Benign prostatic hyperplasia causes, signs and treatments

As a man matures, the prostate goes through two main periods of growth. The first occurs early in puberty, when the prostate doubles in size. Around of the age 25, the gland begins to grow again. This second growth phase often results, years later, in BPH.

Though the prostate continues to grow during most of a man’s life, the enlargement doesn’t usually cause problems until late in life. BPH rarely causes symptoms before age 40, but more than half of men in their sixties and as many as 90 percent in their seventies and eighties have some symptoms of BPH.

As the prostate enlarges, the layer of tissue surrounding it stops it from expanding, causing the gland to press against the urethra like a clamp on a garden hose. The bladder wall becomes irritable and thicker. The bladder begins to contract even when it contains small amounts of urine, causing more frequent urination. Eventually, the bladder weakens and loses the ability to empty itself. Urine remains in the bladder. The narrowing of the urethra and partial emptying of the bladder cause many of the problems associated with BPH. Prostate enlargement is as common a part of aging as gray hair. As life expectancy rises, so does the occurrence of BPH (NucleusMedicalMedia, 2013).

Clinical Findings

Most men with BPH complain of symptoms of the lower urinary tract. Doctors should ascertain whether the symptoms are really caused by BPH or by another pathology. In the assessment, distinction needs to be made between obligatory and optional investigations which follow in the cases where

diagnostic uncertainties persist after the basic examination (Dr. med. Matthias Oelke, 2013).

Obligatory Examinations

Patient history: A family history of prostatic disease and prostatic cancer, a history of lower urinary tract disease such as bladder stones, cystoscopic examination, transurethral surgery, and systemic disease and a history of alpha-blockers, 5-alpha-reductase inhibitors, antimuscarinics, or neurological medications should be recorded (Dr Hann Chorng Kuo, 2008).

In addition to the general and neurourological history, a detailed history with regard to micturition should be taken. In the micturition history, obstructive and irritative symptoms are elicited and possibly quantified (Table 1). The history should also clarify whether drugs are being taken that might affect the functioning of the lower urinary tract (Dr. med. Matthias Oelke, 2013).

Symptom and quality of life questionnaires: The frequency and extent of symptoms can be quantified by using a questionnaire, and changes during therapy can thus be documented. The International Prostate Symptom Score (IPSS) is the most commonly used questionnaire (Table 2). The first 7 questions capture the frequency of symptoms of the lower urinary tract within the preceding 4 weeks, the 8th question the extent to which the patient’s quality of life is compromised. The symptom score is obtained by adding up the answers to questions 1 to 7 and will be a number between 0 and 35 (Dr. med. Matthias Oelke, 2013). On the basis of this score, the symptoms can be classed as mild (IPSS score 0-7), moderate (IPSS score 8-19), or severe (IPSS score 20-35) as shown in the Table 3.

Physical Examination: Patients should be examined systemically and locally. Examination of the abdomen includes checking for a palpable bladder. This may indicate chronic outflow obstruction or a neurogenic bladder. The presence of an abdominal scar, a palpable, distended bladder and genital lesions should be carefully examined. Obviously, any further abnormalities require a full neurological history and examination. In addition to a general physical examination, the patient’s neurourological status should be assessed. This provides information on the anal sphincter muscle tone and the sensorimotor state of the lower extremities, the perineum, and the genitals. During the basic neurological examination, the reflex pathways of the lower extremities should also be assessed (Table 3), to enable conclusions about the functional fitness of the neural pathways in the bladder and the bladder sphincter (Dr. med. Matthias Oelke, 2013).

A digital rectal examination (DRE) of prostatic consistency, prostatic size, surface and abnormal nodularity should be carefully done. It includes noting the tone of the anal sphincter and the pelvic floor (Diagram 2. 2. 1A). It may be poor with a neurogenic bladder. Urologists report their findings in terms of the size of the prostate, a normal gland in a young adult weighing about 20 g. A useful guide for those less familiar with prostates is that a finger’s breadth represents about 15 to 20 g and so a gland that is three fingers in breadth across is 45 to 60 g. Symptoms are unusual below two fingers in breadth. It is also important to note the texture and contour of the gland. It should be firm but not hard, and smooth without nodules. The median sulcus should be clearly defined. A gland that is hard rather than firm, nodular and lacks a clear median sulcus suggests carcinoma of prostate (Dr Laurence

Knott, 2012). Compared with transrectal ultrasonography, the prostate volume is usually underestimated by 10 to 20% on digital rectal examination (Dr. med. Matthias Oelke, 2013).

A Digital rectal exam (DRE) is done to assess the prostate size and shape. After putting on a lubricated glove, the physician gently inserts a finger through the anus into the rectum and assesses the size and hardness of the prostate gland.

Laboratory tests: Urine test (urinalysis). When a patient complains of urethral symptoms (micturition pain, burning sensation) a urinalysis should be performed (Dr Hann Chorng Kuo, 2008). Analyzing a sample of the urine in the laboratory can help rule out an infection or other conditions that can cause similar symptoms (MayoClinic, 2011). When the urinalysis shows a miscroscopic hematuria or pyuria, a KUB radiograpgh should be done to investigate whether there are bladder or lower ureteral stone. Blood urea nitrogen and creatinine levels should be investigated when chronic urinary retention is noted (Dr Hann Chorng Kuo, 2008).

Prostate-specific antigen (PSA) blood test. The prostatic specific antigen (PSA) level is indicated in all patients with an enlarged prostate or abnormal DRE findings (Dr Hann Chorng Kuo, 2008). It’s normal for the prostate gland to produce PSA, which helps liquefy semen. PSA levels increase with an enlarged prostate. However, PSA levels can also be elevated due to prostate cancer, recent tests, surgery or infection (prostatitis) (MayoClinic, 2011). Men with high PSA levels have a higher risk of future growth of the prostate, symptom and flow rate deterioration, acute urinary retention and BPH-

related surgery. BPH levels increase with age and approximately 25% of men with BPH have a PSA of > 4ng/ml. PSA testing is more appropriate for patients whose future natural life span is likely to be more than 10 years (Dr Hann Chorng Kuo, 2008).

Uroflowmetry. It is a dynamic test that measures the volume of urine released from the body, the speed with which it is released, and how long the release takes. Both average and maximum flow rates can be measured (U. S National Library of Medicine, 2012). As shown in the Diagram 2. 2. 1B and Graph 2. 2. 1A, the patient will be asked to urinate into a funnel connected to the electronic uroflowmeter, which records and translates the urine flow into a graph which gives a good indication of the degree of bladder blockage (Chin Chong Min Urology & Robotic Surgery Centre, 2013). The peak flow rate, also known as Qmax is generally used as the basis for determining the severity of any blockage or obstruction. Low flow may indicate such conditions as obstruction of the urethra, enlarged prostate or poor bladder function (UrologyCare, 2011). This technique, which is used to detect an obstruction of the urethra and bladder neck, is widely used in the diagnosis of BPH (EhealthMD, 2012).

A Qmax value over 15 mL/s is usually considered normal. A Qmax below 7 mL/s is accepted as low. Results can vary according to effort and volume and so the usual compromise is to obtain at least two readings with at least 150 mL of urine each time (Dr Laurence Knott, 2012).

Postvoid residual urine: One of the important subjects of tests for urinary incontinence is the postvoid residual urine volume (PVR), the amount of

urine left after urination. Normally, about 50 mL or less of urine is left; more than 200 mL is a definite sign of abnormalities. Measurements in between require further tests. This test is done using ultrasonography or it can also be done with a small tube (catheter), being put into the bladder through the urethra. By using the transabdominal ultrasonography, it uses a device placed over the abdomen. It can give an accurate measure of postvoid residual urine and is less invasive and expensive than transrectal ultrasonography (TRUS) (UrologyCare, 2012). Postvoid residual urine can occur in bladder outlet obstruction in BHP, but also in other forms of bladder outlet obstruction or detrusor underactivity. (Dr. med. Matthias Oelke, 2013).

Urosonography: The bladder and kidneys should be examined in every patient. Since a raised serum creatinine concentration occurs only after about 50% of nephrons have failed, an ultrasound investigation of the kidneys can diagnose upper urinary tract dilatation even in the absence of raised creatinine. Since bladder outlet obstruction results in compensatory hypertrophy of the detrusor muscle, ultrasound measurements of the detrusor thickness when the bladder contains at least 250 ml urine can be used as an additional variable in assessing the degree of obstruction. A detrusor wall thickness of ‰¥ 2 mm indicates a bladder outlet obstruction with 95% certainty (Dr. med. Matthias Oelke, 2013).

Optional Examinations

TRUS: Transrectal ultrasonography (TRUS) can determine the volume of the prostate more precisely than transabdominal volumetry, the methods differ by about 10%. Only TRUS can visualize and assess the zonal anatomy of the

prostate (Dr. med. Matthias Oelke, 2013). Transrectal ultrasonography (TRUS) uses a rectal probe for assessing the prostate. TRUS is significantly the most accurate method for determining prostate volume. It can sometimes detect cancer (UrologyCare, 2012).

Urodynamic studies and pressure flow studies. With these procedures, a catheter is threaded through your urethra into your bladder. Water is slowly injected into your bladder. This allows doctor to measure bladder pressures and to determine how well your bladder muscles are working (MayoClinic, 2011).

These should be used only if standard diagnostic tests have not been able to assess the degree of obstruction. (Dr. med. Matthias Oelke, 2013).

Cystoscopy. Also called urethrocystoscopy, may be performed in men diagnosed with BPH, particularly if they are surgical candidates or if other urinary tract problems are suspected (Chin Chong Min Urology & Robotic Surgery Centre, 2013). This procedure allows your doctor to see inside your urethra and bladder. After you receive a local anesthetic, a lighted flexible telescope (cystoscope) is inserted into your urethra to look for signs of problems as shown in the Diagram 2. 2. 2A (MayoClinic, 2011).

Intravenouspyelogram or CT urogram. These tests can help detect urinary tract stones, tumors or blockages above the bladder. First, dye is injected into a vein, and X-rays or CT scans are taken of your kidneys, bladder and the tubes that connect your kidneys to your bladder (ureters). The dye helps outline the drainage systems of the kidneys (MayoClinic, 2011).

Etiology of Benign Prostate Hyperplasia

The actual cause of prostate enlargement is unknown. However, most urologists agree that age is most definitely a factor in the development of an enlarged prostate (ProstateHealthGuide, 2012). Several theories have been proposed to explain benign cell growth in older men (University of Maryland Medical Center, 2009). Benign prostatic hyperplasia is probably a normal part of the aging process in men, caused by changes in hormone balance and in cell growth (Healthwise, 2012).

Hormonal Changes

Male Hormones. Androgens (male hormones) most likely play a role in prostate growth. The most important androgen is testosterone, which is produced in the testes throughout a man’s lifetime. The prostate converts testosterone to a more powerful androgen, dihydrotestosterone (DHT). DHT stimulates cell growth in the tissue that lines the prostate gland (the glandular epithelium) and is the major cause of the rapid prostate enlargement that occurs between puberty and young adulthood.

DHT is a prime suspect in prostate enlargement in later adulthood (University of Maryland Medical Center, 2009).

Female Hormones. The female hormone estrogen may also play a role in BPH. (Some estrogen is always present in men.) As men age, testosterone levels drop, and the proportion of estrogen increases, possibly triggering prostate growth (University of Maryland Medical Center, 2009).

Late Activation of Cell Growth

Another theory focuses on cells in a certain section of the gland that may become active late in life, signaling other prostate cells to replicate or causing them to be sensitive to growth-stimulating hormones (University of Maryland Medical Center, 2009).

The incidence of Benign Prostate Hyperplasia

Interest in alternative treatments for BPH increased after epidemiologic studies showed a lower incidence of BPH and prostate cancer in Asians compared with persons from Western countries. The incidence of BPH is also low in vegetarian men. It is an interesting finding that BPH incidence is lower in Asian countries than in Western countries whereas Asian immigrants in the United States have the same incidence of clinical BPH as their white American counterparts. It is also to note that the lower incidence of clinical BPH of Asian men increases in immigrant generations after they have started to live in North America. One postulated explanation is the higher soy content of the typical Asian diet. Genistein, a major isoflavone ingredient of tofu, has been found to decrease the growth of hyperplastic prostate tissue in histoculture. Dietary factors are accused to explain this phenomenon since Asian people consume low-fat, high-fiber diets than Western people. In different series, it was shown that high energy and animal product diet increase the risk of BPH while fruit and vegetable based diet has a protective effect against BPH (Dr Praveen R, 2008).

The incidence of BPH is 34. 4 per 1, 000 persons per year in the U. S. in men over age 55. The prevalence of lower urinary tract symptoms secondary to

BPH in the U. S. population is 41% in black men and 34% in white men. The prevalence of BPH increases with age. Histologic BPH is present in approximately 8% of men aged 31 to 40, 50% of men aged 51 to 60, 70% of men aged 61 to 70, and 90% of men aged 81 to 90. Correspondingly, symptomatic (clinical) BPH is present in approximately 26% of men in the fifth decade of life, 33% of men in the sixth decade, 41% of men in the seventh decade, and 46% of men in the eighth decade of life and beyond (Elsevier, 2012).

Mortality and Morbidity

Benign prostatic hyperplasia (BPH) is a common problem among older men, and is responsible for considerable disability. However, it is an infrequent cause of death. According to the World Health Organization database, the mortality rates for most developed countries in the 1980s were 0. 5 to 1. 5/100, 000. Death from BPH is rare in the United States.

The large number of men with the symptoms of this disorder, the easy access to diagnostic tests, and the availability of drug therapy make it appropriate for the primary care provider to participate in the management of men with this disorder (Wolters Kluwer Health, 2012). BPH associated mortality is rare and serious complications are uncommon (Dr. Dan Van Syoc, 2010).

Benign prostatic hyperplasia (BPH) is a common cause of morbidity among older men, (Annual Reviews, 2013) causing morbidity primarily through lower urinary tract symptoms (LUTS). The primary physician should attempt to distinguish LUTS due to BPH from the other causes of such symptoms,

objectively determine symptom severity, and, when the symptoms are bothersome enough, work with the patient on a therapeutic approach to reducing symptoms while minimizing side effects (Lippincott Williams & Wilkins, 2009).

Surgery consists of various approaches that resect or ablate prostate tissue. While effective in expanding the urethral lumen and relieving symptoms, tissue resection or ablation also contributes to significant morbidity (NeoTract, 2011). However, because of the morbidity associated with the surgical treatment of this condition, alternative treatments are being developed and are coming into increasing use (National Health and Medical Research Council, 2011).

Histopathology

Microscopically, the prostate consists of glandular epithelium and fibromuscular stroma elements. Smooth muscle cells, fibroblasts and endothelial cells are in the stroma and the epithelial cells are secretory cells, basal cells and neuroendocrine cells (Diagram 2. 6A) (Mark Frydenberg, Nathan Lawrentschuk, 2012).

Both the glandular epithelial cells and the stromal cells (including muscular fibers) undergo hyperplasia in BPH. Most sources agree that of the two tissues, stromal hyperplasia predominates, but the exact ratio of the two is unclear (Wikipedia, 2013).

The columnar secretory cells are tall with pale to clear cytoplasm. These cells stain positively with prostate specific antigen. Basal cells are less differentiated than secretory cells and so are devoid of secretory products

such as prostate-specific antigen (PSA). Finally, neuroendocrine cells are irregularly distributed throughout ducts and acini, with a greater proportion in the ducts . The prostate has the greatest number of neuroendocrine cells of any of the genitourinary organs.

Glands are structured with open and closed cell types with the open type facing the inside of the duct having a monitoring role over its contents. Most cells contain serotonin but other peptides present include somatostatin, calcitonin, gene-related peptides and katacalcin. The cells co-express PSA and prostatic acid phosphatase.

Their function is unclear but it is speculated that these cells are involved with local regulation by paracrine release of peptides. Prostatic ducts and acini are distinguished by architectural pattern at low power magnification. The prostate becomes more complex with ducts and branching glands arranged in lobules and surrounded by stroma with advancing age (Mark Frydenberg, Nathan Lawrentschuk, 2012).

Pathophysiology

Prostatic enlargement depends on the potent androgen dihydrotestosterone (DHT). In the prostate gland, type II 5-alpha-reductase metabolizes circulating testosterone into DHT, which works locally, not systemically. DHT binds to androgen receptors in the cell nuclei, potentially resulting in BPH.

In vitro studies have shown that large numbers of alpha-1-adrenergic receptors are located in the smooth muscle of the stroma and capsule of the prostate, as well as in the bladder neck.

Stimulation of these receptors causes an increase in smooth-muscle tone, which can worsen LUTS. Conversely, blockade of these receptors (see Treatment and Management) can reversibly relax these muscles, with subsequent relief of LUTS.

Microscopically, BPH is characterized as a hyperplastic process. The hyperplasia results in enlargement of the prostate that may restrict the flow of urine from the bladder, resulting in clinical manifestations of BPH. The prostate enlarges with age in a hormonally dependent manner. Therefore, castrated males (ie, who are unable to make testosterone) do not develop BPH.

The traditional theory behind BPH is that, as the prostate enlarges, the surrounding capsule prevents it from radially expanding, potentially resulting in urethral compression. However, obstruction-induced bladder dysfunction contributes significantly to LUTS. The bladder wall becomes thickened, trabeculated, and irritable when it is forced to hypertrophy and increase its own contractile force.

With the increased sensitivity (detrusor overactivity [DO]), even with small volumes of urine in the bladder, is believed to contribute to urinary frequency and LUTS. The bladder may gradually weaken and lose the ability to empty completely, leading to increased residual urine volume and, possibly, acute or chronic urinary retention.

25In the bladder, obstruction leads to smooth-muscle-cell hypertrophy. Biopsy specimens of trabeculated bladders demonstrate evidence of scarce smooth-muscle fibers with an increase in collagen. The collagen fibers limit

compliance, leading to higher bladder pressures upon filling. In addition, their presence limits shortening of adjacent smooth muscle cells, leading to impaired emptying and the development of residual urine.

Signs and Symptoms

When symptoms (known as lower urinary tract symptoms, or LUTS) occur, they may range from mild and barely noticeable to serious and disruptive. The amount of prostate enlargement not always related to the severity of the symptoms. Some men with only slight enlargement have serious symptoms, and some men with a great deal of enlargement have few symptoms (WebMD, 2010).

The signs and symptoms of BPH (benign prostatic hyperplasia) can vary, but usually involve changes or problems with urination (eMedTV, September 2008). According to eMedTV, the following are the most common symptoms of benign prostatic hyperplasia. However, each individual may experience symptoms differently. Symptoms may include:

- Leaking or dribbling of urine
- More frequent urination, especially at night
- A strong or sudden urge to urinate
- Urine retention – inability to urinate
- A hesitant, interrupted, weak stream of urine
- Trouble starting a urine stream or making more than a dribble
- Feeling that the bladder has not fully emptied
- Stopping and starting again several times while passing urine

At their worst, common BPH symptoms can lead to severe symptoms such as:

- A weak bladder
- Backflow of urine causing bladder or kidney infections
- Complete block in the flow of urine
- Kidney failure.

Symptoms can be quantitated by scores, such as the 7-question American Urological Association Symptom Score in Table 2. As shown in Table 3, this score also allows doctors to monitor symptom progression from mild to severe.

Sometimes these symptoms can reduce the quality of life to such a great extent that those affected build their daily routines around the condition. They avoid drinking or plan their errands around easy access to toilet facilities. If BPH is not treated, it holds considerable risks (Roehrborn CG, McConnell JD, et al. 2010).