PHARMACOLOGY OF THE LOWER URINARY TRACT MUSCULATURE

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BY

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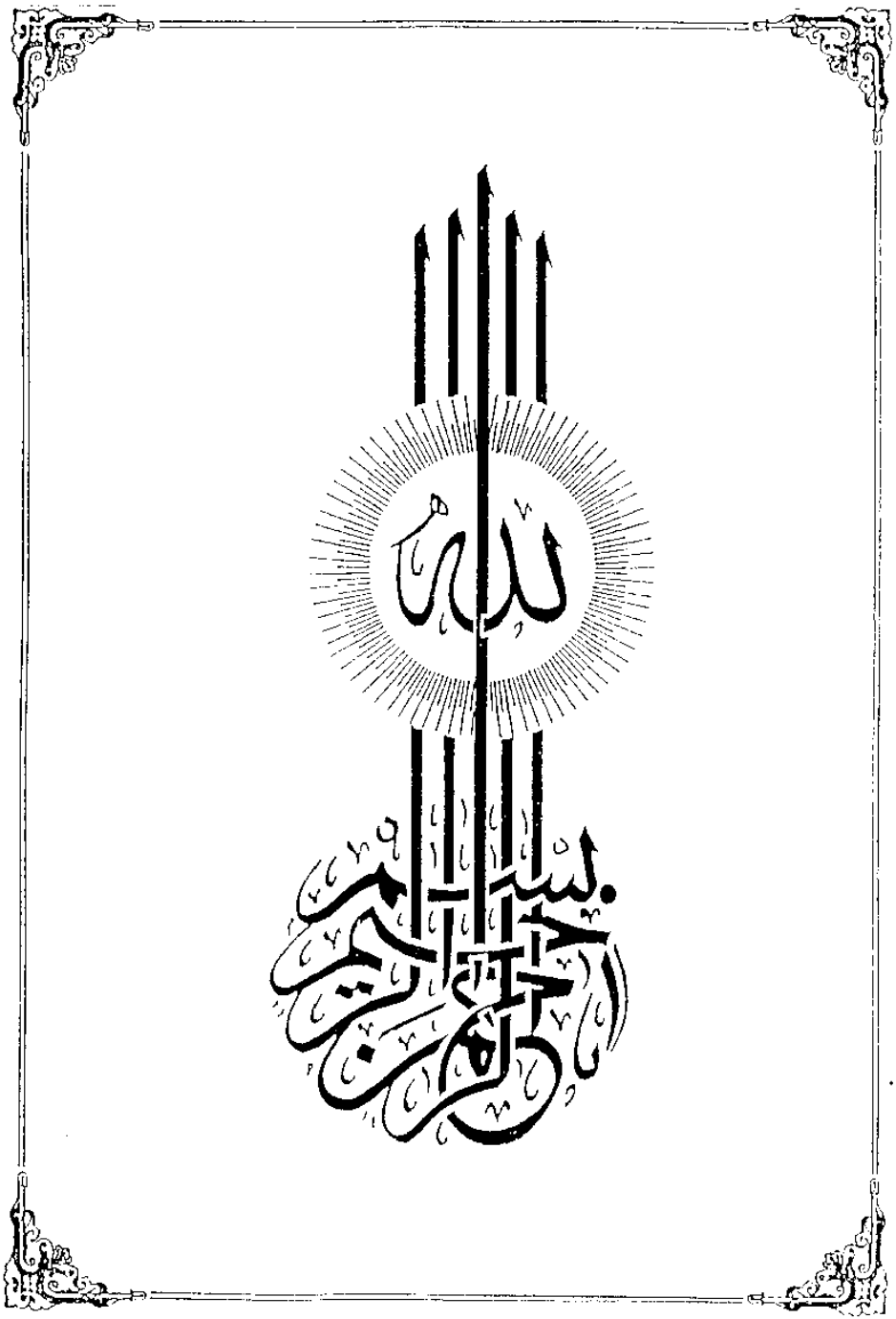

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descend and loop around the proximal urethra and then turn back to the outer surface of the bladder. In the female, the arrangement is the same, except that instead of penetrating the substance of the prostate the fibres end in the vesico-vaginal septum.

2- The trigone:

The trigone seems to be superimposed over the detrusor and is composed of two layers.

The superficial trigone. The fibres of the intravesical ureter diverge at the ureteral orifice. Some of which run across the base of the trigone and the rest fan out and converge at the internal meatus to proceed downward into the urethra in midline posteriorly. In the male, these fibres terminate at the level of the verumontanum, and in the female, some fibres reach the level of the external meatus.

The deep trigone. The fibromuscular fibres of the Waldeyer's sheath continue downward uninterrupted into the base of the bladder forming the deep trigone which ends at the internal meatus as a dense muscular fibrocollagenous structure. Immediately behind the deep trigone some detrusor circular fibres are firmly adherent or actualy fuse with it.

3- The bladder neck and internal urethral sphincter:

There are some controversies as regard the anatomical delineation of the bladder neck and the internal sphincter.

Tanagho discussed the anatomy of the bladder neck under three headings: the trigonal musculature, the detrusor muscle at the bladder outlet ; and the urethral musculature. Also, he denied the prescence of any seperate anatomic entity which can be delineated as the internal urethral sphincter (Tanagho, 1986).

Other authors described the bladder neck musculature in males as being formed by a concentration of detrusor smooth muscles around the internal meatus extending down in the preprostatic portion of the urethra or even up to the verumontanum. The term proximal, internal, or preprostatic urethral sphincter is given to this muscular component. The females do not possess a distinct smooth muscle sphincter at the bladder neck (Mitchell, 1981; Gosling, 1985; and Warwick, 1985).

4- The urethra:

The urethra and the bladder have the same origin and their musculature are directly continuous.

In the male, the urethral musculature is very compact and contains abundant collagen tissue with widespread elastic fibres throughout its entire length.

In the female, urethral musculature consists of two coats: an inner longitudinal coat and an outer semicircular coat.

5- The external sphincter:

The striated skeletal muscle fibres encircle the membranous urethra in males forming an omega-shaped configuration deficient in midline posteriorly. In the female, it is more or less a complete ring surrounding the midurethral portion.

The precise histological nature of the myofibrils is still a matter of controversy. Some authors believe that it is formed of a mixture of : (1) Slow twitch fibres, which on contraction attain a slow amplitude and

can sustain it for a relatively long time; and (2) Fast twitch fibres, which usually attain a higher amplitude but sustain it for a shorter time (Tanagho, 1986; and Atta, 1986).

Other authors state that the external sphincter consists of a single population of slow twitch fibres with a mean diameter of 17.47 um ± 0.7um and the periurethral levator ani muscle consists of a heterogenous population of slow twitch and fast twitch fibres with mean diameters of 45.5 um ± 0.8 um and 59 um ± 3.4 um respectively (Gosling, 1981; Gosling, 1985; and Warwick, 1985).

CHAPTER II

INNERVATION OF URETHRO VESICAL UNIT

A- Peripheral innervation:

I. Autonomic receptors.

II. Motor Innervation.

III. Sensory Innervation.

B. Central Innervation:

I. Conus medullaris

II. Spinal pathway of the detrusor muscles and peri urethral striated muscle.

INNERVATION OF THE VESICO-URETHRAL UNIT

I. Autonomic receptors:

Clarification concerning the distribution of autonomic receptors is an important contribution toward the understanding of lower urinary tract physiology and pharmacology. Autonomic receptors are components in the membrane of the smooth muscle cells that react with specific neurotransmitters to produce specific action. Three main kinds of receptors are considered important to the lower urinary tract: alpha type adrenergic receptors, beta type adrenergic receptors ; and cholinergic receptors. (Raz, 1978).

Others are probably present, which are non-cholinergic, non-adrenergic and non-prostaglandin, but more investigations needs to be done to understand their exact influence on the lower urinary tract. (Klarskov, 1983).

1. The detrusor:-

In the bladder detrusor, both cholinergic, alpha adrenergic and beta adrenergic receptors are present. Cholinergic receptors are distributed generally throughout the detrusor muscle. In the dome of the

bladder, beta-receptors greatly predominate and there are very few alpha-receptors, whereas in the base of the bladder and the region of bladder neck the opposite occurs and the alpha receptors greatly predominate (Caine, 1981).

2. The Urethra:-

It was suggested that the longitudinal fibres of the bladder outlet region that extend down to the urethra are supplied by cholinergic receptors and respond, by contracton, to cholinergic agonists, whereas the circular urethral muscle fibres response is sluggish or not at all. The alpha receptors supply both muscle layers, and the beta type supplies mainly the circular rather than the longitudinal fibres (Hassonna, 1983).

The alpha $_2$ subtype of alpha adrenoceptors and the muscarinic cholinoceptors may be also located prejunctionally on noradrenergic nerve terminals of the urethra controlling noradrenaline release from these nerves. (Mattiasson, 1984).

3. The prostate:-

The alpha receptors supply both the adenomatous, and the peripheral capsule of the prostate, but the

magnitude of receptors is much greater in the capsule. This marked difference may to some extent be explained by the difference in the relative amount of muscular tissue in each of them. (Caine, 1975).

Recently, the binding sites of both alpha $_1$ and alpha $_2$ subtypes of adrenoceptors were demonstrated, and the ratio between alpha $_1$ and alpha $_2$ was 3/2 in non hyperplastic specimens of prostatic tissue (Hedlund, 1985).

Examination of human prostatic adenomas removed by open prostatectomy revealed increased concentration of alpha $_2$ adrenoceptors, which regulate the prostatic urethral resistance. The receptor density was not directly proportional to the weight of the removed adenoma (Lepor, 1984b).

The prostatic capsule showed a marked response to cholinergic stimulation. This way of reaction may be due to the fact that the capsule is not derived from the prostate but is entirely distinct and represent the outer muscle layer of the urethra (Hutch, 1970).

Lepor in (1984a), identified high affinity muscarinic cholinergic receptors in prostates from men with BPH, and these muscarinic cholinergic receptors have been localized to the epithelial components of the prostate.

II- Motor innervation:

1- To the detrusor:

These nerves are part of the parasympathetic nervous system. They arise from S_2-S_4 and pass through the pelvic nerves. The trigonal portion of the bladder, because of its different embryological origin, is innervated by motor fibres from the thoraco-lumbar outflow (T11 to L5) of the sympathetic nerve (Fig. 1) (Tanagho, 1981).

The pelvic ganglia are located in the connective tissue of the pelvis and the interstices of the detrusor muscles. The anatomy of a single pelvic ganglion is believed to be similar to that described for the cervical sympathetic ganglion.

The preganglionic input from the hypogastric and pelvic nerves terminates synaptically on the dendrites

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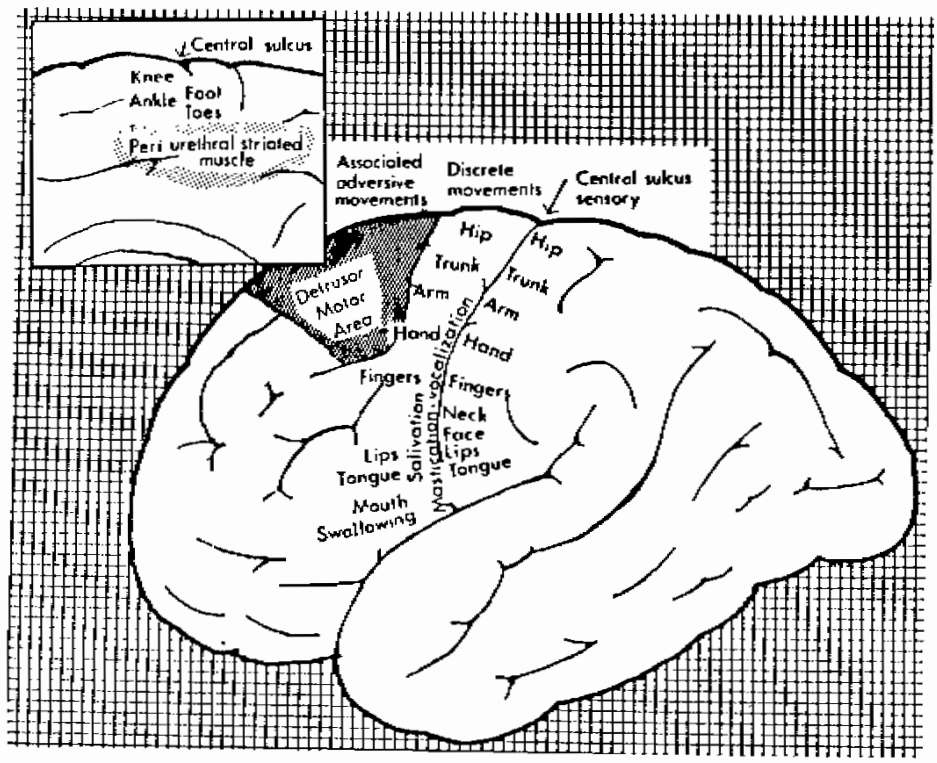

Fig. 1:

Representation of detrusor muscle control and periurethral striated muscle in the cerebral cortex.

(Hald and Bradley, 1982)

of the neurons, axodendritic synapses ; and occasionaly on the cellsoma of the ganglionic neurons (Fig. 2). The pre- and post-ganglionic axons consist of cholinergic and adrenergic nerves (Hald, 1982; and Bradley, 1986).

The interrelationship of post-ganglionic axons to the vesico-urethral lisosphincter (internal sphincter) were studied ultrastructurally in cats and rats of both sexes. Direct axoaxonal contacts between cholinergic and adrenergic axons are more common in preterminal axon bundles and at neuro effector junctions (El badawi, 1984).

2- To the external sphincter:

The motor nerve supply to the external sphincter and perineal muscles is somatic (voluntary) arising from S 2-4, and reaches these structures through the pudendal nerves. However, recent studies on dogs, suggested that the pelvic nerves may contain somatic fibres innervating the external urethral sphincter (Morita, 1984).

3- To the prostate gland:

The human prostate is innervated by both cholinergic and adrenergic fibres. The former fibres are more prevalant in the prostatic capsule than the