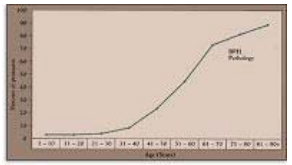
Objectives:

After studying the summary of BPH the student should be able to:

A. Describe the typical symptoms of BPH.
B. State four complications of untreated BPH.
C. Describe the medical therapy for men with symptomatic BPH. Describe the physiologic basis
for the use of these drugs in men with BPH.
D. State four indications for surgical resection of the prostate in men with BPH.

Introduction:

1. There is difficulty arriving at a practical definition of BPH as there is little correlation between the size of the prostate and clinical symptoms in older men. Using a histologic definition, 50% of men aged 50 - 60 years have transition zone hyperplasia. Over 90% of men in their 80's show similar histologic changes. However, only 10% - 15% of men over 50 years have moderate or severe voiding symptoms due to BPH.



Prevalence of BPH pathology with age

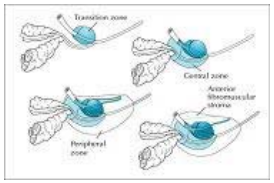
2. Studies have identified 2 factors necessary for the development of BPH:

A. Dihydrotestosterone (DHT)
B. Aging.

· As men get older it appears that the prostate becomes more sensitive to DHT, which decreases cell death in the prostate, therefore, increasing prostate size.

3. BPH develops in the "transition zone".

· It is truly a hyperplastic process resulting from an increase in cell number. Histologically, there is hyperplasia of both the epithelial glands and fibromuscular stroma (containing collagen and smooth muscle), resulting in a nodular expansion of the periurethral portion of the prostate (called the "transition zone"). The outer portions of the prostate become compressed and stretched around the expanding hyperplastic tissue forming the "surgical capsule".
· Mechanical compression of the urethra causing bladder outlet obstruction is the most common explanation for the associated voiding symptoms however there is only a weak correlation between the size of the prostate and the severity of symptoms. Prostatic smooth muscle is now recognized as producing a "dynamic" component of prostatic urethral resistance and may explain why smaller prostates might cause more severe obstruction than larger prostates.



Prostate Anatomy

BPH - Gross Pathology

Clinical Presentation:

1. The most common presentation is a variety of voiding symptoms that include:

   A. **"Obstructive" symptoms** due to mechanical obstruction and/or dynamic obstruction
   caused by the large adrenergic innervation of the smooth muscle of the prostate (the
   dynamic component explains the variable nature of the symptoms experienced by
   patient's with BPH):

   · slow stream
   · hesitancy
   · straining to void

   B. **"Irritative" symptoms** due to outlet resistance and an overactive detruser:

   · nocturia
   · urgency
   · frequency

2. Other ways that BPH may present are the **associated complications of untreated BPH:**

   A. **UTIs**
   B. **renal impairment**
   C. **acute retention**
   D. **gross hematuria**
   E. **bladder stones.**

3. **Differential diagnosis** - There is nothing specific about the voiding symptoms that suggest a diagnosis of BPH and other possibilities must be considered:

   A. prostate cancer F. bladder stones
   B. bladder tumour G. neurogenic voiding dysfunction
   C. prostatitis H. urethral stricture
   D. cystitis I. urethral cancer
   E. distal ureteral stones J. pelvic mass

   F. bladder stones
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Fortunately, non-BPH causes of voiding symptoms in older men can often be excluded by a careful history, physical exam and urinalysis.

BPH Work-up:

History

1. In addition to the typical voiding symptoms, other details that should be questioned include:

A. Hematuria
B. Dysuria
C. Abdominal/flank/pelvic pain
B. Incontinence

· These are not typical of BPH and suggest an alternate diagnosis.

2. The presence of neurologic conditions that may produce voiding symptoms is very important (diabetes, Parkinson's disease, Alzheimer's disease, stroke).
3. Certain medications may produce voiding symptoms similar to BPH (oral decongestants, tricyclic antidepressants).
4. Previous STDs (usually gonorrhea) or perineal trauma may produce urethral strictures resulting in similar voiding symptoms.
5. The severity of the voiding symptoms should be properly evaluated using the IPSS or AUA symptom score.

· The IPSS or AUA symptom index score can be given by answering seven questions about the severity of symptoms, it is possible to define whether the symptoms are mild (0-7 points), moderate (8-19 points) or severe (20-35 points).

International Prostate Symptom Score (I-PSS)

Physical Exam

1. In addition to the general exam, a DRE and focused neurologic exam are required.

   · The DRE not only confirms the presence of prostate enlargement but also examines for any prostate or rectal malignancy.
   · The DRE may be used to evaluate anal sphincter tone, perianal sensation and the bulbocavernosus reflex which are controlled by spinal level S2, S3, S4 and may be abnormal in patients with peripheral neuropathy or spinal cord diseases.

2. The external genitalia should be examined for meatal stenosis or a urethral mass.

Investigations

1. Urinalysis: A urine dipstick should be done to rule out hematuria or

UTIs. While both hematuria and UTIs may be caused by BPH, they warrant further investigation (usually ultrasound of abdomen/pelvis and cystoscopy).
2. Serum Creatinine: This should be done at the initial evaluation to screen for renal insufficiency due to obstructive uropathy. The duration and severity of symptoms are not good indicators of the chances of renal injury.
3. Serum PSA: Prostate cancer may be locally advanced and produce voiding symptoms. Prostate cancer may simply coexist with BPH since both are common conditions in men over 50 years of age. **In men with a greater than ten year life expectancy, knowledge of a concomitant prostate cancer is likely going to alter any planned treatment of BPH.**
4. Other Tests: Abdominal/pelvic ultrasound, cystoscopy, post-void residual measurements and urodynamic testing are all "optional". These tests are used to evaluate men who have features on history, physical, urinalysis, creatinine or PSA that suggest a diagnosis other than BPH or to evaluate possible complications of BPH.

Treatment:

1. **Conservative ("watchful waiting")** for those with mild or no symptoms:

· Mildly symptomatic BPH with no associated complications (i.e.: hematuria, UTI, stones, renal impairment, urinary retention) is unlikely to progress rapidly and many men choose to postpone any medical or surgical treatment. The most common reason for the initiation of medical treatment is patient frustration with the voiding symptoms (most bothersome symptoms are usually nocturia, urgency and frequency).
· 50% of patients symptoms improve spontaneously
· Often, reassurance that there is no other serious illness is all that the patients are interested in.
· The finding of an enlarged prostate on DRE in an asymptomatic man with no associated complications is of no consequence.
· This includes lifestyle changes (evening fluid restriction and planning activities).

2. **Medical therapy consists mainly of alpha-adrenergic antagonists:**

A. The rationale for use of alpha-blockers is that the bladder outlet obstruction is due, in part, to the intrinsic tone of prostate smooth muscle. The tension of prostate smooth muscle is mediated by a1-andrenergic receptors, which are densely localized within the prostate stroma.
B. The three most commonly used are terazosin (Hytrin), doxazosin (Cardura) and tamsulosin (Flomax). All three drugs have been proven effective in double-blinded, placebo controlled trials.

I. **Terazosin (Hytrin)** is the most frequently prescribed of the three.

· The improvement in symptoms and urine flow rate is somewhat dose-dependent; with Hytrin, an initial test dose of 1mg - 2 mg is slowly titrated up to 10 mg daily provided there are minimal side effects. The expected improvement in urine flow rate and symptom score is modest but patient satisfaction is usually very high.
· Important side effects of terazosin include orthostatic hypotension, rhinorrhea and loss of energy. The drug may be given before bed to minimize the orthostatic hypotension problem. Care must be taken in patients who are already taking antihypertensive medication or in patients with poor cardiac function as the blood pressure may become dangerously low.

II. **Tamsulosin (Flomax)** is an alpha-blocker that is specific for the **a1a-(sub-type) adrenergic receptor**, which is

localized to the prostate and urethra and not the cardiovascular system. Therefore, the most difficult side effect (hypotension) of the other alpha-blockers is avoided. Tamsulosin demonstrates equivalent efficacy to the other alpha-blockers in improving flow rates and voiding symptoms.

C. **Finasteride (Proscar or Propecia) is a competitive inhibitor of the enzyme 5-a-reductase, which converts testosterone to dihydrotestosterone.** Reduction in serum and intraprostatic DHT results in a modest regression of BPH in approximately 30% of men. DHT does not fall to castrate levels because there are isomers of 5-a-reductase in the skin and liver that are not blocked by finasteride. It may take up to three months of treatment before improvements in symptoms are noted. For this reason and the fact that two thirds of men show no improvement no matter how long treatment is administered, finasteride is not frequently used.

3. Surgical Therapy

Indications for surgical therapy for BPH are:

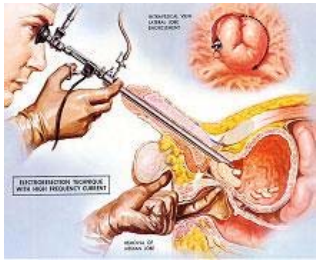
· Symptoms refractory to medical treatment
· Recurrent hematuria
· Recurrent UTIs
· Bladder stones
· Recurrent urinary retention
· Renal impairment.

Various options are available including:

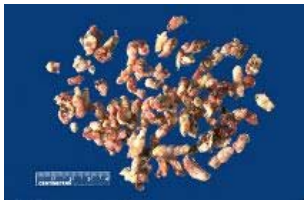
A) Transurethral resection of the prostate ("TURP")

· Done under spinal or general anaesthesia.
· The resection includes the bladder neck and obstructed prostatic urethra. Urinary continence is maintained by the external, striated urethral sphincter.
· Intraoperative and postoperative bleeding is the most common early complication of this surgery.

· Late complications include retrograde ejaculation, urethral strictures and bladder neck contractures. Incontinence is extremely rare (but possible if the resection is carried too distal and includes part of the external striated sphincter).



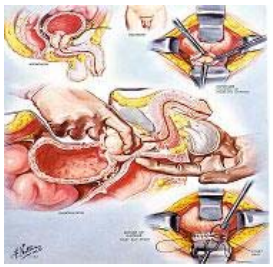
Transurethral Prostate Resection (TUPR)



BPH "chips" from TUPR

B) **Minimally invasive treatments:**

I. Transurethral balloon dilatation
II. Transurethral hyperthermia
III. Transurethral radiofrequency ablation.

· The minimally invasive techniques are usually done as part of a research protocol and are not widely applied.

C) **Open, simple prostatectomy** is reserved for patients with extremely large prostates that cannot be completely resected transurethrally or for patients with other associated complications that need open surgery (i.e.: large bladder stone).