

CHRONIC PROSTATITIS AT AUA 2017

Although somewhat fewer than last year, the studies of chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS) were certainly intriguing at this year's American Urological Association (AUA) meeting. There was a renewed interest in the role of bacteria in the condition, although the story may be much more complicated than pointing to one disease-causing bacterium. One study showed that certain strains of common bacteria may cause symptoms—but probably only in those with a genetic predisposition to CP/CPPS. Bacteria may not be the only microbes to investigate either, implied one study of interstitial cystitis/bladder pain syndrome (IC/BPS) and overactive bladder, which showed a very different fungal mix in patients with these conditions compared with healthy persons. On the other hand, another study suggested that a condition known as small-fiber polyneuropathy might be responsible for pelvic pain symptoms, especially in patients who have other chronic pain problems in addition. Another hint about a cause of symptoms came from the IC/BPS studies: It's long been known that certain foods and beverages can ramp up pain in IC/BPS and in CP/CPPS. But the common factor may not be acid or spice; it may be histamine. Most of the common troublesome foods and beverages for pelvic pain patients are indeed high in histamine, including alcohol, chocolate, mature cheeses, pickled foods, beans, and nuts. This finding may spur more studies looking at the role of mast cells in chronic pelvic pain, but it may also point to histamine-producing bacteria in the urogenital tract, which this study found.

A look-back at a large number of patient histories showed that the nature of CP/CPPS hasn't changed much since 1998, but treatment has been nudged a little. The nudge has come mainly from recognition of muscle tenderness as a contributor to pain in CP/CPPS, and most of the treatment studies presented this year reflected that, showing that physical therapy (PT) and trigger point injections can be helpful and that transcutaneous electrical nerve stimulation (TENS) can help some men who haven't had relief from other treatments. A few medical therapies, however, were studied or proposed. One of the treatments mentioned in the small-fiber polyneuropathy study is intravenous immunoglobulin, but that has not been tried yet in pelvic pain. The sole drug study this year showed better results with one of the erectile dysfunction drugs than with antibiotics and alpha blockers, and a pollen extract supplement bested saw palmetto.

CAUSES, DIAGNOSIS, AND NATURAL HISTORY

Bacteria from Chronic Prostatitis Patients Produce Pelvic Pain in Mice

Clinically Isolated Gram-Positive Prostate Bacteria Induce Chronic Pelvic Pain

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This research group previously showed that only certain strains of *Escherichia coli* bacteria produce the pain and urinary troubles that can come with a urinary tract infection. Now they have found certain pain-inducing strains of common prostate bacteria in men with CPPS. But these pain-inducers may not always produce the symptoms—that may depend on a man's genetics. The researchers isolated common gram-positive bacteria from the prostates of three men with CPPS and one healthy volunteer and then put these bacteria into the urethras of two

different strains of mice. Specifically, *Staphylococcus haemolyticus* 2551, *Enterococcus faecalis* 427 and *S epidermidis* 7244 from the men with CPPS had a dramatically enhanced ability to cause pain in one strain of mice but not another. (And it was clear that the strain did indeed get into the prostate tissues of the unaffected mice.) In the affected mice, the pain started a week after infection and lasted for 28 days. In contrast, *S epidermidis* from the healthy man did not affect either strain of mice. These results indicate that it's the genetic background of the host that determines whether pain-inducing strains of bacteria will cause problems and not the bacteria alone.

Usually Benign Bacteria May Contribute to CP/CPPS

Reassessment of Non-Traditional Uropathogens in Chronic Pelvic Pain Syndrome (CP/CPPS)

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Digging into the records of patients who had CP/CPPS, chronic bacterial prostatitis, recurrent urinary tract infections (UTIs), or high PSA but no pain showed some distinct differences between the types of bacteria these groups had and pointed to some usually benign bacteria as potential culprits in CP/CPPS symptoms. This research team found that gram-positive bacteria accounted for 100% of the prostate bacteria in the CP/CPPS patients and 92% of the prostate bacteria in those with no pain but high PSA. However, gram-negative bacteria were much more common (accounting for 27% of prostate bacteria) in the men with chronic bacterial prostatitis or recurrent UTIs. All of the gram-negative bacteria produced a high level of a certain type of inflammatory response, but a subgroup of gram-positive bacteria also did so (including 11% of *Enterococcus faecalis*, 13% of *Staphylococcus haemolyticus*, and 19% of *S epidermidis*). All of the patients with bacteria in this subgroup reported pain, and 83% reported voiding complaints. That was in contrast with patients who had the low-inflammatory-response gram-positive prostate bacteria, of whom 66% had pain and 69% voiding complaints. A subset of bacteria that aren't normally thought to cause urinary tract problems may contribute to inflammation and symptoms in patients with CP/CPPS, the researchers concluded.

New High-Tech Technique Reveals More Bacteria in Men with CP/CPPS

Next-Generation Sequencing of Chronic Prostatitis: Preliminary Results of Comprehensive Species Level Description in 212 Men with Pelvic Pain

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A new technique called next-generation sequencing revealed numerous bacteria that would be missed by traditional culture methods in prostatic fluid from men with CP/CPPS. The technique detects and identifies bacterial, fungal, and antimicrobial resistance genetic material. Among 212 men with pelvic pain and other symptoms of CP/CPPS, 75% had a significant number of bacteria. Gram-positive anaerobic bacteria were the most abundant (found in 60% of the men), including *Enterococcus faecalis* (30%) and *Escherichia coli* (25%). That's a much greater abundance than the 10% reported from routine cultures in men with possible CP/CPPS. The common *Enterococcus* species in men with possible CP/CPPS were *E faecium* and *E faecalis*,

and these bacteria may form a treatment-resistant biofilm, said the author. Resistance to beta-lactam antibiotics was the highest, occurring in 35% of the samples. The author noted that this type of testing may help distinguish between chronic bacterial and nonbacterial prostatitis.

Small Fiber Polyneuropathy May Be a Treatable Cause of Pelvic Pain

Small Fiber Polyneuropathy—A Big Clue to Etiology and Management of Chronic Pelvic Pain (CPP)

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Widespread damage to small peripheral nerve fibers, which are present in the skin, peripheral nerves, and internal organs, may be responsible for pelvic pain. And that opens the possibility of treatment with immune-based therapies, according to these researchers. (The immune-based treatment studied for SFPN is intravenous immunoglobulin or IVIG therapy.) Of 28 patients (it was not specified how many were men or women) who had hard-to-treat chronic pelvic pain, 17 (61%) had small fiber polyneuropathy (SFPN), which is diagnosed by looking at the nerve fiber density in a small sample of skin. That's very high compared with the "minimum prevalence" of SFPN in the general population—a mere 53 in every 100,000 people. High rates of this condition have also been found in people with fibromyalgia. That pain condition, as well as others, were common in these patients: 29% had migraine, 36% irritable bowel syndrome, 21% endometriosis, 32% fibromyalgia, 14% IC/BPS, 50% gastroesophageal reflux disease (GERD), 7% vulvodynia, 32% low back pain, and 35% other chronic pain syndromes. However, there were no differences in the duration of pain, the number of medical visits, or age between those who had SFPN and those who didn't. The researchers said identifying SFPN should be a priority for people with chronic pelvic pain and suggested that IVIG or other immunomodulatory therapies could be offered to them.

Chronic Prostate Inflammation Promotes Urinary Problems

Expression of Inflammatory Mediators in Sensory Ganglia Innervating Lower Urinary Tract and Dysfunctional Voiding

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Chronic prostate inflammation prompts overproduction of inflammatory chemicals in the nerve roots that carry sensation from the bladder and lower urinary tract, helping explain why urinary troubles go along with an inflamed prostate. This research team demonstrated how this may happen by inducing prostatitis in rats, checking their urination patterns, and analyzing the levels of inflammatory cytokines, chemokines, and growth factors in lumbosacral (L6-S1 in the low back) and cervical (C4 in the neck) nerve root ganglia. In the rats with irritated prostates, expression of inflammatory and growth factors went up into the L6-S1 root, which serves the lower urinary tract, which may be the cause of changes in the urination reflex in chronic prostatitis. There were also increases of a few markers of inflammation in the cervical dorsal root ganglion, possibly indicating a role for generally circulating neurohormones in development of the pain syndrome.

CP/CPPS Hasn't Changed in 16 Years, Although Treatment Has Nudged a Little

The Evolving Clinical Picture of Chronic Prostatitis/Chronic Pelvic Pain Syndrome (CP/CPPS): A look at 1310 patients over 16 years

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At this pelvic pain center, the team took a look back at the symptoms and treatment of 1,310 CP/CPPS patients over 16 years—from 1998 to 2014. There was negligible change in symptom patterns. The UPOINT (urinary, psychosocial, organ, infection, and tenderness) system of classifying the disease brought more recognition of psychosocial, organ, and tenderness problems. The use of alpha-blockers, neuromodulation, and phytotherapy (such as pollen extracts or quercetin) has increased. Despite the increased recognition of pelvic floor tenderness, the use of physical therapy changed little except in the last four years. The most common symptom domain was urinary, and men with high urinary scores tended to have more frequent and painful urination, pain at the tip of the penis, and more treatment with alpha blockers. The more types of symptoms men had (ie, the more UPOINT domains), the higher their total as well as pain and quality-of-life chronic prostatitis symptom index (CPSI) scores were. The age of patients (mean 44.7 years), their CPSI scores, and pain locations have changed little over time.

Vets with PTSD More Likely to Have CP/CPPS

The Association of PTSD and Chronic Prostatitis/Chronic Pelvic Pain Syndrome in Young Male Veterans

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Veterans 18 to 45 years old with PTSD were twice as likely to have CP/CPPS than veterans without, concluded this study of VA records of nearly 400,000 men. The rate of CP/CPPS among those with PTSD was 18.5% compared with 8.7% for veterans without PTSD. Also, those with PTSD were more likely to have a history of military sexual trauma—2.8% versus 0.5%—or nonmilitary sexual trauma—0.4% versus less than 0.1%. Younger veterans with PTSD were also more likely to have had a cystoscopy (0.8% versus 0.5%) and/or to have undergone urodynamic studies (1.0% versus 0.5%)—potential indicators of developing CP/CPPS or IC/PBS. The authors recommended that providers treating young veterans with PTSD improve their assessment for sexual trauma and recommended that urologists consider referring the young PTSD veterans to mental health professionals.

MAPP Researchers Develop Mobile App to Track Pain

Use Of A Mobile App for Ecological Momentary Assessment of Pain and Other Symptoms in Patients with Urologic Chronic Pelvic Pain Syndrome

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These researchers developed and beta-tested a mobile app to capture measurements of pain and symptoms in patients participating in the Multidisciplinary Approach to Pelvic Pain (MAPP) Research Network studies. The 22 participants who had either CP/CPPS or IC/BPS got mobile phone notifications that linked to and opened the app at wake-up, 4 and 8 hours after that, and at bedtime. The participants' ratings and feedback after 15 days suggested that the app was simple and easy to use. The data on pain ratings showed that pain varied significantly during the day.

TREATMENT

Trigger Point Injections Help about Half of Men with CP/CPPS

Utility of Trigger Point Injection as an Adjunct to Physical Therapy in Men with Chronic Prostatitis/Chronic Pelvic Pain Syndrome

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Many men with CP/CPPS have pelvic floor muscle spasm, and physical therapy can be effective at relieving this source of pain. But for some men, that's not enough. They still may have trigger points—muscle “knots”—that are painful. A next step is to inject these knots with small quantities of anesthetic. This review of the records of 37 CP/CPPS patients who had injections aimed to find out how well they work. These injections are done after the patient gets a numbing nerve block. Then, the doctor locates these trigger points by feeling the muscle through the rectum or abdomen and then guides a needle through the skin of the perineum or abdominal skin and injects the knot with between a half to one milliliter of a local anesthetic mixture. Typically, the men were offered three sets of injections 6 weeks apart. Of the 34 men who had follow-up information, 16 had received 1 injection, 11 had 2, and 10 had 3. All of them had pelvic floor injections through the perineum, and 9 also had more frontal trigger points injected through the abdominal skin. Twenty-two of the men had at least some improvement, with 12 reporting significant improvement and 10 having some improvement; 11 had no change, and 1 got worse. On average, CPSI scores dropped from about 29 to 22, with 18 of the men getting a reduction of 6 or more points. None of the three men who did not have physical therapy first got any benefit from the injections. Side effects were few, with 5 men showing temporary numbness on the outer thigh and 1 man having some difficulty bearing weight on a leg for about 30 minutes.

PT May Help Some 80% of Men with Testicular Pain

Physical Therapy for Orchalgia

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Only in the last few years has pelvic pain research and treatment begun to focus on musculoskeletal problems as a source of pain in CP/CPPS and PT as treatment. So we are still learning how successful physical therapy is for pelvic pain. In this study of men with testicular pain at one clinical center, the results look very good, with 83% of the men reporting that their testicular pain was better after treatment. The records the team reviewed were of 392 men treated for testicular pain between 2009 and 2016. Nearly half the men also had urinary complaints. The men had had their symptoms for an average of nearly 3 years before treatment. Of the men whose pain improved with PT, CPSI pain scores dropped from an average of nearly 17 to about 11, urinary scores dropped about a half point, and quality-of-life scores improved from about 8 to 4. Some 16% of men had no change in pain, and for about 1%, pain got worse. The men who had no improvement in pain didn't see improvements in urinary and quality of life scores either. The results are good enough to encourage men with pelvic pain to try PT, although it's not apparent from this study how long PT effects last and which approaches work best, since the length of treatment wasn't reported in the abstract, and these men received a variety of different treatments, including pelvic alignment exercises, therapeutic stretching and strengthening, manual therapy, dry needling, and biofeedback.

TENS Therapy Helpful for Tough-to-Treat CPPS

Transcutaneous Electrical Nerve Stimulation for Treatment of Refractory Chronic Pelvic Pain Syndrome in Men: A Prospective Study.

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In this clinical trial with 42 men with CPPS that had not yielded to other treatments, 12 weeks of transcutaneous electrical nerve stimulation (TENS) yielded some improvements. A third (14) of the men showed more than 50% improvement in CPSI index scores, and 8 had a final score of less than 10. The 8 with the big improvement also showed significant improvements in quality of life and urinary symptoms. To help confirm their findings, the authors called for randomized, placebo-controlled trials.

ED Works Better than Usual Drug Treatment in Small Study

Role of PDE-5 Inhibitor in the Treatment of Chronic Pelvic Pain Syndrome: A Randomized Control Trial

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In this study, 68 men with CP/CPPS took one of two drug treatments for 6 weeks: 32 got the common treatment of the alpha blocker alfuzosin (which is used for enlarged prostates) plus levofloxacin (an antibiotic), and 36 got tadalafil (Cialis, 5 mg), which is one of the erectile dysfunction drugs known as PDE-5 inhibitors. The tadalafil group improved much more after 6 weeks of treatment. This group's CPSI scores dropped 18 points compared with about 8 for the usual treatment group. International prostate symptoms scores (IPSS) were also better for the

men taking tadalafil, dropping nearly 9 points compared with about 3, with the quality-of-life subscore improving by 2 points compared with about a half point. Not surprisingly, erectile function scores for the men taking tadalafil got better, improving by 6 points (out of 30) on the IIEF erectile function scale, whereas erectile function for the other men got slightly worse. In addition, the men taking tadalafil had improved urinary function, with their maximum flow rates going up by a little more than 2 points, while those for the other men went down an average of about 3 points.

Pollen-Vitamin Combo Bests Saw Palmetto for CP/CPPS

Pollen Extract in Association with Vitamins (Deprox 500 ®) Versus *Serenoa Repens* in Chronic Prostatitis/Chronic Pelvic Pain Syndrome; A Single Center Experience

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In a small randomized, controlled clinical trial compared the results of 6 weeks of treatment with a brand of pollen extract plus vitamins (Deprox 500) 500 mg twice a day in 29 men and *Serenoa repens* (saw palmetto) 320 mg once a day in 34 men with CP/CPPS. The IPSS scores dropped about 13 points with the pollen extract and 8 points with the saw palmetto. The corresponding CPSI scores dropped 17 points versus 13 points. When only symptom scores were considered, the improvements were almost 12 points for the pollen combination and 9 points for saw palmetto. In men with hypertension, the scores dropped some 14 points with the pollen supplement versus 9 points for saw palmetto.