PROSTATE DISORDERS OTHER THAN CANCER *Part 1*

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Let's examine what the prostate does and doesn't do as well as some of the things we know and don't know about the prostate. There are three main disorders of the prostate. Inflammatory conditions known as "prostatitis", problems associated with urination as a result of the increasing growth of the prostate known as "Benign Prostatic Hyperplasia "(BPH), and cancer. Most of the readers of Insights have either had their prostates removed, irradiated or treated in some manner that would change its function. Before the cancer was found, many men had one or both of these disorders.

The primary function of the prostate and an associated structure, the seminal vesicles, is to manufacture and store the seminal fluid and all of the enzymes that are involved in the maintenance of reproductive function. The prostate supplies the ingredients that keep the sperm alive and healthy for an extended period of time. The prostate, like the appendix, is not necessary for life and technically, reproduction can occur by extracting sperm directly from the testicles and implanting them into an ovum. Prostate function is influenced by many hormones. The principle ones are androgens which include testosterone. The prostate also produces substances that help regulate testosterone production. It probably makes other substances as well that have yet to be identified.

"Prostatitis" includes a variety of entities. Acute bacterial prostatitis refers to an infection caused by one of the many bacteria that reside in our intestine. The most common organism is E.coli which is the most common bacteria we possess. There are more than 150 types of E.coli and one person's E.coli may differ from someone else's. The symptoms include feeling sick, a high fever, difficulty urinating, painful urination, urgency, pain in the pelvis, rectum and low back and sometimes bloody urine. The urine appears cloudy and when examined under the microscope, there are many white blood cells.

A urine culture confirms the diagnosis and identifies the bacteria and its sensitivity to various antibiotics. On examination the prostate is swollen, hard and painful. One portion of the prostate may be more involved than the remainder of the prostate. Blood tests show a high white blood cell count and usually a very high PSA. The treatment for bacterial prostatitis is antibiotics for 2-4 weeks although the duration of antibiotic therapy is dependent upon the severity of the infection and the response to treatment.

If there is difficulty urinating, agents such as Flomax or Uroxatrol are beneficial. It is often difficult to determine when the prostate has healed, and relapses are common. Patients who have one episode of bacterial prostatitis seem to be more susceptible to further episodes. The bacteria hide inside the prostate by building a protective gel around them that antibiotics cannot penetrate. Chronic, recurrent bacterial prostatitis requires aggressive therapy and frequent follow-up in an attempt to prevent another recurrence.

Patients who have similar symptoms but no bacteria can be found are considered to have non-bacterial prostatitis. These patients are not sick but have urinary frequency, urgency and pressure in the pelvic area and in the rectum. They may have pain or increased sensitivity in the testes. Urine and prostate fluid cultures fail to grow any organisms. On rectal exam, the prostate is soft and congested, and squeezing or massaging the prostate tends to produce a large volume of prostatic fluid which usually shows only a few white blood cells. One of the problems we have is that there are probably many organisms that have yet to be identified. The treatment for this condition ranges from a trial of antibiotics to prostate massages. This tends to be a chronic condition and these patients go from one urologist to another in an attempt to find a beneficial treatment.

Another form of "prostatitis" is has been referred to as prostatodynia, but the current terminology for this entity is "chronic prostatitis or chronic pelvic pain syndrome" (CP/CPPS). This condition produces moderately severe pelvic pain, urinary frequency and urgency and is often associated with erectile dysfunction but is unrelated to BPH or prostate cancer. These people are miserable and the therapies vary widely and often provide limited benefit. Interstitial cystitis is an inflammatory condition of the bladder and may represent another manifestation of this disease. Fibromyalgia involving the pelvic musculature is another disorder that is often included in this syndrome.

The cause of CP/CPPS is unknown. The various possibilities that have been considered include infectious (bacterial or viral), genetic, anatomical, physiological, neuropathic, neuromuscular, endocrine, immune and psychological mechanisms. In other words, any cause is possible and even though some investigators have spent years studying this disease, we still have only hypotheses and no clear answers. Dr. Curtis Nickel, a respected authority on this subject, points out that there is no one unifying mechanism to explain all of the signs and symptoms. He believes that these patients have a genetic or an anatomical abnormality that potentiates an initial triggering event such infection or trauma.

The primary symptom for CP/CPPS is pain. Investigators have been studying changes in the central and peripheral nervous system as a possible cause. Animal studies have shown that inflammation and injury from a single site in the pelvis or around the prostate could result in nervous system inflammation in the spinal cord. This produces an expanded field of pain and inflammation beyond the original site of injury. The theory, offered by Dr. Michel Pontari is that an injury, infection or some unknown inflammatory process starts in one area of the pelvis which expands into a more extensive process. In support of this concept is evidence that the sacral spinal cord appears to develop signs of inflammation that come from a peripheral source. Although the symptoms appear to be coming only from the prostate, it is the pelvic musculature that seems to be responsible for all of the symptoms.

Two studies from the University of Washington have demonstrated neurological abnormalities. Men with CP/CPPS had hypersensitivity to thermal *(Continued on Page 14)*

stimuli (heat) applied to the perineum (the area between a man's scrotum and anus, behind which lies the prostate) compared to asymptomatic controls. These investigators found abnormalities in both the nerves going to the pelvis as well as those leaving the pelvis.

There are important psychological consequences for people suffering from this disease. They must be addressed as a part of the total therapeutic program. There is no doubt that stress can magnify the symptoms but whether or not stress can actually precipitate the syndrome is unclear.

Prostatitis in young men has become a common observation nowadays, as many people below the age of 30 are facing this problem.

Pontari postulates that some men are susceptible because of genetic predisposition or prior injury from infection, local injury, and psychological stress. This results in changes in some areas of the brain and spinal cord. These changes allow stimuli that otherwise would not be perceived as being painful to be interpreted in the brain as painful. Mild pain becomes more exaggerated and the area of pain distribution extends beyond the area of the initial stimulus.

A variety of treatments have been used to minimize the symptoms. Carefully done studies attempting to identify various organisms have shown that there is no difference between these patients and age-match men who have no symptoms. Randomized, placebo controlled clinical trials have failed to demonstrate an effective therapy but some patients do respond to a variety of therapies.

These findings have led to the "Snow Flake Hypothesis" coined by Pontari. Each patient is unique and should be managed accordingly. What seems to work for one person may not be of benefit for anyone else. Nickel has presented a similar concept with the UPOINT system. This refers to six distinct, clinically relevant and identifiable domains that include: Urinary, Psychosocial, Organ specific, Infection, Neurologic and Tenderness of muscles. The percentage of patients identified for each domain was 52%, 34%, 61%, 16%, 37% and 53%. Of the patients studied, 22% were positive for only one domain while the others were positive for two or more domains. Duration of symptoms but not age was associated with the number of domains, while the number of domains was associated with symptom severity. The domains outside the prostate (T) and particularly those outside the pelvis (P and N) had the most impact on the quality of life.

Management of CP/CPPS usually includes a trial of several different antibiotics, anti-inflammatory agents, and alpha blockers such as tamsulosin. Individually, these agents are not very effective but combinations may improve the symptoms in some men. Each patient has to be carefully assessed and managed according to the specific symptoms and stresses that are occurring. There is no data to suggest that this disorder leads to prostate cancer but erectile dysfunction is a frequent accompaniment.

BPH will be covered in Part 2, planned for May 2010 Issue.