State budgetary educational institution of higher professional education

"North Ossetian State Medical Academy" of the Ministry of health of the Russian Federation

Department of surgical diseases № 2

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Tutorial “Urology”

Textbook for students 4 course
medical faculty of Urology

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UDC

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The authors presented modern methods for the research and treatment of different pathological conditions in Urology.
The textbook is developed on the discipline "Urology» in accordance with the requirements of the FSEI HPE, is intended for students at medical Universities and faculties, trained in the specialty 31.05.01 General Medicine using modern content from EAU, AUA guidelines, Campbell-Walsh Urology book and other articles.

The manual is developed in accordance with the requirements of the Federal state educational institution, is intended for senior students at medical Universities and faculties enrolled in the specialty 31.05.01 Medical business.

UDC -

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Contents

AP antegrade pyelography
AR androgen receptors
AUR acute urinary retention
ARPKD autosomal recessive polycystic kidney disease
ADPKD autosomal dominant polycystic kidney disease
AS active surveillance
AT active treatment
ADT androgen deprivation therapy
BRA bilateral renal agenesis
BEEC bladder exstrophy-epispadias-complex
BXO balanitis xerotica obliterans
BPH benign prostatic hyperplasia
BCR bulbocavernosus reflex
CSL cranial suspensory ligament
CT computed tomography
CPRE type of operation (exstrophy)
CIC clean intermittent catheterization
CMA chlormadinone acetate
CKD chronic kidney disease
DSD disorder of sex development
DRE digital rectal examination
DHT dihydrotestosterone
EPS expressed prostatic secretion.
ESWL extracorporal shock wave lithotripsy
EHL electrohydraulic lithotripsy
FSH follicle stimulating hormone.
GnRH gonadotropin- releasing- hormone
GU genitourinary tract
GFR glomerular filtration rate
HU Hounsfield
HPF high-power microscopic field
IPSS international prostate symptom score
IVU intravenous urography
ISUP International society of urological pathology
KUB Kidney-ureter-bladder
LUIS lower urinary tract symptoms
LDR low-dose rate
MCUG mixed cystourethrography
MIS Mullerian- inhibiting substance
MRI magnetic resonance imaging
MSK medullary sponge kidney
MM metanephric mesenchyme
MSRE type of treatment of exstrophy
NCCT non-enhanced computed tomography
NPH juvenile nephronophtisis

PUV posterior urethral valves
PSA prostate specific antigen
PNL percutaneous nephrolithotomy
PKD polycystic kidney disease
PTH parathyroid hormone
PHI prostate health index
PFR peak flow rate
PDEIs phosphodiesterase inhibitors
PN partial nephrectomy
RCC renal cell carcinoma
RAA renal artery aneurism
RPs Randalls plaques
RN radical nephrectomy
RBC red blood cell
SEM scanning electron microscopy
SRY sex-determining region of the Y chromosome
TAPP transabdominal preperitoneal approach
TEP total extraperitoneal approach
TURP transurethral resection of prostate
UPJ ureteropelvic junction
UPJO ureteropelvic junction obstruction
US ultrasound
UTI urinary tract infections
UB ureteric bud
URA unilateral renal agenesis
UC ureterocele
UGS urogenital sinus
VUR vesicoureteral reflux
VCUG voiding cystourethrogram
VB voided bladder
WD wolffian duct
WBC white blood cell
XGP xanthogranulomatous pyelonephritis

Question for check-up input knowledge

1. Anatomical features of kidney, ureter, bladder, urethra and male genital system (follow and describe crucial point).

2. What is a main unit of kidney? (Describe structure and the main function of unit)

3.Explain the main mechanisms of development of genitourinary abnormalities.

4. Embryogenesis of upper and lower urinary tract and male genital system (explain mechanism).

5. The main methods of diagnostic evaluation of abnormalities.

6. The main functions of kidney, bladder (describe).

7. Innervation of bladder, describe mechanism of voiding.

Scheme of answer about anatomy

1. Organ name
2. The main functions of organs.
3. Topography of organ (holotopiya, skeletotopiya, sintopiya).
4. External structure of an organ (form, parts, surfaces, lobes, grooves, hilum, etc.).
5. Internal structure of organ:

a) Structure of the wall coats of tubular organs (characteristic of mucous, fibrous, muscular, adventitia or serosa layers).

b) Internal structure of parenchymatous organs (lobes, hilum, segments, structurally functional units, features of intraorganic blood circulations).

6. Types of a covering of abdominal organs by peritoneum

Embryology of genitourinary tract

Embryologically, all three kidneys develop from the intermediate mesoderm (image 1): **pronephros**, **mesonephros** (regress in utero), **metanephros**. The mammalian *pronephros* is a transitory, nonfunctional kidney, analogous to that of primitive fish, that you may notice from third to five weeks from future region of neck and thoracic. The *mesonephros,* is also transient, but in mammals it serves as an excretory organ for the embryo while the definitive kidney, the metanephros, begins its development.

Development of the *nephric ducts* (also called the *wolffian ducts*) precedes the development of the mesonephric tubules. The nephric ducts can be seen as a pair of solid longitudinal tissue condensations at about the 24th day, developing parallel to the *nephrogenic cords* in the dorsolateral aspect of the embryo (image 2). Its blind distal ends grow toward the primitive cloaca and soon fuse with it at about the 28th day. As the ducts fuse with the cloaca, they begin to form a lumen at the caudal end. This process of canalization then progresses cranially in a reverse direction, transforming the solid tissue condensations into the definitive *nephric ducts with excretory capability*. Soon after the appearance of the nephric ducts during the 4th week, mesonephric vesicles begin to form. By 4 th month, the human mesonephros has almost completely disappeared, except a few elements that persist into part of the reproductive tract (in males, efferent ductules of the testes, epididymis, vas deferens; in females, nonfunctional mesosalpingeal structures) [5].

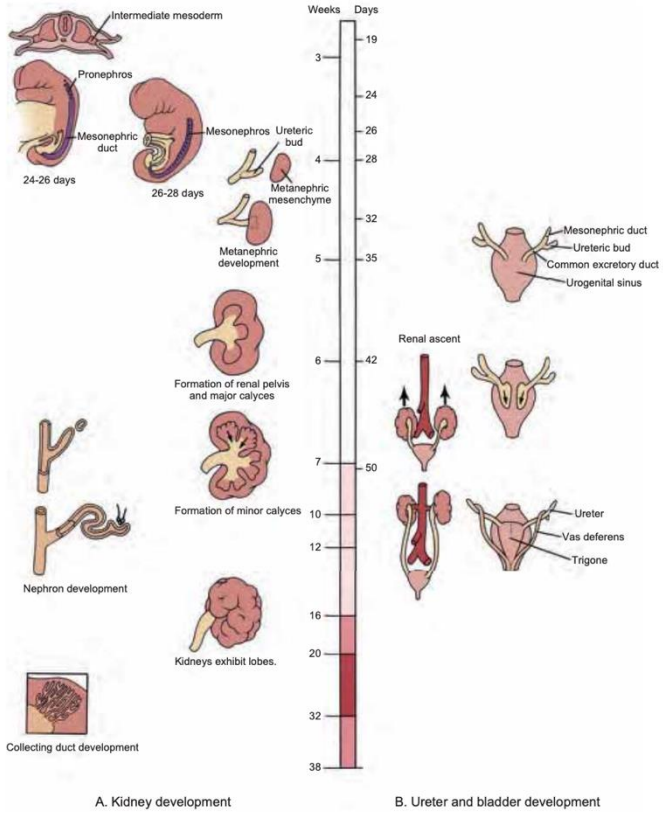


Image 1 – Development of urinary system (Campbell- Walsh Urology, chapter 122, embryology of genitourinary tract).

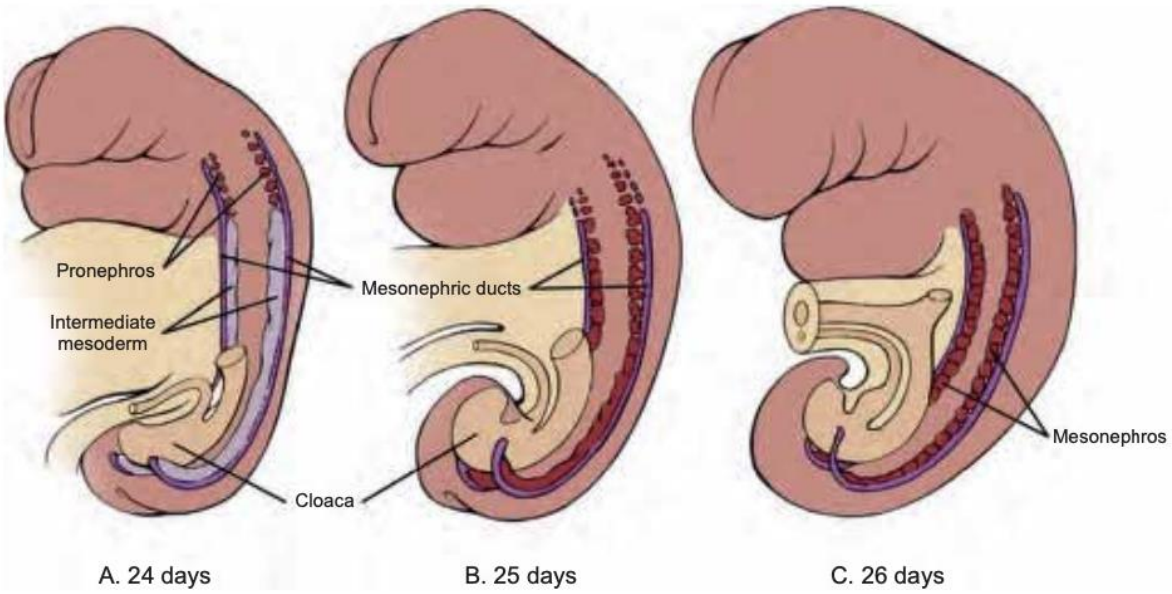


Image 2 – Development of pronephros and mesonephros (Campbell- Walsh Urology, chapter 122, embryology of genitourinary tract)

Development of metanephros. The definitive kidney, or the *metanephros,* forms in the sacral region as a pair of new structures, called the *ureteric buds,* sprout from the distal portion of the nephric duct and come in contact with the condensing blastema of *metanephric mesenchyme* at about the 28th day. The ureteric bud penetrates the metanephric mesenchyme and begins to divide dichotomously. The tip of the dividing ureteric bud, called the *ampulla,* interacts with the metanephric mesenchyme to induce formation of future nephrons via mesenchymal-epithelial interaction (image 3) [5].

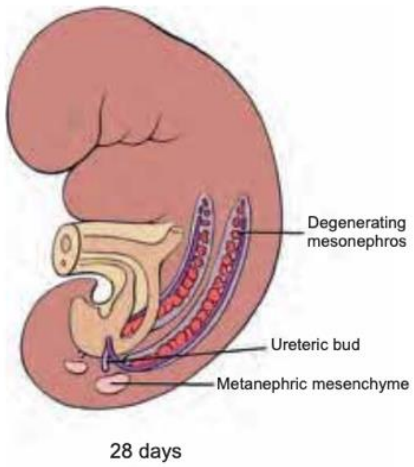


Image 3 – Development of metanephros (Campbell- Walsh Urology, chapter 122, embryology of genitourinary tract).

The nephron, which consists of the glomerulus, proximal tubule, loop of Henle, and distal tubule, is thought to derive from the *metanephric mesenchyme*, while the

collecting system, consisting of collecting ducts, calyces, pelvis, and ureter, is formed from the *ureteric bud* (image 4) [5]. The tip of the dividing ureteric bud induces the metanephric mesenchyme to condense, which then differentiates into a renal vesicle, that coils into an S-shaped tubule (forms a Bowman capsule, proximal convoluted tubules, distal convoluted tubules and loop of Henle). Ureteric bud contributes to the formation of collecting ducts.

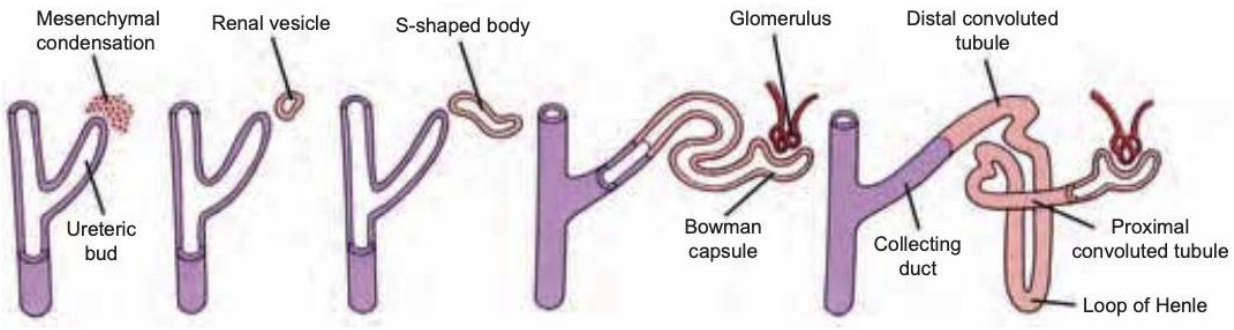


Image 4 – Development of nephrons and collecting duct (Campbell- Walsh Urology, chapter 122, embryology of genitourinary tract).

Renal ascent. The metanephros normally ascends from the sacral region to its definitive lumbar location between the sixth and ninth weeks. As the kidneys migrate, they are vascularized by a succession of *transient aortic sprouts* that arise at progressively higher levels. These arteries do not elongate to follow the ascending kidneys but instead degenerate and are replaced by *successive new arteries*. The final pair of arteries forms in the upper lumbar region and becomes the definitive renal arteries. Occasionally, a more inferior pair of arteries persists as accessory lower pole arteries.

When the kidney fails to ascend properly, its location becomes **ectopic**. If its ascent fails completely, it remains as a pelvic kidney.

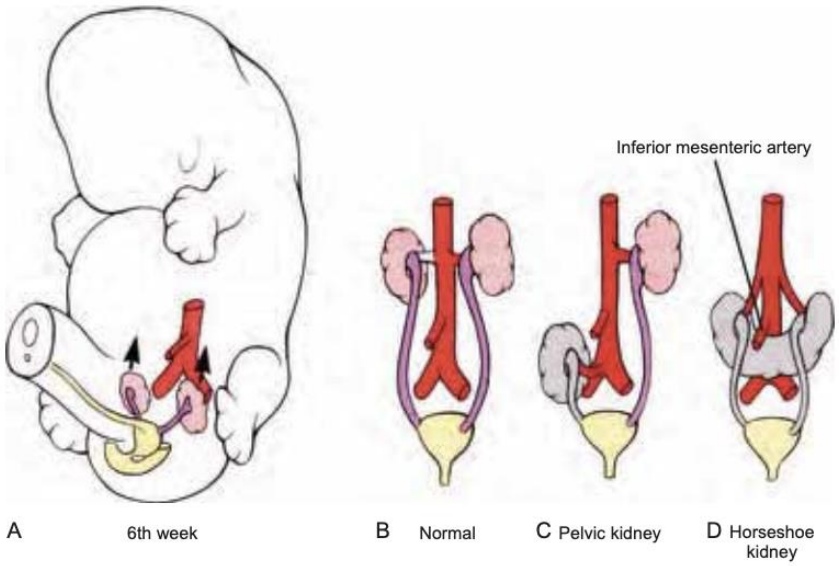


Image 5 – Renal ascent (Campbell- Walsh Urology, chapter 122, embryology of genitourinary tract).

Bladder and ureter development. According to the theories of Rathke and Tourneux regarding embryonic development, the partition of the cloaca into an anterior urogenital sinus and a posterior anorectal canal occurs by the midline fusion of two lateral ridges of the cloacal wall and by a descending urorectal septum. This process is thought to occur during the fifth and sixth weeks, and it culminates with the fusion of this urorectal septum with the cloacal membrane. The superior part of the urogenital sinus, continuous with the allantois, forms the bladder. The constricted narrowing at the base of the urogenital sinus forms the pelvic urethra. The distal expansion of the urogenital sinus forms the vestibule of the vagina in females and the penile urethra in males (Modified from Larsen WJ. Human embryology. New York: Churchill Livingstone; 1997).

The nephric (wolffian) duct fuses with the cloaca by the 24th day and remains with the urogenital sinus during the cloacal separation. The entrance of the nephric duct into the primitive urogenital sinus serves as a landmark distinguishing the cephalad vesicourethral canal from the caudal urogenital sinus. The vesicourethral canal gives rise to the bladder and pelvic urethra, whereas the caudal urogenital sinus forms the phallic urethra for males and distal vaginal vestibule for females [5]

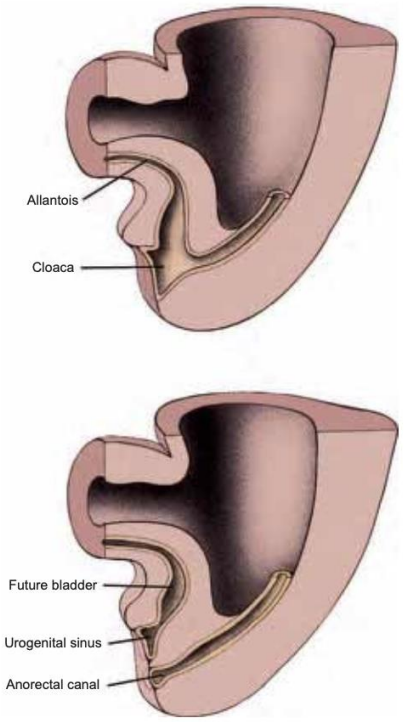


Image 6 – Development of bladder (Campbell- Walsh Urology, chapter 122, embryology of genitourinary tract).

By day 33 of gestation, the *common excretory ducts* (the portion of nephric ducts distal to the origin of ureteric buds) dilate and connect to the urogenital sinus. The formation of these final connections involves apoptosis, which enables the ureters to disconnect from the nephric ducts, and fusion, in which the ureteral orifice inserts into the urogenital sinus epithelium at the level of the trigone. According to the classic view (Weiss, 1988), the right and left common excretory ducts fuse in the

midline as a triangular area, forming the primitive trigone, structurally different from bladder and urethra. The ureteral orifice exstrophies and evaginates into the bladder by day 37 and begins to migrate in a cranial and lateral direction within the floor of the bladder [5].

The embryonic pattern of ureteral orifice incorporation into the developing bladder is inferred primarily from clinical observations of duplex kidneys. The upper pole ureteral orifice rotates posteriorly relative to the lower pole orifice and assumes a more caudal and medial position. Weigert and Meyer recognized the regularity of this relationship between upper and lower pole ureteral orifices, which has come to be known as the ***Weigert-Meyer rule*** (image 7). According to this concept, an abnormally lateral lower pole ureteral orifice may result from a ureteric bud arising too low on the nephric duct, therefore resulting in premature incorporation and migration within the developing bladder. In such a ureteral orifice, vesico-ureteral reflux is more likely to occur because of an inadequate intramural tunnel. In contrast, an abnormally caudal upper pole ureteral orifice may result from a ureteric bud arising too high on the nephric duct.

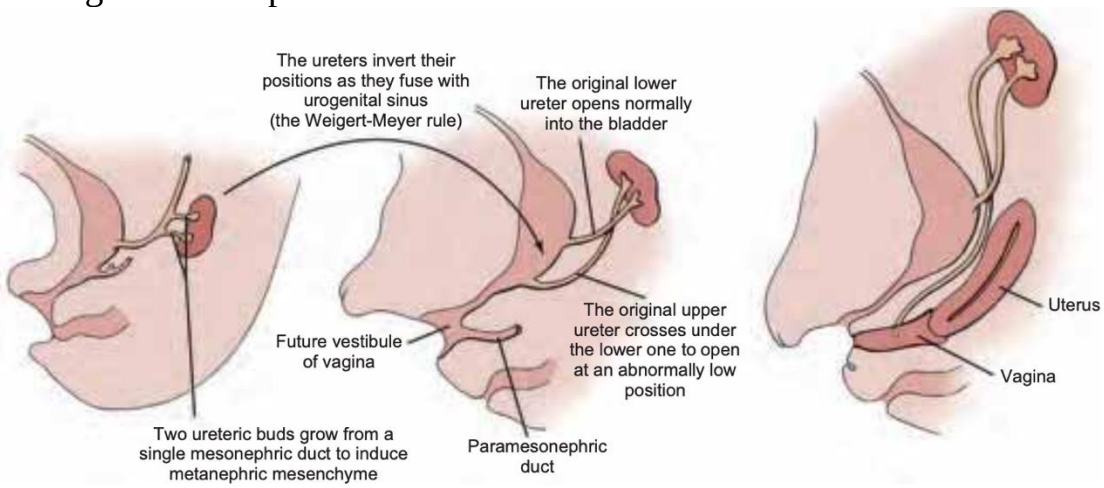


Image 7 – Weigert-Meyer rules (Campbell- Walsh Urology, chapter 122, embryology of genitourinary tract).

By the 10th week of gestation, the bladder is a cylindric tube lined by a single layer of cuboidal cells surrounded by loose connective tissue. The apex tapers as the urachus, which is contiguous with the allantois. By the 12th week the urachus involutes to become a fibrous cord, which becomes the *median umbilical ligament* [5].

Bladder compliance is thought to change during development. During gestation the bladder wall muscle thickness increases and the relative collagen content decreases. The ratio of thick-to-thin collagen fibers also decreases, whereas the amount of elastic fibers increases. These changes in compliance seem to coincide with the time of fetal urine production, suggesting a possible role for mechanical distention. The smooth muscle layer becomes thicker at the level of bladder neck and forms the inner part of the urethral musculature. The urethral sphincter, composed of central smooth muscle fibers and peripheral striated muscle fibers, develops in the anterior wall of the urethra. The urethral sphincter muscle fibers extend to the posterior wall of the urethra. In males these fibers project to the lateral

wall of the prostate, whereas in females the muscle fibers attach to the lateral wall of the vagina.
[5].

Development of male genital structure (image 8).

Under the influence of *SRY* (the *s*ex-determining *r*egion of the *Y* chromosome), cells in the medullary region of the primitive sex cords begin to differentiate into *Sertoli cells* while the cells of the cortical sex cords degenerate. Sex cord cells differentiate into Sertoli cells only if they contain the SRY protein; otherwise, the sex cords differentiate into ovarian follicles [5].

During the seventh week, the differentiating Sertoli cells organize to form the *testis cords.* At puberty these testis cords associated with germ cells undergo canalization and differentiate into **seminiferous tubules**. This interaction occurs shortly after the arrival of the primordial germ cells in the presumptive genital ridge. The vas deferens also develops from the nephric duct. At this time the testis begins to become round, reducing its area of contact with the surrounding mesonephros. As the testis continues to develop, the degenerating cortical sex cords become separated from the coelomic (peritoneal) epithelium by an intervening layer of connective tissue called the *tunica albugineaю* as the developing Sertoli cells begin their differentiation in response to the SRY protein, they also begin to secrete a glycoprotein hormone called *müllerian-inhibiting substance* (MIS). MIS causes the paramesonephric (müllerian) ducts to regress rapidly between the 8th and 10th weeks. Small müllerian duct remnants can be detected in the developed male as a small tissue protrusion at the superior pole of the testis, called the *appendix testis*, and as a posterior expansion of the prostatic urethra, called the *prostatic utricle* [5].

During the 9th and 10th weeks, Leydig cells differentiate from mesenchymal cells of the genital ridge in response to the SRY protein. These endocrine cells produce testosterone. At an early stage of development testosterone secretion is regulated by placental chorionic gonadotropin, but eventually the pituitary gonadotropins assume control of androgen production. Between the 8th and 12th weeks, testosterone secretion by Leydig cells stimulates the nephric (wolffian) ducts to transform into the vas deferens. The cranial portions of the nephric ducts degenerate, leaving a small remnant of tissue protrusion called the *appendix epididymis*, and the region of nephric ducts adjacent to the presumptive testis differentiate into the epididymis. During the 9th week, 5 to 12 nephric ducts in the region of the epididymis contact the sex cords of the future rete testis [5].

Prostate and seminal vesicle development. The seminal vesicles sprout from the distal nephric ducts, whereas the prostate and bulbourethral glands develop from the urogenital sinus. The initial event in prostatic development is an outgrowth of solid epithelial cords from the urogenital sinus epithelium into the surrounding mesenchyme during weeks 10 to 12 of gestation. The solid prostatic ducts are subsequently canalized from their urethral connections, proceeding distally toward the ductal tips. As the solid epithelial cords canalize, the epithelium organizes itself into two distinct cell types—luminal and basal cells. The prostatic mesenchyme

differentiates into a layer of smooth muscle cells that surround the prostatic ducts. At puberty, corresponding to a rise in circulating testosterone, the prostate size increases rapidly, along with functional cytodifferentiation of luminal cells, as evidenced by the expression of prostate-specific secretory proteins. **Circulating androgens produced by fetal testes play a critical role in the development of the prostate.** Cellular responses to circulating androgens are mediated by nuclear androgen receptors that are activated by either testosterone or dihydrotestosterone (DHT). The evidence for the requirement of androgens in establishing the prostate specificity of the urogenital sinus comes primarily from the absence of prostate development in mice and humans who lack functional androgen receptors. In the urogenital sinus, testosterone could activate androgen receptors by directly binding to the receptor and through a local conversion of circulating testosterone into the more potent DHT by the enzyme 5α-reductase [5].

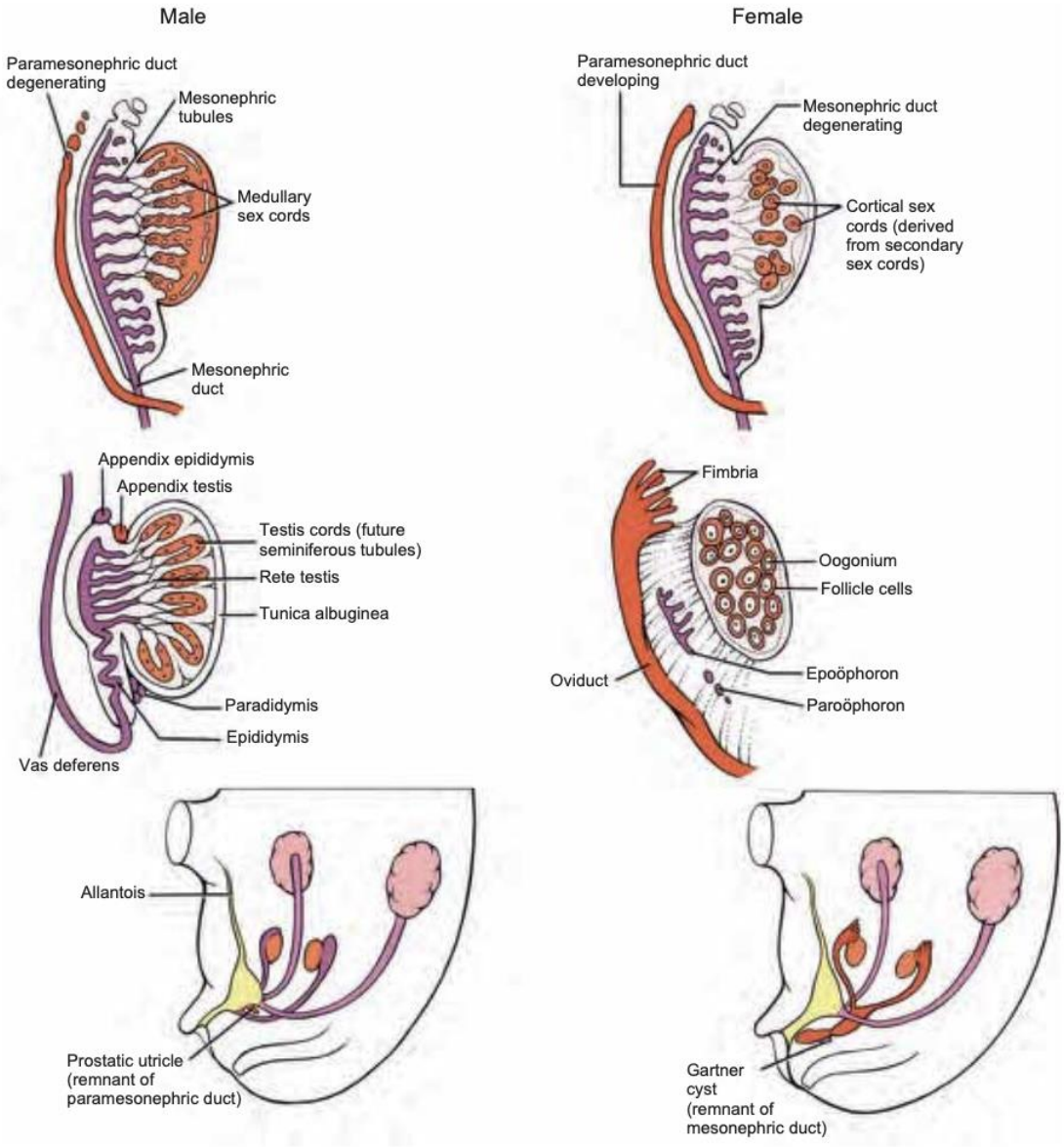


Image 8 – Development of genital organs (Campbell- Walsh Urology, chapter 122, embryology of genitourinary tract).

Development of external genital organs. Bilayered cloacal membrane "retracts" into the perineum as a result of cranial and medial migration of mesodermal cells into the anterior body wall between the ectoderm and the endoderm layers of the cloacal membrane. This mesenchymal migration brings about the closure of the inferior part of the anterior abdominal wall and causes the caudal portion of the cloacal membrane to position itself in the perineal region. These migrating mesodermal cells give rise to the musculature of the medial portion of the anterior abdominal wall, the mesenchymal portion of the anterior bladder wall, the pubic symphysis, and the rudiments of the external genitalia (image 9) [5].

Migrating mesenchymal cells spread themselves around the cloacal membrane and pile up to form swellings. Early in the fifth week, a pair of swellings called *cloacal folds* develops on either side of the cloacal membrane. These folds meet just anterior to the cloacal membrane to form a midline swelling called the *genital tubercle.* During the cloacal division into the anterior urogenital sinus and the posterior anorectal canal, the portion of the cloacal folds flanking the opening of the urogenital sinus becomes the *urogenital folds* and the portion flanking the opening of the anorectal canal becomes the *anal folds.* A new pair of swellings, called the *labioscrotal folds*, appears on either side of the urogenital folds.

Male and female genitalia are morphologically indistinguishable until the seventh week. In males the urogenital folds fuse and the genital tubercle elongates to form the penile shaft and glans. A small region of the distal urethra in the glans is formed by the invagination of surface epithelial tag. The fused labioscrotal folds give rise to the scrotum [5].

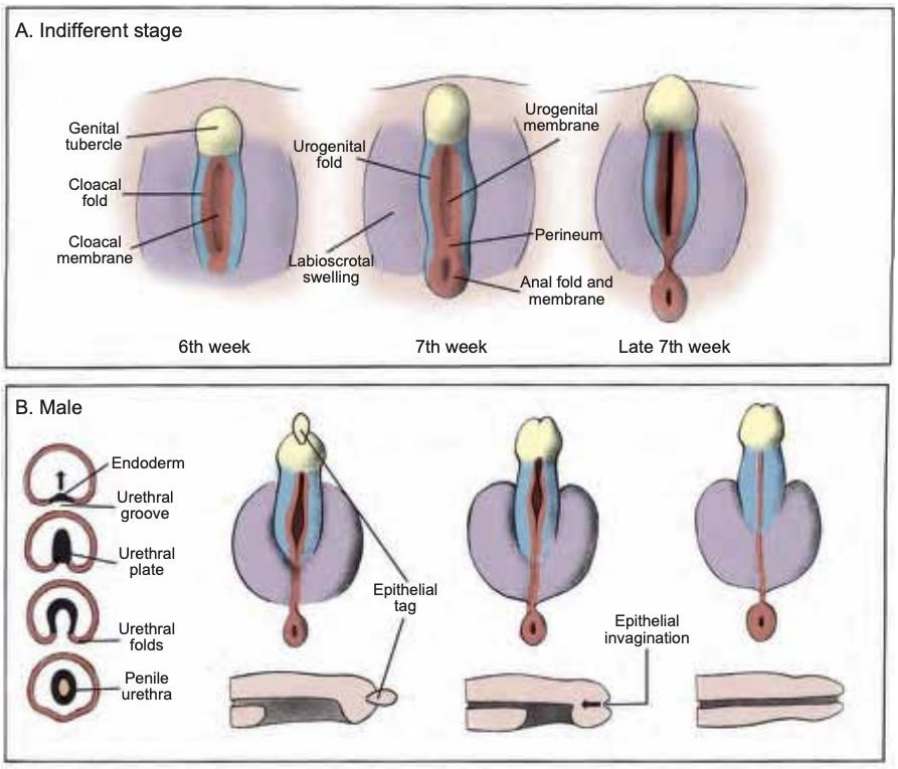


Image 9 – Development of external genitalia (Campbell- Walsh Urology, chapter 122, embryology of genitourinary tract).

Gonadal descent. Before gonadal differentiation, the testis lies near the developing kidney, loosely held in place by two ligamentous structures. The dorsal ligament is referred to as the *cranial suspensory ligament* (CSL), whereas the ventral ligament later develops into the *gubernaculum.* Between 10 and 15 weeks, the testis remains close to the future inguinal region during the enlargement of the abdominal cavity while the ovary moves more cranially. **The testis is anchored near the inguinal region by enlargement of the gubernaculum and regression of the CSL** (image 10).

Starting in the seventh month, the gubernaculum begins to bulge beyond the external inguinal ring and descends to the scrotal location, while simultaneously it is hollowed out by the evaginating peritoneal diverticulum called the *processus vaginalis.* The processus vaginalis allows the intraabdominal testis to exit the abdominal cavity. The bulky distal end of the gubernaculum (known as the *bulb*) is resorbed in humans after completion of inguinoscrotal migration [5].

Although intraabdominal pressure may not be a factor during the initial transabdominal descent, it is thought to be important during transit through the inguinal canal and the subsequent scrotal migration**.** Inguinoscrotal descent requires migration of the gubernaculum over a considerable distance, along with an increase in the length of the processus vaginalis. The force for movement may come from the intraabdominal pressure, transmitted directly and indirectly to the testis via the lumen of the processus vaginalis and the gubernacular cord, respectively. Although patients with defective androgen production or metabolism show varied manifestations of cryptorchidism, the exact role of androgen in testicular descent remains unclear. During intraabdominal testicular descent, androgen appears to play a role in the regression of the CSL [5].

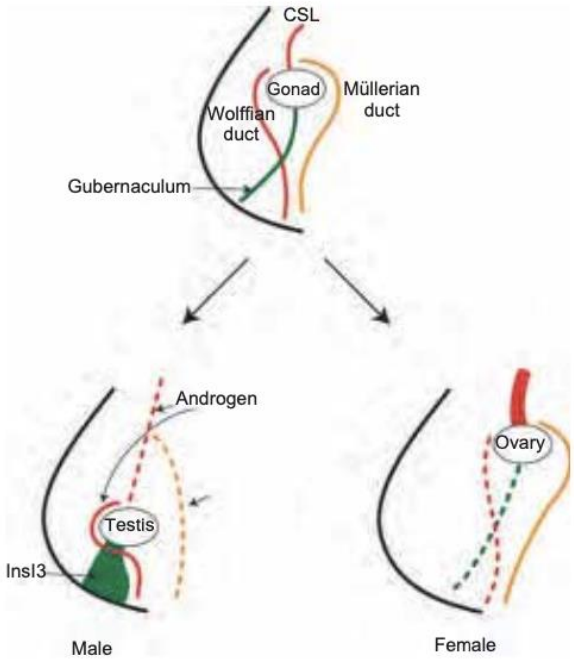


Image 10 – Gonadal descent (Campbell- Walsh Urology, chapter 122, embryology of genitourinary tract).

At the beginning of gestation (first and second week in humans), embryos of the two sexes differ only by their sex chromosomes. The first visible sign of sexual dimorphism in mammalian embryos is when the bipotential gonad starts to develop into either a testis or an ovary in XY and XX individuals, respectively. This occurs at around 6 weeks of development in humans. Differentiation of the gonads leads to testicular and ovarian hormone production and subsequent induction of anatomic and physiologic differences [5].

Both testis and ovarian development involve sex-specific pathways that appear to act antagonistically to one another. The normal role of *SRY* in XY gonads is to tip the balance in favor of the testis-specific pathway. *SRY* expression initiates an upregulation of *SOX9* expression. In mice, *Sox9* has been shown to stimulate *Fgf9* expression and subsequently, both FGF9 and SOX9 act together in a positive feedback loop and are thought to suppresses *Wnt4* (by unknown mechanisms), leading to the establishment of the testis-specific pathway. In the absence of *SRY* in XX individuals, *RSPO1* and *WNT4* are expressed at high levels and stabilize cytoplasmic β-catenin, which is then translocated into the nucleus, where it binds to the TCF/LEF (transcription factor/lymphoid enhancer-binding factor) and activates the transcription of target genes. Both WNT4 and β-catenin suppress (by unknown mechanisms) the SOX9/FGF9 positive feedback loop, allowing the ovarian-specific pathway to progress (image 11). In both sexes, before the expression of the male-determining gene *SRY*, several factors appear to play a role in urogenital ridge specification. Because the urogenital ridge is the primordium for the gonad, kidney, and reproductive tract, multiple organs are affected by mutations of these genes [5].

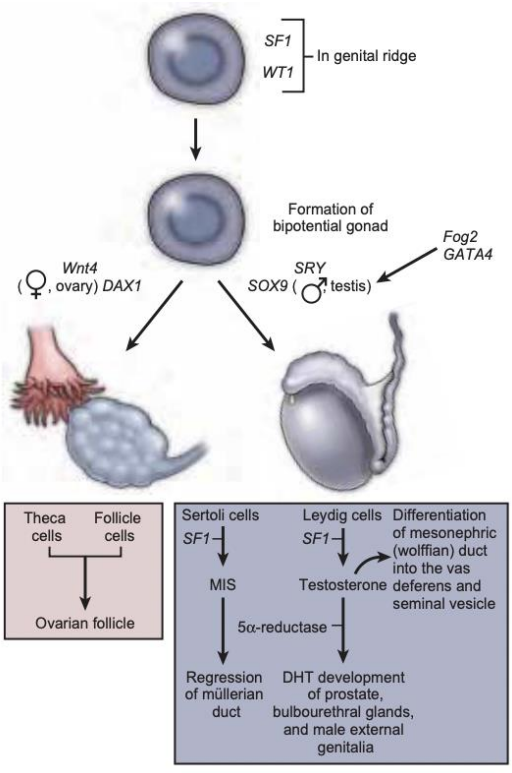


Image 11 – Sex development (Campbell- Walsh Urology, chapter 122, embryology of genitourinary tract).

Surgical anatomy of the kidney.

The kidneys are paired ovoid, reddish-brown retroperitoneal organs situated in the posterior part of the abdomen on each side of the vertebral column. The kidneys lie on the psoas muscles; thus, the **longitudinal axes** of the kidneys are oblique, with the upper poles more medial and posterior than the inferior poles [5].

The exact **position** of the kidney within the retroperitoneum varies during different phases of respiration, body position, and presence of anatomic anomalies. For example, the kidneys move inferiorly approximately 3 cm (one vertebral body) during inspiration and during changing body position from supine to the erect position. The position of the kidneys in the supine end-expiration is described here. Because of the inferior displacement of the right kidney by the liver, the right kidney sits 1 to 2 cm lower than the left kidney [5].

Each kidney measures 10 to 12 cm in length, 5.0 to 7.5 cm in width, and 2.5 to 3.0 cm in thickness.

The kidneys are relatively larger in children and have more prominent fetal lobulations, which generally disappear by the first year of life. In addition, the adult kidney's lateral contour might have a focal renal parenchymal bulge known as a **dromedary hump,** which is more common on the left side and has no pathologic significance. These dromedary humps are thought to be caused by the downward pressure from the liver or the spleen [5].

Superiorly, the kidneys are related to the inferior edge of the diaphragm and the ribs. The right kidney is related to the 12th rib, and the left kidney is related to the 11th and 12th ribs. When the lower ribs are fractured during trauma, associated renal lacerations could occur. The upper poles of the kidneys come close to the diaphragm and underlying pleural cavity containing the lungs; thus, any violations of the diaphragm during excision of large renal masses could lead to pleural tears and pneumothorax [5].

Percutaneous access to the upper pole of the kidneys above the 11th rib (10th intercostal space) is associated with increased risk for injuring pleura and even lungs. Therefore, when possible, subcostal (below the 12th rib) or 11th intercostal space (between the 11th and 12th ribs) access should be achieved.

More inferiorly, the kidneys are related to the psoas major muscle medially and both the quadratus lumborum and aponeurosis of the transversus abdominis muscles laterally. The subcostal nerve and vessels and the iliohypogastric and ilioinguinal nerves descend obliquely across the posterior surfaces of the kidneys [5].

The **right kidney** is related superiorly to the liver (both intraperitoneal and retroperitoneal bare portions) and superomedial to the adrenal gland. Inferiorly, the right kidney is related to the small intestine and hepatic flexure of the colon, and medially it is related to the second stage of the duodenum and head of the pancreas. The parietal peritoneum bridging the upper pole of the right kidney to the liver forms the **hepatorenal ligament.** Therefore, excessive downward traction of the right kidney may cause capsular tear of the liver and may lead to excessive intraoperative bleeding.

The **left kidney** is related to the stomach and spleen superiorly, adrenal gland superomedially, jejunum and splenic flexure of the colon inferiorly, and tail of the pancreas with splenic vessels medially. The parietal peritoneum bridging the upper pole of the left kidney to the spleen forms the splenorenal **ligament.** If excessive downward pressure is applied to the left kidney, splenic capsular tears may occur, leading to hemorrhage from the spleen [5].

The kidneys are surrounded by a smooth, tough **fibrous capsule**, which is easily removed under normal conditions. Each kidney and its vessels are surrounded by a **perinephric fat** that extends into its hollow vertical cleft, the **renal hilum,** which is the entrance to a space within the kidney called the **renal sinus.**

The kidneys and adrenal glands, including the perirenal fat surrounding them, are enclosed by a condensed, membranous layer of **renal (Gerota) fascia,** which continues medially to fuse with the contralateral side. This fascia extends inferomedially along the abdominal ureter as a **periureteral fascia.** The Gerota fascia encasing the kidneys, adrenal glands, and abdominal ureters is closed superiorly and laterally and serves as an anatomic barrier to the spread of malignancy and a means of containing perinephric fluid collections. Because it is open inferiorly, perinephric fluid collections can track inferiorly into the pelvis without violating the Gerota fascia. The Gerota fascia is further surrounded by a layer of condensed fat called the **paranephric fat,** which is most obvious posteriorly and represents the extraperitoneal fat of the lumbar region. Superiorly, the Gerota fascia is continuous with the diaphragmatic fascia on the inferior surface of the diaphragm, and, inferiorly, the anterior and posterior layers of the Gerota fascia are loosely attached. The Gerota fascia is attached with the paranephric fat by collagen bundles. Therefore, the kidneys are relatively kept fixed in position by these collagen bundles, the Gerota fascia, and paranephric fat.

The relationships of the kidneys have important **surgical implications.** To access the kidneys, adrenals, or abdominal ureters, the Gerota fascia must be opened. To access the kidneys transperitoneally, the colon needs to be mobilized from the **white line of Toldt,** which is the lateral reflection of posterior parietal peritoneum over the ascending and descending colon. To access the right renal hilum, the second stage of the duodenum and head of pancreas need to be carefully mobilized using the Kocher maneuver. To access the left renal hilum, the tail of the pancreas together with the spleen and splenic vessels need to be mobilized medially [5].

Anterior relationships of the kidneys and ureters you may see on image 12 (Copyright 2016 Elsevier Inc. All rights reserved. www.netterimages.com.). Posterior abdominal wall showing great vessels, kidneys, and adrenal glands is located on image 13 (Copyright 2016 Elsevier Inc. All rights reserved. www.netterimages.com.)

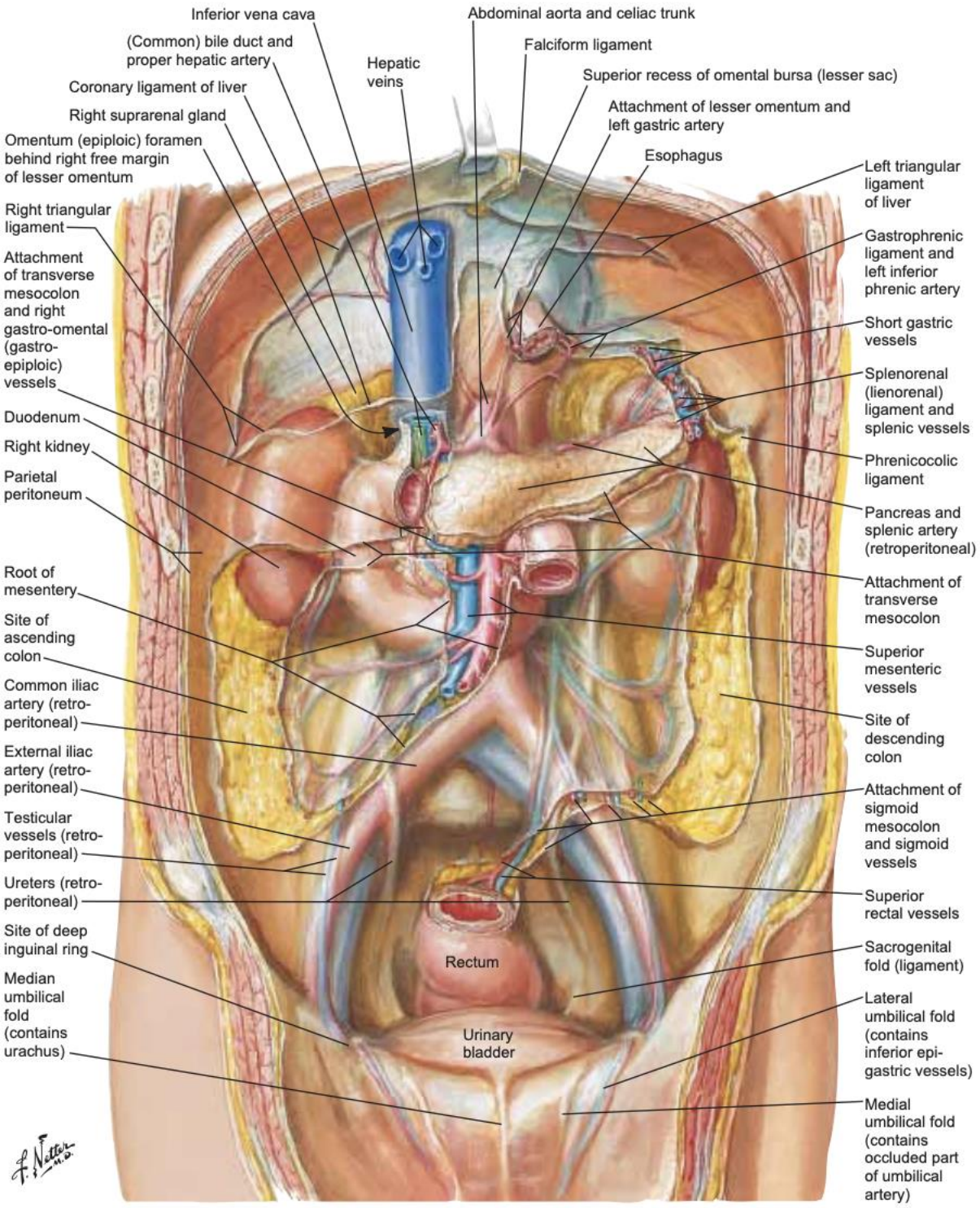


Image 12 - Anterior relationships of the kidneys and ureters (Copyright 2016 Elsevier Inc. All rights reserved. www.netterimages.com.) (Campbell- Walsh Urology, chapter 42).

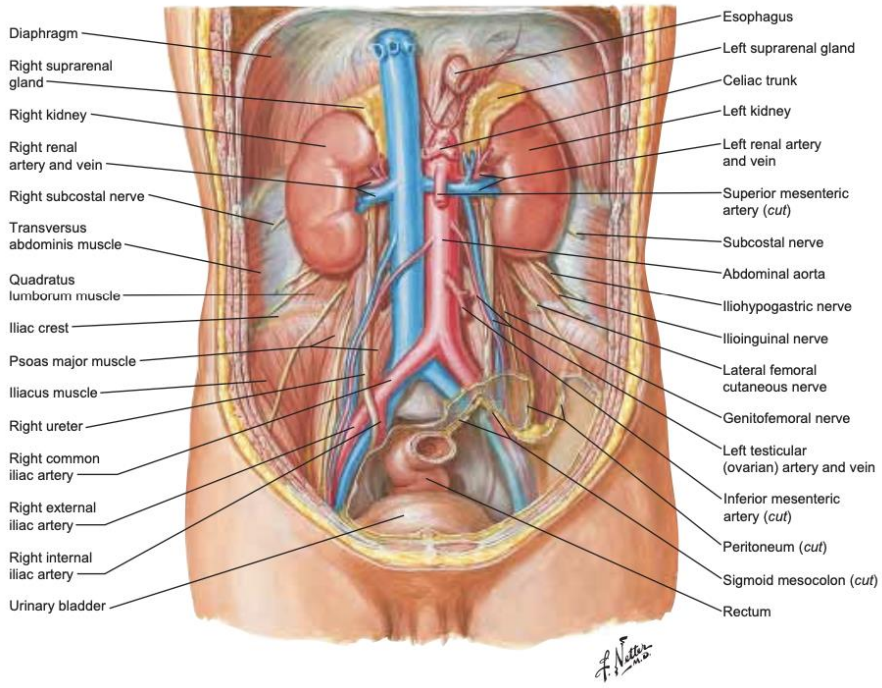


Image 13 - Posterior abdominal wall showing great vessels, kidneys, and adrenal glands (Copyright 2016 Elsevier Inc. All rights reserved. www.netterimages.com.) (Campbell- Walsh Urology, chapter 42).

Two distinct regions can be identified on the cut surface of a bisected kidney: the cortex, which is a pale outer region, and the medulla, which is a darker inner region (image 14). The renal medulla is divided into 8 to 18 striated, distinct, conically shaped areas that are frequently called renal pyramids. The apex of the pyramids forms the renal papilla, and each papilla is cupped by an individual minor calyx. The base of the pyramids is positioned at the corticomedullary boundary. The cortex and the medulla containing the renal pyramids could be differentiated on renal imaging studies [5].

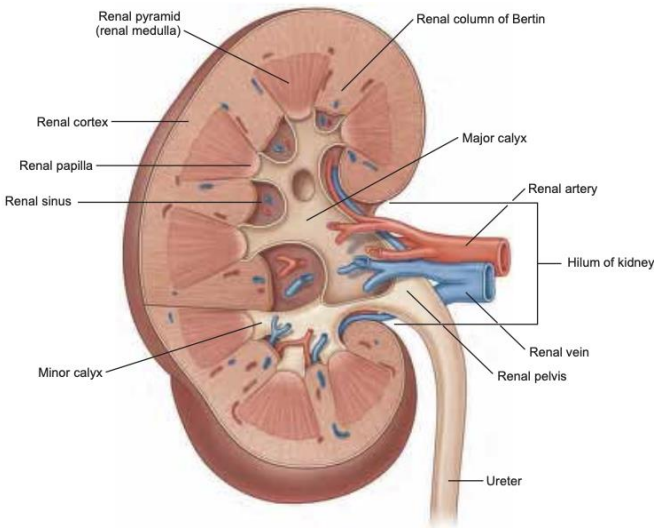


Image 14 - Internal structure of the right kidney (Campbell- Walsh Urology, chapter 42).

The renal cortex is approximately 1 cm in thickness and covers the base of each renal pyramid peripherally and extends downward between the individual pyramids to form the **columns of Bertin**. Interlobar arteries (image 15) traverse these columns of Bertin from the renal sinus to the peripheral cortex and decrease in diameter as they move peripherally. Therefore, percutaneous access to the collecting system is usually performed through a renal pyramid into a calyx to avoid these columns of Bertin containing larger blood vessels. The pyramids and their associated cortex form the lobes of the kidney. The lobes are visible on the external surfaces of the kidneys in fetuses, and evidence of the lobes may persist for some time after birth [5].

The functional unit of the kidney is the nephron (image 16). Approximately 0.4 to 1.2 million nephrons are found in each adult kidney. The nephron consists of a **glomerulus**, which is composed of a capillary tuft surrounded by epithelial cells and the thin, fibrous Bowman capsule. The glomerulus filters the blood at a rate of 125 mL/min, the glomerular filtration rate, which is considered an index of renal function. The filtrate passes into the Bowman space and then into **the proximal convoluted tubule**, through the thin and thick limbs of the **loop of Henle**, to the macula densa adjacent to the glomerulus, and into the **distal convoluted tubule**. It then enters the **collecting tubules** and the ducts of Bellini. After absorption of approximately 90% of this filtrate, the remaining part constitutes the urine, which drips from the collecting ducts into the calyces, then to the renal pelvis, ureter, and bladder. Three layers separate the filtered blood from the Bowman space: a single layer of endothelial cells, a thin glomerular basement membrane, and a layer of podocytes on the other side of that basement membrane. The proximal and distal convoluted tubules and the loop of Henle are lined by a single layer of cubical epithelial cells. The cells lining the collecting ducts are cubical to columnar and are more resistant to damage than those of the renal tubules. The calyces, pelvis, ureters, bladder, and urethra are lined by transitional epithelium, the urothelium, which may change and give rise to a transitional cell carcinoma of the urinary tract or urothelial carcinoma [5].

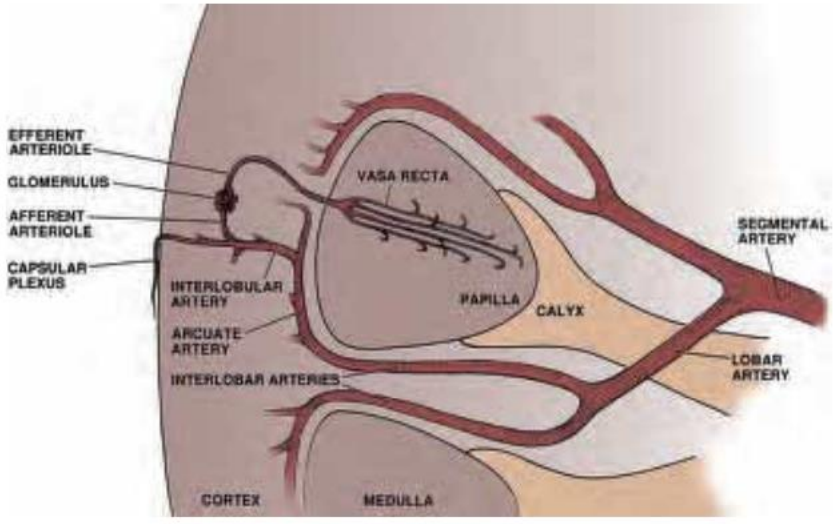


Image 15 – Arterial anatomy of kidney (Campbell- Walsh Urology, chapter 42)

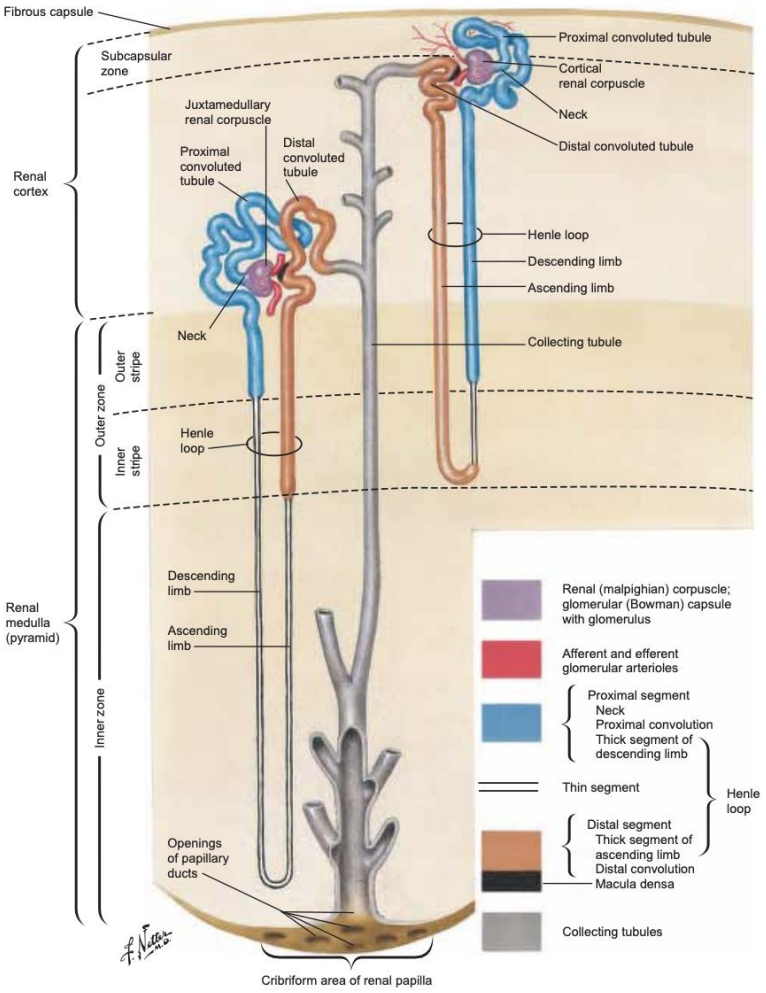


Image 16 - Schematic diagram of the microanatomy of the kidneys. (Copyright 2016 Elsevier Inc. All rights reserved. www.netterimages.com.) (Campbell- Walsh Urology, chapter 42).

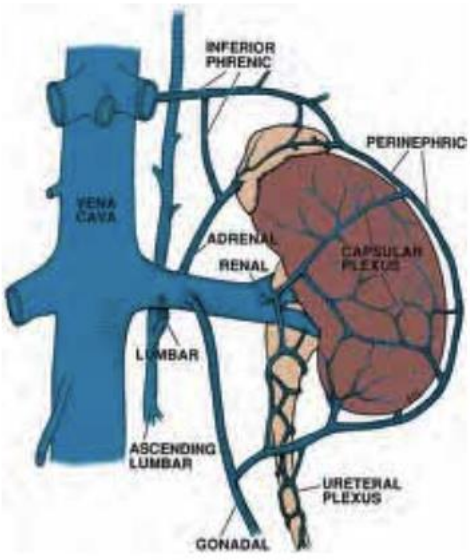


Image 17 – Venous dranage of the kidney (Campbell- Walsh Urology, chapter 42).

The ureters are bilateral muscular retroperitoneal ducts with narrow lumens that carry urine from the kidneys to the urinary bladder (image 18,19). Each ureter runs inferiorly as a narrow continuation of its renal pelvis at the UPJ, passing over the pelvic brim at the bifurcation of the common iliac artery. They then run along the lateral wall of the pelvis to enter the urinary bladder. In adults, the ureter is 22 to 30 cm in length with a diameter of 1.5 to 6 mm; in neonates it measures 6.5 to 7.0 cm long. In the retroperitoneum, the ureter is situated just lateral to the tips of the transverse processes of the lumbar vertebrae [5].

The ureter is arbitrarily divided into proximal (upper), middle (over the sacrum), and distal (lower) segments. However, according to international anatomic terminology the ureter consists of abdominal (from renal pelvis to iliac vessels), pelvic (from iliac vessels to the bladder), and intramural segments [5].

From the back, the surface anatomy of the ureter corresponds to a line joining a point 5 cm lateral to the L1 spinous process and the posterior superior iliac spine. Normally, three constrictions could be identified radiologically in each ureter; at its junction with the renal pelvis (UPJ), where it crosses the iliac vessels, and during its passage through the wall of the urinary bladder (intramural ureter) or ureterovesical junction. These constricted areas are potential sites of obstruction by ureteral calculi [5].

Posteriorly, both ureters descend anterior to the psoas major muscle and then cross the ventral surface of transverse processes of the 3rd to 5th lumbar vertebrae and enter the pelvis at the bifurcation of the common iliac vessels (image 12). The bifurcation of the common iliac vessels is used intraoperatively as a landmark to look for the ureter. The genitofemoral nerve runs on top of the psoas major muscle behind the ureter. The right ureter begins behind the descending part of the duodenum, where it is crossed by the gonadal vessels (testicular or ovarian), which is called "**water under the bridge**." The left ureter is covered at its origin by the initial part of the jejunum. The gonadal vessels cross the left ureter after running parallel to it for a small distance. The inferior mesenteric artery and its terminal branch, the superior rectal artery, follow a curved course close to the left ureter.

The pelvic segment of the ureter is approximately 15 cm long—a half of its total length. At the pelvic inlet, it crosses the common iliac vessels near their bifurcation. The ureter then runs downward and laterally toward the ischial spine on the lateral pelvic wall along the anterior border of the greater sciatic notch, dorsally accompanied by the internal iliac artery and its visceral branches and the venous plexuses as well. It is still closely related to the posterior parietal peritoneum. At the ischial spine, the ureter turns medially to descend in the endopelvic fascia with branches of the hypogastric nerves. At the lateral wall of the pelvis, this part of the ureter crosses the obturator artery, vein, and nerve. In males, the vas deferens loops medially over this part while the ureter passes the ampulla of the vas deferens and the seminal vesicles just before it enters the bladder. The terminal ureter runs forward, accompanied by the neurovascular bundle of the bladder and passes the anterior vaginal fornix just before entering the bladder. Near the bladder, the terminal ureter is enveloped by a muscular layer, the Waldeyer sheath, and then pierces the bladder wall obliquely as the intramural segment (image 20).

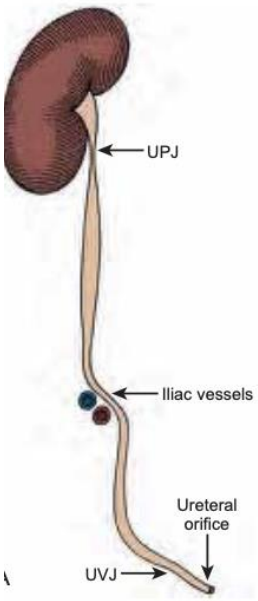


Image 18 – Ureter (Campbell- Walsh Urology, chapter 42).

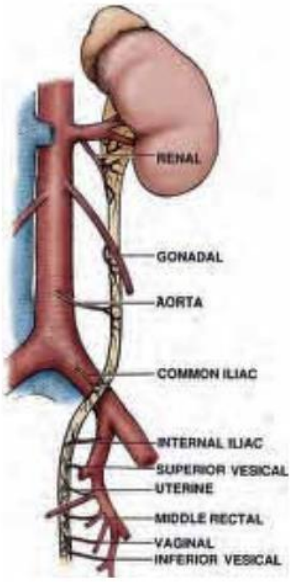


Image 19 – Artery supply of ureter (Campbell- Walsh Urology, chapter 42)

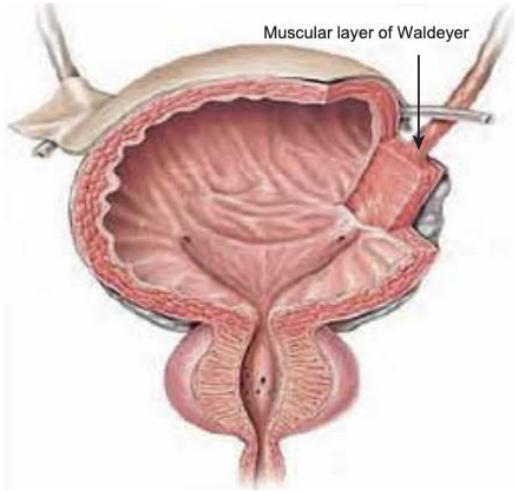


Image 20 – Intramural portion of ureter (Campbell- Walsh Urology, chapter 42)

Classification of abnormalities of kidney [5]

1. Anomalies of number
2.Anomalies of ascent
3. Anomalies of form and fusion
4. Anomalies of rotation
5. Anomalies of renal vasculature
6. Anomalies of the collecting system
7. Cystic disease of the kidney

I. ANOMALY OF STRUCTURE.

Cystic disease of the kidney. Renal cystic disease contains a widespread group of sporadic and genetically determined congenital or acquired conditions that have in common the presence of cysts in one or both kidneys.

Definition. Renal cysts are cavities derived primarily from tubules and are composed of a layer of partially de-differentiated epithelial cells enclosing a cavity filled with urine-like liquid or semisolid material. They may develop in any tubular segment between the Bowman capsule and the tip of the renal papilla, depending on the nature of the underlying disorder [5].

We should differentiate multicystic dysplasia between multicystic. What is the main sign of multicystic dysplasia? Multicystic dysplasia is an exception in that it arises before formation of the nephron, from abnormal induction of metanephric development, from a primary abnormality **of** the nephrogenic blastema, or from obstruction occurring early in renal development. Another exception, benign multilocular cyst, represents a neoplastic growth.

Mechanism. Obstruction any tubules, proliferation of epithelial cells in segments of renal tubule, accumulation of fluid within the expanding tubule segment, and disturbed organization and metabolism of the extracellular matrix [5] (image 21).

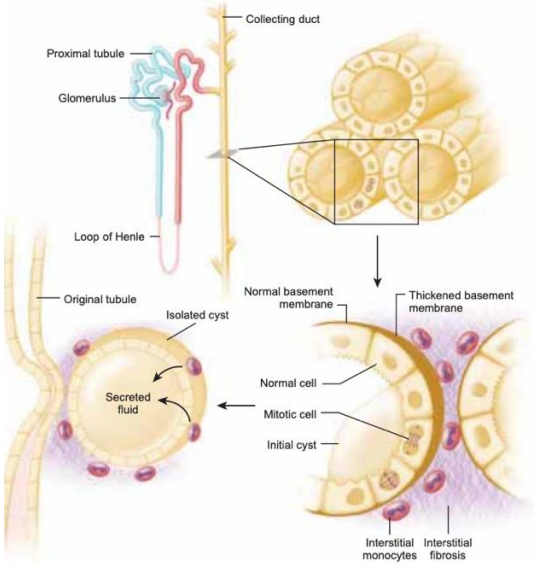


Image 21 – Evolution of cysts (Campbell- Walsh Urology, chapter 131, Renal Dysgenesis and Cystic Disease of the Kidney).

Classification (task1) (according to the classification of renal cystic disease as outlined in 1987 by the Committee on Classification, Nomenclature, and Terminology of the AAP Section on Urology).

Task 1 Classification of Cystic disease of the kidney

Inheritable	Nonheritable
Autosomal recessive (infantile) polycystic kidney disease	Multicystic kidney (multicystic dysplastic kidney)
Autosomal dominant (adult) polycystic kidney disease	Benign multilocular cyst (cystic nephroma)
Medullary cystic disease (autosomal dominant)	Simple cysts
Congenital nephrosis (familial nephrotic syndrome) (autosomal recessive)	Medullary sponge kidney
Familial hypoplastic glomerulocystic disease (autosomal dominant)	Sporadic glomerulocystic kidney disease
Multiple malformation syndromes with renal cysts (e.g., tuberous sclerosis, von Hippel-Lindau disease)	Acquired renal cystic disease
	Calyceal diverticulum (pyelogenic cyst)

Multicystic typically refers to a dysplastic kidney resulting from aberrant renal development. *Polycystic* refers to renal units that developed in a normal fashion, all of which have no dysplasia and have nephrons throughout the kidney. The term *polycystic kidney disease* tradition- ally is used in reference to two conditions: ARPKD and ADPKD. Many of the PKD entities progress to renal failure as the nephrons become more diseased. In other conditions, such as tuberous sclerosis and VHL disease, there are hyperplastic cysts, and the individual nephrons are normal. Only occasionally do the nephrons become compressed by the cysts or by associated tumors, and only in such situations does renal failure ensue.

Among the nonheritable cystic diseases, benign multilocular cysts, cystic renal cell carcinoma (RCC), and other variants are considered neoplasms. Medullary sponge kidney is a disease principally of dilated ectatic collecting ducts, with cysts playing a lesser role, although the size of the ducts makes them cysts. The nephrons initially are normal [5].

Now we are discussing about the most important and frequent forms.

ARPKD.

ARPKD is typified by relatively rapid, symmetrical, and bilateral enlargement of the kidneys in infants secondary to collecting duct cysts. It is invariably associated with some degree of congenital hepatic fibrosis [5].

Epidemiology. ARPKD is one of the most common causes of heritable, infantile cystic renal disease. Despite that, it accounts for only 1 in 20,000 to 50,000 live births. There is no gender or racial predilection [6].

Etiology. All forms of ARPKD are caused by a mutation in the PKHD1 gene on chromosome 6p12.

Pathophysiology. Circumferential proliferation of epithelial cells, which predominantly affects collecting ducts in renal tubules. Variable degrees of collecting duct epithelial proliferation, biliary duct proliferation and ectasia, periportal fibrosis are present in almost all patients [6].

Clinical features. Thirty percent to 50% of the affected individuals die shortly after birth as a result of uremia or respiratory failure. Hypertension and renal insufficiency are the major manifestations in surviving children, with liver disease becoming more prevalent in older patients [5].

Task 2 Features of ARPKD [6]

Perinatal Type (the most common)	Neonatal and Infantile Type	Juvenile Type
oligohydramnios and pulmonary hypoplasia and has a poor prognosis	Minimal to moderate hepatic/periportal fibrosis.	Gross hepatic fibrosis and features of portal hypertension like hepatosplenomegaly and portosystemic varices with less severe renal disease

Diagnostic evaluation. Ultrasound shows bilateral smooth enlarged kidneys with loss of corticomedullary differentiation. CT shows smooth enlarged kidneys with a striated pattern of contrast excretion. Those children who survive the neonatal period and present later with portal hypertension in the infantile or juvenile period, usually have less involvement of kidneys. Their renal ultrasound is usually normal or may show minimal cysts. Other findings which may be associated with ARPKD include; biliary duct ectasia (Caroli disease) and congenital hepatic fibrosis. A subset group of ARPKD patients may show hepatosplenomegaly [6].

Diagnostic management. Management depends on the severity of the clinical manifestations and the organs involved; this involves monitoring respiratory function, renal function tests, liver function tests, infant growth evaluation and blood pressure monitoring, and symptomatic treatment. Dual organ transplant (liver

and kidney) depending on the severity of portal hypertension and end-stage renal disease has shown promising results in a significant number of cases [6].

ADPKD.

ADPKD is by far the most common inheritable form of renal cystic disease, with an incidence of approximately 1 in 400 to 1000 live births. All affected individuals mani- fest the disease (although not necessarily symptomatically) if they live long enough, but renal failure is seldom seen before the age of 40 years, unless the disease manifests during infancy, in which case it is much more aggressive [5].

Several associated anomalies are common, including cysts of the liver, pancreas, spleen, and lungs; aneurysms of the circle of Willis (berry aneurysms); colonic diverticula; aortic aneurysms; and mitral valve prolapse [5].

Etiology. The condition may arise from mutation of either of two genes, PKD 1 and PKD 2. PKD 1 located in the short arm of chromosome 16p and encodes protein polycystic-1 which accounts for most cases (85%). PKD 2 is located on the long arm of chromosome 4q and encodes protein polycystic-2, which accounts for the remaining 15% of cases [6].

Pathophysiology. Polycystin 1 and 2 proteins are components of cell membranes of primary cilia of renal tubular epithelial cells. Deranged production of these proteins results in ciliary dysmotility, which leads to overproduction of epidermal growth factors, which causes proliferation of tubular epithelial cells with increased fluid secretion and cysts formation. Intrarenal cysts distort normal renal architecture and function causes continued activation of the renin-angiotensin-aldosterone system which leads to hypertension. Liver cysts arise by excessive proliferation and dilatation of biliary ductules, caused by a similar mechanism [6].

Gross, histologic specimen reveals bilaterally enlarged kidneys with multiple cysts of varying sizes. On microscopy, renal tubular ectasia and cysts lined by columnar to cuboidal to flattened epithelial cells and thickened basement membrane are the usual findings [6].

Clinical features. Patient may present clinically usually around the third decade of age with hypertension and with or without pain or hematuria of renal origin or other cyst's related complications as infection or rupture. Medical renal disease as renal tubular acidosis is also common in this population. About 45% of patients may progress to end-stage renal disease, which leads to their dependence on hemodialysis or renal transplant. Imaging studies play a vital role in the diagnosis and screening of families at risk [6].

Pain (flank and/or abdominal) is the most common presenting symptom in adults. This results from several possible factors: mass effect (cysts impinging on abdominal wall or neighboring organs), bleeding into the cysts, urinary tract infection (including infected cysts), and nephrolithiasis. Twenty percent to 30% of patients with ADPKD develop stones [5].

The hypertension seems to be renin mediated, secondary to stretching of the intrarenal vessels around cysts, causing distal ischemia [5].

Diagnostic evaluation (images 22,23*)*. US: simple cysts appear anechoic on ultrasound, while complex cysts may show anechoic material and thick septa or calcifications, which require careful assessment to rule out hemorrhage, infection,

or renal malignancy. Ultrasound is also used to assess cysts in other organs like the liver.

CT, MRI - simple cysts appear hyperintense on T2 and hypointense on T1. Hemorrhage in a cyst appears hyperintense on T1; calcification shows blooming on GRE or susceptibility-weighted images. A complex cyst may show thick enhancing septa or enhancing solid nodules which raise suspicion for malignancy [6].

Diagnostic management. The treatment of patients with ADPKD includes managing high blood pressure with medications, a low-salt diet, dietary protein restriction, and statins which may reduce disease progression. Patients with ADPKD who ultimately progress to end-stage renal disease require renal replacement therapy which includes hemodialysis and renal transplantation [6].

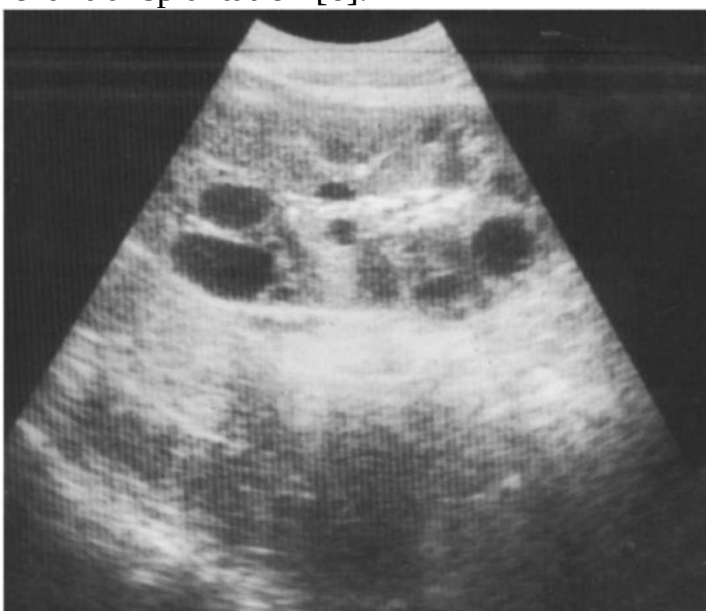


Image 22 – Polycystic kidney disease (Atlas of Pediatic urology, Kulikova T.N.)

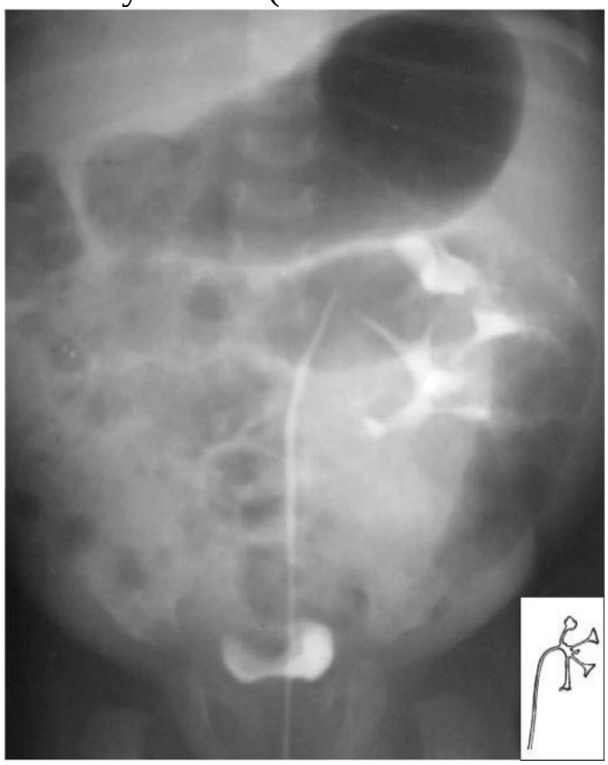


Image 23 - Polycystic kidney disease (Atlas of Pediatric urology, Kulikova T.N.).

Juvenile nepronophtisis (NPH) and medullary cystic disease complex (MCKD).

Group of genetic (inheritable) disorders with both similar and unique characteristics: *similarities* include the gross and histopathologic appearance of the kidneys, with the hallmark being interstitial fibrosis; distinguishing features are the mode of inheritance, the age of onset of end-stage renal disease, and the type of extrarenal organ involvement.

Juvenile NPH (first described by Fankoni) is the more common condition and is responsible for 10% to 20% of cases of renal failure occurring in children and occurs in 1% to 5% of patients undergoing dialysis or transplantation [5].

Pathophysiology. Development of massive interstitial fibrosis with abnormal thickness of the tubular basement membranes, atrophic and/or dilated tubules, and occasionally, formation of cysts mainly distributed at the cortico-medullary junction within normal sized or small kidneys [8].

Etiology. NPH (autosomal recessive kidney disease) is caused by mutations in over 20 different genes, most of which encode components of the primary cilium, an organelle in which important cellular signaling pathways converge. Ciliary signal transduction plays a critical role in kidney development and tissue homeostasis, and disruption of ciliary signaling has been associated with cyst formation, epithelial cell dedifferentiation and kidney function decline [9].

MCKD usually is inherited in an autosomal dominant **(**50% of all offspring will have the disease) and is caused by mutations in either the *MCKD1* or *MCKD2* gene [5].

Clinical features. Patients present with a urine concentration defect leading to polyuria and polydipsia, anemia, proteinuria (in advanced stages) and progressive renal insufficiency [9]. The polyuria is caused by a renal tubular urinary concentrating defect that leads to salt wasting, and this process is resistant to vasopressin. Difference in the two entities is the *presence of hypertension*. There is no hypertension associated with juvenile NPH, whereas patients with MCKD can have significant hypertension. Rarer versions of NPH occur as well: infantile NPH (ESRD in patients 4 years of age or younger) results from a mutation in the *NPHP2/INVS* gene, and adolescent NPH (ESRD variable, occurring in patients ranging from 3 to 13 years old) results from a mutation in the *NPHP3* gene [5].

Renal failure develops in patients with NPH at a mean age of 13 years and almost always before 25 years, otherwise, ESRD in patients with MCKD most often develops in the third or fourth decade.

Pathologically, NPH and MCKD are similar. Grossly, the kidneys are small to normal in size with multiple cysts at the corticomedullary junction. Histologically, there is a characteristic triad present that includes (1) irregular thickening and disintegration of the tubular basement membrane, (2) marked tubular atrophy with cyst development, and (3) interstitial cell infiltration with fibrosis [5].

Diagnostic evaluation. US, CT, MRI. US (image 24): smaller-than-normal kidneys in juvenile NPH. Cysts may be seen on imaging studies if they are large enough, but, early in the disease, cysts are rarely visible [5].

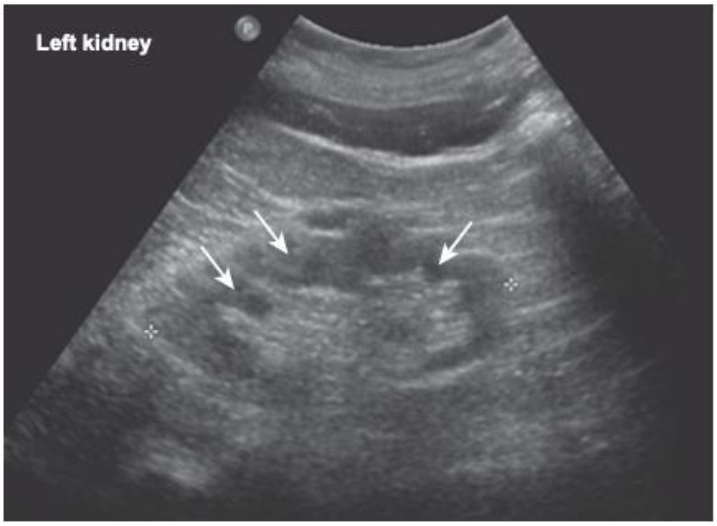


Image 24 – MCKD (corticomedullary cysts (indicated by arrows), hyperechogenicity is secondary to the tubulointerstitial fibrosis (Campbell- Walsh Urology, chapter 131, Renal Dysgenesis and Cystic Disease of the Kidney).

Diagnostic management. The treatment of NPH is supportive. Because of the tendency for sodium wasting, volume contraction, and renal azotemia, sodium replacement is indicated early in the course of the disease, and unnecessary sodium restriction or use of diuretics should be avoided. Later, dialysis and transplantation must be considered [5].

Multicystic dysplastic kidney (MCDK.)

Definition. MCDK- is a developmental anomaly resulting in multiple cysts of differential size, without identifiable normal renal parenchyma. As rules, this is unilateral process. These kidneys have no function and contlateral kidney exhibits compensatory hypertrophy [5].

Renal size is highly variable, ranging from a small nubbin of tissue to a very large mass in abdomen (the second most cause of an abdominal mass in newborn, after hydronephrosis).

This pathological process can be two types:

- infundilopelvic type (atresia of renal pelvis and ureter);
- Hydronephrosis (atresia of only ureter).

In both cases, the ureters are absent or atretic and the renal vessels are hypoplastic.

Etiology. There are many theories explaining the reason of this anomaly. One of them noted, that may result from abnormal interaction between the ureteric bud and metanephric mesenchyme. Mutations in genes such as *EYA1, SIX1, WNT, WT-1*, *GNF, AT2,* and *PAX2* are known to have important roles in ureteric bud development and have been identified in multiple human syndromes with renal dysplasia [5].

Clinical features. The natural history of MCDK is benign; the incidence of complications is extremely rare; and approximately 40% of MCDKs will spontaneously involute [5].
Histopathology. Multicystic kidneys with large cysts tend to be large with little stroma, whereas those with small cysts typically are smaller and more solid. Likewise, the blood supply is variable, ranging from a pedicle with small vessels to no pedicle at all. Usually the ureter is partly or totally atretic, and the renal pelvis may be absent [5].Microscopically, the cysts are lined by low cuboidal epithelium, are surrounded by collars of spindle cells, and are filled with proteinaceous or sanguineous fluid.
Diagnostic evaluation. US, CT scan, MRI.
US: it's necessary to performed prenatal ultrasonography (image 25), repeat after birth (1 month later).
Signs: the multicystic kidney has a haphazard distribution of cysts of various sizes without a larger central or medial cyst and without visible communications among the cysts. Frequently, very small cysts appear among the large cysts. By comparison, in UPJO, the cysts or calyces are organized around the periphery of the kidney; connections usually can be demonstrated between the peripheral cysts and a central or medial cyst that represents the renal pelvis; and there is an absence of small cysts among the larger cysts [5].

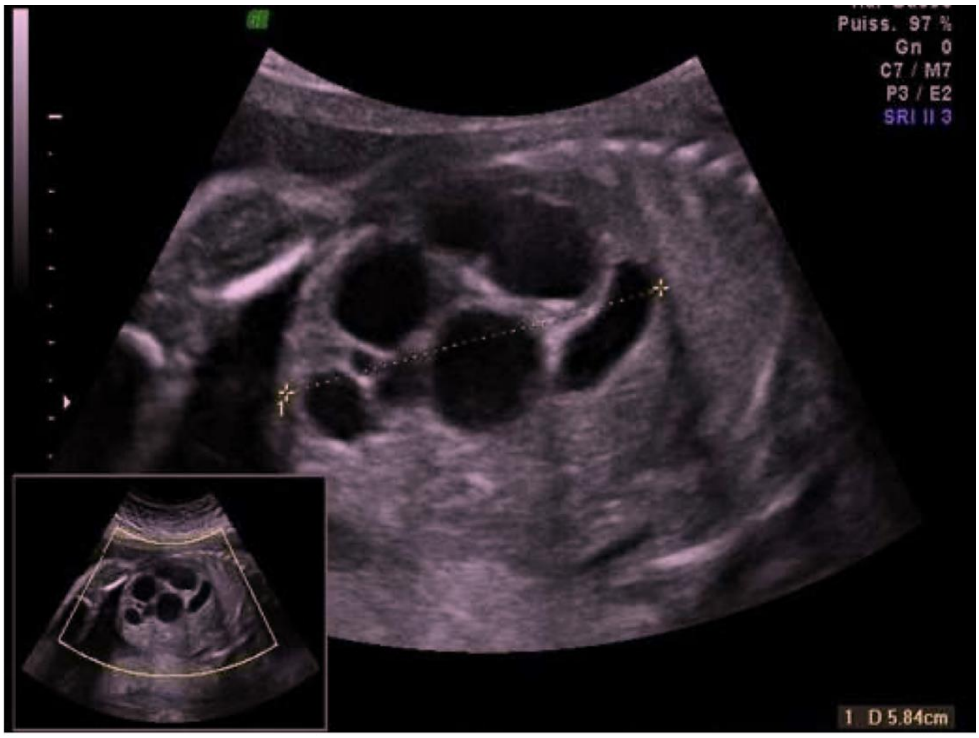


Figure 1: rein multikystique

Image 25 – MCKD (prenatal ultrasonography) (image from article [10].)

Diagnostic management. Nephrectomy for MCDK may also be necessary to correct the rare cases of associated hypertension or if a cyst has ruptured spontaneously or secondary to trauma (to relieve pain or hemorrhage). Therefore, it is reasonable to

follow patients with MCDK conservatively, realizing that hypertension can exist and should be assessed periodically [5].

Simple cysts.

Definition. They are usually oval to round; may be solitary or multiple, unilateral or bilateral; and are filled with plasma-like clear or straw-colored fluid. They are not connected to any part of the nephron, although they may originate initially from a portion of the nephron [5].

Etiology. Simple renal cysts are acquired, not inherited. Risk factors are advancing age and male sex. The presence of simple cysts increases after age 40. Renal cysts are most often identified at autopsy or incidentally in radiological studies [11].

Hystopathology. The wall is fibrous and of varying thickness and has no renal elements. The cyst lining is glistening and usually smooth and histologically is a single layer of flattened or cuboidal epithelium, and the cysts are filled with a clear, serous fluid [5].

Clinical features. They are discovered incidentally on ultrasonography, CT, or urography. However, cysts can produce an abdominal mass or pain, hematuria secondary to rupture into the pelvicalyceal system, and hypertension secondary to segmental ischemia, also cysts can cause calyceal or renal pelvic obstruction as well. Cysts can rupture into the pelvicalyceal system, maintain a communication, and become a *pseudocalyceal diverticulum*. The reverse is also possible: Closure of the communication of a diverticulum can create a simple cyst [5].

Diagnostic evaluation.

Most simple cysts are identified incidentally. One can safely make the diagnosis of a classic benign simple cyst by ultrasonography (image 26) when the following criteria are met:

- absence of internal echoes.
- presence of a sharply defined, thin, distinct wall with a smooth and distinct margin;
-good transmission of sound waves through the cyst with consequent acoustic enhancement behind the cyst.
- a spheric or slightly ovoid shape.

If all these criteria are satisfied, the chance that malignancy is present is negligible [5].

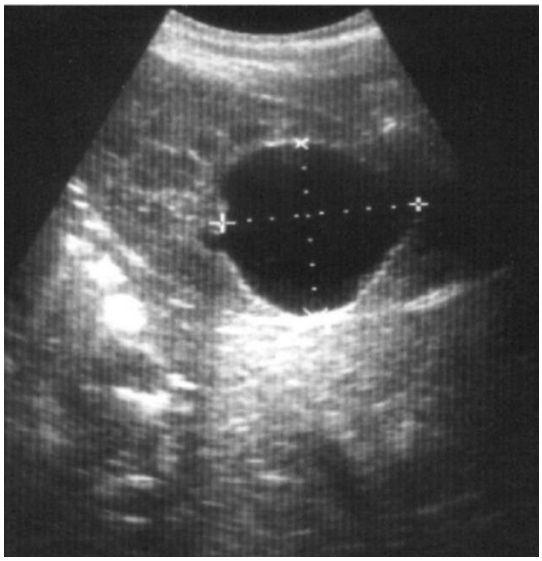


Image 26 – Simple renal cyst (Atlas of Pediatric urology, Kulikova T.N.).

CT scan. The CT (image 18) criteria for a simple cyst are similar to those used in ultrasonography:

-a sharp, thin, distinct, smooth wall and margin.

- a spheric or ovoid shape.

-homogeneous content.

When these criteria are respected, the accuracy of diagnosis of a simple cyst by CT approaches 100%. The density ranges from −10 to +20 HU, like the density of water, and no enhancement should occur after the intravenous injection of contrast medium.

When the cyst fluid is hyperdense (i.e., between 20 and 90 HU), the cyst still is likely to be a simple cyst if no enhancement occurs when intravenous contrast agent is injected and if the other criteria of CT and ultrasonography are met. Because cysts have no blood vessels and do not communicate directly with nephrons, they should not enhance; enhancement therefore implies vascular tissue or contrast medium mixing with fluid.

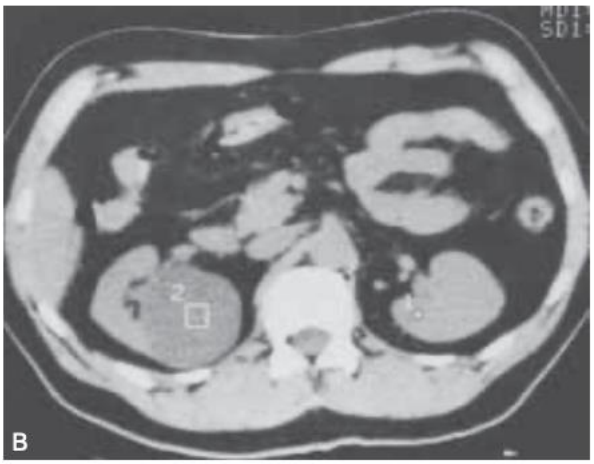


Image 27 – Simple renal cyst (CT scan) (mass in the left kidney) (Campbell-Walsh Urology, chapter 131, Renal Dysgenesis and Cystic Disease of the Kidney).

Classification.

BOX 131-2 Bosniak's Classification of Simple and Complex Cysts

CATEGORY I
Simple benign cyst with (1) good through-transmission (i.e., acoustic enhancement), (2) no echoes within the cyst, (3) sharply marginated smooth wall; requires no surgery.

CATEGORY II
Looks benign with some radiologic concerns, including septation, minimal calcification, and high density; requires no surgery.

CATEGORY II F
Although calcification in wall of cyst may even be thicker and more nodular than in category II, the septa have minimal enhancement, especially those with calcium; requires no surgery.

CATEGORY III
More complicated lesion that cannot confidently be distinguished from malignancy, having more calcification, more prominent septation of a thicker wall than a category II lesion; more likely to be benign than malignant; requires surgical exploration and/or removal.

CATEGORY IV
Clearly a malignant lesion with large cystic components, irregular margins; solid vascular elements; requires surgical removal.

Image 28 – Bosniak classification (Campbell- Walsh Urology, chapter 131, Renal Dysgenesis and Cystic Disease of the Kidney).

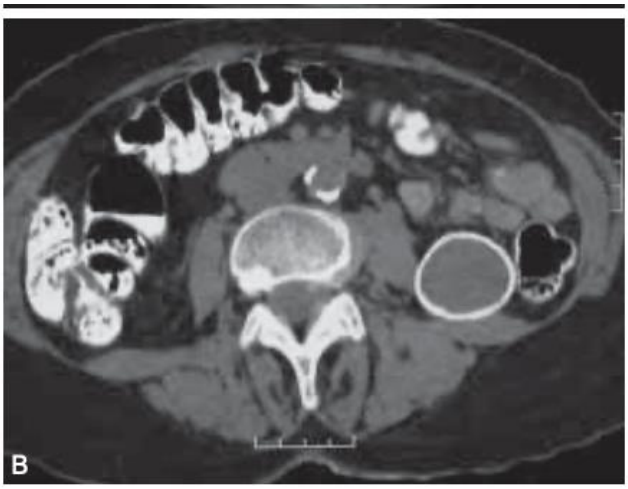


Image 29 - CT scan (category II Bosniak classification, cysts with diffuse calcification but no enhancement of septa on computed tomography) (Campbell-Walsh Urology, chapter 131, Renal Dysgenesis and Cystic Disease of the Kidney).

Diagnostic management. Large renal cysts may cause abdominal or flank pain, although this pain may be caused by a coexisting problem (e.g., nephrolithiasis), and other sources of pain should be ruled out. Other symptoms that may arise as a result of simple cysts are pain resulting from hemorrhage into the cyst or calyceal or infundibular obstruction caused by cyst impingement. In rare cases, hypertension may occur, presumably from cyst compression causing segmental renal ischemia of the surrounding renal parenchyma. Cyst infection is a rare but potentially severe complication, with patients demonstrating fever, flank pain, and often a sympathetic pleural effusion [5].

When a benign simple cyst causes pyelocalyceal obstruction or hypertension, the problem may be corrected either **surgically**, by unroofing the cyst, or percutaneously, by aspirating the fluid and perhaps injecting a sclerosing agent (glucose, phenol, iophendylate (Pantopaque), bismuth phosphate, and absolute ethanol), particularly if fluid has reaccumulated after an earlier aspiration,

laparoscopic unroofing (either transperitoneally or retroperitoneally) are all reasonable options for the treatment of symptomatic simple cysts.

Medullary sponge kidney (MSK)

Definition. **MSK (precalyceal canalicular ectasia)** - tubular dilation of the distal portion of the collecting ducts with numerous associated cysts and diverticula strictly confined to the medullary pyramids with calcifications.
Epidemiology. The disease is often sporadic, rarely familial, and is shown to present bilaterally with a prevalence between 5/10,000 and 5/100,000. Renal anomalies which may be associated with CD include MSK, cortical cysts, adult recessive polycystic kidney disease, and rarely autosomal dominant polycystic kidney disease.
Pathophysiology. Mutations and abnormalities in genes imperative for proper renal formation led to diminished distal nephron development, where precalyceal and collecting ducts are mostly affected. This leads to cyst formation, causing nephro-calcinosis and distal renal tubular acidosis as subsequent consequences of urine concentration defects. The occurrence of distal acidification in the nephron is thought to be the initial cause of the series of events including **hypercalciuria**, **hypocitraturia**, stone formation, and defective bone mineralization [12].
Clinical features. As rules, it's a benign process and may be totally asymptomatic for a long time. Most patients are asymptomatic. Episodic renal stones and recurrent urinary tract infections (UTI) are its common clinical implications. Hyperparathyroidism is a rare secondary manifestation of MSK. Excessive loss of calcium through the crystallization in the nephron can cause an up-regulation of parathyroid hormone (PTH) attempting to readjust the calcium imbalance. Major complications associated with MSK include nephrocalcinosis leading to nephrolithiasis, distal renal tubular acidosis, and UTI secondary to renal stones. Nephrolithiasis can be found in 70% of MSK patients [12].
Diagnostic evaluation.
Features of the disorder are as follows:
-enlarged kidneys, sometimes with calcification, particularly in the papillae.
-elongated papillary tubules or cavities that fill with contrast medium.
-papillary contrast blush and persistent medullary opacification [5].
IVU (image 30).

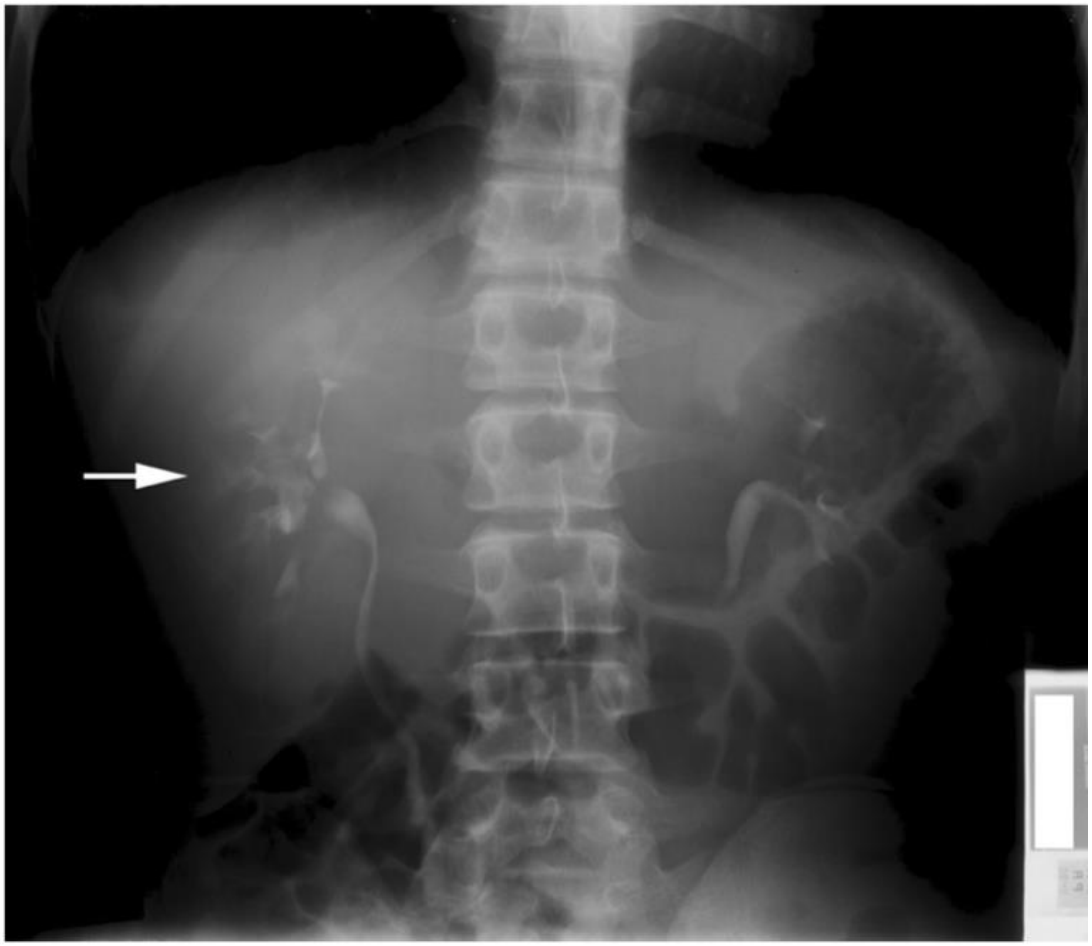


Image 30 - MSK (showed brush-like striations (arrow) within dilated contrast-filled medullary tubules) [12].

CT imaging (image 31) has been proven to better establish diagnoses for most urological conditions, however this unfortunately does not apply to MSK. This transition can negatively affect accurate diagnoses of MSK due to a deviation from contrast mediums [12].

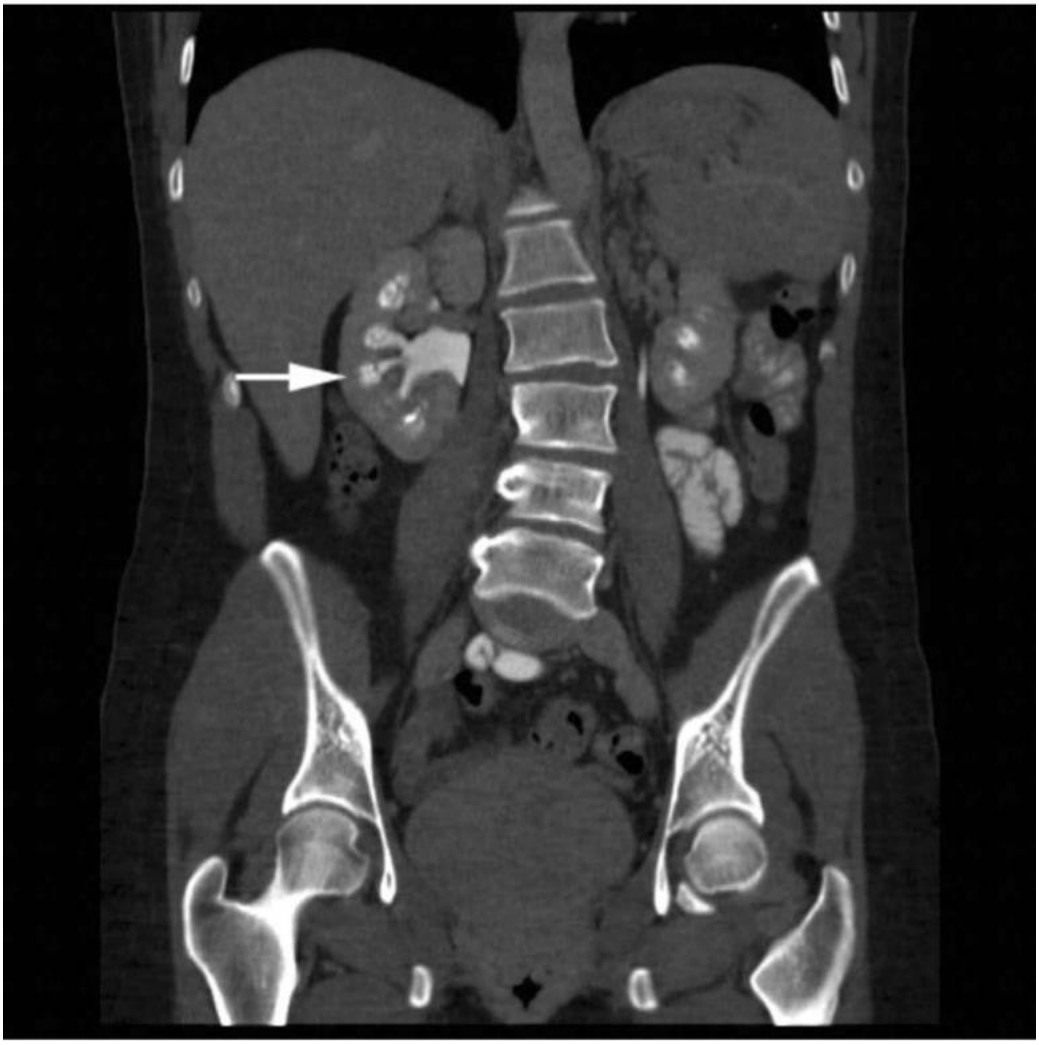


Image 31- CT (MSK) (dilated medullary contrast-filled tubules and medullary calcifications (arrow)[12].

Diagnostic management. MSK treatment remains unclear. Symptomatic care is focused on pH stabilization of urine, resulting in citrate and alkaline compound usage. Potassium citrate has shown to decrease distal renal tubular acidosis and reduce the renal stone precipitation in patients with MSK. When given to patients, citrate compounds have also shown to improve calciuria and decrease the negative effects of calcium mobilization from bone [12].

Thiazide diuretics can be added as an adjunctive measure to decrease rates of calcium stone formation in the distal nephron. Thiazide diuretics allow the reabsorption of calcium in the distal convoluted tubules, ultimately helping in the prevention in the recurrence of new stone formation [12].

II. ANOMALY OF NUMBER.

- **Bilateral renal agenesis**
- **Unilateral renal agenesis**
- **Supernumary kidney**

Bilateral renal agenesis (BRA).

Definition. Bilateral complete absence of the kidney. A study in 8500 pregnancies in Poland documented a higher incidence of 0.25% (Forys et al, 2003). Almost 75% of affected individuals are males. BRA has been detected in higher-than- expected proportions in esophageal atresia, cryptophthalmos or Fraser syndrome, Klinefelter syndrome, and Kallmann syndrome [5].

Mechanism. In a short way let repeat embryology of the kidney: the intermediate kidney, or mesonephros, develops and then regresses except for the mesonephric tubules. In the male, these are the efferent ductules that serve as a link between the gonad and the mesonephric or wolffian duct (WD) structures (the body and tail of the epididymis and vas deferens). In the female, the mesonephric tubules link the ovary through the fimbriated end of the fallopian tube to the reproductive tract. The WD elongates caudally and fuses with the anterior cloaca.

The definitive kidney differentiates from the metanephric blastema, which is a specialized region of the intermediate mesoderm termed the *metanephric mesenchyme* (MM). This process requires the reciprocal induction between the metanephric blastema and the ureteral bud (UB). The metanephric blastema sends signals to the WD to initiate UB formation from its caudal end between 5- and 7-weeks' gestation. The UB evaginates and invades the metanephric blastema and branches repeatedly in a characteristic pattern to form the collecting duct system. The ureteral tips induce nephron differentiation in the adjacent mesenchyme, forming the mature metanephros [5].

The absence of a nephrogenic ridge on the dorsolateral aspect of the coelomic cavity, or the failure of a UB to develop from the WD, will result in **renal agenesis**. Therefore for BRA to occur, there must be an alteration in normal molecular development or a mutation that causes renal or ureteral maldevelopment on both sides of the midline [5].

Potter has extensively described phenotypic features associated with BRA. These infants have low birth weights, ranging from 1000 to 2500 g, and intrauterine growth retardation resulting in part from low iron stores in the liver (Georgieff et al, 1996). At birth, oligohydramnios is present. The characteristic facial appearance and deformity of the extremities distinguishes these neonates from normal newborn**s.** The infants look prematurely senile and have "a prominent fold of skin that begins over each eye, swings down in a semicircle over the inner canthus and extends onto the cheek" (Potter, 1946a, 1946b).

Anomalies of the external genitalia include absence of the scrotum and clitoral hypertrophy. Penile development is usually normal, but in a few cases, penile agenesis or a rudimentary penis and scrotum have been reported [5].

Pulmonary hypoplasia and a bell-shaped chest are commonly associated findings that were thought to be caused by uterine wall compression of the thoracic cage as a

result of oligohydramnios. The anephric fetus fails to produce proline, which is a prerequisite for collagen formation in the bronchiolar tree. The kidney is the primary source of proline, thus pulmonary hypoplasia may result from the absence of renal parenchyma and not from diminished amniotic fluid [5].

Diagnostic evaluation. BRA is being diagnosed by prenatal ultrasonography in the second and third trimesters, when severe oligohydramnios is noted and no renal parenchyma can be identified. Additional diagnostic findings include small lung volumes and chest diameter and abnormal adrenal gland appearance [5].

Renal ultrasonography is the most efficient way to identify the kidneys and bladder and to confirm the presence or absence of urine production.

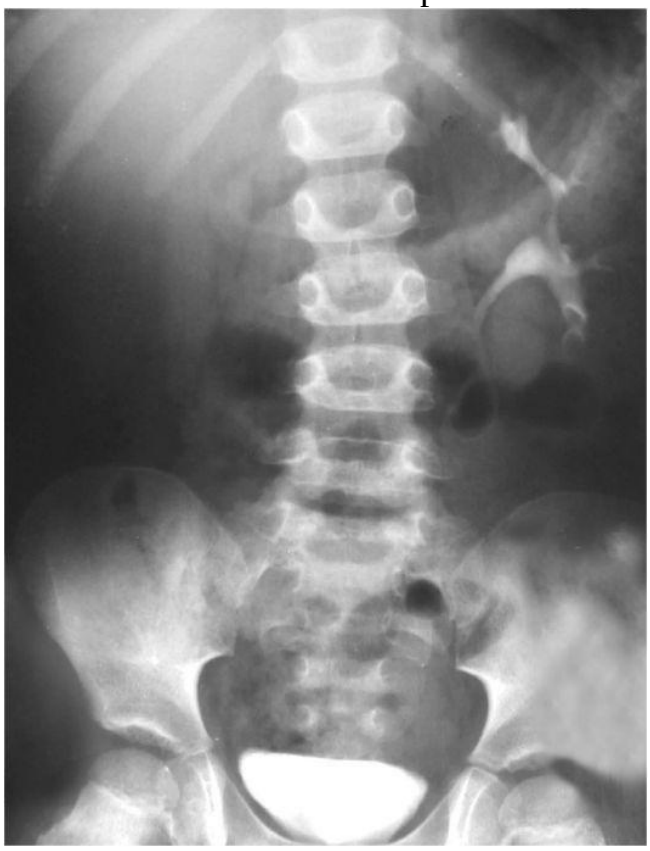


Image 32 – IVU (right renal agenesis) (Atlas of Pediatric urology, Kulikova T.N.).

Unilateral renal agenesis (URA).

Definition. Unilateral absence of the kidney. URA may remain undetected unless examination of the external genitalia and/or radiographic evaluation of the female or male pelvis for other reasons shows an anomaly associated with renal agenesis [5].

Mechanism. Renal aplasia is found in 1 in about 1300 births, which is like the incidence of renal agenesis and may be the most common cause of congenital solitary kidney. Renal aplasia includes those units with rudimentary parenchyma and ureter. It is thought to be a result of early regression of the ureteric bud, altered metanephric differentiation, or defects in the branching ureteric duct and the metanephric blastema to “communicate” and to provide reciprocal induction [5].

Diagnostic evaluation. Postnatally, a ultrasonogram (image 32) with color Doppler will show an absence of the kidney and ipsilateral renal vessels. The diagnosis of URA usually can be confirmed with a DMSA scan showing absent uptake of the

isotope on one side, with the contralateral kidney often showing compensatory hypertrophy.
Angiography (image 33): renal agenesis.

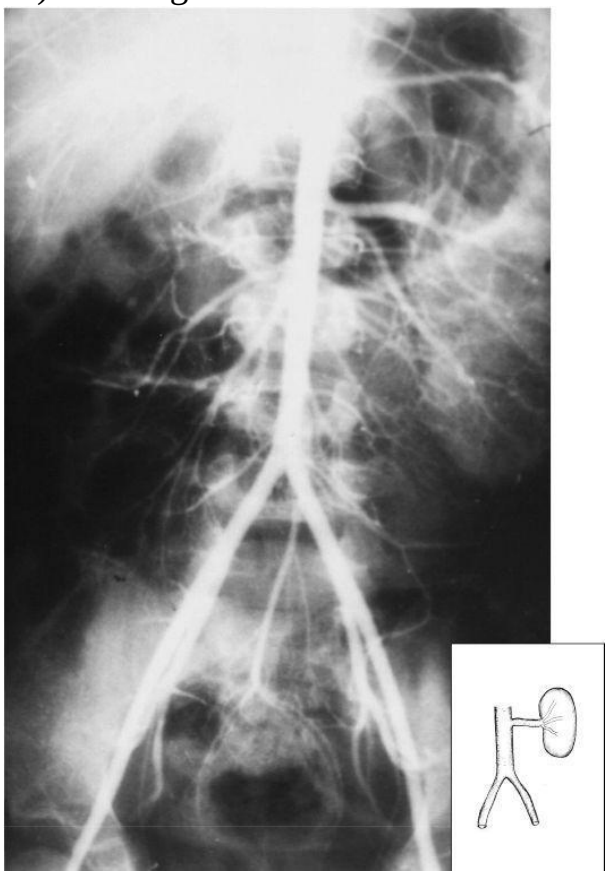


Image 33 -Angiography (right renal agenesis) (Atlas of Pediatric urology, Kulikova T.N.).

Supernumerary kidney.

Definition. Accessory organ with its own collecting system, blood supply, and distinct encapsulated parenchymal mass [5].

The supernumerary kidney is an extremely rare congenital urinary system anomaly in which fewer than 100 cases have been reported in the literature [13].
Mechanism. A second UB or a branching from the initial UB appears as a necessary first step. Next, the nephrogenic anlage may divide into two metanephric tails, which separate entirely when induced to differentiate by the separate or bifid UBs [5].
Clinical features. This anomaly is rarely symptomatic, but it may become symptomatic in early adulthood**.** Pain, fever, hypertension, and a palpable abdominal mass are the usual presenting complaints. Urinary infection, obstruction, or both, are the major conditions that lead to evaluation. Ureteral ectopia from the supernumerary kidney may produce urinary incontinence, but this is extremely rare. A palpable abdominal mass secondary to a carcinoma in the supernumerary kidney has been described in two patients. In 25% of all reported cases, the supernumerary kidney is discovered only at autopsy [5].
Diagnostic evaluation. If the supernumerary kidney is normal and asymptomatic, it is usually diagnosed when radiographic studies are performed for other reasons. The

kidney may be inferior and distant enough from the ipsilateral kidney so that it does not alter the position of the normal kidney [5].
Ultrasound examination (image 34).

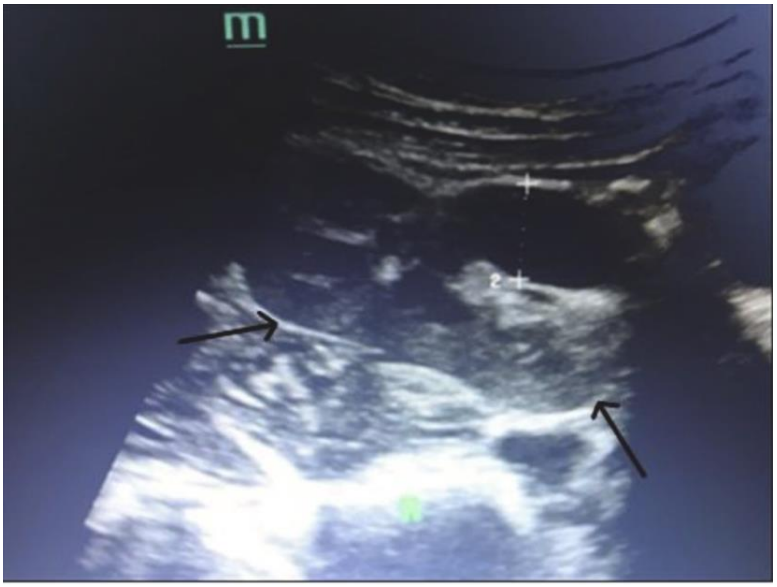


Image 34 – US (supernumerary fusion right kidney)

Computed tomography (image 35) [14].

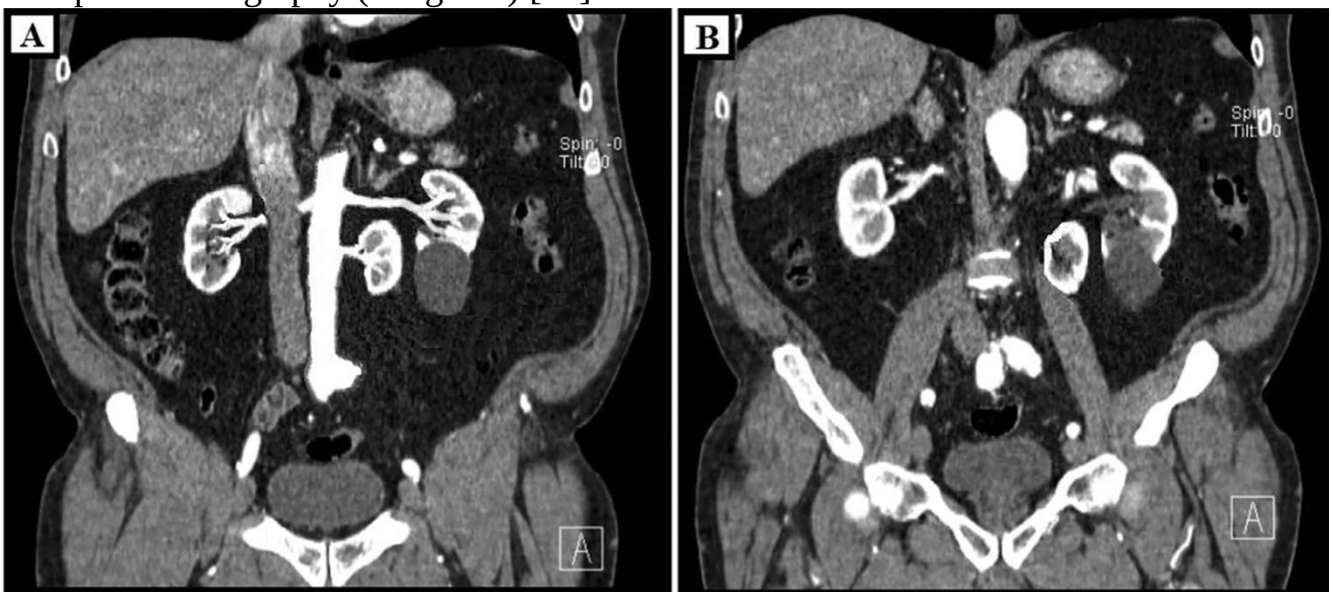


Image 35 – CT scan (arterial phase, the separate ectopic supernumerary left kidney which have own blood supply from aorta) [14].

III. ANOMALY OF ASCENT.

- **Simple renal ectopia**
- **Cephalad renal ectopia**
- **Thoracic kidney**

Simple renal ectopia.

Definition. When the mature kidney fails to reach its normal location in the “renal” fossa, the condition is known as *renal ectopia* (image 36) [5].

Differential diagnosis, as rules, we have performed between renal ptosis, in which the kidney initially is in its proper place (and has normal vascularity) but moves downward in relation to body position. The ectopic kidney has never back in the appropriate location. An ectopic kidney can be found in one of the following positions: pelvic, iliac, abdominal, thoracic, and contralateral or crossed [5]

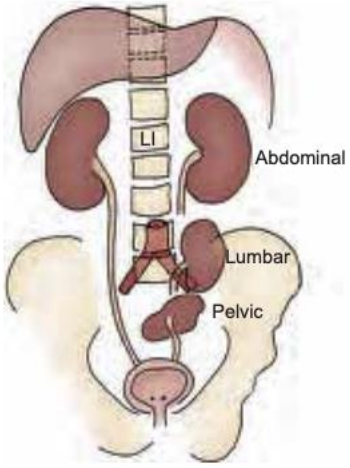


Image 36 – Incomplete ascent of kidney (Campbell- Walsh Urology, chapter 13, Anomalies of the Upper Urinary Tract).

The actual incidence among autopsy series varies from 1 in 500 (Campbell, 1930) **to 1 in 1200** (Bell, 1946a), **with an average occurrence of about 1 in 900** with no significant difference between the sexes [5].

Mechanism. The UB, arising from the WD at the end of the fourth week, grows craniad toward the urogenital ridge, acquiring a cap of metanephric blastema by the fifth week. The developing metanephric tissue and UB migrate cephalad, rotating medially on its long axis. The entire process is completed by 8 weeks' gestation. Factors that may prevent the orderly ascent and rotation of the kidneys include UB maldevelopment (Campbell, 1930), defective metanephric tissue that fails to induce ascent (Ward et al, 1965), genetic abnormalities, and maternal illnesses or teratogenic causes [5].

The **renal pelvis** is usually anterior (instead of medial) to the parenchyma, because the kidney has incompletely rotated. As a result, 56% of ectopic kidneys have a hydronephrotic collecting system. Half of these cases are a result of obstruction of the ureteropelvic or the ureterovesical junction (70% and 30%, respectively), 25% from reflux grade III or greater, and 25% from the malrotation alone (Gleason et al, 1994). Reflux has been found in 30% of children with ectopic kidneys (Guarino et al, 2004) [5].

The **ureter** usually enters the bladder on the ipsilateral side with its orifice positioned normally, except for those unusual cases with ectopic ureters [5].

The **arterial and venous network** is anomalous, and its vascular pattern depends on the ultimate position of the kidney. There may be one or two main renal arteries arising from the distal aorta or from the aortic bifurcation, with one or more aberrant arteries emanating from the common or external iliac or even the inferior

mesenteric artery. The kidney may be supplied entirely by multiple anomalous branches, none of which arise from the aorta. In no instance has the main renal artery arisen from the level of the aorta that would be its proper origin if the kidney were positioned normally [5].

Clinical features. Most ectopic kidneys are clinically asymptomatic, except in cases of associated ectopic ureter. Vague abdominal complaints or ureteral colic secondary to an obstructing stone are the most frequent symptoms leading to the diagnosis of an ectopic kidney. The abnormal position of the kidney results in a pattern of direct and referred pain that is atypical for colic and may be misdiagnosed as acute appendicitis or as pelvic inflammatory disease in female patients. Symptoms rarely occur because of organs that are adjacent to the ectopic kidney. Renal ectopia may also present with a UTI or a palpable abdominal mass. Seven cases of concomitant renal and ureteral ectopia presenting with urinary incontinence have been reported [5].

Diagnostic evaluation. US examination (lumbar or ectopic kidney). IVU (image 37).

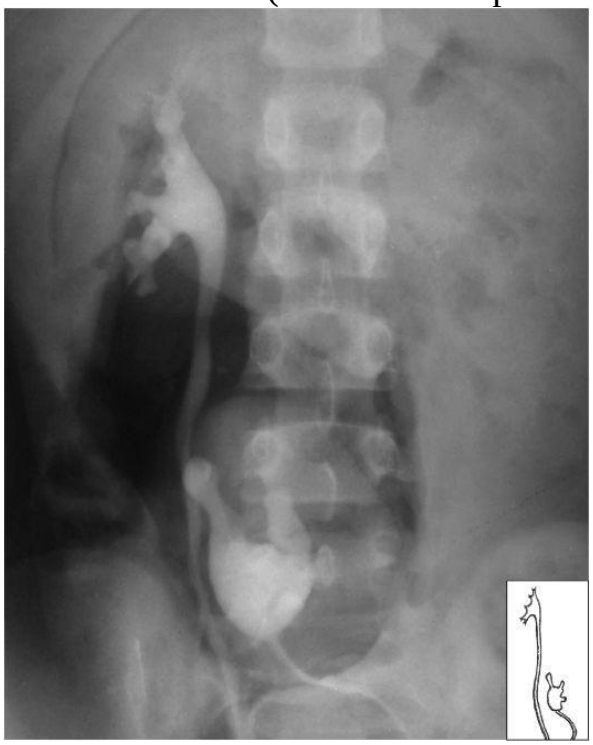


Image 37 – IVU (crossed iliac renal ectopia) (Atlas of Pediatric urology, Kulikova T.N.).

Cystoscopy, when performed, will demonstrate ureteral orifices that are invariably normal unless the ureteral orifice is also ectopic. If surgery is indicated on an ectopic kidney, MR arteriography may be useful preoperatively to define the anatomy of the renal vasculature, especially in cases of solitary ectopia [5].

Cephalad renal ectopia.

Definition. The kidney may be positioned more crania than normal when there is an omphalocele [5].

Mechanism. When the liver herniates into the omphalocele with the intestines, the kidneys continue to ascend until the diaphragm arrests their ascent. Both kidneys are ectopic and are positioned immediately beneath the diaphragm at the level of the 10th thoracic vertebra. The ureters were excessive in length but were otherwise normal. A color Doppler sonogram or MR arteriography demonstrates that the origin of each renal artery is more cephalad than normal. Patients usually have no symptoms caused by malposition, and urinary drainage is not impaired [5].

Thoracic renal ectopia.

Definition. Intrathoracic ectopia denotes either a partial or a complete protrusion of the kidney above the level of the diaphragm into the posterior mediastinum (image 38). It is the rarest form of renal ectopia; fewer than 5% of patients with ectopia have an intrathoracic kidney, with an incidence of 1:13,000 at autopsy [5].

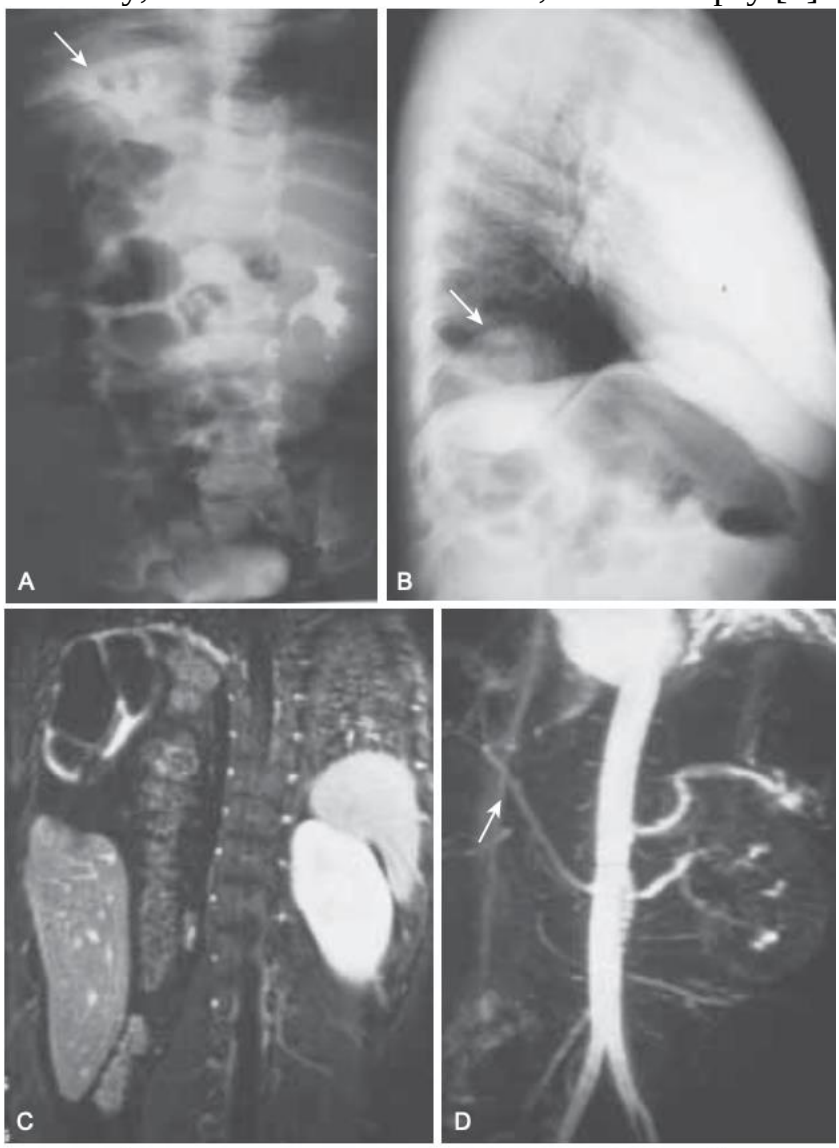


Image 38 – Thoracic renal ectopia (**A**-intravenous pyelogram shows a right thoracic kidney *(arrow)* and left orthotopic kidney. **B** -chest radiograph demonstrates right diaphragmatic eventration and a right intrathoracic kidney *(arrow).* C- magnetic resonance urogram shows coronal T1 fat saturation after contrast images of poorly functioning right hydronephrotic kidney located superior to the liver and inferior to

the right lung with absence of the posterior right hemidiaphragm, permitting the colon to enter the right hemithorax. D - angiographic sequence demonstrating right renal artery *(arrow)* arising from the aorta at the normal level of the left renal artery coursing superiorly to enter the right renal hilum) (Campbell- Walsh Urology, chapter 13, Anomalies of the Upper Urinary Tract).

The kidney is situated in the posterior mediastinum and usually has completed the normal rotation process. The renal contour and collecting system are normal. The kidney usually lies in the posterolateral aspect of the diaphragm in the foramen of Bochdalek. At this point, the diaphragm thins out and a flimsy membrane surrounds the protruding portion of kidney [5].

Clinical features. **Most affected individuals are asymptomatic.** Flank pain was the presenting symptom in a case of UPJ obstruction in a thoracic kidney [5].

IV. ANOMALIES OF FORM AND FUSION.

-L-shaped, S-shaped, horseshoe kidney, disc-kidney, lumb-kidney.

Crossed renal ectopia with and without fusion.

*Definition***.** When a kidney is located on the side opposite that in which its ureter inserts into the bladder, the condition is known as *crossed ectopia*. Ninety percent of crossed ectopic kidneys are fused to their ipsilateral mate [5].

Classification. Fusion anomalies of the kidney were categorized as crossed ectopia with fusion, crossed ectopia without fusion, solitary crossed ectopia, and bilaterally crossed ectopia (image 39) [5].

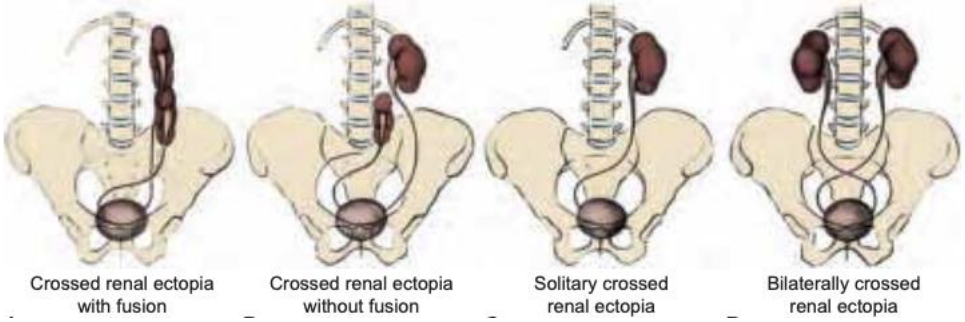


Image 39 – Anomalies of fusion of kidney (Campbell- Walsh Urology, chapter 13, Anomalies of the Upper Urinary Tract).

Also, the fusion anomalies have been designated as (A) unilateral fused kidney with inferior ectopia; (B) sigmoid, or S-shaped; (C) lump or cake; (D) L-shaped, or tandem; (E) disc, shield, or doughnut; and (F) unilateral fused kidneys with superior ectopia (image 40) [5].

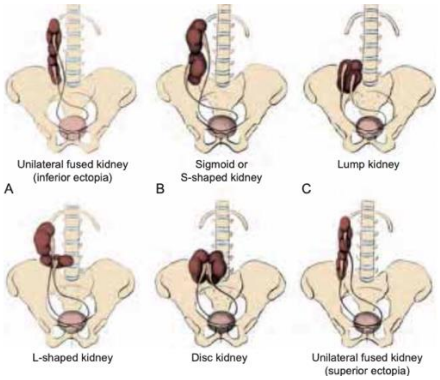


Image 40 - Six forms of crossed renal ectopia with fusion

Mechanism. Fusion of the metanephric masses may occur when the renal anlagen are still in the true pelvis before or at the start of cephalad migration, or it may occur during the latter stages of ascent. The extent of fusion is determined by the proximity of the developing renal anlagen to one another. After fusion, midline retroperitoneal structures, the aortic bifurcation, the inferior mesenteric artery, and the base of the small bowel mesentery impede the advancement of the kidneys toward their normal location. The crossed kidney usually lies caudad to its normal counterpart on that side. It is likely that migration of each kidney begins simultaneously, but ascent of the ectopic renal unit lags because of crossover time. Therefore, it is the superior pole of the ectopic kidney that usually joins with the inferior aspect of the normal kidney. Ascent continues either until the uncrossed kidney reaches its normal location or until one of the retroperitoneal structures prevents further migration of the fused mass. The final shape of the fused kidneys depends on the time and extent of fusion and the degree of renal rotation that has occurred. No further rotation is likely after the two kidneys have joined. An anteriorly placed pelvis suggests early fusion, whereas a medially positioned renal pelvis indicates that fusion probably occurred after rotation was completed [5].

The sigmoid, or **S-shaped**, kidney is the second most common anomaly of fusion. The crossed kidney is inferior, with the two kidneys fused at their adjacent poles, each renal pelvis is oriented correctly, and they face in directions opposite from one another (image 40) [5].

Lump or cake kidney is a relatively rare form of fusion. Ascent usually progresses only as far as the sacral promontory, but in many instances the kidney remains within the true pelvis. Both renal pelves are anterior, and they drain separate areas of parenchyma. The ureters do not cross (image 40) [5].

L – shaped kidney occurs when the crossed kidney assumes a transverse position at the time of its attachment to the inferior pole of the normal kidney. The crossed kidney lies in the midline or in the contralateral paramedian space anterior to the L4 vertebra. Rotation about the long axis of the kidney produces an inverted or a reversed pelvic position. The ureter from each kidney enters the bladder on its respective side (image 40) [5].

The ectopic kidney may have associated UPJ obstruction (29%), reflux (15%), or carcinoma (Abeshouse and Bhisitkul, 1959; Gleason et al, 1994).

Clinical features. **Most individuals with crossed ectopic anomalies present no symptoms.** These anomalies are often discovered incidentally at autopsy, during routine perinatal ultrasound, or after bone scanning. When symptoms occur, they usually develop in the third or fourth decades of life and they include vague lower abdominal pain, pyuria, hematuria, and UTI [5].

Diagnostic evaluation. US, CT scan, MRI, renography.

Horseshoe kidney is the most common of all renal fusion anomalies. The anomaly consists of two distinct renal masses lying vertically on either side of the midline and connected at their respective lower poles by a parenchymatous or fibrous isthmus that crosses the midplane of the body (Natsis et al, 2014). Horseshoe kidney occurs in 0.25% of the population, or about 1 in 400 persons [5].

Mechanism. The abnormality occurs between 4 and 6 weeks' gestation, after the UB has entered the renal blastema. In view of the ultimate spatial configuration of the horseshoe kidney, the entrance of the UB occurred before rotation and before renal ascent [5].

The pelves and ureters of the horseshoe kidney are usually anteriorly placed, crossing ventrally to the isthmus. Very rarely, the pelves are anteromedial, suggesting that fusion occurred after some rotation occurred. **In a small subset, an isthmus connects both upper poles**. The isthmus is generally bulky and consists of parenchymatous tissue with its own blood supply. The isthmus is located adjacent to the L3 or L4 vertebra just below the origin of the inferior mesenteric artery from the aorta. The isthmus most often lies anterior to the aorta and vena cava, but it has been reported to pass between the inferior vena cava and the aorta or even behind both great vessels [5].

The calyces are normal in number and are atypical in orientation. Because the kidney fails to rotate, the calyces point posteriorly, and the axis of each pelvis remains in the vertical or obliquely lateral plane (on a line drawn from the lower to the upper poles) (image 41) [5].

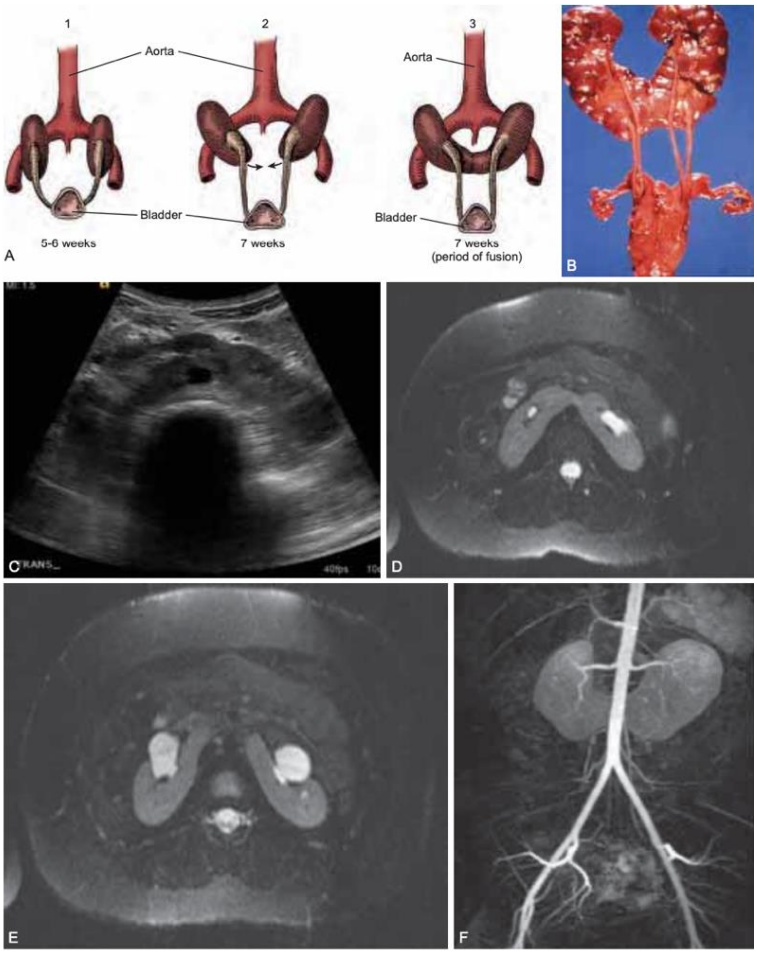


Image 41 – Horseshoe kidney (A – embryology of development of kidney. B - postmortem specimen showing horseshoe kidney with bilateral duplicated ureters. C – US of horseshoe kidney. D, E – MRI. F – angiography) (Campbell- Walsh Urology, chapter 13, Anomalies of the Upper Urinary Tract).

V. ANOMALY OF ROTATION.

Definition. The kidney, as it assumes its final position in the “renal” fossa, orients itself so that the calyces point laterally, and the pelvis faces medially. When this condition is not exact, the process is known as *malrotation* and is often described in conjunction with other renal anomalies, such as ectopia with or without fusion or horseshoe kidney (image 42) .

Mechanism. The kidney starts to turn during the sixth week, just when it is leaving the true pelvis, and it completes this process by rotating 90 degrees toward the midline by the time ascent is complete at the end of 9 weeks’ gestation. Each ureteral branch then induces differentiation of the metanephrogenic tissue. More parenchyma develops ventrally than dorsally, and the pelvis seems to rotate medially. The renal blood supply does not appear to be the cause, nor does it appear to be a limiting factor in malrotation, but rather it follows the course of renal hyporotation, hyperrotation, or reverse rotation [5].

The kidney and renal pelvis normally rotate 90 degrees ventromedially during ascent.

Malrotation does not impair renal function. Hydronephrosis resulting from impaired urinary drainage may lead to infection and calculus formation [5].

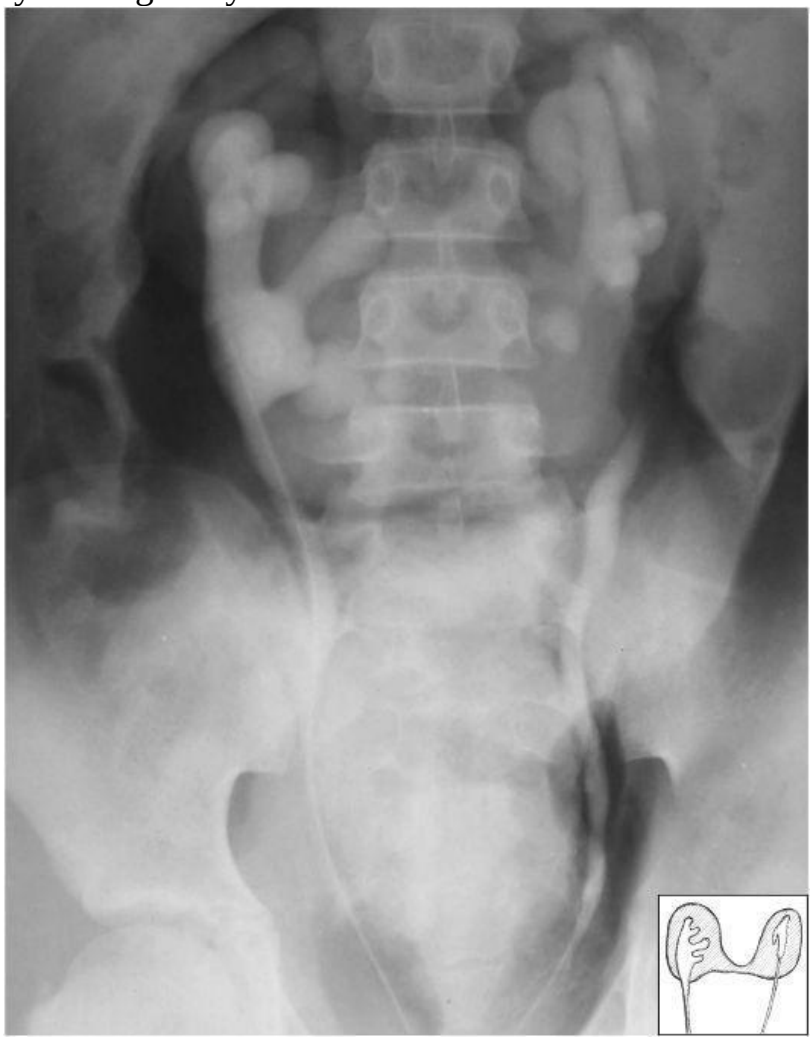


Image 42 – Horseshoe kidney (IVU) (malrotation of renal pelvis) (Atlas of Pediatric urology, Kulikova T.N.)

VI ANOMALY OF RENAL VASCULATURE.

- **Aberrant vessels**
- **Accessory vessela**
- **Multiple vessels**
- **Renal artery aneurism (RAA)**
- **Renal arteriovenous fistula**

*Definition***.** The kidney is divided into various segments, each supplied by a single "end" arterial branch that usually courses from one main renal artery. The correct term to describe any kidney supplied by more than one vessel is *multiple renal arteries*. The terms *anomalous vessels* or *aberrant vessels* should be reserved for those arteries that originate from vessels other than the aorta or main renal artery. The term *accessory vessels* denotes two or more arterial branches supplying the same renal segment [5].

Based on vascular supply, the renal parenchyma is divided into five segments: apical, upper, middle, lower, and posterior. The main renal artery divides initially into an anterior and posterior branch. The anterior branch almost always supplies the upper, middle, and lower segments of the kidney. The posterior branch invariably supplies the posterior and lower segments.

Symptoms attributable to renal vascular anomalies are those that might result from inadequate urinary drainage. Multiple, aberrant, or accessory vessels may constrict an infundibulum, a major calyx, or the UPJ . Pain and hematuria secondary to hydronephrosis, UTI, or calculus may result [5].

Abeshouse (1951) classified *renal artery aneurysms* (RAAs) as follows: saccular, fusiform, dissecting, and arteriovenous. The saccular aneurysm, a localized outpouching that communicates with the arterial lumen by a narrow or wide opening, is the most common type, accounting for 93% of all aneurysms (Zinman and Libertino, 1982). When the aneurysm is located at the bifurcation of the main renal artery and its anterior and posterior divisions, or at one of the more distal branchings, it is congenital in origin and is called the fusiform type [5]. The diagnosis is suspected when a pulsatile mass is palpated in the region of the renal hilum or when a bruit is heard on abdominal auscultation. A wreathlike calcification in the area of the renal artery or its branches (30%) is highly suggestive [5]. Many asymptomatic RAAs are diagnosed during an evaluation of hypertension.

Renal arteriovenous fistula: two types exist, congenital and acquired, with the latter (secondary to trauma, inflammation, renal surgery, or percutaneous needle biopsy) accounting for the increase in incidence. They are identifiable by their cirsoid configuration and multiple communications between the main or segmental renal arteries and the venous channels. The pathophysiology involved in the shunting of blood, which bypasses the renal parenchyma and rapidly joins the venous circulation and returns to the heart, results in a varied clinical picture. The hemodynamic derangement often produces a loud bruit in 75% of cases. Diminished perfusion of renal parenchyma distal to the fistulous site leads to relative ischemia and renin mediated hypertension in approximately 50%. The increased venous return and high cardiac output with concomitant diminution in peripheral resistance may

result in left ventricular hypertrophy and subsequent high-output cardiac failure in 50% of cases [5]. Nephrectomy, partial nephrectomy, vascular ligation, selective embolization and balloon catheter occlusion have been used to obliterate the fistula [5].

VII ANOMALIES OF THE COLLECTING SYSTEM

- **Calyceal diverticulum**
- **Hydrocalycosis**
- **Megacalycosis**
- **Infundibulopelvic stenosis**
- **Bifid pelvis**

Calyceal diverticulum. A calyceal diverticulum is a cystic cavity within the kidney that is lined by transitional epithelium and communicates with a calyx or less commonly with the renal pelvis through a narrow isthmus.
Mechanism. At the 5-mm stage of the embryo, ureteral branches of the third and fourth generation, which ordinarily degenerate, may persist as isolated branches, resulting in the formation of a calyceal diverticulum [5]. Small diverticula are usually asymptomatic and are found incidentally by ultrasonography, CT, or MRI. These diverticula tend to distend progressively with trapped urine. Hematuria, pain, and UTI may be seen in the presence of stones, which may be present in almost 40% of patients [5].
Hydrocalycosis is a rare cystic dilation of a major calyx with a demonstrable connection to the renal pelvis. Dilation of the upper calyx resulting from obstruction of the upper infundibulum by vessels or stenosis has been described [5].
Megacalycosis is a nonobstructive enlargement of calyces resulting from malformation of the renal papillae. Megacalycosis occurs predominantly in males with a ratio of 6:1. Bilateral disease has been seen almost exclusively in males, whereas segmental unilateral involvement occurs only in females. Long-term follow-up of patients with this anomaly does not usually show progression of the anatomic or functional status of the kidney [5].
Infundibulopelvic stenosis most likely forms a link between cystic dysplasia of the kidney and the grossly hydronephrotic organ (Uhlenhuth et al, 1990). This condition includes a variety of radiographically dysmorphic kidneys with varying degrees of infundibular or infundibulopelvic stenosis that may be associated with renal dysplasia. Infundibulopelvic stenosis is usually bilateral and is commonly associated with vesicoureteral reflux, suggesting an abnormality of the entire UB [5].
Bifid pelvis. Approximately 10% of normal renal pelves are bifid**,** the pelvis dividing to form two major calyces first at, or just within, its entrance to the kidney. A bifid pelvis should be considered a normal variant. If further division of the renal pelvis occurs, triplication of the pelvis may result, but this is extremely rare [5].

ANOMALIES OF URETER

-Anomalies of number
-Anomalies of position
-Ectopic ureters
-Ureterocele
-Ureteropelvic junction obstruction (UPJO)
-Ureterovesical junction obstruction (we are talking about in chapter " Hydronephrosis").

I ANOMALIES OF NUMBER

Definition. Bifid ureters (duplication of ureter) are a common condition, when it was found duplex of ureter. Also, may be associated with ectopia or a ureterocele but is also compatible with a normally functioning renal system if both ureters enter orthotopically or if there is partial duplication [5]. A bifid renal pelvis includes only a single ureter, but with confluence of the upper and lower ureters lower than the ureteropelvic junction (UPJ) constitutes partial duplication of the ureter or bifid ureter.

Mechanism. The ureteric bud, from which the collecting system of kidney will form, arises from the caudal end of the mesonephric duct around the 5th week of development and grows into the nephrogenic cord, meanwhile the metanephric blastema, which will evolve into nephron, is formed around the tissue from the nephric cord surrounds the ureteric bud. The fact that the ureteric bud divides prematurely before penetrating into metanephric blastema will result in duplex ureter. There are 2 types of complete and incomplete duplex ureter. The incidence of incomplete duplex ureter, including 3 subtypes, such as proximal, middle, and distal, depending on the location that bifid ureters join a single unit, is 3 times more than the complete [15].

Clinical features. The upper pole is more likely affected by conditions resulting from abnormal ureteral formation, including ectopic and ureterocele. Lower pole UPJO evaluation and management are like those for a single-system UPJ obstruction. Lower pole UPJO may be identified with partial and complete ureteral duplication. Recognition of the presence of the duplication may be challenging with massive hydronephrosis, but in most cases the normal upper pole will be identified on functional imaging such as a renal scan, even if not detected on ultrasound [5].

Although asymptomatic patients with duplex ureter could be found incidentally by excretory urography (image 43), ultrosonography, computed tomography (CT), and magnetic resonance imaging (MRI), preoperative assessment of the anatomic variations and function of duplex renal and ureters is often difficult in symptomatic patients with urinary obstruction, vesicoureteral reflux, and urinary tract infection [15].

Triplication. Triplication of the ureter, either complete or partial, is very rare. Type 1 constitutes three entirely separate ureters with unique attachment to the bladder or distally and accounts for 35% of triplications.

Type 2 is an incomplete separation with two ureteral orifices, occurring in 21%. Type 3 is a trifid ureter with a single ureteral orifice, seen in 31%.
Type 4 describes two ureters with three orifices [5].

The ureters may be associated with ureteroceles and may be ectopic to the bladder neck, urethra, or vagina. Lower pole and mid-pole UPJ obstruction may be present, as well as ureterovesical obstruction. VUR is also described, as well as contralateral duplication [5].

Even more rare is ureteral *quadruplication*, with only eight cases reported [5].

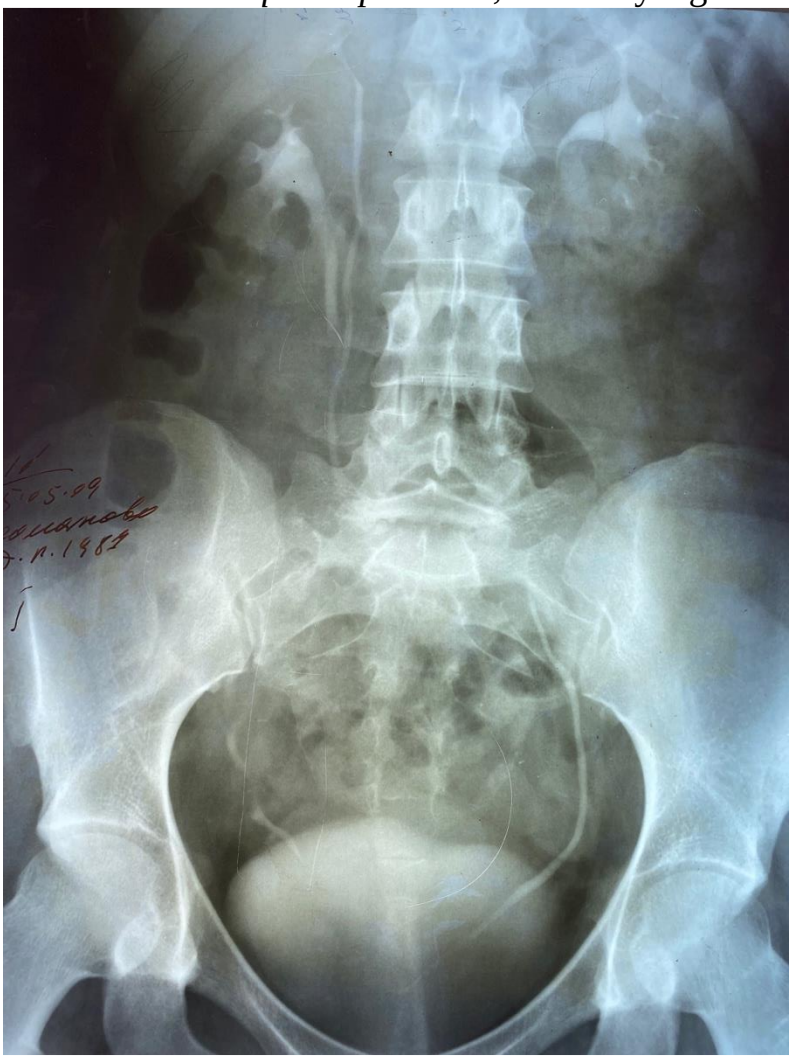


Image 43 – Duplication of ureter (partial) (the own materials from department).

II ANOMALIES OF POSITION

*Retrocaval ureter***.** This disorder involves the right ureter, which typically deviates medially behind (dorsal to) the inferior vena cava, winding about and crossing in front of it from a medial to a lateral direction, to resume a normal course, distally, to the bladder. The renal pelvis and upper ureter are typically elongated and dilated in a J or fishhook shape before passing behind the vena cava [5].

Mechanism. The definitive inferior vena cava develops on the right side from a plexus of fetal veins (image 44). Initially, the venous retroperitoneal pathways consist of symmetrically placed vessels, both central and dorsal. The posterior cardinal and supracardinal veins lie dorsally, and the subcardinal veins lie ventrally.

These channels, with their anastomoses, form a collar on each side through which the ascending kidneys pass. Normally the left supracardinal veins and the lumbar portion of the right posterior cardinal vein atrophy. The subcardinal veins become the internal spermatic veins. The definitive right-sided inferior vena cava forms from the right supracardinal vein. **If the subcardinal vein in the lumbar portion fails to atrophy and becomes the primary right-sided vein, the ureter is trapped dorsal to it [5].**

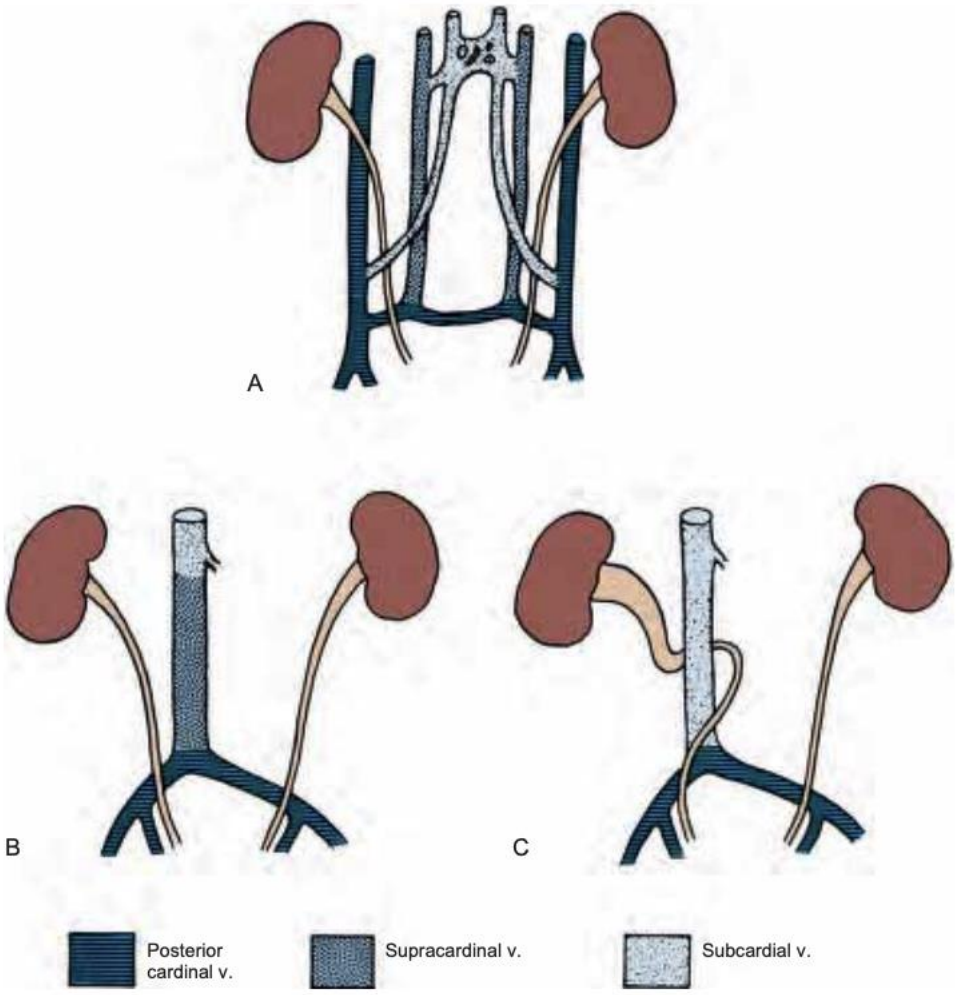


Image 44 – Development of vena cava (Campbell- Walsh Urology, chapter 134, Ectopic ureter, ureterocele and ureteral anomalies).

The symptoms of preureteral vena cava are those of obstruction (flank or abdominal pain or infection).

Surgical correction involves ureteral division, with relocation and ureteroureteral or ureteropelvic reanastomosis, usually with excision or bypass of the retrocaval segment, which can be aperistaltic [5].

Retroiliac ureter. Like the preureteral cava, the preureteral iliac artery is of vascular origin without definitive proof. Normally, the primitive ventral root of the umbilical artery is replaced by development of a more dorsal branch between the aorta and the distal umbilical artery. Persistence of the ventral root as the dorsal root fails to form traps the ureter dorsally [5].

Obstruction occurs at the level of L5 or S1 as the ureter is compressed behind the artery. Coexisting anomalies are common.

Ectopic ureter.

Definition. An ectopic ureter is any ureter, single or duplex, that does not enter the trigonal area of the bladder (image 45).

In a duplex system the ectopic ureter is inevitably the upper pole ureter owing to its budding from the mesonephric duct later (more cephalad) than the lower pole ureteral bud.

In females, the ectopic ureter may enter anywhere from the bladder neck to the perineum and into the vagina, uterus, and even rectum. One of the classic symptoms is continuous wetting.

In males, the ectopic ureter always enters the urogenital system above the external sphincter or pelvic floor and usually into the wolffian structures, including vas deferens, seminal vesicles, or ejaculatory duct. Clinical presentation is not incontinence but infection.

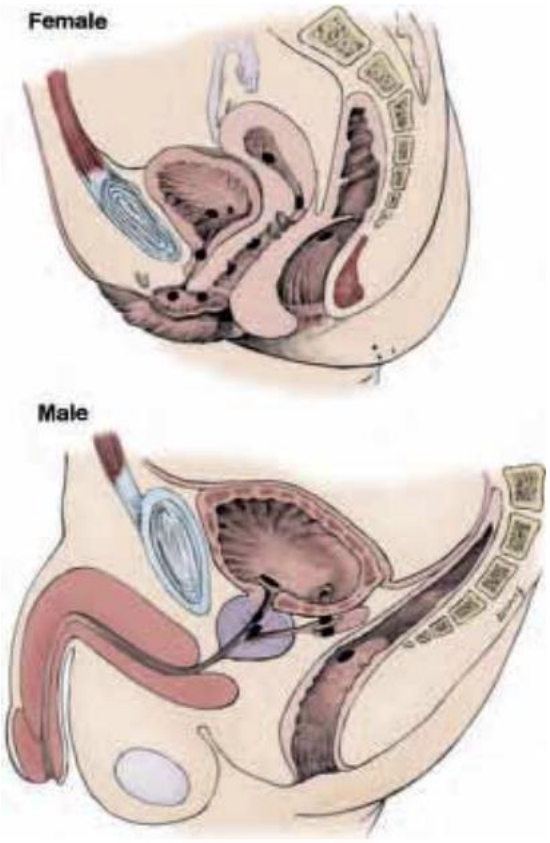


Image 45 – Sites of ureteral ectopic orifices (Campbell- Walsh Urology, chapter 134, Ectopic ureter, ureterocele and ureteral anomalies).

Ureterocele.

Definition. Ureteroceles (image 46) represent a version of the ectopic ureter with a cystic dilation of the distal aspect of the ureter that is located either within the bladder or spanning the bladder neck and urethra. As with the ectopic ureter,

ureteroceles may be associated with a single or duplex system, and in duplex systems are associated with the upper [5].

Classification. Several classification systems exist for ureteroceles, but the most useful one for clinical practice separates intravesical from extravesical ureteroceles [5].

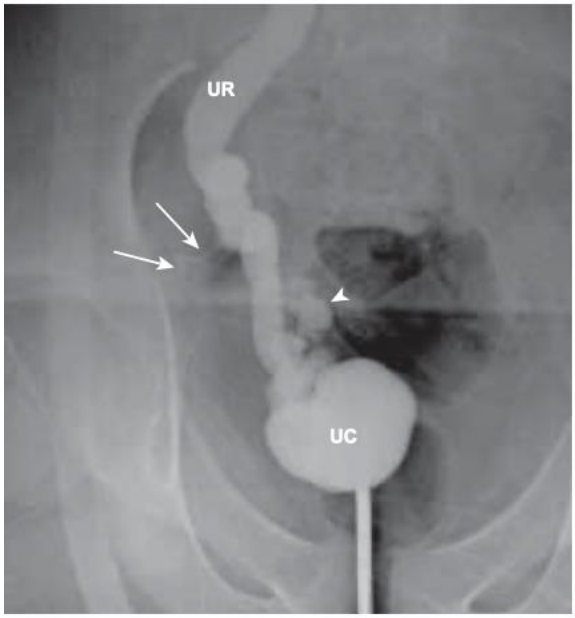


Image 46 – Retrograde injection study of a boy with abdominal pain and a ureterocele associated with a hypoplastic right kidney. The intravesical ureterocele (UC) is being injected and demonstrates communication with the right seminal vesicle *(arrowhead)* and vas deferens *(arrows)*, with the ureter (UR) leading to the dysplastic kidney. At surgical resection, the ureter and vas joined just above the seminal vesicles (Campbell- Walsh Urology, chapter 134, Ectopic ureter, ureterocele and ureteral anomalies).

Mechanism. The pathogenesis of ureteral ectopia with or without ureterocele results in renal maldevelopment caused by defective ureterotrigonal connections [5].

Function of the urinary tract depends on patent ureterobladder connections and an antireflux mechanism that prevents backflow of urine to the ureter and kidneys. The antireflux valve is formed by intersecting ureteral and bladder muscle fibers, hence malpositioned ureters that do not follow a precise trajectory through the bladder wall or terminate outside the normal insertion site in the trigone can cause obstruction or vesicoureteral reflux (VUR). Renal defects associated with ureteral ectopia, ureterocele, or VUR can be caused by obstruction that damages renal cell types or mutations in genes that are required independently for normal kidney development and ureter insertion, including *Ret, Fgfr2, Gata3* and several others [5].

Because the ureteral bud derives from the wolffian duct, the ectopic ureter will not insert directly into the müllerian structures (vagina, cervix, uterus), but will be associated with them through the remnant of the wolffian duct, the Gartner duct, that runs alongside the mature müllerian structures. The Weigert-Meyer rule

describes the inverse relationship of the duplex ureteral orifices, in which the ectopic ureter or ureterocele associated with the upper pole is caudal to the lower pole ureteral orifice [5].

Diagnostic evaluation and management. The majority of ureteroceles and ectopic ureters are detected through prenatal ultrasound imaging, even if the specific diagnosis is not made until after birth. Ectopic ureters will frequently manifest with a less acute pattern evidenced by ongoing low-grade fever with periodic spikes. In some cases, urine cultures will be negative because the infected ectopic system is not draining into the bladder.

In boys, a similar subacute pattern of infection may be present, but more often these boys have epididymitis.

Urinary incontinence may be caused by an ectopic ureter in a girl but not in a boy. The toilet-trained girl with verified continuous urinary leakage must be evaluated for an ectopic ureter. Ureterocele prolapse is an unusual but distinctive presenting sign; these are usually smooth, congested mucosa-covered intralabial masses, and the child may be having trouble voiding [5].

The ultrasound image will usually provide the anatomic diagnosis of an ectopic ureter or ureterocele and permit an inference of renal function. The typical findings are of a dilated upper pole with ureteral dilation or a dilated single system. The ureterocele is characterized by a thin-walled, cystic dilation within the bladder and not extending beyond its walls. A very dilated ectopic ureter may produce an impression on the bladder and appear as a ureterocele.

Radionuclide renal imaging remains the gold standard for renal functional assessment, and this is usually best provided by DMSA imaging.

The function of the affected upper pole is the principal focus, but the health of the other renal moieties must be determined as well.

VCUG provides the most definitive evaluation of the bladder and distal ureters, as well as the urethra.

The appearance of the bladder base with filling and voiding demonstrated on VCUG will also be useful in therapeutic decisions, as massive eversion indicates a weak trigonal floor that may be more likely to require surgical repair.

Endoscopy should take note of the character of the urethra, bladder neck, and trigone relative to the ureterocele or ectopic ureter [5].

The goals of therapy are preservation of renal function; elimination of infection, obstruction, and reflux; and maintenance of urinary continence (total reconstruction, upper pole partial (total) nephrectomy open or laparoscopic, ureterocele excision and common-sheath reimplantation, pyeloureterostomy,ureterureterostomy).

Anatomy of bladder

The bladder is a unique organ of the human body in that not only does it carry a dual function of both storage and emptying of urine but it also has a complex innervation of voluntary and involuntary control of function, wall consists of three layers: mucosa, detrusor, and adventitia [5].

The detrusor consists of a meshwork of smooth muscle fibers arranged into a single functioning unit with an ability to elicit nearly maximum active tension over a wide range of length. This allows the bladder to fill with urine from the upper tract at low pressures (compliance). The ability of the bladder to store urine (reservoir function) is determined by the concomitant activity of the detrusor muscle and the bladder outlet (consisting of the bladder neck, proximal urethra, and striated muscle of the pelvic floor) (image 47) [5].

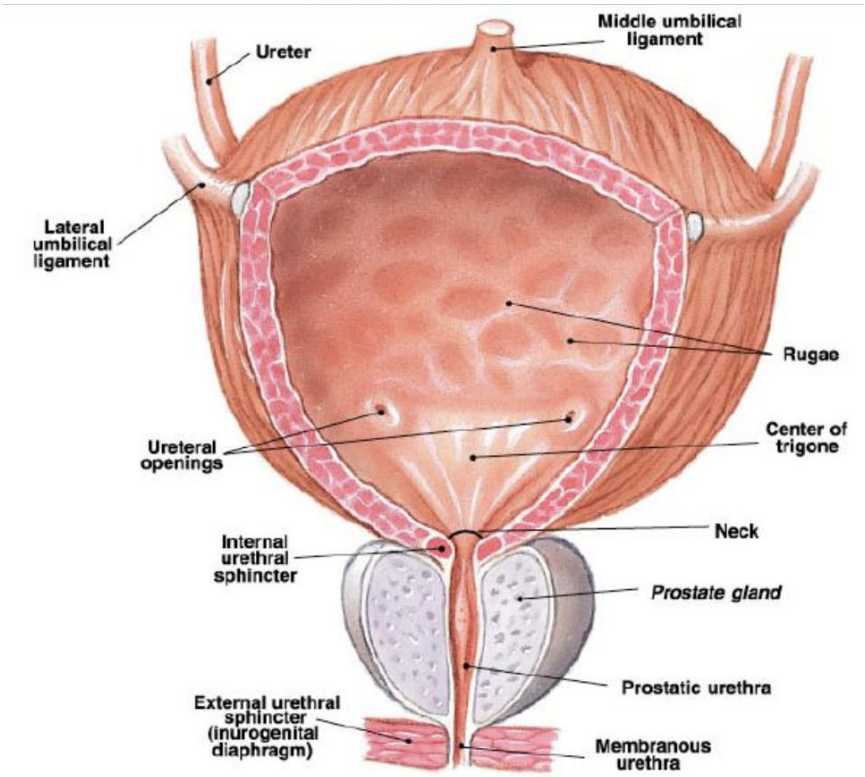


Image 47 – Bladder (medstudentnotes.com)

The anatomy of the external urinary sphincter consists of a cylindric structure, which is accentuated anteriorly and thinned or absent posteriorly, thus giving a characteristic horseshoe or ω shape on cross section. It has an inner layer of smooth muscle and an outer layer of striated muscle, extending from the apex of the prostate to invest the length of the membranous urethra in males. In females this is less well developed and extends from the bladder neck to the mid-urethra [5].

The internal sphincter has not been well delineated anatomically. It has generally been accepted that it consists of smooth muscle fibers continuing from the bladder base and trigone that traverse inferiorly through the bladder neck to extend toward the proximal urethra [5].

Innervation of bladder. Activation, coordination, and integration of various parts of the bladder-sphincteric complex involves both the central somatic and autonomic nervous systems through three sets of peripheral nerves: sacral parasympathetic (pelvic nerve), thoracolumbar sympathetic (hypogastric nerves and sympathetic chain), and sacral somatic nerves (primarily the pudendal nerve).

Parasympathetic nerve fibers run in the pelvic nerve (S2 to S4) to supply the pelvic and vesical plexuses before entering the bladder. Parasympathetic ganglia are found within these plexuses and in the bladder wall.

Sympathetic nerves arise from segments T10 to L2 of the spinal cord and go to the inferior mesenteric ganglion through the sympathetic trunk. From the inferior mesenteric ganglion, the nerve fibers pass to the pelvic plexus and bladder through the hypogastric nerves. There is also sympathetic innervation originating from T10 to L2 supplying the detrusor and urethral sphincter.

The somatic nervous system (pudendal nerve) supplies the periurethral pelvic floor musculature. The sensory and motor nerve fibers carried by all three nerves innervate both the bladder and urethral sphincter. They originate from parasympathetic ganglia located in the second, third, and fourth segments of the sacral spinal cord. Within the spinal cord, information from bladder afferents is integrated with that from other viscera and somatic sources and projected to the brainstem centers that coordinate the micturition cycle (image 48) [5].

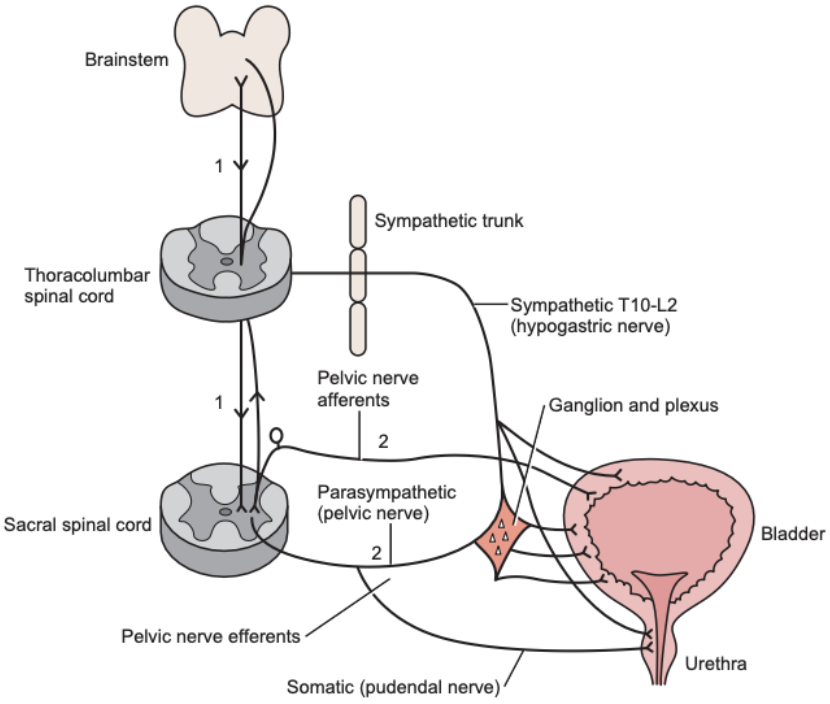


Image 48 – Innervation of bladder ((Campbell- Walsh Urology, chapter 136, development and assessment LUT function).

ANOMALIES OF BLADDER

-Urachal abnormalities
-Bladder diverticulum
-Bladder duplication
-Extrophy
-Vesicoureteral reflux

I. URACHAL ABNORMALITIES.

Bladder and urachal development. Between the 4th and 6th weeks of gestation, the urorectal septum divides the endodermal cloaca into a ventral urogenital sinus and a dorsal rectum.

The cranial part of the urogenital sinus is continuous with the allantois and develops into the bladder and pelvic urethra.

The caudal portion gives rise to the phallic urethra in males and the distal vagina in females. Unlike in males, the entire female urethra is derived from the pelvic part of the urogenital sinus. The allantois develops as an extraembryonic cavity from the yolk sac and connects with the cranioventral portion of the cloaca, the future bladder.

Around the 4th to 5th month of gestation, the allantoic duct and ventral cloaca involute as the bladder descends into the pelvis. The descent causes the allantoic duct to elongate because it does not grow with the embryo. This epithelialized fibromuscular tube continues to become narrower until it obliterates into a thick fibrous cord, the urachus. The obliterated urachus becomes the median umbilical ligament and connects the apex of the bladder with the umbilicus [5].

The urachus is located pre-peritoneally in the center of a pyramid-shaped space. This space is lined by the obliterated umbilical arteries, with its base on the anterior dome of the bladder and the tip directed toward the umbilicus (image 49) [5].

Image 49 – Urachus ((Campbell- Walsh Urology, chapter 138, bladder anomalies in children).

The urachus can remain either completely open or obliterate partially, leading to the formation of cystic structures at any site throughout its course. The following four different urachal anomalies have been describepatients urachus, umbilical-urachus sinus, urachal cyst, vesicourachal diverticulum (image 50) [5].

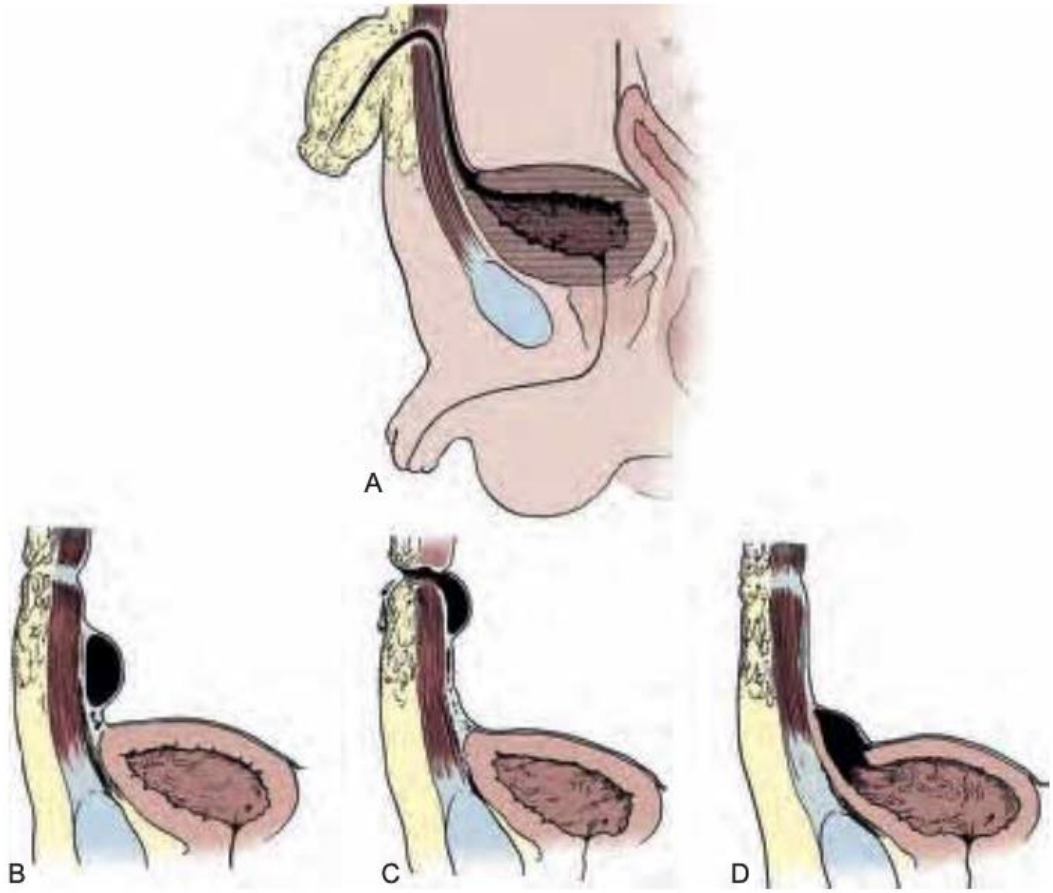


Image 50 – Anomalies of Urachus **(A** Patent urachus. B, Urachal cyst. C, Umbilical-urachus sinus. D, Vesicourachal diverticulum) (Campbell- Walsh Urology, chapter 138, bladder anomalies in children).

Patent Urachus is explained by nondescent of the bladder or, more commonly, failure of the epithelial-lined urachal canal to obliterate . This patology is suspected in the neonatal period as continuous or intermittent drainage of fluid from the umbilicus. The most common organisms cultured from the umbilical drainage include *Staphylococcus aureus, Escherichia coli, Enterococcus, Citrobacter,* and, rarely, *Proteus* species . Additional manifestations include an enlarged or edematous umbilicus and delayed healing of the cord stump. The diagnosis is confirmed by demonstration of the fluid- filled canal on longitudinal ultrasound or contrast filling on retrograde fistulogram or VCUG (image 51) [5].

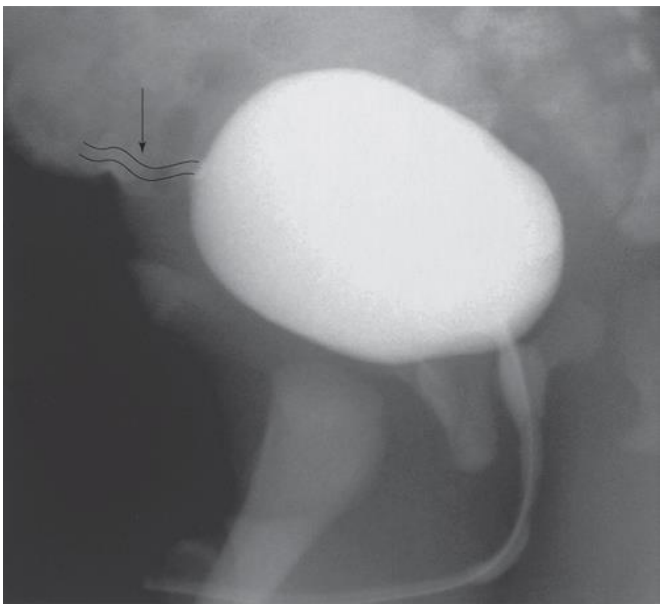


Image 51 - Urachus (vesicoureterogram image of patent urachus in a newborn. Retrograde contrast filling of patent canal with contrast pooling in umbilicus.)) (Campbell- Walsh Urology, chapter 138, bladder anomalies in children).

In the umbilical-urachus sinus, the urachus obliterates at the bladder level but remains open at the umbilical site, causing a continuously draining sinus. The manifestation is like that of the patent urachus. The diagnosis is made by sinugram. The caudal part of the urachus is filled with desquamated epithelial cells, and no connection to the bladder can be identified [5].

There is no communication of the *cyst with the bladder or umbilicus*. However, the fluid-filled cyst can drain through the umbilicus or into the bladder intermittently. Urachal cysts are found more commonly in the distal part of the urachus and manifest more commonly in adults than in infants or children. The cyst material consists of desquamated epithelial cells. These cells can become infected; *Staphylococcus aureus* has been identified as the most common organism.

Once infected, urachal cysts can manifest as umbilical abscess formation or bladder infections. Additional symptoms include localized lower abdominal pain, voiding symptoms, or even a painful and palpable mass. The diagnosis is confirmed by ultra-sound, demonstrating the localized cyst between the anterior abdominal wall and the peritoneum [5].

The urachus obliterates almost completely, except at the level of bladder apex. Here it forms a *diverticulum* of varying size. These lesions are usually nonsymptomatic and found incidentally on nonrelated radiographic workups. Although the diverticulum can enlarge in the case of urinary obstruction, this rarely causes problems because they tend to have a large opening and drain into the bladder well. Stone formation and urinary tract infections have been reported, especially in the case of a narrowed neck causing the need for intervention [5].

II BLADDER DIVERTICULUM. Bladder diverticula (image 52) are caused by infravesical obstruction, iatrogenic after bladder surgery, or as a congenital defect. Independent from the cause, all diverticula develop as herniation of bladder mucosa between defects of bladder smooth muscle fibers [5].

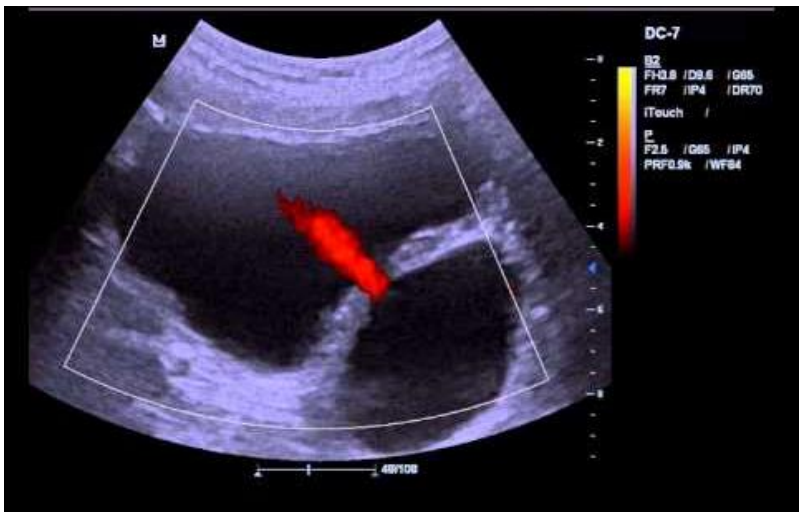


Image 52 – US of bladder (diverticulum of bladder) (material is from internet).

Hutch (1961) describes the following two kinds of diverticula at the ureteral hiatus (task 2) [5]:

Task 2 Types of diverticula of bladder

Primary paraureteral diverticula	**Secondary paraureteral diverticula**
Arise as a localized herniation of bladder mucosa through the ureteral hiatus between the intravesical ureter and the roof of the ureteral hiatus due to congenital deficient of the bladder wall (*congenital diverticula*)	Acquired and develop as a result of existing infravesical obstruction. The resulting increased infravesical pressure forces the bladder mucosa to bulge between the muscle fibers (image 53).

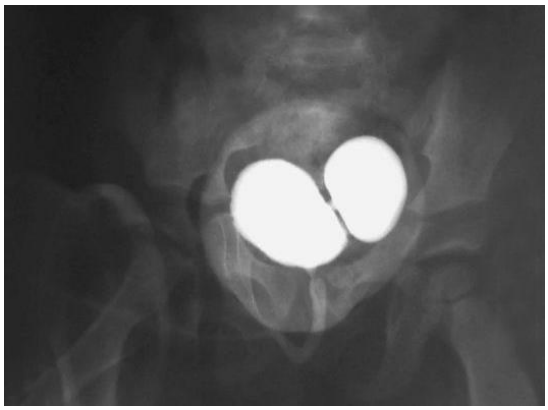


Image 53 – Voiding cystourethrogram (Atlas of Pediatric urology, Kulikova T.N.)

III DUPLICATION OF BLADDER AND URETHRA. These conditions can be complete or incomplete. It can occur in either the coronal or sagittal plane. Abrahamson (1961) attempted to classify the various bladder duplication anomalies and found complete duplication in the sagittal plane the most common [5]. In incomplete duplications, the two bladder halves communicate and are usually drained by a single urethra. In complete duplications, the two bladders are fully separated entities with normal mucosa and a full-thickness musculature wall divided by a peritoneal fold (image 54) [5].

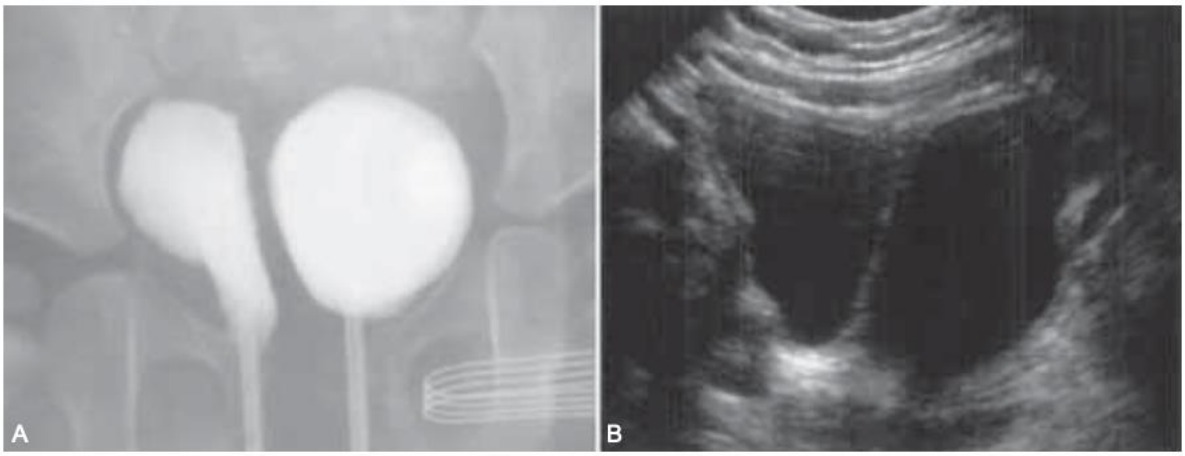


Image 54 – Duplication of bladder (A – retrograde vesicourethrogramm, B -US) (complete duplication))(Campbell- Walsh Urology, chapter 138, bladder anomalies in children).

IV EXTROPHY.

Definition. Patological conditions characterized by a spectrum of anomalies involving the ventral body wall, urinary tract, genitalia, bony pelvis, spine, anus, etc.
Embriology. According to the Marshalls theories, an abnormally large cloacal membrane causes a wedge effect and prevents the medial migration of the mesenchymal tissue. As a result, the lower abdominal wall is not well-formed. A subsequent rupture of the cloacal membrane results in herniation of all the contents and leading to the clinical picture of bladder-exstrophy-epispadias complex [16].

Recently, a new hypothesis has been suggested by Varma et al, that have been proposed that pubic diastasis is central to the occurrence of exstrophy bladder, and it precedes exstrophy development [16].
Patomorphology. The classical bladder (image 55) exstrophy is characterized by abnormalities involving the lower urinary tract, abdominal wall, bony pelvis, genitalia, pelvic floor, spine, and the anus.
Clinical features. A fleshy, red mass prolapsing out of the suprapubic region represents the open bladder plate (continuous urine leakage from the mass). The testis may not be descended at birth, and occasionally there may be the presence of bilateral inguinal hernias. In females, the clitoris is bifid with a slightly anterior vaginal opening [16].

Diagnostic evaluation. The diagnosis of exstrophy bladder is clinical and does not require any other additional investigations. Routine hemogram and blood chemistry are performed as a part of the preoperative work-up, an ultrasound KUB to rule out associated anomalies of the upper urinary tract should be done [16].

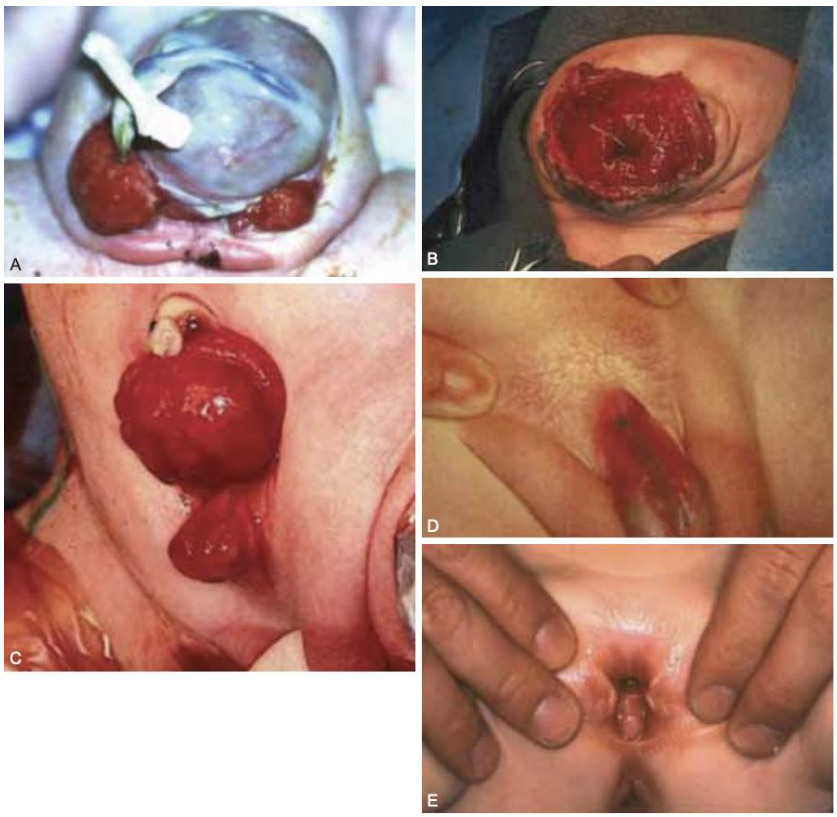


Image 55 – Extrophy – epispadias complex (a – cloacal extrophy, b- superior vesical fissure, c - classic bladder exstrophy , d -Male epispadias, e - female epispadias))(Campbell- Walsh Urology, chapter 138, bladder anomalies in children).

Diagnostic management. Surgical treatment of classical bladder exstrophy includes two main categories: the reconstructive procedures and the diversion procedures.

Among the reconstructive procedures, the two procedures that are commonly performed by pediatric surgeons across the globe are modern staged repair of exstrophy (MSRE) and complete primary repair of exstrophy (CPRE) [16].

MSRE. The main principle is to perform a staged repair (in three separate procedures) at appropriate times. The ideology is each procedure will **provide some degree of outlet resistance and will help the bladder to grow**.

The first step is the primary turn-in, which is performed in the first three days, might avoid osteotomy, protect the lower abdominal skin from ammoniacal contents, and prevent the bladder from trauma. Although the first stage is performed in the newborn age, occasionally it must delay. This is done where the bladder template is very small, and the closure is technically not feasible.

The second stage, epispadias repair or genitalia reconstruction, is performed at 6 to 9 months of age. This ensures early bladder cycling and provides outlet resistance for the bladder to grow. Bladder neck reconstruction is the third procedure and is

performed at a time when the child has sufficient bladder capacity (at least 100 ml) and has attained a certain age [16].

CPRE - also is known as Mitchell's repair as it was first performed by Michael Mitchell. The procedure aims at performing the **complete repair, including bladder turn-in, bladder neck repair, and epispadias repair in a single sitting**. The ideology is the initiation of early bladder cycling to ensure the optimal development of the bladder. The subsequent surgeries are also avoided. The procedure utilizes complete penile disassembly and division of the intersymphyseal bands, such that the vesicourethral unit is buried deep into the pelvis [16].

Osteotomy (image 56): due to abnormalities of the bony pelvis, there is tension on the bladder and the abdominal wall following turn-in. The issue can be solved by performing an osteotomy. However, this is not universally performed the procedure and depends on the surgeon's preference along with the child's age. Different types of osteotomies have been performed by different surgeons including anterior osteotomy of the pubic ramus, anterior innominate osteotomy (with or without vertical posterior osteotomy), posterior iliac osteotomy, etc. Among these, the anterior innominate osteotomy offers various advantages including less blood loss, easy external fixation, and no need to turn the patient to perform the osteotomy, etc [16].

Prognosis. **Hydronephrosis** or upper tract dilatation is commonly seen after the repair of exstrophy. After CPRE, it was seen in 53% of the patients during follow-up. Overall, 30% had bilateral hydronephrosis [16].

Recurrent urinary tract infection (UTI) and renal scarring occur in approximately 11.5% and 5.7% of the patients, respectively, after MSRE [16].

According to the Johns Hopkins group, continence was defined as the dry period of at least 3 hours during the day, dry during the night, able to void without clean intermittent catheterization (CIC), and no need for augmentation. They have shown that 70% of their patients had continence as per this definition [16].

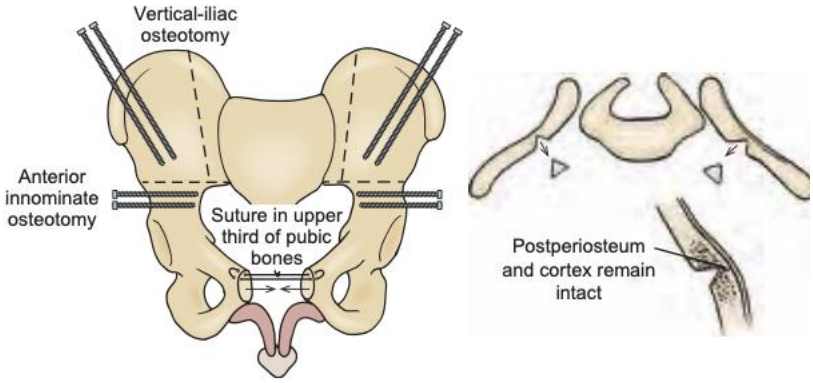


Image 66 – Combined osteotomy ((Campbell- Walsh Urology, chapter 138, bladder anomalies in children).

V. VESICOURETERAL REFLUX (VUR).

Definition.VUR is a retrograde flow of urine from bladder to upper urinary tract. Its clinical challenges arise from the fact that it is usually asymptomatic. When it is not,

however, it is responsible for pyelonephritic scarring and can be associated with congenital renal dysmorphism [5].

Embryology. At one point, the embryonic ureter buds from the mesonephric or wolffian duct to define the metanephric duct or early fetal ureter. The wolffian duct (early vas deferens) and early ureter can be thought of as forming the two upper arms of a Y with the distal mesonephric duct as the stem of the Y. While budding is occurring, the distal mesonephric duct is being drawn and incorporated into the region of the urogenital sinus (UGS), which later becomes the bladder. Incorporation continues until the entire stem is absorbed, leaving the two arms of the Y to enter the bladder separately—one as the ureter and the other as the vas and ejaculatory duct in the male prostatic urethra (or the vestigial Gartner duct in the female vagina). The two arms of the Y also rotate relative to each other once they contact the UGS/bladder wall, resulting in the ureteric orifice being proximal to the ejaculatory duct orifice. If the ureteric bud reaches the UGS too soon (thought to be due to early budding), over-rotation draws it high and lateral in the bladder wall, leading to inadequate incorporation, insufficient intramural length in the bladder wall, and reflux (Mackie et al, 1975). If the ureteric bud reaches the UGS too late (because of budding late), insufficient rotation occurs, resulting in an ectopic ureter that is drawn distally and medially, often obstructing in the bladder neck region or elsewhere. Furthermore, early or late budding is also thought to mistarget the contact between bud epithelium and the metanephros, leading to renal malformations, dysplasia, hypoplasia, or even agenesis [5].

Anatomy. For purposes of reflux prevention, the ureter represents a **dynamic conduit**, which adequately propels the urine presented to it in a bolus fashion, antegrade, by neuromuscular propagation of peristaltic activity. Also, the anatomic design of the UVJ (intramural portion of ureter that travels within the detrusor muscle as it traverses the bladder wall).

At the extravesical bladder hiatus, the three muscle layers of the ureter separate. The outer ureteral muscle merges with the outer detrusor muscle to form the Waldeyer sheath, which contributes to formation of the deep trigone. The intramural ureter remains passively compressed by the bladder wall during bladder filling, preventing urine from entering the ureter. Adequate intramural length and fixation of the ureter between its extravesical and intravesical points is required to create this antirefluxing compression valve (image 57).

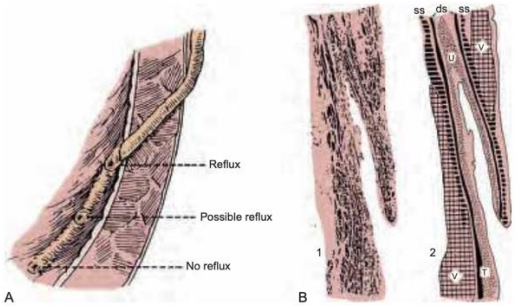


Image 57 – Anatomical features of prevention VUR (Campbell- Walsh Urology, chapter 138, bladder anomalies in children).

Task 3 Cause of vesicoureteral reflux.

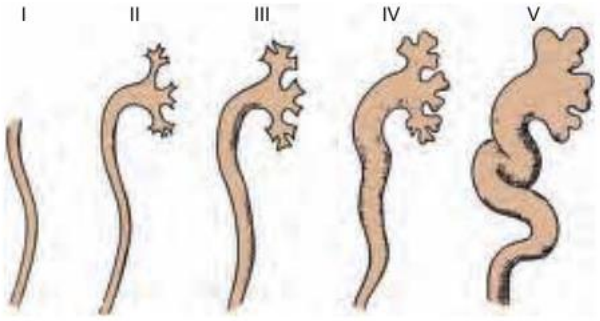
Primary reflux	Second reflux
A congenital defect in the structure and therefore function of the UVJ. Although inadequate tunnel length rather than excessive ureteral diameter usually underlies primary reflux, the dilated ureter often poses a challenge when a nonrefluxing ureterovesicostomy is required. This has traditionally prompted both long tunnels (>5 cm) or reduction of ureteral diameter by tapering, plication, or both to reconstruct a successful antireflux mechanism. On the other hand, construction of a new tunnel with a full 5:1 length-to-diameter ratio may not be absolutely required to correct reflux [5].	Any number of obstructing bladder pathologic processes can create hostile and excessive storage and emptying pressures that eventually overwhelm a normal antirefluxing intramural flap-valve mechanism. Such abnormalities can be functional or anatomic [5]. The most common anatomic obstruction of the bladder in the pediatric population is posterior urethral valves (PUVs). Reflux is present in 48% to 70% of patients with PUV patients [5]. Relief of PUV obstruction appears responsible for resolution of reflux in about one third of the patients. In females, anatomic bladder obstruction is rare. The most common structural obstruction is from a ureterocele that prolapses into the bladder neck [5]. In contrast to anatomic obstruction, neurofunctional causes of elevated bladder pressures also predispose to VUR. Neurogenic bladder associated with spina bifida is at risk for reflux [5].Some studies suggest that a secondary aspect to neonatal reflux is a peculiarity of male infants [5].

Grading of reflux.

Grading systems generally exist to help prognosticate the behavior of the disease they classify. In 1981 the International Reflux Study Committee proposed a

system of five grades of reflux that remains in current use today in North America (Duckett and Bellinger, 1982; Lebowitz et al, 1985). Five grades of reflux are currently used to depict the appearance of the ureter, renal pelvis, and calyces as seen on the radiographic contrast images generated by the voiding cystourethrogram (image 58)(VCUG) (image 59).

GRADE	DESCRIPTION
1	Into a nondilated ureter
2	Into the pelvis and calyces without dilation
3	Mild-to-moderate dilation of the ureter, renal pelvis, and calyces with minimal blunting of the fornices
4	Moderate ureteral tortuosity and dilation of the pelvis and calyces
5	Gross dilation of the ureter, pelvis, and calyces; loss of papillary impressions; and ureteral tortuosity



GRADES OF REFLUX

Image 58 – Grades of reflux (Campbell- Walsh Urology, chapter 138, bladder anomalies in children).

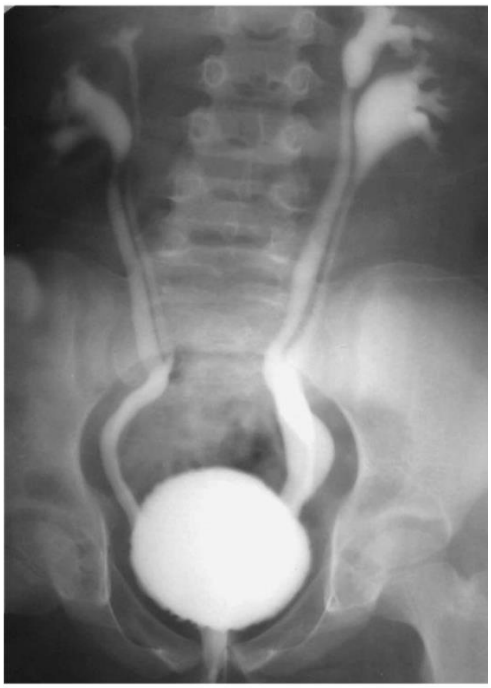


Image 59 – Voiding cystourethrogram (bilateral VUR complete duplex kidney) Atlas of Pediatric urology, Kulikova T.N.).

The principles of surgical correction of reflux include the following:

- Exclusion of causes of secondary VUR
- Adequate mobilization of the distal ureter without tension or damage to its delicate blood supply
- Creation of a submucosal tunnel that is generous in caliber and satisfies the 5:1 ratio of length to width recommended by Paquin (1959)
- Attention to the entry point of the ureter into the bladder (hiatus), the direction of the submucosal tunnel, and the ureteromucosal anastomosis to prevent stenosis, angulation, or twisting of the ureter
- Attention to the muscular backing of the ureter to achieve an effective antireflux mechanism
- Gentle handling of the bladder to reduce postoperative hematuria and bladder spasms [5].

ANOMALIES OF URETHRA

- **Epispadias**
- **Hypospadias**
- **Posterior urethral valves**
- **Urethral atresia**
- **Urethral duplication**

I. EPISPADIAS.

Definition. Epispadias is a rare urogenital anomaly characterized by the failure of the urethral tube to tubularize on the dorsal aspect. Although commonly associated as a part of bladder exstrophy-epispadias-complex (BEEC), isolated epispadias occurs less frequently. Its diagnosis is clinical and does not require any additional investigations [16, 17]. Unlike in hypospadias, where the meatus is on the ventral aspect, children with epispadias have a wide-open urethral plate on the dorsum [17].
Characteristics. Males have characteristic anatomic abnormalities, including a short-stubby phallus with a dorsally located meatus, upward-pointing phallus, and ventral hooding of the prepuce (image 60).

Girls have a bifid clitoris, patulous urethral opening, anteriorly placed vaginal opening, and ill-formed or absent mons. Pubic diastasis is seen in both males and females with epispadias [17].
Epidemiology. Epispadias is a rare congenital birth defect with an estimated prevalence of 1 in 10,000 to 50,000 [17].
Pathophysiology. Isolated male epispadias is characterized by a short phallus, an abnormal dorsally located urethral meatus, dorsal chordee, and a ventrally hooded prepuce (categorized into glandular, penile, and penopubic forms). Urinary incontinence is almost always seen in the penopubic forms due to the incompetent bladder neck [17].
Diagnostic evaluation. The diagnosis of epispadias is clinical and does not require any other additional investigations for diagnosis. A plain radiograph should always

be performed to document pubic diastasis. Other investigations, including cystourethrography (MCUG) and nuclear scintigraphy scans, should be performed to assess the baseline renal function in children with continent epispadias, as tubularizing the open urethral plate will further increase the outlet resistance and may lead to upper tract damage. However, it has been shown that the incidence of vesicoureteric reflux before surgery ranges from 35% to 85%, due to lateral ureteral ectopia. Due to this, some surgeons perform MCUG and nuclear scintigraphy scans in all children [17].

Diagnostic management. The surgery aims to reconstruct the genitalia and urethra, providing optimal functional and cosmetic outcomes. Modified Cantwell-Ransley repair: the initial procedure of mobilizing the urethral plate followed by tubularization and ventral movement between the corpora was described by Cantwell. Ransley changed the procedure to include mobilization of the urethral plate with separation of the corporal bodies, leaving the distal portion of the plate attached to the glans. Lateral glans wings are developed. A reverse-MAGPI (meatal advancement and granuloplasty) procedure is performed on the distal urethra. Cavernostomies are required to correct persistent chordee. The corporal bodies are medially rotated and reapproximated [17].

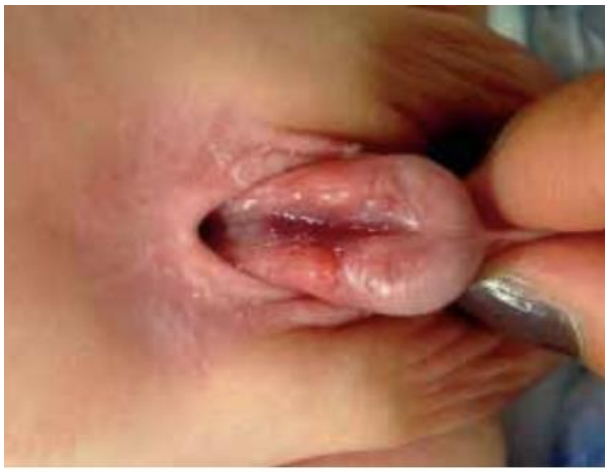


Image 60 – Complete epispadias Campbell- Walsh Urology, chapter 139, exstrophy-epispadias complex).

II. HYPOSPADIAS.

Definition. Anomally, that characterized by three typical anatomical features define hypospadias: ectopic location of the urethral meatus, irregular distribution of the foreskin and abnormal ventral curvature of the penis [18].

This patological condition is one of the commonest congenital malformations affecting the penis, with a reported incidence of 1/250 newborns, and yet unknown etiology [18].

In newborn males, hypospadias is the second most common congenital anomaly after undescended testis [19].

Classification. Hypospadias is often classified in posterior, penile, and anterior according to the preoperative meatal position (image 61) [20].

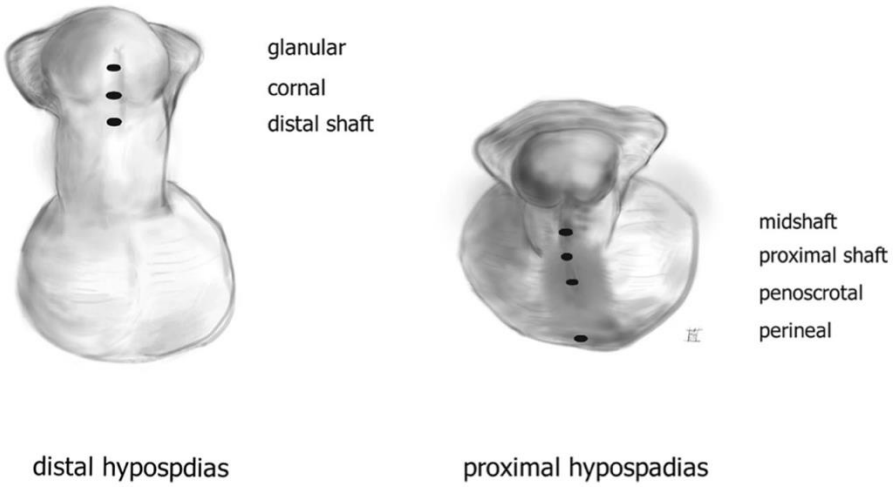


Image 61 – Classification of hypospadias [20]

Embryology. The first, hormone-independent stage of genital development consists of forming a urethral plate in the midline of the genital tubercle. This takes place during weeks 8 and 12 of gestation in both male and female fetuses.

During the second stage, between 11 and 16 weeks of gestation, the genital tubercle elongates under the influence of fetal testicular androgens. The urethral plate elongates into a groove towards the tip of the phallus. Fusion of the labioscrotal folds in the midline forms the scrotum, and fusion of the urethral folds adjacent to the urethral plate results in creation of the penile urethra. Eventually, the glans of the penis and the foreskin close in the midline [20].

Most hypospadias occur as an isolated condition, but associated anomalies include uni-bilateral cryptorchidism and micropenis. The occurrence of these co-morbidities suggests a deficiency of hormonal influences during embryogenesis. Androgens and estrogens both play a critical role in genital development, and in case of disbalance, different entities can be seen within the spectrum of congenital penile anomalies like hypospadias, micropenis, and ambiguous genitalia [20].

Diagnostic evaluation. In case of concomitant unilateral or bilateral undescended testis, one should always be aware of a disorder of sex development (DSD).

In proximal and complex hypospadias, further diagnostic evaluation is advised, such as ultrasonography of the urinary tract and internal genital organs to detect other nephrourological malformations. Endoscopic examination of the urethra at the time of surgery can exclude the presence of urethral anomalies not detected by ultrasound [20].

Diagnostic management. The main goal for hypospadias repair is to achieve both cosmetic and functional normalities. Reasons for treating hypospadias include spraying of urinary stream, inability to urinate in standing position, curvature leading to difficulties during intercourse, fertility issues because of difficulty with sperm deposition, and decreased satisfaction with genital appearance (image 62) [20].

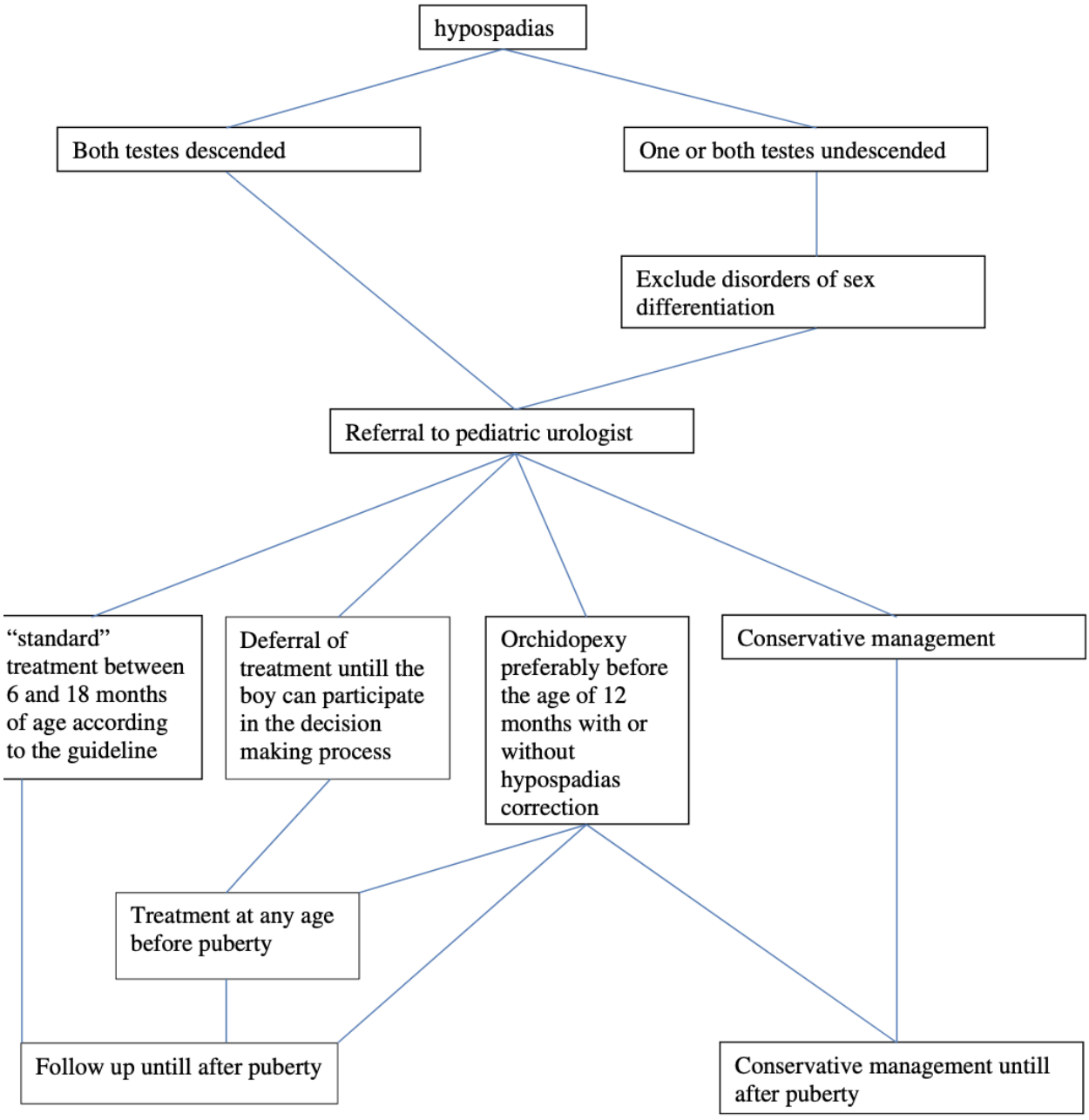


Image 62 – Proposed algorithm of treatment of hypospadias [20]

III. POSTERIOR URETHRAL VALVES.

Definition. The prostatic urethra is markedly dilated. The vesical neck raised and bladder orifice relaxed. Deep pittings penetrate down into either lateral wall of the prostatic urethra and at the extremity the verumontanum is seen a fine frenulum which extends distally for about 1 cm, and in dividing, forms what is apparently a definite valve on either side of the urethra, rising from the floor to each side wall. (Randall, 1921) [5].

Classification. Type 1 valves are the most common variant of posterior urethral valves and appear as leaflets that arise from the verumontanum and fuse anteriorly just proximal to the external urethral sphincter.

Type 3 valves present as a congenitally obstructing membrane that is likely perforated at the time of the initial postnatal catheterization (image 63) [5].

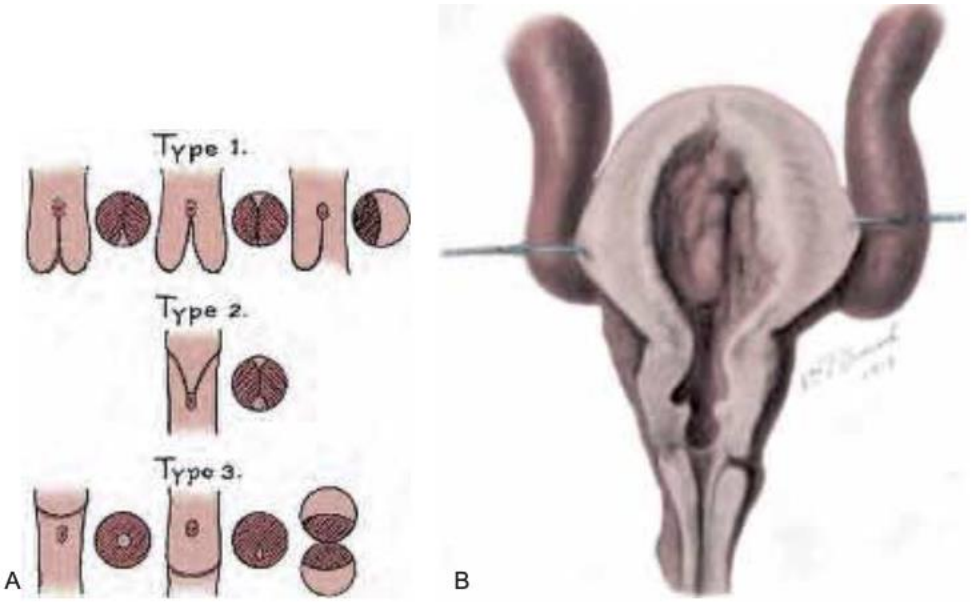


Image 63 – Types of posterior urethral valves (Campbell- Walsh Urology, chapter 141, urethral anomalies in children).

It cannot be overstated that the potential comorbidities arising from posterior urethral valves—renal dysfunction, urine reflux, worsening hydronephrosis—are due to bladder dysfunction. Mitchell (1982) coined the term ***valve bladder syndrome*** when he described 11 patients in whom bladder filling and emptying were noted to be intricately related to extent of renal pelvocaliectasis and overall renal function and dysfunction. This concept was subsequently illustrated as a "vicious cycle" leading to the valve bladder syndrome [5]. What is apparent is that a sustained increase in intravesical storage pressures over prolonged time intervals transmits that pressure to the ureter, the renal pelvis, and ultimately the glomerular units—causing architectural and functional changes at each ascending structure. The renal dysfunction seen in posterior urethral valves has two specific etiologies: (1) obstructive uropathy and (2) renal dysplasia [5].

Diagnostic evaluation (image 64).

Description of image 64:

A, Voiding cystourethrogram image shows a bladder affected by multiple diverticuli and a dilated posterior urethra narrowing at the site of valvular obstruction.

B, Cystoscopic image corresponding to the point of obstruction in A. *Arrows* indicate valve leaflet that would be fulgurated at the time of valve ablation. The urethral valves are seen as leaflets arising from the verumontanum and fusing in the midline, just proximal to the striated sphincter. The verumontanum is noted just proximal to the valve leaflets.

C, Voiding cystourethrogram image shows an elevated bladder neck and dilated posterior urethral funneling to a point of obstructed flow. These are typical radiologic findings of posterior urethral valves.

D, Cystoscopic image corresponding to point of obstruction in C. The concentric narrowing is classically associated with a type 3 valve but is also considered consistent with the congenital obstructing posterior urethral membrane that may have been perforated at the time of initial catheter placement.

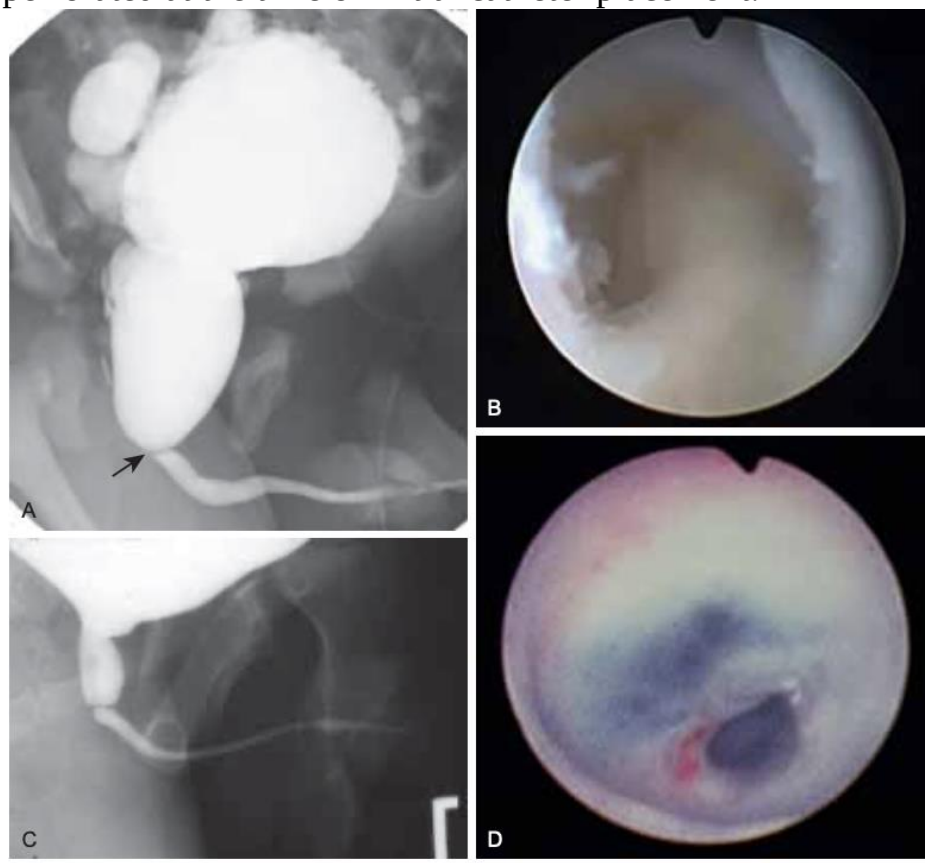


Image 64 – Diagnostic evaluation of posterior urethral valves (Campbell- Walsh Urology, chapter 141, urethral anomalies in children).

Diagnostic management. Today, cystoscopy with ablation of the valves is considered the preferred initial surgical option in any neonate diagnosed with posterior urethral valves. The treatment goal is to restore flow of urine through the urethra and enable normal cyclic filling and emptying of the bladder, which is superior to urinary diversion and passive urine drainage [5].

IV URETHRAL ATRESIA

Urethral atresia or congenital urethral stricture is a rarely described entity, likely because of its high associated mortality. When an infant survives—because the obstruction is incomplete or because there was decompression owing to an antenatal shunt placement or a patent urachus—the outcome can be like that of a child with obstructing posterior urethral valves (González et al, 2001).

V URETHRAL DUPLICATION

Urethral duplication is another rare anomaly of the urethra with several known anatomic variants. The duplication may begin at the bladder neck or within the more distal urethra. Whereas one urethra usually terminates on the glans near its orthotopic position, another urethra may end in a meatus placed on the glans or more ventrally along the shaft of the penis. In the most severe cases, the duplicated urethra may even be as proximal as the anal sphincter. The duplication occurs in a sagittal plane, with the ventral urethra usually the functional meatus containing the sphincteric complex and verumontanum [5].

ANOMALIES OF EXTERNAL GENITALIA IN BOY

-Phimosis and paraphimosis
-Undescended testis
- Hernia and hydrocele
-Varicocele

I. PHIMOSIS

Definition. At birth, a physiologic phimosis with either partial or complete inability to retract the prepuce exists owing to natural adhesions between the glans and inner preputial skin and/or due to a preputial ring.

Two factors are involved in the separation of the prepuce from the glans:

(1) epithelial debris, referred to as smegma, accumulates under the prepuce during the first 3 to 4 years of age.

(2) intermittent penile erections.

Classification. Primary phimosis commonly resolves during childhood.

Secondary phimosis may result from several causes, including forceful retraction and balanitis xerotica obliterans (BXO). Forceful preputial retraction should be discouraged to avert cicatrix formation [5].

Conditions associated with the uncircumcised penis include paraphimosis, infection, urinary tract infection (UTI), and cancer. Paraphimosis (image 65), the entrapment of the prepuce behind the glans penis, can result in gangrene if not reduced in a timely fashion by manipulation, dorsal slit procedure, or circumcision [5].

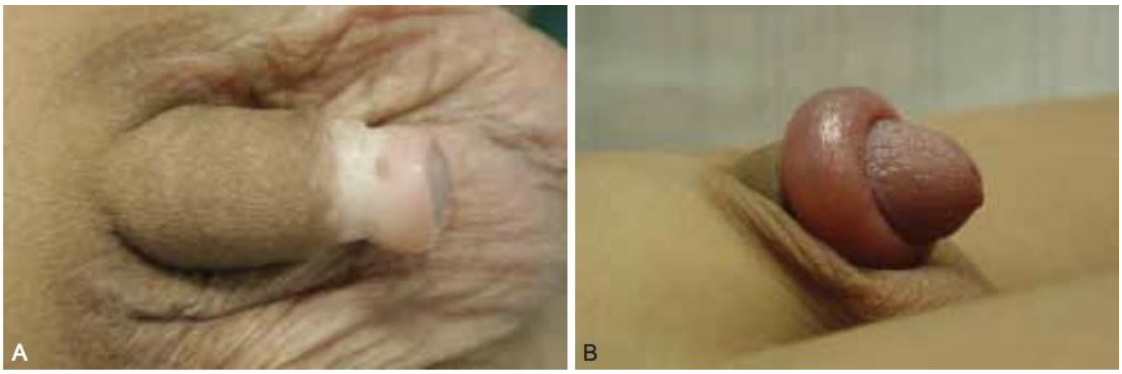


Image 65 – Phimosis (a), paraphimosis (b) (Campbell- Walsh Urology, chapter 146).

Diagnostic management. **Indications to enhance preputial retractability** include persistent primary phimosis, secondary phimosis, balanitis, posthitis (i.e., inflammation of the prepuce), BXO, and UTIs [5].

Several topical corticosteroid creams with different regimens have been successfully used to treat phimosis with a relatively small number of side effects. Palmer and Palmer (2008) compared the efficacy of two different topical betamethasone (0.05%) treatment regimens (twice daily for 30 days or three times daily for 21 days) and found an 84.5% and 87% response rate, respectively. Only one child had an untoward effect (candidal dermatitis) [5].

There are several techniques and devices for neonatal **circumcision**, including the Gomco clamp, Mogen clamp, and Plastibell device (image 66). There should be complete separation of the prepuce from the glans and complete inspection of the meatus and the corona to confirm the absence of anomalies, including hypospadias. **When neonatal circumcision is performed, local anesthesia is recommended.**

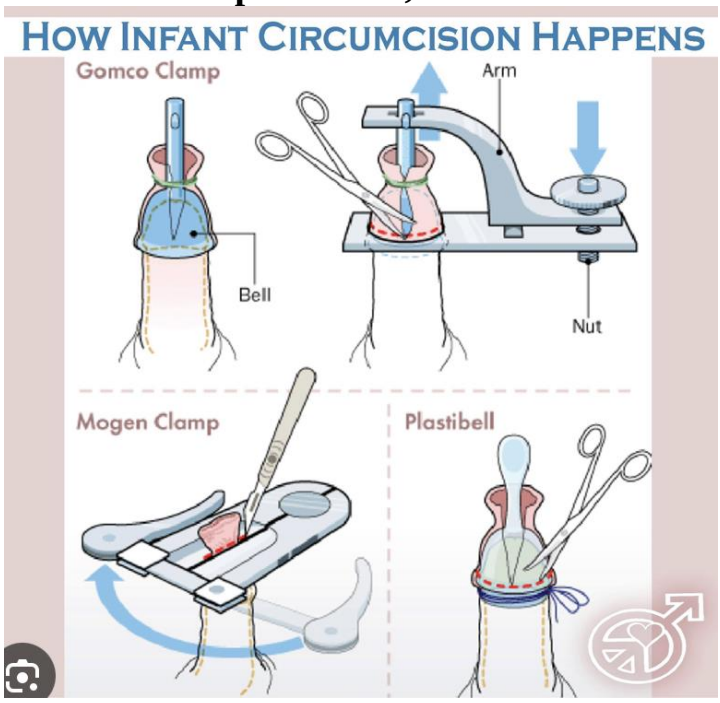


Image 66 – Types of circumcision
(https://cincycircinfo.org/circumcision/procedure)

Circumcision should not be performed in neonates with other penile conditions that require surgical correction. These conditions include hypospadias, penile curvature, dorsal hood deformity, buried penis, and webbed penis [5].

II. HERNIA AND HYDROCELE

Embryology. **The processus vaginalis** forms during the third month of gestation as the peritoneum bulges into the inguinal canal just before the onset of testicular descent. On completion of testicular descent, the processus vaginalis obliterates and the portion adjacent to the testes becomes the tunica vaginalis. Obliteration of the processus vaginalis continues postnatally, and its failure to obliterate accounts for nearly all inguinoscrotal abnormalities seen in infancy and childhood. In an autopsy

series, Mitchell found closure of the processus vaginalis in 18% of full-term infants at birth (image 67) (task 4) [5].

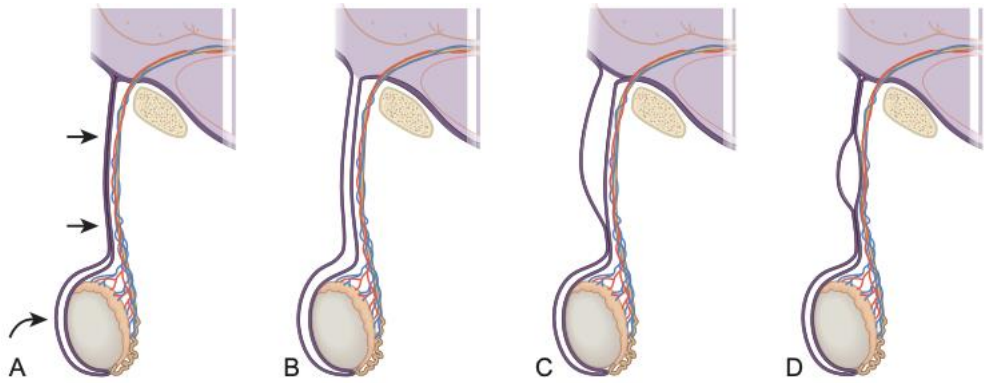


Image 67 – Processus vaginalis in hydrocele (A- normal closure of the processus vaginalis; *straight arrows* indicate the funicular process; *curved arrow* is the tunica vaginalis. B, Communicating hydrocele with complete patency of the processus vaginalis. C, Funicular hydrocele with distal closure of the processus vaginalis; communication with the peritoneal cavity may also result in hernia. D, Encysted hydrocele of the spermatic cord) (Campbell- Walsh Urology, chapter 146).

Task 4 Pathological types of process vaginalis [5]

Indirect inguinal hernia	a widely patent processus vaginalis extending beyond the internal inguinal ring containing abdominal contents (bowel, omentum, gonads) which may pass into the inguinal canal, labia, or scrotum
Communicating hydrocele	a patent processus vaginalis extending beyond the internal inguinal ring containing peritoneal fluid alone, which extends to the testis, with fluid within the tunica vaginalis
Hydrocele of the spermatic cord	fluid contained within a segment of patent processus vaginalis with obliterated processus distally and proximally

Scrotal hydrocele	fluid contained within the tunica vaginalis surrounding the testis without communication proximally
Abdominoscrotal hydrocele	a large scrotal hydrocele that extends proximally across the internal inguinal ring into the abdomen without communication with the peritoneum

Diagnostic evaluation. Inguinal hernias and communicating hydroceles typically manifest as a painless bulge found in the groin or extending along the cord to the scrotum. The bulge may be present only during periods of increased intra-abdominal pressure (crying or bowel movements); the supine position facilitates reduction of peritoneal fluid and intra-abdominal contents. **The presence of an intermittent bulge helps to distinguish a reducible inguinal hernia and communicating hydrocele from a scrotal hydrocele or hydrocele of the spermatic cord [5].**

Ultrasonography may identify a large elongated echolucent area from the groin extending anteromedially in the spermatic cord; omentum or bowel with peristalsis can be found in a large hernia sac (image 68, 69). **In the presence of a presumed hydrocele, a sonogram can aid in identifying an unpalpable testicle surrounded by hydrocele fluid [5].**

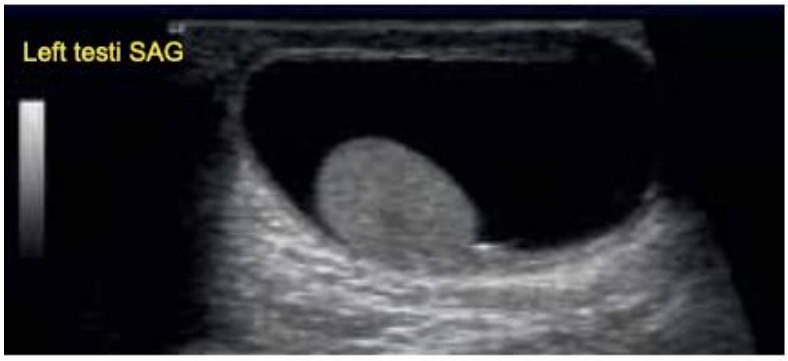


Image 68 – Hydrocele (Campbell- Walsh Urology, chapter 146).

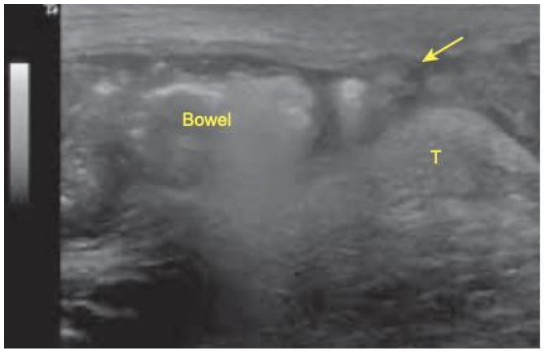


Image 69 – Inguinal hernia (Campbell- Walsh Urology, chapter 146).

Diagnostic management. Lets discuss about surgical treatment of indirect unguinal hernia (image 70). The hernia repairs (Bassini, McVay and Shouldice techniques) involve opening the external oblique aponeurosis and freeing the spermatic cord. The transversalis fascia is then opened, facilitating inspection of the inguinal canal, the indirect space and the direct space. The hernia sac is usually ligated, and the canal floor is subsequently reconstructed. Posterior repair (iliopubic tract repair and Nyhus technique) is performed by dividing the layers of the abdominal wall superior to the internal ring and entering the properitoneal space. Dissection then continues behind and deep to the entire inguinal region. Like the anterior approach, the posterior approach provides excellent visualization of the areas of concern in herniorrhaphy. The major difference between this technique and the anterior approach is that reconstruction is performed from the "inside."

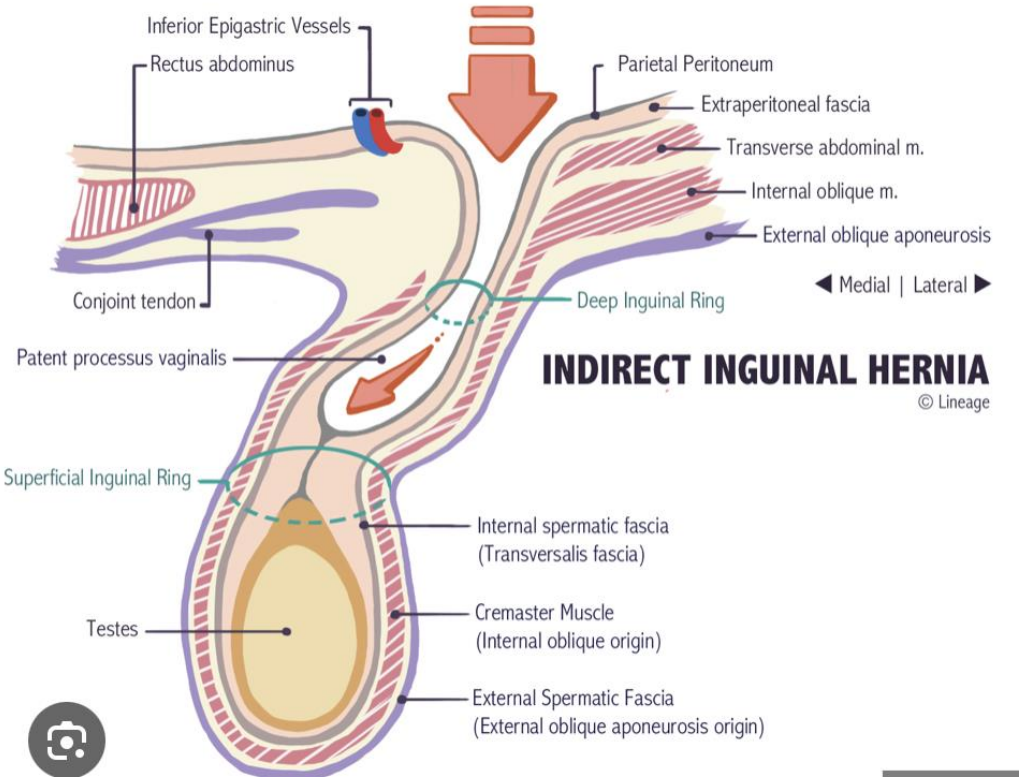


Image 70 – Anatomy of indirect unguinal hernia (internet)

Laparoscopic approach (image 71).

Today, most laparoscopic herniorrhaphies are performed using either the transabdominal preperitoneal (TAPP) approach or the total extraperitoneal (TEP) approach. The TAPP approach involves placing laparoscopic trocars in the abdominal cavity and approaching the inguinal region from the inside. This allows the mesh to be placed and then covered with peritoneum. While the TAPP approach is a straightforward laparoscopic procedure, it requires entrance into the peritoneal cavity for dissection. Consequently, the bowel or vascular structures may be injured during the procedure [21].

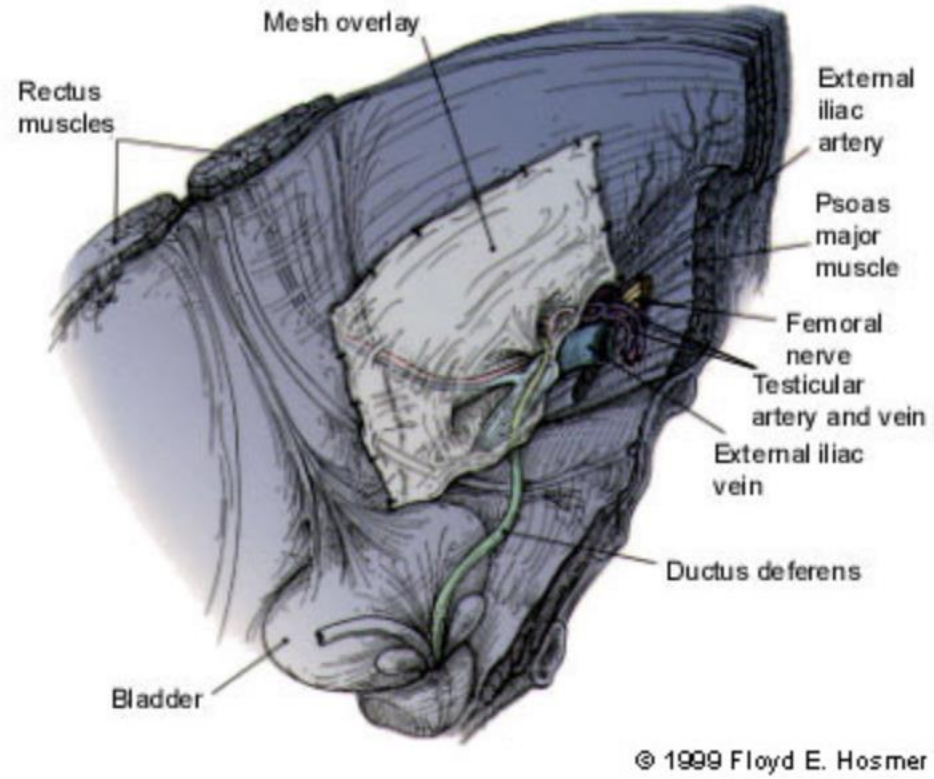


Image 71- Laparoscopic approach for treatment of inguinal hernia [21]

III. VARICOCELE.

Definition. An abnormal dilation and tortuosity of the internal spermatic veins within the pampiniform plexus, is common among adolescents and may contribute significantly to the risk of subfertility in adulthood [5].

Pathophysiology of the adolescent varicocele is likely to be multifactorial**. The primary factors are believed to be increased venous pressure in the left renal vein, collateral venous anastomoses, and valvular incompetence of the left internal spermatic vein at its junction with the left renal vein.**

The "nutcracker phenomenon" (compression of the left renal vein between the aorta and superior mesenteric artery) may account for the varicocele in some boys (Coolsaet, 1980; Kim et al, 2006).

Diagnostic evaluation. Most varicoceles in children and adolescents are **identified incidentally** by a primary care practitioner [5].

The patient should be examined in both the supine and standing positions. The scrotum is inspected for visible swelling, followed by palpation of the spermatic cord at rest and during the Valsalva maneuver.

The clinical grading system defines varicoceles as *grade 0* (subclinical), nonpalpable and visualized only by CDUS; *grade 1*, palpable only with Valsalva maneuver; *grade 2*, easily palpable but not visible; and *grade 3*, easily visible. The veins should decompress in the supine position; failure to do so, particularly on the right side, warrants evaluation (CT or sonogram) for an abdominal or pelvic mass [5].

The ultrasound criteria for diagnosing a varicocele—spermatic vein diameter and retrograde blood flow—are controversial in adults and more so in adolescents. Niedzielski and colleagues (1997) measured spermatic vein diameter in the standing position and spermatic venous reflux with Valsalva maneuvers in 625 boys with varicoceles and 50 normal controls. They found normal spermatic vein diameter (<2 mm in normal boys) in 95%, 70%, and 4% of boys with grades 1, 2, and 3 varicocele and spermatic venous blood reflux in two thirds of boys with grade 2 or 3 varicoceles; flow velocity measured while the patient was standing correlated with varicocele grade and sperm motility [5].

Diagnostic management. **Despite the limitations regarding testicular hypotrophy, the main indications for surgical intervention remain significant left (≥20%) or bilateral testicular hypotrophy, pain, or abnormal semen analysis findings; the last is most reliable in boys of Tanner stage 5 and/or at least 18 years of age.**

Several approaches exist to correct the adolescent varicocele: inguinal or subinguinal, laparoscopic or retroperitoneal, or venographic. The surgical decision revolves around (1) whether to spare the testicular artery and/or lymphatics using the available approaches, and (2) the effect on the rate of recurrence and hydrocele formation (image 72,73) [5].

PROCEDURE	RECURRENCE OR PERSISTENCE	HYDROCELE	TESTICULAR ATROPHY
Open suprainguinal (Palomo)	2%-4%	0%-30% (10%)*	
Laparoscopic:			
Nonlymphatic or artery sparing	0%-9%	11%-32% (7%)*	
Artery and/or lymphatic sparing	1%-7%	0%-4%	
Microscopic subinguinal	0%-10%	0%-6%	Rare
Nonmicroscopic inguinal	7%-33%	8%-14%	
Sclerotherapy	6%-35%	Occasional	Rare

*Number in parentheses refers to meta-analysis of Barroso et al, 2009.

Image 72 – Results of varicocele repair [5].

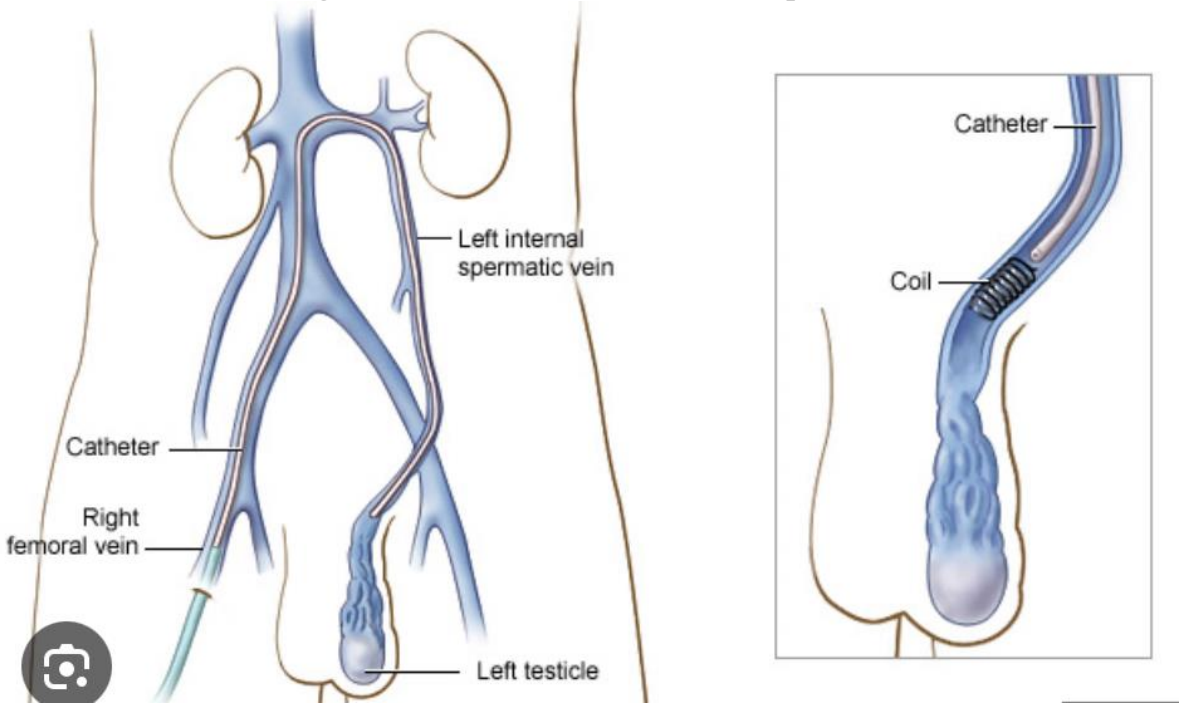


Image 73 – Sclerotherapy (https://www.virchicago.com/treat/varicocele/)

IV. UNDESCENDED TESTIS

Definition. The absence of one or both testes in normal scrotal position and during initial clinical evaluation may refer to palpable or nonpalpable testes, which are either cryptorchid or absent. Most absent testes are **vanishing** or **vanished,** being present initially in development but becoming lost as a result of vascular accident or torsion unilaterally **(monorchia)** or, very rarely, bilaterally **(anorchia) [5].**

Retractile testes are scrotal testes that retract easily out of the scrotum but can be manually replaced in a stable scrotal position and remain there at least temporarily until there is recurrent stimulation. Testes that are significantly retractile—that is, those that rarely remain in a stable scrotal position (spontaneously or with manipulation) and/or are located at rest in the high scrotum—may or may not be diagnosed as cases of acquired cryptorchidism on longitudinal examination [5].

Classification. (image 74)

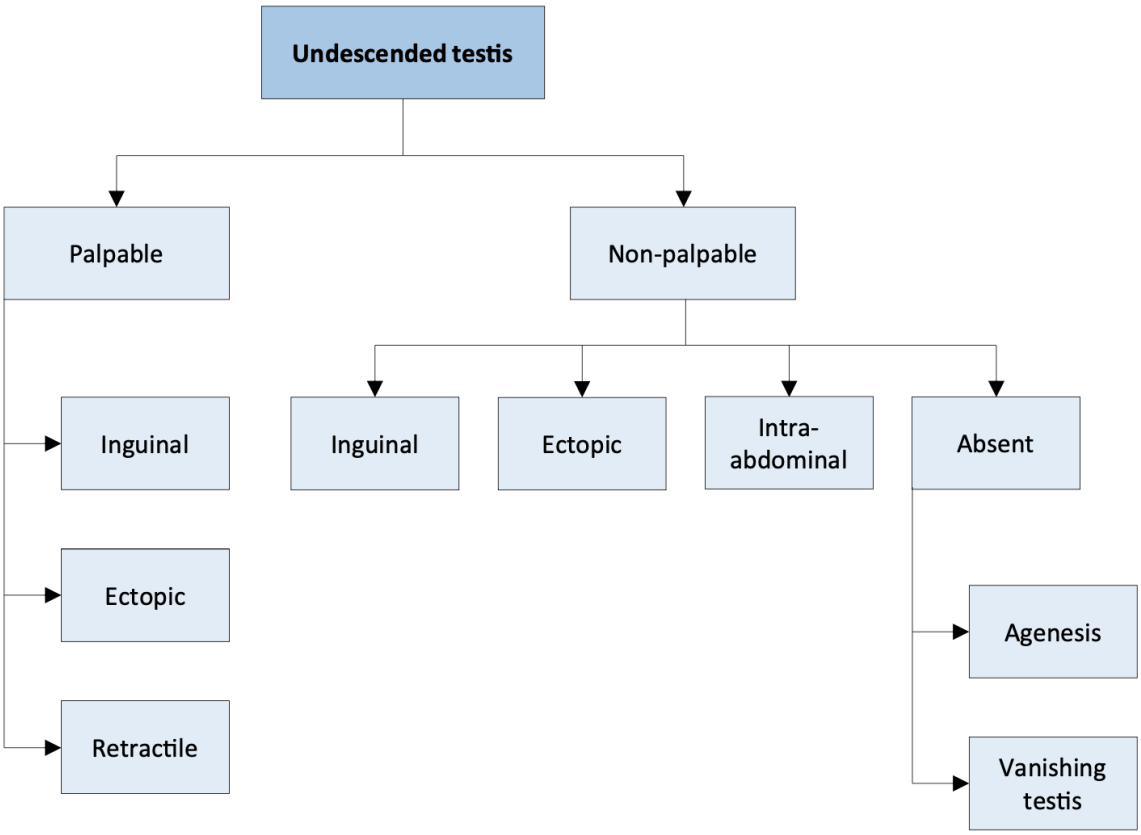


Image 74 – Classification of undescended testis (EAU guidelines, 2023).

Diagnostic evaluation. History taking and physical examination are key in evaluating boys with undescended testes. Localization studies using different imaging modalities are usually without any additional benefit [22]. An undescended testis is pursued by carefully advancing the examining fingers along the inguinal canal towards the pubis region, perhaps with the help of lubricant. A possible inguinal testis can be felt to bounce under the fingers. Ultrasound (US) lacks the diagnostic sensitivity to detect the testis confidently or establish the absence of an intra-abdominal testis. Consequently, the use of different imaging modalities, such

as US or magnetic resonance imaging (MRI), for undescended testes is limited and only recommended in specific and selected clinical scenarios [22].

Diagnostic management.

Hormonal therapy using hCG or gonadotropin-releasing hormone (GnRH) is based on the hormonal dependence of testicular descent, but has a limited success rate of only 20%. Human chorionic gonadotropin stimulates endogenous testosterone production and is administered by intramuscular injection. Several dose and administration schedules are reported. There is no proven difference between 1.5 IU and weight-based doses up to 3.0 IU every other day for fourteen days [22].

If a testis has not concluded its descent at the age of six months (corrected for gestational age), and since spontaneous testicular descent is unlikely to occur after that age, surgery should be performed within the subsequent year, and by age eighteen months at the latest. In addition, early **orchidopexy** can be followed by partial catch-up testicular growth, which is not the case in delayed surgery. All these findings recommend performing early orchidopexy between the ages of six and twelve month. Surgery for palpable testes includes orchidofunicolysis and orchidopexy, either via an inguinal or scrotal approach (image 75, 76,77) [22].

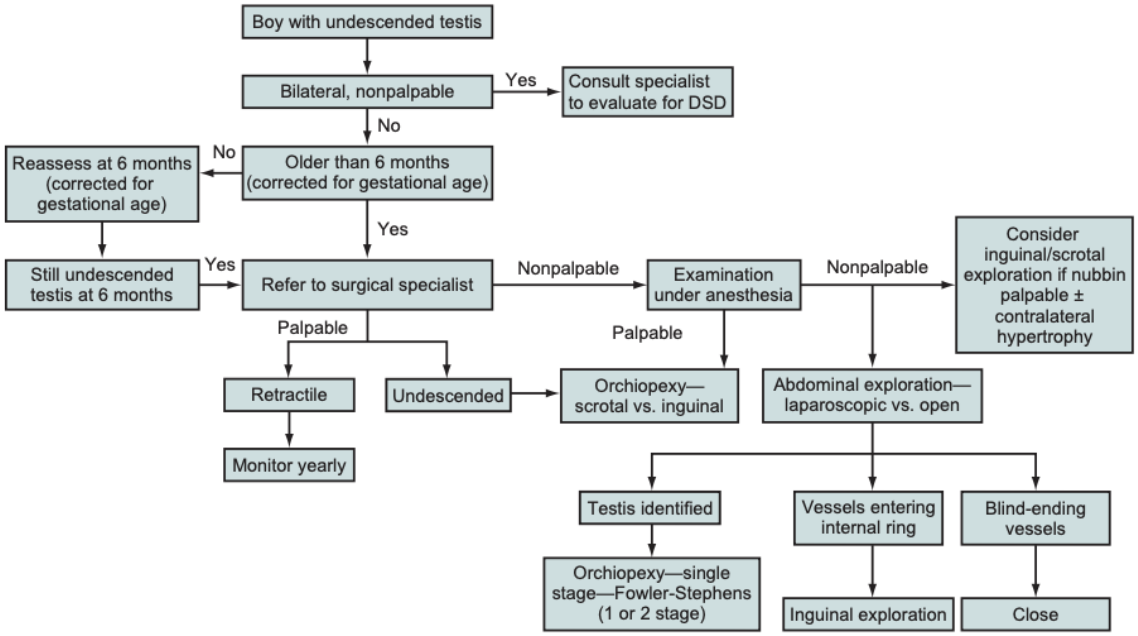


Image 75 - Algorithm for management of the undescended testis (The American Urological Association guideline algorithm for diagnosis and treatment of palpable and nonpalpable testes in patients confirmed to have undescended testis by an experienced examiner) (Campbell- Walsh Urology, chapter 148).

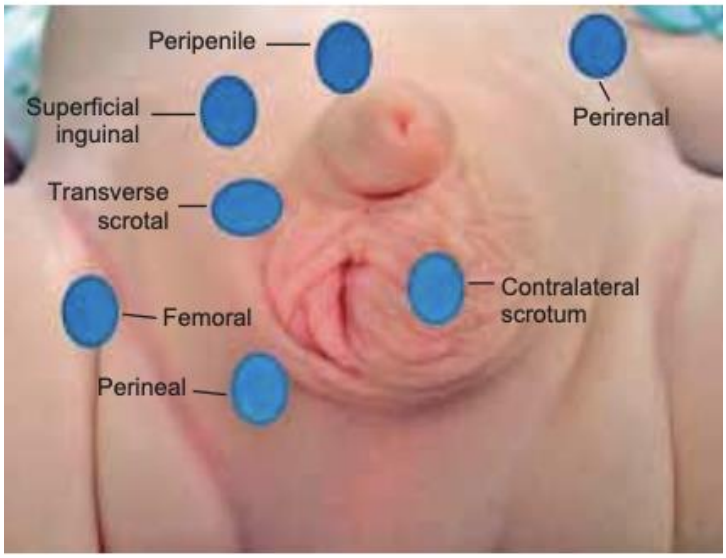


Image 76 – Positions of ectopic testis (Campbell- Walsh Urology, chapter 148).

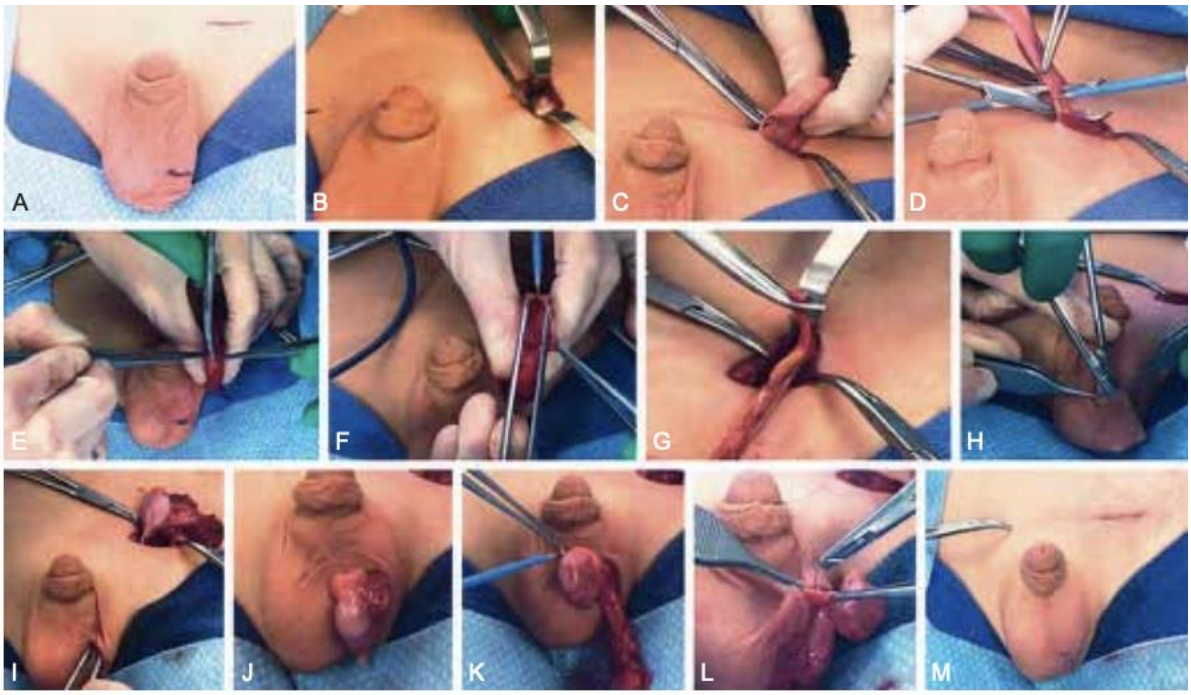


Image 77 - Inguinal orchiopexy. A, an incision is made at or below the inguinal crease superolateral to the pubic tubercle. B, the external oblique fascia is incised to expose the canal. C, the gubernaculum is transected distal to the sac. D, the internal spermatic fascia is incised. E, the tunica vaginalis is opened over the testis, and F, the incision is extended proximally along the length of the cord. G, the sac is mobilized to the level of the internal inguinal ring and suture-ligated. H, A transverse scrotal incision is made and a subdartos pouch created. I, A large clamp or a finger can be used to create a tunnel just anterior to the pubis. J, the testis is passed into the scrotum. K, Existing appendages are excised. L, the testis is secured within the pouch. M, Closure is completed with absorbable sutures (Campbell- Walsh Urology, chapter 148).

Surgical anatomy of the scrotum

The availability of multiple blood supplies to the testis allows continued testicular viability when one or two of the arteries are compromised by injury or ligation (image 78) [5].

TESTIS
Testicular (internal spermatic) artery from aorta
Deferential artery from internal iliac/superior vesical artery
Cremasteric (external spermatic) artery from inferior epigastric artery

EPIDIDYMIS
Superior epididymal artery from testicular artery
Inferior epididymal artery from deferential artery

VAS DEFERENS
Seminal vesicle region: deferential artery from internal iliac/superior vesical artery
Testicular region: deferential artery and inferior epididymal artery

Image 78 – Blood supply of testis. (Campbell- Walsh Urology, chapter 41).

There is a predictable pathway for the spread of scrotal infections including Fournier gangrene and necrotizing fasciitis of the scrotum and postoperative fluids based on scrotal anatomy. Anatomic barriers to the spread of necrotizing fasciitis include the dartos fascia of the penis and scrotum, Colles fascia of the perineum, and Scarpa fascia of the anterior abdominal wall. The testicles and epididymis are frequently spared in cases of necrotizing fasciitis of the scrotum (image 79) [5].

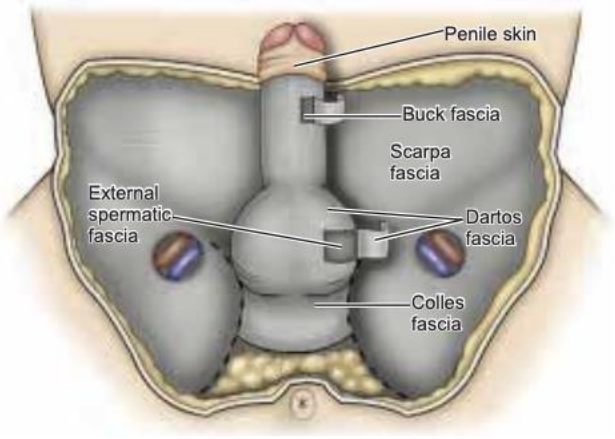


Image 79 – Anatomic barrier to the spread of infection (Campbell- Walsh Urology, chapter 41).

Scrotum is a sac of skin and muscle that hangs in front of the pelvis, between the legs. The scrotum is divided into two haves by the *scrotal septum*. In most men, one testicle sits on either side of the scrotal septum. It is common for one side of the scrotum to hang slightly lower than the other side (image 80).

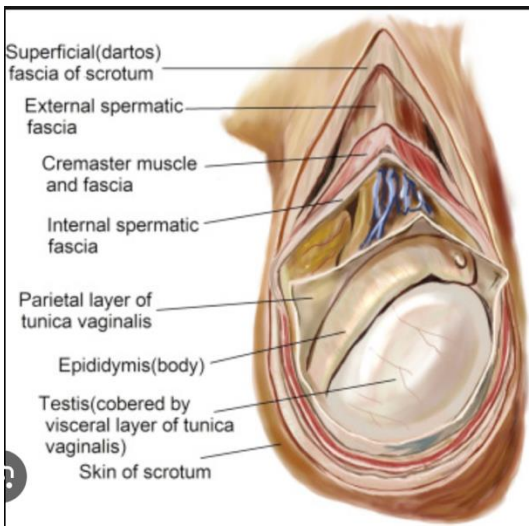


Image 80 – Anatomy of scrotum (Scrotumhttps://www.sciencedirect.com/science/article/abs/pii/B9780128150085000017).

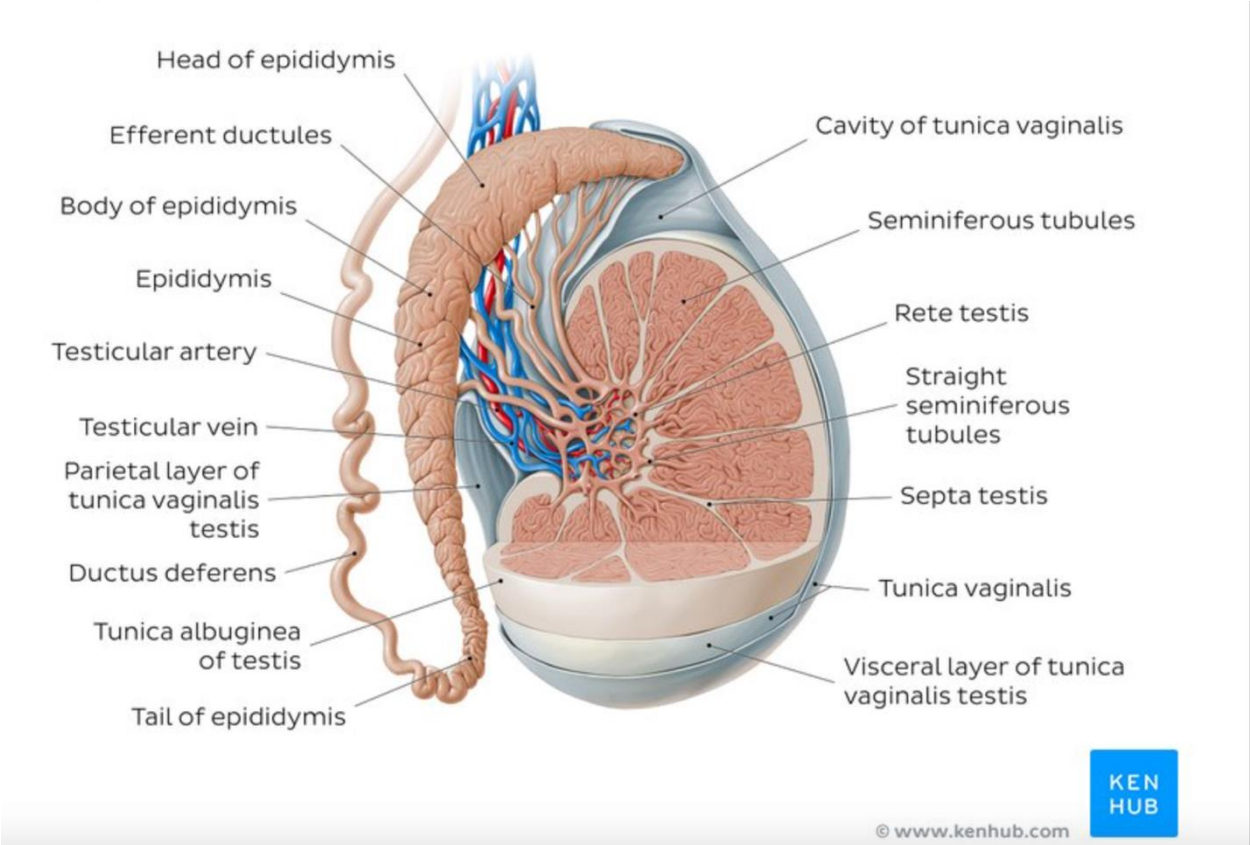


Image 81- Anatomy of testis (https://www.kenhub.com/en/library/anatomy/the-testes).

On the testis, we can observe two sides (medial and lateral) that are separated by two edges (anterior and posterior). We can also observe superior and inferior poles since it is an ovoid organ. On the posterior edge and superior pole of the testis is a structure called the epididymis. Also on the inferior pole is the scrotal ligament (a remnant of the gubernaculum testis) and serves to fix the testis to the bottom of the scrotum [23].

Each of the 200-300 lobules of the testis are filled with one to four highly convoluted seminiferous tubules which each course towards the mediastinum testis. Before entering the mediastinum, they change to a straight course, so in this segment, each convoluted tubule becomes a straight seminiferous tubule. Straight tubules enter the mediastinum, and by interconnecting they form a collecting chamber called rete testis [23].

The tubules are surrounded by the connective tissue stromal cells which contain testosterone secreting Leydig (interstitial) cells. The tubules are lined with a layer of seminiferous epithelium, which contains supporting Sertoli (sustentacular) cells, and spermatogenic cells. The spermatogenic cells constantly multiply and through several phases of spermatogenesis differentiate into mature sperm, while the Sertoli cells nourish them.

Histology: *Spermatogenic cells:* cells in all phases of spermatogenesis (from stem cell to mature spermatozoa)
Leydig cells: secrete testosterone
Sertoli cells: blood-testis barrier, support and nurture maturing spermatogenic cells
Function: Production of sperm and androgens (testosterone) [23].

Anatomy of prostate (image 82)

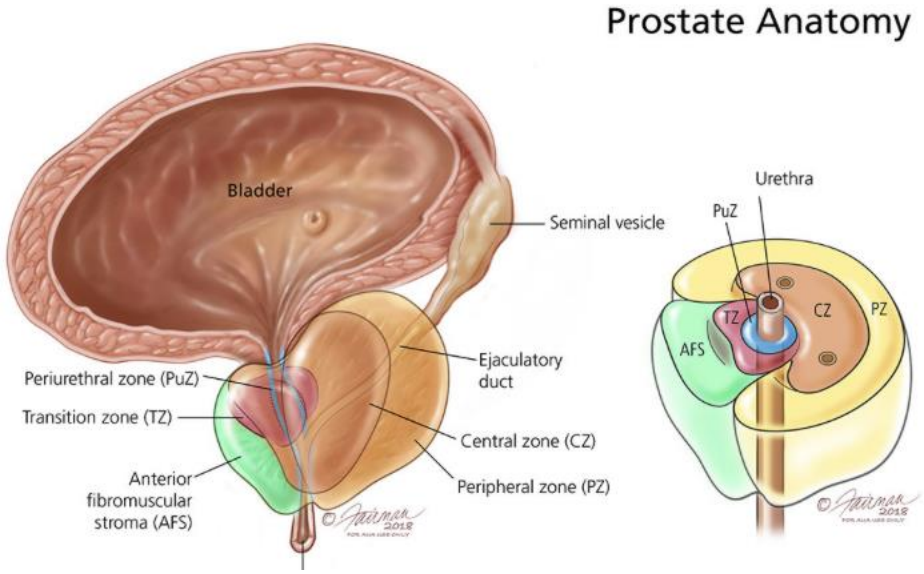


Image 82 – Anatomy of prostate (https://www.ncbi.nlm.nih.gov/books/NBK540987/)

The prostate gland is situated in the true pelvis and plays a supportive role in the male reproductive system. Its principal purpose is to secrete alkaline solution protective for sperm in the acidic environment of the vagina. The fluid acts to balance the acidity of the vagina, which increases the overall lifespan of the sperm, allowing the greatest length of time to fertilize an egg successfully. The fluid also contains supportive proteins and enzymes that provide nourishment to sperm. The

added volume of the prostatic fluid to the seminal fluid and sperm allow for easier mechanical propulsion through the urethra [24].

Topography anatomy: anteriorly, it is posterior to the pubic symphysis, separated by a pad of fat (retropubic fat) and venous plexus (prostatic venous plexus). Posteriorly it is in a close relationship to the rectum and is separated by fascia of Denonvilliers. The external urethral sphincter muscle is beneath the prostate where it wraps around the urethra help to control ejaculatory and urinary flow. On the lateral aspects, the gland is related to the levator ani muscle of the pelvic floor covered by endopelvic fascia [24].

The prostate gland idivides anantomically into five lobes: anterior and posterior lobes, two lateral lobes, and one median lobe. This description is in many anatomical textbooks. In clinics, it is described as having two lateral lobes right and left and a median lobe [24].

The prostate gland is composed of histologically different zones; based on these, the gland divides into three anatomical zones:

- The central zone forms the base of the gland that surrounds the ejaculatory ducts
- The peripheral zone is the largest zone making up 70% of the gland and surrounds most of the central zone and partially surrounds the distal part of the prostatic urethra
- The transition zone is a small glandular zone that surrounds a portion of the urethra between the urinary bladder and verumontanum.
- There is an area denoted as the anterior fibromuscular stroma within the prostate; this area is not glandular, and contains mostly muscular and fibrous tissue and surrounds an inferior portion of the prostate called the apex.
- Lastly, the prostate is encompassed by a fibrous layer called a capsule [24].

Importantly, the prostate gland has multiple tubular structures passing within it, including the proximal urethra and two ejaculatory ducts. The ejaculatory ducts enter the prostate immediately as it emerges from the seminal vesicles. Both of these ducts travel from posterior and lateral to medial and inferior. They ultimately converge at the urethra within the prostate gland on an area called the seminal colliculus [24].

As the prostate gland shares a close anatomical relationship with the bladder, it also shares a portion of the bladder's blood supply. The inferior vesical artery is the major blood supply for the prostate, and it also receives blood supply from the middle rectal and internal pudendal arteries. Veins around the prostate form the prostatic plexus which drains into internal iliac veins. The prostate drains to the internal iliac lymph nodes and the sacral lymph nodes [24].

TEST

1. List anomaly of number of the kidney

a) agenesis of kidney
b) duplex kidney
c) horseshoe kidney
d) lumb-kidney
e) supernumery kidney

2. Which of methods you should take to diagnostic evaluation of anomaly of the kidney?

a) intravenous urography
b) retrograde pyelography
c) ultrasound examination
d) rectoscopy
e) angiography

3. Which anomaly of ascent do you know?

a) pelvic ectopic
b) iliac ectopic
c) horseshoe kidney
d) polycystic diseases
e) abdominal ectopic

4. Which anomaly of shape and fusion do you know?

a) horseshoe kidney
b) lumb-kidney
c)agenesis of kidney
d) thoracic ectopia
e) disc-kidney

5. Follow the anomaly of structure of kidney

a) polycystic disease
b) multicystic disease
c) medullary sponge kidney
d) simple renal cyst
e) hydronephrosis

6. What clinical features of polycystic disease do you know?

a) flank pain
b) hematuria
c) low gravity density of urine
d) enuresis
e) nocturia
f) palpable mass

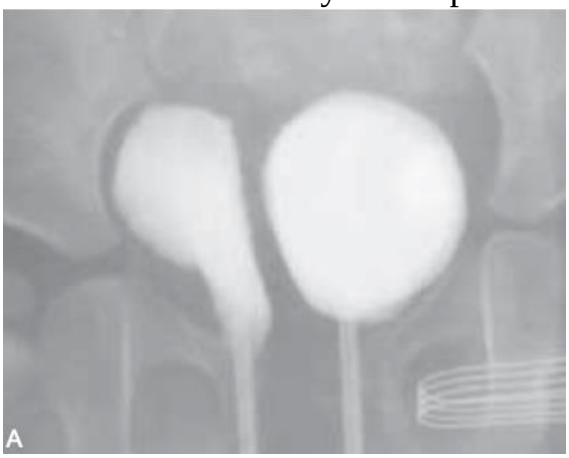
7. Which anomaly of ureter you may list?

a) duplex ureter
b) retrocaval ureter
c) ectopic ureter
d) exstrophy
e) phymosis

8. Which anomaly of scrotum you may follow?

a) hydrocele
b) hernia
c) phymosis
d) ectopic of testis
e) undescended testis

9. What is the anomaly on the picture ?



10. Specify complications of kidney anomalies (follow and describe).

TASKS

1. A 4-year-old boy has a dense elastic formation in the right inguinal canal. One testicle is palpable in the left half of the scrotum. Diagnosis and tactics?

2. A 13-year-old girl was admitted in emergency room with pains in the right side of the abdomen. During physical examination, painless, elastic, palpable mass is in the right iliac region. Laboratory: erythrocytes in the urine. What diseases you may suspect? Differential diagnosis.

3. A 3-year-old boy was admitted in emergency room with urinary retention. Physical examination: the edematous and hyperemic foreskin is displaced; the glans of the penis cannot be found. Diagnosis, diagnostic management.

Check your answers:

1. abe
2.abce
3.abe
4.abe
5. abcd
6. abcf
7. abc
8. abde

1. Undescended testis
2. ectopic kidney
3. phymosis

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Diagnostic evaluation of the urologic patient.

Firstly, before you will make decision about patients' hospitalization, it is very necessary to obtain accurate information and make physical examination.

A complete history can be divided into the chief complaint and history of the present illness, the patient's past medical history, and a family history. Each segment can provide significant positive and negative findings that will contribute to the overall evaluation and treatment of the patient [5].

Chief Complaint and Present Illness

Most urologic patients definite their symptoms as arising from the urinary tract and frequently present to the urologist for the initial evaluation. The chief complaint is a constant reminder to the urologist as to why the patient initially sought care.

Pain arising from the genitourinary tract may be quite severe and is usually associated with either urinary tract obstruction or inflammation. You should describe the duration, severity, chronicity, periodicity, and degree of disability are important considerations (task 5).

Task 5 Reasons of pain

Obstruction	Inflammation
1. Urinary calculi Urinary calculi cause severe pain when they obstruct the upper urinary tract. Large, nonobstructing stones may be totally asymptomatic. Thus a 2-mm-diameter stone located at the ureterovesical junction may cause excruciating pain, whereas a large staghorn calculus in the renal pelvis or a bladder stone may be totally asymptomatic [5] 2. Tumors (Usually do not cause pain unless they produce obstruction or extend beyond the primary organ to involve adjacent nerves) [5]	Inflammation of the GU tract is most severe when it involves the parenchyma of a GU organ (due to edema and distention of the capsule surrounding the organ). Thus pyelonephritis, prostatitis, and epididymitis are typically quite painful. Inflammation of the mucosa of a hollow viscus such as the bladder or urethra usually produces discomfort, but the pain is not nearly as severe [5]

Features of renal pain:

- Pain may radiate across the flank anteriorly toward the upper abdomen and umbilicus and may be referred to the testis or labium.
- Pain of renal origin may be associated with gastrointestinal symptoms because of reflex stimulation of the celiac ganglion and because of the proximity of adjacent organs (liver, pancreas, duodenum, gallbladder, and colon).

Differential diagnosis: pain that is due to a perforated duodenal ulcer or pancreatitis may radiate into the back, but the site of greatest pain and tenderness is in the epigastrium. Pain of intraperitoneal origin is seldom colicky, as with obstructive renal pain. Furthermore, pain of intraperitoneal origin frequently radiates into the shoulder because of irritation of the diaphragm and phrenic nerve; this does not occur with renal pain. Typically, patients with intraperitoneal pathology prefer to lie motionless to minimize pain, whereas patients with renal pain usually are more comfortable moving around and holding the flank.

- Renal pain may also be confused with pain resulting from irritation of the costal nerves, most commonly T10-T12.

Ureteral pain is usually acute and secondary to obstruction. The pain results from acute distention of the ureter and by hyperperistalsis and spasm of the smooth muscle of the ureter as it attempts to relieve the obstruction, usually produced by a stone or blood clot [5].

The pain may be referred to the scrotum in the male or the labium in the female. Lower ureteral obstruction frequently produces symptoms of vesical irritability, including frequency, urgency, and suprapubic discomfort that may radiate along the urethra in men to the tip of the penis.

Vesical pain is usually produced either by overdistention of the bladder as a result of acute urinary retention or by inflammation [5].

Prostatic pain. Pain of prostatic origin is poorly localized, and the patient may complain of lower abdominal, inguinal, perineal, lumbosacral, penile, and/or rectal pain. Prostatic pain is frequently associated with irritative urinary symptoms such as frequency and dysuria, and, in severe cases, marked prostatic edema may produce acute urinary retention [5].

Penile pain. Pain in the flaccid penis is usually secondary to inflammation in the bladder or urethra, with referred pain that is experienced maximally at the urethral meatus. Pain in the erect penis is usually due to Peyronie disease or priapism [5].

Scrotal pain may be either primary or referred. Primary pain arises from within the scrotum and is usually secondary to acute epididymitis or torsion of the testis or testicular appendices. Because of the edema and pain associated with both acute epididymitis and testicular torsion, it is frequently difficult to distinguish these two conditions. For differential diagnosis, as a rules, we may make ultrasound diagnostic to measure blood supply of testis.

Chronic scrotal pain is usually related to noninflammatory conditions such as a hydrocele or a varicocele, and the pain is generally characterized as a dull, heavy sensation that does not radiate [5].

Hematuria is the presence of blood in the urine; greater than three red blood cells (RBCs) per high-power microscopic field (HPF) is significant [5].

In evaluating hematuria, several questions should always be asked:

-Is the hematuria gross or microscopic?

-At what time during urination does the hematuria occur (beginning or end of stream or during entire stream)?

-Is the hematuria associated with pain?

-Is the patient passing clots?
-If the patient is passing clots, do the clots have a specific shape (task 6)?

Task 6 Classification of hematuria

The timing of hematuria (image 83)	As rules indicates the site of origin: *Initial hematuria* usually arises from the urethra. *Total hematuria* is most common and indicates that the bleeding is most likely coming from the bladder or upper urinary tracts. *Terminal hematuria* occurs at the end of micturition and is usually secondary to inflammation in the area of the bladder neck or prostatic urethra. It occurs at the end of micturition as the bladder neck contracts, squeezing out the last amount of urine.
The association with pain	*Painful hematuria* (usually results from upper urinary tract hematuria with obstruction of the ureters with clots) *Painless hematuria*
The shape of clots	The presence of *vermiform (wormlike) clots*, particularly if associated with flank pain, identifies the hematuria as coming from the upper urinary tract with formation of vermiform clots within the ureter. *Nonshaped clots*, as usual, indicates on bleeding from bladder.

Fever and chills may occur with infection anywhere in the GU tract but are most observed in patients with pyelonephritis, prostatitis, or epididymitis. **When associated with urinary obstruction, fever and chills may portend septicemia and necessitate emergency treatment to relieve obstruction [5].**

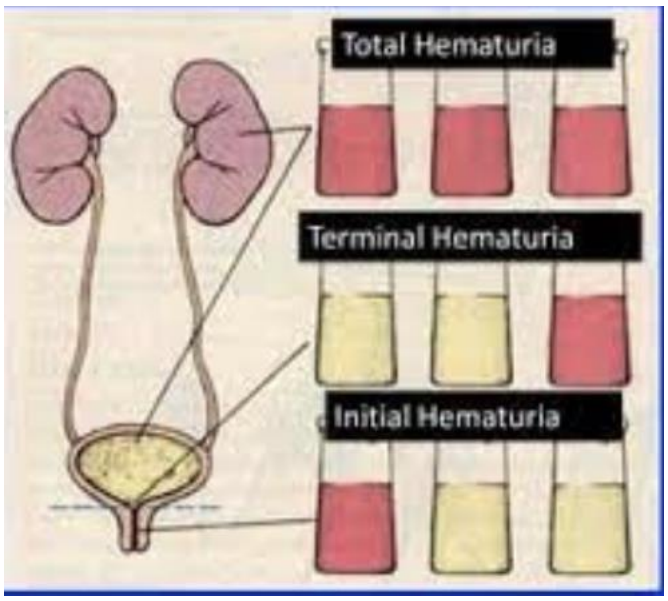


Image 83 – Timing of hematuria (slideshare, material from internet).

Voiding:

- storage phase (bladder filling) (accommodation and compliance)
- voiding phase (bladder emptying; coordinated detrusor contraction, synchronous relaxation of outlet sphincter) (task 7).

Task 7 Lower Urinary Tract Symptoms

Irritative symptoms	Obstructive symptoms
Frequency Nocturia Dysuria Urgency Incontinence Enuresis	Decreased force of urination Urinary hesitancy Intermittency Postvoid dribbling. Straining Sense of residual urine

Frequency is one of the most common urologic symptoms. The normal adult voids five or six times per day, with a volume of approximately 300 mL with each void. **Urinary frequency is due to either increased urinary output (polyuria) or decreased bladder capacity.** If voiding is noted to occur in large amounts frequently, the patient has polyuria and should be evaluated for diabetes mellitus, diabetes insipidus, or excessive fluid ingestion. Causes of decreased bladder capacity include bladder outlet obstruction with decreased compliance, increased residual urine, and/or decreased functional capacity due to irritation, neurogenic bladder with increased sensitivity and decreased compliance, pressure from extrinsic sources, or anxiety. By separating irritative from obstructive symptoms, the astute clinician should be able to arrive at a proper differential diagnosis [5].

Nocturia is nocturnal frequency. Normally, adults arise no more than twice at night to void. As with frequency, nocturia may be secondary to increased urine

output or decreased bladder capacity. Nocturia may also occur in people who drink large amounts of liquid in the evening, particularly caffeinated and alcoholic beverages, which have strong diuretic effects. In the absence of these factors, nocturia signifies a problem with bladder function secondary to urinary outlet obstruction and/or decreased bladder compliance [5].

Dysuria is painful urination that is usually caused by inflammation. **This pain is usually not felt over the bladder but is commonly referred to the urethral meatus.** Pain occurring at the start of urination may indicate urethral pathology, whereas pain occurring at the end of micturition (strangury) is usually of bladder origin. Dysuria is frequently accompanied by frequency and urgency [5].

Urgency is a sense of immediate, strong feeling of voiding due to either decrease of capacity of bladder or having of inflammation of lower urinary tract, for example.

Incontinence.

Urinary incontinence is the involuntary loss of urine. A careful history of the incontinent patient will often determine the etiology. Urinary incontinence can be subdivided into four categories (task 8).

Task 8 Classification of incontinence

Continuous incontinence	Stress Incontinence	Urgency incontinence	Overflow Urinary Incontinence
- A urinary tract **fistula** that bypasses the urethral sphincter (vesicovaginal fistula usually secondary to gynecologic surgery, radiation, or obstetric trauma) - **A**n **ectopic ureter** that enters either the urethra or the female genital tract [5].	Sudden leakage of urine with coughing, sneezing, exercise, or other activities that increase intra-abdominal pressure. During these activities, intra-abdominal pressure rises transiently above urethral resistance, resulting in a sudden, usually small amount of urinary leakage (after childbearing or menopause and is related to a loss of anterior vaginal support and weakening of pelvic tissues)	Loss of urine preceded by a strong urge to void. This symptom is commonly observed in patients with cystitis, neurogenic bladder, and advanced bladder outlet obstruction with secondary loss of bladder compliance [5].	*paradoxical incontinence*, is secondary to advanced urinary retention and high residual urine volumes. The bladder is chronically distended and never empties completely. Urine may dribble out in small amounts as the bladder overflows [5].

	In men after prostatic surgery, most commonly radical prostatectomy, in which there may be injury to the external urethral sphincter [5].		

Enuresis refers to urinary incontinence that occurs during sleep. It occurs normally in children up to 3 years of age **but persists in about 15% of children at age 5 and about 1% of children at age 15** (Forsythe and Redmond, 1974). Enuresis must be distinguished from continuous incontinence, which occurs in the day and night and which, in a young girl, usually indicates the presence of an ectopic ureter. All children older than age 6 years with enuresis should undergo a urologic evaluation, although the vast majority will be found to have no significant urologic abnormality [5].

Obstructive Symptoms.

Decreased force of urination is usually secondary to bladder outlet obstruction and commonly results from benign prostatic hyperplasia (BPH) or a urethral stricture.

Urinary hesitancy refers to a delay in the start of micturition. Normally, urination begins within a second after relaxing the urinary sphincter, but it may be delayed in men with bladder outlet obstruction.

Intermittency refers to involuntary start-stopping of the urinary stream. It most commonly results from prostatic obstruction with intermittent occlusion of the urinary stream by the lateral prostatic lobes.

Postvoid dribbling refers to the terminal release of drops of urine at the end of micturition. In men with bladder outlet obstruction, this urine escapes into the bulbar urethra and leaks out at the end of micturition. Men will frequently attempt to avoid wetting their clothing by shaking the penis at the end of micturition.
Postvoid dribbling is often an early symptom of urethral obstruction related to BPH, but seldom necessitates any further treatment [5].

Straining refers to the use of abdominal musculature to urinate. Normally, it is unnecessary for a man to perform a Valsalva maneuver except at the end of urination. Increased straining during micturition is a symptom of bladder outlet obstruction. This most frequently occurs in evaluating men with benign prostate hyperplasia.

Male sexual dysfunction is frequently used synonymously with *impotence* or erectile dysfunction, although impotence refers specifically to the inability to achieve and maintain an erection adequate for intercourse. Patients presenting with "impotence" should be questioned carefully to rule out other male sexual disorders, including loss of libido, absence of emission, absence of orgasm, and, most

commonly, premature ejaculation. It is important to identify the precise problem before proceeding with further evaluation and treatment [5].

The original AUA symptom score is based on the answers to seven questions concerning frequency, nocturia, weak urinary stream, hesitancy, intermittency, incomplete bladder emptying, and urgency. The International Prostate Symptom Score (I-PSS) includes these seven questions, as well as a global quality-of-life question. The total symptom score ranges from 0 to 35 with scores of 0 to 7, 8 to 19, and 20 to 35 indicating mild, moderate, and severe lower urinary tract symptoms, respectively. The I-PSS is a helpful tool both in the clinical management of men with lower urinary tract symptoms and in research studies regarding the medical and surgical treatment of men with voiding dysfunction (image 84).

International Prostate Symptom Score (I-PSS)

In the past month:	Not at All	Less than 1 in 5 times	Less than Half the Time	About Half the Time	More than Half the Time	Almost Always	Your Score
1. Incomplete Emptying How often have you had the sensation of not emptying your bladder?	0	1	2	3	4	5	
2. Frequency How often have you had to urinate less than every two hours?	0	1	2	3	4	5	
3. Intermittency How often have you found you stopped and started again several times when you urinated?	0	1	2	3	4	5	
4. Urgency How often have you found it difficult to postpone urination?	0	1	2	3	4	5	
5. Weak Stream How often have you had a weak urinary stream?	0	1	2	3	4	5	
6. Straining How often have you had to strain to start urination?	0	1	2	3	4	5	
	None	1 time	2 times	3 times	4 times	5 times	
7. Nocturia How many times did you typically get up at night to urinate?	0	1	2	3	4	5	
Total I-PSS Score							
Score:	1-7 Mild		8-19 Moderate		20-35 Severe		

The first seven questions of the I-PSS are from the American Urological Association (AUA) Symptom Index

Quality of Life Due to Urinary Symptoms

	Delighted	Pleased	Mostly Satisfied	Mixed	Mostly Dissatisfied	Unhappy	Terrible
If you were to spend the rest of your life with your urinary condition just the way it is now, how would you feel about that?	**0**	**1**	**2**	**3**	**4**	**5**	**6**

Image 84 – IPSS score (https://www.ciccenters.com/ipss-score/).

Hematospermia refers to the presence of blood in the seminal fluid. **It almost always results from nonspecific inflammation of the prostate and/or seminal vesicles and resolves spontaneously, usually within several weeks.** A genital and rectal examination should be done to exclude the presence of tuberculosis; a prostate-specific antigen (PSA) and a rectal examination done to exclude prostatic carcinoma; and a urinary cytology done to exclude the possibility of transitional cell carcinoma of the prostate. It should be emphasized, however, that hematospermia

almost always resolves spontaneously and rarely is associated with any significant urologic pathology [5].

Pneumaturia is the passage of gas in the urine. In patients who have not recently had urinary tract instrumentation or a urethral catheter placed, this is almost always **due to a fistula between the intestine and the bladder. Common causes include diverticulitis, carcinoma of the sigmoid colon, and regional enteritis (Crohn disease).** In rare instances, patients with diabetes mellitus may have gasforming infections, with carbon dioxide formation from the fermentation of high concentrations of sugar in the urine [5].

The past medical history is extremely important because it frequently provides clues to the patient's current diagnosis. The past medical history should be obtained in an orderly and sequential manner.

*Previous Medical Illnesses with Urologic Sequelae (*many diseases may affect the GU system, and it is important to listen to the patient and record previous medical illnesses). **Patients with diabetes mellitus frequently develop autonomic dysfunction that may result in impaired urinary and sexual function.** Patients with hypertension have an increased risk of sexual dysfunction because they are more likely to have peripheral vascular disease and because many of the medications that are used to treat hypertension frequently cause impotence. Patients with neurologic diseases such as multiple sclerosis are also more likely to develop urinary and sexual dysfunction) [5].

*Family History (*It is similarly important to obtain a detailed family history because many diseases are genetic and/or familial. Examples of genetic diseases include adult polycystic kidney disease, tuberous sclerosis, von Hippel-Lindau disease, renal tubular acidosis, and cystinuria; these are but a few common and well-recognized examples, urolithiasis, prostate cancer) [5].

Medications (most of the antihypertensive medications interfere with erectile function, and changing antihypertensive medications can sometimes improve sexual function. Similarly, many of the psychotropic agents interfere with emission and orgasm) [5].

Previous Surgical Procedures.

Smoking and Alcohol Use (Cigarette smoking is associated with an increased risk of urothelial carcinoma, most notably bladder cancer, and it is also associated with increased peripheral vascular disease and erectile dysfunction. Chronic alcoholism may result in autonomic and peripheral neuropathy with resultant impaired urinary and sexual function. Chronic alcoholism may also impair hepatic metabolism of estrogens, resulting in decreased serum testosterone, testicular atrophy, and decreased libido**)** [5].

*Allergies (*All medicinal allergies should be marked boldly on the front of the patient's chart to avoid potential complications from inadvertent exposure to the same medications) [5].

Physical examination.

The visual inspection (task 9) of the patient provides a general overview. The skin should be inspected for evidence of jaundice or pallor. The nutritional status of the patient should be noted. Cachexia is a frequent sign of malignancy, and obesity may be a sign of underlying endocrinologic abnormalities**.** In this instance, one should search for the presence of truncal obesity, a "buffalo hump," and abdominal skin striae, which are stigmata of hyperadrenocorticism. In contrast, debility and hyperpigmentation may be signs of hypoadrenocorticism.

Gynecomastia may be a sign of endocrinologic disease and a possible indicator of alcoholism or previous hormonal therapy for prostate cancer.

Edema of the genitalia and lower extremities may be associated with cardiac decompensation, renal failure, nephrotic syndrome, or pelvic and/or retroperitoneal lymphatic obstruction.

Supraclavicular lymphadenopathy may be seen with any GU neoplasm, most commonly prostate and testis cancer; inguinal lymphadenopathy may occur secondary to carcinoma of the penis or urethra [5].

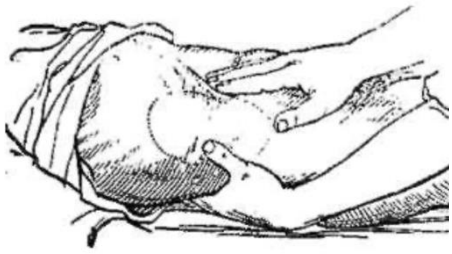
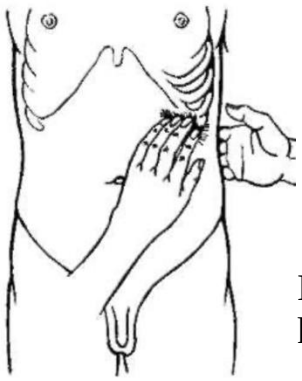
Task 9 Visual inspection

Abdomen	Lumbar region	Penis	Scrotum
-Palpable mass due to renal cancer, polycystic disease, simple renal cyst, hydronephrosis - In a lower part of abdomen, you may find bladder due to acute urinary retention	-Signs of operation, trauma -Palpable mass due to inflammation disease of kidney, for example, paranephritis ("psoas-symptom").	- Signs of phymosis, paraphymosis -anomaly of development, for example,epispadias, hypospadias -inflammation disease, for example, balanopostittis	- Signs of epidydimoorchitis (pain, increase in sizes, hyperemia) - Hernia -Hydrocele -Varicocele -Cancer of testis -Cyst of epididymis

Palpation.

The kidneys are fist-sized organs located high in the retroperitoneum bilaterally. In the adult, the kidneys are normally difficult to palpate because of their position under the diaphragm and ribs with abundant musculature both anteriorly and posteriorly. Because of the position of the liver, the right kidney is somewhat lower than the left. **In children and thin women, it may be possible to palpate the lower pole of the right kidney with deep inspiration.** However, it is usually not possible to palpate either kidney in men, or the left kidney is almost always impalpable unless it is abnormally enlarged (task 10) [5].

Task 10 Types of bimanual palpation of kidney

Palpation in the supine position (The best way)	Palpation in stand position	Palpation on the side
The kidney is lifted from behind with one hand in the costovertebral angle **i**n deep inspiration, the examiner's hand is advanced firmly into the anterior abdomen just below the costal margin. At the point of maximal inspiration, the kidney may be felt as it moves downward with the diaphragm. With each inspiration, the examiner's hand may be advanced deeper into the abdomen. (image 85)  Image 85 – Palpation kidney in the supine position [10].	 Image 86 – Palpation of kidney [10].	 Image 87 - – Palpation of kidney [10].

Every patient with flank pain should also be examined for possible nerve root irritation. The ribs should be palpated carefully to rule out a bone spur or other skeletal abnormality and to determine the point of maximal tenderness. Unlike renal pain, radiculitis usually causes hyperesthesia of the overlying skin innervated by the irritated peripheral nerve. This hypersensitivity can be elicited with a pin or by pinching the skin and fat overlying the involved area. Finally, the pain experienced during the presumptive phase of herpes zoster involving any of the segments between T11 and L2 may also simulate pain of renal origin [5].

Palpation of bladder.

A normal bladder in the adult cannot be palpated or percussed until there is at least 150 mL of urine in it. Percussion is better than palpation for diagnosing a distended bladder (image 88).

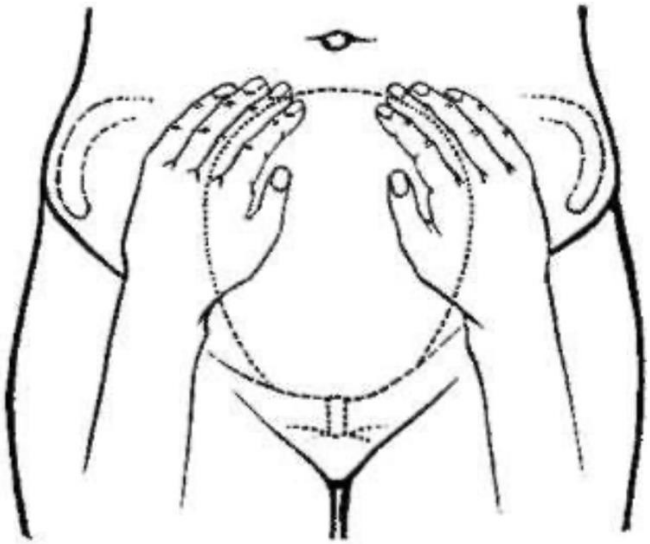


Image 88 – Palpation of bladder [10].

If the patient has not been circumcised, the foreskin should be retracted to examine for tumor or balanoposthitis (inflammation of the prepuce and glans penis). **Most penile cancers occur in uncircumcised men and arise on the prepuce or glans penis.** The position of the urethral meatus should be noted. It may be located proximal to the tip of the glans on the ventral surface (hypospadias) or, much less commonly, on the dorsal surface (epispadias). The penile skin should be examined for the presence of superficial vesicles compatible with herpes simplex and for ulcers that may indicate either venereal infection or tumor [5].

The scrotum is a loose sac containing the testes and spermatic cord structures. The scrotal wall is made up of skin and an underlying thin muscular layer. The testes should be palpated gently between the fingertips of both hands. The testes normally have a firm, rubbery consistency with a smooth surface. Abnormally small testes suggest hypogonadism or an endocrinopathy such as Klinefelter disease. **A firm or hard area within the testis should be considered a malignant tumor until proved otherwise.** The epididymis should be palpable as a ridge posterior to each testis. Masses in the epididymis (spermatocele, cyst, and epididymitis) are almost always benign.

To examine for a hernia, the physician's index finger should be inserted gently into the scrotum and invaginated into the external inguinal ring (image 89) [5].

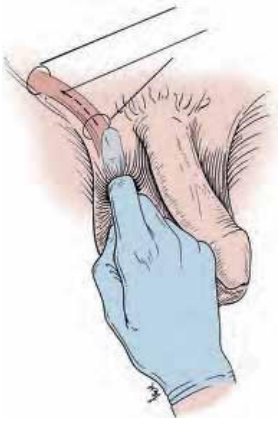


Image 89 – Palpation of scrotum, spermatic cord [5].

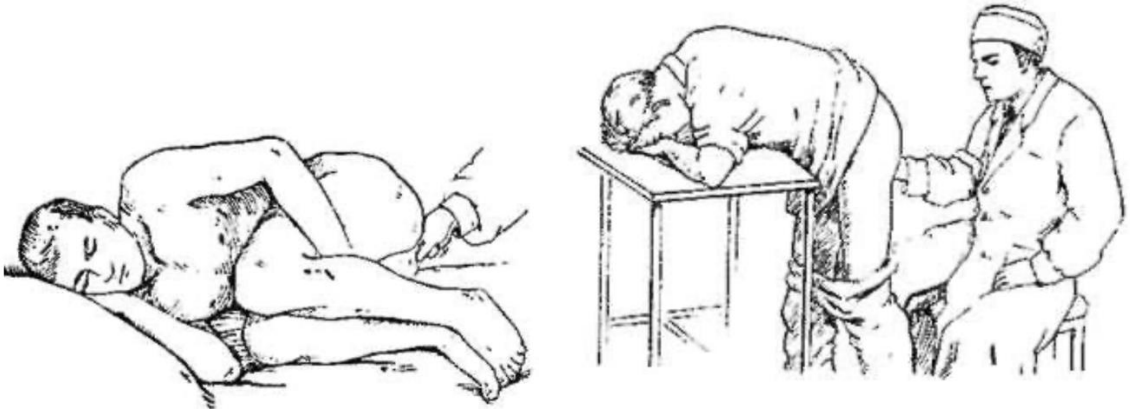
The scrotum should be invaginated in front of the testis, and care should be taken not to elevate the testis itself, which is quite painful. Once the external ring has been located, the physician should place the fingertips of his or her other hand over the internal inguinal ring and ask the patient to bear down (Valsalva maneuver). A hernia will be felt as a distinct bulge that descends against the tip of the index finger in the external inguinal ring as the patient bears down [5].

The spermatic cord is also examined with the patient in the standing position. A varicocele is a dilated, tortuous spermatic vein that becomes more obvious as the patient performs a Valsalva maneuver. The epididymis can again be palpated as a ridge of tissue running longitudinally, posterior to each testis. The testis should be palpated again between the fingers of both hands, once again taking care not to exert any pressure on the testis itself to avoid pain [5].

Transillumination is helpful in determining whether scrotal masses are solid (tumor) or cystic (hydrocele, spermatocele). A small flashlight or fiberoptic light cord is placed behind the mass. A cystic mass transilluminates easily, whereas light is not transmit- ted through a solid tumor.

Digital rectal examination (DRE) should be performed in every male after age 40 years and in men of any age who present for urologic evaluation. Prostate cancer is the second most common cause of male cancer deaths after age 55 years and the most common cause of cancer deaths in men older than 70 years [5].

DRE should be performed at the end of the physical examination. It is done best with the patient standing and bent over the examining table or with the patient in the knee-chest position. The physician should place a glove on the examining hand and should lubricate the index finger thoroughly (image 90) [5].



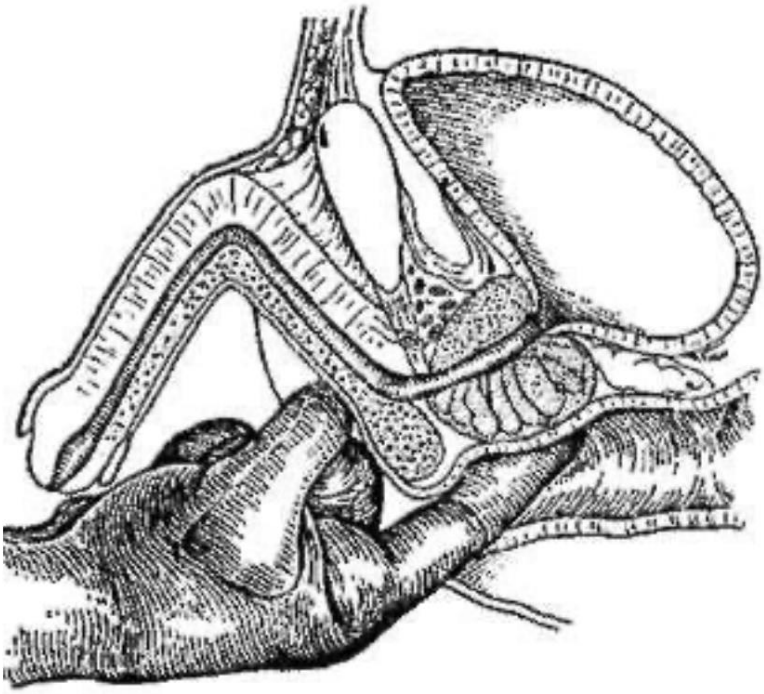


Image 90 – Digital rectal examination (prostate palpation) [10].

Sensory deficits in the penis, labia, scrotum, vagina, and perianal area generally indicate damage or injury to sacral roots or nerves. In addition to sensory examination, testing of reflexes in the genital area may also be performed. The most important of these is the bulbocavernosus reflex (BCR), which is a reflex contraction of the striated muscle of the pelvic floor that occurs in response to various stimuli in the perineum or genitalia. This reflex is most tested by placing a finger in the rectum and then squeezing the glans penis or clitoris. If a Foley catheter is in place, the BCR can also be elicited by gently pulling on the catheter. If the BCR is intact, tightening of the anal sphincter should be felt and/or observed. The BCR tests the integrity of the spinal cord–mediated reflex arc involving S2-S4 and may be absent in the presence of sacral cord or peripheral nerve abnormalities [5].

The cremasteric reflex can be elicited by lightly stroking the superior and medial thigh in a downward direction. The normal response in males is contraction of the cremasteric muscle that results in immediate elevation of the ipsilateral scrotum and testis. There is limited clinical utility for testing superficial reflexes such as the cremasteric when investigating neurologic dysfunction. However, there may be a role for testing this reflex when assessing patients with suspected testicular torsion or epididymitis. Finally, an overly active cremasteric reflex in children can lead to the mistaken diagnosis of an undescended testis in some cases (image 91) [5].

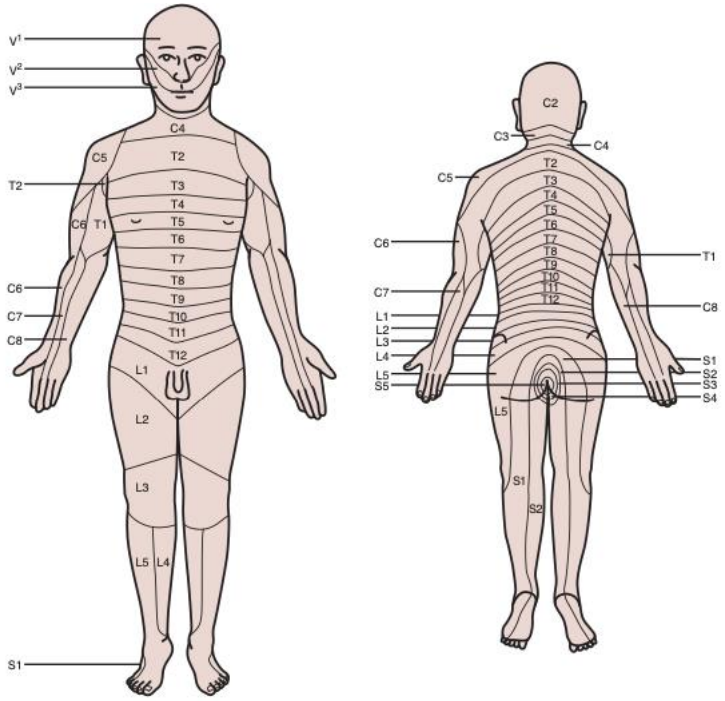


Image 91 – Neurologic examination (Campbell- Walch Urology, chapter1, evaluation of the urologic patients).

Urinalysis.

The urinalysis is a fundamental test (image 92) that should be performed in all urologic patients. Although in many instances a simple dipstick urinalysis will provide the necessary information, **a complete urinalysis includes both chemical and microscopic analyses [5].**

In the male patient, a midstream urine sample is obtained. The uncircumcised male should retract the foreskin, cleanse the glans penis with antiseptic solution, and continue to retract the foreskin during voiding. The male patient begins urinating into the toilet and then places a wide-mouth sterile container under his penis to collect a midstream sample. This avoids contamination of the urine specimen with skin and urethral organisms [5].

The VB1 (voided bladder) is the initial 5 to 10 mL of urine voided, whereas the VB2 is the midstream urine. The EPS (expressed prostatic secretion) is the secretions obtained after gentle prostatic massage, and the VB3 specimen is the initial 2 to 3 mL of urine obtained after prostatic massage. The value of these cultures for localization of UTIs is that the VB1 sample represents urethral flora; the VB2, bladder flora; and the EPS and VB3 samples, prostatic flora. The VB3 sample is particularly helpful when little or no prostatic fluid is obtained by massage. To better obtain prostatic secretions, patients should be instructed to attempt to void during prostatic massage and to avoid tightening the anal sphincter and pelvic floor muscles. The four-part urine sample is particularly useful in evaluating men with suspected bacterial prostatitis (Meares and Stamey, 1968) [5].

PATIENT INFORMATION

REPORT STATUS: FINAL

SPECIMEN INFORMATION

ORDERING PHYSICIAN

SPECIMEN:

DOB:

REQUISITION:

AGE:

LAB REF NO:

GENDER:

FASTING:

CLIENT INFORMATION

Clinical Info:

ACCESA LABS

Order Today

www.accesalabs.com/general

COLLECTED:

RECEIVED:

REPORTED:

Test Name	Result	Flag	Reference Range	Lab
URINALYSIS, COMPLETE				
COLOR	YELLOW		YELLOW	01
APPEARANCE	CLEAR		CLEAR	01
SPECIFIC GRAVITY	1.023		1.001-1.035	01
PH	6.0		5.0-8.0	01
GLUCOSE	NEGATIVE		NEGATIVE	01
REDUCING SUBSTANCES	DNR		NEGATIVE %	01
BILIRUBIN	NEGATIVE		NEGATIVE	01
KETONES	NEGATIVE		NEGATIVE	01
OCCULT BLOOD	NEGATIVE		NEGATIVE	01
PROTEIN	NEGATIVE		NEGATIVE	01
NITRITE	NEGATIVE		NEGATIVE	01
LEUKOCYTE ESTERASE	NEGATIVE		NEGATIVE	01
WBC	0-5		< OR = 5 /HPF	01
RBC	NONE SEEN		< OR = 3 /HPF	01
SQUAMOUS EPITHELIAL CELLS	0-5		< OR = 5 /HPF	01
TRANSITIONAL EPITHELIAL CELLS	DNR		< OR = 5 /HPF	01
RENAL EPITHELIAL CELLS	DNR		< OR = 3 /HPF	01
BACTERIA	FEW	ABNORMAL	NONE SEEN /HPF	01
CALCIUM OXALATE CRYSTALS	DNR		NONE OR FEW /HPF	01
TRIPLE PHOSPHATE CRYSTALS	DNR		NONE OR FEW /HPF	01
URIC ACID CRYSTALS	DNR		NONE OR FEW /HPF	01
AMORPHOUS SEDIMENT	DNR		NONE OR FEW /HPF	01
CRYSTALS	DNR		NONE SEEN /HPF	01
HYALINE CAST	NONE SEEN		NONE SEEN /LPF	01
GRANULAR CAST	DNR		NONE SEEN /LPF	01
CASTS	DNR		NONE SEEN /LPF	01
YEAST	DNR		NONE SEEN /HPF	01
COMMENTS	DNR			01
NOTE	DNR			01

Image 92 – Simple urinary test (material from internet Accesa laboratory).

Task 11 Referent meaning

Parameters	Meanings
Colour	Pale yellow, yellow
Cloudy/milky	negative
PH	pH <7.0
Specific gravity	1010–1025
Protein	No more than 0,03 g/l
Glucose	negative
Bilirubine	negative
Ketone	negative
Erythrocytes	No more than 3 per
Leucocytes	M: No more than 3 per ; W: No more than 5 per

Hyaline casts	No more than 1-2
Granular casts	Negative
Wax casts	Negative
Bacteria	Negative
Yeast	Negative
Crystals	negative

The physical examination of the urine includes an evaluation of color, turbidity, specific gravity and osmolality, and pH. **Chemical examination** in urine include blood, protein, glucose, ketones, urobilinogen and bilirubin, and white blood cells [5].

Hematuria may reflect either significant **nephrologic** or **urologic** disease. Hematuria of nephrologic origin is frequently associated with casts in the urine and almost always associated with significant proteinuria. Even significant hematuria of urologic origin will not elevate the protein concentration in the urine into the 100 to 300 mg/dL or 2+ to 3+ range on dipstick, and proteinuria of this magnitude almost always indicates glomerular or tubulointerstitial renal disease [5].

Morphologic evaluation of erythrocytes in the centrifuged urinary sediment also helps localize their site of origin. Erythrocytes arising from **glomerular disease** are typically **dysmorphic and show a wide range of morphologic alterations**. Conversely, erythrocytes arising from **tubulointerstitial renal disease** and of urologic origin have a **uniformly round shape**; these erythrocytes may or may not retain their hemoglobin ("ghost cells"), but the individual cell shape is consistently round [5].

Proteinuria may be the first indication of renovascular, glomerular, or tubulointerstitial renal disease, or it may represent the overflow of abnormal proteins into the urine in conditions such as multiple myeloma [5].

Normally, urine protein is about 30% albumin, 30% serum globulins, and 40% tissue proteins, of which the major component is Tamm-Horsfall protein .

Glomerular proteinuria occurs in any of the primary glomerular diseases such as IgA nephropathy or in glomerulopathy associated with systemic illness such as diabetes mellitus. Glomerular disease should be suspected when the 24-hour urine protein excretion exceeds 1 g and is almost certain to exist when the total protein excretion exceeds 3 g [5].

Tubular proteinuria results from failure to reabsorb normally filtered proteins of low molecular weight such as immunoglobulins. In tubular proteinuria, the 24-hour urine protein loss seldom exceeds 2 to 3 g and the excreted proteins are of low molecular weight rather than albumin. Disorders that lead to tubular proteinuria are commonly associated with other defects of proximal tubular function such as glucosuria, aminoaciduria, phosphaturia, and uricosuria (Fanconi syndrome) [5].

Overflow proteinuria occurs in the absence of any underlying renal disease and is due to an increased plasma concentration of abnormal immunoglobulins and other low-molecular-weight proteins. The increased serum levels of abnormal proteins result in excess glomerular filtration that exceeds tubular reabsorptive capacity. The most common cause of overflow proteinuria is multiple myeloma, in

which large amounts of immunoglobulin light chains are produced and appear in the urine (Bence Jones protein).

Conventional radiography.

Conventional radiography includes abdominal plain radiography, intravenous excretory urography, retrograde pyelography, loopography, retrograde urethrography, and cystography.

PLAIN ABDOMINAL RADIOGRAPHY

The plain abdominal radiograph is a conventional radiography study, which is intended to display the kidneys, ureters, and bladder.

Plain films are widely used in the management of renal calculus disease.

Technique

An abdominal plain radiograph is obtained with the patient in the supine position, using an anterior to posterior exposure. The study typically includes that portion of the anatomy from the level of the diaphragm to the inferior pubic symphysis. It may occasionally be necessary to make two exposures to cover the desired anatomic field. Depending on the indication for the study, oblique films are obtained to clarify the position of structures in relation to the urinary tract. If small bowel obstruction or free peritoneal air is suspected, upright films will be obtained (image 93, 94) [5].

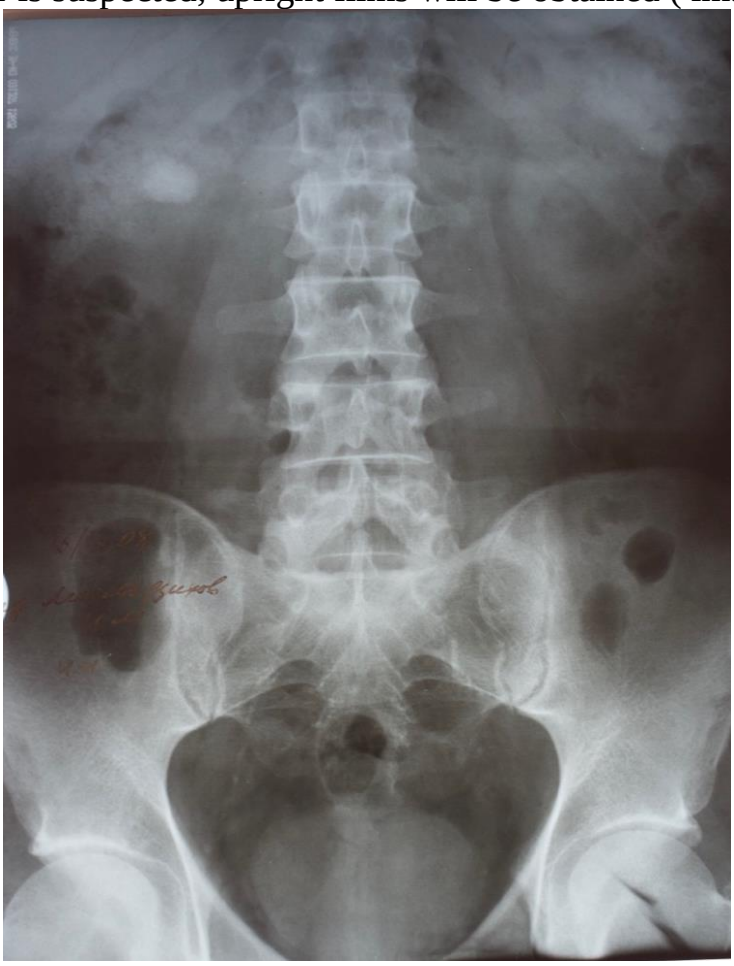


Image 93 – Plain abdominal urography (own material from department).

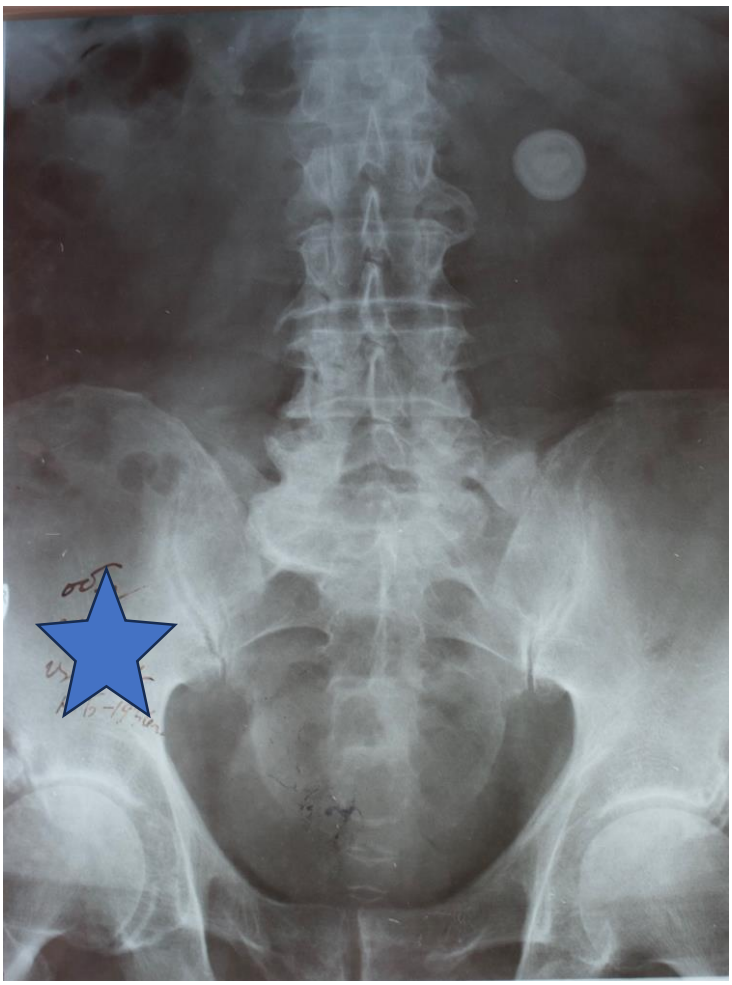


Image 94- Plain abdominal urography (own material from department).

INTRAVENOUS UROGRAPHY.

Before injection of contrast, a plain abdominal radiography or KUB (kidney-ureter-bladder) film is taken demonstrating the top of the kidneys and the entire pelvis to the pubic symphysis. This allows determination of adequate bowel prep, confirms correct positioning, and exposes kidney stones or bladder stones.

Contrast is injected as a bolus of 50 to 100 mL of contrast.

1. After contrast is given, radiographs are obtained at 1, 3, 5, and 10 minutes.
2. By 1 minute, the glomeruli and tubules begin to opacify (nephrographic phase).
3. By 5 minutes, the calyces and renal pelvis should be seen bilaterally (pyelographic phase). If there is an obstruction, a delay in the pyelographic phase on the affected side will be noted.
4. By 10 minutes, the ureters and bladder are visible. If there is obstruction, the ureter on the affected side may not yet be opacified or it may be seen to be dilated (ureter ectasis).
5. If there is an obstruction, it may be necessary to obtain delayed radiographs up to several hours to visualize the ureter and the site of obstruction.
6. The bladder should be distended by 10 minutes. Assess the bladder for filling defects that may reflect a stone or tumor.
7. Finally, the post void film is obtained to determine the ability of the patient to empty the bladder.

Indications

- Demonstration of renal collecting systems and ureters
- Investigation of level of ureteral obstruction
- Demonstration of intraoperative opacification of collecting system during extracorporeal shock wave lithotripsy or percutaneous access to the collecting system
- Demonstration of renal function during emergent evaluation of unstable patients
- Demonstrate renal and ureteral anatomy in special circumstances (e.g., ptosis, after transureteroureterostomy, and after urinary diversion) (image 95,96)[5].

Epinephrine can be administered IV in the dose of 0.01mg/ kg of 1:10,000 dilution or 0.1 mL/kg slowly into a running infusion of saline and can be repeated every 5 to 15 minutes as needed. If no IV access is available, the recommended IM dose of epinephrine is 0.01 mg/kg of 1:1000 dilution (or 0.01 mL/kg to a maximum of 0.15 mg of 1 : 1000 if less than 30 kg; 0.3 mg if weight is greater than 30 kg) injected in the lateral thigh [5].

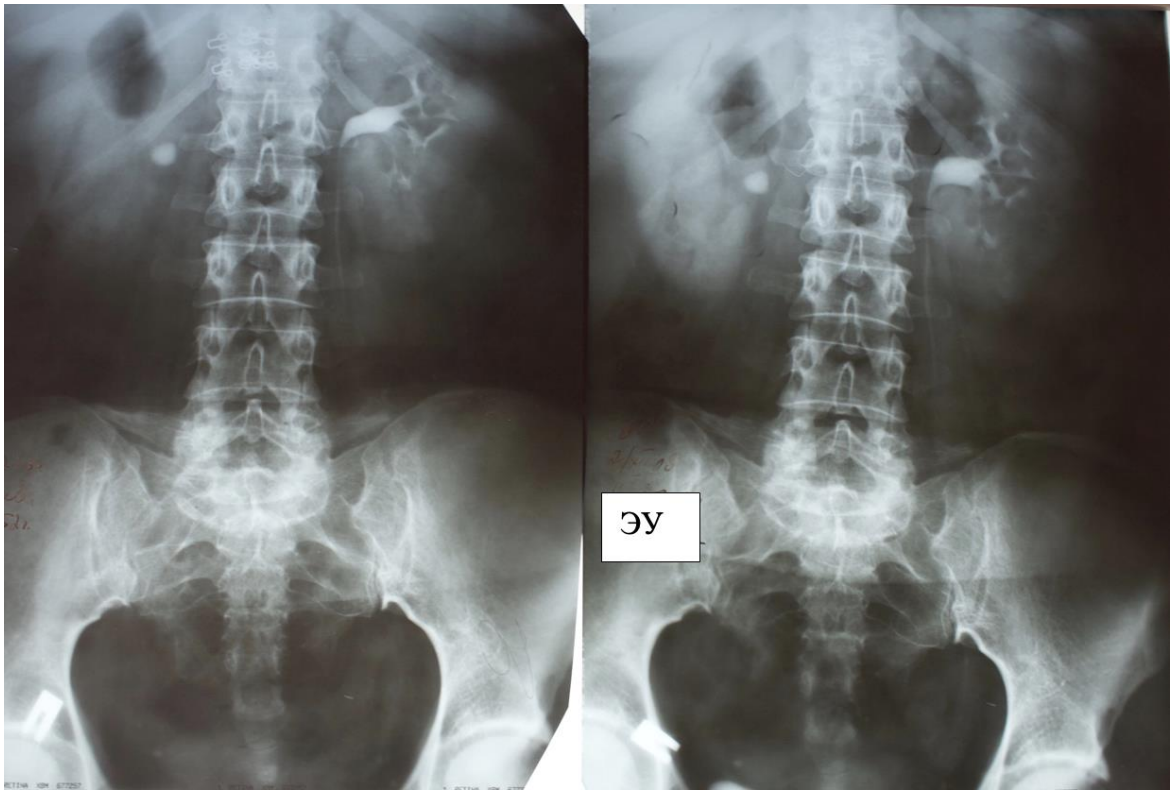


Image 95 – IVU (first list – after 10m, second – after 60m)(own materials)(stone in right UPJ, complete obstruction).

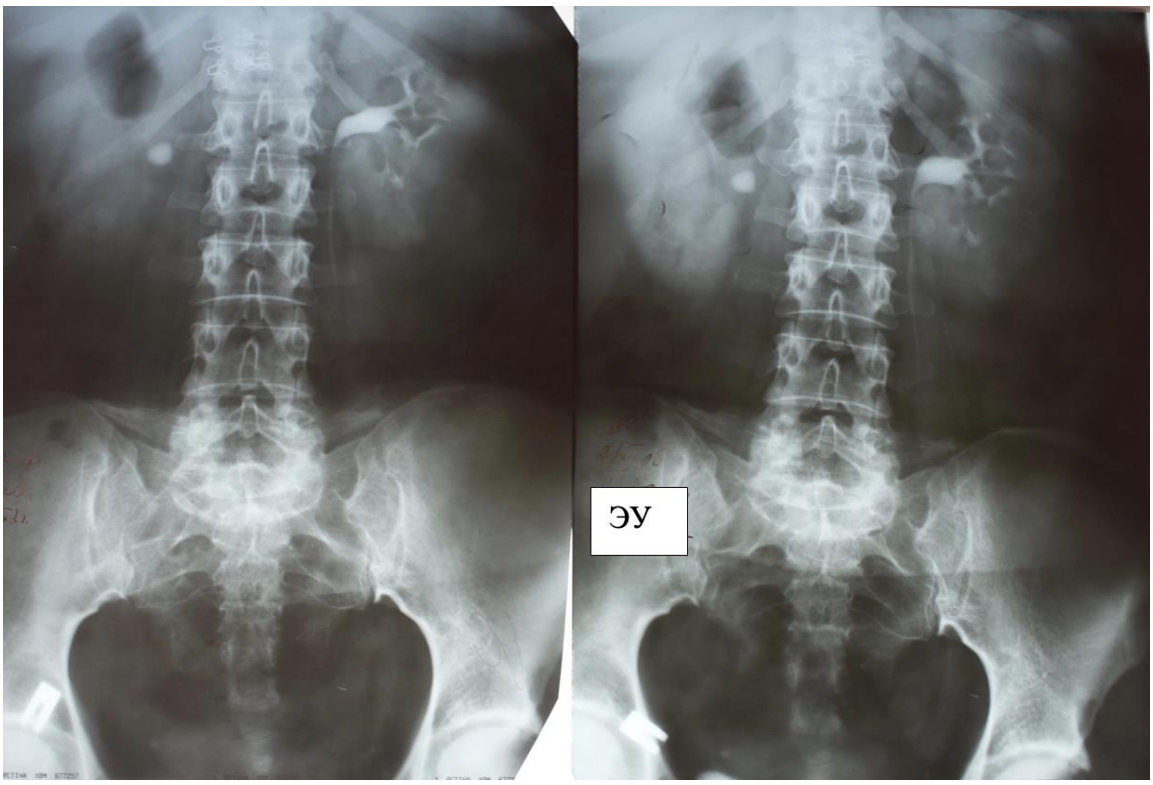


Image 96 - IVU (first list – after 1 hours, second – after 2 hours) (own materials)(stone in right UPJ, complete obstruction, symptom “white kidney”).

RETROGRADE PYELOGRAPHY

Retrograde pyelograms are performed to opacify the ureters and intrarenal collecting system by the retrograde injection of contrast media. Any contrast media that can be used for excretory urography is also acceptable for retrograde pyelography [5].

Technique

Retrograde pyelography is usually performed with the patient in the dorsal lithotomy position. An abdominal plain radiograph (KUB film) is obtained to ensure that the patient is in the appropriate position to evaluate the entire ureter and intrarenal collecting system. Cystoscopy is performed and the ureteral orifice is identified [5].

Contrast may be injected (5 – 8 ml) through either a nonobstructing catheter or an obstructing catheter.

Complications

Backflow occurs during retrograde pyelography when contrast is injected under pressure and escapes the collecting system. Contrast may escape the collecting system by one of four routes: **Pyelotubular** backflow occurs when contrast fills the distal collecting ducts producing opacification of the medullary pyramids.

Pyelosinus backflow occurs when a tear in the calyces at the fornix allows contrast to leak into the renal sinus.

Pyelolymphatic backflow is characterized by opacification of the renal lymphatic channels . **Pyelovenous** backflow is seen when contrast enters the venous system, resulting in visualization of the renal vein (image 97) [5].

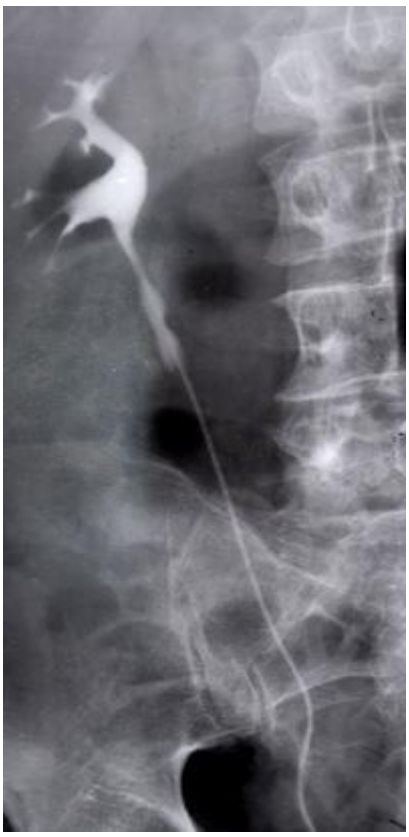


Image 97 – Retrograde pyelography (material from internet)

Antegrade pyelography.

Antegrade pyelograms are performed to opacify the ureters and intrarenal collecting system by the antegrade injection of contrast media via nephrostomy (image 98).

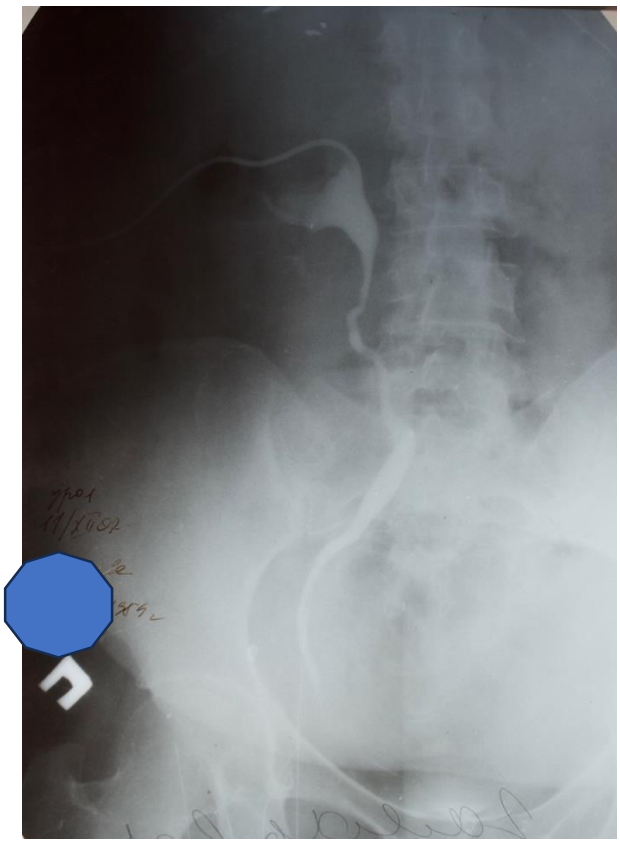


Image 98 - Antegrade pyelogram (own materials from department).

RETROGRADE URETHROGRAPHY.

A retrograde urethrogram is a study to evaluate the anterior and posterior urethra. Retrograde urethrography may be particularly beneficial in demonstrating the total length of a urethral stricture that cannot be negotiated by cystoscopy. Retrograde urethrography also demonstrates the anatomy of the urethra distal to a stricture that may not be assessable by voiding cystourethrography, may be performed in the office or in the operating room before performing visual internal urethrotomy or formal urethroplasty [5].

Technique

A plain film radiograph is obtained before injection of contrast. The patient is usually positioned slightly obliquely to allow evaluation of the full length of urethra. The penis is placed on slight tension. A small catheter may be inserted into the fossa navicularis with the balloon inflated to 2 mL with sterile water. Contrast is then introduced via a catheter-tipped syringe. Alternatively, a penile clamp (e.g., Brodney clamp) may be used to occlude the urethra around the catheter (image 99).

Indications

1. Evaluation of urethral stricture disease
a. Location of stricture
b. Length of stricture
2. Assessment for foreign bodies
3. Evaluation of penile or urethral penetrating trauma
4. Evaluation of traumatic gross hematuria [5].

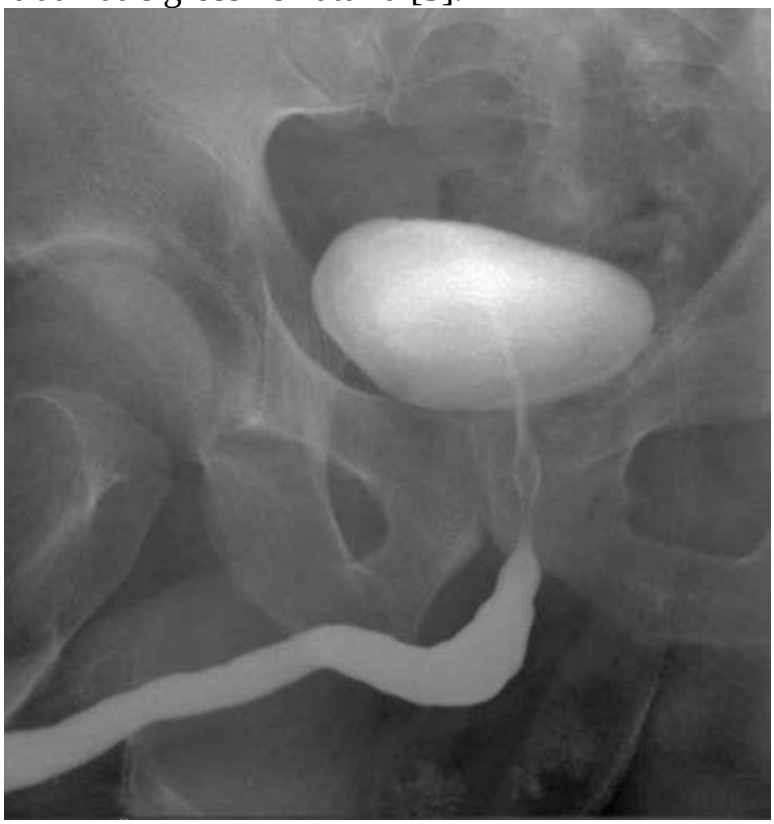


Image 99 – Retrograde urethrogram (material from internet) (stricture of membranous part of urethra).

Cystography is used primarily to evaluate the structural integrity of the bladder. The shape and contour of the bladder may give information about neurogenic dysfunction or bladder outlet obstruction. Filling defects such as tumors and stones may be appreciated [5].

Technique

The patient is positioned supine. A plain radiograph is performed to evaluate for stones and residual contrast and to confirm position and technique. The bladder is filled with 200 to 400 mL of contrast, depending on bladder size and patient comfort. Adequate filling is important to demonstrate intravesical pathology or bladder rupture. Oblique films should be obtained because posterior diverticula or fistulae may be obscured by the full bladder. A postdrainage film completes the study (image 100) [5].

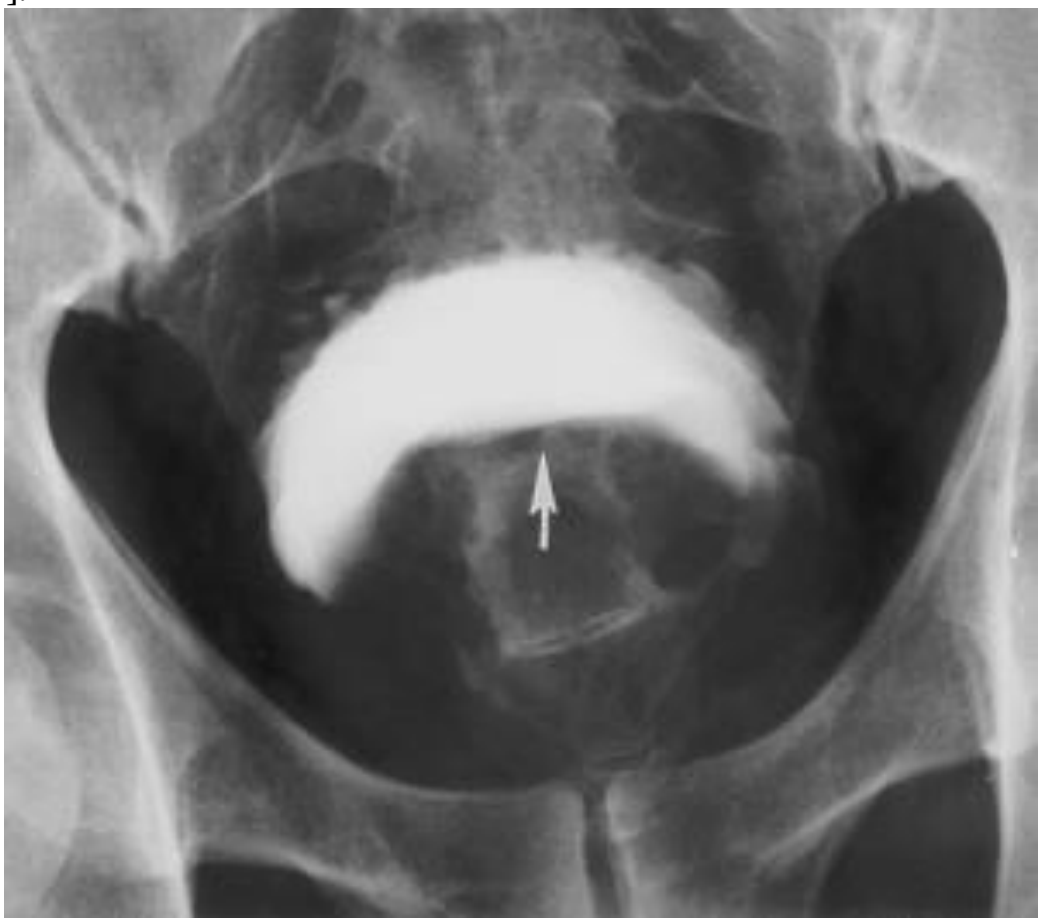


Image 100 – Cystography (material from internet)(BPH elevated bladder).

A **voiding cystourethrogram** (VCUG) is performed to evaluate the anatomy and physiology of the bladder and urethra. The study provides valuable information regarding the posterior urethra in pediatric patients. VCUG has long been used to demonstrate vesicoureteral reflux [5].

Technique

The study may be performed with the patient supine or in a semi upright position using a table capable of bringing the patient into the full upright position. A preliminary pelvic plain radiograph is obtained. In children, a 5- to 8-Fr feeding tube is used to fill the bladder to the appropriate volume. Patient comfort should be considered when determining the appropriate volume. In the adult population a

standard catheter may be placed, and the bladder filled to 200 to 400 mL. The catheter is removed, and a film is obtained. During voiding, AP and oblique films are obtained. The bladder neck and urethra may be evaluated by fluoroscopy during voiding. Bilateral oblique views may demonstrate low-grade reflux, which is not able to be appreciated on the AP film. In addition, oblique films will demonstrate bladder or urethral diverticula, which are not always visible in the straight AP projection. Postvoiding films should be performed.

Indications

1. Evaluation of structural and functional bladder outlet obstruction
2. Evaluation of reflux
3. Evaluation of the urethra in males and females [5].

NUCLEAR SCINTIGRAPHY

Radionuclide imaging (image 101) is the procedure of choice to evaluate renal obstruction and function. It is very sensitive to changes that induce focal or global changes in kidney function. Because neither Gd nor iodinated IV contrast agents are used, scintigraphy does not damage the kidney, has no lingering toxicity, results in minimal absorbed radiation, and is free from allergic reactions [5].

Once the agent is injected gamma scintillation cameras measure radiation emitted from the radioisotope, and digital workstations gather, process, and display the information. There is an extensive list of radiopharmaceuticals used for renal scintigraphy. This section will be limited to those agents most used in urologic practice.

Technetium 99m-diethylenetriamine pentaacetic acid (99mTc- DTPA) is primarily a glomerular filtration agent (Peters, 1998; Gates, 2004). It is most useful for evaluation of obstruction and renal function. Because it is excreted through the kidney and dependent on GFR, it is less useful in patients with renal failure because impaired GFR may limit adequate evaluation of the collecting system and ureters. It is readily available and relatively inexpensive (Klopper et al, 1972) [5].

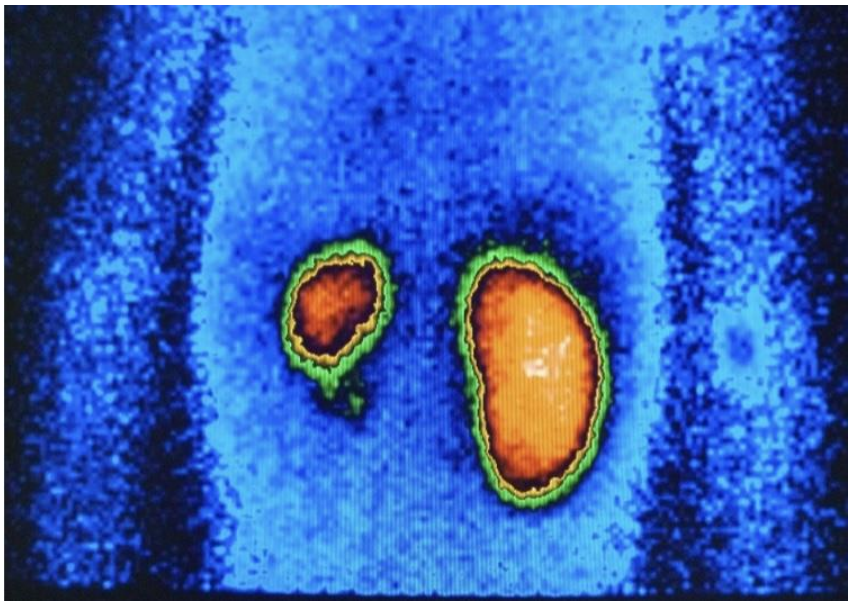


Image 101 – Nephroscingraphy (hypoplasia of right kidney)(: https://2gdkb.by/o-клинике/отделения/изотопная-лаборатория)

Diuretic scintigraphy.

The diuretic renal scan using ^{99m}Tc- MAG3 can provide differential renal function and clearance time comparing right and left kidneys, which is pivotal in-patient management.

The initial phase is the flow phase where 2-second images are gathered for 2 minutes and then 1-second images for 60 seconds. The flow phase shows renal uptake, background clearance, and abnormal vascular lesions, which may indicate arteriovenous malformations, tumors, or active bleeding.

In the second phase, **the renal phase**, time-to-peak uptake is typically between 2 and 4 minutes. The renal phase is the most sensitive indicator of renal dysfunction. One-minute images are taken for 30 minutes. In the final phase, **the excretory phase**, 1-minute images are taken for 30 minutes [5].

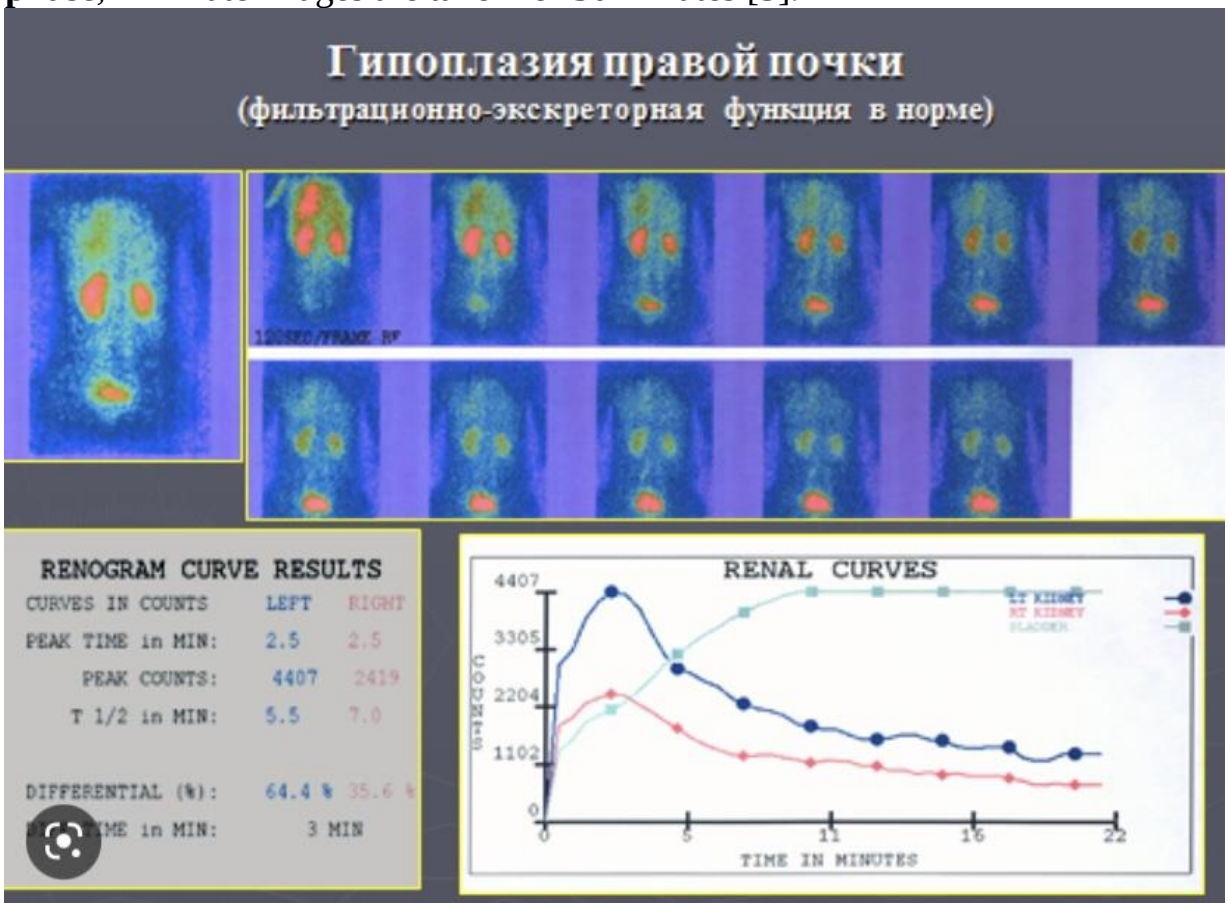


Image 102 - Diuretic scintigraphy

Источник: https://2gdkb.by/о-клинике/отделения/изотопная-лаборатория)

A diuretic (usually furosemide 0.5 mg/kg) is administered when maximum collecting system activity is visualized. The T1/2 is the time it takes for collecting system activity to decrease by 50% from that at the time of diuretic administration. This is highly technician dependent because the diuretic must be given when the collecting system is displaying maximum activity. Transit time through the collecting system in less than 10 minutes is consistent with a normal, nonobstructed collecting system. T1/2 of 10 to 20 minutes shows mild to moderate delay and may be a mechanical obstruction. The patient's perception of pain after diuretic administration can be helpful for the treating urologist to consider when planning

surgery in the patient with mild to moderate obstruction. A $T_{1/2}$ of greater than 20 minutes is consistent with a high-grade obstruction. The level of obstruction can usually be determined, as can abnormalities such as ureteral duplication (Ell and Gambhir, 2004) [5].

Whole-Body Bone Scan

Conventional radionuclide imaging in urologic malignancy has long been the standard for detecting bone metastasis. The whole- body bone scan or skeletal scintigraphy is the most sensitive method for detecting bone metastasis (Narayan et al, 1988). A "positive" bone scan is not specific for cancer and may require plain film radiography, CT, or MRI to confirm, as well as correlation with prior history of bone fractures, trauma, surgery, or arthritis. In patients with diffuse metastatic bone involvement, the bone scan can be mistaken for normal because there is uniformly increased uptake in the bony structures (Kim et al, 1991) [5].

Computed tomography.

Urologists often request a CT evaluation of the abdomen and pelvis. An abdominal CT starts at the diaphragm and ends at the iliac crest. If the pelvis is to be imaged, a separate request is usually required. The pelvic CT begins at the iliac crest and terminates at the pubis symphysis. Intravenous contrast may be required for better delineation of soft tissue. Oral contrast is not commonly used in urology but may be helpful in certain patients to differentiate bowel from lymph nodes, scar, or tumor .

CT urogram (CTU) has replaced IVU as the imaging modality of choice in modern urology for the workup of hematuria, urologic malignancies, detection of kidney stones, and preoperative planning. As in the case of conventional radiographic imaging, the basis for CT imaging is the attenuation of x-ray photons as they pass through the patient. Tomography is an imaging method that produces 3D images of internal structures by recording the passage of x-rays as they pass through different body tissues. In the case of CT, a computer reconstructs cross-sectional images of the body based on measurements of x-ray transmission through thin slices of the body tissue [5].

Hounsfield Units

A single CT image generated by the scanner is divided into many tiny blocks of different shades of black and white called pixels. The
actual gray scale of each pixel on a CT depends on the amount of radiation absorbed at that point, which is termed an attenuation value. **Attenuation values are expressed in Hounsfield units (HU). The HU scale, or attenuation value, is based on a reference scale in which air is assigned a value of −1000 HU and dense bone is assigned the value of +1000 HU. Water is assigned 0 HU (image 103).**

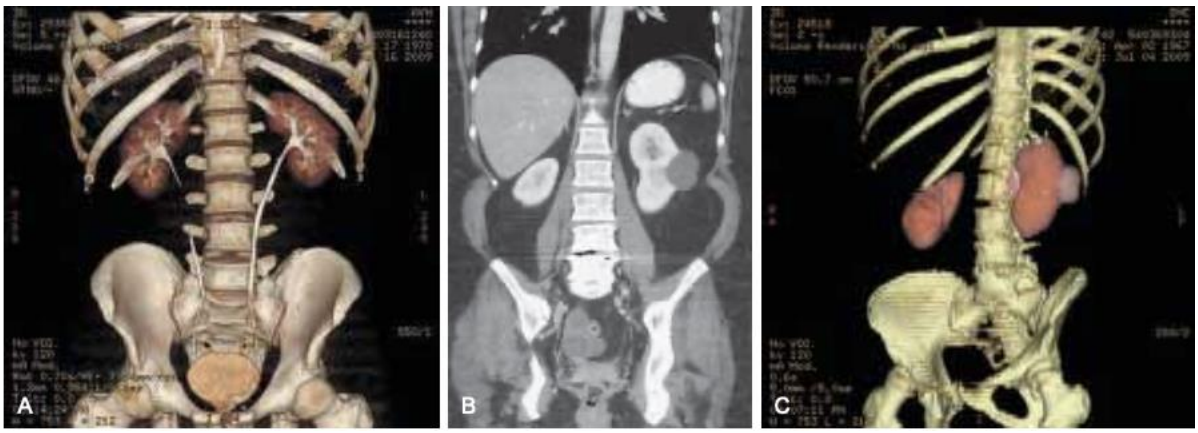


Image 103 – CT (A, Three-dimensional (3D) colored reconstruction of the kidneys, ureters, and bladder from computed tomography urogram. B, Coronal reconstruction in a patient with a clear cell renal cell carcinoma in a complex renal cystic mass and enhancing mural nodule. C, 3D reconstruction of the same patient with slight posterior rotation). (Campbell- Walch Urology, chapter 2, urinary tract imaging).

MRI.

To obtain MR images, the patient is placed on a gantry that passes through the bore of the magnet. When exposed to a magnet field of sufficient strength, the free water protons in the patient orient themselves along the magnetic field's z-axis. This is the head- to-toe axis, straight through the bore of the magnet. An RF antenna or "coil" is placed over the body part to be imaged. It is the coil that transmits the RF pulses through the patient. When the RF pulse stops, protons release their energy, which is detected and processed to obtain the MR image. Currently, some coils can transmit and receive a signal, which is referred to dual channel RF. An MR sequence exploits the body's different tissue characteristics and the particular manner that each type of tissue absorbs and then releases this energy. Weighting of the image depends on how the energy is imparted through the physics of the pulse sequence and whether the energy is released quickly or slowly. Images are described as being T1 or T2 weighted. The T1-weighted images are generated by the time required to return to equilibrium in the z-axis. The T2-weighted images are generated by the time to return to equilibrium in the xy-axis. **On T1-weighted MR images, fluid has a low SI and appears dark. T2-weighted MR images have a high SI and appear bright. In the kidney this translates into the cortex having a higher SI or being brighter than the medulla, which gives off a lower signal and is darker [5].** MRI has significant advantages over other imaging modalities. First, and most importantly, no risks are associated with secondary malignancies from radiation exposure (Berrington de González and Darby, 2004). It is the modality of choice in patients who are pregnant, suffer from renal insufficiency, and/or have an iodine contrast allergy (image 104) [5].

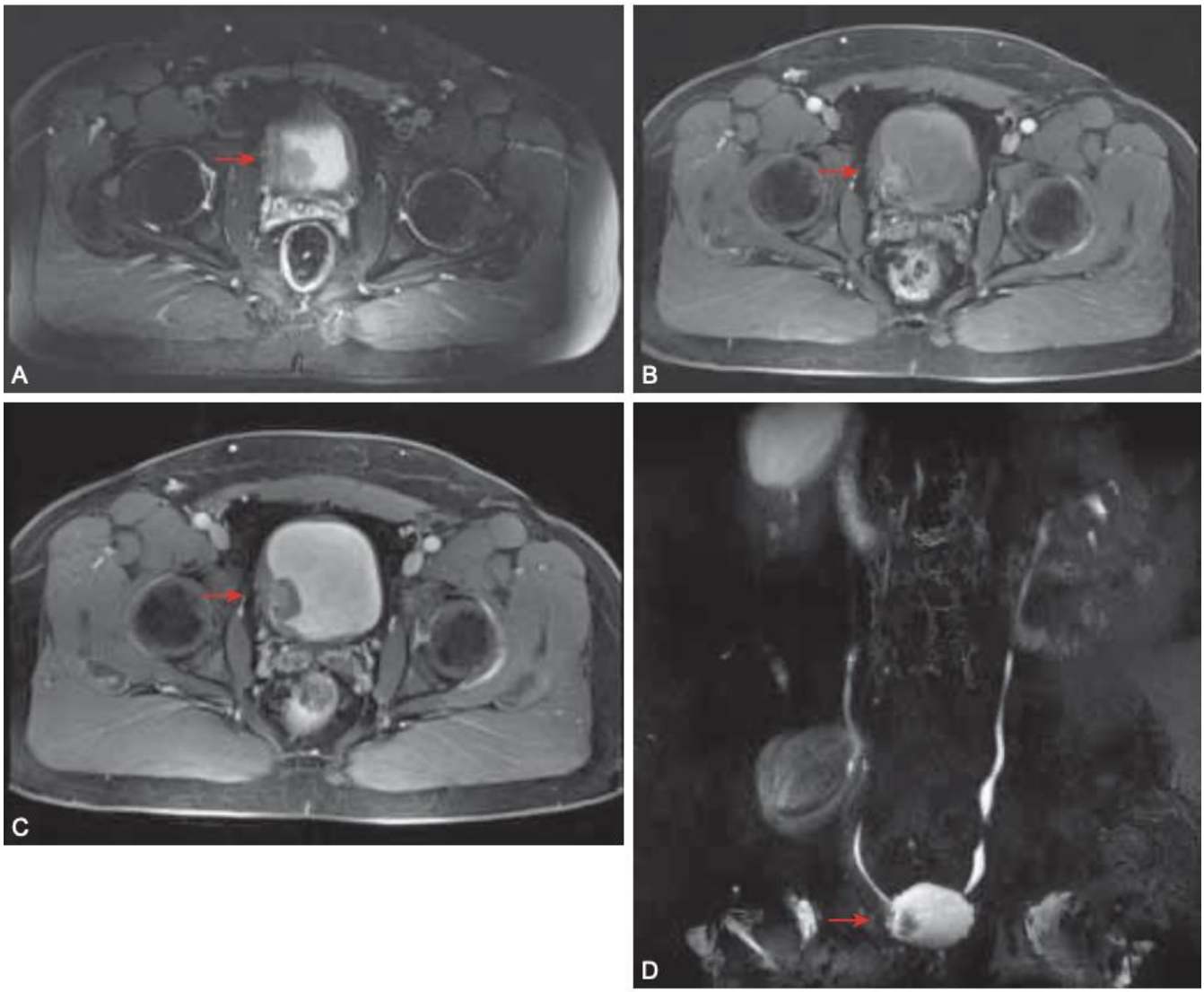


Image 104 – MRI (A 51-year-old man with a history of gross hematuria underwent a 1.5-tesla magnetic resonance urogram. A, T2 fat-saturated sequence with high T2 signal in bladder (urine). Right bladder wall low signal intensity filling defect *(red arrow)*.
B, Fat-suppressed T1 postcontrast arterial phase shows enhancing right bladder wall polypoid mass and is without bladder wall invasion.
C, Fat-suppressed T1 delayed contrast imaging shows high signal in bladder consistent with intravenous contrast excretion. Mild persistent signal in right bladder wall mass. D, Heavily weighted T2 urogram selectively demonstrates high signal of fluid within the ureters and bladder. Right wall bladder filling defect *(red arrow)* is evident. Transurethral resection of bladder tumor confirmed no bladder wall invasion of a high-grade papillary urothelial carcinoma.) (Campbell- Walch Urology, chapter 2, urinary tract imaging).

Ultrasound examination.

All ultrasound imaging is the result of the interaction of sound waves with tissues and structures within the human body. Ultrasound waves are produced by applying short bursts of alternating electrical current to a series of crystals housed in

the transducer. Alternating expansion and contraction of the crystals via the piezoelectric effect creates a mechanical wave that is transmitted through a coupling medium to the skin and then into the body. The waves that are produced are longitudinal waves. In a longitudinal wave, the particle motion is in the same direction as the propagation of the wave (image 105, 106) [5].

The appearance of the image produced by ultrasonography is the result of the interaction of mechanical ultrasound waves with biologic tissues and materials. Because ultrasound waves are transmitted and received at frequent intervals, the images can be rapidly reconstructed and refreshed, providing a real-time image. The frequencies of the sound waves used for urologic ultrasound imaging are in the range of 3.5 to 12 MHz.

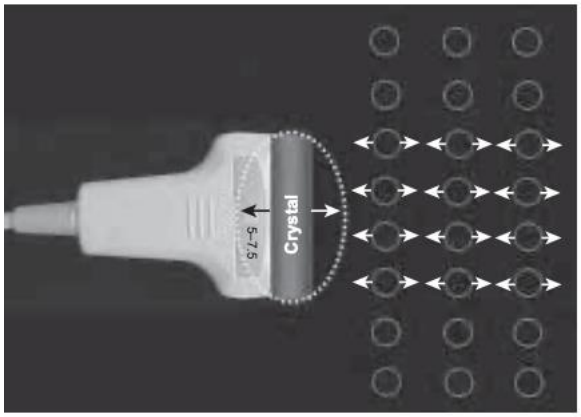


Image 105 – Formation of US waves (Campbell- Walch Urology, chapter 2, urinary tract imaging).

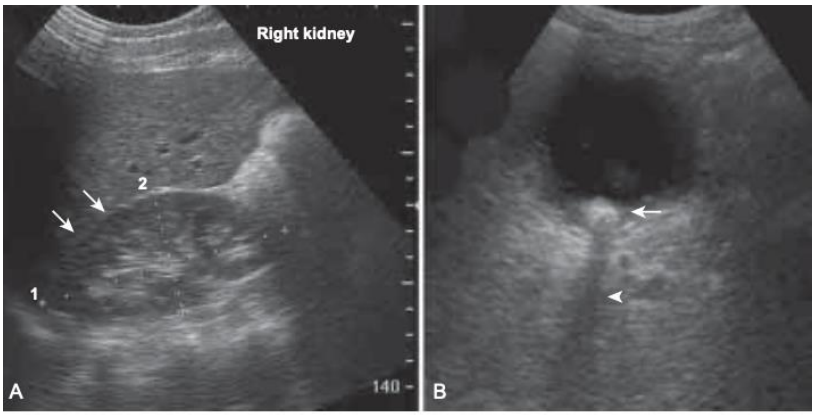


Image 106 - A, In this sagittal view of the right kidney, the paucity of perinephric fat and the small impedance difference make it difficult to distinguish the interface between the kidney and the liver *(arrows)*. B, The large impedance difference at the interface between urine and a bladder stone *(arrow)* result in significant reflection and attenuation of the sound wave. An acoustic shadow is seen distal to the stone *(arrowhead)*.

Endoscopic examination.

The average length of the male urethra is 17.5 to 20 cm from bladder neck to external urethral meatus from postmortem studies as reported in *Gray's Anatomy* (Standring, 2008). In general, the male urethra is divided into segments: bladder neck or preprostatic urethra, prostatic urethra, membranous urethra, and penile or spongy urethra, which in turn can be subdivided into the bulbous urethra, pendulous urethra, and fossa navicularis. An alternative classification for urethral segments is anterior and posterior urethra; the posterior segment consists of the prostatic and membranous urethra, and the anterior segment equates to the penile urethra [5].

The indications for inserting a bladder catheter (image 107) can conveniently be divided into two categories: therapeutic or diagnostic catheterization.

The most common indication for transurethral bladder catheterization is for drainage of an acute or chronic urinary retention or postvoid residual volume. Drainage can be accomplished by an indwelling catheter or by intermittent catheterization, depending on the pathology, the recurring need for drainage, and the dexterity of the patient or caregivers [5].

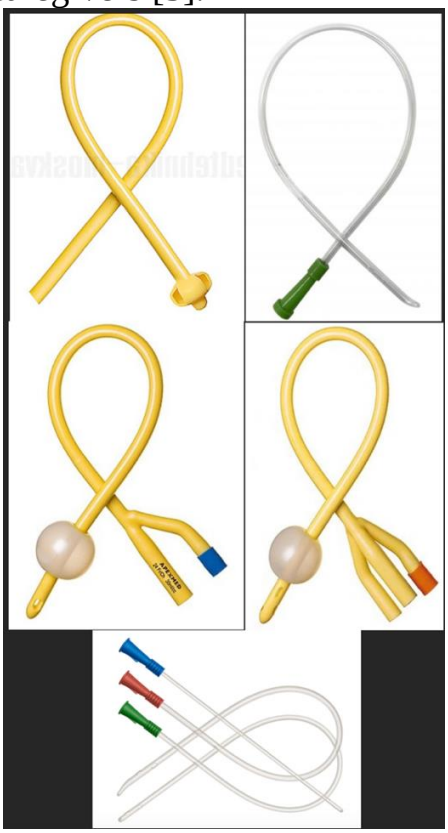


Image 107 – Catheters (Foley(two-way, three-way), Pizzer, Nelaton, Timan)

Cystourethroscopy.

At minimum, cystourethroscopy requires irrigation fluid, a light source, and an endoscope. Typical irrigation fluids include sterile water, glycine ,and normal saline.If electrocautery is needed, a solution free of electrolytes should be used. Cystourethroscopy is one of the most common procedures in urology. Routinely performed in both the office and operating room setting, cystourethroscopy provides

direct visualization of the urethra and bladder. The upper urinary tract may be evaluated fluoroscopically by ureteral catheterization with retrograde instillation of contrast material (image 108, 109, 110) [5].

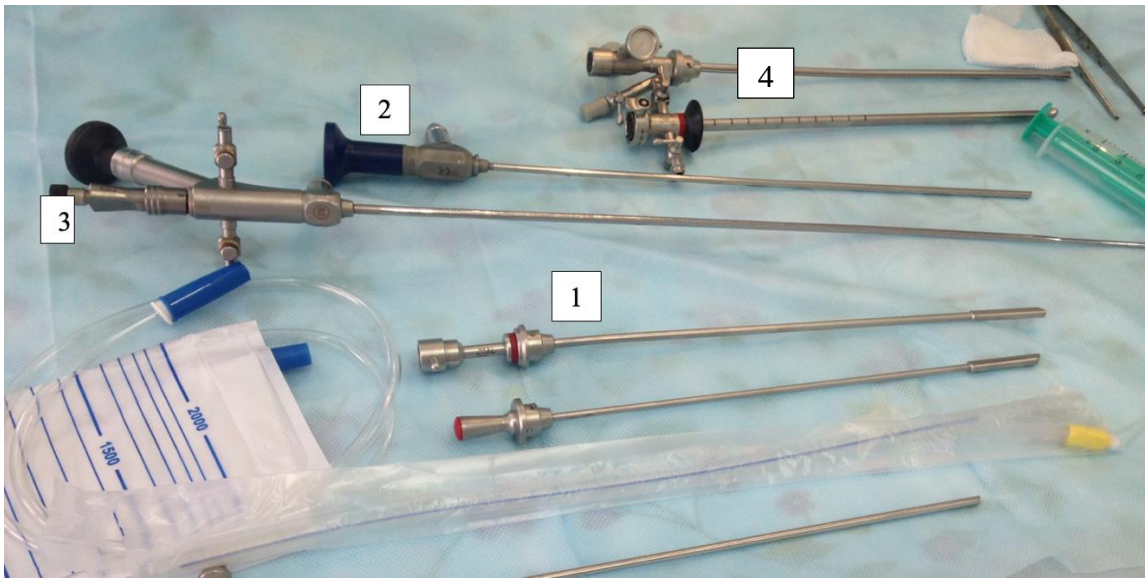


Image 108 – Urethrocystoscopy (1- obturator, 2 – lenses,3 – ureteroscopy, 4 – sheath for urethrocystoscopy) (own material)

	KARL STORZ	OLYMPUS	GYRUS/ACMI	WOLF
Lenses	0, 12, 30, 70, 120 Diameter: 4 mm Length: 30 cm	0, 12, 30, 70, 110 Diameter: 4 mm Length: 28 cm	0, 12, 30, 70, 110 Diameter: 4 mm Length: 28 cm	0, 12, 30, 70 Diameter: 4 mm Length: 29.5 cm
Bridges	Telescopic • Diagnostic • Single and dual channel Deflecting (Albarran lever) • Single and dual channel	Telescopic • Diagnostic • Single and dual channel Deflecting (Albarran lever) • Single and dual channel	Telescopic • Diagnostic • Single and dual channel Deflecting (Albarran lever) • Single and dual channel	Telescopic • Diagnostic • Single and dual channel Deflecting (Albarran lever) • Single and dual channel
Sheaths and working channels	17 Fr SB: 5 Fr DB: 5 Fr × 1 19 Fr SB: 6 Fr DB: 5 Fr × 2 20 Fr SB: 7 Fr DB: 6 Fr × 2 22 Fr SB: 10 Fr DB: 7 Fr × 2 25 Fr SB: 12 Fr DB: 8 Fr × 2	15 Fr SB: none DB: none 17 Fr SB: none DB: none 19.8 Fr SB: 6 Fr DB: 5 Fr, 6 Fr 21 Fr SB: 8 Fr DB: 6 Fr, 7 Fr 22.5 Fr SB: 10 Fr DB: 8 Fr x 2 25 Fr SB: 12 Fr DB: 8 Fr × 2	17 Fr SB: 5 Fr DB: 4 Fr × 2 21 Fr SB: 9 Fr DB: 6 Fr × 2 23 Fr SB: 10 Fr DB: 8 Fr × 2 25 Fr SB: 12 Fr DB: 8 Fr × 2	16 Fr SB: 5 Fr DB: none 17.5 Fr SB: 5 Fr DB: 4 Fr × 2 19.5 Fr SB: 7 Fr DB: 5 Fr x 2 21 Fr SB: 10 Fr DB: 6 Fr × 2 23 Fr SB: 12 Fr DB: 7 Fr × 2 25 Fr SB: 15 Fr DB: none

Image 109 – Types of rigid cystoscopes ((Campbell- Walch Urology, chapter 7, principles of urologic endoscopy).

Task 12 Indications for cystoscopy [5]

Hematuria	Malignancy	Lower Urinary tract symptoms	Miscellaneous
Gross Microscopic	Urethral cancer	Recurrent urinary tract infections	Trauma Bladder abnormalities seen

	Bladder cancer Atypical cytology Upper tract transitional cell carcinoma surveillance	Obstructive voiding symptoms Irritative voiding symptoms Urinary incontinence Chronic pelvic pain syndrome Urethral stricture disease	on imaging Removal of foreign bodies and small bladder stones Hematospermia Obstructive azoospermia

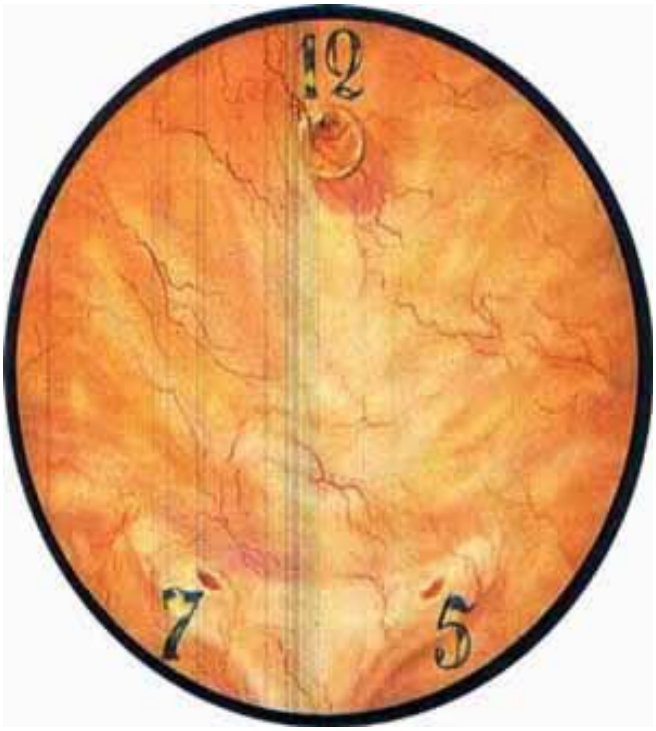


Image 110 – Normal view of bladder

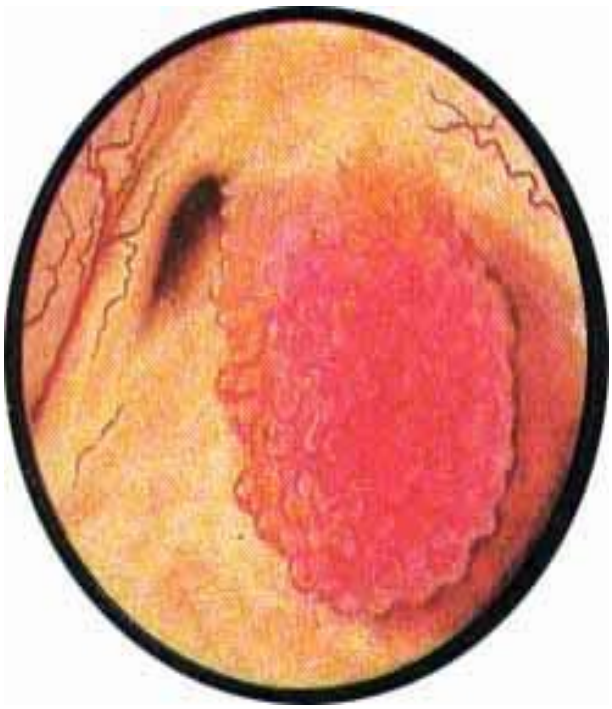


Image 111– Bladder cancer

Performance of successful **ureteroscopy** requires a variety of instrumentation—most important, appropriate and modern ureteroscopes (image 112). Although larger rod-lens rigid ureteroscopes are still available in some operating rooms, the smaller-diameter fiberoptic ureteroscopes are less traumatic, less often require ureteral dilation, and are equally effective.

Semirigid ureteroscopes are smaller in diameter because of the incorporation of fiberoptics into their construction. Fiberoptic bundles are created from molten glass that has been pulled into small-diameter fibers. Each individual glass fiber is "cladded" with a second layer of glass of a different refractive index. This cladding improves the internal reflection, light transmission, and durability of the fiberoptic bundle. The meshlike appearance of the image from fiberoptic image bundles is caused by the lack of light transmission through this cladding. These fibers uniformly transmit light from one end of the fiber to the other proportional to the light input. The glass fibers of a fiberoptic bundle can be arranged randomly or in a precise orientation with identical location at each end of the fiber (i.e., coherent). When the fibers are grouped randomly, such as those within the light bundle, they provide excellent light transmission for illumination, but no image. When the fibers are arranged in a coherent fashion, the light from each fiber within the bundle will coalesce to transmit images [5].

B

Image 112 – Ureteroscopy (B -semirigid ureteroscope with an offset eyepiece, which has a straight working channel permitting passage of rigid instruments).

Current semirigid ureteroscopes typically have tip diameters of 7 Fr or smaller and working channels larger than 3 Fr. Semirigid ureteroscopes have either large single or two smaller individual working channels. An advantage of the separate working channels is the ability to irrigate through one unrestricted channel while a working instrument occupies the other. Separate working channels also permit passage of a lithotripsy device through the separate channel to fracture a stone that cannot be disengaged from a basket in the other channel. With a single channel, this can be difficult because of entanglement between the two working instruments [5]. Eyepieces are commonly “in line” with the ureteroscope, which allows easy introduction of the scope . Offset eyepiece design makes possible a straight working channel for the use of more rigid working instruments such as rigid biopsy forceps or a pneumatic lithotripsy probe . Increased availability and use of the holmium laser for ureteroscopic lithotripsy has decreased the need for ureteroscopes with offset eyepieces [5].

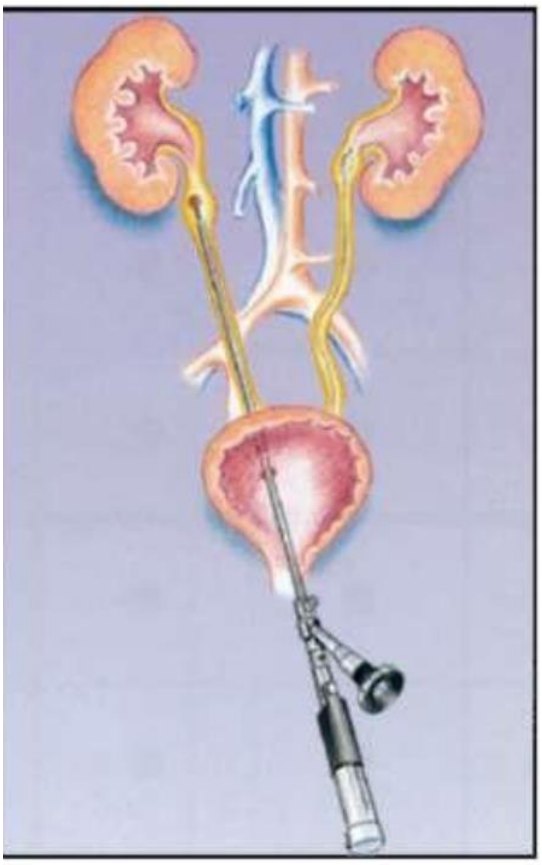


Image 113 – Ureterolithotripsy of UPJ stone

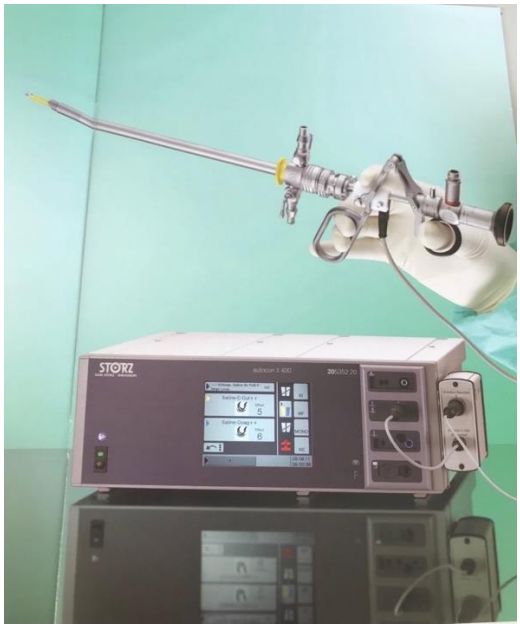


Image 114 - Resectoscopy

Tests

1. What is the character of pain during renal colic?

a) acute pain
b) excruciating pain
c)temporary pain
d)periodic pain

2. What kind of hematuria do you know?

a) initial
b) terminal
c) total
d)intermittent

3. Indicate the types of instrumental of diagnostic evaluation?

a) laparoscopy
b) cystoscopy
c) intravenous urography
d) uretroscopy
e) retroperitoneal nephroscopy

4. Which are the methods, that you may use to evaluate functional conditions of kidney?

a) chromocystoscopy
b) retrograde pyelography
c) intravenous urography
d) plain abdominal urography
e) nuclear scintigraphy

5. Tell us about complications, those may arise during retrograde urography?

a) attack of pyelonephritis
b) renal colic
c) pulmonary embolism
d) heart failure
e) nocturia

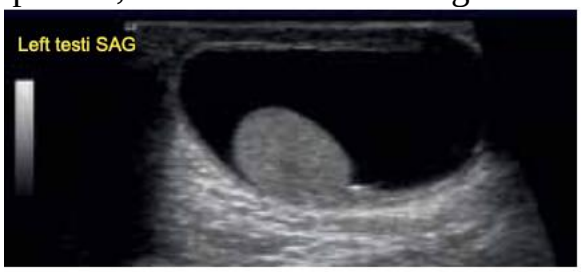
6) Indicate the types of anuria?

a) prerenal anuria
b) renal anuria
c) postrenal anuria
d) painless anuria
e) painful anuria

7) What does it mean term “dysuria”?

a) painful voiding
b) painless voiding
c) frequency
d) urgency
e) nocturia

8) Name, according to picture, the method of investigation



9)Describe in scheme the blood supply of the kidney.

10)What is the most wideaspread reason of renal colic?

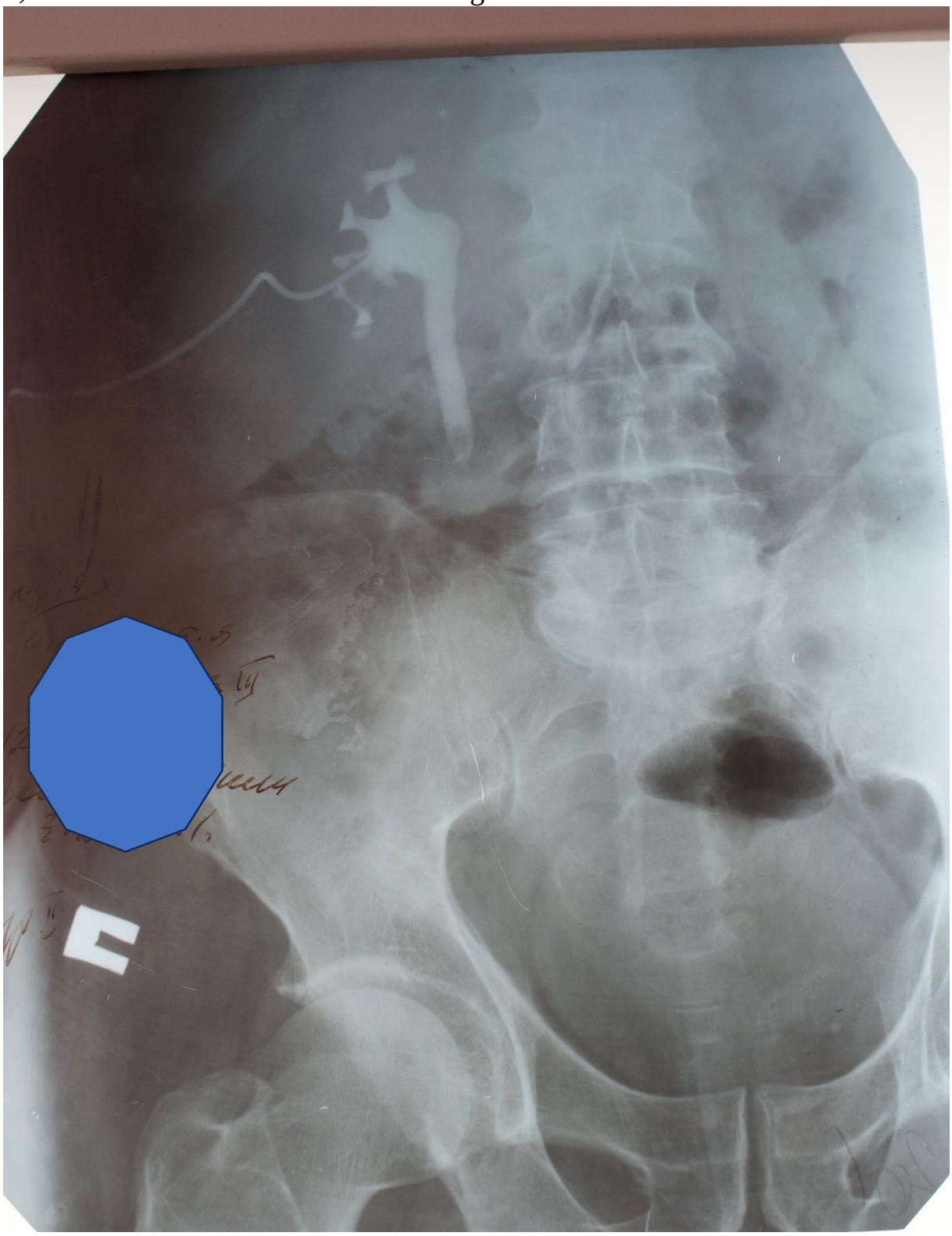
a) urinary stones
b) renal cancer
c)hydronephrosis
d)clots in the UPJ

Tasks

1. The patient has persistent arterial hypertension. Excretory urograms of the left kidney show no contrast agent. There are no pathological changes in the urine. What methods can determine the nature of hypertension.

2. The patient has frequently voided with pain and blood at the beginning of the act of urination. What types of hematuria does the patient have and what the reason may cause this pathological condition?

3, Name and describe the method of diagnostic evaluation.



Check your answers:

1. abd.
2. abc.
3. abde.
4. ace.
5. a.
6. abc
7. a
8. Ultrasound of scrotum
10. a

1. check the concentration of renin
2. initial hematuria
3. antegrade pyelography

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Acute pyelonephritis

Definition. Pyelonephritis is defined as inflammation of the kidney and renal pelvis. The diagnosis is clinical.

Etiology. E. coli, Proteus spp., Klebsiella spp., Pseudomonas spp., Serratia spp. and Enterococcus spp. are the most common species found in cultures [13].

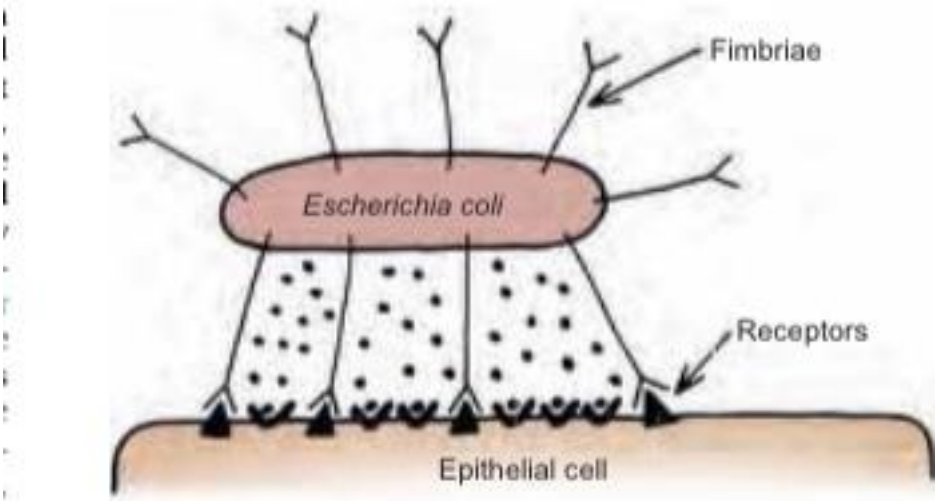


Image 115 – Bacterial adherents(adhesins on pili) [5]

Clinical Presentation. The classic presentation is an abrupt onset of chills, fever (100.3° (100 F=37,7 C) F or greater), and unilateral or bilateral flank or costovertebral angle pain and/or tenderness. These so-called upper tract signs are often accompanied by dysuria, increased urinary frequency, and urgency [5].

According to the EAU: Pyelonephritis is suggested by fever (> 38°C), chills, flank pain, nausea, vomiting, or costovertebral angle tenderness, with or without the typical symptoms of cystitis [13]. Pregnant women with acute pyelonephritis need special attention, as this kind of infection may not only have an adverse effect on the mother with anaemia, renal and respiratory insufficiency, but also on the unborn child with more frequent pre-term labour and birth [13].

Upper tract symptoms are caused by activation alfa and beta adrenoreceptors of bladder, urethra and prostate due to differential pathological conditions, in our cases, we are talking about inflammation. These symptoms also are called lower tract symptoms.

Now the question arises, why patient with acute pyelonephritis may have dysuria?

It means that firstly patient had inflammation of bladder, prostate or urethra and secondly was acquired pyelonephritis. This route of spread of infection called ascending route (task 13).

Task 13 The types of routes of infection

Ascending route	Hematogenous route.	Lymphatic Route
Most bacteria enter the urinary tract from the bowel reservoir via ascent through the urethra into the bladder. The most episodes of pyelonephritis are caused by retrograde ascent of bacteria from the bladder through the ureter to the renal pelvis and parenchyma. Although reflux of urine is probably not required for ascending infections, edema associated with cystitis may cause sufficient changes in the ureterovesical junction to permit reflux. Bacteria that reach the renal pelvis can enter the renal parenchyma by means of the collecting ducts at the papillary tips and then ascend upward within the collecting tubules.	The kidney is occasionally secondarily infected in patients with *Staphylococcus aureus* bacteremia originating from oral sites or with *Candida fungemia*. Experimental data indicate that infection is enhanced when the kidney is obstructed.	

On **physical examination**, there often is tenderness to deep palpation in the costovertebral angle. Variations of this clinical presentation have been recognized. Acute pyelonephritis may also simulate gastrointestinal tract abnormalities with abdominal pain, nausea, vomiting, and diarrhea.

Diagnostic evaluation.

Laboratory Diagnosis.

Urinalysis usually reveals numerous WBCs, often in clumps, and bacterial rods or chains of cocci. The presence of large amounts of granular or leukocyte casts in the urinary sediment is suggestive of acute pyelonephritis [5].

Blood tests may show leukocytosis with a predominance of neutrophils, increased erythrocyte sedimentation rate, elevated C-reactive protein levels, and

elevated creatinine levels if renal failure is present. In addition, creatinine clearance may be decreased. Blood cultures may be positive.

Urine cultures are positive, but about 20% of patients have urine cultures with fewer than 105 cfu/mL and therefore negative results on Gram staining of the urine.

E. coli, which constitutes a unique subgroup that possesses special virulence factors, accounts for 80% of cases. E. coli have P pili , Bacterial K antigens and endotoxins that may contribute to pathogenicity (Kaijser et al, 1977). Many cases of community-acquired pyelonephritis are caused by a limited number of multiantimicrobial-resistant clonal groups (Manges et al, 2004) [5].

More resistant species, such as Proteus, Klebsiella, Pseudomonas, Serratia, Enterobacter, or Citrobacter, should be suspected in patients who have recurrent UTIs, are hospitalized, or have indwelling catheters, as well as in those who required recent urinary tract instrumentation. Except for E. faecalis, S. epidermidis, and S. aureus, gram-positive bacteria rarely cause pyelonephritis.

Renal Ultrasonography and Computed Tomography.

These studies are commonly used to evaluate patients initially for complicated UTIs or factors or to reevaluate patients who do not respond after 72 hours of therapy. later). Ultrasonography and CT show renal enlargement, hypoechoic or attenuated parenchyma, and a compressed collecting system, delineate focal bacterial nephritis and obstruction.

Differential Diagnosis.

Acute appendicitis, diverticulitis, and pancreatitis can cause a similar degree of pain, but the location of the pain often is different. Results of the urine examination are usually normal. Herpes zoster can cause superficial pain in the region of the kidney but is not associated with symptoms of UTI; the diagnosis will be apparent when shingles appear.

Diagnostic management

Initial Management. Infection in patients with acute pyelonephritis can be subdivided into:

1) uncomplicated infection that does not warrant hospitalization.

2) uncomplicated infection in patients with normal urinary tracts who are ill enough to warrant hospitalization for parenteral therapy.

3) complicated infection associated with hospitalization, catheterization, urologic surgery, or urinary tract abnormalities [5].

However, if there is any reason to suspect a problem or if the patient will not have reasonable access to imaging if there should be no change in condition, we prefer renal ultrasonography to rule out stones or obstruction. In patients with known or suspected complicated pyelonephritis, CT provides excellent assessment of the status of the urinary tract and the severity and extent of the infection [5].

Diagnostic management

1. Ciprofloxacin 500-750 mg b.i.d 7 days (twice daily)

Levofloxacin 750 mg q.d 5 days (Fluoroquinolone **resistance should be less than 10%.)** in our country more than 10%, that is why first line (image 116):

Cefotaxime 2 g t.i.d
Ceftriaxone 1-2 g q.d(every day)
Gentamicin. 5 mg/kg q.d
Amikacin. 15 mg/kg q.d

Antimicrobial	Daily dose	Duration of therapy	Comments
Ciprofloxacin	500-750 mg b.i.d	7 days	Fluoroquinolone resistance should be less than 10%.
Levofloxacin	750 mg q.d	5 days	
Trimethoprim sulfamethoxazol	160/800 mg b.i.d	14 days	If such agents are used empirically, an initial intravenous dose of a long-acting parenteral antimicrobial (e.g. ceftriaxone) should be administered.
Cefpodoxime	200 mg b.i.d	10 days	
Ceftibuten	400 mg q.d	10 days	

b.i.d = twice daily; q.d = every day.

Image 116 - Suggested regimens for empirical oral antimicrobial therapy in uncomplicated pyelonephritis (EAU)

If a gram- positive organism is suspected, amoxicillin or amoxicillin/clavulanic acid is recommended.

If a patient has an uncomplicated infection but is sufficiently ill to require hospitalization (high fever, high WBC count, vomiting, dehydration, evidence of sepsis), has complicated pyelonephritis, or fails to improve during the initial outpatient treatment period, a parenteral fluoroquinolone, an aminoglycoside with or without ampicillin, or an extended-spectrum cephalosporin with or without an aminoglycoside is recommended (Warren et al, 1999) [5,13] (image 117).

Antimicrobials	Daily dose	Comments
First-line treatment		
Ciprofloxacin	400 mg b.i.d	
Levofloxacin	750 mg q.d	
Cefotaxime	2 g t.i.d	Not studied as monotherapy in acute uncomplicated pyelonephritis.
Ceftriaxone	1-2 g q.d	Lower dose studied, but higher dose recommended.
Second-line treatment		
Cefepime	1-2 g b.i.d	Lower dose studied, but higher dose recommended.
Piperacillin/tazobactam	2.5-4.5 g t.i.d	
Gentamicin	5 mg/kg q.d	Not studied as monotherapy in acute uncomplicated pyelonephritis.
Amikacin	15 mg/kg q.d	
Last-line alternatives		
Imipenem/cilastatin	0.5 g t.i.d	Consider only in patients with early culture results indicating the presence of multi-drug resistant organisms.
Meropenem	1 g t.i.d	
Ceftolozane/tazobactam	1.5 g t.i.d	
Ceftazidime/avibactam	2.5 g t.i.d	
Cefiderocol	2 g t.i.d	
Meropenem-vaborbactam	2 g t.i.d	
Plazomicin	15 mg/kg o.d	

b.i.d = twice daily; t.i.d = three times daily; q.d = every day; o.d = once daily.

Image 117 - Suggested regimens for empirical parenteral antimicrobial therapy in uncomplicated pyelonephritis (EAU).

If gram-positive cocci are causative, ampicillin/sulbactam with or without an aminoglycoside is recommended.

An obstructed kidney has difficulty concentrating and excreting antimicrobial agents. Any substantial obstruction must be relieved expediently by the safest and simplest means. A Gram stain of the urine sediment is helpful to guide the selection of the initial empirical antimicrobial therapy. In all cases, antimicrobial therapy should be active against potential uropathogens and achieve antimicrobial levels in renal tissue and urine.

A **complicated UTI (image 118)** occurs in an individual in whom factors related to the host (e.g., underlying diabetes or immunosuppression) or specific anatomical or functional abnormalities related to the urinary tract (e.g., obstruction, incomplete voiding due to detrusor muscle dysfunction) are believed to result in an infection that will be more difficult to eradicate than an uncomplicated infection.

Factors .

Functional or anatomic abnormality of urinary tract
Male gender
Pregnancy
Elderly patient
Diabetes
Immunosuppression
Childhood urinary tract infection
Recent antimicrobial agent use
Indwelling urinary catheter
Urinary tract instrumentation
Hospital-acquired infection
Symptoms for more than 7 days at presentation

Use the combination of:

• amoxicillin plus an aminoglycoside.
• a second-generation cephalosporin plus
an amino-glycoside.
• a third generation cephalosporin intravenously as empirical treatment of complicated UTI with systemic symptoms.

Recommendations	Strength rating
Use the combination of: • amoxicillin plus an aminoglycoside; • a second generation cephalosporin plus an aminoglycoside; • a third generation cephalosporin intravenously as empirical treatment of complicated UTI with systemic symptoms.	Strong
Only use ciprofloxacin provided that the local resistance percentages are < 10% when: • the entire treatment is given orally; • patients do not require hospitalisation; • patient has an anaphylaxis for beta-lactam antimicrobials.	Strong
Do not use ciprofloxacin and other fluoroquinolones for the empirical treatment of complicated UTI in patients from urology departments or when patients have used fluoroquinolones in the last six months.	Strong
Manage any urological abnormality and/or underlying complicating factors.	Strong

Image 118 - Suggested regimens for empirical antimicrobial therapy in complicated pyelonephritis (EAU).

Subsequent Management.

Patients with complicated pyelonephritis and positive blood cultures should be treated with parenteral therapy until clinically stable. If blood cultures are negative, 2- to 3-day parenteral therapy is sufficient.

Unfavorable Response to Therapy.

When the response to therapy is slow or the urine continues to show infection, an immediate reevaluation is mandatory:

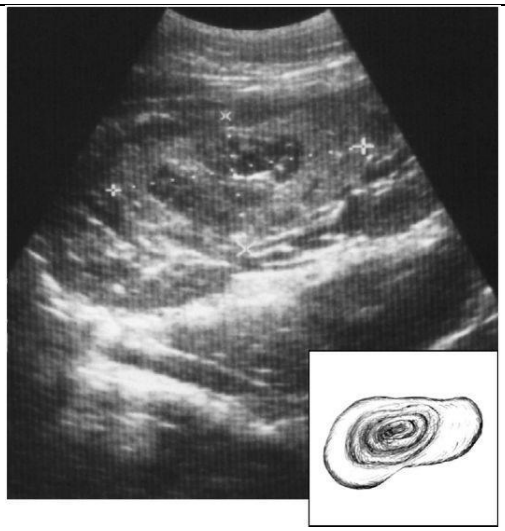
-urine and blood cultures must be repeated and appropriate alterations in antimicrobial therapy made based on susceptibility testing.

-CT is indicated to attempt to identify unsuspected obstructive uropathy, abscess formation, urolithiasis, or underlying anatomic abnormalities that may have predisposed the patient to infection, prevented a rapid therapeutic response, or caused complications of the infectious process, such as renal or perinephric abscess. [5].

In patients with fever lasting longer than 72 hours, CT is most helpful for ruling out obstruction and identifying renal and perirenal infections (Soulen et al, 1989). Radionuclide imaging may be useful to demonstrate functional changes associated with acute pyelonephritis (decrease in renal blood flow, delay in peak function, and delay in excretion of the radionuclide) (Fischman and Roberts, 1982) and cortical defects associated with vesicoureteral reflux.

Task 14 Types of acute pyelonephritis

Acute focal or multifocal bacterial nephritis (image 119)	A heavy leukocyte infiltrate is confined to a single renal lobe (focal) or multiple lobes (multifocal). *Clinical presentation* is similar to acute pyelonephritis. On *ultrasonography*, the lesion is typically poorly marginated and relatively sonolucent with occasional low-amplitude echoes that disrupt the cortical medullary junction [5]. *Treatment* includes hydration and IV antimicrobial agents for at least 7 days, followed by 7 days of oral antimicrobial therapy. Failure to respond to antimicrobial therapy is an indication for appropriate studies to rule out obstructive uropathy, renal or perirenal abscess, renal carcinoma, or acute renal vein thrombosis [5].
Renal abscess or carbuncle (image 120)	A collection of purulent material confined to the renal parenchyma.

 Image 120 - Carbuncle (Atlas of pediatrician Urology, Kulikova T.N.)	*Clinical presentation*: fever, chills, abdominal or flank pain, and occasionally weight loss and malaise. Complicated UTIs associated with stasis, calculi, pregnancy, neurogenic bladder, and diabetes mellitus also appear to predispose the patient to abscess formation [5]. *Diagnostic evaluation*. *Blood tests* - leukocytosis. Pyuria and bacteriuria may not be evident unless the abscess communicates with the collecting system. *Ultrasonography* is the quickest and least expensive method to demonstrate a renal abscess. An echo-free or low-echodensity space-occupying lesion with increased transmission is found on the ultrasound image. *Treatment.* Although the classic treatment for an abscess has been percutaneous or open incision and drainage, there is good evidence that use of IV antimicrobial agents and careful observation of a small abscess less than 3 cm or even 5 cm in a clinically stable patient is appropriate. Percutaneous drainage, however, remains the first-line procedure of choice for most renal abscesses greater than 5 cm in diameter. [5].
Emphysematous pyelonephritis	An acute necrotizing parenchymal and perirenal infection caused by gas-forming uropathogens (usually occurs in diabetic patients), (E. coli, which can produce carbon dioxide by the fermentation of sugar) [5]. *Clinical presentation*. Almost all patients display the classic triad of fever, vomiting, and flank pain. Pneumaturia is absent unless the infection involves the collecting system. Results of urine cultures are invariably

	positive. E. coli is most identified. Klebsiella and Proteus are less common [5]. *Diagnostic evaluation*. Tissue gas that is distributed in the parenchyma may appear on abdominal radiographs as mottled gas shadows over the involved kidney. CT is the imaging procedure of choice in defining the extent of the emphysematous process and guiding management [5]. *Treatment*. Emphysematous pyelonephritis is a surgical emergency. Most patients are septic, and fluid resuscitation and broad-spectrum antimicrobial therapy are essential. If the kidney is functioning, medical therapy can be considered. Nephrectomy is recommended for patients who do not improve after a few days of therapy [5].
Infected hydronephrosis (the end-stage called pyonephrosis) (image 121)	Infected hydronephrosis associated with suppurative destruction of the parenchyma of the kidney, in which there is total or nearly total loss of renal function. Where infected hydronephrosis ends and pyonephrosis begins is difficult to determine clinically [5]. *Clinical presentation*. The patient is usually very ill, with high fever, chills, flank pain, and tenderness. Bacteriuria may not be present if the ureter is completely obstructed. *Diagnostic evaluation*. The ultrasonographic diagnosis of infected hydronephrosis depends on demonstration of internal echoes within the dependent portion of a dilated pyelocalyceal system [5]. *Treatment.* Antimicrobial drugs and drainage of the infected pelvis. A ureteral catheter can be passed to drain the kidney, but if the obstruction

	prevents this, a percutaneous nephrostomy tube should be placed.

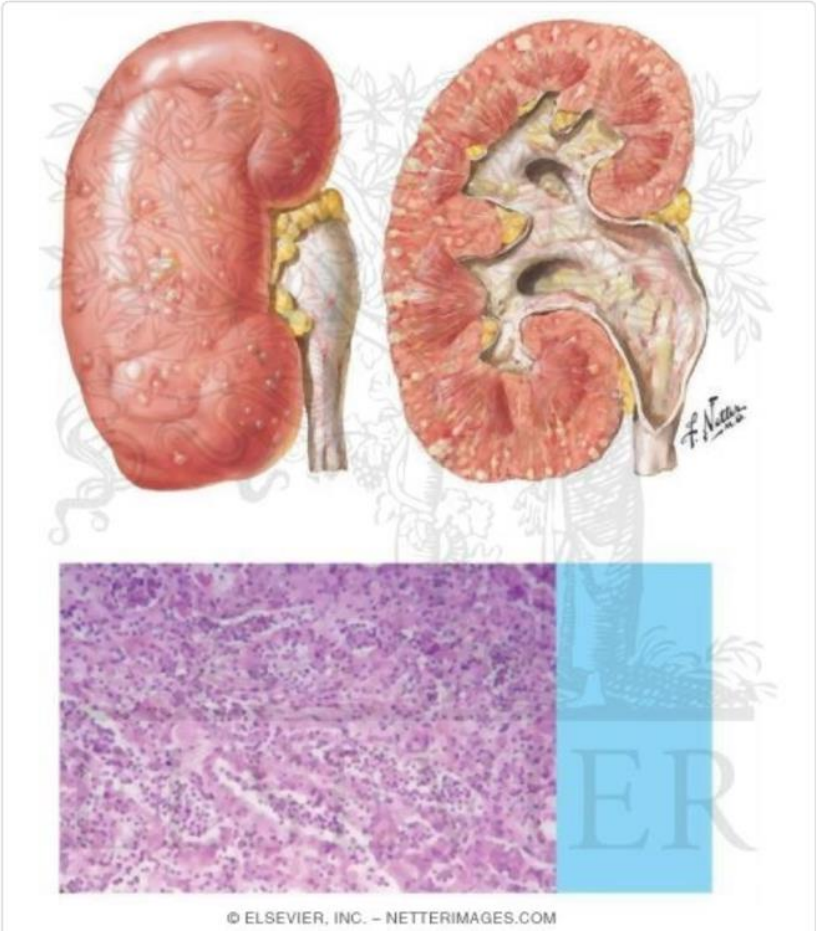


Image 119 - Acute focal or multifocal bacterial nephritis (https://www.netterimages.com/acute-pyelonephritis-pathology-unlabeled-histology-frank-h-netter-2414.html).

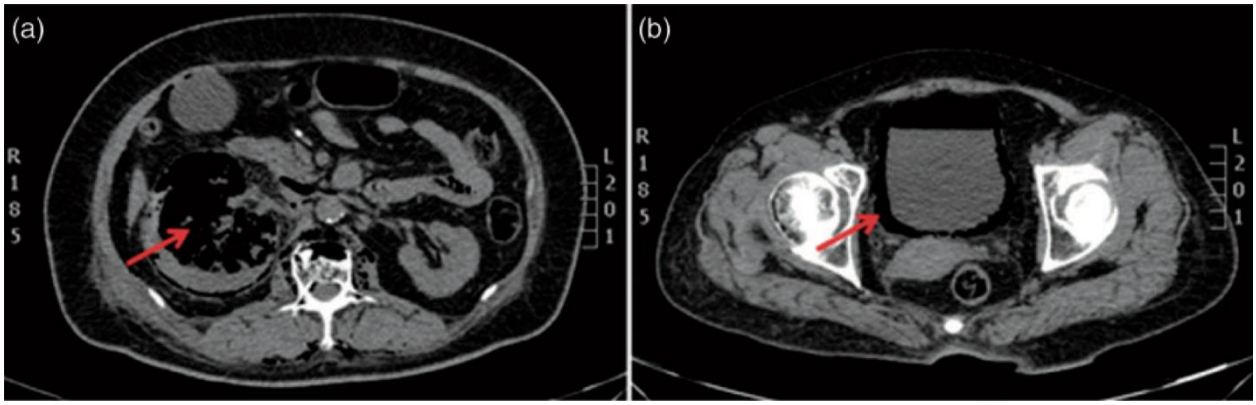


Image 121 – CT scan (emphysematous pyelonephritis) **(images** showing gas in the right kidney (red arrows) (a) and in the urinary bladder wall (red arrows) (b) (case report [11]).

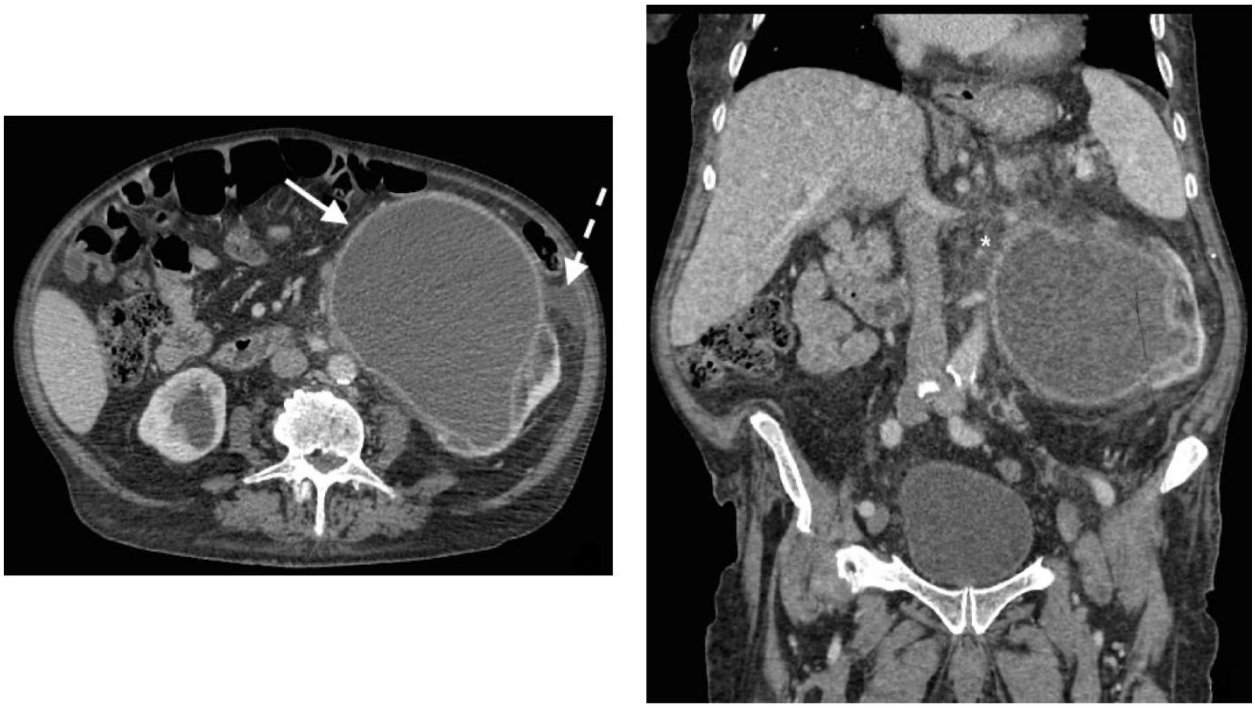


Image 122 – CT scan axial and coronal (right image - high grade hydronephrosis, diffuse parietal thickening of the calico-pelvic system (white arrow), fat stranding of perirenal and renal hydronephrosis, diffuse parietal thickening of the calico-pelvic system (white arrow), fat stranding of perirenal and renal sinus fat. Small amount of free fluid is appreciated anteriorly (dashed arrow) [12].

The following classification of UTIs is adopted in the EAU Urological Infections Guidelines:

Classification of UTI	
Uncomplicated UTIs	Acute, sporadic or recurrent lower (uncomplicated cystitis) and/or upper (uncomplicated pyelonephritis) UTI, limited to non-pregnant women with no known relevant anatomical and functional abnormalities within the urinary tract or comorbidities.
Complicated UTIs	All UTIs which are not defined as uncomplicated. Meaning in a narrower sense UTIs in a patient with an increased chance of a complicated course: i.e. all men, pregnant women, patients with relevant anatomical or functional abnormalities of the urinary tract, indwelling urinary catheters, renal diseases, and/or with other concomitant immunocompromising diseases for example, diabetes.
Recurrent UTIs	Recurrences of uncomplicated and/or complicated UTIs, with a frequency of at least three UTIs/year or two UTIs in the last six months.
Catheter-associated UTIs	Catheter-associated urinary tract infection (CA-UTI) refers to UTIs occurring in a person whose urinary tract is currently catheterised or has had a catheter in place within the past 48 hours.
Urosepsis	Urosepsis is defined as life threatening organ dysfunction caused by a dysregulated host response to infection originating from the urinary tract and/or male genital organs [12].

Image 123 – Definition of different types of UTIs according to EAU.

Chronic Pyelonephritis

In patients without underlying renal or urinary tract disease, chronic pyelonephritis secondary to UTI is a rare disease and an even more rare cause of chronic renal failure [5].

Huland and Busch (1982) evaluated 161 patients with end-stage renal disease and found that 42 had chronic pyelonephritis. However, in addition to a history of UTIs, these 42 patients had complicating defects, such as vesicoureteral reflux, analgesic abuse, nephrolithiasis, or obstruction. Nonobstructive uncomplicated UTI alone was never found to be the cause of renal insufficiency. Thus, using end-stage renal disease seen at autopsy or at the dialysis clinic as an indicator, the prevalence of uncomplicated chronic bacterial pyelonephritis is rare [5].

Clinical Presentation. There are no symptoms of chronic pyelonephritis until it produces renal insufficiency, and then the symptoms are like those of any other form of chronic renal failure. If a patient's chronic pyelonephritis is thought to be a result of many episodes of acute pyelonephritis, a history of intermittent symptoms of fever, flank pain, and dysuria may be elicited [5].

Radiologic Findings. The diagnosis of chronic pyelonephritis can be made with the greatest confidence based on pyelographic findings. The essential features are **asymmetry and irregularity of the kidney outlines, blunting and dilation of one or more calyces, and cortical scars at the corresponding site** [5].

In the absence of stones, obstruction, and tuberculosis, and with the single exception of analgesic nephritis with papillary necrosis (which can be readily excluded by history), chronic pyelonephritis is virtually the only disease that produces a localized scar over a deformed calyx.

Pathology. In chronic pyelonephritis, the gross kidney is often diffusely contracted, scarred, and pitted.

Histologic changes are patchy. There is usually an interstitial infiltrate of lymphocytes, plasma cells, and occasional polymorphonuclear cells. Portions of the parenchyma may be replaced by fibrosis, and, although glomeruli may be preserved, periglomerular fibrosis is often seen. In some affected areas, glomeruli may be completely fibrosed and tubules atrophied. Leukocyte and hyaline casts are sometimes present in the tubules; the latter may cause resemblance to the thyroid colloid, hence the description renal thyroidization.

Management. Management of radiographic evidence of pyelonephritis should be directed at treating infection if present, preventing future infections, and monitoring and preserving renal function.

The treatment of existing infection must be based on careful antimicrobial susceptibility tests and selection of drugs that can achieve bactericidal concentrations in the urine and yet are not nephrotoxic [5].

Xanthogranulomatous pyelonephritis (XGP) is a rare, severe, chronic renal infection typically resulting in diffuse renal destruction. Most cases are unilateral and result in a nonfunctioning, enlarged kidney associated with obstructive uropathy secondary to nephrolithiasis. XGP is characterized by accumulation of lipid-laden foamy macrophages. It begins within the pelvis and calyces and subsequently extends into and destroys renal parenchymal and adjacent tissues. It has been known

to imitate virtually every other inflammatory disease of the kidney, as well as renal cell carcinoma, on radiographic examination [5].

Clinical Presentation. XGP should be suspected in patients with UTIs and a unilateral enlarged nonfunctioning or poorly functioning kidney with a stone or a mass lesion indistinguishable from malignant tumor. Most patients present with flank pain (69%), fever and chills (69%), and persistent bacteriuria (46%) (Malek and Elder, 1978). Additional vague symptoms, such as malaise, may be present. On physical examination, 62% of the patients had a flank mass and 35% had previous calculi [5].

CT is probably the most useful radiologic technique in evaluating patients with XGP. Fifty to eighty percent of patients show the classic triad of unilateral renal enlargement with little or no function and a large calculus in the renal pelvis (Elder, 1984). CT usually demonstrates a large, reniform mass with the renal pelvis tightly surrounding a central calcification but without pelvic dilatation [5].

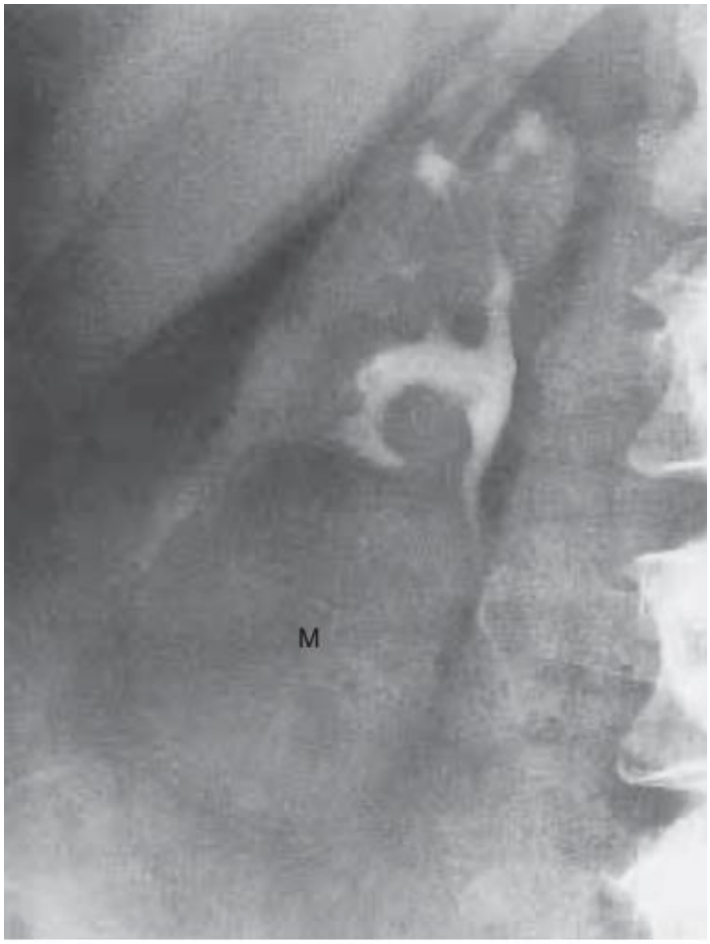


Image 124 – Chronic pyelonephritis (ten-minute excretory urogram demonstrates irregular renal outline with upper pole parenchymal atrophy. Note significant loss of renal cortical thickness over blunted and dilated calyces. Lower pole mass (M) is a simple cyst) (Campball -Walsh urology, chapter 12)[5].

Tests

1. You should follow the routes of widespread of infections:
a) hematogenous route
b) lymphtatic route
c) ascending route
d) contact route

2. What are the main types of pyelonephritis do you know?
a) acute
b) chronic
c) recurrent
d)subclinic

3. Follow 3 main signs of acute pyelonephriris.
a) flank pain
b) fever
c) dysuria
d) nausea
e) chills
f) leukocyturia

4. What are the methods of diagnostic evaluation do you know?
a) common blood test
b) urine culture
c) urinalysis
d) plain abdominal radiography
e) retrograde urethrography
f) coprogramm

5. What is the normal value of leucocytes in urine (women)
a) no more than 2
b) no more than 3
c) no more than 4
d) no more than 5

6. Follow the complications of acute pyelonephritis?
a) pneumonia
b) carbuncle of kidney
c) paranephritis
d) epididimytis
e) otitis
f) peritonitis

7. Follow the complications of chronic pyelonephritis?
a) renal insufficiency
b) arterial hypertension
c) peritonitis
d) urinary stones

8. What types of surgical treatment of acute pyelonephritis do you know?
a) laparotomy
b) nephrostomy
c) nephrectomy
d) remove capsule of kidney

9. What type of antibiotics you don't administer for pregnant due to contraindications?
a) penicillin
b) aminoglycoside
c) levofloxacin
d) cefuroxime
e) gentamycin

10. What type of antibiotics you don't administer for child due to contraindications?
a) penicillin
b) aztreonam
c) levofloxacin
d) cefuroxime
e) gentamycin

Tasks

A 42- year-old patient was admitted to the hospital with complaints of acute pain in the lumbar region on the left side, temperature to 40C, chills. He fell ill 3 days ago when he had an attack of renal colic. Oliguria. History of a pelvic stone of the left kidney. What examinations are necessary to clarify the diagnosis? What is your diagnosis and tactics?

A 33-year-old patient was admitted to the urological clinic in serious condition on the 2nd day from the onset of the disease. The disease was preceded by tonsillitis. Objectively: temperature 40.3C, chills with profuse sweating. The lower pole of the right kidney is palpated. Pasternatsky's symptom is positive. ROE-56 mm / hour, leukocytosis 24700. Pyuria. What examinations are necessary to clarify the diagnosis? What is your diagnosis and tactics?

A 53-year-old patient complains of constantly pain in the lumbar region, lack of appetite, general weakness, increased blood pressure for several years. Objectively:

the patient is pale, subfebrile condition, ROE 32 mm / hour. Leukocytosis 24700. Pyuria. Common blood test without changes. What the main examination is necessary to identify the diagnosis? What is your diagnosis and tactics?

Check your answers:

1.acd.	6. bc	1. CT scan
2.ab.	7. ab	2. US, common urine analysis, urine culture
3. abf.	8. bcd	3. CT scan or US, concenteration of renin
4. abcde.	9. bce	
5. d.	10. ce	

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Urolithiasis

Stone incidence depends on geographical, climatic, ethnic, dietary, and genetic factors. Accordingly, the prevalence rates for urinary stones vary from 1% to 20% [5].

Classification of urinary stones.

Urinary stones can be classified according to the following aspects: aetiology of stone formation, stone composition (mineralogy), stone size, stone location, and X-ray characteristics of the stone. The recurrence risk is basically determined by the disease or disorder causing the stone formation [5].

Stone composition is the basis for further diagnostic and management decisions. Stones are often formed from a mixture of substances. It has been two names (chemical name and mineral name). For example: the chemical name is Calcium oxalate monohydrate, and the mineral name is Whewellite.

Stone size is usually given in one or two dimensions, and stratified into those measuring up to 5, 5-10, 10-20, and > 20 mm in largest diameter.

Stones can be classified according to **anatomical position**: upper, middle, or lower calyx; renal pelvis; upper, middle, or distal ureter; and urinary bladder.

Stones can be classified according to **plain X-ray appearance** [kidney-ureter-bladder (KUB) radiography]), which varies according to mineral composition. Non-contrast-enhanced computed tomography (NCCT) can be used to classify stones according to density, inner structure, and composition, which can affect treatment decisions (task 15).

Task 15 Classification of urinary stones according to X-ray [11]

Radiopaque	Calcium oxalates dehydrate. Calcium oxalate monohydrate Calcium phosphates
Poor radiopacity	Magnesium ammonium phosphate Apatite Cystine
Radiolucent	Uric acid Ammonium urate Xanthine 2,8-Dihydroxyadenine Drug-stones

Etiology.

High-risk stone formers

General factors [11]

Early onset of urolithiasis (especially children and teenagers)
Familial stone formation
Recurrent stone formers

Short time since last stone episode
Brushite-containing stones (CaHPO4.2H2O)
Uric acid and urate-containing stones
Infection stones
Solitary kidney (the kidney itself does not particularly increase the risk of stone formation, but prevention of stone recurrence is of more importance)

Diseases associated with stone formation [11].

Hyperparathyroidism
Metabolic syndrome
Nephrocalcinosis
Polycystic kidney disease (PKD)
Gastrointestinal diseases (i.e., jejuno-ileal bypass, intestinal resection, Crohn's disease, malabsorptive conditions, enteric hyperoxaluria after urinary diversion, exocrine pancreatic insufficiency) and bariatric surgery
Increased levels of vitamin D
Sarcoidosis
Spinal cord injury, neurogenic bladder Genetically determined stone formation Cystinuria (type A, B and AB)
Primary hyperoxaluria (PH)
Renal tubular acidosis (RTA) type I 2,8-Dihydroxyadeninuria
Xanthinuria
Lesch-Nyhan syndrome
Cystic fibrosis

Anatomical abnormalities associated with stone formation [11].

Medullary sponge kidney (tubular ectasia) Ureteropelvic junction (UPJ) obstruction Calyceal diverticulum, calyceal cyst Ureteral stricture
Vesico-uretero-renal reflux
Horseshoe kidney
Ureterocele

Environmental and professional factors High ambient temperatures [11].

Chronic lead and cadmium exposure

Kidney stones form at a foundation of Calcium phosphate termed Randall's plaques (RPs), which begins at the basement membranes of thin limbs of the loop of Henle on the renal papillary surface [12]. Regardless of the type, kidney stone formation is a complex and multistep process that includes urinary supersaturation, crystal nucleation, growth and aggregation. Kidney stone formation is associated with systemic disorders, including diabetes, obesity, cardiovascular diseases, hypertension and metabolic syndrome [12].

Stone formation. Urinary supersaturation and crystallization are the driving force for intrarenal crystal precipitation and is mainly caused by inherited or acquired diseases associated with renal function impairment. Additionally, urinary supersaturation and crystallization are influenced by urine pH and specific concentrations of substance excess, including calcium oxalate, calcium phosphate, uric acids and urates, struvite, amino acids (cysteine), purines (2,8-

dihydroxyadenine and xanthine) and drugs (e.g., atazanavir, sulfamethoxazole, amoxicillin, ceftriaxone) (image 124,125) [12].

Normal urine contains numerous inhibitors that act both in competition and cooperation, consequently, decrease crystallization and inhibit crystals aggregation: anions (citrate), metallic cations (magnesium) and macromolecules (Tamm-Horsfall protein (THP), urinary prothrombin fragment 1 (UPTF-1), nephrocalcin (Nc) et. al.). Alkali supplements are widely used for hypocitraturic recurrent nephrolithiasis patients to restore citrate excretion [12].

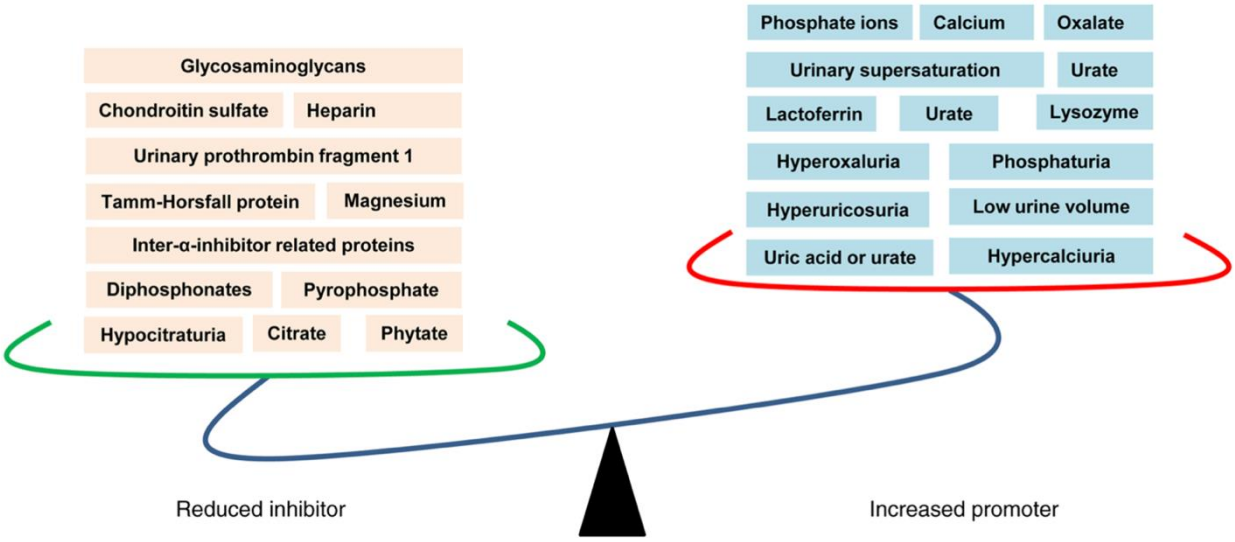


Image 124 – Stone formation [12].

Randall's plaque (RP). Scanning electron microscopy (SEM) examination has shown that RP are made of a mixing of tubules with calcified walls and of tubules obstructed by calcium phosphate plugs. RP consists of calcium phosphate crystals mixed with an organic matrix that is rich in various proteins and lipids, and includes membrane-bound vesicles or exosomes, collagen fibers, as well as other components of the extracellular matrix [12].

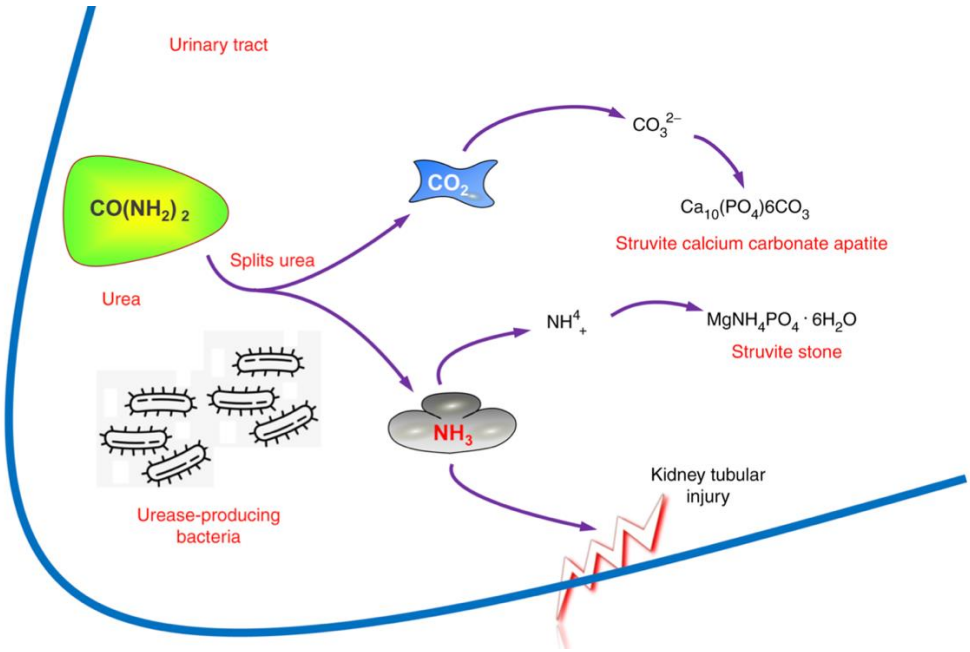


Image 125 – Role of urease-producing bacteria in stone formation [12].

Diagnostic evaluation

Standard evaluation includes a detailed medical history and physical examination. Patients with ureteral stones usually present with loin pain, vomiting, and sometimes fever, but may also be asymptomatic. Immediate evaluation is indicated in patients with solitary kidney, fever or when there is doubt regarding a diagnosis of renal colic [11].

Ultrasound (US) should be used as the primary diagnostic imaging tool, although pain relief, or any other emergency measures, should not be delayed by imaging assessments. Ultrasound is safe (no risk of radiation), reproducible and inexpensive. It can identify stones located in the calyces, pelvis, and pyeloureteric and vesico-ureteral junctions (US with filled bladder), as well as in patients with upper urinary tract (UUT) dilatation.

Plain abdominal radiography (image 126, 127,), **intravenous urography** (image 128), antegrade or retrograde pyelography has been performed for identify pathological condition.

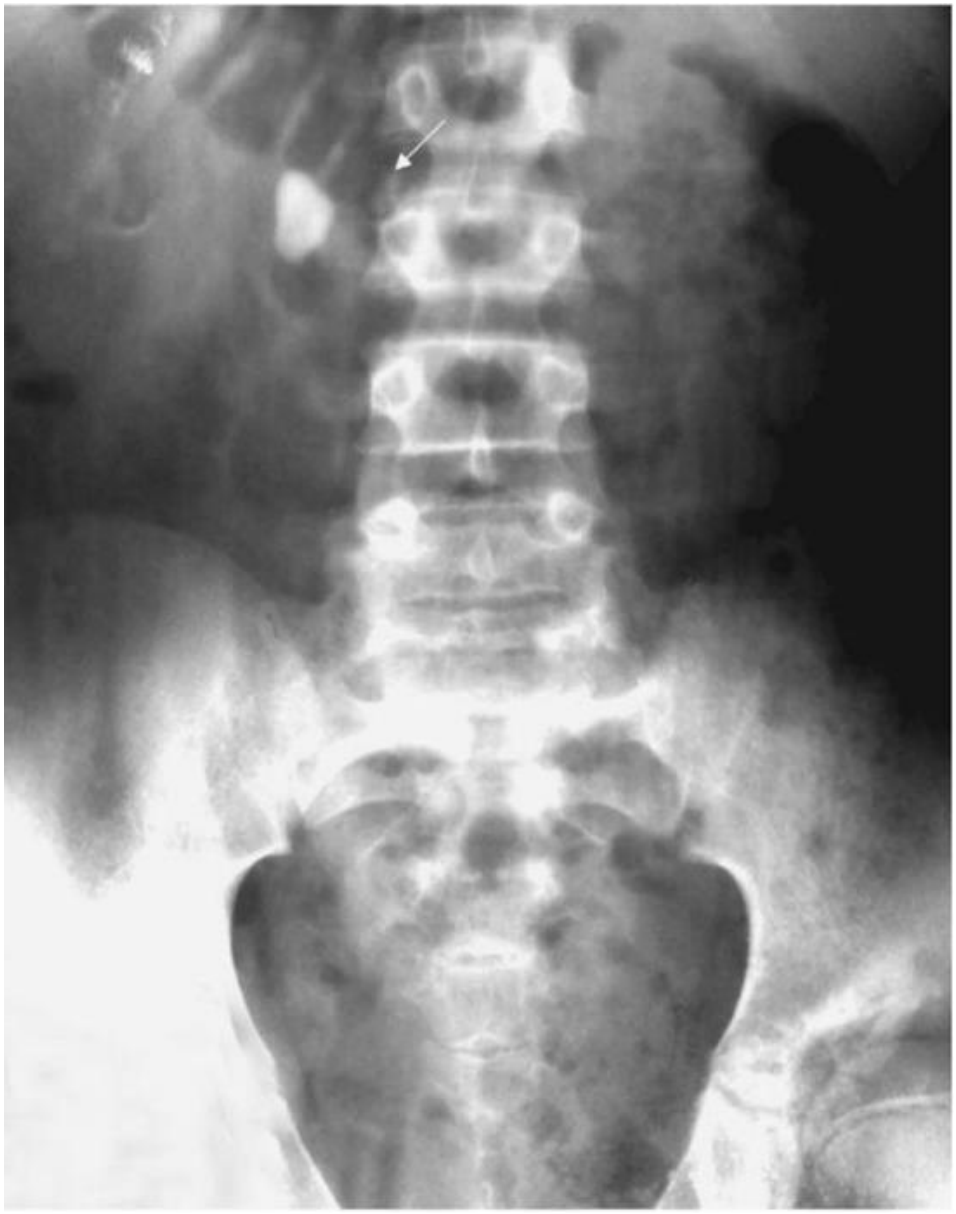


Image 126 – Plain abdominal radiography (KUB- kidney-ureter-bladder)
Stone in pelvis of the right kidney (Atlas of pediatrician urology, KulikovaT.N.)

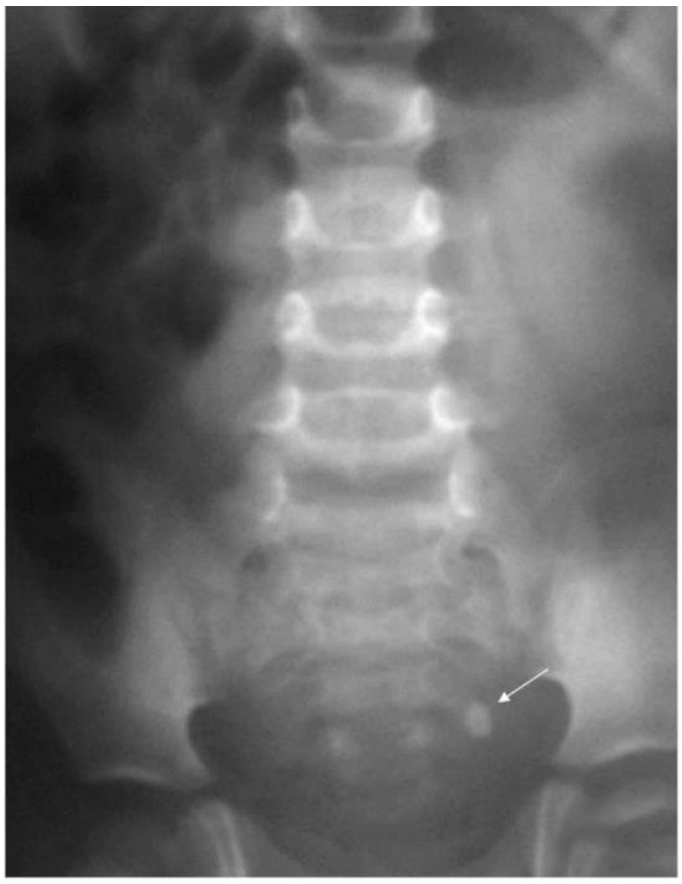


Image 127 – KUB (stone in a lower part of left ureter) (Atlas of pediatrician urology, KulikovaT.N.)

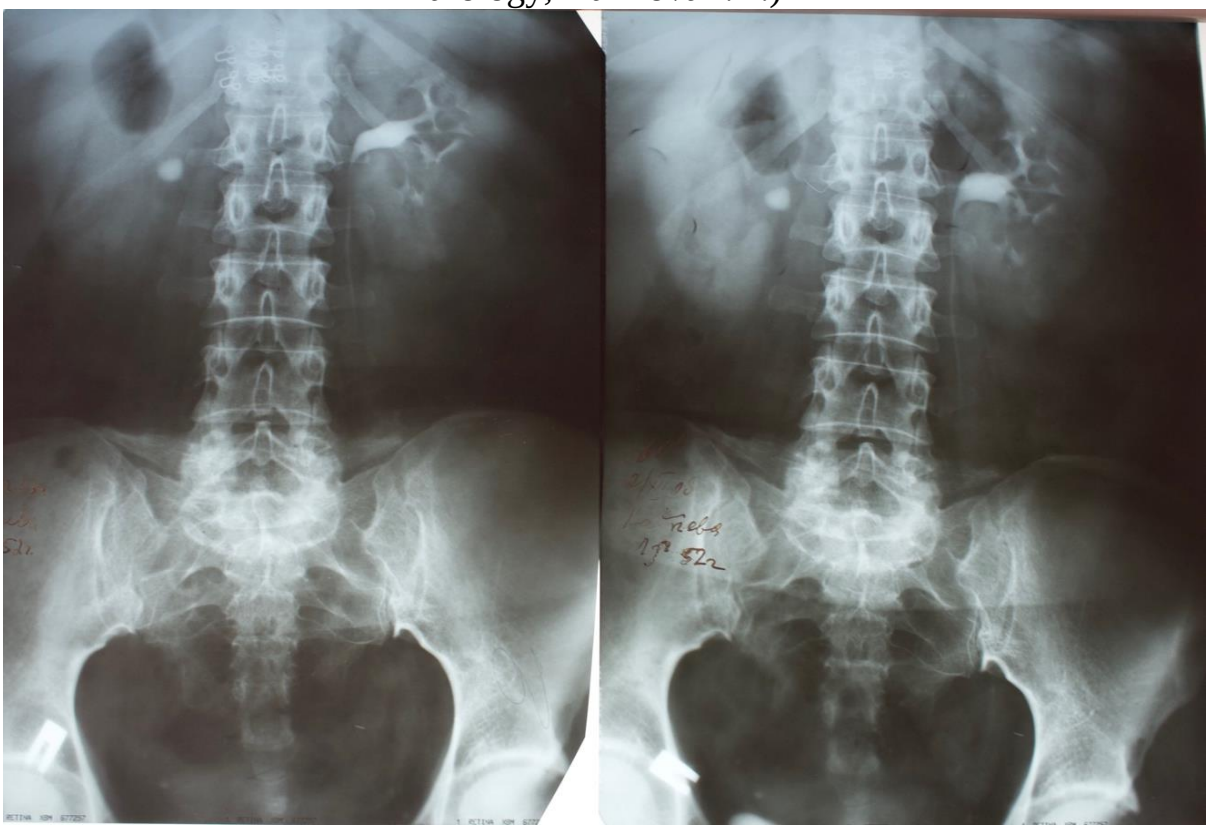


Image 128 – Intravenous urography (stone in pelvis of the right kidney, complete obstruction, symptom called " white kidney") (own material)

Use non-contrast-enhanced computed tomography **to confirm** stone diagnosis in patients with acute flank pain following initial ultrasound assessment (image 129) [11].

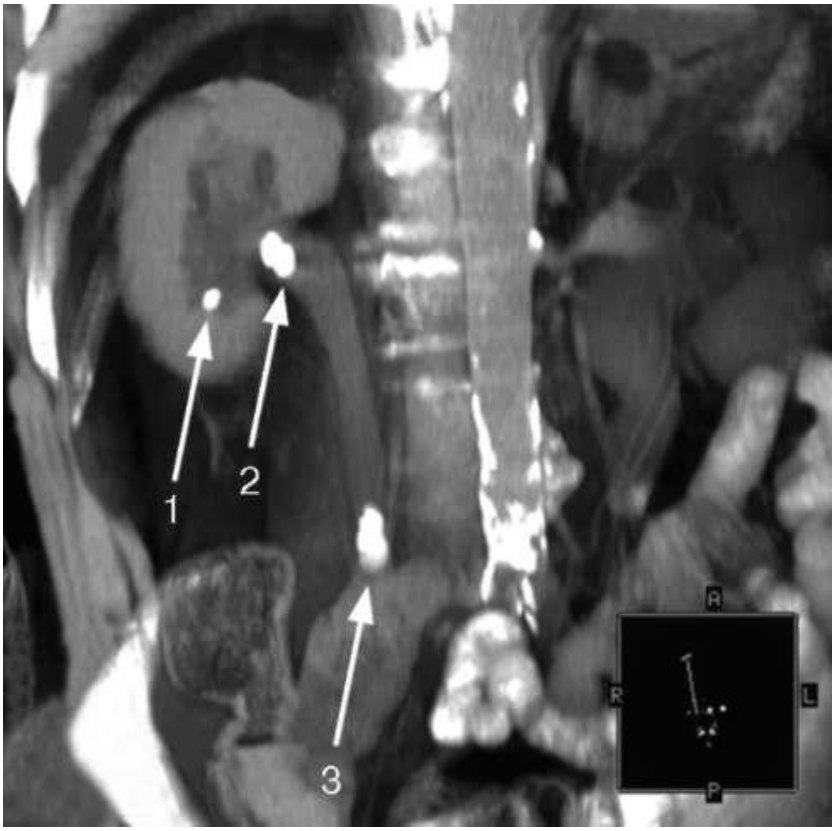


Image 129 – CT scan (1 – stone in lower calyces of the right kidney, 2 - stone in pelvis, 3 – stone in a middle part of the right ureter) (internet).

Basic laboratory analysis - non-emergency urolithiasis patients:

-Urine:

Dipstick test of spot urine sample:

- red cells;
- white cells;
- nitrites;
- approximate urine pH;
- urine microscopy and/or culture.

-Blood:

Serum blood sample:

- creatinine.
- uric acid.
- level of calcium.
- sodium.
- potassium.
- blood cell count.
- C-reactive protein.

-Perform a coagulation test (partial thromboplastin time and international formalized ratio) if intervention is likely or planned [11].

-Perform stone analysis in first-time formers using a valid procedure (X-ray diffraction or infrared spectroscopy).

Diagnostic imaging during pregnancy [11[.

-Use ultrasound as the preferred method of imaging in pregnant women.

-Use magnetic resonance imaging as a second-line imaging modality in pregnant women.

-Use low-dose computed tomography as a last-line option in pregnant women.

Disease Management [11].

Renal colic

-Offer a non-steroidal anti-inflammatory as the first drug of choice e.g., metamizole (dipyrone); alternatively, paracetamol or, depending on cardiovascular risk factors, diclofenac, indomethacin or ibuprofen.

-Offer opioids (hydromorphine, pentazocine or tramadol) as a second choice.

-Offer renal decompression or ureteroscopic stone removal in case of analgesic refractory colic pain.

Pathophysiology of urinary tract obstruction.

The clinical presentation of urinary tract obstruction can be quite variable depending on the site, degree, and chronicity of the obstruction. Flank pain secondary to stretching of the collecting system is the most common symptom in patients with acute obstruction; is typically an unrelenting, excruciating pain that can radiate to the lower abdomen and testicles or labia on the affected side; and is often associated with nausea or vomiting. Pelvis has been numerous receptors, that has been activated due to stretching , and compressed on the parenchyma, caused activation receptors from under capsule of kidney.

The histologic derangements associated with obstruction are localized primarily to the interstitial compartment of the kidney and include massive tubular dilation, progressive interstitial fibrosis, and a loss in renal mass secondary to apoptotic cell death (Misseri et al, 2004). These changes and any resulting impact on renal function are collectively referred to as obstructive nephropathy.

The obstructed kidney with all signs of urinary tract infection (UTI) and/or anuria is a urological emergency. Urgent decompression is often necessary to prevent further complications in infected hydronephrosis secondary to stone-induced, unilateral or bilateral, renal obstruction.

Decompression

Currently, there are two options for urgent decompression of obstructed collecting systems:

• placement of an indwelling ureteral stent.

• percutaneous placement of a nephrostomy tube

Then,

-Collect (again) urine for antibiogram test following decompression.

-Start antibiotics immediately (+ intensive care, if necessary).

-Re-evaluate antibiotic regimen following antibiogram findings.

Medical expulsive therapy

Medical expulsive therapy seems to be efficacious for treating patients with distal ureteral stones less or more than 5mm approximately.

Consider α-blockers for medical expulsive therapy as one of the treatment options for (distal) ureteral stones > 5 mm [11].

Chemolysis

Percutaneous chemolysis is rarely used nowadays, for practical reasons. Percutaneous irrigation chemolysis may be an option for infection-stones and theoretically also for uric acid stones. For dissolution of struvite stones, Suby's G solution (10% hemiacidrin; pH 3.5-4) can be used. The method has been described in case series and literature reviews.

Oral chemolysis

Stones composed of uric acid can be dissolved by oral chemolysis.

Oral chemolitholysis is based on alkalinisation of urine by application of alkaline citrate or sodium bicarbonate. The pH should be adjusted to 7.0-7.2. Chemolysis is more effective at a higher pH, which might, however, promote calcium phosphate stone formation. Patients will need to adjust the dosage of alkalising medication by self-monitoring the pH of their urine.

In the case of uric acid obstruction of the collecting system, oral chemolysis in combination with urinary drainage is indicated. A combination of alkalinisation with tamsulosin can increase the frequency of spontaneous passage of distal ureteral uric acid stones.

If you can't application conservative therapy or it was ineffective, it has been necessary consider the following ways.

Extracorporeal shock wave lithotripsy (ESWL)

The purpose of treatment are fragmentation of stones and safety removal.

The uniqueness of the shock wave lithotripter is in its exploitation of shock wave focusing. Relatively weak, nonintrusive waves are generated externally and transmitted through the body. The shock waves build to sufficient strength only at the target, where they generate enough force to fragment a stone (image 130).

Image 130 – Shock wave lithotripsy [10].

-Stepwise power ramping prevents renal injury.
-Clinical experience has shown that repeat sessions are feasible (within one day for ureteral stones).
-Optimal shock wave frequency is 1.0 to 1.5 Hz.
-Proper acoustic coupling between the cushion of the treatment head and the patient's skin is important.
-Careful imaging control of localisation of stone contributes to outcome of treatment. -Careful control of pain during treatment is necessary to limit pain-induced movements and excessive respiratory excursions.
-Antibiotic prophylaxis is recommended in the case of internal stent placement, infected stones, or bacteriuria [11].
Ureteroscopy and percutaneous nephrolithotomy (PNL) occupy an essential place in the treatment of urinary calculi as increasing technologic advancements allow easier access to stones in all parts of the kidney and ureter (image 130).
Smaller ureteral stones can be extracted intact with endoscopic baskets or grasping devices after ureteral dilation, if necessary.
The larger ureteral stones require lithotripsy (fragmentation of stones by using energy) to permit the safe extraction of calculus fragments, for example, it is ureteral intracorporeal lithotripsy. Four techniques are available for intracorporeal lithotripsy: electrohydraulic lithotripsy (EHL), laser lithotripsy, ultrasonic lithotripsy, and ballistic lithotripsy.
Indications for active stone removal of renal stones
Indications for the removal of renal stones, include:
• stone growth.
• stones in high-risk patients for stone formation.
• obstruction caused by stones.
• infection.
• symptomatic stones (e.g., pain or haematuria)
• stones > 15 mm.
• stones < 15 mm if observation is not the option of choice.
• patient preference;
• comorbidity;
• social situation of the patient (e.g., profession or travelling);
• choice of treatment.
Evaluate stone composition before deciding on the method of removal, based on patient history, former stone analysis of the patient or Hounsfield unit (HU) on unenhanced CT. Stones with density > 1,000 HU (and with high homogeneity) on non-contrast-enhanced CT are less likely to be disintegrated by shock wave lithotripsy (SWL).
Perform percutaneous nephrolithotomy (PNL) as first-line treatment of larger stones > 2 cm [11].

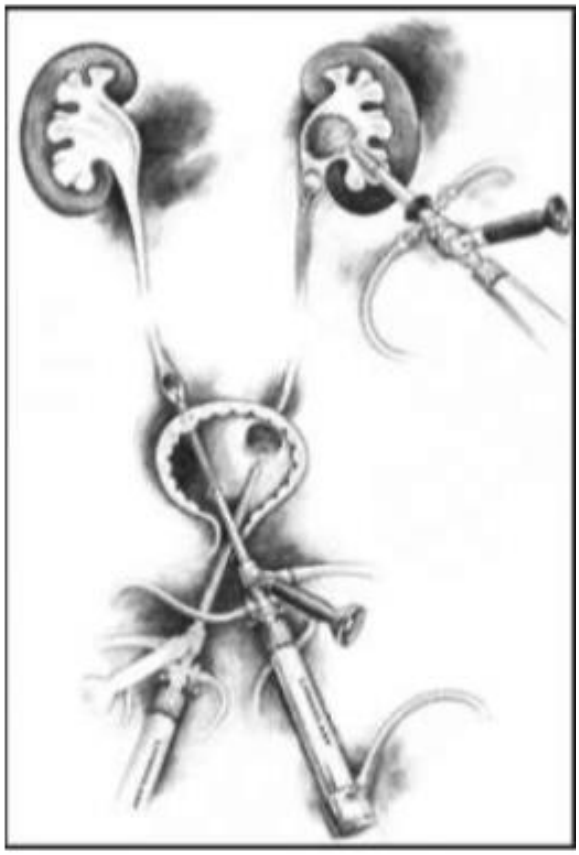


Image 131 - Ureteroscopy and percutaneous nephrolithotomy (PNL) [10].

Tests

1. What is the character of flank pain patient may observe having staghorn stone?

a) temporary pain
b) permanent pain
c) severe pain
d) pain with irradiation to labia or glans of penis
e) chronic pain

2. Which symptoms are most characteristic for renal colic?

a) severe flank pain
b) dysuria
c) nocturia
d) liquorrhea
e) vomiting
f) enuresis

3. Indicate the most specific symptoms in urinalysis for urolithiasis?

a) hematuria
b) proteinuria

c) crystals of salt
d) glucosuria

4. Which X-ray methods you may use for diagnostic evaluation of ureteral stone?

a) plain abdominal radiography
b) intravenous urography
c) retrograde pyelography
d) CT scan

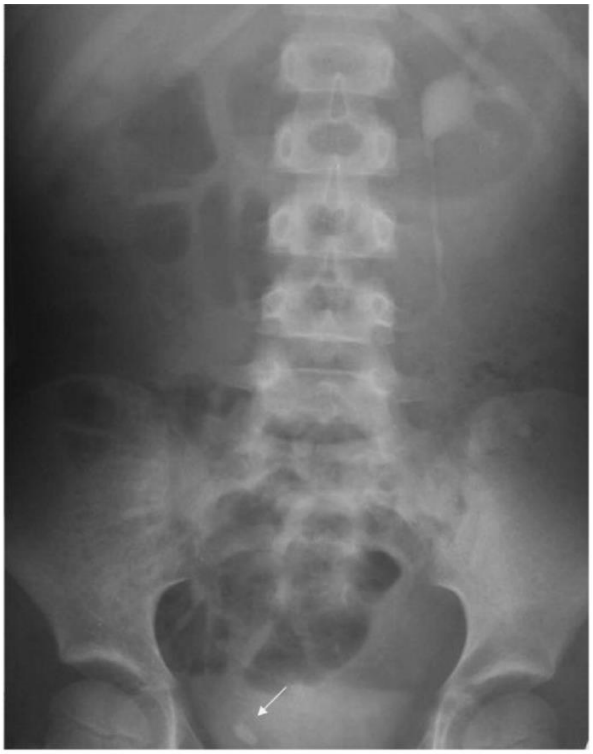
5. How you may perform diagnostic evaluation of radiolucent stone?

a) antegrade pyelography
b) pneumopyelography
c) CT scan
d) ultrasound diagnostic

6. Follow the complications of acute pyelonephritis?

a) focal or multifocal bacterial nephritis
b) hydronephrosis
c) nephrogenic hypertension
d) ectopia of kidney
e) anuria
f) SIRS

7. Describe the X ray list



Task

Woman was admitted in emergency room with the main complaints, such as colicky pain on the right lumbar region with radiate in inner part of right femur and labia for 3 hours.

Anamnesis morbi. Patient tried to remove this pain with drotaverine hydrochloride, without effect. This pain has been affecting for five years. As for chronic disease, patient has disease of joints, dolyhosigma.

Physical examination: the general condition of patient is satisfactory, t. 36,8 C. Heart rate is 75 in min, blood pressure 130/80 mm.hg.

Auscultation: breathing is vesicular, without wheezing.

The tongue is clean, wet. The abdomen is symmetrical, painful with deep palpation in the right upper quadratum, kidneys don't palpate. Murphys percussion test (costovertebral angle tenderness) is positive on the right side.

Voiding is frequency, painless. Patient tends to constipation.

Urinalysis. Gravity density 1021, pH- 5,0, protein – 0,07 g/l, leu – 7-8 per field of view, Er 15-20 per field of view, crystals of uric acid +++.

Plain abdominal radiography is without radiopaque shades.

Ultrasound examination is demonstrated hyperechoic formation with shade from 7 to 9 mm in the upper and middle segments of kidney, pelvis is 23 mm.

Questions:

1. Diagnosis.
2. What is additional method you should administer for proper diagnostic of this pathological condition?
3. What do you think about level of obstruction?

Check your answers:

1. be.
2. ae.
3. ac
4. abcd.
5. cd
6. abef

1. Urinary stone. Renal colic. Stone in a lower part of ureter, concentration of uric acid.

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Hydronephrosis

Definition. Hydronephrosis is a common phenomenon. The renal pelvis or calices (or both) become distended with urine because the pelviureteric junction cannot conduct it correctly [12].

Hydronephrosis is the most common genitourinary tract anomaly detected on prenatal ultrasound studies, reported in approximately 1–5% of all pregnancies [13]. The most common causes of hydronephrosis in neonates in order of frequency are ureteropelvic junction obstruction (UPJO) (35 %), ureterovesical junction anomalies, vesicoureteral reflux, multicystic kidney, and posterior urethral valves. Other causes include obstructive and non-obstructive megaureter, ureterocele, neurogenic bladder, prune-belly syndrome, and urethral atresia (image 131) [14].

Lower polar vessels are often found across the ureter at or just below the pelviureteric junction and are probably far too often blamed as the prime cause of obstruction [14].

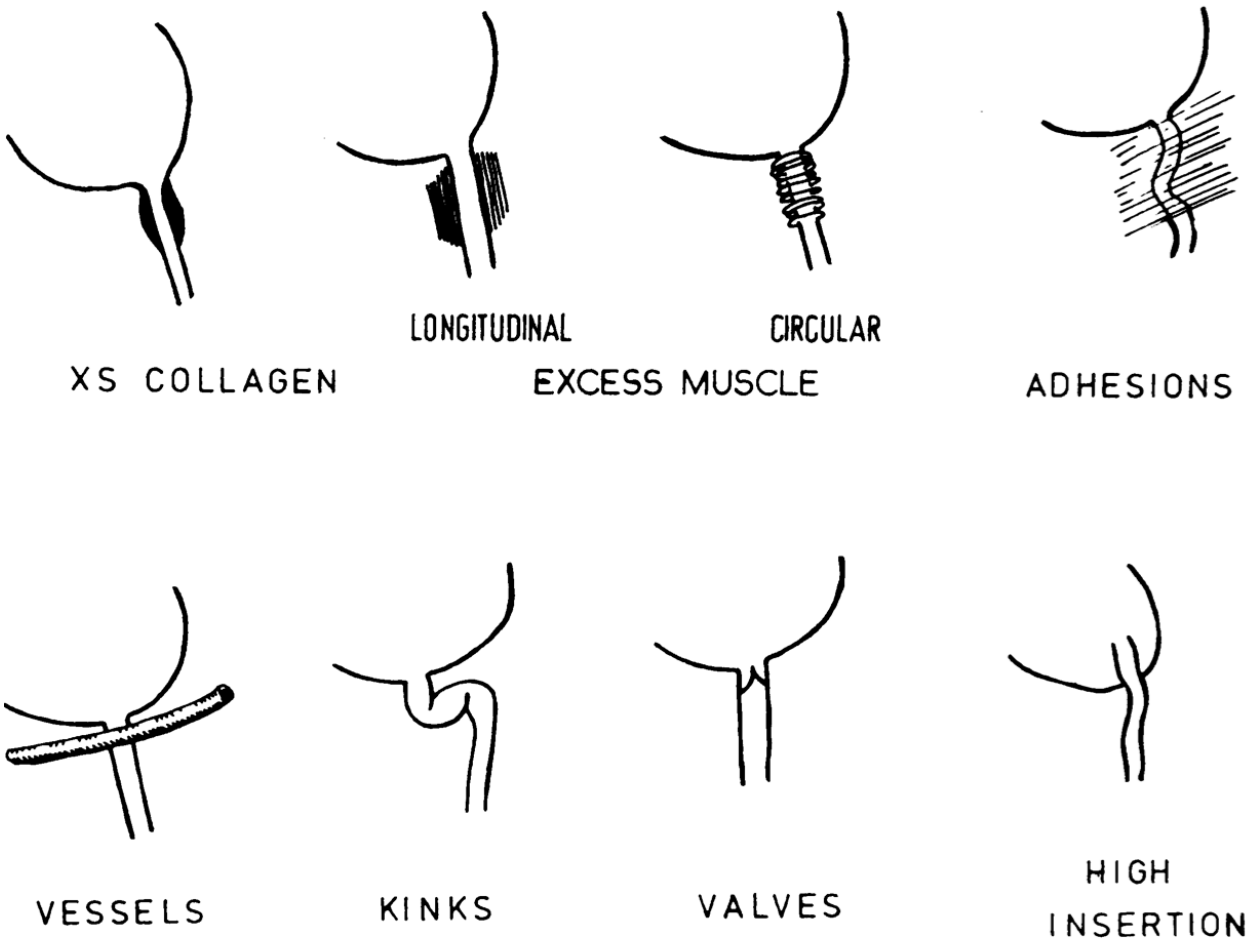


Image 131 – Possible factors in the production of pelviureteric junction (Robert H Whitaker, 1977).

Pathophysiology of ureteral obstruction.

The pathological changes include interstitial inflammation, tubular apoptosis, and interstitial fibrosis, and the cellular and molecular events are dependent on

interstitial cells and a variety of locally and systematically produced molecular products. These signaling molecules include an endless list of cytokines that act as intercellular mediators of paracrine communication [14].

The initial reaction to an acute obstruction of the ureter with the subsequent increase in pressure is a prompt renal hemodynamic response, mediated by increased activity of the renin- angiotensin system, which leads to an increase in the renal vascular resistance of the obstructed kidney. Various vasoactive mediators such as angiotensin, thromboxane, and endothelin contribute to this complex and not completely understood response. As mentioned previously, this is followed by an interstitial inflammatory response that is initially characterized by macrophage infiltration, tubular dilatation, and renal tubular apoptosis, leading to tubular atrophy and interstitial fibrosis with nephron loss [14].

Classification. SFU radiology grading system (image 132) [16].

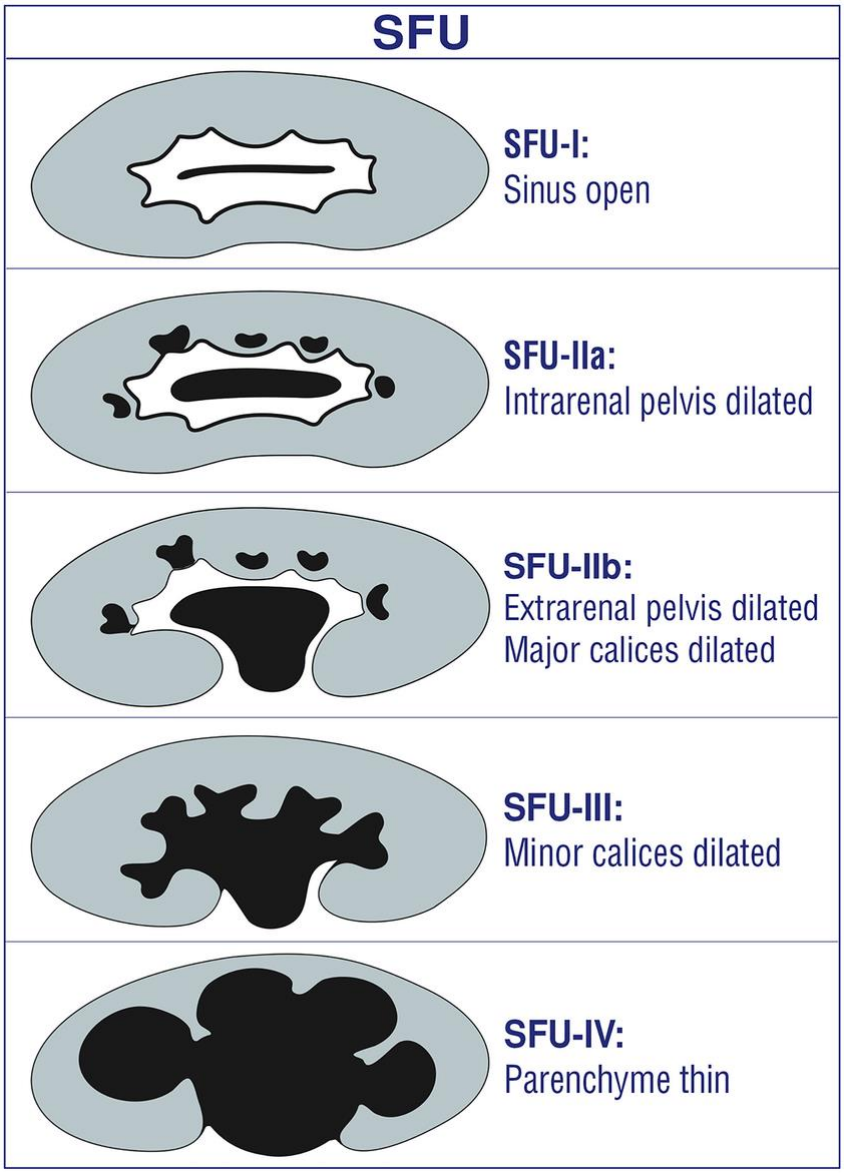


Image 132 - SFU radiology grading system

This grading system has been developed in 1993. It is quantitative and subjective. All grades of SFU are very variable between operators and clinicians.

Therefore, it is not popular between disciplines other than pediatric urologists.
Disadvantages/limitations of SFU
• *SFU-1 and SFU-2a:* Both indicate different degrees of renal pelvic dilation. Therefore, it is confusing and very difficult to differentiate each other. Moreover, follow-up, treatment, and prognosis of these two degrees are similar; all of them resolve spontaneously without renal damage [16].
• *SFU-2b and SFU-3*: Both represent different degrees of calyceal dilation. It is very operator dependent in differentiating the dilation of peripheral (minor) calices from those of central (major) calices due to a high discrepancy within and between raters for interpretation of the two types of calyceal dilation. Therefore, it is subjective and confusing, and it is very difficult to differentiate each other [16].
• *SFU-3:* Although it represents only calyceal dilation, the pictures used for SFU-3 in the original article clearly show severe medullary thinning. This causes significant confusion among clinicians and radiologists [16].
• *SFU-4:* It represents minimal thinning of the medullary parenchyma (e.g., 6 mm) and severe thinning of the cortical parenchyma (e.g., 2 mm) and cyst-like hydronephrotic kidneys at the same grade. The wide definition of SFU-4 fails to demonstrate accurately the severity of hydronephrosis and thus significant misleads from a prompt treatment. It does not suggest who need surgery and who can safely be followed non-operatively. The first example (medulla thin) can safely be followed non-operatively while the second (cortex thin) clearly need surgery. This wide definition makes prognosis difficult to predict in UPJHN cases [16].

The radiology grading system has partially been modified from SFU for post-natal use (image 133) [16].

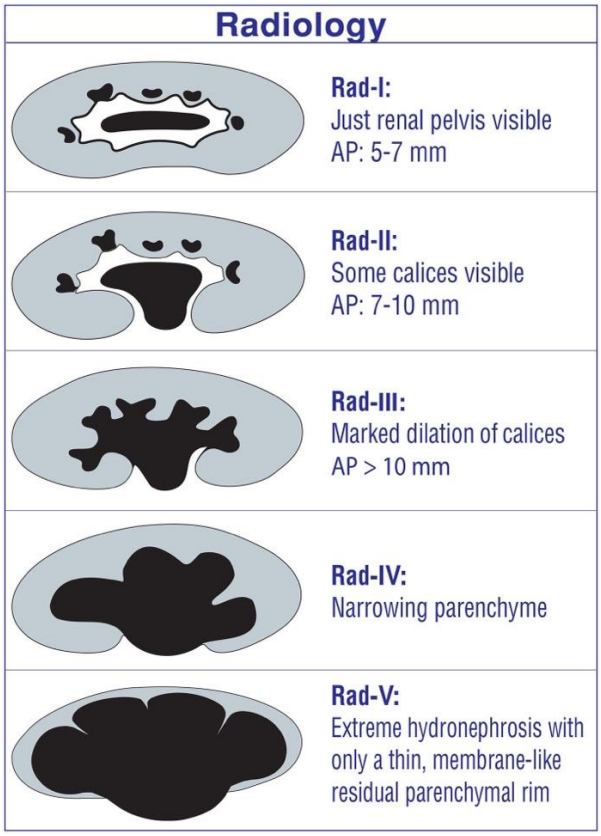


Image 133 – Radiology grading system [16]

It has the same grades 1, 2, and 3 as the SFU grading system. In addition, it includes anterior-posterior diameter of the pelvis for the grades 1, 2, and 3 [16].

UTD classification (image 134).

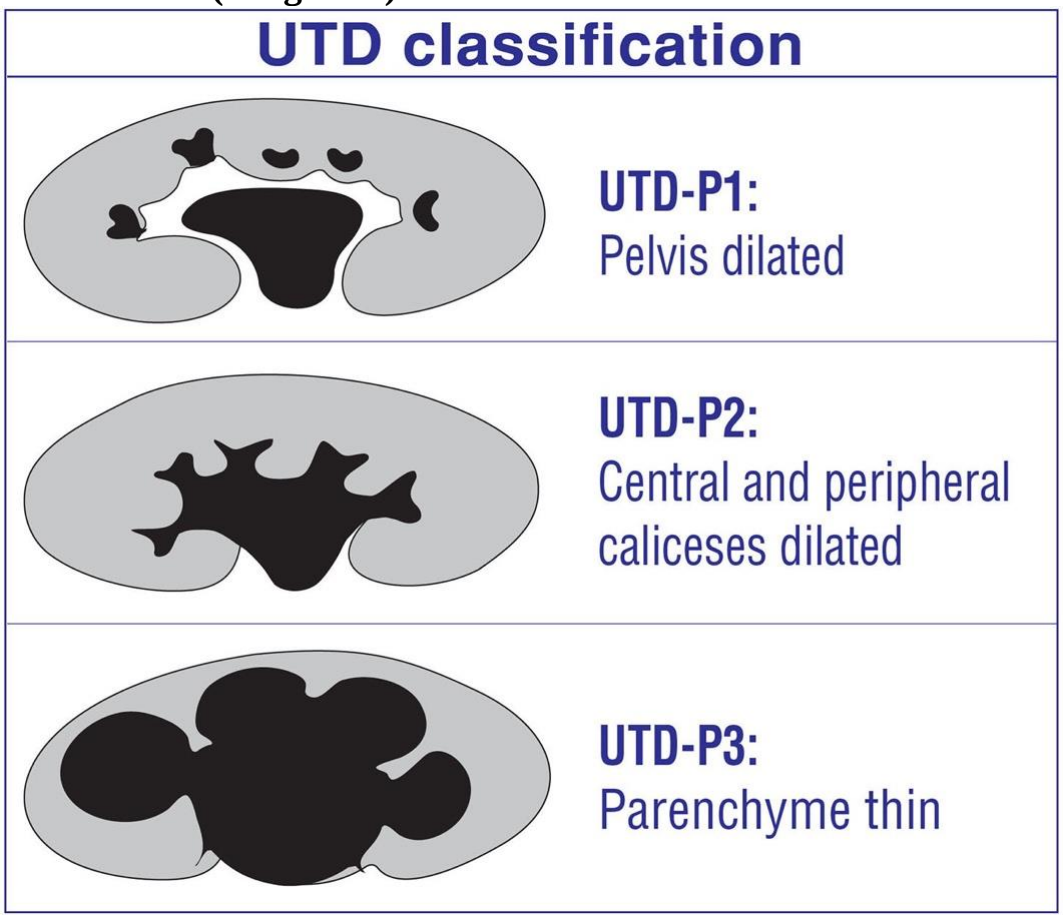


Image 134 - UTD classification [16].

This classification suggests the general term “urinary tract dilation” to indicate ultrasound findings that include all ureteral and kidney dilations. UPJ-type hydronephrosis, UVJ-type hydroureteronephrosis, vesicoureteral reflux, bladder pathologies (ureterocele, diverticula, etc.), and posterior urethral valve cause hydronephrosis in very different ways. They may cause different levels and types of renal damage and prognosis [16].

Onen-grading system.

The Onen grading system is terminologically simple and clear. Therefore, all disciplines including radiology, perinatology, pediatric nephrology, and pediatric urology can easily use not only for clinical practice but also for future researches [16].

The Onen grading system has evidence-based standardized objectives and reproducible parameters. It includes two categories of kidney findings. The first is dilation of the pelvicalyceal system; the second which is the most important category is the quality of the renal parenchyma (thickness and appearance). This grading system divides thinning of the renal parenchyma into two grades: medullary thinning and cortical thinning. In addition, the appearance of the parenchyma (echogenicity, cortical cysts, corticomedullary differentiation) which is suggestive of renal damage is also considered in this grading system [16].

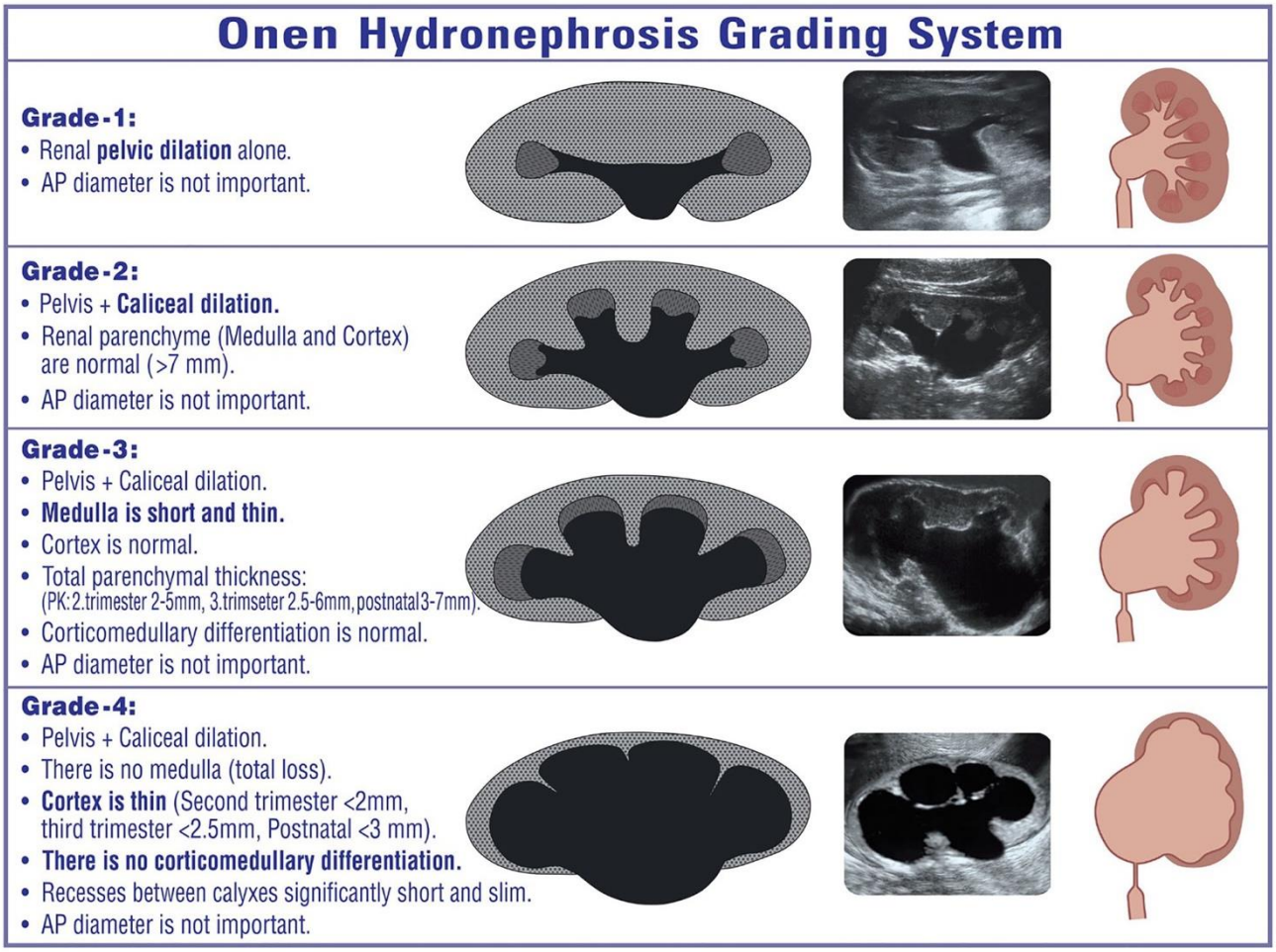


Image 135 – Onen grading system [16].

Clinical features.

Symptoms of obstructive hydronephrosis show a wide spectrum from asymptomatic patients to patients with flank pain, urinary tract infection (UTI), a palpable abdominal mass, hematuria or symptoms of impaired kidney function. The obstruction may change temporally, i.e., diminish over time, become progressive, or occur intermittently. Previously, patients with hydronephrosis presented with one or more of these symptoms, which were the compelling indications for surgical intervention. Occasionally, patients with a severe obstruction were diagnosed and/or treated too late, resulting in impaired renal function and, in a few of the worst cases, renal insufficiency [14].

Diagnostic evaluation.

The aim is to preserve renal function by selecting the 15–20% of children who require early surgical intervention from those for whom watchful waiting may be appropriate because of spontaneous resolving/stabilization without a significant loss of renal function. Today this requires repetitive **ultrasonography,** diuretic renographies and, in selected cases, determinations of the glomerular filtration rate (GFR) [14]. To exclude UTI, it is important to performed common blood tests, urinalysis, urine culture (image 136).

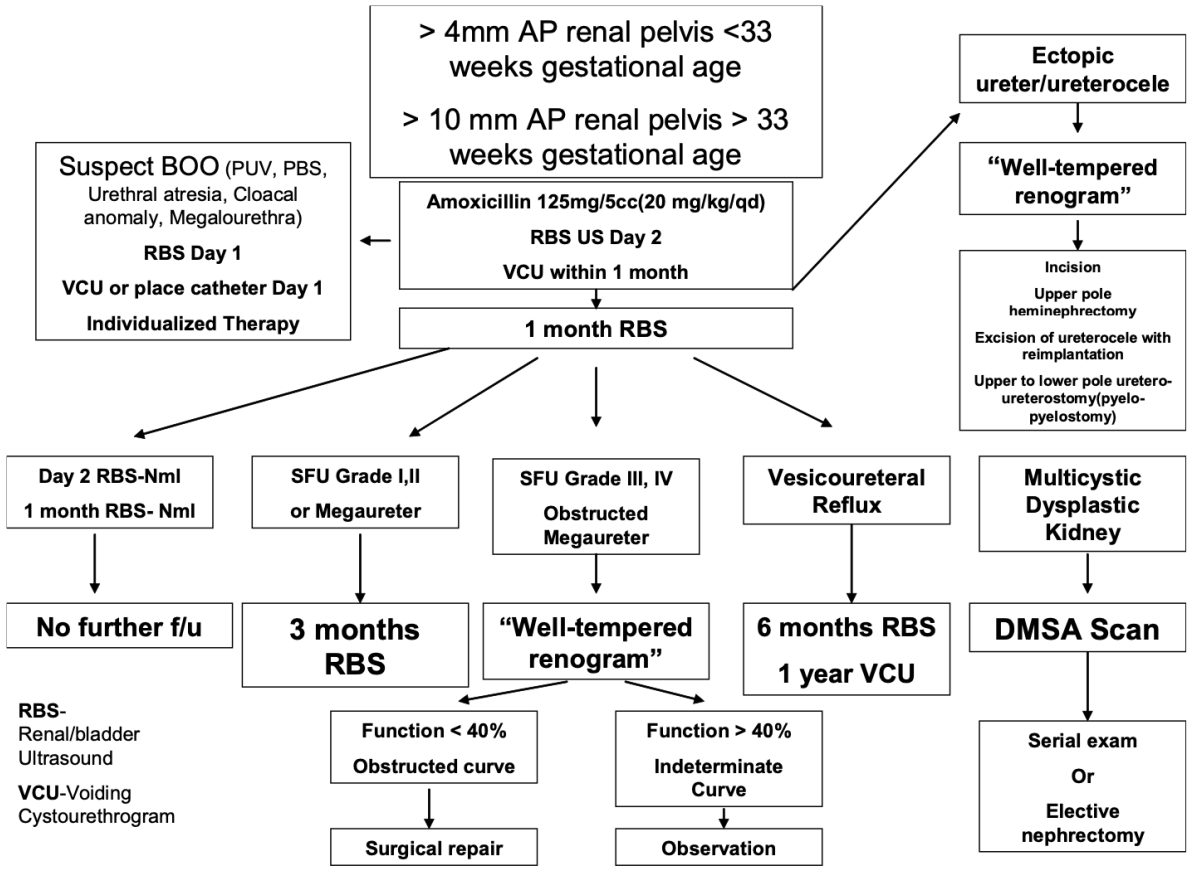


Image 136 – Diagnostic evaluation of hydronephrosis

Diagnostic management.

Based on EAU and ESPU 2019 Guidelines on pediatric urology, surgical indications for UPJHN are impaired renal function (<40%), significant renal functional decrease (>10%) in control scans, poor drainage after furosemide injection, increased AP diameter, and SFU-III/IV [16].

Surgical Indications for UPJHN Based on the Hydronephrosis Severity Score (HSS):

-Onen-4(thincortex)(<3mm)
-Onen-3(thinmedulla)(3–7mm)plus
-Presence of symptom (UTI,pain,stone)or
->20% compensatory growth in contralateral kidney or
->10 units decrease in renal function or
-Renal function <35%.

All patients were operated on by a pediatric urologist with open or laparoscopic, or retroperitoneoscopic Anderson-Hynes pyeloplasty with the insertion of a thin stent (Salle Pyeloplasty Stent 4.7 Cook Urological, Spencer, IN, USA) which was inserted to reduce the load on the anastomosis between the pelvis and ureter (image 7). After the retroperitoneal approach (for example), the ureter and pelvis were exposed. The ureter was spatulated at 1–2 cm past the stenotic area. After the stent was inserted, the anastomosis was sutured, and the stent was guided through the skin and carefully attached with a bandage. The stent was closed on the first postoperative day and removed at the outpatient clinic after 3 weeks without anesthesia. It was

possible to collect urine samples (e.g., in case of fever), and to rinse the stent in case of blockage due to blood- clots.

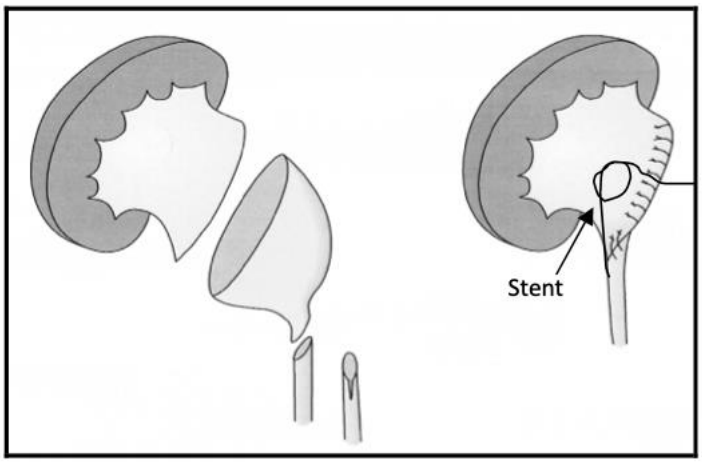


Image 137 – Anderson – Hynes pyeloplasty [14].

TEST

1. The etiology of secondary hydronephrosis DOES NOT APPLY to:
a) urolithiasis
b) BPH
c) stricture of urethra
d) accessory inferior polar vessel

2. Ultrasound screening of the fetus to detect primary hydronephrosis is carried out starting from:
a) 20–21 weeks
b) 8–9 weeks
c) 16–17 weeks
d) 30–31 weeks

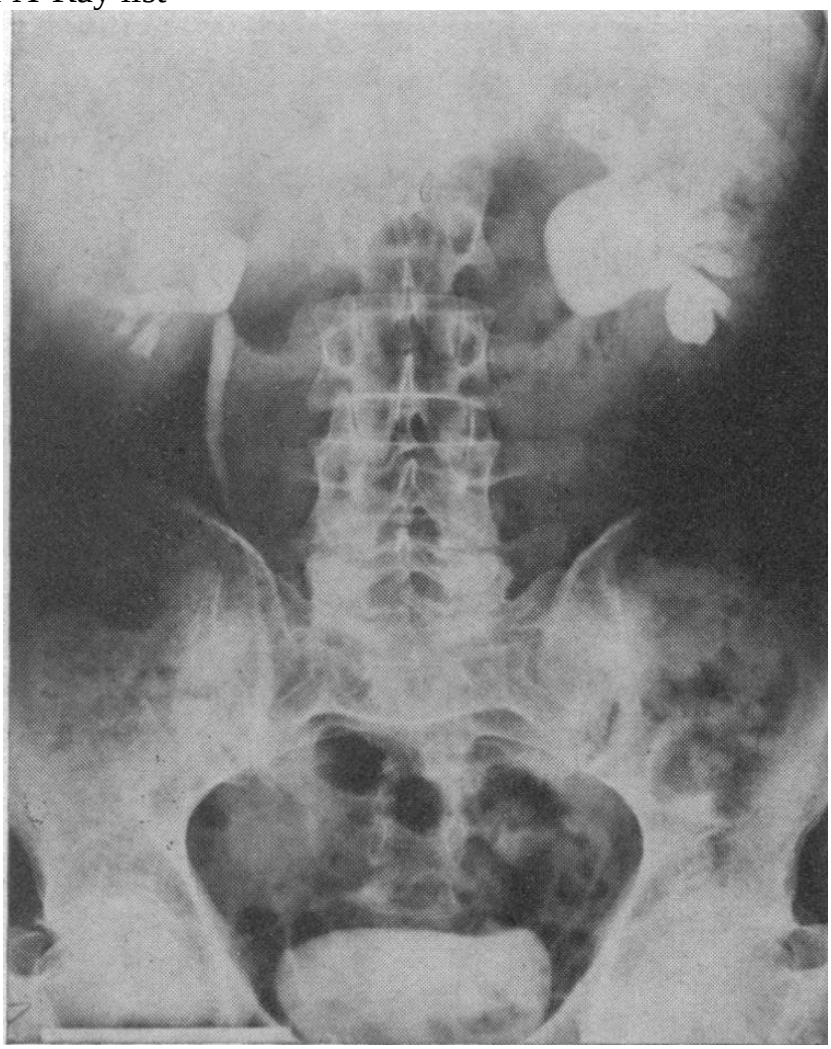
3. According Onen grading classification dilatation of pelvis and calyces with normal renal parenchyma consist of?
a) grade 1
b) grade 2
c) grade 3
d) grade 4

4. To assess the functional capacity of the kidneys, the following is carried out:
a) plain abdominal urography
b) intravenous urography
c) cystoscopy
d) dynamic nephroscintygraphia

d) CT scan

5. Indications for surgical treatment of hydronephrosis are:
a) pain in the lumbar region, leading to social desadaptaion
b) urinary stones
c) attacks of pyelonephritis
d) pyelocalicoectasia on ultrasound examination
e) development of chronic renal failure

6. Describe of X-Ray list



7. Which symptoms are most likely for hydronephrosis?

a) flank pain
b) dysuria
c) hematuria
d) palpable mass
e) nocturia

TASK

Patient I, 32 years old, consulted a urologist with a complaint of pain in the lumbar region on the left. History of the present illness: these symptoms have been presenting for two months. In December 2015 (7 years ago), an ultrasound examination was revealed stones in the left kidney and and pyeloectasia up to 25 mm.

Physical examination: the condition is satisfactory. Body temperature 36.6 C, heart rate 83 in minute, blood pressure – 120/70 mm. Hg. On auscultation, there is vesicular breathing in the lungs, no wheezing. The tongue is clean. The abdomen is symmetrical, soft and painless on palpation.

The kidney is palpable on the left, smooth and painless. The costovertebral angle tenderness is negative on both sides. Voiding without pathology.

In urine analysis - specific gravity 1021, PH - 5.5, protein 0.02 g/l, Leu - 3-4 per field of view, Er - 1-2 per field of view.

Ultrasound and multiCT scan revealed duplication of the upper urinary tract on the left, stenosis of the ureteropelvic segment of the lower pole of the double kidney, numerous stones of the left kidney up to 2 to 5-6 mm in diameter, density 600 HU, pelvis dilated to 44 mm, calyces up to 9 mm (material from telegramm chanel Russian society Urology).

Questions:

1) Diagnosis.

2) Describe further tactics of examination and treatment of a patient with this pathology.

3) What diseases will you carry out differential diagnosis with?

Check your answers:

1. abc.
2. a.
3. b
4. bd
5. abce
7. acd

1.Duplication of the upper urinary tract. Hydronephrosis of the lower part of kidney. Urinary stones.

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Benign prostate hyperplasia

Histopathologically, BPH is characterized by an increased number of epithelial and stromal cells in the periurethral area of the prostate and thus correctly referred to as hyperplasia and not hypertrophy, as is often found in the older literature. The observed increase in cell number may be due to epithelial and stromal proliferation or to impaired programmed cell death leading to cellular accumulation [5].

Etiology. Androgens, estrogens, stromal-epithelial interactions, growth factors, and neurotransmitters may play a role, either singly or in combination, in the etiology of the hyperplastic process [5].

Active form of testosterone is DHT.

The formation of DHT involves the reduction of the double bond in the A ring of testosterone through the enzymatic action of the enzyme 5α-reductase. There are at least two isoforms of this enzyme (type 1 and type 2). Type 2 5α-reductase expression predominates in human accessory sex tissues and is localized to the fibromuscular stromal compartment. The type 1 isoform predominates n skin, in prostatic epithelia, and to a lesser extent in prostatic fibromuscular stroma [5].

DHT levels were associated with an increased risk of BPH and activate AR receptors, which is cause of growth of tissue. Age- related increases in estrogen, as well as other factors, may increase AR expression in the aging prostate, leading to further growth (or to a decrease in cell death), despite decreasing levels of androgen in the peripheral circulation and “normal” levels of DHT in the prostate [5] (image 138).

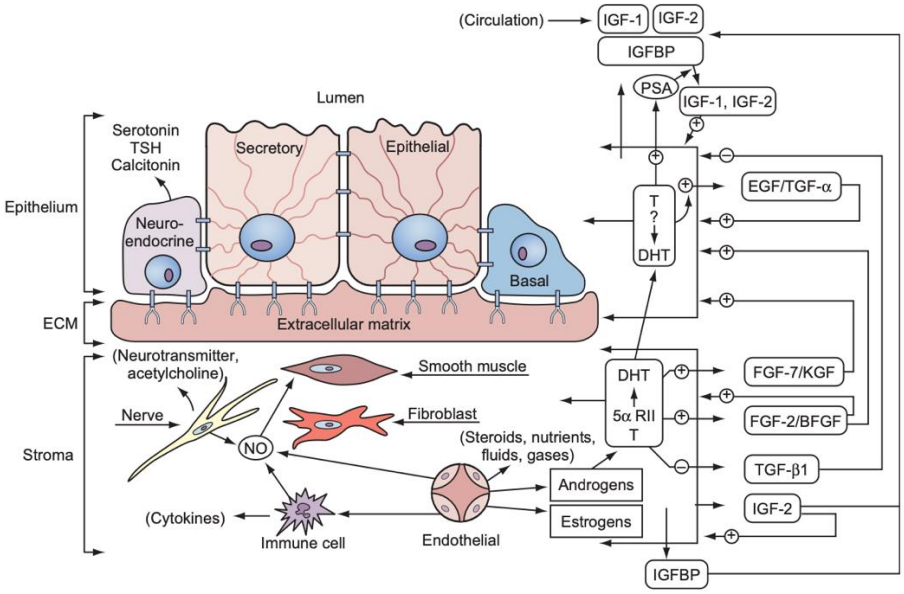

Image 138 - Stromal-epithelial interactions (Campbell – Walsh urology)

BPH first develops in the periurethral *transition zone* of the prostate (image 139).

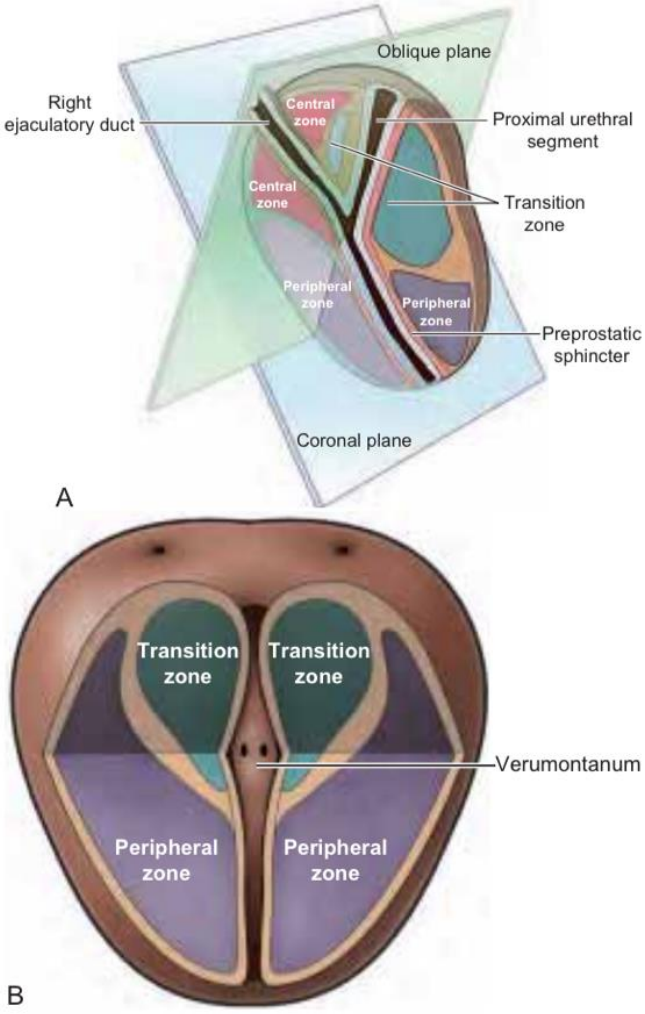

Image 139 – Anatomy of prostate [5]

One of the unique features of the human prostate is **the presence of the prostatic capsule, which plays an important role in the development of lower urinary tract symptoms. T**he capsule transmits the "pressure" of tissue expansion to the urethra and leads to an increase in urethral resistance [5].

Prostatic hyperplasia increases urethral resistance, resulting in compensatory changes in bladder function. However, the elevated detrusor pressure required to maintain urinary flow in the presence of increased outflow resistance occurs at the expense of normal bladder storage function.

Obstruction-induced changes in detrusor function, compounded by age-related changes in both bladder and nervous system function, lead to urinary frequency, urgency, and nocturia, the most bothersome BPH-related complaints< for example development of hydronephrosis (image 140).

Histologic Features

BPH is a hyperplastic and not a hypertrophic process; that is, there is a net increase in the number of cells and not in the size of the cells.

Regardless of the exact proportion of epithelial to stromal cells in the hyperplastic prostate, there is no question that prostatic smooth muscle represents a significant volume of the gland (image 141).

Symptoms.

The symptoms of BPH can be divided into two group: obstructive (hesitancy, decreased force and caliber of stream, sensation of incomplete bladder emptying, double voiding straining) and irritative symptoms (frequency, urgency, nocturia).

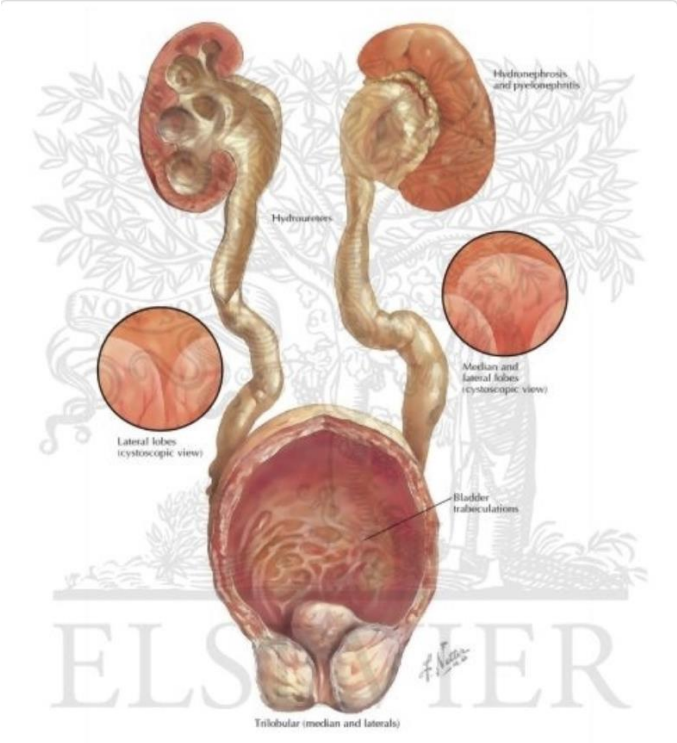

Image 139 – BPH with ureterohydronephrosis (https://www.netterimages.com/benign-prostatic-hyperplasia-iii-complications-and-medical-treatment-labeled-smith-gb-2e-obstetrics-gynecology-frank-h-netter-58444.html).

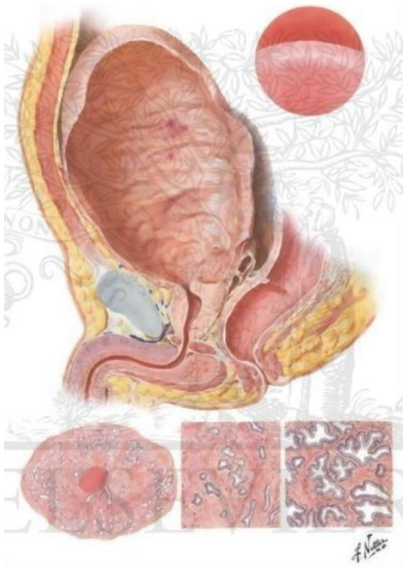

Image 141 – Histologic features of BPH (https://www.netterimages.com/benign-prostatic-hypertrophy-i-histologic-structure-median-bar-unlabeled-histology-frank-h-netter-2989.html).

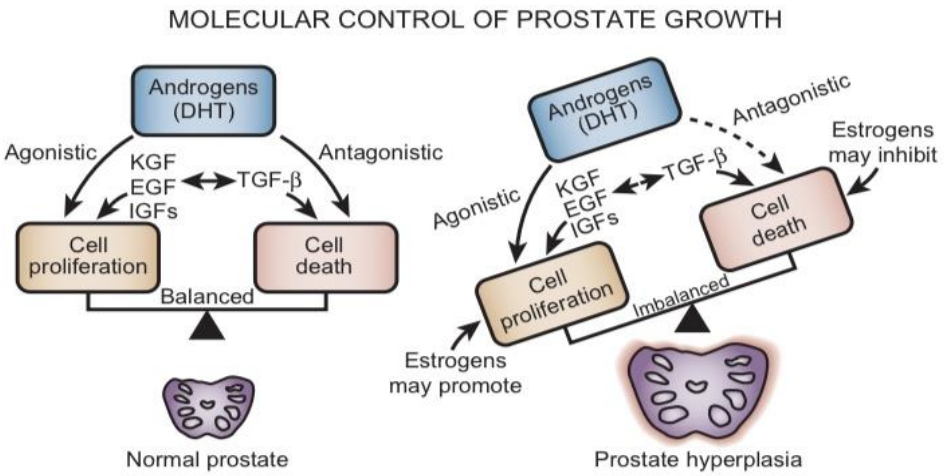

Image 142 – Molecular control of prostate growth [5]

Diagnostic evaluation

- BPH can most easily be identified by *digital rectal examination* (DRE) (image 143). DRE establishes the approximate size of the prostate gland. Estimation of prostate size is important to guide the most appropriate pharmacologic or interventional approach. In addition, examination of the external genitalia is indicated to exclude meatal stenosis or a palpable urethral mass, and an abdominal examination is necessary to exclude an overdistended, palpable or percussable bladder, to evaluate anal sphincter tone, and to rule out any neurologic problems that may cause the presenting symptoms (task 16).

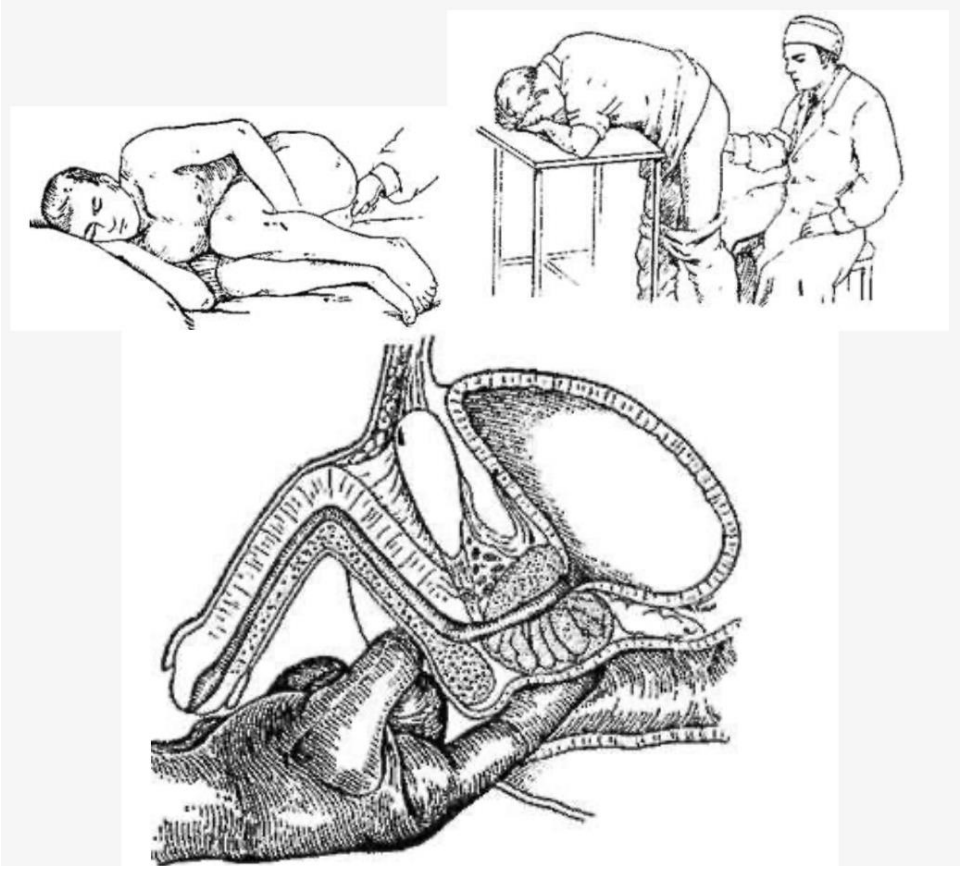

Image 143 – Digital rectal examination [15].

Task 16 Characteristic of prostate (DRE)

	Physiologic condition	BPH	Prostate cancer
Size	Normal size	Enlarged	Enlarged/ normal size
Symmetrically	Symmetrically	Symmetrically	Symmetrically/not a symmetrically
Consistency	Elastic	Tight elastic	Density consistency
Painfull/painless	Painfull	Painfull	Painfull/painless
Moving of mucosa of recti during palpation	Moving mucosa	Moving mucosa	Moving mucosa/not moving mucosa

- A **urinalysis** *should* be done by use of either a dipstick test or microscopic examination of the spun sediment to rule out UTI and hematuria, either of which strongly suggests a non-BPH pathologic process as a cause of symptoms.

Urine cytology should always be requested in men with severe storage symptoms and dysuria, especially if they have a smoking history. Carcinoma in situ of the bladder may have serious consequences if overlooked. More important, urinalysis assists in distinguishing UTIs and bladder cancer from benign prostate disease. These conditions may produce urinary tract symptoms (e.g., frequency and urgency) that mimic LUTS or BPH [5].

- Although the measurement of **serum creatinine** was recommended in the initial evaluation of all patients with LUTS to exclude renal insufficiency caused by the presence of obstructive uropathy. Elevated serum creatinine in a patient with LUTS is an indication for imaging studies (usually ultrasound) to evaluate the upper urinary tract [5].
- **Serum Prostate-Specific Antigen (PSA)**. Serum PSA trends over time (PSA velocity), measurement of free versus complexed PSA, and PSA density may help to improve the specificity of PSA in men with BPH. Newer markers such as the p2PSA and Prostate Health Index (PHI) score or urinary PCA3 test result can also help to differentiate BPH from prostate cancer [5].
- Use a **validated symptom score questionnaire** including bother and quality of life assessment during the assessment of male LUTS and for re-evaluation during and/or after treatment. When this system is used, symptoms can be classified as mild (0 to 7), moderate (8 to 19), or severe (20 to 35) (Barry et al, 1992b). The symptom score should also be the primary determinant of treatment response or disease progression in the follow-up period. the IPSS is a good instrument to grade baseline symptom severity, assess the response to therapy, and detect symptom progression in men managed by watchful waiting [5] (image 144).
- Uroflowmetry involves the electronic recording of the urinary flow rate throughout the course of micturition. It is a common, noninvasive urodynamic test used in the diagnostic evaluation of patients with symptoms of BOO. The results of uroflowmetry are nonspecific for causes of the symptoms. For example, an

abnormally low flow rate may be caused by an obstruction (e.g., hyperplastic prostate, urethral stricture, meatal stenosis) or by detrusor hypocontractility. *The peak flow rate* (PFR; Qmax) more specifically identifies patients with BOO than does the average flow rate (Qave) (meaning more than 15 mL/sec) [5] (image 145,146).

IPSS	Not at all	Less than 1 time in 5	Less than half the time	About half the time	More than half the time	Almost always	Your score (BT)	Your score (AT)
Incomplete emptying Over the past month, how often have you had a sensation of not emptying your bladder completely after you finish urinating?	0	1	2	3	4	5		
Frequency Over the past month, how often have you had to urinate again less than two hours after you finished urinating?	0	1	2	3	4	5		
Intermittency Over the past month, how often have you found you stopped and started again several times when you urinated?	0	1	2	3	4	5		
Urgency Over the last month, how difficult have you found it to postpone urination?	0	1	2	3	4	5		
Weak stream Over the past month, how often have you had a weak urinary stream?	0	1	2	3	4	5		
Straining Over the past month, how often have you had to push or strain to begin urination?	0	1	2	3	4	5		
Nocturia Over the past month, many times did you most typically get up to urinate from the time you went to bed until the time you got up in the morning?	0	1	2	3	4	5		

Image 144 – IPSS (https://www.researchgate.net/figure/International-prostate-symptom-score-IPSS_tbl2_272498677).

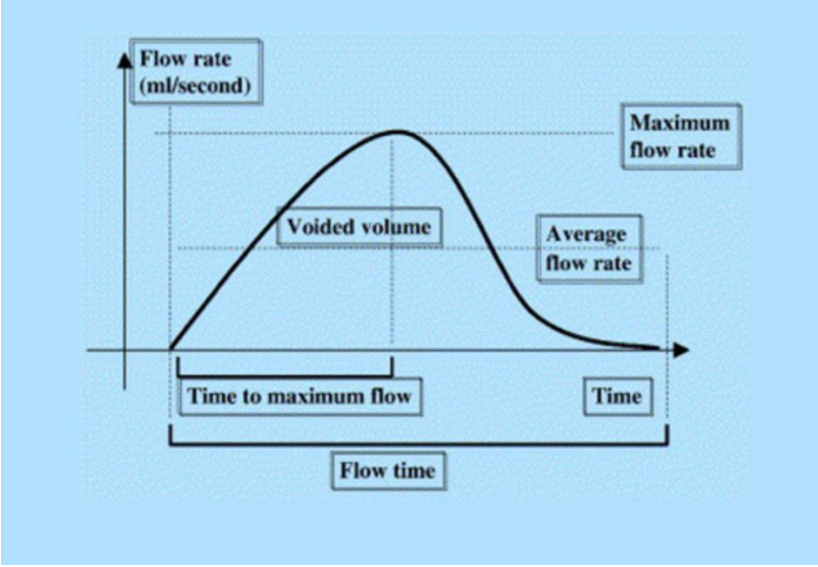

Image 145 – Uroflowmetry (https://advinurology.com/wp-content/uploads/2015/07/PC-Based-Uroflow-2.jpg).

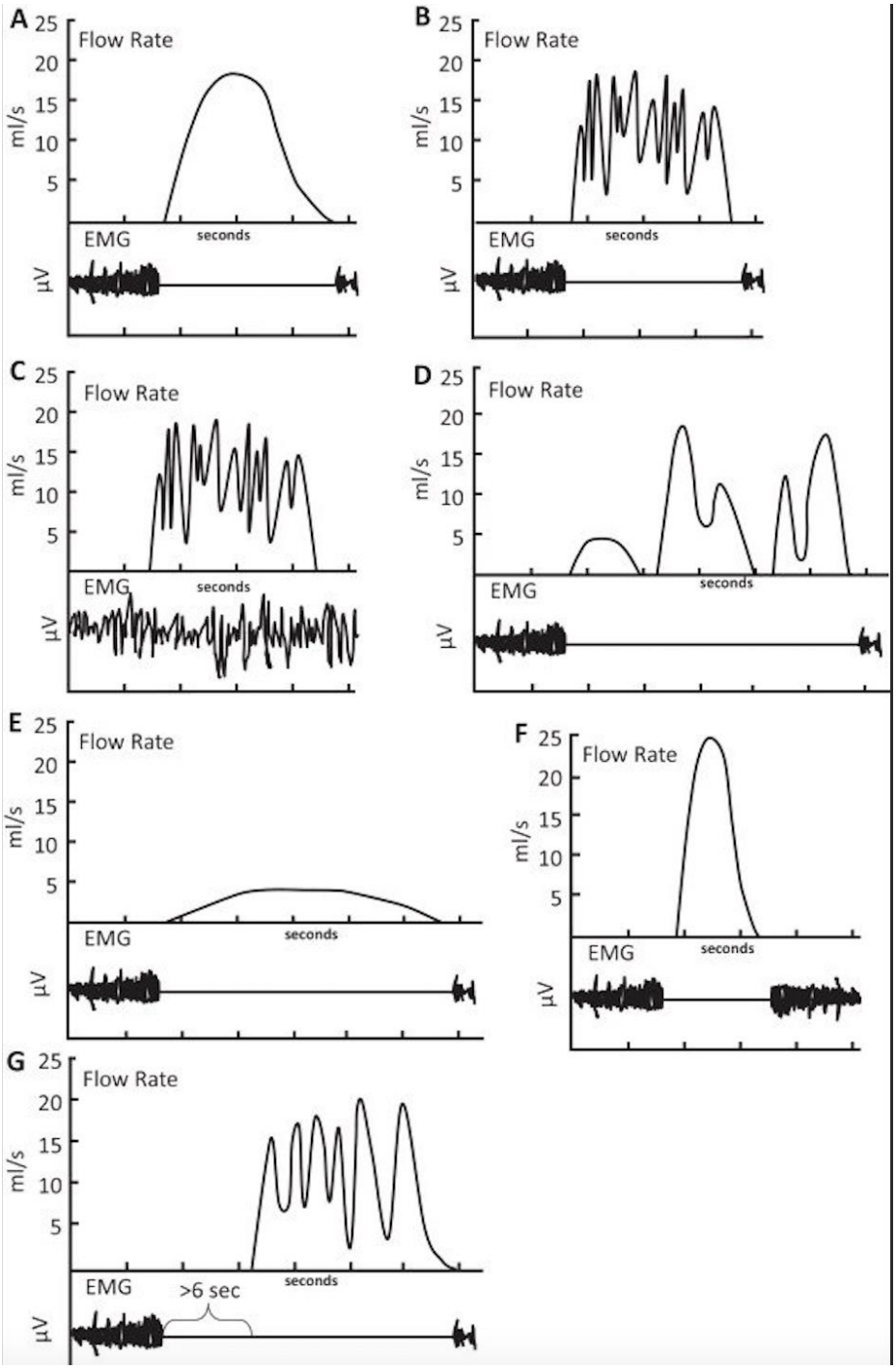

Image 146 – Results of uroflowmetry Descripton:(A- Normal flow showing bell-shaped curve and cessation of external sphincter activity. B, C - staccato shaped flow, which can occur with a weak or unsustained detrusor contraction but quiet external urethral sphincter (as in B) or with periodic bursts of sphincter activity on EMG while voiding with a continuous but varying flow rate (as in C). D - Interrupted or fractionated voiding notable for periods of no urine flow in the absence of EMG activity. Like the Staccato pattern, this can occur with an unstained detrusor contraction but also result when voiding is achieved via abdominal muscle contractions in the presence of an acontractile bladder. (E) Plateau shaped flow showing low amplitude, prolonged void and cessation of sphincter activity on EMG. This occurs as a result of a fixed anatomic obstruction or a weak detrusor

contraction. Plateau shaped flow can also occur with a tonically active external sphincter (not depicted). (F) Tower shaped flow with a high amplitude, short duration of flow caused by detrusor overactivity; may result in urge incontinence. (G) Primary bladder neck dysfunction with urine flow beginning at least 6s after the cessation of sphincter activity on EMG (https://www.researchgate.net/figure/Examples-of-uroflowmetry-in-children-A-Normal-flow-showing-bell-shaped-curve-and_fig1_260012810).

- **PVR** urine is the volume of fluid remaining in the bladder immediately after the completion of micturition. PVR measurement can be performed by noninvasive (ultra- sound) and by invasive (catheterization) methods.

If the initial evaluation, flow rate, and PVR are not sufficiently suggestive of BOO, further urodynamic assessment by pressure-flow studies should be considered, especially if an invasive treatment is considered (i.e., surgery) or if surgical treatment has failed. Pressure-flow studies differentiate between patients with a low Qmax secondary to obstruction and those who's low Qmax is caused by impaired detrusor contractility [5].

-**Urethrocystoscopy** is **not recommended** to determine the need for treatment because the linkage between the endoscopic appearance of the lower urinary tract and the treatment outcome is poorly documented and available information suggests that the relationship is minimal. The test is recommended for men with LUTS who have a history of microscopic or gross hematuria, urethral stricture disease (or risk factors such as history of urethritis or urethral injury), bladder cancer or suspicion of carcinoma in situ, or prior lower urinary tract surgery (especially prior TURP). Urethrocystoscopy may be considered in men with moderate to severe symptoms who have chosen (or require) surgical or other invasive therapy to help the surgeon determine the most appropriate technical approach (image 147)[5].

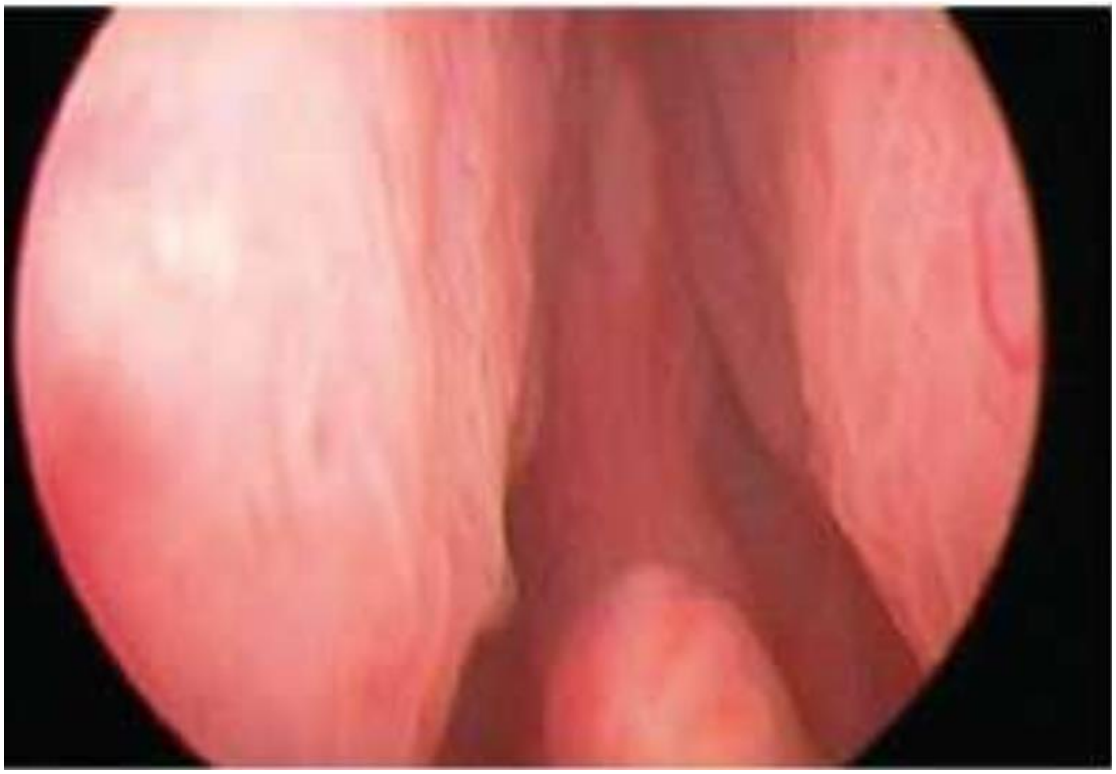

Image 147 – Urethrocystoscopy (BPH)

- Upper urinary tract imaging is not recommended in the routine evaluation of men with LUTS unless they also have one or more of the following: hematuria, UTI, renal insufficiency (ultrasound recommended), history of urolithiasis, or history of urinary tract surgery (image 148, 149).

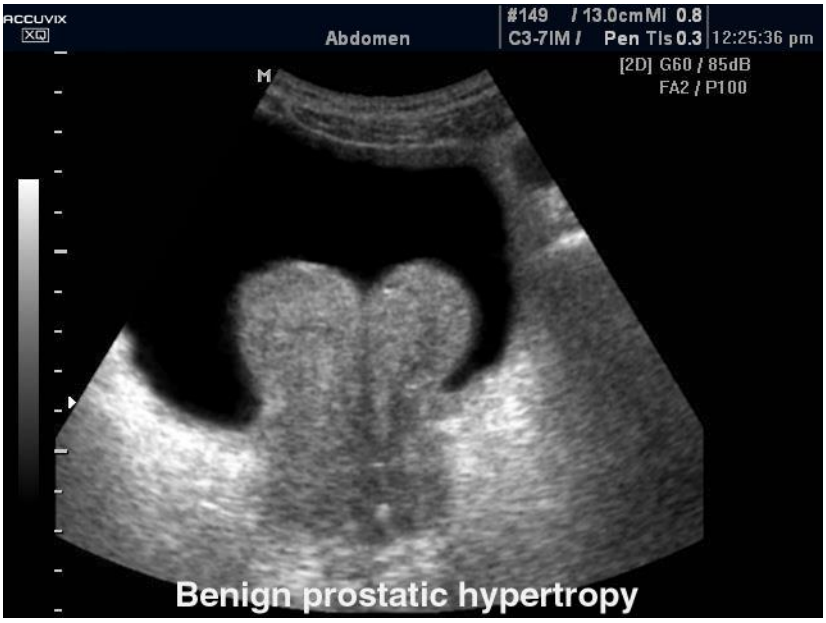

Image 148 – Ultrasound examination of prostate (BPH) (symptom «curtain» (Internet)

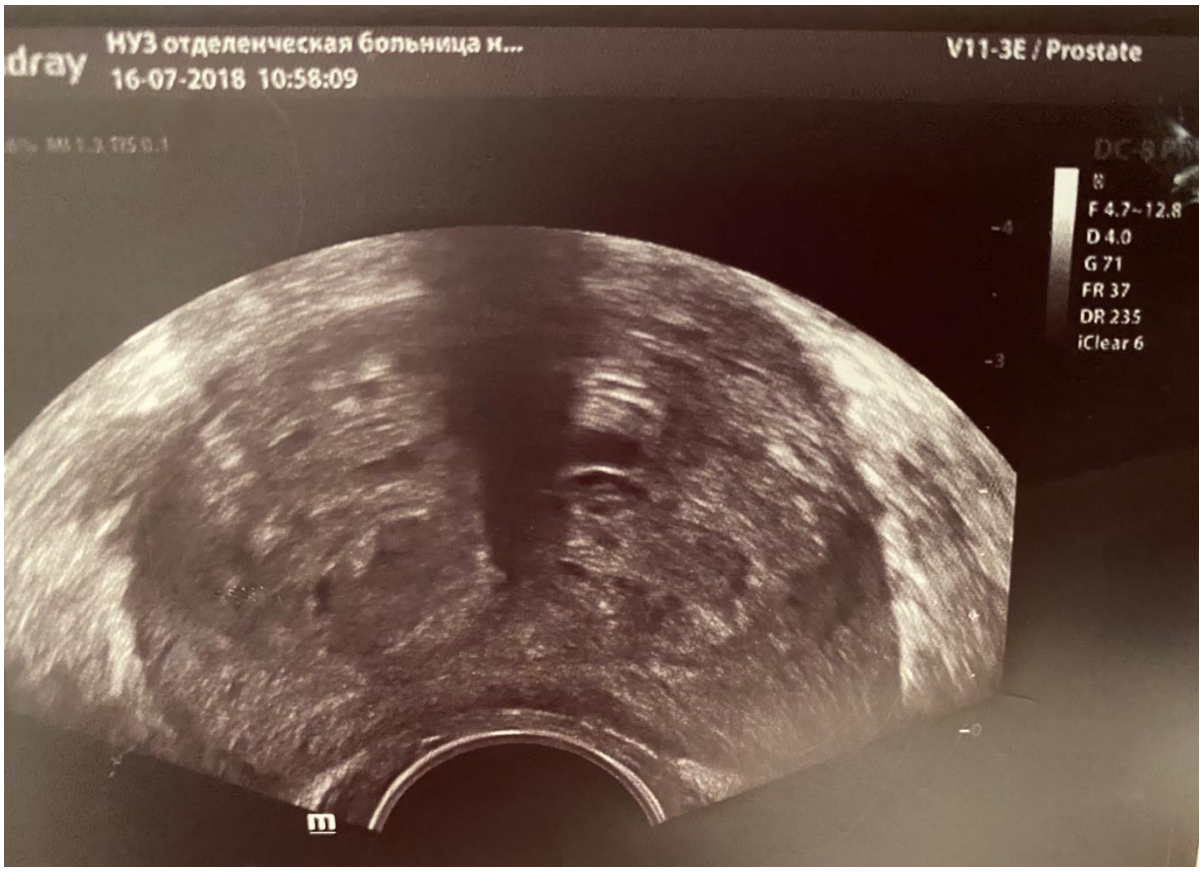

Image 149 – Transrectal ultrasound examination of prostate (BPH) (own material).

Diagnostic management.

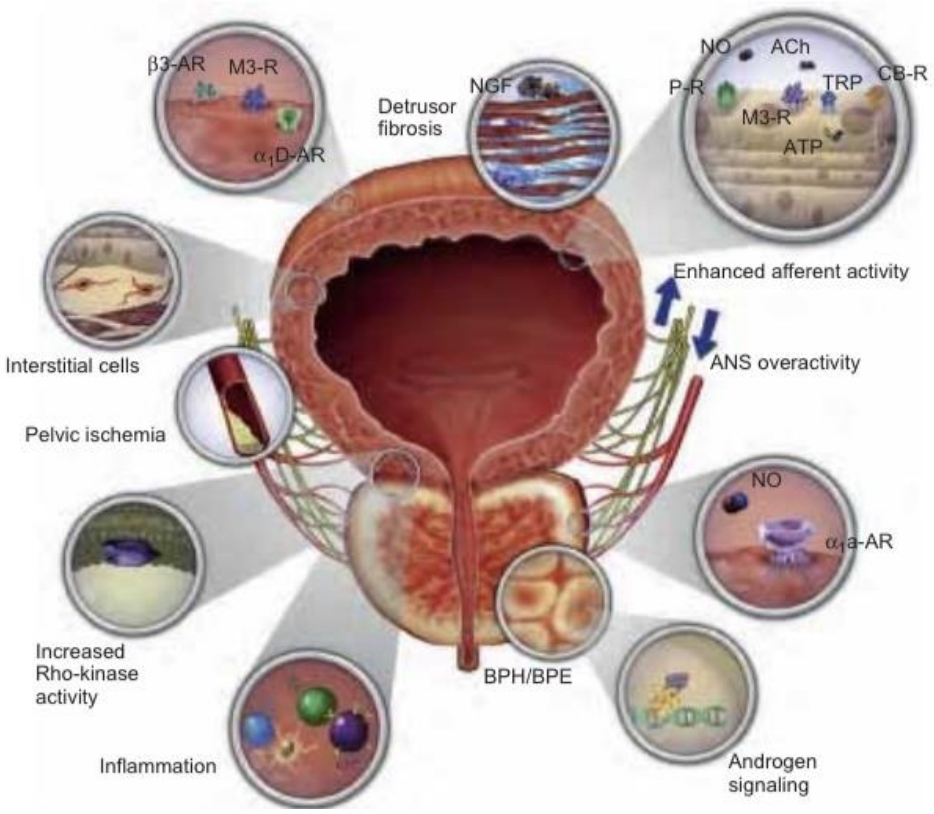

Image 150 – Pathophysiological mechanisms of nonsurgical treatment [5].

The goals of treatment include relieving LUTS, decreasing BOO, improving bladder emptying, ameliorating detrusor overactivity, reversing renal insufficiency, and preventing disease progression, which may include a deterioration of symptoms, future episodes of gross hematuria, UTI, AUR, or the need for surgical intervention. The definition of *detrusor overactivity* is the development of a detrusor contraction exceeding 15 cm H2O at a bladder volume less than 300 mL [5].

NONSURGICAL THERAPY FOR BENIGN PROSTATIC HYPERPLASIA

Education and Reassurance

• Discuss the causes of LUTS, including normal prostate and bladder function.
• Discuss the natural history of BPH and LUTS, including the expected future symptoms.
• Reassure that no evidence of a detectable prostate cancer has been found.

Fluid Management

• Advise a daily fluid intake of 1500 to 2000 mL (minor adjustments made for climate and activity).
• Avoid inadequate or excessive intake based on a frequency- volume chart.
• Advise fluid restriction when symptoms are most inconvenient (e.g., during long journeys or when out in public).
• Advise evening fluid restriction for nocturia (no fluid for 2 hours before retiring).

Caffeine and Alcohol

• Avoid caffeine by replacing with alternatives (e.g., decaffeinated or caffeine-free drinks).
• Avoid alcohol in the evening if nocturia is bothersome.
• Replace large-volume alcoholic drinks (e.g., pint of beer) with small-volume alcoholic drinks (e.g., wine or spirits).

Concurrent Medication

• Adjust the time when medication with an effect on the urinary system is taken, to improve LUTS at times of greatest inconvenience (e.g., during long journeys and when out in public).
• Replace antihypertensive diuretics with suitable alternatives with fewer urinary effects (via the patient's general practitioner).

Types of Toiletings and Bladder Retraining

• Advise men to double-void.
• Advise urethral milking for men with postmicturition dribble.
• Advise bladder retraining. Using distraction techniques (predetermined mind exercise, perineal pressure or pelvic floor exercises), aim to increase the minimum time between voids to 3 hours (daytime) and/or the minimum voided volume to between 200 and 400 mL (daytime). The urge to void should be suppressed for 1 minute, then 5 minutes, then 10 minutes, and so on, increasing on a weekly basis. Use frequency-volume charts to monitor progress.

Miscellaneous

• Avoid constipation in men with LUTS.

MEDICAL THERAPY FOR LOWER URINARY TRACT SYMPTOMS AND BENIGN PROSTATIC HYPERPLASIA

Medical therapies extensively investigated for LUTS and BPH include α-adrenergic blockers, 5α-reductase inhibitors, aromatase inhibitors, and numerous plant extracts. Newer therapies include antimuscarinic drugs, β3-agonists, phosphodiesterase inhibitors (PDEIs), and several combinations of these agents.

A potential role of medical therapy is to prevent the development of LUTS or BPH or its progression.

The rationale for *α-adrenergic blockers* in the treatment of LUTS is based on the hypothesis that the pathophysiology of LUTS is in part caused by BOO, which is mediated by α1 adrenoceptors associated with prostatic smooth muscle. The importance of this dynamic obstruction was supported by morphometric studies demonstrating that smooth muscle is one of the dominant cellular constituents of BPH, accounting for 40% of the area density of the hyperplastic prostate.
α-Adrenergic blockers may be classified according to α adrenoceptor selectivity and serum elimination half-life.

The advance in the development of α-blockers was the development of advanced drugs with serum elimination half-lives that allowed for once-a- day administration [5].

ANDROGEN MANIPULATION

The development of BPH is also an androgen-dependent process. Castration and pharmacologic agents suppressing testosterone and DHT synthesis or action have been shown to reduce prostate volume in men with established LUTS or BPH. Peters and Walsh (1987) demonstrated that androgen suppression causes regression primarily of the epithelial elements of the prostate. Reducing prostate volume is thought to decrease the static component of BOO resulting from BPE (task 17).

Task 17. Androgen deprivation

5α-REDUCTASE INHIBITORS	Finasteride 5 mg PO qd Dutasteride 0.5 mg PO qd
ANTIANDROGENS	Flutamide 100 mg tid, 250 mg tid Oxandrolone 200 mg IM weekly Bicalutamide 50 mg qd
GONADOTROPIN-RELEASING HORMONE ANALOGUES	Leuprolide 3.75 mg IM qd mo

Maximal reduction of prostate volume after initiation of androgen suppression is achieved within 6 months (Peters and Walsh, 1987; Gormley et al, 1992).
Dutasteride is an inhibitor of both type 1 and type 2 5α-reductase and has efficacy and side effects like those of finasteride. *Finasteride* and dutasteride alter the natural history of urinary retention in men with LUTS and enlarged prostates. In selected patients with larger prostates, over longer time periods, dutasteride appears to have symptomatic benefits greater than tamsulosin [5].

OAB symptoms may coexist with LUTS and BPH or BOO and may be either secondary to that obstruction or unrelated. Traditionally, in the treatment of OAB symptoms the use of **antimuscarinic** (commonly called anticholinergic) agents is often used. Current European guidelines suggest that antimuscarinics can be added to α-blockers to address storage symptoms when monotherapy with α-blockers is inadequate.

Mirabegron is the first of a new class of drugs. β3 agonists enhance bladder relaxation during bladder filling by blocking the β3 adrenoreceptors in the detrusor muscle. Mirabegron can increase bladder capacity without blocking contractility [5].

AUR is the commonest urologic emergency managed by most urologists worldwide, may be spontaneous, in which case it is usually associated with previous LUTS or BPH. Alternatively, it may be precipitated by some other factor such as the effects of various medications, particularly anticholinergic or sympathomimetic agents, commonly found in cough and cold remedies. Urinary infection, excessive fluid intake, and the consequences of surgery (postoperative pain or the effects of anesthesia or analgesia or loss of mobility) may precipitate AUR.

Analysis of the placebo arms of a series of large studies such as the PLESS evaluation of finasteride, MTOPS, and the CombAT study indicate that increasing

age, the presence of LUTS, a low Qmax, and prostatic enlargement and/ or raised PSA increase the risk of AUR [5].

When AUR develops, most men are catheterized for a period or taught intermittent self-catheterization. If urinary retention is caused by increased sympathetic activity at the level of the prostatic smooth muscle, an α-blocker should increase the likelihood of spontaneous voiding after catheter removal.

The trial data suggest a role for 5α-reductase inhibitor drugs in the prevention of AUR [5].

SURGICAL TREATMENT OF BPH

TURP (image 152) involves an endoscopic approach via the patient's urethra to surgically remove the inner portion (primarily the transition zone) of the prostate that encircles the urethra. An electrified wire loop is used to remove the portion of the prostate between the bladder neck and the verumontanum to a depth of the surgical capsule [5].

Offer bipolar- or monopolar-transurethral resection of the prostate to surgically treat moderate-to-severe LUTS in men with prostate size of 30-80 mL [15].

The original M-TURP (monopolar) requires the use of a nonionic irrigant (water, glycine, sorbitol) to allow electroresection of the prostate. The use of an ionic solution (i.e., normal saline) leads to dissipation of the cutting current and poor cutting efficacy.

Offer open prostatectomy (image 151) in the absence of bipolar transurethral enucleation of the prostate and holmium laser enucleation of the prostate to treat moderate-to-severe LUTS in men with prostate size > 80 mL [15].

Technique.

In general, TURP is performed using general or spinal anesthesia. Traditionally, TURP was accomplished with the patient under spinal anesthesia so the anesthesiologist could monitor for signs of transurethral resection (TUR) syndrome resulting from hyponatremia (nonionic solutions are hypoosmolar and can be problematic when absorbed through open prostate sinuses into the systemic circulation) [5].

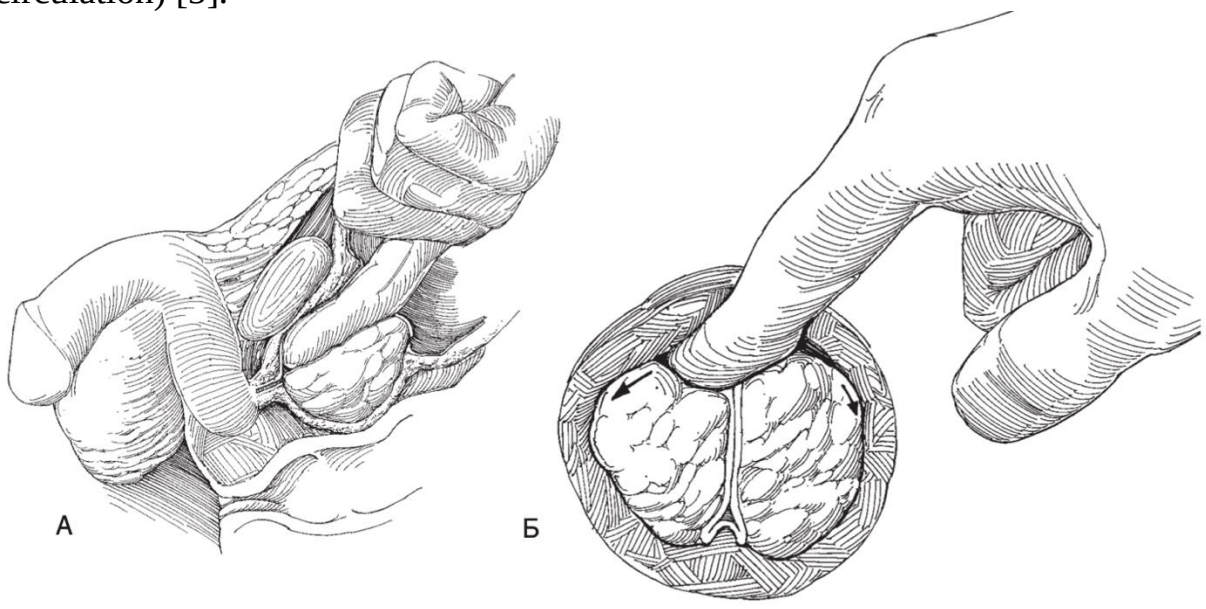

Image 151 – Open adenomectomy.

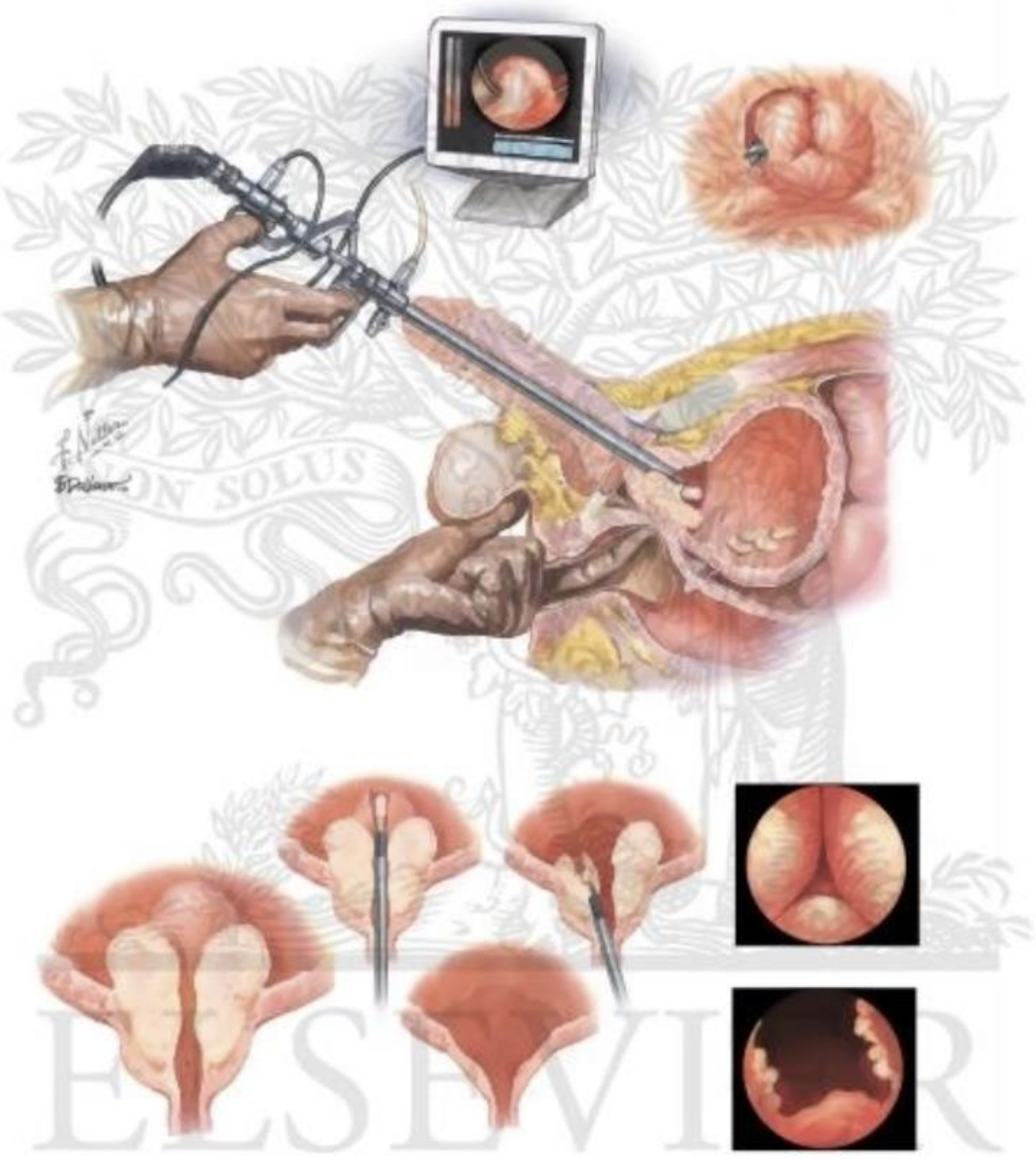

Image 152 – TURP (https://www.netterimages.com/benign-prostate-surgery-iv-transurethral-unlabeled-surgery-frank-tiffany-56957.html)

Prostate cancer

Prostate cancer is the second most common cancer in males. It is a major health concern, especially in developed countries due to the greater proportion of elderly men in the general population, and the potential risk of over-treatment following early diagnosis. There are three well-established risk factors for PCA: increasing age, ethnic origin, and genetic predisposition [15].

The 2017 Tumour Node Metastasis (TNM) classification is used for staging (image 153).

T - Primary Tumour (stage based on digital rectal examination [DRE] only)		
TX	Primary tumour cannot be assessed	
T0	No evidence of primary tumour	
T1	Clinically inapparent tumour that is not palpable	
	T1a	Tumour incidental histological finding in 5% or less of tissue resected
	T1b	Tumour incidental histological finding in more than 5% of tissue resected
	T1c	Tumour identified by needle biopsy (e.g. because of elevated PSA)
T2	Tumour that is **palpable** and confined within prostate	
	T2a	Tumour involves one half of one lobe or less
	T2b	Tumour involves more than half of one lobe, but not both lobes
	T2c	Tumour involves both lobes
T3	Tumour extends through the prostatic capsule	
	T3a	Extracapsular extension (unilateral or bilateral)
	T3b	Tumour invades seminal vesicle(s)
T4	Tumour is fixed or invades adjacent structures other than seminal vesicles: external sphincter, rectum, levator muscles, and/or pelvic wall	
N - Regional (pelvic) Lymph Nodes[1]		
NX	Regional lymph nodes cannot be assessed	
N0	No regional lymph node metastasis	
N1	Regional lymph node metastasis	

M - Distant Metastasis[2]		
M0	No distant metastasis	
M1	Distant metastasis	
	M1a	Non-regional lymph node(s)
	M1b	Bone(s)
	M1c	Other site(s)

[1] Metastasis no larger than 0.2 cm can be designated pNmi.
[2] When more than one site of metastasis is present, the most advanced category is used. (p)M1c is the most advanced category.

Image 153- TNM (2017) [15].

Definition			
Low-risk	**Intermediate-risk**	**High-risk**	
PSA < 10 ng/mL and GS < 7 (ISUP grade 1) and cT1–2a	PSA 10-20 ng/mL or GS 7 (ISUP grade 2/3) or cT2b	PSA > 20 ng/mL or GS > 7 (ISUP grade 4/5) or cT2c	any PSA any GS (any ISUP grade) cT3–4 or cN+
Localised			**Locally advanced**

GS = Gleason score; ISUP = International Society for Urological Pathology; PSA = prostate-specific antigen.

Image 154 - EAU risk groups for biochemical recurrence of localized and locally-advanced prostate cancer [15].

Prostate cancer grades were described according to the **Gleason Score**, a system named for the pathologist who developed it in the 1960s. Dr. Donald Gleason realized that cancerous cells fall into 5 distinct patterns as they change from normal cells to tumor cells. The cells are graded on a scale of 1 to 5. Grade 1 cells resemble normal prostate tissue. Cells closest to 5 are considered "high-grade" and have mutated so much that they barely resemble normal cells [16] (image 155).

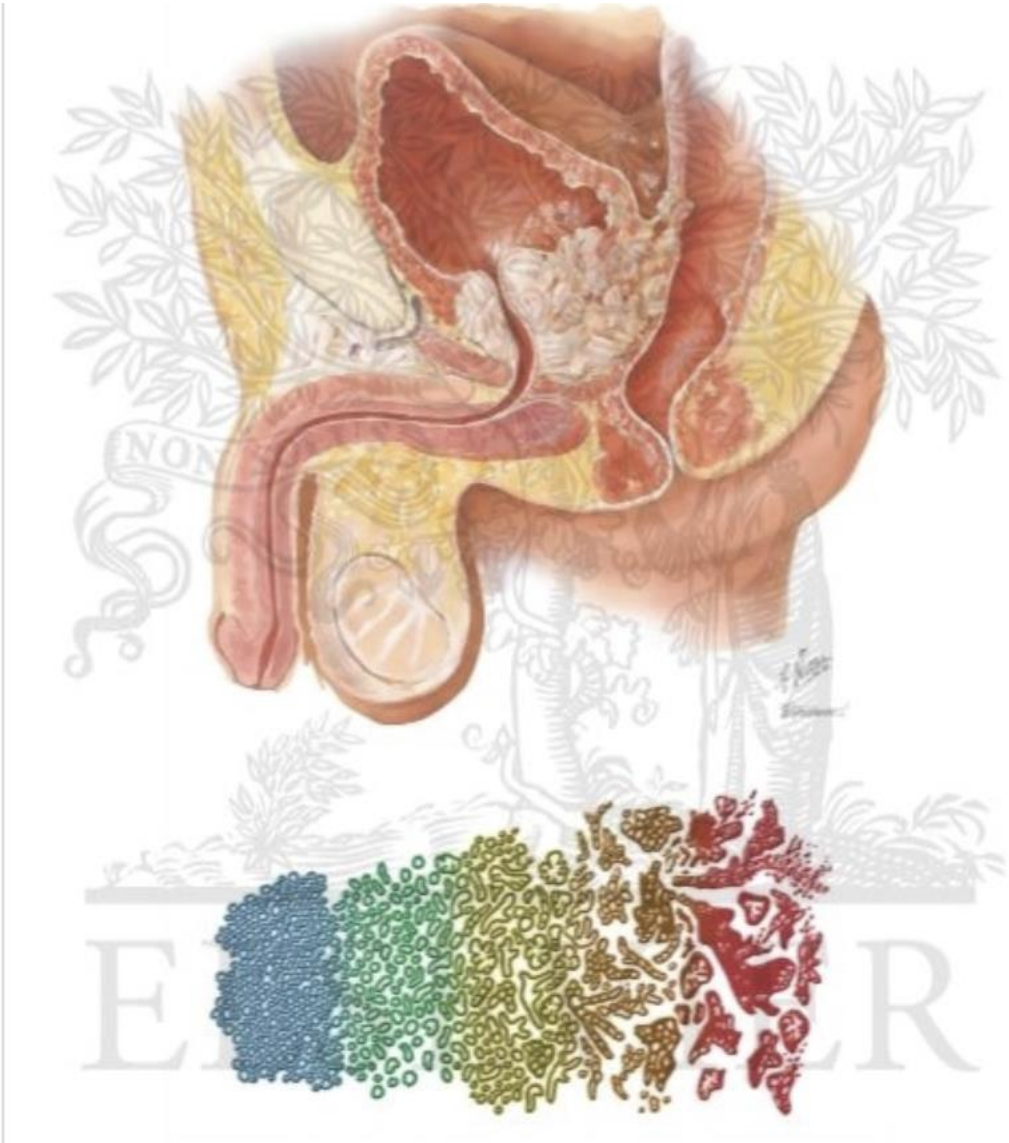

Image 155 – Gleason score (https://www.netterimages.com/carcinoma-of-prostate-i-epidemiology-prostate-specific-antigen-staging-and-grading-unlabeled-epidemiology-frank-tiffany-58213.html)

The International Society of Urological Pathology (ISUP) World Health Organization (WHO) 2014 grade groups have been adopted which allow patients to better understand the behaviour of their diagnosed prostate carcinoma, while separating GS 7 adenocarcinoma into two prognostically very distinct categories; grade group 2 for GS 7(3+4) and grade group 3 for GS 7(4+3) (image 156)[15].

Gleason score	ISUP grade
2–6	1
7(3+4)	2
7(4+3)	3
8(4+4 or 3+5 or 5+3)	4
9–10	5

Image 156 – ISUP grade 2014 [15].

Early detection [15].

Offer early PSA testing to well-informed men at elevated risk of having PCa:
- men from 50 years of age;
-men from 45 years of age and a family history of PCa;
-men of African descent from 45 years of age;
-men carrying *BRCA2* mutations from 40 years of age.

Diagnostic evaluation.

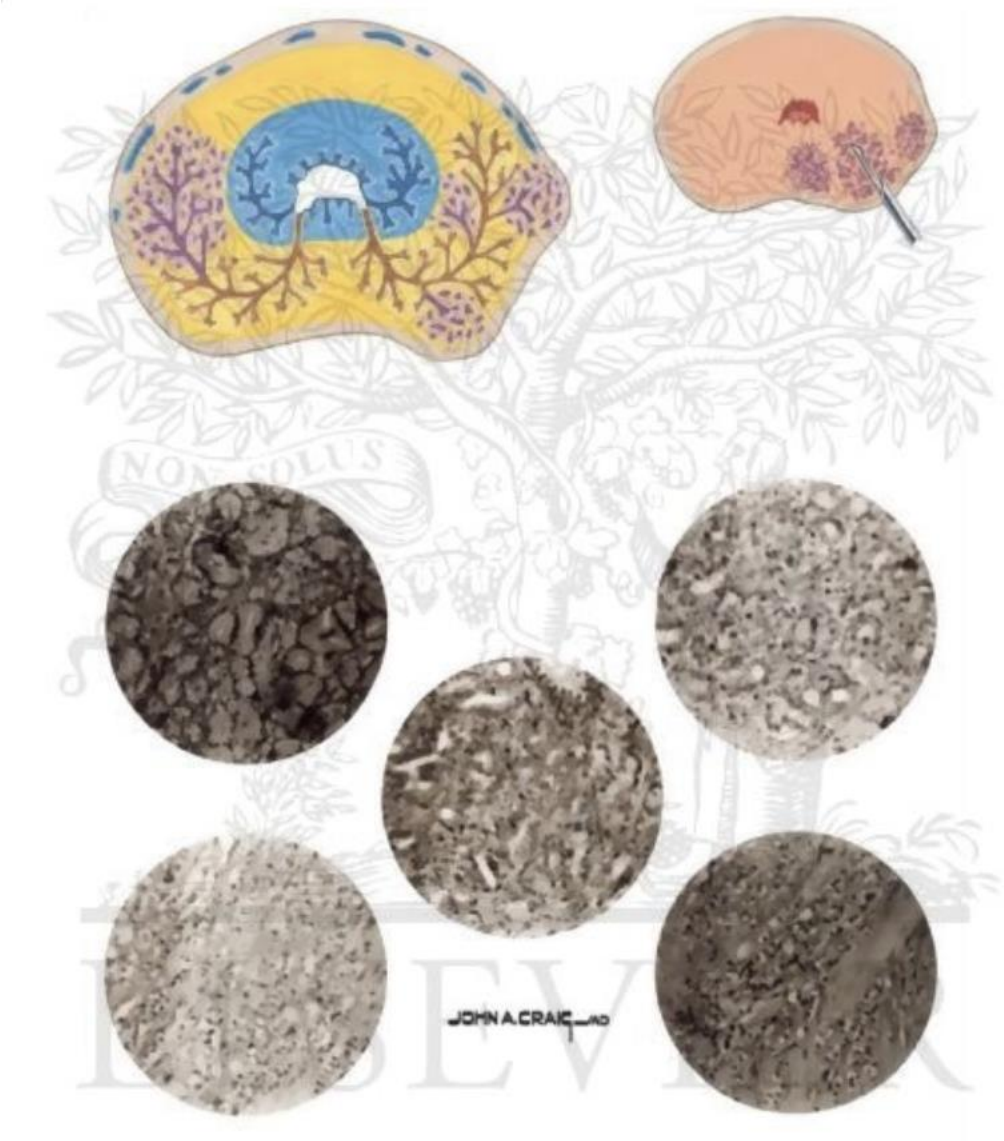

Image 157 – Prostate cancer (https://www.netterimages.com/carcinoma-of-prostate-i-epidemiology-prostate-specific-antigen-staging-and-grading-unlabeled-epidemiology-frank-tiffany).

Prostate cancer is usually suspected based on DRE and/or PSA levels. Definitive diagnosis depends on histopathological verification of adenocarcinoma in prostate

biopsy cores, specimens from transurethral resection of the prostate, or prostatectomy for benign prostatic enlargement [15].

Adhere to PI-RADS guidelines for MRI acquisition and interpretation and evaluate MRI results in multidisciplinary meetings with pathological feedback [15].

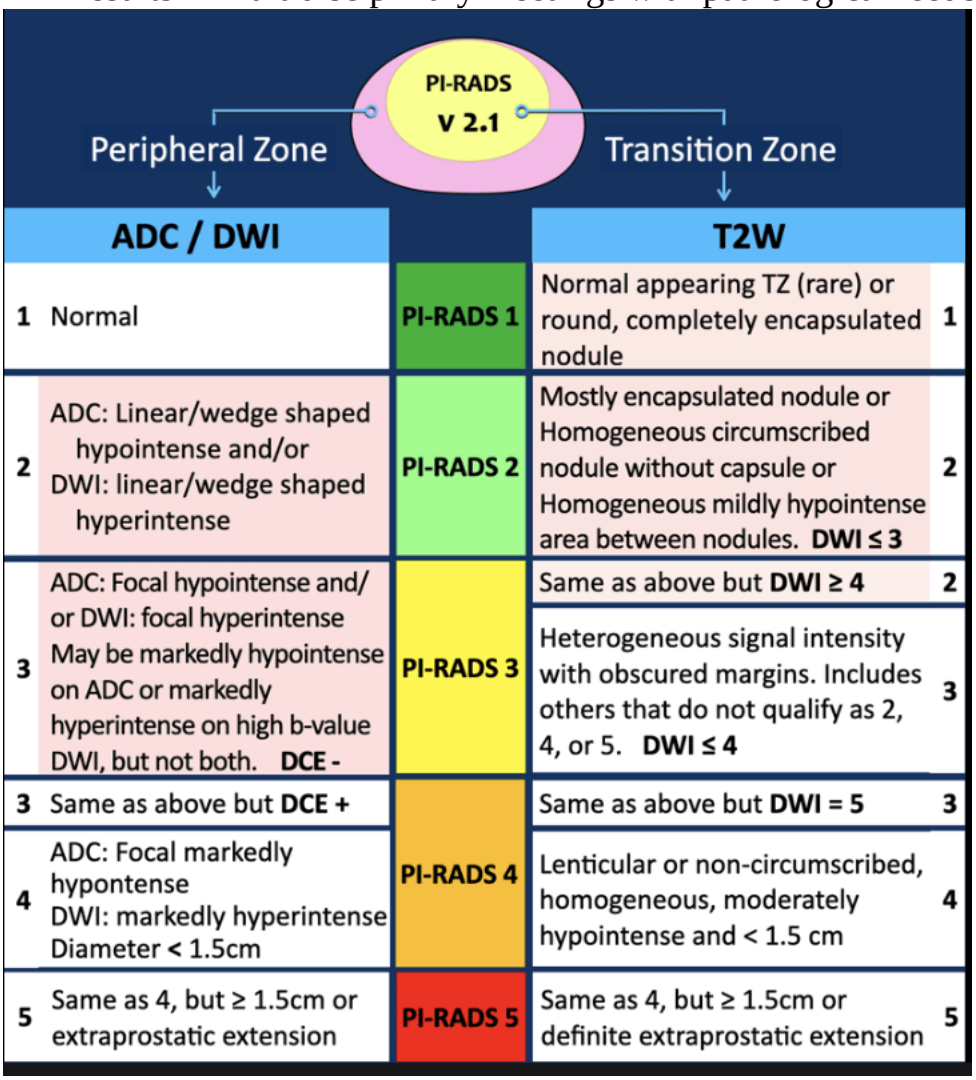

Image 158 – Pi RADS (https://www.google.com/search?client=safari&sca_esv=565268182&rls=en&q=pi+rads+prostate+cancer&tbm=isch&source=lnms&sa=X&ved=2ahUKEwjOkqzY0amBAxVCJBAIHYnRB2oQ0pQJegQIDBAB&biw=1023&bih=725&dpr=2#imgrc=iMCPSEGsOYN-pM).

Perform MRI before prostate biopsy.

When MRI is positive (i.e., PI-RADS ≥ 3), combine targeted and systematic biopsy [15].

Prostate biopsy. At least 8 systematic biopsies are recommended in prostates with a size of about 30 cc and 10 to 12 core biopsies are recommended in larger prostates, with > 12 cores not being significantly more conclusive [15] (Use rectal cleansing with povidone-iodine in men prior to transrectal prostate biopsy).

Disease management.

Active surveillance (AS).

-Offer AS to patients with a life expectancy > 10 years and low- risk disease.
-Perform an MRI before a confirmatory biopsy if no MRI has been performed before the initial biopsy.
-Repeat biopsies should be performed at least once every 3 years for 10 years.
-In case of PSA progression or change in DRE or MRI findings, do not progress to active treatment without a repeat biopsy [15].

Offer AS to highly selected patients with ISUP grade group 2 disease (i.e. < 10% pattern 4, PSA < 10 ng/mL, ≤ cT2a, low disease extent on imaging and low biopsy extent[defined as ≤ 3 positive cores and cancer involvement ≤ 50% core involvement [CI]/per core]), or another single element of intermediate-risk disease with low disease extent on imaging and low biopsy extent, accepting the potential increased risk of metastatic progression [15].

Active treatment (AT)
Radiotherapy.

Offer low-dose rate (LDR) brachytherapy to patients with low risk PCa and good urinary function.	Strong
Use intensity-modulated radia- tion therapy (IMRT)/ volumetric modulated arc therapy (VMAT) plus image-guided radiation therapy (IGRT) with a total dose of 74-80 Gy or moderate hypofractionation (60 Gy/20 fx in4weeksor70Gy/28fxin6 weeks), without androgen deprivation therapy (ADT).	

[15].

Radical prostatectomy is the procedure of medically removing the prostate gland by open and/or laparoscopic surgery. The procedure requires making small incisions on the abdomen or via the perineum.
Salvage radical prostatectomy is usually recommended to patients with local recurrence in the absence of metastases after undergoing external beam radiation therapy, brachytherapy, or cryotherapy. This may, however, lead to increased morbidity. Patients younger than age 70 with organ-confined prostate cancer, with a life expectancy higher than 10 years who have little to no comorbidities, are best suited for radical prostatectomy. However, there are a few complications associated with its use. These complications include incontinence and erectile dysfunction arising from surgical damage to the urinary sphincter and erectile nerves [17].

Cryoptherapy. This method involves the use of surgical insertion of cryoprobes into the prostate under ultrasound guidance. It involves freezing of the prostate gland to a temperature from −100 ˚C to −200 ˚C for about 10 min. However, there are reports of complications as- sociated with the use of this method, including urinary incontinence and urinary retention, erectile dysfunction, fistula, and rectal pain [17].

Brachytherapy includes the direct placement of radioactive sources into the prostate gland with the aid of seeds, injections, or wires under the guidance of transrectal ultrasound. This often involves two techniques: low dose and high dose rates. The low dose rate refers to the permanent implantation of seeds in the prostate tissue, which loses radioactivity gradually , and the latter refers to the supply of a dose of radiation to the prostate tissues with significant risk of leakage to other surrounding organs. The advantage associated with brachytherapy is that it can be completed within a day or less. There is a minimal risk of incontinence in patients without a previous transurethral resection of the prostate (TURP). Erectile function is also not affected. Its disadvantages are usually a requirement for general anesthesia, acute urinary retention risks, and persistent irritative voiding symptoms [17].

Hormonal therapy is also known as androgen deprivation therapy (ADT). This technique is applied in the treatment of advanced and/or metastasized prostate cancer. Its therapeutic mechanism is based on the blockage of testosterone production and other male hormones, preventing them from fueling prostate cancer cells. Therefore, significantly decreased male hormonal levels are responsible for inhibition of the action of androgen on the androgen receptor. This is often achieved using bilateral orchiectomy or medical castration via administration of luteinizing hormone-releasing hormone (LHRH) analogs or antagonists. LHRH analog primarily elevates the luteinizing hormone (LH) and follicle- stimulating hormone (FSH) by stimulating hypophysis receptors, thus, enabling the drug to downregulate the hypophysis receptors with concomitant reduction of LH and FSH levels, leading to suppressed testosterone production. Leuprolide, goserelin, triptorelin, and histrelin are among the common LHRH agonists. The antagonists cause action by block- ing the hypophysis receptors, thereby triggering the immediate inhibition of testosterone synthesis. ADT has, however, been associated with acute and long-term side effects, such as hyperlipidemia, fatigue, hot flashes, flare effect, osteoporosis, insulin resistance, cardiovascular disease, anemia, and sexual dysfunction. **Flutamide** is a type of drugnthat is nonsteroidal and pure antiandrogenic lacking hormonal agonist activity. Flutamide is antiandrogen at the androgen-dependent accessory genitals. Its biological activity is based on 2-hydroxyflutamide. Treating prostate cancer with flutamide and an (LHRH) agonist has produced promising results. In vivo studies of flutamide have shown certain antagonist at the ventral prostate and androgen-dependent seminal vesicles. Flutamide is known to result in hepatic dysfunction; however, a study on antiandrogen therapy (AAT) in combination with flutamide indicated that flutamide could be successful when performing regular hepatic function testing during treatment periods. Maximum androgen blockade (MAB) using flutamide as a second- line hormonal therapy can

give a prostate-specific antigen response without side effects, making this a possible treatment option for patients with HRPC with no bone metastases or whose cancer has progressed more than a year following first-line therapy. **Chlormadinone acetate (CMA**) is an oral steroidal antiandrogen. Chlormadinone has proven to have anticancer activity. Similar to progesterone used in maximum androgen blockade (MAB) therapy as well as monotherapy for prostate cancer in Japan. To determine the success of the antiandrogen chlormadinone acetate in treating stage A prostate cancer, a study of 111 patients who received chlormadinone acetate was conducted. The progression rates linked to antiandrogen therapy for stage A1 and A2 patients were lesser in non-treatment receiving groups, concluding that antiandrogen treatment with chlormadinone acetate inhibited the progression. Chlormadinone is also used to treat benign prostatic hyperplasia, it decreases testosterone level, prostate-specific antigen (PSA) level, and prostate volume, in benign prostatic hyperplasia slowing the progression of Prostate cancer.

Chemotherapy uses anticancer drugs to kill or inhibit the growth of cancerous cells. There has been progress in treatment of prostate cancer after decades of learning and understanding genetics, diagnosis, and treatment. The most common chemotherapy drug for prostate cancer is docetaxel (Taxotere) [17].

TEST

1. A 71-year-old, previously healthy man comes to his physician for a routine health examination. On palpation, there is a nodule in his normal-sized prostate. Laboratory studies show a serum prostate-specific antigen (PSA) level of 17 ng/mL. A routine urinalysis shows no abnormalities. Which of the following histologic findings is most likely to be found in a subsequent biopsy specimen of his prostate?

A Acute prostatitis
B Adenocarcinoma
C Chronic abacterial prostatitis
D Nodular hyperplasia
E Prostatic intraepithelial neoplasia

2. A 65-year-old man has had multiple, recurrent urinary tract infections for the past year. *Escherichia coli* and streptococcal organisms have been cultured from his urine during these episodes, with bacterial counts of more than 10^5/mL. He has difficulty with urination, including starting and stopping the urinary stream. Over the past week, he has again developed burning pain with urination. Urinalysis now shows a pH of 6.5, and specific gravity of 1.020. No blood or protein is present in the urine. Tests for leukocyte esterase and nitrite are positive. Microscopic examination of the urine shows numerous WBCs and a few WBC casts. Which of the following is the most likely condition predisposing him to recurrent infections?

A Epispadias

B Nodular prostatic hyperplasia
C Phimosis
D Posterior urethral valves
E Prostatic adenocarcinoma
F Vesicoureteral reflux

3. Which symptoms are most likely for benign prostatic hyperplasia?

a) nocturia
d) acute urinary retention
c) renal colic
d) frequency
e) urgency

4. Which diseases are contraindications for open adenomectomy?

a) renal insufficiency
b) chronic bronchitis
c) stone in a bladder
d) chronic pyelonephritis, active phase

5. Indicate a normal size of prostate?

a) 10-15 sm 3
b) 15-20 sm 3
c) 20-25 sm 3
d) 30-40 sm 3

6. Which medications consist of conservative treatment of BPH?

a) tamsulosin
b) sertraline
c) dutasteride
d) finasteride
e) tadalafil
f) ampicillinum

7. A 72-year-old man has had increasing difficulty with urination for the past 10 years. Now he must get up several times each night because of a feeling of urgency, but each time the urine volume is not great. He has difficulty starting and stopping urination. On physical examination, the prostate is enlarged to twice its normal size, but is not tender to palpation. One year ago, his serum prostate-specific antigen

(PSA) level was 6 ng/mL, and it is still at that level when retested. Which of the following drugs is most likely to be effective in treatment of this man?

A Estrogen (hormone)
B Finasteride (5α-reductase inhibitor)
C Mitoxantrone (chemotherapy agent)
D Nitrofurantoin (antibiotic)
E Prednisone (corticosteroid)

8. What a method confirms a diagnosis “prostate cancer”?

a) retrograde urethrography
b) PSA
c) intravenous urography
d) transrectal biopsy of prostate
e) DRE

TASKS

1. A 71-year-old, previously healthy man comes to his physician for a routine health examination. On palpation, there is a nodule in his normal-sized prostate. Laboratory studies show a serum prostate-specific antigen (PSA) level of 17 ng/mL. A routine urinalysis shows no abnormalities. Indicate potential diagnosis. Which of the following histologic findings is most likely to be found in a subsequent biopsy specimen of his prostate?

2. An 85-year-old man has experienced urinary hesitancy and nocturia for the past year. He has had increasing back pain for the past 6 months. On digital rectal examination, there is a hard, irregular prostate gland. A bone scan shows increased areas of uptake in the thoracic and lumbar vertebrae. Laboratory studies show a serum alkaline phosphatase level of 300 U/L, and serum prostate-specific antigen (PSA) level of 72 ng/mL. The blood urea nitrogen concentration is 44 mg/dL, and the serum creatinine level is 3.8 mg/dL. Transrectal biopsy specimens of all lobes of the prostate are obtained. Microscopic examination shows that more than 90% of the tissue has a pattern of cords and sheets of cells with hyperchromatic pleomorphic nuclei, prominent nuclei, and scant cytoplasm. Which of the following is the best classification for this patient’s disease?

Check your answers:

1. b	5. b
2. b.	6. acde

3. abde 7. b
4. ad 8. d

1. prostate cancer
2. prostate cancer. TNM

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Renal masses

Definition. The modern era has brought an appreciation that renal cell carcinoma (RCC) includes several distinct subtypes derived from the various parts of the nephron, each with a unique genetic basis and tumor biology (Rini et al, 2009; Linehan and Ricketts, 2013). Other major advances in the past several decades have included the introduction of radical nephrectomy (RN) followed by a trend toward less radical approaches, including kidney-sparing surgery and a variety of minimally invasive approaches (Robson, 1963; Novick, 2007; Volpe et al, 2011). One common theme that has persisted is that RCC remains primarily a surgical disease and, although immune-based and targeted molecular approaches can provide durable clinical responses, cure is rarely seen without complete surgical excision of RCC (Rini et al, 2009; Kroeger et al, 2014). Unfortunately, the incidence of RCC is gradually increasing and, despite a trend toward earlier detection, mortality rates remain high [5].

Renal masses can be malignant, benign, or inflammatory as classified by Barbaric (1994) (image 159), or they can be classified based on radiographic appearance (simple cystic, complex cystic, solid) [5].

Malignant renal tumors include RCC, urothelium-based malignancies, sarcomas, embryonic or pediatric tumors, lymphomas, and metastases [5].

BOX 57-1 Renal Masses Classified by Pathologic Features

MALIGNANT
- Renal cell carcinoma
- Urothelium-based cancers
  - Urothelial carcinoma
  - Squamous cell carcinoma
  - Adenocarcinoma
- Sarcomas
  - Leiomyosarcoma
  - Liposarcoma
  - Angiosarcoma
  - Hemangiopericytoma
  - Malignant fibrous histiocytoma
  - Synovial sarcoma
  - Osteogenic sarcoma
  - Clear cell sarcoma
  - Rhabdomyosarcoma
- Wilms tumor
- Primitive neuroectodermal tumor
- Carcinoid tumor
- Lymphoma/leukemia
- Metastasis
- Invasion by adjacent neoplasm

BENIGN
- Cystic lesions
  - Simple cyst
  - Hemorrhagic cyst

BENIGN—cont'd
- Solid lesions
  - Angiomyolipoma
  - Oncocytoma
  - Renal adenoma
  - Metanephric adenoma
  - Cystic nephroma
  - Mixed epithelial-stromal tumor
  - Reninoma (juxtaglomerular cell tumor)
  - Leiomyoma
  - Fibroma
  - Hemangioma
- Vascular lesions
  - Renal artery aneurysm
  - Arteriovenous malformation
- Pseudotumor

INFLAMMATORY
- Abscess
- Focal pyelonephritis
- Xanthogranulomatous pyelonephritis
- Infected renal cyst
- Tuberculosis
- Rheumatic granuloma

BOX 57-2 Radiologic and Pathologic Correlates for Renal Masses

SIMPLE CYSTIC
- Benign cyst
- Parapelvic cyst
- Hydronephrosis
- Caliceal diverticulum

COMPLEX CYSTIC
- Cystic RCC
- Hemorrhagic cyst
- Hyperdense cyst
- Benign complex cyst
- Cystic nephroma
- Mixed epithelial-stromal tumor
- Cystic Wilms tumor
- Infected cyst/abscess
- Hydrocalix
- Arteriovenous malformation
- Renal artery aneurysm

STRONGLY ENHANCING SOLID MASS
- Clear cell RCC
- Angiomyolipoma
- Oncocytoma (occasionally)
- Papillary RCC (occasionally)
- Chromophobe RCC (occasionally)

MODERATELY ENHANCING SOLID MASS
- Papillary RCC
- Chromophobe RCC
- Oncocytoma
- Other benign tumors
  - Fat-poor angiomyolipoma
  - Adenoma
  - Metanephric adenoma
- Unifocal lymphoma
- Sarcoma
- Lobar nephronia
- Infarct

MULTIFOCAL/BILATERAL MASSES
- Familial RCC
- Metastases
- Sporadic, multifocal RCC
- Angiomyolipomas (tuberous sclerosis)
- Lymphoma
- Cystic tumors (autosomal dominant polycystic kidney disease)

INFILTRATIVE MASS
- Lymphoma
- High-grade urothelial carcinoma
- Sarcomatoid differentiation
- Collecting duct carcinoma
- Renal medullary carcinoma
- Xanthogranulomatous pyelonephritis
- Metastasis (occasionally)

CALCIFIED MASS
- RCC
- Urothelial carcinoma
- Benign complex cyst
- Xanthogranulomatous pyelonephritis
- Renal artery aneurysm
- Concomitant nephrolithiasis

FAT-CONTAINING MASS
- Angiomyolipoma
- Liposarcoma
- Lipoma

RCC, renal cell carcinoma.
Modified from Simmons MN, Herts BR, Campbell SC. Image based approaches to the diagnosis of renal masses [lesson 39]. AUA Update Se 2007;26:382–91.

Image 159 – Classification of renal masses (Campbell – Walsh Urology, chapter 57, malignant renal tumors).

Ultrasonography is a noninvasive and relatively inexpensive modality that can differentiate cystic versus solid renal masses, and it continues to play an important role for such lesions. Strict ultrasonographic criteria for simple cysts have been defined and include a smooth cyst wall, a round or oval shape without internal echoes, and through-transmission with strong acoustic shadows posteriorly [5].

If these criteria are met, observation is sufficient in an asymptomatic patient. In evaluating complex renal cysts, important ultrasonographic features include thickness and contour of the cyst wall, number and thickness of any septa, presence of any calcifications, density of cyst fluid, and presence of solid or nodular components [5].

A renal mass that is not clearly a simple cyst by strict ultrasound criteria should be evaluated further with computed tomography (CT).

Magnetic resonance imaging (MRI) is the alternate standard imaging modality for the characterization of a renal mass. Enhancement indicative of malignancy can also be assessed by MRI with intravenous gadolinium-labeled diethylenetriaminepentaacetic acid, although the assessment is qualitative rather than quantitative . One concern with MRI with gadolinium is the uncommon but potentially serious complication of nephrogenic systemic fibrosis, which is more common in patients with chronic kidney disease (CKD) [5].

Evaluation of Cystic Renal Lesions

The differentiation between benign renal cysts and cystic RCC remains one of the more common and difficult problems in renal imaging (Bosniak, 2012). When a complex renal cyst is identified, determination of its benign or malignant nature is based on evaluation of the wall of the lesion; its thickness and contour; the number, contour, and thickness of any septa; the amount, character, and location of any calcifications; the density of fluid in the lesion; the margination of the lesion; and the presence of solid components. Bosniak developed a useful classification scheme primarily based on CT imaging criteria that divides renal cystic lesions into categories that are distinct from one another in terms of the likelihood of malignancy (Israel and Bosniak, 2005) (image 160).

Category I lesions are uncomplicated, simple, benign cysts of the kidney that are straightforward to diagnose on ultrasonography, CT, or MRI. These are by far the most common renal cystic lesions, and in the absence of associated symptoms, no treatment is necessary.

Category II lesions are minimally complex cysts that are generally benign but have some radiologic findings that cause concern. These lesions include septated cysts, cysts with calcium in the wall or septum, infected cysts, and hyperdense (high-density) cysts (Israel and Bosniak, 2005). Hyperdense cysts are benign lesions that contain old, degenerated, or clotted blood; therefore, the CT attenuation of their contents is increased (>20 HU). Classic hyperdense renal cysts are small (<3 cm), round, and sharply marginated and do not enhance after the administration of contrast material.

Category III lesions are more complex renal cysts that cannot be confidently distinguished from malignant neoplasms. The radiographic features include thickened irregular or smooth walls or septa in which measurable enhancement can be observed [5].

Category IV lesions have large cystic components; irregular, shaggy margins; and most important, solid enhancing portions that provide a definitive diagnosis of malignancy (Israel and Bosniak, 2005). Category IV lesions are almost invariably cystic RCCs that, if localized, require surgical treatment [5].

TABLE 57-1 Classification of Complex Renal Cysts

BOSNIAK CLASSIFICATION	RADIOGRAPHIC FEATURES	RISK OF MALIGNANCY	MANAGEMENT
I	Water density Homogeneous, hairline thin wall No septa No calcification No enhancement	None	Surveillance not necessary
II	Few hairline septa in which "perceived" enhancement may be present Fine calcification or short segment of slightly thickened calcification in wall or septa No unequivocal enhancement	Minimal	Surveillance not necessary
	Hyperdense lesion: ≤3 cm, well marginated, with no unequivocal enhancement	Minimal	Periodic surveillance
IIF	Multiple hairline thin septa Minimal smooth wall thickening "Perceived" enhancement of wall or septae may be present Calcification may be thick or nodular, but must be without enhancement Generally well marginated No unequivocal enhancement	3%-5%	Periodic surveillance
	Hyperdense lesion: >3 cm or totally intrarenal, with no enhancement	5%-10%	Periodic surveillance
III	"Indeterminate," thickened irregular or smooth walls or septa in which measurable enhancement is present	50%	Surgical excision
IV	Clearly malignant lesions that can have all the criteria of category III but also contain enhancing soft-tissue components	75%-90%	Surgical excision

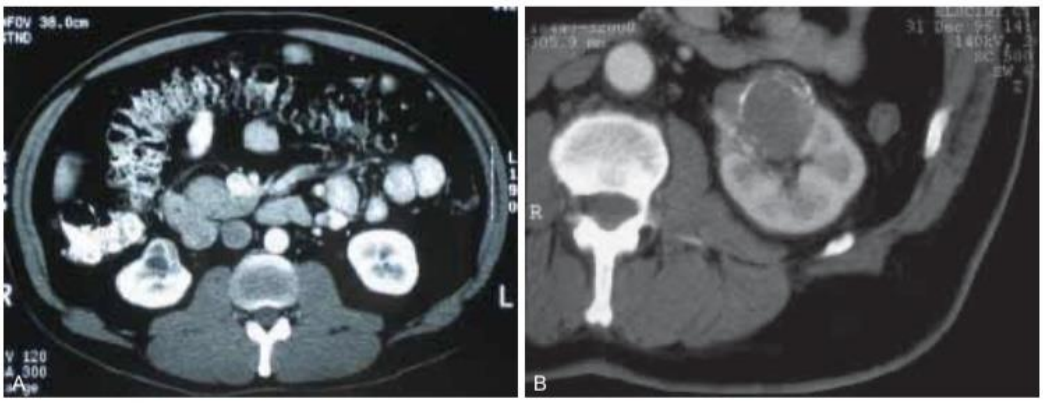

Figure 57-5. **Bosniak category III cysts. A, Computed tomography (CT) scan shows complex right renal cyst with thick and irregular septa and inhomogeneous character. B, CT scan shows somewhat thick-walled, complex left renal cyst also exhibiting irregular calcification and moderate heterogeneity. (Courtesy Dr. Terrence Demos, Maywood, IL.)**

Image 160 – Bosniak category (Campbell – Walsh Urology, chapter 57, malignant renal tumors).

RENAL CELL CARCINOMA

Incidence

Overall, approximately 12 new cases are diagnosed per 100,000 population per year, with a male-to-female predominance of 3: 2 (Siegel et al, 2013). This is

primarily a disease of older adults, with typical presentation between 50 and 70 years of age (Pantuck et al, 2001b; Wallen et al, 2007; Siegel et al, 2013) [5].
RCC in childhood is uncommon, representing only 2.3% to 6.6% of all renal tumors in children (Broecker, 2000). Mean age at presentation in children is 8 to 9 years, and the incidence is similar in boys and in girls. Although Wilms tumor is much more common in younger children, RCC is as common as Wilms tumor during the second decade of life. RCC in children and young adults is more likely to be symptomatic, locally advanced, high grade, and of unfavorable histologic subtypes [5].

Etiology

RCCs were traditionally thought to arise primarily from the proximal convoluted tubules, and this is probably true for the clear cell and papillary variants. However, we now know that other histologic subtypes of RCC, such as chromophobe RCC and collecting duct carcinoma, are derived from the more distal components of the nephron.

The most generally accepted environmental risk factor for RCC is *tobacco exposure*, although the relative associated risks have been modest, ranging from 1.4 to 2.5 compared with controls [5].

Obesity is now accepted as another major risk factor for RCC, with an increased relative risk of 1.07 for each additional unit of body mass index. Potential mechanisms linking obesity to RCC include increased insulin-like growth factor-1 expression, increased circulating estrogen levels, and increased arteriolar nephrosclerosis and local inflammation (Calle and Kaaks, 2004; Ljungberg et al, 2011) [5].

Hypertension appears to be the third major etiologic factor for RCC. The proposed mechanisms are hypertension- induced renal injury and inflammation or metabolic or functional changes in the renal tubules that may increase susceptibility to carcinogens (Lipworth et al, 2006; Ljungberg et al, 2011) [5].

Other potential iatrogenic causes include regular *usage of non- steroidal anti-inflammatory drugs*, which was associated with a relative risk of 1.51, while aspirin and acetaminophen were not associated with any increased risk (Cho et al, 2011). Retroperitoneal radiation therapy, typically administered for Wilms tumor or testicular cancer, appears to be a risk factor for RCC, although the relative risks are low (Romanenko et al, 2000). An increased incidence of RCC is also observed in patients with end-stage renal disease and certain familial syndromes such as tuberous sclerosis, as discussed later (Linehan and Ricketts, 2013) [5].

Since the early 1990s, significant advances have been made in our understanding of the molecular genetics of RCC. We now, more than ever, recognize the distinct nature of the various subtypes of RCC, and advances in molecular genetics have contributed to a major revision in the histologic classification of this malignant neoplasm. A direct and beneficial impact on patient management has also been achieved, with targeted molecular agents now extending survival for patients with advanced RCC [5].

The familial form of **clear cell RCC** is *von Hippel-Lindau disease*.

This is a relatively rare autosomal dominant disorder that occurs with a frequency of 1 per 36,000 population. Major manifestations include the development of RCC, pheochromocytoma, retinal angiomas, and hemangioblastomas of the brainstem, cerebellum, or spinal cord (Kim et al, 2010; Linehan and Ricketts, 2013). All these tumor types are highly vascular and can lead to substantial morbidity, much of which can be avoided with prompt recognition and careful, skilled management. Central nervous system lesions can lead to paralysis or death and retinal lesions to blindness if they are not identified and managed in an expedient manner. Other common or important manifestations of von Hippel-Lindau disease include renal and pancreatic cysts, inner ear tumors, and papillary cystadenomas of the epididymis (Neumann and Zbar, 1997). An increased incidence of neuroendocrine tumors of the pancreas has also been reported in von Hippel-Lindau disease (Zbar et al, 1999) [5].

RCC develops in about 50% of patients with von Hippel-Lindau disease and is distinctive for early age at onset (often in the third, fourth, or fifth decade of life) and bilateral and multifocal involvement.

Early clues to the genetic elements involved in RCC development came from **cytogenetics**. These studies demonstrated a common *loss of chromosome 3* in kidney cancer, particularly the clear cell variant, and led to intensive efforts to find a tumor suppressor gene in this region (image 161) [5].

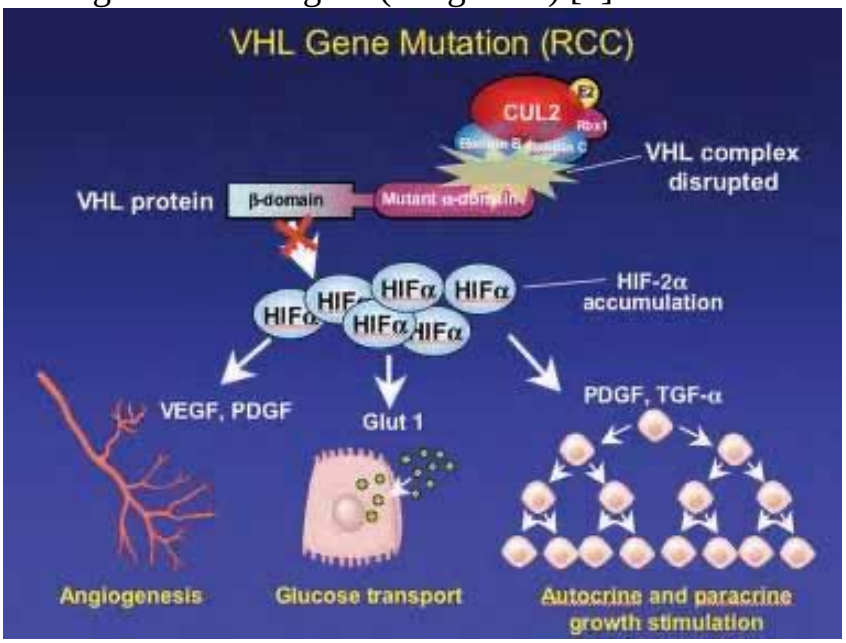

Image 161 – Genetic reason of RCC (Campbell – Walsh Urology, chapter 57, malignant renal tumors).

Several lines of evidence demonstrate that RCC is immunogenic, and this knowledge has stimulated intensive efforts to harness the immune system to improve outcomes for patients with advanced disease (1862).

RCC has long been recognized as one of the most vascular of cancers, as reflected by the distinctive neovascular pattern exhibited on renal angiography and robust enhancement observed on dedicated renal CT. The primary angiogenesis inducer in clear cell RCC is VEGF, which is suppressed by the wild-type VHL protein under normal conditions and is dramatically upregulated during tumor

development (Gnarra et al, 1996; Iliopoulos et al, 1996). Functional relevance of VEGF has been demonstrated by studies showing increased levels of VEGF in the serum and urine of patients with RCC. Increased expression of VEGF is also found in hypervascular tumors when compared to hypovascular tumors (Takahashi et al, 1994) [5].

Clear cell RCC accounts for 70% to 80% of all RCCs, representing the garden variety of RCC formerly known as "conventional" RCC (Störkel et al, 1997; Deng and Melamed, 2012). These tumors are typically yellow when they are bivalved and are highly vascular, containing a network of delicate vascular sinusoids interspersed between sheets or acini of tumor cells. On microscopic examination, clear cell RCC can include clear cell, granular cell, or mixed types.

Clear cells are typically round or polygonal with abundant cytoplasm containing glycogen, cholesterol, cholesterol esters, and phospholipids, all of which are readily extracted by the solvents used in routine histologic preparations, contributing to the clear appearance of the tumor cells (Farrow, 1997). In general, patients with clear cell RCC have a worse prognosis compared with papillary or chromophobe RCC, even after stratification for stage and grade (Cheville et al, 2003; Deng and Melamed, 2012). Chromosome 3 alterations occur in more than 90% of clear cell RCCs, leading to mutation or inactivation of the *VHL, PBRM1, SETD2,* or *BAP1* genes, which are all present on this portion of the genome (Cancer Genome Atlas Research Network, 2013; Linehan and Ricketts, 2013). The familial form of clear cell RCC, the von Hippel-Lindau syndrome, in which the *VHL* tumor suppressor gene is inactivated, has already been reviewed (image 162).

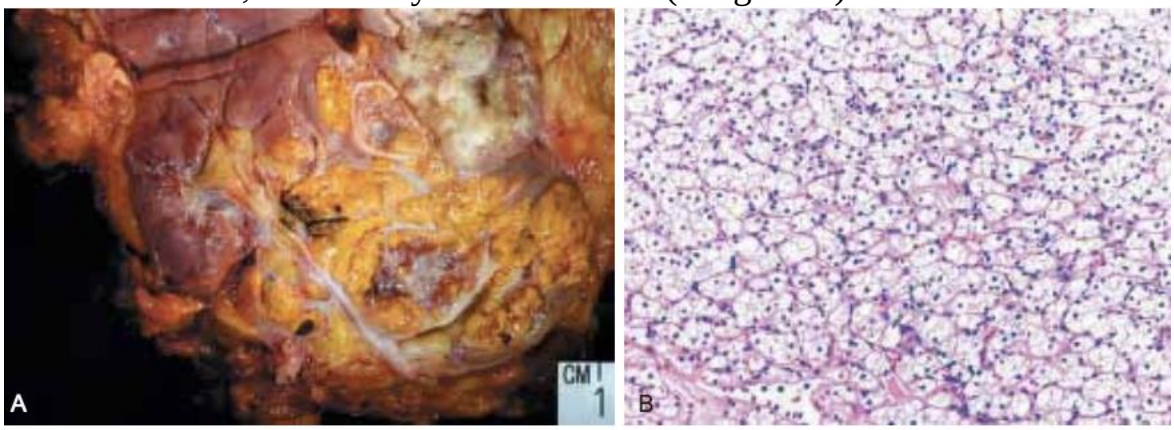

Image 163 – Clear cell RCC (A – macroscopic (typicall yellow color. B – microscopic (homogeneous nests of cells with clear cytoplasm)

Papillary RCC, which was also designated chromophilic RCC in previous classification schemes, is the second most common histologic subtype (Sukov et al, 2012). It represents 10% to 15% of all RCCs, with several features that distinguish it from clear cell RCC [5].

On microscopic examination, most tumors in this category consist of basophilic or eosinophilic cells arranged in papillary or tubular configuration. Gross features of **papillary RCC** include beige to white color, spherical boundary, and frequent hemorrhage, which may mimic cystic components radiologically. One unique

feature of papillary RCC is its tendency toward multicenricity, which approaches 40% in many series and occurs more commonly in patients with end-stage renal failure and acquired renal cystic disease (Deng and Melamed, 2012) [5].
Type 1 papillary RCC, the more common form, consists of basophilic cells with scant cytoplasm; type 2 papillary RCC includes potentially more aggressive variants with eosinophilic cells and abundant granular cytoplasm (Pignot et al, 2007).
The cytogenetic abnormalities associated with the more common type 1 papillary RCC are characteristic and include trisomy of chromosomes 7 and 17 and loss of the Y chromosome (Kovacs et al, 1989b) (image 164) [5].

At present, most authors believe that papillary RCC, and type 1 papillary RCC, carries a better prognosis than clear cell RCC when compared grade for grade and stage for stage (Deng and Melamed, 2012).
Papillary adenomas are small (≤5-mm) tumors that resemble papillary RCC under the microscope, are often well encapsulated and low grade, and are commonly found at autopsy (Algaba et al, 2011).

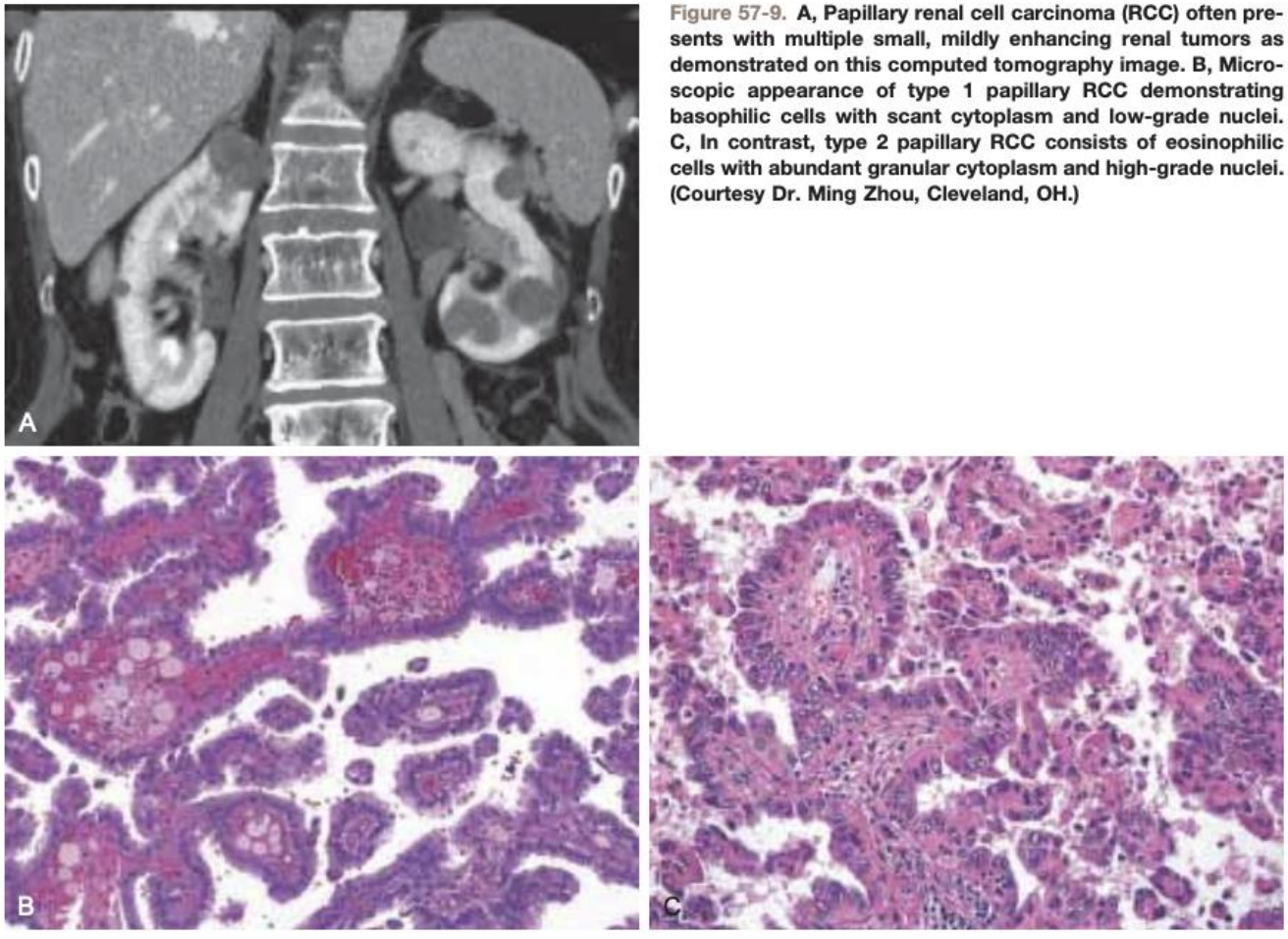

Figure 57-9. **A, Papillary renal cell carcinoma (RCC) often presents with multiple small, mildly enhancing renal tumors as demonstrated on this computed tomography image. B, Microscopic appearance of type 1 papillary RCC demonstrating basophilic cells with scant cytoplasm and low-grade nuclei. C, In contrast, type 2 papillary RCC consists of eosinophilic cells with abundant granular cytoplasm and high-grade nuclei. (Courtesy Dr. Ming Zhou, Cleveland, OH.)**

Image 164 – Papillary RCC [5].

Chromophobe RCC, first described by Thoenes and colleagues in 1985, is a distinctive histologic subtype of RCC that represents 5% of all RCCs and appears to be derived from the cortical portion of the collecting duct (Algaba et al, 2011).
The tumor cells typically exhibit a relatively transparent cytoplasm with a fine reticular pattern that has been described as a “plant cell” appearance. Most

chromophobe RCCs are resistant to the pigment used during typical hematoxylin and eosin staining, but eosinophilic variants constitute about 30% of cases (Thoenes et al, 1988; Nagashima, 2000). In either case, a perinuclear clearing o**r "halo" is typically found and electron microscopic findings consist of numerous 150- to 300-nm microvesicles, which are the single most distinctive and defining feature of chromophobe cell carcinoma. These microvesicles characteristically stain positive for Hale colloidal iron, indicating the presence of a mucopolysaccharide unique to chromophobe RCC (image 165) [5].**

Genetic analysis typically reveals massive chromosomal losses, most frequently the whole chromosomes 1, 2, 6, 10, 13, 17, 21, and Y, and flow cytometric analysis has demonstrated hypodiploid DNA content in most cases (Bugert et al, 1997). Most studies of the clinical behavior of chromophobe RCC suggest a better prognosis for localized chromophobe RCC than for clear cell RCC but a poor outcome in the subset of patients with sarcomatoid features or metastatic disease (Renshaw et al, 1996; Klatte et al, 2008) [5].

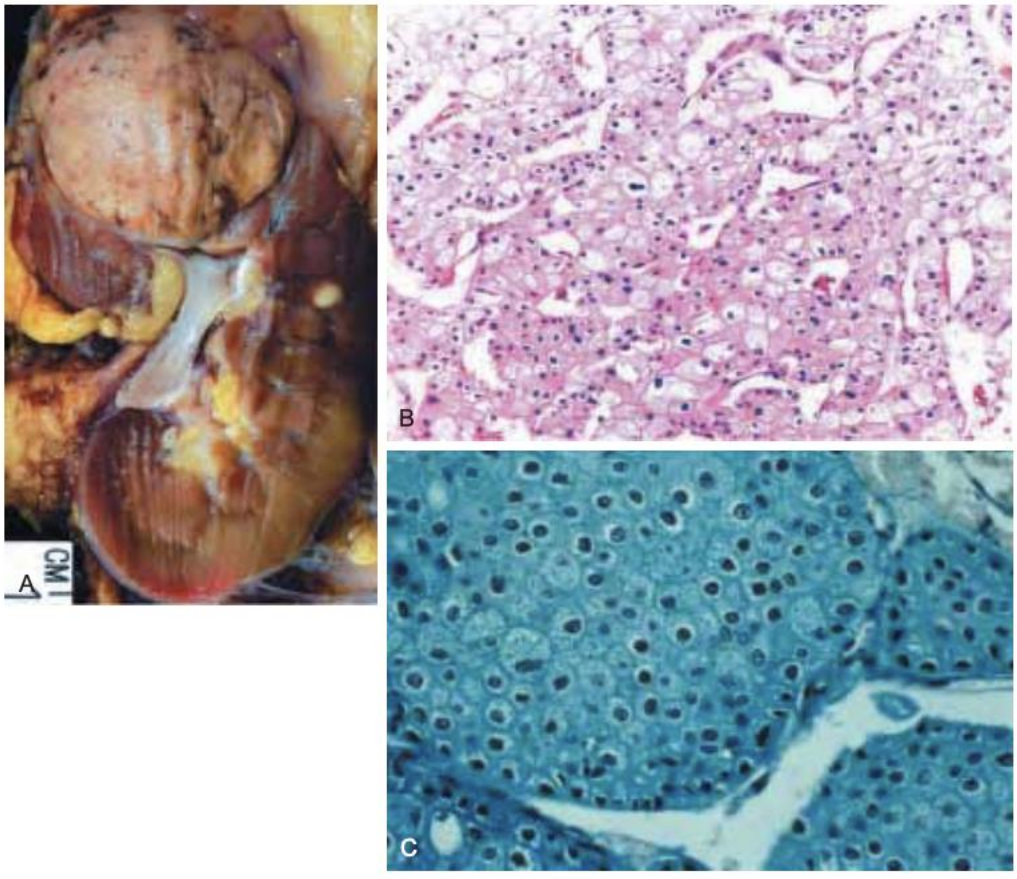

Image 165 – Chromophobe RCC (a – macroscopic, b- distinct cytoplasmic borders, perinuclear "halos," and nuclear "raisins." , c- chromophobe RCC stains positive for Hale colloidal iron and demonstrates multiple microvesicles on analysis by electron microscopy).

Carcinoma of the collecting ducts of Bellini is a relatively rare subtype of RCC, accounting for less than 1% of all RCCs (Algaba et al, 2011). Collecting duct carcinoma often presents earlier in life and with advanced stage (Tokuda et al, 2006; Karakiewicz et al, 2007c; Wright et al, 2009). Small collecting duct carcinomas can arise in a medullary pyramid, but most are large, infiltrative masses and extension

into the cortex is common (Pickhardt et al, 2001; Deng and Melamed, 2012). On microscopic examination, these tumors consist of an admixture of dilated tubules and papillary structures typically lined by a single layer of cuboidal cells, often creating a cobblestone appearance. Deletions on chromosome 1q and monosomy of chromosomes 6, 8, 11, 18, 21, and Y have been reported, but the number of tumors analyzed thus far has been limited (Fuzesi et al, 1992; Steiner et al, 1996; Polascik et al, 2002) [5].

Most reported cases of collecting duct carcinoma have been high grade, advanced stage, and unresponsive to conventional therapies (Tokuda et al, 2006; Karakiewicz et al, 2007c; Wright et al, 2009) [5].

Sarcomatoid differentiation is found in 1% to 5% of RCCs, most commonly in association with clear cell RCC or chromophobe RCC, but variants of most other subtypes of RCC have been described (Ro et al, 1987; Shuch et al, 2012a).

Clinical Presentation

Because of the sequestered location of the kidney within the retroperitoneum, many renal masses remain asymptomatic and nonpalpable until they are locally advanced. With the more pervasive use of noninvasive imaging for the evaluation of a variety of nonspecific symptom complexes, more than 60% of RCCs are now detected incidentally (Silverman et al, 2008) [5].

Symptoms associated with RCC can be due to local tumor growth, hemorrhage, paraneoplastic syndromes, or metastatic disease.

Flank pain is usually due to hemorrhage and clot obstruction, although it can also occur with locally advanced or invasive disease.

The classic triad of flank pain, gross hematuria, and palpable abdominal mass is now rarely found. This is fortunate because this constellation of findings almost always denotes advanced disease, and some refer to it as the “too late triad.” Other indicators of advanced disease include constitutional symptoms such as weight loss, fever, and night sweats, and physical examination findings such as palpable cervical lymphadenopathy, nonreducing varicocele, and bilateral lower extremity edema resulting from venous involvement [5].

THUS:

Incidental presentation

Symptoms of localized disease:

Hematuria Flank pain

Abdominal mass

Perirenal hematoma

Obstruction of the inferior venal cava:

Bilateral lower extremity edema

Nonreducing or right-sided varicocele

Symptoms of systemic disease:

Persistent cough Bone pain Cervical lymphadenopathy

Constitutional symptoms

Weight loss/fever/malaise

Paraneoplastic syndromes

A less common but important presentation of RCC is that of spontaneous perirenal hemorrhage, in which the underlying mass may be obscured. Zhang and colleagues (2002) have shown that more than 50% of patients with perirenal hematoma of unclear etiology have an occult renal tumor, most often AML or RCC. Repeat CT a few months later will often provide a definitive diagnosis [5].

Paraneoplastic syndromes are found in 10% to 20% of patients with RCC. Under normal circumstances, the kidney produces 1,25-dihydroxycholecalciferol, renin, erythropoietin, and various prostaglandins, all of which are tightly regulated to maintain homeostasis. RCC may produce these substances in pathologic amounts, and it may also elaborate a variety of other physiologically important factors, such as parathyroid hormone– like peptides, lupus-type anticoagulant, human chorionic gonadotropin, insulin, and various cytokines and inflammatory mediators. These substances are believed to be responsible for the development of constitutional symptoms such as weight loss, anemia, and paraneoplastic syndromes [5].

Hypercalcemia has been reported in up to 13% of patients with RCC and can be due to either paraneoplastic phenomena or osteolytic metastatic involvement of the bone (Klatte et al, 2007c; Schwarzberg and Michaelson, 2009) [5].
The signs and symptoms of hypercalcemia are often nonspecific and include nausea, anorexia, fatigue, and decreased deep tendon reflexes. Medical management predominates and includes vigorous hydration followed by diuresis with furosemide and the selective use of bisphosphonates, corticosteroids, or calcitonin. Bisphosphonate therapy is now established as a standard of care for patients with hypercalcemia of malignancy, if renal function is adequate (Schwarzberg and Michaelson, 2009). Zoledronic acid, 4 mg intravenously every 4 weeks, appears to be particularly effective in patients with RCC but must be withheld in the presence of renal insufficiency [5].

Hypertension and polycythemia are other important paraneoplastic syndromes commonly found in patients with RCC (Moein and Dehghani, 2000).
Hypertension associated with RCC can be secondary to increased production of renin directly by the tumor; compression or encasement of the renal artery or its branches, effectively leading to renal artery stenosis; or arteriovenous fistula within the tumor. Less common causes include polycythemia, hypercalcemia, ureteral obstruction, and increased intracranial pressure associated with cerebral metastases. Polycythemia associated with RCC can be due to increased production of erythropoietin, either directly by the tumor or by the adjacent parenchyma in response to hypoxia induced by tumor growth (Wiesener et al, 2007) [5].

One of the more fascinating paraneoplastic syndromes associated with RCC is **nonmetastatic hepatic dysfunction, or Stauffer syndrome**, which has been reported in 3% to 20% of cases (Giannakos et al, 2005; Kranidiotis et al, 2009). Almost all patients with Stauffer syndrome have an elevated serum alkaline phosphatase level, 67% have elevated prothrombin time or hypoalbuminemia, and 20% to 30% have elevated serum bilirubin or transaminase levels. Other common findings include thrombocytopenia and neutropenia, and typical symptoms include fever and weight loss, which is not surprising given that many patients are found to harbor discrete regions of hepatic necrosis. **Hepatic metastases must be excluded**.

Biopsy, when indicated, often demonstrates nonspecific hepatitis associated with a prominent lymphocytic infiltrate. Elevated serum levels of IL-6 have been found in patients with Stauffer syndrome, and it is believed that this and other cytokines may play a pathogenic role. Hepatic function normalizes after nephrectomy in 60% to 70% of cases. Persistence or recurrence of hepatic dysfunction is almost always indicative of the presence of viable tumor and thus represents a poor prognostic finding [5].

A variety of other less common but distinct paraneoplastic syndromes associated with RCC include Cushing syndrome, hyperglycemia, galactorrhea, neuromyopathy, clotting disorders, and cerebellar ataxia (Sufrin et al, 1989). **In general, treatment of paraneoplastic syndromes associated with RCC has required surgical excision or systemic therapy and, except for hypercalcemia, medical therapies have not proved helpful.**

Diagnostic evaluation

Review of the literature describing the use of dipstick analysis for hematuria and **ultrasonography or CT for screening for RCC supports these conclusions** (Herts and Baker, 1995; Cohn and Campbell, 2000; Carrizosa and Godley, 2009).
Several investigators are now reporting novel molecular assays to detect RCC-related biomarkers in the urine or serum that may substantially alter our perspective about screening for RCC. These assays can detect microsatellite alterations in the DNA, *VHL* gene mutations or hypermethylation, upregulation of angiogenic factors (including VEGF), or expression of RCC-specific proteins such as CA-IX and aquaporin-1 (Jonasch et al, 2012) [5].

Staging

The tumor, node, and metastasis (TNM) system proposed by the Union International Contre le Cancer represents a major improvement because it defines the anatomic extent of disease more explicitly (Leung and Ghavamian, 2002; Nguyen and Campbell, 2006; Decastro and McKiernan, 2008).

Other major revisions in 2009 included a reclassification of tumors with adrenal metastasis, venous thrombi, and lymphatic involvement, representing a substantial departure from previous staging paradigms for RCC. Contiguous extension of tumor into the ipsilateral adrenal gland is now classified as T4 and metastatic involvement of either adrenal as M1, reflecting likely patterns of dissemination (image 166).

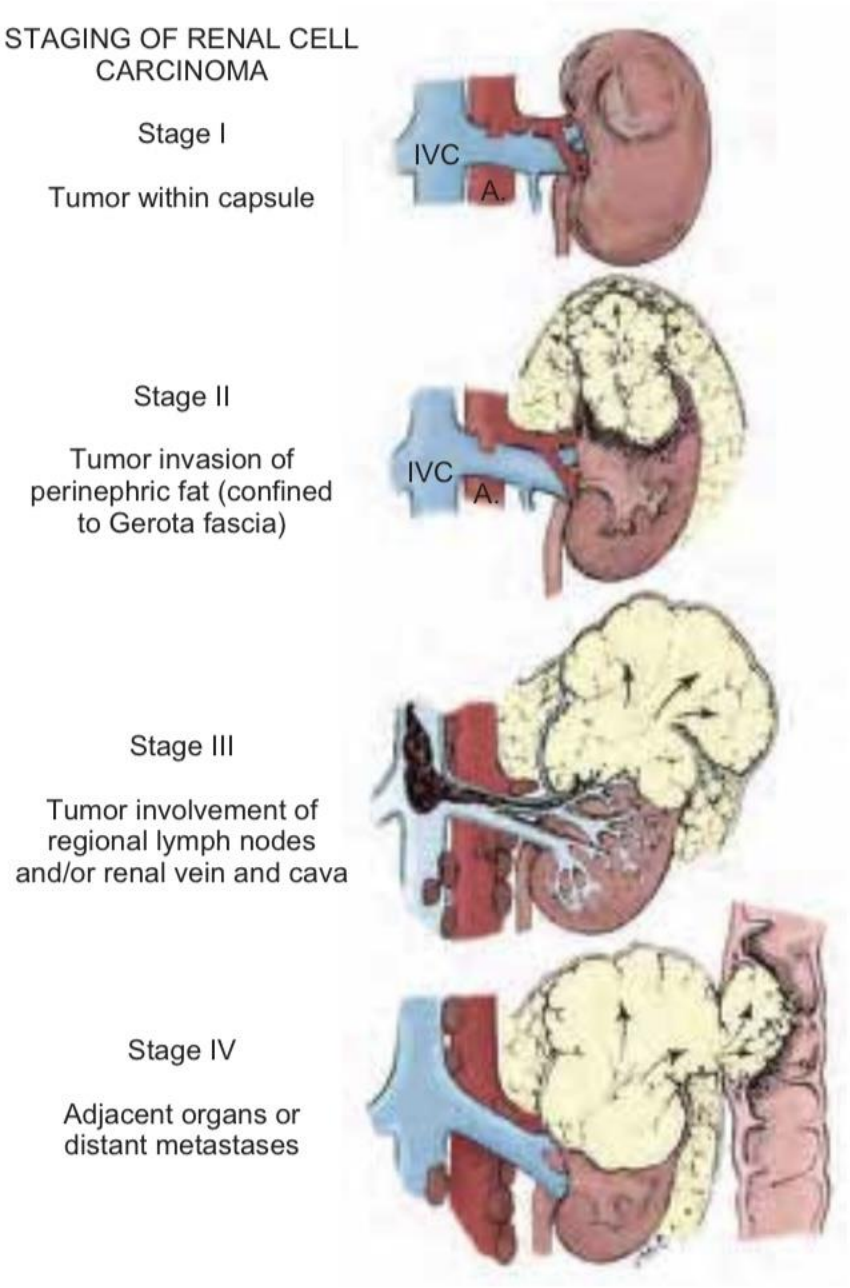

Figure 57-12. Staging of renal cell carcinoma as proposed by Holland, in accordance with classification systems developed by Robson, Murphy, and Flocks and Kadesky. A, aorta; IVC, inferior vena cava. (From Holland JM. Cancer of the kidney: natural history and staging. Cancer 1973;32:1030. Copyright © 1973 American Cancer Society.)

Image 166 – Staging of RCC [5].

Perform a genetic evaluation in patients aged ≤ 46 years, with bilateral or multifocal tumours and/or a first or second-degree relative with RCC and/or a close blood relative with a known pathogenic variant and/or specific histologic characteristics which suggest the presence of a hereditary form of RCC.

Disease Management

Treatment of localised RCC

Localised RCCs are best managed with partial nephrectomy (PN) rather than radical nephrectomy (RN), irrespective of the surgical approach. Partial nephrectomy is unsuitable in some patients with localised RCC due to:

• locally advanced tumour growth;
• unfavourable tumour location;
• significant health deterioration.

PN is preferred for small renal masses (T1a, <4.0 cm) whenever feasible, because RN represents gross overtreatment for most such lesions, which tend to have limited biologic potential (image 167).

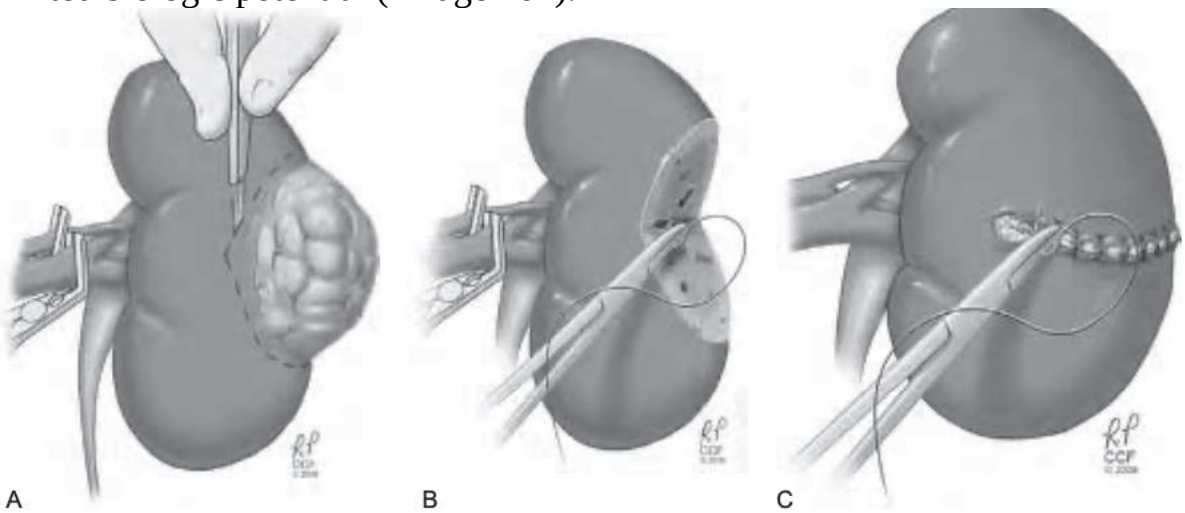

Image 167 – Partial nephrectomy [5].

• PN is also strongly preferred whenever preservation of renal function is potentially important, such as patients with preexisting CKD, those with an abnormal contralateral kidney, or those with multifocal or familial RCC.

• Larger renal tumors (clinical stages T1b and T2) have increased oncologic potential and have often already replaced a substantial portion of the parenchyma, leaving less to be saved by PN. In the setting of a normal contralateral kidney, the relative merits of PN versus RN can be debated in this population.

• Well-designed randomized, prospective trials will be required to provide higher quality data and to allow for more rational management of patients with localized renal tumors [5].

The prototypical concept of RN encompasses the basic principles of early ligation of the renal artery and vein, removal of the kidney with primary dissection external to the Gerota fascia, excision of the ipsilateral adrenal gland, and performance of an extended lymphadenectomy from the crus of the diaphragm to the aortic bifurcation (O'Malley et al, 2009b) [5].

-Offer laparoscopic radical nephrectomy (RN) to patients with T2 tumours and localised masses not treatable by partial nephrectomy (PN) [13].

-Offer nivolumab or cabozantinib for immune checkpoint inhibitor-naïve vascular endothelial growth factor receptor (VEGFR)-refractory cc-mRCC after one or two lines of therapy [13].

-Interferon-α monotherapy and combined with bevacizumab, has been superseded as standard treatment of advanced cc-mRCC by ICI combinations and combinations with ICI and targeted therapies [13].
-Offer active surveillance (AS) or thermal ablation (TA) to frail and/or comorbid patients with small renal masses [13].

T2 tumours (>7 cm)

Laparoscopic RN is the preferred option [14].

Locally advanced RCC (T3 and T4)

Open RN remains the standard of care, even though a laparoscopic approach can be considered [14].

Systematic adrenalectomy or extensive lymph node dissection is not recommended when abdominal CT shows no evidence of adrenal or lymph node invasion [14].

The evidence regarding management of venous tumour thrombus is based on retrospective studies with significant risks of bias and confounding. Resection of venous thrombi is challenging and associated with a high risk of complications. Surgical intervention should be considered, but the most effective approach remains unknown, and outcome depends on tumour thrombus level [14].

An algorithm for first-line systemic treatment in ccRCC is presented in image 9. Three vascular endothelial growth factor (VEGF)-targeted agents have demonstrated efficacy in pivotal phase III trials, mostly focused on good and intermediate patients: bevacizumab (combined with IFN), sunitinib and pazopanib [14].

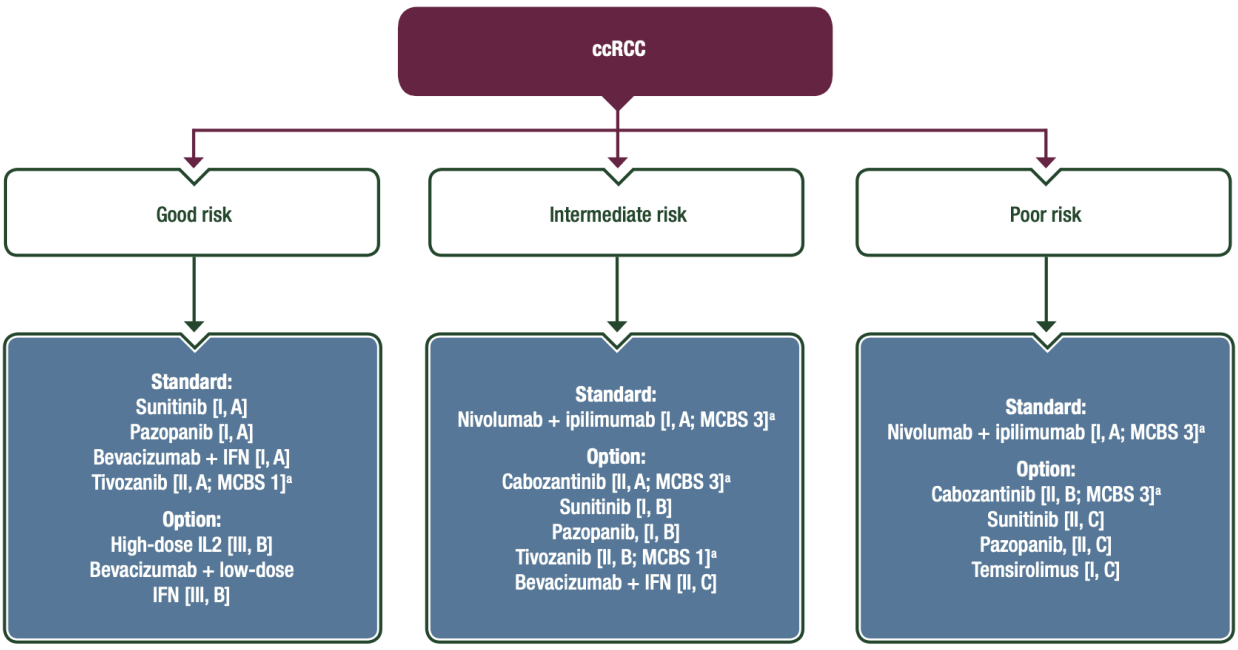

Image 168 – First-line treatment of ccRCC [14].

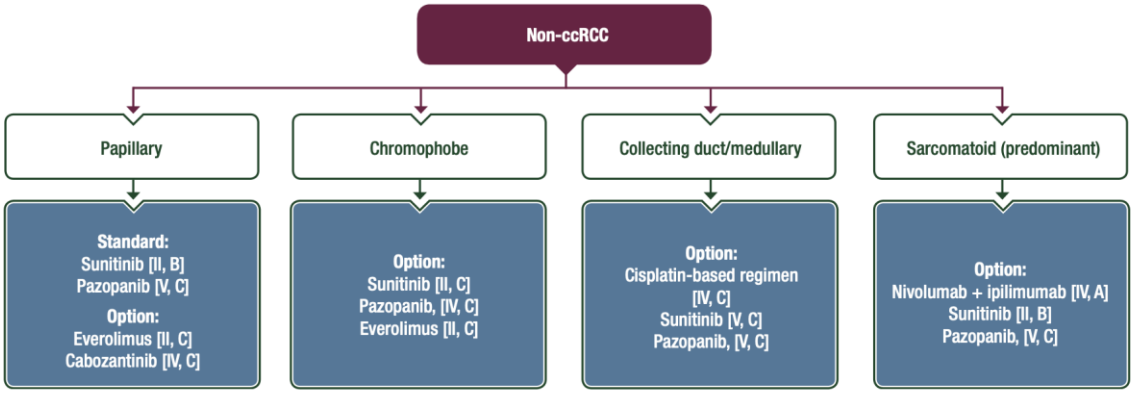

Image 169– Systematic treatment of non cc-Rcc [14].

TEST

1. Which are following methods using for diagnostic evaluation of renal cancer?

a) CT scan
b) ultrasound diagnostic
c) intravenous urography
d) angiography

2. Which symptoms are most likely for renal cancer?

a) palpable mass
b) hematuria
c) nocturia
d) flank pain
e) urgency

3. Which blood symptoms of renal cancer do you know?

a) headache pain
b) “head of Medusa”
c) swelling of the lower
d) varicocele

4. What is the widest spreading type of renal cancer?

a) cc- Rcc
b) chromophobe Rcc
c) papillary 1 type
d) papillary 2 type
e) carcinoma of collecting ducts of Bellini

5. Choose the type of treatment RCC of solitary kidney?

a) partial nephrectomy
b) radical nephrectomy
c) laparoscopic radical nephrectomy (RN)
d) open radical nephrectomy (RN) with adrenalectomy

6. A 60-year-old man has a feeling of fullness in his abdomen and a 5-kg weight loss over the past 6 months. He has a 50 pack-year smoking history. Physical examination is normal. Laboratory studies show hemoglobin of 8.3 g/dL, hematocrit of 24%, and MCV of 70 μm^3. Urinalysis shows 3+ hematuria, but no protein, glucose, or leukocytes. Abdominal CT scan shows an 11-cm mass in the upper pole of the right kidney. A right-sided nephrectomy is performed, and gross examination reveals that the mass has invaded the renal vein. Microscopic examination of the mass shows cells with abundant clear cytoplasm. Indicate a full diagnosis?
a) cc- Rcc
b) chromophobe Rcc
c) papillary 1 type
d) papillary 2 type
e) carcinoma of collecting ducts of Bellini
7. A 60-year-old man has noted a nonproductive cough along with back pain for 4 months. He has passed darker urine for 1 month. He has a 50 pack/year history of smoking. On examination, his blood pressure is 175/110 mm Hg. He has tenderness to percussion of the upper back. Urinalysis shows 3+ blood but no casts or crystals. Chest CT imaging shows a 4-cm solid nodule in the right lower lobe of his lung, as well as 1- to 2-cm lytic lesions in thoracic vertebrae. A neoplasm is most likely to have arisen in which of the following urinary tract locations in this man?
A Bladder
B Calyx
C Penile urethra
D Renal cortex
E Urachus
F Ureter

TASK

A 42-year-old man has had right flank pain for the past 2 days. On physical examination, his temperature is 37.1° C, pulse is 70/min, respirations are 14/min, and blood pressure is 130/85 mm Hg. Laboratory studies show a serum creatinine level of 1.1 mg/dL. Urinalysis shows no blood, protein, or glucose, and microscopic examination of the urine shows no WBCs or RBCs. Abdominal CT scan shows a 7-cm eccentric lesion of the upper pole of the right kidney. The lesion is well circumscribed and cystic with a thin wall and focal hemorrhage. What is the most likely diagnosis? What type of treatment you should perfumed?

Check your answers:

1. abc 6.a
2. abd 7.a
3. bcd
4. a
5.a

Maybe simple cyst with hemorrage or angiomyolipoma

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