The MAPP Research Network Continues Its Work to Unravel Chronic Prostatitis

Researchers, patients, and health care providers alike face an enormous challenge when it comes to chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS) and interstitial cystitis/painful bladder syndrome (IC/PBS). While estimated to affect millions of Americans, these two urologic chronic pelvic pain conditions are not well understood and remain difficult to diagnose and treat. The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) at the National Institutes of Health (NIH) in Bethesda, Maryland, spearheads the public investment in biomedical research that we hope will lead to relief for people suffering from CP/CPPS and IC/PBS, and possibly ways to prevent these conditions altogether.

In a major effort to address the many long-standing questions regarding CP/CPPS and IC/PBS, in 2008, the NIDDK established the Multidisciplinary Approach to the Study of Chronic Pelvic Pain (MAPP) Research Network. The MAPP Research Network is comprised of six Discovery Sites across the United States that conduct research studies and two Core Sites that coordinate data collection, analyze tissue samples, and provide technical support. This innovative research program embraces a systemic, or whole-body, approach to understanding CP/CPPS and IC/PBS. To implement this approach, MAPP Research Network leaders have developed a highly collaborative and integrated study design for use by the Network sites. This study design not only incorporates new and novel approaches employed by investigators from traditional urologic disciplines, but also relies heavily on broad non-urologic expertise: Network investigators include experts in pain, neurobiology, infectious disease, biomarker discovery, animal modeling, epidemiology, psychology, immunology, and many other areas.

Network investigators are conducting numerous complementary studies to investigate questions of significant clinical relevance to CP/CPPS and IC/PBS. They pursue these studies with the view that CP/CPPS and IC/PBS may involve areas of the body beyond the bladder and prostate. One key objective of these studies is to advance our understanding of underlying causes, symptom variation, and risk factors for CP/CPPS and IC/PBS. Another key objective is to provide a comprehensive description of patient characteristics and—based on differing symptom profiles—identify potential patient sub-groupings. A third key objective is to address the relationships between CP/CPPS, IC/PBS, and other chronic pain syndromes commonly found in persons with urologic chronic pelvic pain conditions. The overarching goal of the MAPP Research Network is to provide findings useful for designing future, targeted clinical trials and ultimately to improve clinical management. Importantly, this effort is also generating a unique national resource of highly detailed clinical data associated with biological samples, which may be studied well beyond the lifetime of the Network.

The MAPP Research Network studies are all well underway. Already, Network investigators have collected extensive baseline and follow-up data from participants. The researchers are now analyzing this complex data and developing numerous scientific manuscripts for publication. Indeed, thanks to the hard work of Network investigators, the cooperation of the Prostatitis Foundation and other patient advocacy groups, and the strong commitment of the patient community, the MAPP Research Network has met its recruitment goals—critical to completion of Network studies. To date, the network has recruited over 1,100 individuals. This includes nearly 200 CP/CPPS patients, which exceeds the Network’s original goals!

NIDDK plans to support the MAPP Research Network for an additional 5 years, once the current phase is completed. In the second phase, the MAPP Research Network will design more focused studies to uncover the causes of, and potential treatments for, CP/CPPS and IC/PBS. NIDDK will again ask for the help of the Prostatitis Foundation and the CP/CPPS patient community. These studies are only possible with your participation.

Thanks to all for your continued support.

Chris Mullins, PhD
MAPP Network Project Scientist
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Chronic Pain Management: A Realistic Way Forward

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Chronic pain has become a progressively more prominent issue in medical care. This is due, currently, to persistent media attention regarding the abuse of prescription pain medications. This trend is significant, especially at a time when the Affordable Care Act has been purported to offer broader access to medical care. The "significant trend" that I spoke of is related to the need for clinicians to balance the need to treat pain against the fear of addiction and law enforcement concerns associated with the treatment of chronic pain. The end result, it is becoming progressively harder for people with legitimate chronic pain to obtain pain medications.

Given current concerns regarding prescription-drug abuse, it isn't surprising that clinicians are apprehensive when large amounts of pain medication are required. Studies have shown that most healthcare providers are open to providing low potency medications such as ibuprofen, they are generally unwilling to prescribe more potent varieties, particularly when patients require constant pain coverage.

Chronic pain results from the combination between a prior injury, inflammatory disorder or surgery in combination with a prominent affective, or mood related, element. These patients frequently suffer emotional as well as physical manifestations of pain. Many chronic pain patients are stigmatized as "drug seekers", and are often accused of simulating pain in an effort to obtain medications due to their addiction. This can lead to the under-treatment of pain, which can result in patients requiring progressively larger doses of medication to treat their pain. This dynamic, wherein the patient seeks medication to relieve legitimate pain, but appears to be an addict, often strains the healthcare provider-patient relationship.

Patients frequently receive medications that are inappropriate for the treatment of chronic pain. For instance many medications are compounds of acetaminophen (Tylenol) and hydrocodone or oxycodone. These medications are designed for short-term use. Their long-term use can result in suboptimal pain control, severe addiction and liver injury due to the ingestion of large amounts of acetaminophen (Tylenol). In truth, longer-acting medications that require twice daily or daily dosing, offer a safe alternative. For instance, these medications contain no acetaminophen (Tylenol), and offer analgesic without the profound peak effects and short duration that we see with shorter acting medications. Sustained-release oral forms of morphine and oxycodone address this need. Additionally, transdermal fentanyl offers stable pain control with patch application every 72 hours.

So, what are patients to do. After all, chronic pain is a very real problem that can absolutely diminish quality of life. For starters, it is important for patients to become educated. It is not reasonable, for instance, for patients to repeatedly request short-term medications when longer term medications are indicated. Patients should be willing partners in the transition to a more appropriate and more effective pain management.

The key to this transition is partnership with one's healthcare provider. Patients must provide an honest accounting of their struggles over the years, and their wish to have their pain, underlying disease process and their overall health managed. This may well require individual patients to consult with a variety of healthcare providers until that find one who is willing to assist them.

Clinicians, for their part, often employ a variety of techniques to attempt to diminish their own professional risk when they choose to manage chronic pain. First off, they need clear documentation of the reason for the chronic pain syndrome. This will require patients' cooperation in gaining previous health records to substantiate the nature of their condition.

As well, clinical agencies often resort to contracts that specify the nature of the treatment plan, and the need for patients' to adhere to the plan, and refrain from seeking medications elsewhere. Some clinics even perform urinalysis to verify
that the patient is taking the medication. Extra medications, whether prescription or illicit, are potentially harmful and alter the dynamics of a carefully thought-out treatment.

Patients are not criminals. The system, however, dictates that clinicians carefully prescribe pain medications. The full engagement of patients in the treatment plan, and their embracing of transition from acute to appropriate chronic pain treatments is essential. Only when healthcare providers and patients partner, can we maximize pain management.

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**DIAGNOSIS OF CHRONIC PROSTATITIS**

**1. HISTO-PATHOLOGY**

In order to learn more about the pathophysiology of "chronic" prostatitis, we examined the cytology of expressed prostatic secretions (EPS). In the EPS from most patients with chronic prostatitis, we have observed cohesive aggregates of polymorphonuclear (PMN) leukocytes within a proteinaceous matrix. We call these aggregates prostatic inflammatory aggregates (PIAs). PIAs are frequently associated with corpora amylacea, concretions known to form inside the prostate. We believe that PIAs may be pathognomonic for prostate inflammation because we have observed, histopathologically, remarkably similar aggregates in prostate tissue obtained surgically. These are normally ignored by surgical pathologists when they are searching for cancer. We find it remarkable that PIAs can be expressed by massage. We have observed in the surgically obtained prostate tissue that most PIAs are located in the periphery of the prostate gland. Prostatic ducts are tortuous, branching, and very long relative to their narrow diameter. In fact, prostatic ducts appear smaller in diameter than PIAs. Therefore, the ducts must expand and/or the PIAs must deform in order for the PIA to be expressed.

Based on preliminary studies, we believe the following conclusions are likely:

A. The inflammatory process in chronic prostatitis is persistently active because the lifespan of PMNs is known to be short, approximately 5 days.

B. The inflammatory process is likely triggered by a bacteria or a bacteria-like organism because of the predominance of PMNs, not lymphocytes.

C. Finding PIAs in EPS may prove to be a specific clinical test of disease activity. We have already found it useful in the management of patients.

D. Because PIAs are found in most prostates with BPH, a relationship could exist between BPH and prostatitis.

Finally, we note the disparity between the clinical disease (chronic symptoms and signs) and its pathology (an acute-inflammatory process). Perhaps the disorder, therefore, should be called "chronic active prostatitis" (CAP).

**2. DIAGNOSIS OF CHRONIC PROSTATITIS**

**MULTIPLE MASSAGES ARE REQUIRED**

**INTRODUCTION AND OBJECTIVES:** For the past 20 years, I have been studying the cause of Chronic Prostatitis. Symptomatic patients have come to our Center from all 50 states of the United States, as well as from the Americas, Europe, Asia, Africa, the Pacific and Australia seeking a diagnosis (and then treatment).

**METHODS:** In order to make a specific etiologic diagnosis, a vigorous prostate massage was done on each patient daily for at least 5 consecutive days. The expressed prostatic secretions (EPS) were collected and cultured for bacteria and bacteria-like organisms. 671 patients were so studied.

**RESULTS:** Bacteria and/or bacteria-like organisms were isolated from the EPS in almost all patients who were not on antibiotics at the time of their presentation. However, we have observed that it was not uncommon for the first culture to be negative. Furthermore, we will present evidence that these bacteria were from the prostate itself and not from the bladder nor the urethra.

**CONCLUSIONS:** Bacteria play an important etiologic role in chronic prostatitis. To
succeessfully identify those causative organisms, however, patients require multiple prostate massages done on several, not only one, occasion.

3. GRAM-POSITIVE BACTERIA ARE COMMONLY ASSOCIATED WITH CHRONIC PROSTATITIS

BACKGROUND: For the past 20 years, we have been studying chronic prostatitis. Symptomatic patients have come to The Prostatitis Center in Tucson, Arizona, from all 50 states of the United States, as well as from the Americas, Europe, Asia, Africa, the Pacific and Australia seeking a diagnosis (and then treatment).

METHODS: We have studied 797 patients. For each patient, a vigorous prostate massage was done daily for 5 consecutive days. The expressed prostatic secretions (EPS) were collected and cultured.

RESULTS: Bacteria and/or bacteria-like organisms were isolated from 99 percent of the patients who were not already on antibiotics at the time of presentation. Furthermore, the EPS from a great majority of the patients contained more than one organism (average 2.46 organisms per patient). We have strong evidence that these organisms originated in the prostate gland itself, and were not from the bladder nor the urethra. The most common species so isolated were Staphylococcus (from 78% of patients) and Streptococcus (from 62%). On the other hand, Gram negative rods, which had been expected to be common, were isolated from only 13%. Diphtheroids were isolated from only 13% and anaerobes from only 5%. Other bacterial species were only rarely isolated.

CONCLUSIONS: We conclude that common gram positive organisms are associated with most patients suffering with chronic prostatitis. Furthermore, we speculate that these bacteria likely play an important etiologic role.

4. THE ETIOLOGY OF CHRONIC PROSTATITIS

ABSTRACT: For the past 20 years, I have been studying the cause of Chronic Prostatitis. Symptomatic patients have come to our Center from all 50 states of the United States, as well as from the Americas, Europe, Asia, Africa, the Pacific and Australia seeking a diagnosis (and the treatment). In order to make a specific etiologic diagnosis, a vigorous prostate massage was done daily for one week. The expressed prostatic secretions (EPS) were collected and cultured for bacteria and bacteria-like organisms. I would like to report the results from 600 consecutive patients: over 99 percent were found to have a bacteria or bacteria-like organism, and many patients had multiple organisms.

Therefore, this disorder should properly be called: Chronic Bacterial Prostatitis.

Dr John Polachen, www.prostate-usa.com

The previous three articles have been submitted at the Prostatitis Foundation's request. We were searching for answers to the question, "What have we done or learned so far about prostatitis?" We hope these articles will answer some of those questions for many patients. It seems the research to find a cause and cure for prostatitis has taken a lot longer than we anticipated. Many advocacy groups probably are saying that very same thing. If you think about it, cancer, diabetes, heart disease, and the common cold are all still present. They have all had more funding than prostatitis has, and are still searching for solutions. We will not give up; any progress at all is welcome. Medical research has made some giant strides. Some body tissue is now being produced in the lab.

We are trying to provide information to assist patients but cannot endorse any doctor, medicine or treatment protocol.

We have received a complimentary copy of the Urology Health extra. It is published by the Urology Care Foundation as a service to patients, health care professionals and the public. To receive this magazine, call 1-800-828-7866 or visit WWWUrologyHealth.org.
We want to call your attention to the Moderated Forum we maintain for patient discussion. Go to the top of the website www.prostatitis.org and click on the forum. You can find the rules to participate there. Following are random samples of topic submissions:

Hello, My husband has been suffering from non bacterial prostatitis for years now... sometimes it is tolerable, but when he has a flare up it can be unbearable... Pain in his hips, groin, lower back... pain in his buttocks and perineum feeling unwell... my question is has anyone tried or know of any treatment...........

Prostatitis Question
I have been trying to clear my prostate from clogged ducts due to non-bacterial prostatitis. Recently I noticed in my ejaculate 3 small white colored "rice shaped pieces" shaped like a piece of uncooked rice, similar to the little juice jackets found in an orange. They had a softer outside layer but were hard on the inside. I separated them out of the ejaculate and placed them on a plate to study. Within an hour they had basically melted on the plate and dried up. I believe these were plugging three of the ducts in my prostate. However there are several more ducts that must be clogged as well because I still suffer with horrible pain after ejaculation.

"Are there any drugs on the market specifically for loosening up these clogged ducts similar to a stool softener? If not, I am wondering why? Seems to me it wouldn't be rocket science."

I am using prostate massage to help, but without a "softener" for the hardened semen clogging the ducts they are next to impossible to clear. Any help would be appreciated.

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.

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