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Anatomy of the Upper and Lower Urinary Tract

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1.1 Introduction

Urine is produced in the two kidneys, conveyed by their respective pelvises and ureters to the bladder where it is stored temporarily, and finally exuded via the unique urethra at the individual's convenience. The kidneys and the ureters form the paired upper urinary tract; the bladder and the urethra build up the unpaired lower urinary tract.

The urethra shows distinct sex differences. Whereas the female urethra is purely urinary, the male urethra serves both urinary and reproductive purposes, of which the latter one is essential, the former merely the use of a tube almost entirely genital.

1.2 Upper Urinary Tract

1.2.1 The Kidneys

The kidneys are composed of structures which passively filtrate the blood plasma forming the primary urine, of structures which actively modify this primary urine by resorption and secretion forming the secondary urine, and several endocrine structures which release erythropoietin, renin, 1,25-dihydroxycholecalciferol and various other soluble factors with metabolic actions.

The kidneys are situated paravertebral in the upper retroperitoneal space, well wrapped up in a specialized adipose tissue. This adipose capsule also embeds the suprarenal glands. In supine position, the cranial border of the upper poles is approximately on the same level with the upper border of the 12th thoracic vertebral body, caudally with the third lumbar vertebra and therefore about 2.5 cm above the iliac crest. The right kidney is usually positioned about 1.5 cm inferior, probably due to the liver's volume on this side. In upright position, the kidneys are situated about 2.5 cm lower; they can ascend and descend slightly with respiration. The left kidney is slightly longer [1, 2] and wider [3] and lies nearer to the median-sagittal plane. Sex differences in renal dimensions are mainly due to the different body height [1]. Renal length decreases with age, and the decrease rate seems to accelerate at 60 years and upward [1, 4].

The long axis of each kidney is orientated infero-laterally, the transverse axis postero-laterally, due to the underlying psoas major muscle.

Each kidney consists of an upper and a lower pole, a convex anterolateral surface, a more or less flat posteromedial surface and a continuously convex lateral border. The medial borders are convex at the poles and concave in between. In this concavity, the renal hilum opens to the renal sinus bounded by anterior and posterior lips. Through the hilum pass the renal vessels, nerves and the renal pelvis, the renal vein usually anteriorly and the renal pelvis posteriorly, with the renal artery in an intermediate position. The renal sinus is lined with the renal capsule and contains the main part of the renal pelvis and vessels. Into the sinus project 4–19 renal papillae (median: 8) resembling the tips of the renal pyramids [5].

1.2.1.1 The Renal Medulla

The renal medulla consists of 4–19 renal pyramids. Each pyramid is cone-shaped with the blunt apex forming the renal papilla. Except for this papilla, the renal cortex surrounds each pyramid forming a renal lobe (renunculus). By fusing several lobes side by side, the cortical tissue in between the pyramids forms the so-called renal columns, which are in fact not columns but partitions or septa ("cloisons de Bertin") [6]. Eight to 130 papillary ducts (of BELLINI) open out at each papilla into the minor calices of the renal pelvis [5].

1.2.1.2 The Renal Cortex

The renal cortex embraces each of the renal pyramids except for their papilla. The interpyramidal portions of the cortical tissue are called renal columns. The subcapsular portion of the cortex itself is subdivided into an outer and an (inner)

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L. Liao, H. Madersbacher (eds.), *Neurourology*, https://doi.org/10.1007/978-94-017-7509-0_1

juxtamedullary cortex around the bases of the renal pyramids. The arcuate arteries and veins demarcate these two portions. Out of the pyramids' bases medullary rays rise up into the subcapsular cortex.

1.2.1.3 The Renal Parenchyma

The renal parenchyma is composed of a huge number of uriniferous tubules, bound by a little connective tissue comprising blood vessels, lymphatics, and nerves. Each of these uriniferous tubules consists of two embryologically distinct components: the urine-producing nephron and a collecting tubule. These collecting tubules drain several nephrons towards a terminal papillary duct.

The Nephron

The nephron consists of a renal corpuscle, responsible for the initial filtration from the plasma (primary urine), and a renal tubule, concerned with the selective absorption from and secretion into the glomerular filtrate to form the final (or secondary) urine.

There are a half to one million of renal corpuscles per kidney; their number declines significantly with age [7]. They can be found throughout the renal cortex with the exception of a narrow peripheral cortical zone. They have an average diameter of about 200 µm. The (parietal) corpuscular wall (of Bowman) resembles the initial expanded end of the renal tubule and is lined with a squamous epithelium. The visceral sheet engulfing the convoluted glomerular blood vessels is composed of specialized epithelial podocytes. These are flat, stellate cells. Their major processes curve around the glomerular capillaries and interdigitate tightly with each other, forming narrow gaps between these cellular extensions.

The glomerulus is a lobulated collection of convoluted capillary blood vessels covered by the podocytes. Scant connective tissue unites these vascular loops forming a mesangium. The glomerulus is feed by an afferent arteriole which usually enters the corpuscle opposite the exit of the renal tubule; an efferent arteriole emerges at the same site.

The proper renal tubule consists of:

1. a proximal convoluted tubule;
2. a proximal straight tubule entering the medulla;
3. the ansa nephroni (loop of Henle) with
   (a) a thick segment of the descending limb;
   (b) a thin segment of the descending limb;
   (c) the U-turn;
   (d) a thin segment of the ascending limb; and
   (e) a thick segment of the ascending limb.
4. a distal straight tubule;
5. an intermediate macula densa, where the tubule comes close to a glomerulus, and finally;
6. a distal convoluted tubule which finally enters via a junctional tubule into a collecting tubule.

A single layer of mainly isoprismatic epithelium lines the renal tubules, where the type and specific form of the epithelial cells vary according to the functional roles of the different segments.

The mitochondria of proximal convoluted tubule cells are the production site of circulating 1α,25-dihydroxycholecalciferol ($1{,}25(OH)_2D_3$) [8]. The production of $1{,}25(OH)_2D_3$ at this site is strictly regulated. The parathyroid hormone markedly stimulates $1{,}25(OH)_2D_3$ production, whereas $1{,}25(OH)_2D_3$ itself suppresses production.

The collecting tubules hold different cell types, the principal epithelial cells and the intercalated cells [9]. These intercalated cells (IC), also known as mitochondria-rich cells or dark cells, are the "professional" H^+ and HCO_3 transporting cells [10]. The IC exist in two canonical forms: α and β. The α form secretes H^+ into the urine, whereas the β form secretes HCO_3^- into the lumen [10]. Under normal conditions erythropoietin production also occurs mainly in these intercalated cells [11]. In severe hypoxic condition erythropoietin production also takes place in peritubular fibroblastic cells [11].

1.2.1.4 The Juxtaglomerular Apparatus as Site of Renin Production

The afferent and efferent arterioles of a glomerulus enter the mesangium at the vascular pole of a renal corpuscle. In each nephron, the ascending limb of its ansa (loop of Henle) returns from the medulla towards its glomerulus and the intermediate macula densa of the distal tubule and comes in close contact with the afferent and efferent vessels. In this contact area, the cells of the tunica media of the afferent arteriole—and to a lesser extend also the efferent arteriole—differ from smooth muscle cells elsewhere in being large, rounded and granulated with large spherical nuclei and dense vesicles positive for renin. In between the macula densa and the afferent and efferent arterioles lie the so-called Goormaghtigh (G) cells, forming parts of a sensitive nervous body ("corpuscules nerveux sensitifs") [12, 13].

Morphologically and functionally, the afferent arteriole can be divided into a proximal—renin-negative—and a distal—renin-positive—portion. Whereas the media of the proximal portion consists of a monolayer of plain smooth muscle cells not different from those of other resistance vessels, the media of the distal afferent arteriole is composed of renin-producing, granulated cells which are negative for smooth muscle myosin. These cells are often arranged asymmetrically. This distal portion is not limited to the juxtaglomerular region itself but is also found further upstream.

In addition, the efferent arteriole can be divided into a proximal and a distal portion. The proximal portion also comprises renin-positive cells and is not limited to the juxtaglomerular apparatus itself but spreads further downstream.

The G cells show scanty cytoplasm and a chromatin-rich nucleus. They pile up to a cone with the base facing the macula densa and its apex merging continually into the glomerular mesangium. Human G cells have the shape of a flatly pressed cylinder and are oriented parallel to the basis of the macula densa.

The whole juxtaglomerular apparatus is densely innervated by sympathetic fibers, where single individual axons contact multiple vascular cells and renal tubules [14]. The activation of renal sympathetic nerves leads to volume retention via sodium reabsorption, a reduction in renal blood flow, and activation of the renin-angiotensin-aldosterone system through stimulatory effects on the juxtaglomerular apparatus and subsequent renin release [15]. Additionally to these postganglionic efferent sympathetic fibers, the renal nerves also contain sensory afferent ones [16].

At least two ways of signaling are known, one to the arteriolar smooth muscle cells and another one to the renin producing cells in the glomerular arterioles [17]. Long-term decreases of NaCl intake lead to a reduced NaCl concentration at the macula densa site leading to renin secretion, while increases in the distal delivery of NaCl activate the tubuloglomerular feedback mechanism and contract the afferent arteriole, thereby regulating the single nephron glomerular filtration rate. This latter effect strongly contributes to the autoregulation of the renal blood perfusion and filtration rate.

1.2.1.5 The Renal Vascular System

The complex renal vascular patterns show regional specializations, closely adapted to the spatial organization and functions of the renal corpuscles, tubules, and ducts, and prone to a huge variability.

A single renal artery to each kidney is present in about 70% of individuals, with the others having one to four accessory renal arteries. Whereas the renal artery generally enters the renal sinus via the renal hilum, aberrant renal arteries pierce the fibrous renal capsule outside this hilum; such aberrant renal arteries may arise either directly from the aorta or from the pre-renal branches of the (proper) renal artery. Each renal artery gives off one or more inferior suprarenal arteries and branches which supply the perinephritic tissues, the renal capsule, pelvis, and the proximal part of the ureter. Near to the renal hilum the renal artery splits into an anterior and a posterior division, the primary branches of which (segmental arteries) supply the renal vascular segments. There have been different definitions of arterial segmentation, with the most common distinguishing an apical, a superior, an inferior, a middle, and a posterior segment. Each segment is supplied by a virtual end-artery. In contrast, the larger intrarenal veins have no segmental organization and anastomose freely. The initial branches of the segmental arteries are lobar, usually one to each renal pyramid, but before entering they subdivide into two or three interlobar arteries, extending towards the cortex around each pyramid. At the junction of the cortex and the medulla, interlobar arteries split into arcuate arteries, which diverge at right angles; as they arch between the cortex and the medulla, each divides further, and from their branches, interlobular arteries diverge radially into the cortex. These interlobular arteries ascend towards the superficial cortex or may branch a few times en route. Some traverse the surface as perforating arteries to anastomose with the capsular plexus [18]. Afferent glomerular arterioles are mainly the lateral branches of interlobular arteries. From most glomeruli, efferent glomerular arterioles soon divide to form a dense peritubular capillary plexus around the proximal and distal convoluted tubules. Thus there are two sets of capillaries in series, glomerular and peritubular, linked by efferent glomerular arterioles in the main renal cortical circulation.

From the venous ends of the peritubular capillary plexus fine radicles converge to form interlobular veins, one with each interlobulary artery. Many interlobular veins begin beneath the fibrous renal capsule by the convergence of several stellate veins, draining the most superficial zone of the renal cortex. Proceeding to the corticomedullary junction, interlobular veins also receive some ascending vasa recta and end in arcuate veins which accompany the arcuate arteries, but, in contrast to the arteries, anastomose with neighboring veins. Arcuate veins drain into interlobar veins, which anastomose and converge to form the renal vein.

Efferent arterioles of the glomeruli near the corticomedullary junction provide the vascular supply of the renal medulla, supplemented by some efferent arterioles for more superficial glomeruli, and ‘aglomerular’ arterioles. These efferent arterioles entering the medulla are relatively long, wide vessels, which, before they enter the medulla, contribute side branches to the neighboring capillary plexus where each of them divides into 12–25 descending vasa recta. These descend to varying depths into the renal medulla, contributing side branches to a radially elongated capillary plexus surrounding the descending and ascending limbs of the renal loops and collecting ducts. The venous outflow converges to the ascending vasa recta which drain into arcuate or interlobular veins. Especially in the outer medulla, the descending and ascending vessels form vascular bundles. As these bundles converge centrally into the renal medulla, they contain fewer vessels, some terminating at successive levels in the neighboring capillary plexus.

Renal lymphatics start with three different plexuses of initial lymphatics: (a) one around the renal tubules; (b) a second one under the fibrous renal capsule; and (c) a third perirenal one within the adipose capsule connecting freely with the second plexus. Within the kidney’s parenchyma, lymphatics occur between the tubules of the cortex, accompanying the interlobular and interlobar vessels, but extremely rarely in the medulla [19]. No lymphatics are present in the superficial cortex, the glomeruli and the interstitial tissue between the tubuli [20]. During inflammatory injury, new routes are created by the de novo formation of lymphatic vessels [21]. Lymphatic collectors from the intrarenal plexus form four or five trunks following the renal vein and end in the lateral aortic nodes. When these trunks leave the renal hilum, the subcapsular collectors join them. The perirenal plexus drains directly into the lateral aortic nodes.

1.2.1.6 The Renal Innervation

The renal plexus is formed by branches from the coeliac ganglion and plexus, the aorticorenal ganglion, the last thoracic and first lumbar splanchnic nerves, and the aortic plexus. Within the renal plexus there are small ganglia; the largest of them is usually situated behind the renal artery's outflow (aortico-renal ganglia) [22].

The lesser thoracic splanchnic nerve, derived from the 9th and 10th or 10th and 11th thoracic paravertebral ganglia, innervates the coeliac and aorticorenal ganglia, which send branches to the renal plexus. The last thoracic splanchnic nerve, derived from the 12th thoracic paravertebral ganglion, synapses directly on the renal plexus. The upper lumbar splanchnic nerve, derived from the first lumbar paravertebral ganglion, sends fibers to the intermesenteric plexus as well as branches that synapse directly on the renal plexus. Fibers from the superior portion of the intermesenteric plexus also run directly to the renal plexus. Additional fibers from the greater splanchnic nerve, the inferior portion of the intermesenteric plexus and the superior portion of the hypogastric plexus may be present in some cases.

As the renal nerves course toward the kidney, the majority of the nerve fibers converges around the renal artery within the adventitia and continues into the kidney around the arterial branches. Contributions from the inferior intermesenteric or superior hypogastric plexus may pass via the gonadal artery and plexus to the superior ureter and inferior aspect of the renal pelvis. There are more nerve fibers on the ventral aspect of the main renal artery than on the dorsal one.

The renal nerves supply the vessels, the juxtaglomerular apparatus, and—mainly—the cortical tubules. They are mostly vasomotoric, but afferent fibers have also been isolated.

1.2.2 The Renal Pelvis

The revulsive urinary system actually starts with the papillary ducts (of Bellini). Nevertheless, the initial isolable part is the renal pelvis within the renal sinus. The renal pelvis consists of the minor and major renal calices and the proper pelvis, which leaves the renal sinus by the renal hilum. Medially to and at the height of the inferior pole of the kidney the renal pelvis proceeds into the ureter.

The minor calices surround the renal papillae. Here, the (internal) renal capsule covering the renal columns in the sinus fuses with the adventitia of the minor calices. A minor calix is trumpet-shaped and surrounds either one or, more rarely, groups of two or three papillae. The minor calices fuse with others, thus forming two or possibly three larger major calices. These major calices fuse again within the renal sinus and thus form the final renal pelvis. Several analyses of the kidney structure showed that the calices and the renal pelvis are extremely variable in shape, ramified (94%) or ampullary (6%), number (3–22, mean 8.15) and location (2–5 groups in case of a ramified shape) [23]. Barcellos Sampaio and Mandarim-de-Lacerda [24] found perpendicular minor calices draining into the surface of the collecting system (11.0%), crossed calices in the mid kidney with the consequent formation of a region that they termed the interpelviocaliceal region (17.1%), calices related to the lateral kidney margin (in 52.9% the anterior and posterior calices were superimposed or alternately distributed), calices related to the polar regions (the superior pole with a midline caliceal infundibulum in 98.6% and the inferior pole with paired calices in 57.9%) and to the mid kidney (with paired calices in 95.7%), and bilateral symmetry of the casts (37.1%).

When the renal pelvis leaves the hilum, it tapers and finally continues into the ureter. Normally, the exact border between the pelvis and the ureter cannot be determined; thus, the term of a 'pelviureteric region' should be used [25].

The wall comprises three distinct histological layers, namely an adventitia being a sheet of connective tissue, a muscular lamina, and an inner mucosal layer. The latter consists of the transitional epithelium (or uroepithelium) and the underlying lamina propria, a sheet of fibro-elastic connective tissue. Although the urothelium appears to be built up by four or five separate layers of cells, all cells reach down to the basal membrane, thus forming a pseudostratified epithelium. The urothelium is composed of three cell types: the cuboidal basal precursor cells, the smaller and spindle-shaped intermediate cells, and the large polyhedral superficial umbrella cells [26]. Each of them may cover one or several cells of the underlying layer. They contain one to two round nuclei, while the cytoplasm presents, at the free surface under the apical plasma membrane, a condensation (the cuticle) that has the function of sealing the mucosa [27]. They are attached to one another near the luminal side by a junctional complex composed of zonulae occludentes, zonulae adherentes and maculae adherentes. These umbrella cells line the lumina of the urinary organs and are responsible for the main specific urothelial functions [26].

Within the muscular wall of the renal pelvis, an autonomous pacemaker system for the pelviureteric peristalsis is located at the border of the minor and major calices [28, 29]. This pacemaker system comprises a specialized type of smooth muscle in the wall of the renal calices and pelvis devoid of non-specific cholinesterase and possessing a number of unusual morphological features. 'Atypical' cells alone form the muscle coat of each minor calix and extend proximally into the wall of the caliceal fornix. These ‘atypical’ cells do not form compact bundles; instead, they are separated from one another by connective tissue forming a thin sheet of muscle. However, the inner layer of ‘atypical’ cells extends only as far as the pelviureteric region, leaving the proximal ureter devoid of a morphologically distinct inner layer [30].

Within the innermost part of the submucosa, nerve fibers (7–8 μm thick) run in longitudinal direction from the calices throughout the pelvis with many transverse interconnections, thus forming a 3-dimensional network or plexus also continuing into the ureter [28].

1.2.3 The Ureter

The ureter is a muscular tube of about 25–30 cm length which conveys urine from the renal pelvis to the urinary bladder by peristaltic contractions. The ureter has a downward inferior and medial trajectory, in the shape of the italic letter “S”, both in the transverse and in the sagittal plane [27, 31]. There are three ureteral inflexions: at the level of the inferior pole of the kidney, the marginal flexure (over the pelvic brim) and within the pelvis [27]. The ureter begins in the pelviureteric region; a slight constriction may mark this transition. It descends slightly medially and anteriorly to the psoas major muscle, enters the pelvic cavity by passing over the common iliac vessels, follows the pelvic floor in an anterior direction and finally opens into the base of the urinary bladder. The ureter’s diameter is about 3 mm (1.5–6 mm), slightly thinner in the pelviureteric region, the rim of the lesser pelvis near the medial margin of the psoas major muscle, and during its passage through the vesical wall.

Urologists arbitrarily divide the ureter beyond the pelviureteric region into the proximal, middle and distal part whereas in anatomical terminology the course of the ureter comprises three parts: the abdominal, the pelvic and the intramural part. The abdominal part descends retroperitoneally on the medial part of the psoas major muscle, separated from the tips of the lumbar costal processes. The ureter crosses in front of the genitofemoral nerve and is itself crossed by the gonadal vessels. At its origin, the right ureter is overlapped by the descending part of the duodenum. It descends lateral to the inferior vena cava, passes behind the right colic and ileocolic vessels and passes near the pelvic brim behind the caudal part of the mesentery and terminal ileum. The left ureter passes behind the left colic vessels and descends behind the mesosigmoideum in the posterior wall of the intersigmoid recess. The inferior mesenteric artery and its terminal branch, the superior rectal artery, follow a curved course close to the left ureter.

When the ureter passes over the division of the common iliac vessels, either slightly medially over the common iliac vessels (commonly left) or slightly laterally over the external iliac vessels (commonly right), its pelvic part starts. Often underestimated, the pelvic segment of the ureter is approximately 15 cm long and accounts for roughly half of the ureter’s total length. At first, it descends posterolaterally in the retroperitoneal tissue (descending part or parietal segment), ventrally to the internal iliac vessels and their visceral branches, along the anterior margin of the greater sciatic notch. Dorsally, marked venous plexuses also accompany it. Projected on to the lateral wall of the pelvis, the descending part of the ureter crosses the obturator artery, vein and nerve. Then, roughly at the level of the ischial spine, the pelvic ureter turns anteromediad into the subperitoneal tissue covering the levator ani muscle and internally towards the base of the bladder (bent part or visceral segment). Progressively it crosses, medially of the umbilical artery, the obturator neurovascular bundle, and the inferior vesical and middle rectal arteries. In males, the bent part of the ureter is crossed anterosuperiorly by the ductus deferens. Then it passes in front and somewhat above the upper pole of the seminal gland and finally enters the bladder wall, accompanied by inferior vesical vessels and the inferior hypogastric (pelvic) plexus. In females, the pelvic ureter initially has the same topographical relations as in males, but anterior to the internal iliac artery, it courses immediately behind the ovary, thus forming the posterior boundary of the ovarian fossa. In its bent part towards the bladder it under-crosses the uterine artery, the uterine cervix, and the vaginal fornices, passing through the broad ligament of the uterus (parametrium), approximately 1.5–2 cm (occasionally even 1–4 cm) away from the margin of the cervix of the uterus. The inferior hypogastric (pelvic) nerve plexus is positioned a little lower than the ureter, with the middle rectal vessels piercing almost at its center. Finally, the terminal female ureter runs forward, accompanied by the neurovascular bundle of the bladder. Just before entering the bladder it passes the anterior vaginal fornix. As a rule, the left ureter has a closer relation to the anterior wall of the vagina than the right one [32].

The intramural segment of the ureter runs obliquely through the bladder wall. Near the bladder, the muscular layer of Waldeyer envelops the terminal ureter. It coalesces with bundles of the detrusor muscle in the bladder wall and consists of coarser longitudinally arranged muscle bundles. Urine reflux is prevented since the ureter passes diagonally through the bladder wall musculature for a short distance before entering the bladder lumen. The length of this intramural part of the ureter in adults is 1.2–2.5 cm (in neonates approximately 3 mm [33]).

At the periureteric region, branches of the renal artery, which supply the renal pelvis, anastomose with the adventitial vascular plexus of the proximal descending part of the ureter (superior ureteral artery). Sometimes, even major descending branches participate in the blood supply of the upper ureter (30.7%). Branches of the gonadal arteries (middle ureteral artery) supply the following abdominal segment (7.7%). Additional branches derive from the aorta, sometimes forming a proper middle ureteral artery, and the common iliac arteries (15.4%). Overall, the nutrient branches for the abdominal segment of the ureter generally move up from the medial side. By contrast, the descending portion of the pelvic segment of the ureter is supplied by branches of the internal iliac artery (8.5%). These nutrient branches generally move up to the ureter from the lateral side. The bent portion of the pelvic segment of the ureter is supplied by branches of the internal iliac artery, especially the superior vesical artery (inferior ureteral artery) arising from the umbilical artery (12.8%). Moreover, the inferior vesical artery is chiefly engaged in supplying the lower wall of the retrovesical ureter (12.9%). Occasionally, the middle rectal artery also supplies the terminal segment of the ureter. In males, another nutritive branch is the artery to the vas deferens, which can arise directly from the internal iliac or from the umbilical artery. When running together with the vas deferens to the seminal vesicles, it extends branches to the wall of the bent part of the ureter. In females, the uterine artery, additionally supplies the bent portion of the pelvic segment of the ureter as it crosses the ureter. As the crossing is oblique, the ureter is contiguous to the uterine artery for 1–2.5 cm. All these arterial sources present multiple anastomoses, thus forming a periureteral arterial plexus. From this an inner plexus emerges which is characterized by densely convoluted, partly corkscrew-like arteries with small perforating arteries running radially and obliquely upwards and downwards through the intrinsic musculature and continuing to the mucosal vascular plexus.

Venous vessels accompanying the arteries provide the venous drainage towards the inferior vena cava, the iliac veins, and the vesico-genital plexus.

The lymphatic system starts with a network of initial lymphatics in the submucosa, the muscular layer, and the adventitia, and continues with collectors towards the para-aortic, lumbar and iliac lymph nodes. The collecting vessels of the upper ureter mainly join the renal collecting system or pass directly to the lateral aortic nodes near the origin of the gonadal artery; the collecting vessels of the lower abdominal part join the common iliac nodes; the collecting vessels of the pelvic part end in the common, external or internal iliac nodes.

The wall of the ureter comprises an external adventitia, a non-striated muscular layer and an inner mucosa. The ureteric adventitia is assembled by elongated fibrocytes and interwoven bundles of collagenous and elastic fibrils, and is approximately 2.5 mm thick. Numerous blood vessels, lymphatics and nerves intersperse it, mainly orientated parallel to the ureter's long axis. The muscular layer is uniform in thickness and about 750–800 µm in width. In the upper two thirds, a thin superficial circular and a thick deep longitudinal layer can be distinguished. In the inferior third, an additional external layer with longitudinal fibers is added (muscular layer of WALDEYER); it consists of coarser muscle bundles which emerge funnel-shaped from the most external musculature of the bladder wall onto the ureter, separated by a sleeve of connective tissue [27, 34]. The muscle bundles are frequently separated from each other by relatively large amounts of connective tissue. On the other hand, these muscle bundles often form interconnections. Due to the extensive branching, individual muscle bundles do not completely spiral around the ureter [25]. Ureteric muscle bundles consist of closely packed fusiform cells of about 300–400 µm length and 4–7 µm widest diameter. The ureteral mucosa is puckered in longitudinal folds and consists of the transitional epithelium (or urothelium) and the underlying lamina propria, a sheet of irregularly arranged fibro-elastic connective tissue [27]. The latter varies in thickness from 350 to 700 µm. The mucosa contains a vast amount of small blood vessels, many of them accompanied by small non-myelinated nerve fibers.

The ureteric nerves derive from the renal, aortic, and superior and inferior hypogastric plexus. Thus, the ureter is innervated by the lower three thoracic and first lumbar and the second to fourth sacral segments of the spinal cord. The superior hypogastric plexus is a delicate network of sympathetic preganglionic and visceral afferent fibers which are located beneath the level of the peritoneum, just inferior to the bifurcation of the aorta. The hypogastric nerves exit bilaterally at its inferior poles as one to three nerve strands which are the origin of the inferior hypogastric plexus. The pelvic splanchnic nerves (usually arising from the second to fourth sacral segment) traverse the inferior hypogastric plexus before its partition into its specific plexuses for the pelvic viscera. In the female, the branches of the uterovaginal plexus lie a little lower than the uterine artery and the ureter. The branches of the vesical plexus run inferior to the terminal ureter and extend to the trigone of the bladder. In the male, the inferior hypogastric plexus is located 1.5–2 cm dorsal and medial to the vesico-ureteric junction. From its ventrocranial portion the plexus releases the branches to the bladder, the terminal ureter, the seminal vesicle and the vas deferens. The pelvic splanchnic nerves traverse first the dorsocaudal portion of the inferior hypogastric plexus. From there the branches extend to the rectum and the prostate gland as far as the corpus cavernosum of the penis, the so-called erigent nerve(s).

In the adventitia the nerves consist of relatively large axon bundles forming an irregular plexus from which numerous smaller branches penetrate the ureteric muscular layer. These adventitial nerves either accompany the blood vessels or lie free in the adventitia around the ureter, unrelated to the vascular supply. Autonomic ganglion cells can be found only at the extreme lower end of the ureter. Within the ureter, two distinct neuronal networks exist which are in continuity with the plexus of the renal pelvis. The more prominent plexus sits in the submucosa between the lamina propria and the tunica muscularis, whereas the smaller plexus lies within the smooth muscle fibers of the muscular layer. Both plexuses show frequent interconnections [28]. In the muscularis, the nerve fibers can be found both between and within the non-striated muscle bundles. There is a gradual increase in innervation from the renal pelvis and upper ureter to a maximum in the juxtavesical segment. There are at least three different types of autonomic innervation: a cholinergic, a noradrenergic, and a peptidergic (substance P) innervation. Recently, also a purinergic signaling was described [35]. The intramural plexus consists of unmyelinated visceromotor and viscerosensory fibers.

1.3 Lower Urinary Tract

1.3.1 The Urinary Bladder

The urinary bladder solely serves as reservoir and varies in size, shape, position and relations, according to the volume of the contained urine and the state of the neighboring viscera. When it is empty, it is located entirely in the lesser pelvis but as it distends it expands anterosuperiorly into the abdominal cavity and the preperitoneal space. When empty, it is somewhat tetrahedral and has a fundus, a neck, an apex, a superior and two inferolateral surfaces.

The fundus or base is triangular in shape and oriented posteroinferiorly. In females it is closely related to the anterior vaginal wall, in males to the rectum but its upper section is separated from the rectum by the rectovesical pouch and below that by the vesicular glands (seminal vesicles) and deferent ducts. In a triangular area between the deferent ducts, only the rectovesical fascia separates the rectum and the bladder. The female analogue is the rectovaginal septum [36]; thus the sex-independent common term of a rectogenital septum should be used. The rectogenital septum (known in clinical literature as DENONVILLIERS' fascia) forms an incomplete partition between the rectum and the urogenital organs in both men and women. Ventrocranially the rectogenital septum constitutes an incomplete partition between the rectum and the urogenital organs, and it is caudally completed by the perineal body [37, 38]. It is composed of collagenous and elastic fibers and smooth muscle cells intermingled with nerve fibers emerging from the autonomic inferior hypogastric plexus [36].

Although the vesical fundus should, by definition, be the lowest part, in fact the neck is lowest and also the most fixed; it is located 3–4 cm behind the lower part of the pubic symphysis. It is pierced by the internal urethral orifice and even with varying conditions of the bladder and rectum it does not alter its position very much. In males, the neck rests on its wall and is in direct continuity with the base of the prostate; in females, it is related to the pelvic fascia which surrounds the upper urethra.

The vesical apex in both sexes faces towards the upper part of the pubic symphysis.

The superior surface, approximately triangular, is covered completely by the peritoneum in males. In females, the superior surface is also largely covered by the peritoneum, but posteriorly this is reflected to the uterus at the level of the internal os of the uterus, thus forming the vesicouterine pouch. The remaining posterior part of the superior surface, devoid of the peritoneum, is separated from the supravaginal cervix by fibroareolar tissue.

The inferolateral surfaces are separated anteriorly from the pubis and puboprostatic ligaments in males or pubovesical ligaments in females, respectively, by a retropubic fat pad and posteriorly by the fasciae of the levator ani and obturatorius internus muscles.

As the bladder fills, it becomes ovoid in shape. It detaches the parietal peritoneum from the suprapubic anterior abdominal wall and slips in-between. In extensive filling, the apex of the bladder may reach the umbilicus or even climb above it. The full bladder's apex points up und forwards above the attachment of the median umbilical ligament; thus, the peritoneum forms a supravesical recess of varying depth between the apex and the anterior abdominal wall.

In both sexes, strong bands of fibromuscular tissue extend from the bladder neck towards the inferior aspect of the pubic bones. These structures are called pubovesical ligaments and constitute the superior extensions of the pubourethral ligaments in females or the puboprostatic ligaments in males. The bilateral pubovesical ligaments lie one on each side of the median plane, leaving a midline hiatus passed through by numerous small veins.

From the apex, the median umbilical ligament, the remnant of the urachus, ascends on the inside of the anterior abdominal wall towards the umbilicus; the covering peritoneum forms the median umbilical fold. The urachus is an embryonic remnant resulting from the involution of the allantoic duct and the ventral cloaca and becomes progressively obliterated during fetal life [39]. The lumen of the lower part of the urachus may persist throughout life and communicate with the bladder cavity [40]. Towards the umbilicus the urachus and the obliterated umbilical arteries blend in a plexus of fibrous bands [41].

The vesical muscosa, attached only loosely to the subjacent musculature for the most part, folds when the bladder empties; as it fills, these folds spread. An exception is the vesical trigone where the mucosa tightly adheres to the subjacent muscular layer and is always smooth.

The internal urethral orifice forms the antero-inferior angle of the trigone, the ureteric orifices its postero-lateral angles. The interureteric crest forms the superior boundary of the trigone. This crest connects the two ureteric orifices and extends laterally as the ureteric folds, produced by the terminal intramural parts of the ureters. The ureteric musculature contributes directly to the superficial inner layer of the trigonal musculature. Most fascicles run to the midline and blend with those of the opposite side in the interureteric crest. Others spread through the trigone, its lateral margin being formed of somewhat more numerous fascicles directed toward the vesical orifice; yet very few fibers actually descend into the urethra itself [42].

The ureteric orifices are usually slit-like. In an empty bladder, they are about 2.5 cm apart and about the same distance from the internal urethral orifice; when filled, these distances may double.

The internal urethral orifice is usually found in the lowest part of the bladder. In adult males, particularly in those past middle age, immediately behind a slight elevation emerges, caused by the median prostatic lobe, the uvula of the bladder.

The wall of the bladder comprises three distinct layers: an outer adventitial layer, sometimes replaced by a serosal, peritoneal coating, a non-striated muscular layer, commonly known as detrusor muscle, and an inner mucous membrane (mucosa) lining the interior of the bladder.

Relatively thick interlacing bundles of non-striated muscle cells arranged as a complex meshwork construct the detrusor muscle; they are electrically coupled by gap-junctions [43]. This meshwork consists of a substantial middle circular layer and both an indistinct outer and inner layer of predominantly longitudinal muscle bundles. The caudal looping of the middle layer ventrally forms the thickest portion of musculature in both sexes. These muscle lamellae eccentrically encircle the internal urethral orifice perpendicular to the longitudinal axis of the urethra. However, the lamellae of the middle circular layer never directly adjoin the internal urethral orifice. The internal urethral or vesical sphincter, which elliptically encloses the internal urethral orifice, is located dorsally, laterally, and ventrally between the orifice itself and the middle layer of the bladder musculature [44].

The internal longitudinal layer is the thinnest of the three layers. The muscle bundles taper from cranial to caudal and end in the form of fibrous tendons at the dorsal circumference of the interureteric muscle [44]. Posteriorly, some of the outer bundles pass over the base of the bladder and fuse with the capsule of the prostate or with the anterior vaginal wall, respectively. Other bundles extend onto the anterior aspect of the rectum (rectovesical muscle). Anteriorly, some of the outer bundles join the pubovesical ligaments, thus contributing to the muscular components of these structures. At the entrance of the ureters into the bladder wall, some bundles of the outer layer extend funnel-shaped onto the outer surface of the ureters (muscular layer of WALDEYER). Similar to the muscular coat of the ureter, an exchange of fibers between adjacent muscle bundles within the bladder wall frequently occurs, thus forming a coherent unit of interlacing smooth muscle.

The smooth musculature of the trigone comprises two distinct layers: a deep outer layer, principally composed of muscles cells of the detrusor muscle and a superficial inner layer consisting of relatively thin muscle bundles continuing from the ureteric musculature (see above). This layer thickens along its superior border to form the interureteric muscle, thus elevating the interureteric crest. Similar, but less prominent, thickenings take place along the lateral margins of the trigone. The overall thickness of the musculature in the trigone increases with age and declines to a low level in the senium; it is higher in males than in females [45].

The ureterovesical junction is quite complex. The ureters pierce the posterior aspect of the bladder and run obliquely through its wall for a distance of 1.5–2.0 cm before terminating at the ureteric orifices. When passing through the detrusor muscle, the ureter is encircled by a sheet of connective tissue, which itself is in continuation with the sheet of connective tissue separating the proper ureteric musculature from the outermost muscular layer of WALDEYER of the terminal or juxtavesical ureter [46]. The mucosa of the ureters continues into the mucosa of the bladder itself, with the anterior-internal portions forming a tender mucosal falciform fold (or valve) over the orifices. The ureteric musculature continues into the superficial inner trigonal musculature, whereas the outer layer of the detrusor muscle encircles the juxtavesical part of the pelvic ureter [47].

The non-striated musculature of the bladder neck is distinct from that which comprises the detrusor proper [48]. In the male bladder neck, the non-striated muscle cells form a complete elliptical collar, which extends distally to surround the pre-prostatic section of the urethra. They form the internal urethral sphincter or vesical sphincter [44]. Distally, the bladder neck musculature merges with the stroma and capsule of the prostate gland. The female bladder neck seems generally more thickset due to the clearly shorter urethra compared to the male. This is also reflected in the course of the vesical sphincter. The muscle bundles embrace the bladder outlet in a more circular, less elliptical fashion. They are located around the proximal third of the urethra and are directly adjacent to the external urethral sphincter. As a whole, the vesical sphincter is clearly less distinctive in women than in men, however, it corresponds in all age groups to those in the male [44]. As in males, the female internal urethral sphincter does not originate from the bladder detrusor [49].

Throughout the detrusor muscle, c-kit-immunoreactive interstitial cells can be found. These cells are located at the junctional area between the inner circular and outer longitudinal smooth muscle fibers. They display the morphologic characteristics of cells that were formerly defined as the interstitial cells of Cajal or pacemaker cells in the gastrointestinal tract. In the superior vesical wall, an accumulation of such c-kit-immunoreactive interstitial cells was identified. It consists of small groups of accumulated cells surrounded by layers of connective tissue cells and fibers [50].

The mucosa of the bladder has a structure similar to that of the ureters and consists of a transitional epithelium, supported by a layer of loose connective tissue. This lamina propria consists of loose fibro-elastic connective tissue and forms a relatively thick layer, varying in thickness from 500 µm in the fundus and inferolateral walls to about 100 µm in the trigone. Small bundles of non-striated muscle cells occur in this submucosa, forming an incomplete and rudimentary muscularis mucosae. The connective tissue elements immediately below the transitional epithelium, particularly in the trigonal region, are densely packed. At deeper levels, they are more loosely arranged. Thereby the bladder mucosa is able to form numerous thick folds when the volume contained within the lumen is small. Throughout the submucosa an extensive network of blood vessels is present and supplies a plexus of thin-walled fenestrated capillaries lying in the grooves at the base of the urothelium. Besides this plexus, the lamina propria contains several types of cells, including fibroblasts, adipocytes, interstitial cells, and afferent and efferent nerve endings [51].

Outside the trigone, the urethelium comprises up to six cell layers; one layer of umbrella cells, one or more layers of smaller intermediate cells, and one layer of undifferentiated basal cells. Within the trigone the urothelium is flat and usually consists of only two or three cell layers. Additionally, in the neck and trigone a fourth cell type occurs. This consists of flask-shaped cells which extend throughout the whole depth of the urothelium. Numerous large membrane-bound vesicles, each containing a central dense granule, characterize them.

The identification of functional receptors/ion channels in the urothelial cells of the bladder and the involvement of these sensor molecules in the release of chemical mediators (nitric oxide, NO; ATP) suggest that urothelial cells exhibit specialized sensory and signaling properties. Such mechanisms might allow them to respond to their chemical and physical environments and to engage in reciprocal communication with neighboring urothelial cells as well as nerves in the bladder wall [52].

The principal arteries supplying the bladder are the superior and inferior vesical arteries. The superior vesical artery is the major and final branch of the patent rest of the umbilical artery, which originates from the anterior trunk of the internal iliac artery. The inferior vesical artery originates directly from the internal iliac artery, often together with the middle rectal artery, and supplies the vesical fundus, prostate, seminal gland, and the lower ureter. The inferior vesical artery sometimes provides the artery to the ductus deferens. Two major vascular plexuses (adventitial/serosal and mucosal) and two distinct capillary networks (muscular and subepithelial) can be distinguished in the successive layers of the wall. Almost all bladder vessels except the capillaries show an extensive tortuosity ranging from waviness to tight coiling. Larger branches of the main extravesical arteries and veins form the adventitial/serosal plexus characterized by a highly tortuous course of the vessels and numerous anastomoses. This plexus supplies and drains the capillary network of the detrusor muscle and sends long, perpendicular vessels piercing the detrusor muscle itself and communicating directly with the mucosal plexus. The perpendicular vessels are almost straight, wavy, tortuous, or tightly coiled, depending on whether they join the mucosal plexus near the top or near the base of the respective mucosal fold. The mucosal plexus consists of some capillaries, thin arteries and more numerous, thicker veins, presenting a tortuous appearance and frequent interlacements; it forms a distinct vascular layer parallel to the inner surface of the bladder, following the profiles of the mucosal folds. Short non-anastomosing arteriolar and venular twigs, often perpendicular to the surface plane and sometimes forming a palisade-like pattern, leave the upper aspect of the plexus and communicate with the subepithelial capillary network. The subepithelial capillaries form an extremely dense, planar meshwork. Only in the trigonal area and around the urethral orifice are they arranged in the form of a looser network with elongated meshes. The detrusor muscle itself contains occasional, very tortuous arterial and venous branches mostly derived from the adventitial/serosal plexus, and a poorly developed, irregular capillary network consisting of thin, uniform vessels. The vessels of the detrusor muscle are distributed in flat sheets probably corresponding to the connective tissue septa between the smooth muscle bundles [53].

The initial lymphatics start in the mucosal, intramuscular and extramuscular plexus. In the subepithelial layer lymphatics are rare. Within the deeper submucosa lymphatics are consistently present. They are often adjacent to and intermingled with arterioles and venules [54]. Lymphatic vessels, although small, are predominantly distributed in the detrusor muscle compared with the other layers; the tightest plexuses are situated at the borders between the submucosa and the detrusor as well as the detrusor and the adventitia [55]. Almost all collecting vessels end in the external iliac nodes. There are three sets: lymphatics from the trigone emerge on the vesical exterior to run superolaterally; those from the superior surface converge to the posterolateral angle and pass superolaterally across the lateral umbilical ligament towards the external iliac nodes; those from the inferolateral surface ascend to join those from the superior surface.

The nerves supplying the bladder form the vesical plexus and contain both efferent and afferent fibers. This vesical plexus from the anterior part of the inferior hypogastric plexus comprises many filaments which pass along the vesical arteries to the bladder. Branches also supply the seminal glands and deferent ducts. In addition to the branches from the vesical plexus, small groups of autonomic neurons occur throughout all regions of the bladder wall. Numerous preganglionic autonomic fibers form both axosomatic and axodendritic synapses with these ganglion cells. The bladder, including the trigone, is profusely supplied with nerves forming a dense plexus among the detrusor smooth muscle cells. Terminal regions approach to within 20 nm of the surface of the muscle cells and are either partially surrounded by or more often totally denuded of Schwann cell cytoplasm. The lamina propria of the fundus and inferolateral walls is virtually devoid of autonomic nerve fibers, whereas at the bladder neck and the trigone a nerve plexus extends throughout the lamina propria.

1.3.2 The Female Urethra

The female urethra is about 4 cm in length and 6 mm in diameter. It starts at the internal urethral orifice of the bladder and runs antero-inferiorly behind the pubic symphysis, embedded in the anterior wall of the vagina. It traverses the urogenital diaphragm and ends at the external urethral orifice, an antero-posterior slit with rather prominent margins. This orifice lies directly anterior to the opening of the vagina and about 2.5 cm behind the glans clitoridis. Except for the passage of urine, the lumen forms a transverse slit with the anterior and posterior wall in apposition. Many small mucous urethral glands and small lacunae open into the female urethra. Near the lower end, a couple of these glands are grouped together on each side and open into the para-urethral duct; each duct descends in the submucosal tissue and ends in a small aperture on the lateral margin of the external urethral orifice.

Throughout its pelvic course the female urethra has no direct ligamentous fixation to the pubic bone. Ventrolaterally, the urethra is enclosed by the ventral parts of the levator ani, its fasciae, and a ventral urethral connective tissue bridge connecting both sides. Dorsally, the urethra is intimately connected to the wall of the vagina [56].

The muscular wall of the female urethra consists of an outer sleeve of striated muscle, the external urethral sphincter, together with an inner layer of non-striated muscle fibers. The constituent fibers of this external urethral sphincter are circularly arranged and form a sleeve which is thickest in the middle first third of the urethra. The female external urethral sphincter system includes a true annular sphincter around the urethra (urethral sphincter, a part that passes anterior to the urethra and attaches to the ischial rami (compressor urethral muscle), and a part that encircles both the urethra and the vagina (urethrovaginal sphincter) [57].

As in males, the muscle fibers are quite thin and of the slow twitch type. The inner smooth muscle layer extends throughout the length of the female urethra and consists of thin muscle bundles which are orientated obliquely or longitudinally.

The mucous membrane is continuous with that of the bladder. It consists of a stratified transitional epithelium and a supporting layer of loose fibro-elastic connective tissue (lamina propria). This lamina propria contains an abundance of elastic fibers, which are arranged either longitudinally or circularly around the urethra, as well as numerous thin-walled veins. Proximally the female urethra is lined by the characteristic urothelium; nevertheless, distally the epithelium changes into a non-keratinized stratified epithelium lining the major portion of the female urethra. At the external urethral orifice this epithelium keratinizes and becomes continuous with the skin of the vestibule.

The constitution of the glands surrounding the human female urethra has been under debate; especially regarding as to what extent they equal the male prostate; a female prostate was found in a majority of women and can be distinguished from other urethral caverns and immature paraurethral ducts. Their glands consist of tubulo-alveolar acini at the end of one excretory duct, leading to the urethral lumen and are distributed mainly laterally or dorsolaterally of the urethral axis [58, 59].

A large number of unmyelinated nerve fibers are scattered throughout the connective tissue at the level of the proximal urethra. These nerve fibers are distributed in the smooth muscle layers of the vagina and urethra. Although these autonomic nerve fibers are predominantly located at 4 o'clock and 8 o'clock, they tend to spread throughout the periurethral connective tissue. Several myelinated nerve fibers accompany the unmyelinated fibers in the space between the anterior vaginal wall and the posterior surface of the urethra. At the level of the sphincter and distal urethra unmyelinated nerve fibers travel along the lateral vaginal walls and on the posterior surface of the urethra. These fibers penetrate the smooth muscle layers through the lateral walls and spread in the submucosa, smooth muscle layer and the transitional zone between the external smooth and the internal striated circular fibers [60].

Lymphatics from the complete female urethra pass mainly to the internal iliac nodes; a few may end in the external iliac nodes. Lymphatics from the membranous urethra accompany the internal pudendal artery.

1.3.3 The Male Urethra

The male urethra extends from an internal orifice in the urinary bladder to an external orifice, or meatus, at the end of the penis. Four distinct sections can be described:

a pre-prostatic, a prostatic, a membranous, and a spongiose section. When the penis is in its usual flaccid state, these sections form a double curve. Except during the passage of fluid, the urethral canal is a mere slit. In the prostatic section, this slit is transversely arched, in the membranous section it is stellate, in the spongiose section again transverse, while at the external orifice it is sagittal in orientation.

The pre-prostatic section of the male urethra has a stellate lumen. It is about 1–1.5 cm long, extending almost longitudinally from the bladder neck to the superior aspect of the prostate gland. The non-striated musculature surrounding the pre-prostatic urethra forms a distinct elliptical collar which distally becomes continuous with the capsule of the prostate gland. The bundles forming this internal urethral sphincter (or vesical sphincter) are separated by connective tissue containing many elastic fibers.

The prostatic section of the male urethra is approximately 3–4 cm long and, behind the fibromuscular stroma of the isthmus tunnels, through the prostate. Throughout most of its length the posterior urethral wall shows a midline ridge, the urethral crest, which projects into the lumen causing it to appear crescent in transverse section. On each side of the crest there is a shallow depression, the prostatic sinus, into which enter the orifices of the prostatic ducts. About the middle of the length of the urethral crest the colliculus seminalis (or verumontanum) forms an elevation on which the slit-like orifice of the prostatic utricle is situated. On both sides of or just within this orifice enter the ejaculatory ducts. Distally the prostatic urethra possesses an outer layer of circularly disposed striated muscle cells which are continuous with a prominent collar of striated musculature, the external urethral sphincter, within the wall of the membranous urethra. The urethra leaves the prostate slightly anterior to its apex, the most inferior point.

The membranous section is the shortest, least dilatable and, with the exception of the external orifice, the narrowest section. It descends with a slight ventral concavity from the prostate gland to the bulb of the penis, passing through the urogenital diaphragm about 2.5 cm postero-inferior to the pubic symphysis. The posterior part of the bulb is closely apposed to the inferior aspect of the urogenital diaphragm but anteriorly it is slightly separated from it, so that anteriorly the wall of the urethra is related neither to the urogenital diaphragm nor the penile bulb. This part of the anterior wall of the urethra is regarded as the ‘membranous’ part; anteriorly it is about 2 cm long, whilst posteriorly it is only 1.2 cm. The wall of the membranous urethra consists of a muscle coat which is separated from the urothelial lining by a narrow layer of fibroelastic connective tissue. This muscular coat consists of a relatively thin layer of non-striated muscle bundles continuous proximally with those of the prostatic urethra, and a prominent outer layer of circularly orientated, usually quite thin striated muscle fibers forming the external urethral sphincter. This external urethral sphincter, composed of slow twitch fibers, is devoid of muscle spindles and supplied by the pelvic splanchnic nerves.

The spongiose section is embedded in the corpus spongiosum penis. It is about 15 cm long. Commencing below the urogenital diaphragm, it continues the ventrally concave curve of the membranous urethra to a point anterior to the lowest level of the pubic symphysis. From there the urethra curves downwards in the ‘free’ part of the penis, when it is flaccid. The spongiose section is quite narrow (6 mm in diameter), and is dilated at its beginning forming the intrabulbar fossa and again within the glans penis forming the navicular fossa (up to 8–9 mm in diameter). The bulbourethral glands (Cowper) open into the spongiose section about 2.5 cm below the urogenital diaphragm; their orifices are 2–3 mm apart. The external orifice is the narrowest part of the urethra: it is a sagittal slit, about 6 mm long and bounded on each side by a small labium.

Except for the most anterior part within the glans penis, the epithelium of the urethra exhibits the orifices of numerous small mucous glands and follicles situated in the submucous tissue (urethral glands). Additionally, there are three to eleven small pit-like lacunae of varying sizes; the largest of them, the lacuna magna, is situated at the roof of the navicular fossa. The epithelial lining of the pre-prostatic and proximal prostatic urethra is of urethelial type as in the bladder. Below the openings of the ejaculatory ducts the epithelium changes to a patchily pseudostratified or stratified columnar variety which lines the membranous urethra and the major portion of the spongiose urethra. Mucus-secreting cells are common throughout this epithelium and frequently form small clusters in the spongiose urethra. Here the mucous membrane shows many recesses which continue into deeper branching tubular mucous glands (of Littré) which are especially numerous on the dorsal aspect. Within the proximal navicular fossa, the epithelial lining changes, sharply demarcated, to a non-keratinized, stratified squamous epithelium with well-defined connective tissue papillae. At the external urethral orifice, the epithelium keratinizes.

At the level of the bladder neck nerve fibers run under the pelvic fascia on either side of the rectovesical pouch, lateral and cranial to the rectum and the seminal vesicles, and penetrate into the bladder neck at 5 o’clock and at 7 o’clock. The autonomic nerves run beneath the fascia of the levator ani muscle along the posterolateral surface of the rectum, around the anterolateral aspects of the seminal vesicles and over the inferolateral aspect of the prostate. At this level nervous myelinated and unmyelinated fibers can be found on the posterior face of the bladder neck. Some unmyelinated fibers follow the ejaculatory ducts of the cranial prostate to reach the prostate and the prostatic urethra. At the level of the prostate and of the prostatic apex unmyelinated nerve fibers are situated outside and behind the prostatic capsule.

They send numerous branches following the ejaculatory ducts through the prostate gland until they reach the urethra at the level of the seminal colliculus. These branches also innervate the smooth muscular fibers of the prostatic urethra and the submucosa. At the level of the membranous urethra most of the autonomic nerve fibers penetrate the urethral sphincter muscle from the posterolateral surface and most of the myelinated nerves enter the urethral sphincter from the anterolateral surface [61].

Lymphatics from the prostatic and membranous urethra pass mainly to the internal iliac nodes; as in females, a few may end in the external iliac nodes. Lymphatics from the spongiose urethra accompany those of the glans penis, ending in the deep inguinal nodes. Some of them end up in medial superficial nodes; others traverse the inguinal canal and end in the external iliac nodes.

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