases that have no known cause or cure. Their website can be found at www.researchamerica.org There you will find their activities via weekly email alerts, blogs, monthly newsletters and policy updates. Their information can be a lot of help to us as we share many of their goals. Check out their webpage www.researchamerica.org We ask every patient or family member every year to write their senators, members of congress, and the National Institute of Health (NIH) to ask for research to find a cause and cure for prostatitis. We still prefer handwritten letters but email is acceptable. Tell them how much you have suffered and the consequences for your work and family. Ask for more research.

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Commentary on Chronic Prostatitis/Chronic Pelvic Pain Syndrome: The Status Quo Is Not Good Enough (But It Can Be)

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ABSTRACT

Prostatitis is the name given to a group of disorders that share surprisingly little in the way of etiology, symptoms, and treatment. Frequently, the diagnosis and management of these conditions is empiric, inadequate, ineffective, and contrary to the published literature of the past 10 years. In the present commentary, 23 "theses" are presented as a plea to physicians managing these patients to modify their ingrained approaches and incorporate simple evidence-based changes that can greatly improve outcomes and patient quality of life.

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In 1517, Martin Luther posted on the local church his 95 theses entitled, "Disputation on the Power

and Efficacy of Indulgences." Luther was outraged that members of the Catholic Church were selling indulgences by telling parishioners that their sins would be absolved following payment. Well, 493 years later patients are coming to the "Church of Urology" with prostatitis, and in return for their pieces of silver they are often handed similar pieces of paper (antibiotic prescriptions) and told that they are absolved of their illness. Although I cannot comment on whether Renaissance-era indulgences bought their holders relief from temporal punishment in purgatory, the modern-day indulgences are not buying our patients relief from their punishment on Earth. Based on some published data and the histories of hundreds of patients I have seen with prostatitis, I believe that the typical standard of care ignores important published advances in our knowledge of diagnosis, classification, and therapy over the past 15 years. Enough is enough; we need a broad reformation of the medical community's management of these disorders. Here are my (fewer than 95) theses.

1. Stop telling everyone that they have prostatitis as though it is one disease. The National Institutes of Health (NIH) classification may not be perfect, but it is a start and simple to use [1]. Category I is an acute febrile urinary tract infection (UTI). Category II is recurrent UTI with the same bacteria that is recovered from the prostate between acute bladder infections. Category III is persistent pain with or without lower urinary tract symptoms (LUTS) in men without UTI who have no other demonstrable cause. Category IV is asymptomatic and found during semen analysis or prostate biopsy. Stop telling everyone that they have the same condition and treating them all the same.

2. You should not tell a man with pain between his nipples and knees that he has prostatitis without doing a proper history and physical examination.

3. Nobody has to do a full Meares-Stamey 4-glass test. Who cares if there is Escherichia coli in VB1 vs VB2? It makes no difference. You should test at least a midstream sample of urine and then obtain a culture of either prostate fluid or postmassage

urine [2]. Unless you want false negatives, do the test after the patient has been antibiotic-free for at least 2 weeks.

4. Do you think that doing a prostate massage and getting some fluid is difficult and time consuming? It is not. If you cannot do it, get a postmassage urine sample instead.

5. Just because the patient complains of pain during a rectal exam, it does not mean that they have prostatitis.

6. While your finger is in the rectum, palpate the muscles to either side of the prostate. If they feel rock hard or if the patient reacts and says, "That is my prostate pain," then the patient has pelvic floor spasm. At least half of men with category III prostatitis have this condition [3], and it can get better with pelvic floor physical therapy [4]. This is NOT a subtle finding; if you look for it, you will easily find it.

7. Not everyone with prostatitis needs a cystoscopy. However, if you do a cystoscopy, stop telling patients that their prostate has the "classic appearance of prostatitis." There is no such thing.

8. If the patient has true category II chronic bacterial prostatitis, do not give them 5 days of antibiotics. They need 2-4 weeks of antibiotic medication [5]. Advise the patient of potential side effects (eg, tendinitis with quinolones, sun sensitivity with tetracyclines, diarrhea with any antibiotic).

9. Do not try to eradicate category II prostatitis with nitrofurantoin. It does not penetrate the prostate [6].

10. Everyone is busy; many men have a simple urethritis and a few have UTI. It is alright to give a course of antibiotics empirically the first time. However, if it does not work and cultures are negative, STOP GIVING THEM.

11. Just because a patient feels a bit better on antibiotics and feels worse the day after stopping them does not mean that he has an infection. Quinolones, macrolides, and tetracyclines are powerful anti-inflammatory drugs that block

cytokines directly [7]. These antibiotics kill bacteria in the prostate for up to 2 weeks, so if the patient has pain the day after stopping them but does not have a fever, IT IS NOT AN INFECTION.

12. The normal prostate is not a sterile place. It has been reported that 68% of healthy men have gram-positive bacteria in their prostate fluid, and 8% of healthy men have classic uropathogens [8]. Every bacteria found on culture is not necessarily the cause of symptoms, especially if appropriate treatment does not improve the symptoms.

13. Do not treat men who have pelvic pain with empiric interstitial cystitis therapies unless their symptoms actually suggest bladder involvement (eg, severe refractory frequency; pain that worsens with bladder filling and improves with emptying) [9].

14. Do not forget to tell men about simple and often effective supportive measures such as sitting on a donut-shaped cushion and avoiding caffeine and spicy foods.

15. Consider using a clinical phenotyping system to stratify patients for therapy, such as the one found at <http://www.upointmd.com>. This website gives a complete, simple algorithm for the diagnosis and multimodal therapy of chronic pelvic pain syndrome (CPPS) [10].

16. Learn and use simple and effective therapies for the different clinical domains:

Urinary symptoms: alpha blockers or antimuscarinics

Prostate pain or inflammation: quercetin [11] and cernilton [12]

Systemic neurologic symptoms: pregabalin or amitriptyline [13]

Pelvic floor spasm: pelvic floor physical therapy (myofascial release, NOT Kegel's) [4]

17. Patients with longstanding chronic pain can get depression and feel helpless or hopeless. This reaction is called catastrophizing [14]. Find out if they are feeling these emotions with a few simple questions and refer those with symptoms to other professionals for treatment.

18. Help patients to be optimistic, because most will eventually get better. Do not tell them that this is a condition they will have until the day they die.

19. Take new symptoms seriously. Patients with prostatitis also can develop kidney stones and genitourinary (GU) cancers.

20. In patients without UTI, do not treat an elevated prostate-specific antigen (PSA) with antibiotics to see if the PSA will drop. The PSA may drop but the cancer risk does not [15].

21. Use the NIH Chronic Prostatitis Symptom Index to monitor symptom severity, but NOT to diagnose the condition [16].

22. Prostate consistency varies among men. Having an isolated finding of a “boggy prostate” is meaningless and does not diagnose prostatitis or any other condition.

23. Assemble a good referral team. Urologists cannot be expected to treat the parts of these conditions that do not pertain to the GU system. Team members may include physical therapists who know myofascial release therapy, pain management specialists, and psychologists who have experience with catastrophizing, chronic pain, or stress.

Conflict of Interest: Dr. Shoskes is a paid consultant to Farr Laboratories, LLC.

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CHRONIC PROSTATITIS AT AUA 2015

CHRONIC PROSTATITIS AT AUA 2015

This past May, research presentations on chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS) at the American Urological Association Meeting were few - even fewer than in 2014. Just two of presentations on CP/CPPS came from the Multidisciplinary Approach to Pelvic Pain (MAPP)

program, where most of the federal research dollars are now going.

MAPP is aimed at looking for the cause or causes of CP/CPPS and interstitial cystitis/bladder pain syndrome (IC/BPS), so we won't hear about potential treatments from this program for a long time. However, there was an encouraging, although small, study on testosterone treatment in men with CP/CPPS who had hypogonadism (low testosterone levels). Another study showing some relationship between low testosterone levels and CP/CPPS symptoms seems to bolster this treatment approach.

Some preliminary animal studies on the IC/BPS side of pelvic pain research hold out some promise for mesenchymal stem cell therapy. These cells were either instilled into the bladder or injected into the bladder muscle. The treatments calmed bladder contractions and increased the bladder's elasticity. Because the MAPP research this year shows that men with pelvic pain may have urinary symptoms more often than many thought, this approach could be a boon to men with CP/CPPS in the future. And we may also see studies of mesenchymal stem cell therapy directed at the prostate itself.

Another intriguing study on the IC/BPS side of the research showed that a virus injected into the colon of mice then infected the bladder by traveling along the nerves that make connections from each organ at the L6 to S2 spinal nerve roots. That one of this year's presentations showed connections between the nerves from the prostate and bladder that might explain urinary troubles in CP/CPPS makes this idea all the more interesting. A next step may be looking for a virus that could be responsible for symptoms or testing antiviral medications to see if they have any effect on symptoms.

TREATMENT

Testosterone Helps Some Men with CP/CPPS
Testosterone Replacement Therapy for Hypogonadal Patients with Chronic Prostatitis/Chronic Pelvic Pain Syndrome

Ran Pang, Jianxin Lu, Xinyao Zhou, Xiaosong Gao, Yaqiang Zhang, Beijing, People's Republic of China

These investigators had success treating men who had CP/CPPS and low testosterone (less than 3.5 ng/mL, called "hypogonadism"). The men treated in the study were 18 to 60 years old, had had CP/CPPS for at least a year, had a score of at least 15 on the CPSI (which is moderate), testosterone levels in the hypogonadism range, and no evidence of other problems such as prostate cancer and severe bladder outlet obstruction. The men took 80 mg of oral testosterone undecanoate twice a day for 12 weeks. After the 12 weeks, their average total NIH Chronic Prostatitis Symptom Index (CPSI) scores fell from 7.8 to 3.8, their pain scores from 11.9 to 5.3, their quality of life scores from 7.8 to 3.8, and their urinary scores from 2.3 to 2.0 - all significant. They also had improvements in scores on the Hamilton Anxiety Scale (19.7 to 8.3) and Hamilton Depression Scale (16.9 to 10.1) that the investigators called "dramatic." Testosterone levels also improved.

ORIGINS AND NATURAL HISTORY

Low Testosterone Could Play a Role in Chronic Prostatitis

Relationship between Testosterone and Prostatitis-like Symptoms Assessed by the National Institutes of Health Chronic Prostatitis Symptom Index

Gyeong Eun Min, Jun Ho Lee, Koo Han Yoo, DongGi Lee, HyungLae Lee, Seoul, Republic of Korea

Because research has hinted that men with CP/CPPS have low testosterone and more cardiovascular disease, these researchers analyzed health data from a large population of men to see what the relationships were between testosterone levels and prostatitis symptoms. Some 9,000 middle-aged men (average age 52) underwent health screenings that included measuring testosterone levels, aspects of metabolic syndrome (such as high cholesterol), and prostatitis-like symptoms (using the CPSI). Out of that total, about 18% had prostatitis-like symptoms, and 7% had moderate to severe symptoms. The men with symptoms were more likely to have low testosterone levels (less than 3.5 ng/mL, called "hypogonadism"), especially the men with moderate to severe symptoms, who were about 40% more likely to have hypogonadism than the men without symptoms. Men with hypogonadism were also much more

likely to have higher CPSI scores (9.25 versus 8.65) and higher pain scores (3.9 versus 3.7) and to be older than men without hypogonadism. These differences were statistically significant but relatively small. The investigators called for further study on the role of testosterone in the development of CP/CPPS.

Prostate-to-Bladder Nerve Connections May Explain Bladder Troubles in CP/CPPS

Enhanced bladder pain sensitivity due to the prostate-to-bladder afferent cross sensitization in a rat model of prostatitis

Tsuyoshi Majima, Pittsburgh, PA, Yasuhito Funahashi, Nagoya, Japan, Katsumi Kadekawa, Pittsburgh, PA, Momokazu Gotoh, Nagoya, Japan, Naoki Yoshimura, Pittsburgh, PA

Men with CP/CPPS have pain not just from the prostate but from the urinary tract as well, and nerve connections between the prostate and bladder may explain why. In this study some rats had their prostates irritated, whereas controls did not, and the investigators looked at the rats' voiding behavior for a week. The volume of urine with each void went down in the rats with irritated prostates but did not in the others. Then, both groups of rats had their bladders irritated. All showed some signs of pain, but the rats that already had irritated prostates showed much more of that behavior. Markers of activation and pain went up in prostate as well as bladder nerves but much more so in the rats that had irritated prostates. The results indicate that prostatic inflammation enhances pain sensitivity of the bladder and induces bladder overactivity, something often seen in CP/CPPS patients, said the researchers.

Prostate Fibrosis May Play a Role in CP/CPPS Urinary Troubles and Pain

Models of Lower Urinary Tract Symptoms in the Presence and Absence of Pain

Daniel J. Mazur, Anthony J. Schaeffer, Praveen Thumbikat, Chicago, IL

To test a theory that prostate inflammation prompts fibrosis (thickening and scarring), which may play a role in pain, these researchers used bacteria from a CP/CPPS patient to induce temporary prostatitis in two different strains of mice. On strain

did not develop pain, but the other did, and both strains showed more bladder contractions. The mice also showed an increase in cells that play a role in fibrosis in the prostate as well as in the bladder, although there were differences between the strains in when these increases occurred. And one strain showed a large increase in markers of collagen. The study showed that urinary frequency can develop with prostatitis with or without pain and that fibrosis in the prostate may play a role. The researchers are doing more studies to find out how lower urinary tract symptoms develop when inflammation and pain are present.

Sensitized Nerves from Inflamed Prostate May Cause Urinary Troubles in CP/CPPS

Prostatic Inflammation Evokes Upregulation of Neurotrophins in Sensory Ganglia: Possible Contribution to Dysfunctional Voiding

Pradeep Tyagi, Mahendra Kashyap, Subrata Pore, Zhou Wang, Naoki Yoshimura, Pittsburgh, PA

Sensitizing the roots of the nerves that bring sensory information back from the prostate to the spine is thought to contribute to urinary troubles. To test the idea that this may happen when the prostate is inflamed, these researchers injected an irritant into prostates of rats and then looked at their behavior and at levels of two nerve activation proteins in the nerve roots. A week after the irritant injection, the rats urinated more frequently with less volume than the control rats (who got an injection of plain saline). In addition, the rats that had the irritant had both proteins overexpressed in the L6 to S1 spinal nerve roots. The investigators concluded that this might explain the long-lasting effects of prostate inflammation, including urinary problems.

Urinary Pains Spell Worse Symptoms and Quality of Life

Painful Bladder Filling and Painful Urgency Are Distinct Characteristics in Men and Women with Urologic Chronic Pelvic Pain Syndromes (UCPPS), A MAPP Research Network Study

H. Henry Lai, St Louis, MO, John Krieger, Seattle, WA, Michel Pontari, Philadelphia, PA, Dedra Buchwald, Seattle, WA, Xiaoling Hou, J. Richard Landis, Philadelphia, PA

Men and women with CP/CPPS or IC/BPS don't

all have pain as the bladder fills or the urge to urinate because of pain, pressure, or discomfort. To find out how common these symptoms are and how they relate to other conditions these patients have, MAPP researchers asked 233 female and 191 male patients if they had these symptoms. Thirty-five percent of the men and 37% of the women had one or the other symptom, and 41% of the men and 50% of the women reported both. The percentage of men who had bladder pain was "surprisingly high" - about 75%. Both men and women who reported painful filling or painful urgency had worse urologic symptoms (pain, frequency, urgency), more physical symptoms, more depression, and worse overall physical health. The likelihood that men had irritable bowel syndrome, "catastrophizing," or a current "flare" increased with these urinary symptoms - from having neither to one to both. But that did not hold true for women. On the other hand, the women were more likely to have chronic fatigue syndrome, higher fatigue scores, negative mood, and worse mental health as these urinary symptoms added up. Overall, men and women with "painful filling" and/or "painful urgency" have more severe urologic symptoms, more generalized symptoms, and poorer quality of life than those with neither of these bladder characteristics.

OTHER

MAPP Develops Questionnaires that Fit for Future Pelvic Pain Research

A psychometric analysis of pain and urinary symptoms in patients with interstitial cystitis/ bladder pain syndrome and chronic prostatitis/ chronic pelvic pain syndrome: Findings from MAPP Research Network

James Griffith, Chicago, IL, Todd Edwards, Seattle, WA, Barry Hong, Siobhan Sutcliffe, St Louis, MO, Michel Pontari, Philadelphia, PA, Niloofar Afari, San Diego, CA, John Krieger, Seattle, WA, Robert Lloyd, Chicago, IL, Frank Tu, Evanston, IL, David Williams, Ann Arbor, MI, Donald Patrick, Seattle, WA, Jayoung Kim, Bruce Naliboff, Los Angeles, CA, Henry Lai, St Louis, MO, Catherine Bradley, Iowa City, IA, Chris Mullins, Bethesda, MD, Richard Landis, Philadelphia, PA

Out of the results from an extensive set of

questionnaires answered by both CP/CPPS and IC/BPS patients, the MultiDisciplinary Assessment of Pelvic Pain (MAPP) Research Network developed two simple questionnaires that help capture the most meaningful symptoms, one for pain and one for urinary symptoms. These two categories of symptoms show different relationships with other problems patients often have, such as depression. Based on this work, MAPP will look at changes in symptoms over time and study how these symptoms relate to other symptoms and biomarkers.

We have listed below the members of The Appropriations Subcommittee for Labor, Health and Human Services, Education, and Related Agencies.

It would be a good idea for every patient or someone in his family to write the people below who control the funding for the NIH. If you are in any of the States they represent It would be especially important for them to hear from you. They feel compelled to reply to a constituent.

The NIDDK (a branch of The NIH) has maintained the MAPP Research Network. (Look it up on Google) A group who are currently working to find the cause and a cure for Prostatitis. Funding should be maintained and expanded to speed up that research.

Republicans:

Tom Cole, Oklahoma, Chairman
Mike Simpson, Idaho
Steve Womack, Arkansas, Vice Chair
Chuck Fleischmann, Tennessee
Andy Harris, MD, Maryland
Martha Roby, Alabama
Charlie Dent, Pennsylvania
Scott Rigell, Virginia

Democrats

Rosa DeLauro, Connecticut, Ranking Member
Lucille Roybal-Allard, California
Barbara Lee, California
Chaka Fattah, Pennsylvania

Tell them how you suffer. How it has affected your daily life, and work day, your family and social responsibilities. A handwritten letter is best. Email is acceptable.

The Prostatitis Foundation webpage hosts a forum for prostatitis patients to discuss the disease and its possible treatment. This post was picked from a heading submitted: Re: Life sucks - Depressed. This is the most horrible, depressing, helplessness inducing condition I know that isn't terminal even though it feels like it is. I told my urologist's nurse Friday I can't go on much longer if we don't fix this. She said let's do one month of massages and abxs (which I have been on for over seven months this time with little relief) and if you aren't better we can explore removing it. I am sure the doc will say no cause I am yet to hear of an urologist who would do it for chronic prostatitis even though it is ironic that they will do it for an appendix, gall bladder, tonsils, adenoids, etc. For some reason the medical establishment doesn't understand the horrors of chronic prostatitis.

In our local paper they run a syndicated column by Dr. Komarof and he was asked the question, "Dear Dr. Komarof: I am a man and sex is often painful. Why? What can I do to make sex pleasant and pleasurable again?" After much comment about possible causes he concludes by saying, "It is probably obvious from what I have said that the medical field remains mostly ignorant about the causes of pelvic pain and what to do about them. The only solution to that is more research. You might want to investigate his website."

In the February 2015 issue of Fast Company (for and about entrepreneurs) there is an article by John Gartner titled: *Gut Check*. It is a long article and sheds a lot of light on what ideas and prospects their new research entails. You could find it pretty easily at your local library or possibly on the website at gertner@fastcompany.com

The Prostatitis Foundation does not endorse any medicine, doctor or treatment protocol. Please consult with your doctor for these decisions.

(please clip and mail)

Enclosed is my tax deductible gift to support The Prostatitis Foundation, 1063 30th Street, Smithshire, Illinois 61478. Yes, please keep me on the mailing list for updates, newsletters, meeting notices _____. I cannot contribute now _____. I do _____, do not _____ have access to the internet. My e-mail address is _____.

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