PHARMACOLOGICAL THERAPY OF BENIGN PROSTATIC HYPERPLASIA [BPH]

ESSAY

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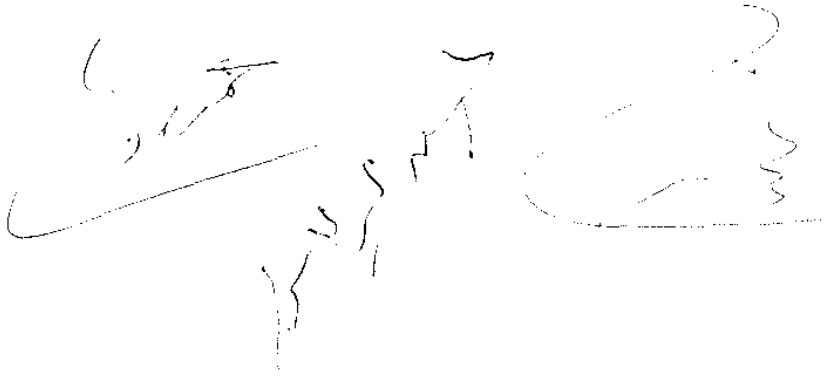

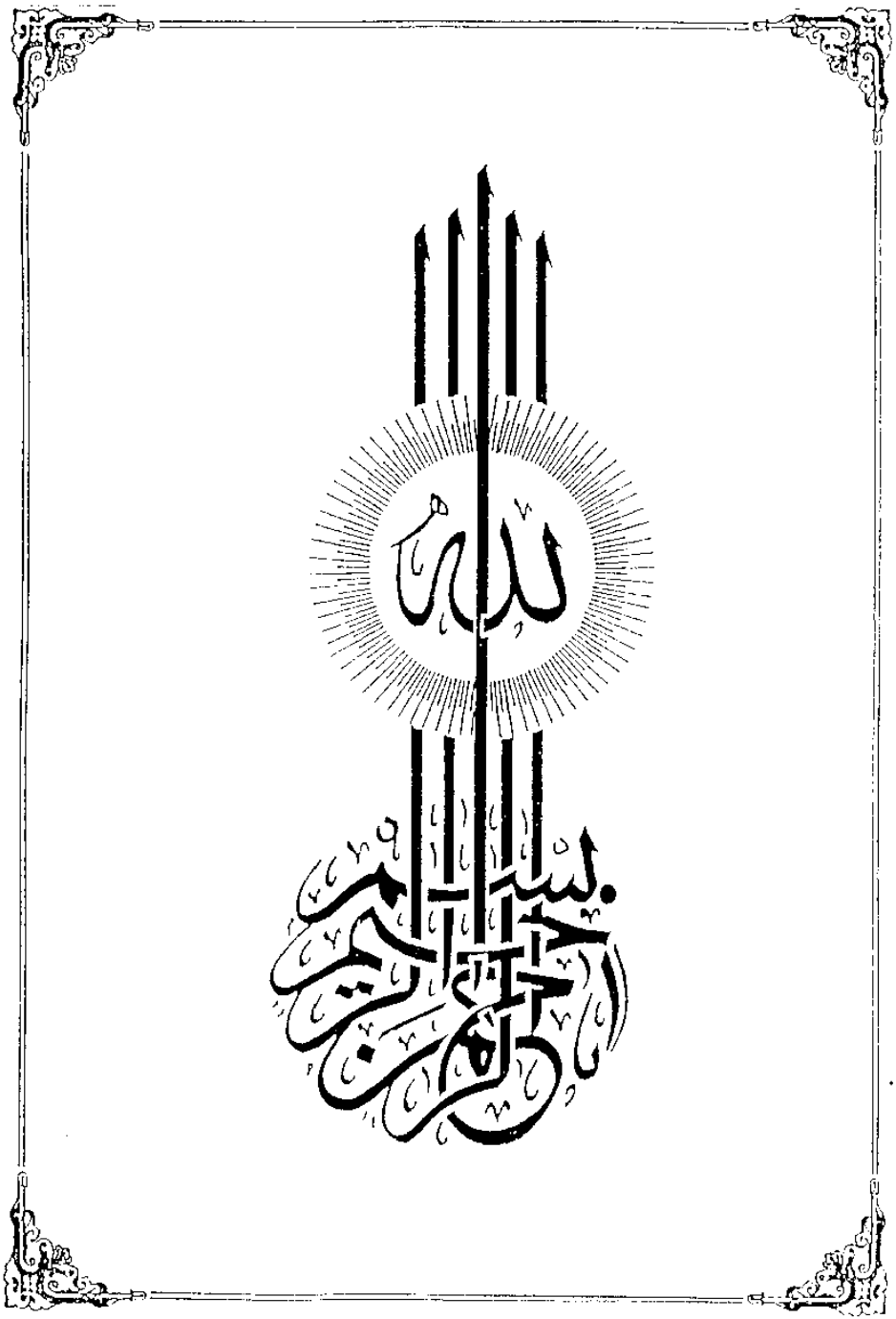

Dedication

To the Sole of my father
Who dreamed of what
I'm hardly trying to be.

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INTRODUCTION AND AIM OF THE WORK

BPH is the most common benign tumor in men. It is responsible for out flow obstructive urinary symptoms in the majority of men older than 50 y of age, and results in the need for prostatectomy in 20 to 30 percent of men who live to age of 80 y [1] . Recently there has been an explosion of interest in BPH, where new pharmacological and non operative approaches, to management of the disease have been developed.

The etiology of BPH in men is undoubtly multifactorial. However, it is well recognized that the two important factors necessary for the induction of BPH in men are the testes and aging. These 2 factors had built up the assumption that BPH is under endocrinal control [1]. According to the degree of hyperplasia symptoms of lower urinary tract obstruction occurs. The severity of these symptoms are variable.

Early in the disease process, the patient usually has minimal symptoms because the detrusor musculature is capable of compansating for the increase in outlet resistance to urine flow, with progressive obstruction a constellation of symptoms called prostatism develop with diminution in the caliber and force of urinary stream, hesitancy, post voiding dribbling, sensation of uncomplete emptying of the bladder and occasionally urinary retention. In addition to development of vesical instability with

increased frequency nocturia, urgency and urgency incontinance.

Features of renal insufficiency may also be present as, BPH is considered to be the 2nd cause of renal insufficiency after urinary Lithiasis [1].

This wide range of symptoms with variable severity, are due to obstructive mechanisms caused by the hyperplastic prostate, which is maintained by a static component related to the anatomic obstruction of the enlarging adenoma and by the dynamic component related to the tone of the smooth muscles in the prostatic capsule [2].

Based on the facts, that BPH is under endocrinal control, and that the prostatic capsule is a dynamic organ composed of smooth muscles fibers, collagen, and varying amount of glandular tissue [3], and that it is rich in adrenergic receptors, which can produce various degree of tension, according to the degree of autonomic stimulation. Pharmacological therapy for BPH can be interpreted as a line of management for BPH, through these two main general lines by interfering with the endocrinal control of BPH which is mainly played by the high levels of the active metabolite of testosterene DHT [4], and by interfering with the dynamic component of BPH obstruction which is mainly alpha adrenergic dependent 2ry to alpha-1 receptors present in smooth muscles of the adenoma and capsule [5].

However, surgical removal of the prostatic adenomas is the mainstay of therapy, especially when absolutly indicated, as in presence of azotema, hydronephrosis, bladder decompensation with overflow incontinance [1].

Simple prostatectomy has been the major form of treatment for BPH for almost a decade. Today 95% of these procedures can be performed transurethrally [1]. Transurethral resection of prostate is associated with a very low mortality when performed for BPH (0.1%) and low morbidity (18%) [6].

However, some patient may not be fit for surgical intervention, as a result of various medical problems, as BPH is a disease of aging men. Also some patients may refuse surgical intervention. For various personal reasons including phobia. Therefore it was a must for urologists to search for the non surgical methods for treatment of BPH as pharmacological treatment, TUBD, microwave hyperthermia and intraurethral stents [7].

Therefore, this assey will discuss the various lines of pharmacological therapy for BPH, as regard mode of action, side effect and complications.

EMBRYOLOGY OF THE PROSTATE

The prostate starts to appear and develop at the 12th week of embryonic life from the urogenital sinus, its development is directed primarily by DHT, which is produced from metabolic conversion of fetal testosterone, through the action of 5 alpha reductase enzyme, located within the urogenital sinus [8]. (Fig. 1).

By the 10th week, epithelial outgrowth from the prostatic segment of the urethra, grow and branch out. By the 12th week, five groups of tubules form the lobes of the prostate [9].

Group 1, the middle lobe is made up of about 10 branching tubules that originate on the floor of urethra between the bladder and the orifices of ejaculatory ducts.

Group 2 & 3, the lateral lobes originate from about 38 tubules on the lateral well of the urethra.

Group 4, the posterior lobe originate from the floor of the urethra distal to the opening of the ejaculatory ducts. The tubules of posterior lobe grow back behind those of the lateral lobes. As the tubules grow out they push the circular urethral musculature and scatter the fibers. These scattered fibers of the circular urethral muscle become the prostatic capsule [10]. The scattered fibromuscular tissue between the tubules are originally continuous

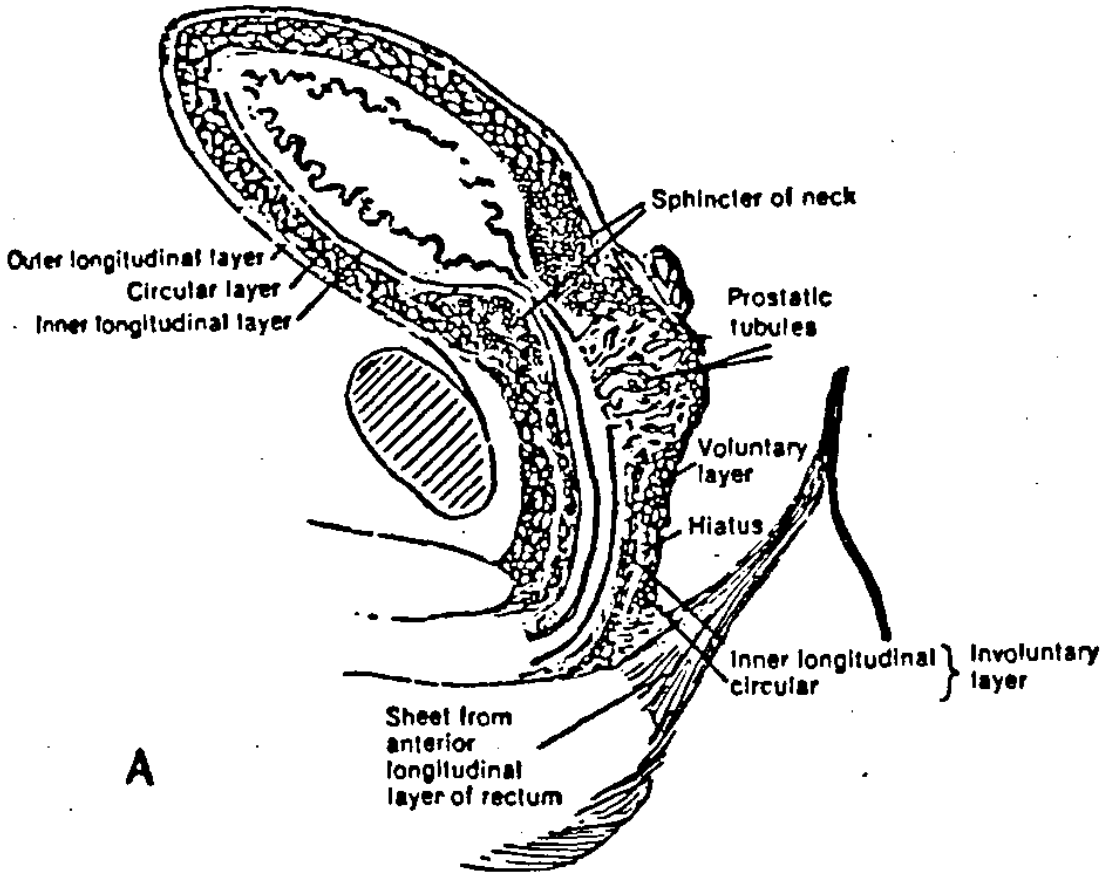

Fig. 1 : Semidiagrammatic longitudinal section of a human bladder and adjacent urethra (9 month gestation).
(From Wood-Jones, F. : J. Anat. Physiol., 36:51(2), 1901-02.

with the bladder, and now to prostatic stroma proper, have a primarily sphincteric function [15], (Fig. 2).

The 5 epithelial buds, are formed in a paired manner on the posterior side of the urogenital sinus, on both sides of veromontanum. The top pair form the inner zone of the prostate, and appear to be of mesoderm origin. The lower buds form the outer zone of the prostate and appear to be of endodermal origin [8]. This is of potential importance, because the inner zone gives tissue of BPH origin, whereas the outer zone contain the primary origin of cancer.

It is worth noting that the prostate embryologically develop from the embryonic urogenital sinus except for the acini of central zone, which are related in their embryologic development into the embryonic Wolffian duct [8].

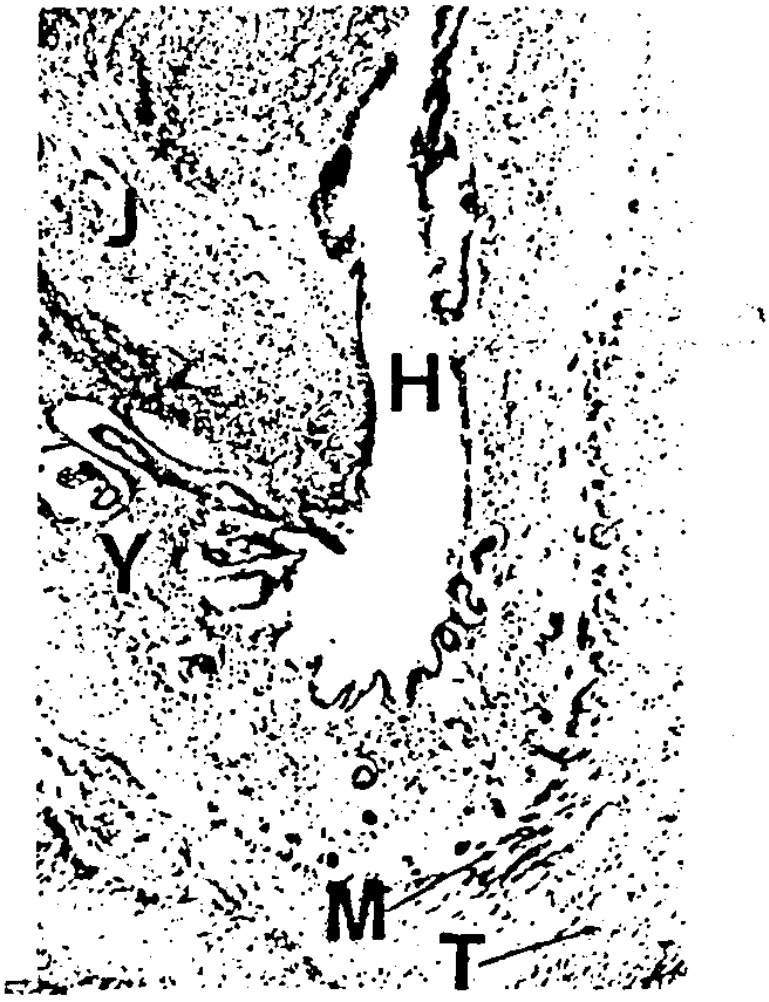

Fig. 2 : Posterior urethra of human fetus at 16 weeks' gestation (sagittal orientation). Prostate buds (Y); straited muscle around the urethra (T), which bounds an inner layer of circular smooth muscle (M); and ejaculatory duct (J) are apparent. (H, lumen of urethra).
(From Matsuno, T., Tokunaka, S., and Koyanagi, T.: J. Urol., 132:148, 1984).

ANATOMY OF THE PROSTATE

The prostate gland, is classically described as a compressed inverted cone. It is a firm, partly glandular, and partly fibromuscular body surrounding the very begining of the male urethra. It is situated in the true pelvis, behind the inferior border of the symphesis pubis and the pubic arch, lying infront of the ampulla of the rectum.

It has its continuity with the neck of the urinary bladder, its apex is inferior, lying on the superior aspect of superior fascia of the urogenital diaphragm (Fig. 3).

The gland has a posterior, an anterior, and two infero-lateral surfaces. The posterior surface is flattened transversally and convex vertically. It lies infront of the ampulla of the rectum, separated from it by its own capsule, and the Denonvillier's fascia.

The anterior surface is relatively narrow and convex, and extends from the apex to the base. It is about 2 cm behind symphesis pubis, separated from it by rich plexus of viens, and some loose adipose tissue. Its apex is connected to the pubic bone by pubo-prostatic ligement.

The urethra traverses the substance of the prostate, and emerges a little antero-superior to the apex.

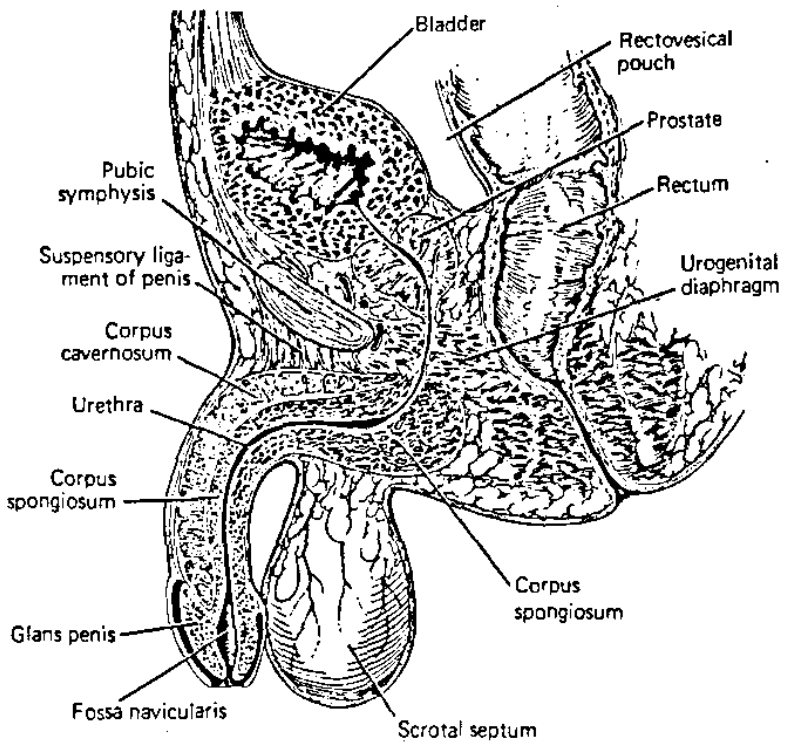

Fig. 3 : Relations of the bladder, prostate, seminal vesicles, penis, urethra, and scrotal contents.
(After Wesson).

The inferolateral surfaces are prominant, and related to the anterior part of the levator ani muscles.

The prostate measures about, 3.5 cm transversely at its base and 2.5 cm in its vertical and anteroposterior dimensions. Its normal weight is 18 gm.

It has fibro-muscular stroma, directly related to the fibromuscular element of the gland it self, which is inturn, is directly contuinuous with the smooth musculature of the bledder neck. This fibro-muscular stroma condenses on the periphery of the gland, to form the prostatic capsule proper [11].

The prostate is surrounded by prostatic sheath; made up primarily of fibrous tissue in which, rich plexus of veins are embedded. The prostatic sheath is continuous anteriorly, with the puboprostatic ligement, and inferiorly blends with the fascia on the deep surface of transversus perinii muscle. Posteriorly it fuses with, the obliterated recto-vesical pouch [11].

Blood supply of the prostate, is mainly from the inferior vesical artry, which is a branch of the hypogastric artry. It penetrates the substance of the prostate, at the prostato-vesical junction at about 4 & 8 o'clock positions. The main trunk of the prostatic artry, devides into central branch supplying the urethral wall, and the periurethral prostatic glands, and a periphral branch which supply the main bulk of the prostate.