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A STUDY OF THE EFFECTS OF TOTAL PROSTATECTOMY
ON URETHRAL FUNCTION OF THE DOG

A thesis presented in partial fulfillment
of the requirements for the degree of Master of
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Abstract

The function of the proximal urethra was studied in twelve dogs both before and after prostatectomy by means of repeated intraurethral pressure recordings and micturating cystograms. The animals were destroyed at times from one to three months after surgery and their pelvic urethrae were studied histologically and compared with a further group of intact dogs. Throughout the experiments, a series of routine urine chemical, physical and bacteriological tests and blood chemical and cytological examinations were performed. In addition, daily observations were made of the clinical state of urinary control.

A general pattern of intraurethral pressure was found to exist. Although individual variations occurred, the pattern recorded from a given animal was reproducible. In general, pressures were higher within the penile urethra than within the pelvic portion. A small pressure rise occurred at the bladder neck and another near the membranous and prostatic urethral junction. Preoperative intraurethral pressure was relatively constant within the membranous urethra. Micturating cystography revealed the prostatic urethra to be a distensible structure and the penile urethral lumen was generally narrower than the pelvic region both before and after surgery.

Following prostatectomy, lower pressures were recorded throughout the pelvic urethra. Mean pre- and postoperative pressures at specific locations were subjected to statistical comparison and a significantly lower pressure was found following surgery at only one of the areas considered, that one near the mid-pelvic urethra. Pressure recordings performed soon after surgery were found to be invalid, probably due to postoperative swelling within the urethra. Areas of postoperative stricture formation, when they occurred, were marked by spikes on the pressure

tracing.

The histological structure of the pelvic urethra was characterized by a predominant striated muscle component extending from the caudal aspect of the prostate to the urethral bulb. Smooth muscle fibers of the prostate were continuous cranially with the bladder and caudally with the membranous urethra where they formed a minor portion of the wall. After surgical removal of the gland, striated muscle fibers constituted the main urethral muscular component. A highly vascular submucosal layer was conspicuous throughout the pelvic urethra. Diagrams of urethral muscular arrangement were composed from a study of the intact and prostatectomized animals.

There were few clinical complications following the initial recovery period after prostatectomy. One dog exhibited mild stress incontinence. Two others developed urethral strictures. All animals were in good physical condition when electively destroyed.

The results of the experiment suggest that the prostatic urethra is not an essential structure for urine control although the slightly higher urethral pressures in the caudal prostatic urethra where there is both a smooth and striated muscle component, imply that this region normally plays some role in urethral closure. The function of striated muscle tone in urinary control is probably increased after prostatectomy.

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Introduction

Man and his best friend, the dog, are unique in the animal world, for they both frequently suffer from benign prostatic hyperplasia, while other species are relatively free of this malady. But while the condition in man has been extensively studied and various surgical techniques perfected for his relief, his canine friend is not so fortunate. The treatment of benign canine prostatic hyperplasia has been limited primarily to injections of female hormones or total castration, therapeutic measures from which man himself would cringe. However, man has been blessed with a prostate gland which is both more accessible and more submissive to the surgeon's hand than that of his unfortunate friend. In fact, surgical correction of benign prostatic hyperplasia in the dog necessitates removal of the entire gland and the effect of this procedure on the animal's urinary continence has been open to question. The interpretation of follow-up studies has been clouded by the fact that the animals were often severely affected by the disease and the extent of the nerve damage occurring during surgical excision was frequently unknown (Pettit, 1960).

It is the purpose of this study to determine the effect of total prostatectomy on the normal dog. Attention is directed specifically toward the structural and functional changes occurring in the proximal urethra following surgery. In addition, the role of the urethra in urinary control is investigated.

The preparation for this study required a background knowledge of the anatomy and physiology of the lower urinary tract. For this reason, a review of the scientific literature relating to these areas is presented at the outset.

Literature Review

Anatomical Considerations

The urinary bladder is composed of two distinct regions of smooth muscle, the detrusor muscle forming the vesical wall and the trigone which overlies the inner surface of the detrusor in the region of the uretero-vesical junction and bladder neck (Tanagho and Smith, 1966). Both the urinary bladder and urethra arise from the endodermal urogenital sinus of the embryo, unlike the trigone which is a mesodermal structure incorporated into the sinus wall during the transposition of the ureters and mesonephric ducts (Arey, 1965).

In reviewing the knowledge of urinary bladder anatomy prior to 1891, Griffiths (1891) pointed out that Ellis in 1856 described the bladder wall as being composed of three strata or planes, with muscular fasciculi passing from one stratum to another, binding them closely together. Three muscular planes can be grossly delineated, two longitudinal layers separated by a coat of circularly oriented fibers, but recent studies (Hunter, 1954; Woodburne, 1960) have confirmed the concept that muscle fibers are continuous between layers forming an intimately woven meshwork.

Coarse smooth muscle fascicles and relatively scanty amounts of connective tissue characterize the histological appearance of the detrusor muscle (Woodburne, 1965; Hutch and Rambo, 1967). Trigonal muscle is easily distinguished by its fine fasciculation and higher concentration of connective tissue (Hutch and Rambo, 1967; Tanagho, Smith and Meyers, 1968). Some elastic fibers can be found associated with the muscle bundles and beneath the mucosa, and are present in especially high concentration at the bladder neck (Woodburne, 1960).

The inner longitudinal bundles of the detrusor musculature are scanty and widely separated. Their orientation appears to be haphazard, but they converge at the bladder neck in a radial fashion and then continue into the urethra as the inner longitudinal muscle layer of the urethra (Woodburne, 1961; Hutch, 1966; Tanagho and Smith, 1966; Hutch and Rambo, 1967). The trigone also contributes fibers to the urethra; superficial fibers of the trigone from the region of both urethral orifices converge medially, then sweep over the dorsal aspect of the internal meatus and pass into the urethra. In the male, these fibers form a prominence, the cresta urethralis, which continues to the verumontanum, whereas the fibers continue throughout the length of the urethra in the female (Tanagho and Smith, 1966; Hutch and Rambo, 1967; Tanagho, Smith, and Meyers, 1968).

Outer longitudinal detrusor muscle bundles are thought by certain authors (Hutch, 1966; Tanagho and Smith, 1966; Hutch and Rambo, 1967; Tanagho and Smith, 1968; Kleeman, 1970; Droes, 1971; Van Ulden, 1971) to be continuous with outer circular fibers of the urethra. From studies of human bladders, Hutch and Rambo (1967) describe the fibers as having a spiral arrangement around the urethra, but according to Tanagho and Smith (1966), the "sliding fibers" loop around the bladder neck and proximal urethra and then continue back onto the bladder again. Woodburne (1960) noticed fascicles of canine detrusor muscle directed toward the bladder neck which swung away from it and back toward the apex rather than continuing onto the urethra.

Of the three muscle layers of the bladder, only the middle circular one does not continue into the urethra, but ends abruptly at the bladder neck (Hutch, 1966; Tanagho, Smith, and Meyers, 1968). Tanagho, Smith, and Meyers (1968) describe an arc-like arrangement of muscle fibers around the internal meatus, well developed

ventrally, but poorly developed dorsally. Hutch (1966) and McNeal (1972) contend that these smooth muscle fibers form complete concentric circles around the internal meatus. However, there appears to be nearly general agreement that no band of constricting circular fibers exist at the bladder neck, which contract and relax reciprocally with the detrusor, as was once thought to constitute the internal sphincter.

The musculature of the urethra can be considered in three zones and appears to have a similar arrangement in the human and the dog. The proximal urethra is composed primarily of smooth muscle fibers which are continuations of the vesical musculature (Lapides, 1958; Woodburne, 1960; Hutch, 1966; Tanagho and Smith, 1966; Hutch and Rambo, 1967; Van Ulden, 1971; Leverett and Halverstadt, 1972). Striated muscle, which in the human arises from the urogenital diaphragm, forms the distal urethra (Hutch and Rambo, 1967). The middle region consists of both striated and smooth muscle fibers, the striated muscle lying more peripherally and covering the smooth muscle located central to it (Droes, 1971). The cranial limit of striated muscle fibers, as seen in human subjects (Van Ulden, 1971; Ellis, 1972), extends to within a few millimeters of the internal urethral orifice on the ventral and lateral aspects but not so far cranially on the dorsal side. In males, striated fibers of the urethra can be seen joining the prostatic capsule (Ellis, 1972) and inserting into the glandular tissue (McNeal, 1972). Striated muscle is more abundant in the ventral urethral wall than dorsally in both males and females (Hutch and Rambo, 1967).

The anatomy of the male urethra is complicated by the presence of the prostate gland in the proximal portion. The prostate develops from buds growing from the urethral epithelium, incorporating muscle fibers of the urethral wall in

its substance as it enlarges (Arey, 1965; Tanagho and Smith, 1968). According to Tanagho and Smith (1968), about one-third of the musculature of the urethra is included in the substance of the prostate in this manner.

Few detailed descriptions of the canine male urethra exist in the literature, the most complete reports being those of Trautman and Fiebiger (1957) and of G. C. Christensen (1964). Christensen divided the male urethra into prostatic, membranous and cavernous (or penile) portions, whereas Trautman and Fiebiger consider the prostatic and membranous urethrae together as the pelvic urethra. The wall of the pelvic portion is muscular and corresponds to the entire female urethra, whereas the penile portion of the urethra is surrounded by cavernous tissue with trabeculae rich in elastic fibers and blood vessels.

Both reports describe longitudinal folds of transitional urethral mucosa at rest, between which are crypts known as lacunae of Morgagni. The folds disappear with distention of the urethra leaving the cresta urethralis protruding into the lumen on the dorsal aspect. A prominence of the cresta urethralis is the seminal hillock (colliculus seminalis) on which is located the minute opening into the uterus masculinis. Lying beneath the mucosa is a submucosal layer, the stratum vasculare, composed of a dense plexus of veins interconnected in a manner characteristic of erectile tissue with smooth muscle fibers present in the trabeculae. Elastic fibers are prominent in the bladder neck area of this layer, but not so evident in distal portions (Leverett and Halverstadt, 1972). According to Christensen (1964), the stratum vasculare extends cranially from the urethral bulb, one-half to one-third the distance to the prostate gland and is continuous with the corpus cavernosum urethra of the penis. Peripheral to the stratum vasculare is the glandular layer, containing prostatic glands in the cranial pelvic urethra and some urethral glands

more caudally. Urethral muscle surrounds the glandular layer, smooth muscle lying central to striated muscle. Christensen states that the muscular layer overlaps the prostate slightly and ends caudally at the urethral bulb. He describes the smooth muscle as having primarily a longitudinal orientation with striated muscle fibers directed transversely and separated dorsally by a longitudinal fibrous raphe. In a histological study of the female canine urethra, Leverett and Halverstadt (1972) noted that all muscle layers were better developed ventrally, and striated muscle appeared in more cranial sections of the ventral aspect than dorsally.

The canine prostate gland is a musculo-glandular body incorporating the proximal part of the male urethra and bladder neck (Christensen, 1964). It consists of numerous compound tubular glands enclosed by interstitial connective tissue containing smooth muscle fibers. The gland is surrounded by a fibromuscular capsule which is partly covered on the dorsal surface by smooth muscle fibers from the wall of the urinary bladder. The precise arrangement of urethral musculature, both striated and smooth, in relation to the prostate gland is not described in the available accounts of canine male urethral anatomy.

Physiological Considerations

Pressure within the bladder is greater than atmospheric pressure and is equivalent to the sum of the tone of the bladder musculature plus the intraabdominal pressure. Changes in intraabdominal pressure due to coughing, sneezing, abdominal muscle tone, diaphragmatic movement and weight of abdominal viscera on the bladder are transmitted to intravesical pressure (Enhorning, Miller, and Hinman, 1964; Susset, Rabinovitch, and MacKinnon, 1965; Lewin, Culp, and Flocks, 1967).

From measurements of resting intravesical pressure listed in Table I, it is evident that the range of pressures is very wide.

TABLE I
RESTING INTRAVESICAL PRESSURES
RECORDED IN HUMANS AND DOGS

Species	Intravesical Resting Pressure (Mean or Range)	Reference
Human	15 cm H ₂ O	Tanagho <u>et al.</u> , 1966
Human	5-10mm H _g	Susset, Rabinovitch, and MacKinnon, 1965
Human (female)	4 [±] 1 cm H ₂ O	Enhorning, 1961
Human (female)	17 cm H ₂ O	Lapides <u>et al.</u> , 1960
Human (male)	13 cm H ₂ O	Lapides <u>et al.</u> , 1960
Human (female)	8.9 [±] 1.5 cm H ₂ O	Toews, 1967
Human	2 - 8 cm H ₂ O	Murphy and Schoenberg, 1962
Human ^a	25 cm H ₂ O	Tanagho <u>et al.</u> , 1966
Human ^b	20 cm H ₂ O	Tanagho <u>et al.</u> , 1966
Canine ^c	10 cm H ₂ O	Tanagho <u>et al.</u> , 1966
Canine ^c	11 - 28 cm H ₂ O	Lapides, 1958
Canine ^c	16 mm Hg	Holmquist and Olin, 1968
Canine ^{c, d}	< 10 cm H ₂ O	Fredericks <u>et al.</u> , 1969
Canine ^{c, e}	8.6 cm H ₂ O	Cass and Hinman, 1968

^a Standing

^b Seated

^c Anesthetised

^d After voiding

^e After injection of 85 ml radioopaque medium into bladder

Although the intravesical pressure exceeds atmospheric pressure, urine does not leak out of the normal resting bladder. Since there is no anatomical sphincter at the bladder neck, a physiological sphincter must operate to maintain continence, but its nature is unclear. Pressure within the urethra at rest has been shown to exceed intravesical pressure and since fluid will not flow from an area of lower to higher pressure, prevention of urine leakage has been attributed to this pressure gradient (Enhorning, 1961; Enhorning, Miller, and Hinman, 1964, Tanagho et al., 1966; Toews, 1967; Tanagho et al., 1969). The difference between intraurethral and intravesical pressures is known as closure pressure and it has been shown that this value is always greater than zero when urine is not flowing (Enhorning, Miller and Hinman, 1964). Examination of factors accounting for the creation of intra-urethral pressure is of great interest to the study of the physiology of the lower urinary tract.

The pressure development within both the bladder and urethra can be explained by the law of Laplace as applied to the sphere and the cylinder respectively. The pressure within the bladder remains relatively low as filling occurs, due to the development of tension in the wall (Claridge, 1965). The law of Laplace applied to a sphere is expressed $P = \frac{2T}{r}$ (P=pressure, T=tension, r=radius). As the radius increases, tension in the wall increases also and the intravesical pressure changes very little. As the bladder volume approaches capacity, the development of tension approaches its physical limit and the pressure then begins to rise rapidly. The law of Laplace for a cylinder is expressed $P = \frac{T}{r}$ and can be applied to the female urethra and the prostatic and membranous urethra in the male. Assuming that the urethral lumen is closed, as it is in the resting state, this allows for a very high

intraurethral pressure, even in the presence of low intramural tension (Claridge and Martin, 1965).

Woodburne (1960) believes that the high concentration of elastic tissue in the bladder neck and urethra maintains urethral closure. In fact, smooth muscle and elastic tissue are both well suited to such a function, having an inherent ability to maintain structural tone without expenditure of much energy, and without central nervous stimulation (Lapides, 1958).

All the structural components of the urethra contribute to intraurethral pressure to some extent, including tension of the fibro-elastic tissues, muscle tone and filling of the vessels of the stratum vasculare (Berkow, 1953; Enhorning, 1961; Tanagho, Meyers, and Smith, 1969^a; Tanagho, Meyers, and Smith, 1969^b; Raz, Caine, and Zeigler, 1972). The contribution of the muscle layers can be assessed by using selective neuromuscular blocking agents. Tanagho et al. (1969) found that administration of curare to female dogs would cause a profound pressure decrease at mid-urethra, but had little effect in the proximal urethra, reflecting the role played by striated muscle in each area. Atropine, which blocks smooth muscle activity, was found to have the most significant effect in the proximal urethra. Occlusion of the internal iliac arteries caused the intraurethral pressure to drop sharply by nearly one-third, indicating the significant contribution of the vascularity of the submucosal layer to urethral pressure (Raz, Caine, and Zeigler, 1972). The extrinsic pressure remaining when these three components have been eliminated is due to the physical characteristics of the collagenous and elastic components of the urethral tube.

Studies of intraurethral pressures in humans and dogs have shown that a definite pattern of intraurethral pressures exists (Enhorning, 1961; Enhorning, Miller, and Hinman, 1964; Tanagho et al. 1966; Toews, 1967). Enhorning believes

that the urethra is responsible for continence because his studies in women revealed the highest pressures in the system, not at the bladder neck, but within an area 1.5 - 3.5 cm distal to the vesicourethral junction. He showed that as long as there was a point in the urethra where the pressure exceeded that in the bladder, the individual would be continent at that instant. Toews (1967) made similar observations localizing the high pressures 1.5 - 2 cm from the bladder neck. Closure pressures were found to be significantly lower in women with stress incontinence¹ in both these studies. In anesthetized female dogs, Tanagho et al. (1966) recorded an average intravesical pressure of 10 cm H₂O and intraurethral pressures of 25 and 40 cm H₂O at one and two centimeters, respectively, from the bladder neck. He considers that the highest pressures represent the combined sphincteric action of striated and smooth muscle in the mid-urethra, and distal to this area the pressure declines rapidly.

There is evidence that pressure in the urethra increases during bladder filling. Tanagho et al. (1969) noted that a marked increase in proximal intraurethral pressure occurred during filling, although intravesical pressure rose only slightly. This effect is attributed to tightening of the "sling fibers" extending from the bladder to encircle the proximal urethra as tension increases in the bladder wall, and supports the concept that a urethral sphincteric mechanism exists which functions closely with the detrusor muscle.

The theory of the urethral sphincteric mechanism was tested by Lapidès (1958) who performed a series of urethral amputations in female dogs. He found that the bladder would contain fluid as long as a segment of urethra 2cm long was left intact.

¹ Leakage when intraabdominal pressure is suddenly increased.

If the urethra was cut shorter than this, urine would leak out of the bladder; stretching the segment would cause the leakage to stop, presumably by increasing tension in the segment.

Several investigators (Flocks and Culp, 1953; Lapidès, 1958; Tanagho et al., 1969; Islam, Boyd, and Laughlin, 1971) have fashioned tubular structures from sections of bladder wall to serve in place of the natural urethra. These neourethrae were found to maintain continence, resist increases in abdominal pressure, and permit voiding during detrusor contraction. The ability of these structures fashioned from detrusor muscle to simulate normal urethral function supports the theory of a natural urethral sphincter acting in concert with the detrusor.

When a neourethra was attached directly to the abdominal wall of dogs (Lapidès, 1958) the length was found to be critical to its efficiency: a 4cm tube permitted nearly normal urinary control, whereas a 1cm tube leaked badly. The significance of urethral length to continence was also emphasized by a follow-up study of human patients having undergone radical prostatectomy (Hutch and Fisher, 1968). The average urethral length was found to be significantly longer in the patients who were continent following surgery than in those who were incontinent.

Other authors (Jeffcoate, 1965; Hutch, 1966; Ardran et al., 1967) refute the concept of the urethra as internal sphincter. Ardran et al. (1967) repeated the urethral amputations in female dogs and found that continence was maintained at the bladder neck. Hutch (1966) describes a structure composed of the middle circular fibers of the detrusor musculature and the trigone which causes the base of the bladder to lie flat during rest. To this structure, the base plate, he attributes the function of the internal sphincter. Hutch recognizes a urethral sphincteric mechanism

but regards this as secondary and supplementary to the role of the base plate in maintaining continence.

Since it is believed that no actively constricting mechanism exists which seals the bladder neck during filling, relaxation of such a structure cannot explain the opening of the internal meatus during voiding. Based on anatomical considerations of the bladder neck area, it is now thought that contraction of the detrusor and trigonal musculature is responsible for opening the bladder neck (Hutch, 1966). In fact, Lapidès' experiment (1958) fashioning urethrae from detrusor musculature lends strong support to this concept. At the internal meatus inner longitudinal detrusor fibers continuing into the urethra can open the bladder neck when contracting around the globular bladder (Lapidès, 1958; Tanagho et al., 1966). Outer longitudinal fibers which attach to the trigone as well as contraction of the trigonal extension into the urethra can funnel the bladder base and contribute to opening the bladder neck, although the latter mechanism may not be significant in the dog (Woodburne, 1964; Homsey, 1967). Contraction of outer longitudinal fibers which arc around the bladder neck and do not extend onto the urethra may also assist in opening the bladder neck (Woodburne, 1960). Shortening of the urethra due to contraction of longitudinal fibers from the detrusor decreases the tension in the urethral walls, and thereby decreases intraurethral pressure and resistance (Lapidès, 1958; Woodburne, 1960; Claridge, 1965). Tanagho, Meyers, and Smith (1969^b) showed that the intravesical pressures necessary to open the canine bladder neck without concomitant detrusor contraction are much higher than normal micturition pressures.

In the human, the term "external sphincter" generally refers to striated muscle of the urogenital diaphragm which exerts a compressing effect on the urethra

when it contracts (Hutch and Rambo, 1967). The striated muscle of the urethra is continuous with that of the urogenital diaphragm and Hutch (1966) considers it to be a part of the external sphincter, calling it paraurethral striated muscle. The levator ani muscle has no direct connection with the urethra but is closely associated with it and its tone contributes to urethral resistance in humans (Lapides et al., 1960).

In the normal human at rest, the urogenital diaphragm is in a state of tonic contraction (Lapides et al., 1960; Woodburne, 1960; Tanagho et al., 1966; Tanagho and Smith, 1968). When the bladder becomes very full, or during coughing or straining, striated muscle contraction increases urethral resistance by compressing the distal urethra and lengthening it (Lapides et al., 1960; Woodburne, 1961). Prior to voiding, relaxation of pelvic striated musculature causes urethral resistance to decrease (Lapides et al., 1960; Tanagho et al., 1966; Tanagho et al., 1969). Shortening of the urethra occurs and the urethro-vesical angle is altered so that the vesical base becomes coned rather than flat (Tanagho and Smith, 1968). Under these conditions, contraction of the trigone and detrusor opens the bladder neck. At the end of voiding, pelvic striated musculature contraction precedes cessation of detrusor contraction and stops the flow of urine (Lapides, Gray, and Rawlings, 1955; Lapides, Sweet, and Lewis, 1957). Any urine remaining in the urethra is returned to the bladder (Corriere, McClure, and Lipshultz, 1972). The pelvic striated musculature then returns to its normal tonic resting state.

Paralysis of the striated musculature of the pelvis does not cause incontinence or difficulty in initiating micturition in normal individuals (Lapides, Gray, and Rawlings, 1955; Lapides, Sweet, and Lewis, 1957; Krahn and Morales, 1965; Kleeman, 1970). The primary function of striated muscle contraction appears to be stopping the flow of urine. Under the effects of skeletal muscle paralyzing agents, human

patients are still capable of initiating and halting the urinary stream on command; only in stopping the stream is there a delay (Lapides, Sweet, and Lewis, 1957). This is strong evidence that detrusor activity alone is sufficient to cause micturition, and that such activity is under cortical control. The delay in stopping the stream without striated muscle contraction is due to the slower response time of smooth muscle. However, with the pelvic musculature constantly in the relaxed state, the individual cannot respond to sudden increases in intraabdominal pressure. This is the situation in stress incontinence in which the urethral resistance is decreased by weakening of the urogenital diaphragm and the levator ani muscles. The urethra is perpetually in a state normally found preparatory to voiding (Woodburne, 1965; Tanagho and Smith, 1968).

Certain investigators have stated that because the external sphincteric mechanism is composed of striated muscle and therefore subject to fatigue, it cannot be responsible for continence on a long term basis (Claridge, 1965; Hutch, 1966). Nevertheless, if the internal sphincteric mechanism is destroyed, as by prostatectomy of the human, the individual is not incontinent as long as the external sphincter is intact. Abolition of the external sphincteric mechanism produces incontinence only if the internal sphincter is already nonfunctional (Lapides, Sweet, and Lewis, 1957).