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Atlas of Imaging in Infertility

A Complete Guide Based in Key Images

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Foreword

Over the last two generations there has been a dramatic change in reproductive patterns worldwide – mainly postponing pregnancy. In Brazilian society, as in many other developing countries, birth rates have plummeted to unprecedented levels, and the age for first pregnancies has matched European customs. What does a decrease in the ability to conceive due to oocyte aging mean, especially when it requires increasingly assisted reproductive treatments?

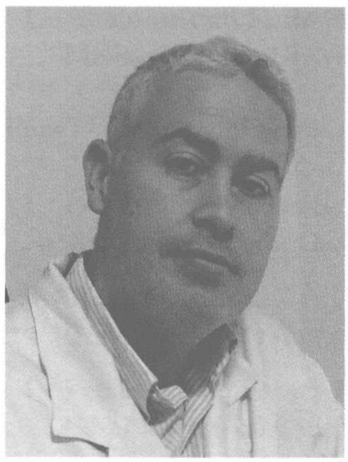
Within this context, considering the routine use of laparoscopy in the late 1970s, from the diagnostic work-up to follicular aspiration for *in vitro* fertilization, remarkable advances were made during the last few decades. At IVF laboratories it is possible to cryopreserve gametes and embryos with the same recovery rates, to fertilize oocytes from severe sperm conditions, or to take biopsies from embryos in order to avoid a host of genetic diseases. On a daily basis, ultrasound guidance estimates ovarian stimulation, and permits oocyte recovery or the correct embryo placement in the uterine cavity.

Imaging techniques also experienced a true revolution in evaluating the pelvic cavity with great detail and accuracy, making it possible to detect pathologies at the very early stages of pregnancy. This new approach has changed the understanding of reproduction and promoted better decisions to enhance pregnancy outcomes. Perhaps endometriosis may represent this new trend, where the precise initial diagnosis could modify the therapeutic management, but also prevent surgeries without the correct approach.

However, all these advances require the proper training of qualified professionals to correctly transmit this range of information and to put new technologies and equipment to proper use. A continuous exchange between imaging specialists and gynecologists, endocrinologists, urologists, or anyone else dealing with infertility, will promote ideal interaction for the benefit of infertile patients.

São Paulo, Brazil — Eduardo Leme Alves da Motta

About the Editors



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Anatomy and Embryology

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Mariana Kefalas Oliveira Gomes and Luis Ronan Marquez Ferreira de Souza

Anatomy of the Genital System

The female pelvis comprises organs that produce gametes and are responsible for their transport, as well as the bone and muscle support structures. The pelvis can be divided into the pelvic structure and internal and external genitalia [1, 2].

Pelvic Structure

Hip Bone

The skeleton of the pelvis is formed by the sacrum, coccyx, and the hip bones (ilium, ischium, and pubis) that previously merged to form the pubis symphysis.

The sacrum and coccyx are an extension of the backbone, resulting from the five fused sacral vertebrae; they are connected by a symphysis type of articulation that allows for some movement.

One of the key points of the sacrum is the promontory, the most prominent and anterior projection, which is located just below the bifurcation of the level of the common iliac arteries. It is an important point of reference for the insertion of a laparoscope and for sacrocolpopexy.

The two hip bones are then posteriorly articulated to the sacrococcygeal region of the spine, and previously between themselves, through the pubic symphysis, both being semimobile joints. A plane passing through the arched line, and the top edge of the pubic symphysis, divides the pelvis into the greater pelvis (above it) and lower pelvis (below it); this is known as the true pelvis.

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Muscles, Support Structures, and Ligaments

The muscles of the pelvis include those of the sidewall and pelvic floor (Fig. 1.1). They pass into the gluteal region in order to help thigh rotation and adduction. They include the piriformis, the internal stop valve, and the iliopsoas.

The pelvic and urogenital diaphragms form the pelvic floor. The former is a funnel-shaped fibromuscular partition that creates the primary support structure for the pelvic organs. It comprises the anus levator muscles (pubococcygeus, puborectal, and iliococcygeal) and coccyx, together with its upper and lower fascia. The loss of normal tonus of the anus levator, by direct muscle denervation or injury, results in sagging of the urogenital gap that is involved in the beginning of prolapse in females.

The muscles of the urogenital diaphragm (deep transverse perineal muscle and urethral sphincter) reinforce the front of the pelvic diaphragm, and are protected by upper and lower fascia of the urogenital diaphragm-pubovesicocervical ligament.

The urogenital diaphragm is closely related to the vagina and urethra, and an injury to the diaphragm is associated with cystocele and urethrocele.

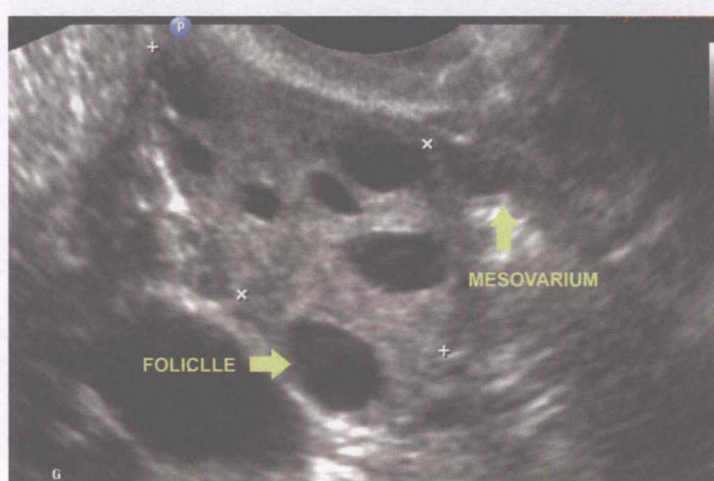

Fig. 1.1 Transvaginal ultrasound of the ovary, showing the normal anatomy

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Vascularization and Lymphatic Drainage

The main arteries that irrigate the pelvic structures and the organs are shown in Fig. 1.2:

(a) Median sacral artery – a single vessel located on the mid-line, emerging from the posterior part of the terminal aorta. It supplies the bone and muscular structures of the posterior pelvic wall.
(b) Internal iliac arteries (hypogastric) – originate from the common iliac arteries (terminal division of the aorta at the level of the fourth lumbar vertebra). They move down close to the ureter, and branch out into further divisions consisting of the following arteries: superior gluteal, lateral sacral, iliolumbar, and its previous division consisting of the obturator artery, internal pudendal, umbilical, superior, media and inferior bladders, rectal media, uterine, and vaginal and inferior gluteal.
(c) Ovarian arteries – originate at the ventral surface of the aorta, just below the origin of the renal vessels. They cross near the common iliac vessels; in proximity to the ureter, it departs from its course, crossing over the ureter while running superficial to the psoas muscle, and then laterally to the ureter, where it enters the pelvis as part of the infundibulopelvic ligament. They supply with blood the ovaries, fallopian tubes, and broad ligament. If the hypogastric arteries, ovarian arteries, sacral or inferior mesenteric need suturing, direct branches of the aorta will supply blood to the pelvic structures once irrigated by the hypogastric arteries.

The venous system accompanies the arteries, except for the ovarian arteries, in which the right one opens into the inferior vena cava, and the left into the left renal vein. Lymphatic drainage, however, is accomplished by lymph vessels that originate in the walls of the uterus, fallopian tubes, ovaries, and vagina, heading for the internal and external iliac, common iliac, aortic (para-aortic), and superior and profound inguinals. Among the most important lymph nodes, Cloquet's (or Rosenmüller's) can be mentioned; these are the highest of the deep inguinal lymph nodes, located at the opening of the femoral canal.

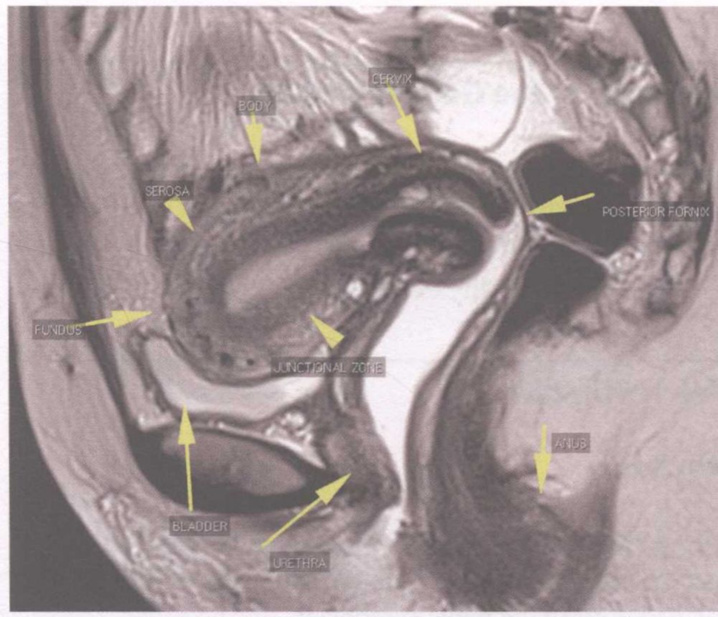

Fig. 1.2 Pelvic MRI, Sagittal TSE T2 weight, demonstrating the normal zonal anatomy of the uterus

Innervation

The pelvis is innervated by both the autonomic and somatic nervous systems.

Somatic innervation is carried by the lumbosacral plexus, which provides motor and sensory innervation to the lower wall, the pelvic and urogenital diaphragms, the perineum and the hip, and the lower extremities. The responsible nerves are the iliohypogastric, ilioinguinal, side femoral cutaneous, femoral, genitofemoral, obturator,superior and inferior gluteus, posterior cutaneous of the thigh, sciatic, and pudendal.

Autonomic innervation, however, is accomplished by the following plexus:

(a) Aortic, located laterally to the spine;
(b) Ovarian, responsible for the innervation of the ovaries, fallopian tubes and part of the broad ligament;
(c) Inferior mesenteric, which innervates the left colon, the sigmoid and rectum;
(d) Superior hypogastric or pre-sacral plexus is responsible for pelvic innervation. It is the continuation of the aortic plexus, under the peritoneum in front of the terminal aorta, the fifth lumbar vertebra and the promontory, medial to the ureters. Just below the promontory, the superior hypogastric plexus is divided into two loosely arranged nerve trunks, the hypogastric nevi. These nerves course below and laterally, to connect themselves to the inferior hypogastric plexus, a dense network of nerves and ganglia that are situated at the side wall of the pelvis, superposing the internal iliac vessels.

The inferior hypogastric plexus includes efferent, afferent (sensory), and parasympathetic fibers that emerge from the splanchnic pelvic nerves. It is divided into the bladder plexus, middle rectal plexus, and uterovaginal plexus.

Internal Genitalia

Ovary

The ovaries are a pair of gonadal structures that are suspended between the pelvic wall and the uterus by the infundibulopelvic ligament, laterally, and by the utero-ovarian ligament, medially. At the bottom, the hilar surface connects to the broad ligament by its mesentery, in a dorsal position to meso fallopian tubes and the uterine tube. Primary neurovascular structures – the ovarian arteries that supply the ovaries – reach the ovary through the infundibulopelvic ligament. The size of the ovaries are approximately 3–4 cm long, 2 cm wide, and 1 cm thick; they weigh 3–9 g.

Each ovary consists of a cortex and a medulla, and is covered by a single layer of cuboidal epithelium. The cortex consists of specialized stroma and follicles in various stages of development or regression. The medulla is located in the hilar portion and consists of fibromuscular tissue and blood vessels (Fig. 1.1).

Uterine Tubes

The uterine tubes are hollow, paired structures located in the mesofallopian tubes. They range from 7 to 12 cm in length and are about 1 cm in diameter [3]. They are divided into four parts: infundibular – terminal where the fimbriae approach the ovarian surface, aiding in the capture of gametes; ampullary – longest portion, with a more tapered diameter, and greater lateral walls; isthmic – shorter, and with thicker walls, closer to the uterine wall; and interstitial, which lies within the uterine wall, and forms the tubal ostia in the endometrial cavity (Fig. 1.3).

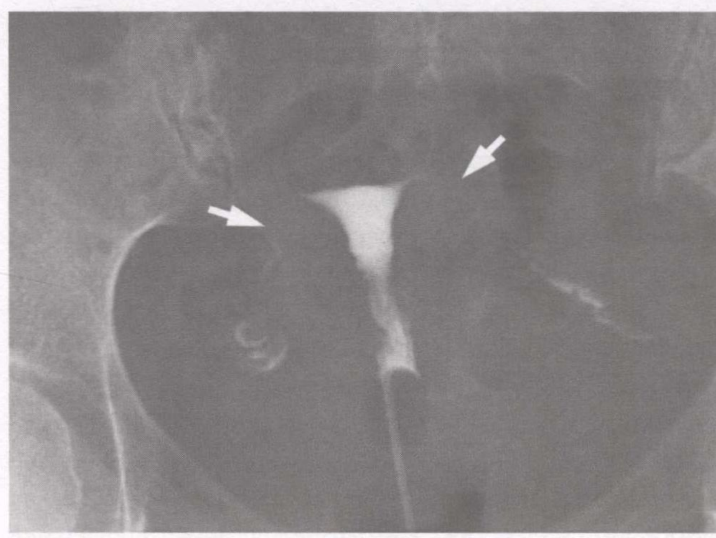

Fig. 1.3 Hysterosalpingography of a normal uterus. The *arrow* are demonstrating the uterine tubes

located in the vagina, approximately 3 cm in length, consisting of a few muscle fibers, but large amounts of connective tissue.

The uterus is lined internally by the endometrium (mucosa and submucosa), and externally by serosa, a peritoneum that covers the uterus and determines the appearance of recto-uterine and vesicouterine reflections. The smooth muscles that compose the myometrium (smooth muscle layer between the endometrium and serous) intertwine in all directions, and form four layers: submucosal stratum, vascular stratum (where the arcuate arteries are identified), supravascular stratum, and subserosal stratum.

The irrigation of the uterus is performed by the uterine arteries that direct themselves superior to the uterus, tortuously, through the lateral margin, resulting in anterior and posterior rami. They terminate with the tubal and ovarian rami (anastomosis with ovarian artery). The initial ramus of the uterine arteries are the arcuate arteries, which are divided into the radial arteries that penetrate deep into the myometrium and come from the following radial arteries: straight arterioles, that reach deep into the endometrial third (and are responsible for constant movement, not being affected by changes in the menstrual cycle), and the spiral arterioles, which reach the upper third of the endometrium and change with the menstrual cycle.

The lymphatic drainage of the body goes to the para-aortic lymph nodes, while those that drain the region of the isthmus and cervix head to the hypogastric lymph nodes, obturators, and external iliac.

Vagina

The vagina is a fibromuscular tubular organ located inferiorly between the vulvar vestibule and the uterus, located superiorly, just above the cervix. It is about 10 cm long and extends in a superposterior direction; it is 3 cm longer at the posterior wall. The spaces between the cervix and the vagina are known as the anterior, posterior, and lateral vaginal fornix. The posterior fornix is of essential importance since it is a means of easy access to the peritoneal cavity.

The vagina is linked to the side pelvic wall by fascial endopelvic connections, and to the tendinous arch (white line), which extends from the pubis to the ischial spine. This connection converts the vaginal lumen into a transverse opening, with the anterior and posterior walls in apposition; the lateral space where the two walls meet is called the vaginal sulcus. The lower vagina is slightly narrowed as it passes through the urogenital hiatus in the pelvic diaphragm; the upper vagina is more spacious.

The vaginal mucosa consists of a mucous layer of stratified squamous non- keratinized epithelium, without glands; a muscular layer of connective tissue and smooth muscle; and the adventitia, composed of endopelvic fascia that separate the lower urinary and gastrointestinal systems. Before that, the vagina is in close contact with the urethra, bladder neck, trigonal region, and posterior bladder; later, it is associated with the perineal body, anal canal, lower rectum, and posterior fornix.

The vagina is irrigated by the vaginal artery and branches that derive from the uterine arteries, rectal media, and internal pudenda. The lymphatic drainage of the lower portion of the vagina is done for femoral and inguinal lymph nodes, while the upper two-thirds drain into the hypogastric lymph nodes, obturators, and external iliac.

External Genitalia

Vulva

The vulva consists of the mons pubis, larger and smaller labia, clitoris, hymen, greater vestibular glands orifice, posterior labial commissure, para-urethral glands orifice, vaginal ostium, and urethral ostium. Its lymphatic drainage leads to the superficial inguinal lymph nodes.

Perineum

The perineum is located at the lower end of the trunk, between the buttocks. Its bony boundaries include (anteriorly) the inferior edge of the pubis symphysis, (posteriorly) the tip of the coccyx, and (laterally) the ischial spines. These reference points correspond to the pelvis output limits, and, looking at it, it is the area between the anus and the vagina, which receives the inserts of the urogenital diaphragm muscle (Fig. 1.4). It is bounded (anteriorly) by the urogenital trigones, and (posteriorly) by the anal trigone.

Urogenital Trigone

The perineal floor is composed of skin and two layers of superficial fascia. The superficial perineal compartment lies between the superficial perineal fascia and the lower fascia of the urogenital diaphragm (perineal membrane). It includes:

(a) Erectile bodies – the vestibule bulbs, which are 3 cm. highly vascularized structures,that surround the vestibule and are located under the bulbospongiosus muscle;
(b) Muscles – ischicavernous, bulbospongiosus, and perineal superficial transverse; and
(c) Vestibular glands – located on each side of the vestibule, under the rear end of the vestibule bulb. They drain the region between the hymen and labia, and their secretion helps maintain proper lubrication.

In the next depth level is the urogenital diaphragm, which contains the urethra, the vagina, two fascias, and support muscles (described above). They are located between the ischiopubic rami, covered by the triangular membrane, which complete the pelvic support.

Perineal Body

The perineal body, or central tendon perineum, is critical for the rear support of the lower portion of the anterior vaginal wall. It is a triangle-shaped structure that separates the distal portion of the anal and vaginal canals, beginning at the convergence of tendon fixations of the bulbospongiosus muscle, external anal sphincter, and perineal superficial transverse muscle. It is the central connection between the two support layers of the pelvic floor – the pelvic and urogenital diaphragms [4].

Anal Trigone

The anal trigone includes the lower end of the anal canal. The external anal sphincter that surrounds the anal trigone, and the ischiorectal fossa, are found on each side.

The ischiorectal fossa is bound, laterally, by the fascia of the internal obturator, and, medially, by the anus elevator muscles, coccyx, and anal sphincter. It is a space outlined by fascias, inferiorly located between the skin of the perineum, and, superiorly, by the pelvic diaphragm. The latter comprises the levator muscle of the anus and the coccyx.

The urinary and genital systems have a common dependency of several interdependent structures for support. The cardinal and uterosacral ligaments are condensations of the endopelvic fascia, that support the cervix and upper vagina, on the anus levator. The anterior distal vagina and the urethra are anchored to the urogenital diaphragm, and the posterior distal vagina to the perineal body. Laterally, the middle vagina is connected through the paracolpos to the tendinous arch of the upper pelvic fascia.

Embryology of the Genital System

The sex of the embryo, determined at fertilization – 46XX or 46XY – remains indistinguishable between the female and male genders in the embryonic stage. Male sexual differentiation is an active process, requiring the presence of the SRY gene, located on the short arm of chromosome Y.

For the development of internal reproductive organs, primordial germ cells derived from the primitive ectoderm, migrate from the yolk sac, by the mesentery of the hindgut to the mesenchyme of the posterior body wall, near the level of the tenth thoracic vertebra. In a sequence around the fifth week of pregnancy, the proliferation of cells in the adjacent mesonephros and coelomic epithelium are induced to form the genital ridges, medial to the mesonephros. Stem cells are the precursors of oocytes and spermatogonials.

The testicular differentiation begins around the sixth week of intrauterine life, with the presence of the testicular determining factor, present in the SRY region of the Y chromosome. By the seventh week, the degeneration of the gonadal cortex and medullary differentiation of gonads in the Sertoli region cells occur, forming the testicular cords, where the germ cells are located. Sertoli cells produce the androgen-binding protein, which maintains a high local concentration of androgens, and it will be important to form the male internal genitalia and spermatogenesis. The production of androgen will depend on the Leydig cells, formed from the mesenchyme of testicular cords, after the eighth week of pregnancy.

The ovarian differentiation, which takes place passively, 2 weeks after testicular differentiation (by the absence of the testicular determining factor), begins with the transformation to oogonia. The oogonia are surrounded by cells of the superficial epithelium (future granulosa cells), and form the primordial follicles. Oogonia enter the first meiotic division (prophase 1) as primary oocytes, at which point the development is suspended until puberty. There are six to seven million of them in the first half of pregnancy, but by undergoing intensive atresia during the second half of pregnancy, there are around one to two million at birth.

Differentiation of the Internal Genitalia

Initially, every human being has two pairs of genital ducts, which are the mesonephric (Wolffian) ducts and the paramesonephrics (Mullerian) ducts (Fig. 1.4). The Wolf ducts produce the epididymis, seminal vesicle, and vas deferens. In females, the fallopian tubes, uterus, and upper part of the vagina originate from paramesonephric ducts.

In the male embryo, Leydig cells begin to produce testosterone around the eighth week of intrauterine life, and the Sertoli cells produce the anti-Müllerian hormone (AMH); the latter causes regression of the paramesonephric ductal system. The inhibitory action of AMH on Müller canals is local and unilateral, influencing canalicular differentiation, according to the ipsilateral gonad. Thus, testosterone becomes responsible for the evolution of the mesonephric duct system, vas deferens, epididymis, seminal vesicles, and ejaculatory duct.

In the female embryo, the absence of the Y chromosome and functional testicle determines the absence of AMH, thus allowing the differentiation of paramesonephric ducts. These are formed on the sides of the mesonephric ducts; they grow caudally, and then medially to fuse the medical line. They join the urogenital sinus in the posterior urethra region, in a slight thickening known as genital tubercle.

Cranially, the Müllerian ducts open into the abdominal cavity. At the midline they come into close contact with the paramesonephric duct from the opposite side. The two ducts are separated by a septum that disappears in week 9 to form the uterine canal. With the descent of the ovaries, the first two parts develop into the uterine tubes and the caudal part fuses to form the uterine canal, giving rise to the body and cervix of the uterus. The endometrial stroma and myometrium are differentiated from the surrounding mesenchyme. There is an initial permanence of a vertical septum fusion, which disappears cranially, with full vaginal canalization between the 18th and 22nd weeks of gestation, ending the formation of the internal genitalia.

The remnants of Wolf ducts in females (present in 25% of adult women) are Morghani hydatids, paraooforo, and Gartner ducts.

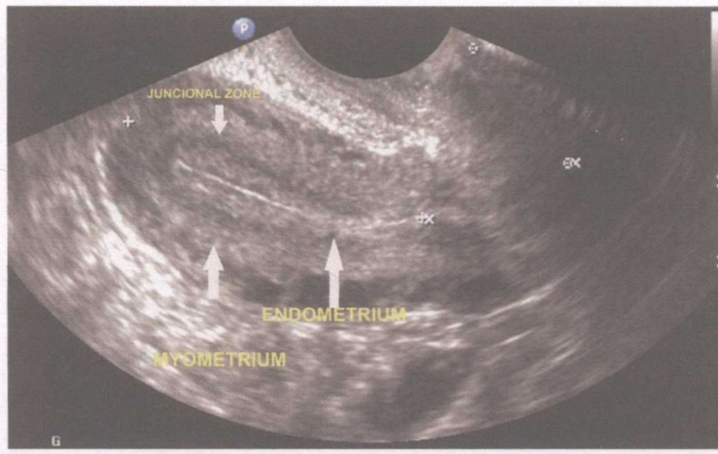

Fig. 1.4 Transvaginal ultrasound of the uterus

Differentiation of the External Genitalia

At the beginning of the fifth week of embryonic life, tissue folds are formed on each side of the cloaca, and they meet above the midline to create the genital tubercle. With the division of the cloaca by the urorectal septum and consequent formation of the perineum, these cloacal folds were previously known as the "anal folds." By the eighth week, the genital tubercle begins to grow, and at the same time labioscrotal bumps and urogenital folds emerge.

In the female embryo, the genital tubercle's growth diminishes and becomes the clitoris, and the urogenital folds become the labia minora. On the sides of the urogenital folds, another pair of dilatations develop - the labioscrotal saliences - and the labia majora develop in the absence of androgens. The final urogenital sinus originates in the vaginal vestibule, into which the urethra, the vagina, and the larger glands open. The external genitalia differentiation process will end around the 20th week in females.

The masculinization of the external genitalia takes place by the action of dihydrotestosterone – a testosterone metabolite – through the action of a 5α-reductase enzyme. Its end occurs around the 14th week of gestation. The genital tubercle creates the penis, and the labioscrotal saliences are responsible for the development of the scrotum, the urogenital folds, and the urethra.

Abnormalities in the development of the urinary and genital systems can be explained and understood after taking into account male and female embryonic development. Due to the intertwined development of these two systems, abnormalities in one may be associated with abnormalities in the other. About 10% of infants are born with some abnormality of the genitourinary system.

Development problems, apart from having a significant role in the differential diagnosis of certain clinical signs and symptoms, have special implications for reproductive life and pelvic surgery. For this reason, it is important to have basic knowledge of the embryology of the genital system.

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Part I

Imaging of Female Infertility