Testis, Epididymis, Vas Deferens

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1. Embryology

Early in fetal development, the gonadal ridge, germ cells, internal ducts and external genitalia are bipotential in both 46 XY and 46 XX embryos. Around the third to fifth week of gestation, a prominence, known as the gonadal ridge, arises on the superomedial portion of each urogenital ridge.[1] The gonadal ridge is composed of proliferating germinal epithelial cells and mesenchyme. Germ cells migrate from the yolk sac into this mesenchyme around the sixth to eighth week, yielding an undifferentiated gonad.[2,3] Around the same time, Müllerian (paramesonephric) ducts develop lateral to the Wolffian (mesonephric) ducts in the bipotential embryo.[1]

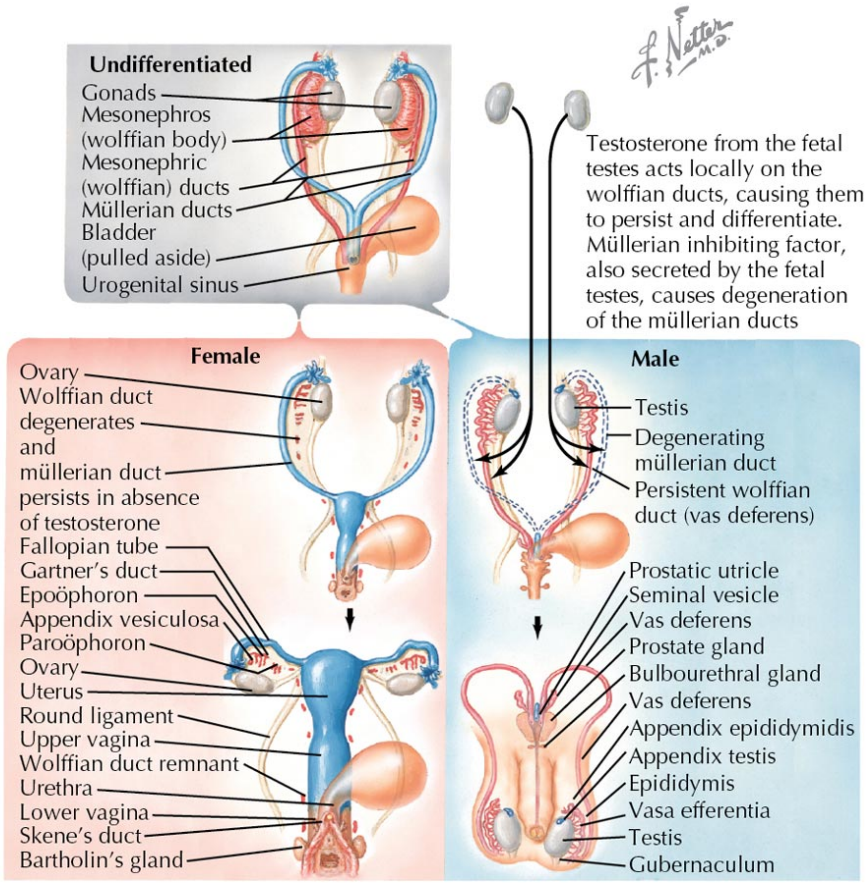

Figure 1: Testis Epidydimis

1.1 Development of Male Gonads

Under the influence of the SRY gene (sex-determining region of the Y chromosome), in the 7th to 8th week, cells in the genital ridge differentiate into seminiferous tubules containing spermatogonia and Sertoli cells (**Table 1**).[2,3] Without the SRY protein, ovarian follicles form. As the testis develops, a connective tissue layer, known as the tunica albuginea, invaginates between the seminiferous tubules and the rest of the gonad, compartmentalizing them. The Sertoli cells begin to secrete Müllerian-inhibiting substance (MIS), acting locally and causing the Müllerian ducts to regress between 8-10 weeks, thus contributing to normal male phenotypic development. The only remnants of these which may persist in the adult male are the appendix testis and prostatic utricle. [1]

More proximal portions of the seminiferous tubules narrow to form the tubuli recti, which converge to form the rete testis. Medial to the developing gonad, the rete testis tubules connect with 5-12 residual tubules of Wolffian ducts, called efferent ductules.

In the 9th-10th weeks, Leydig cells differentiate from genital ridge cells in response to SRY protein and are located between the seminiferous tubules. These cells begin to produce testosterone. There is a rise in both serum and testicular testosterone that peaks at 13 weeks before beginning to decline.

Between the 8th and 12th week, testosterone secretion stimulates the virilization of the wolffian ducts into the vas deferens, seminal vesicles, and ejaculatory ducts. The cranial-most portion eventually degenerates and becomes the appendix epididymis, whereas the portion adjacent to the testis elongates and convolutes to become the epididymis. Around 3 months of gestational age, the rete testes communicate with the seminiferous tubules via the efferent ductules, which open into the epididymis, yielding continuity of the male gonadal tract.

Table 1. Male Gonadal Development

Time	Development
7-8 weeks	Genital ridge SRY protein --> seminiferous tubules (spermatogonia and Sertoli cells) - SRY protein --> ovarian follicles
8-10 weeks	Sertoli cells MIS --> Müllerian duct regression
9-10 weeks	Genital ridge SRY protein --> Leydig cells --> testosterone
8-12 weeks	Wolffian ducts testosterone --> vas deferens, seminal vesicles, ejaculatory ducts

1.2 Gonadal Descent

Around 7-8 weeks of gestation, the testis is situated near the developing kidney, but then begins to migrate caudally. [2] The gubernaculum facilitates this descent. As a mesenchymal thickening, it surrounds the inferior pole of the developing testis, descends along the urogenital ridge, and extends several branches, most notably to the labioscrotal area. By 10-15 weeks of gestation, the testis has completed its transabdominal descent and it has migrated inferiorly near the internal inguinal ring. This phase is thought to be influenced by MIS and descendin. [4,5] From the third to seventh month, the gubernaculum swells and fills the inguinal canal, clearing a path for the testicle's descent. By the end of this swelling process, the gubernaculum is attached proximally to the testis, but has no distal attachments. Around the same time as the gubernaculum swells, an outpouching of the peritoneum known as the processus vaginalis grows caudally into the developing scrotum. [1] The testis passes through the inguinal canal between 20 and 28 weeks. Around six to seven months, the testis descends from the external inguinal ring into the scrotum, its path canalized by the processus vaginalis. Testicular descent from the inguinal canal into the scrotum is not clearly understood, but is thought to be androgen dependent. Prior theories of a caudal pull from the gubernaculum, a pull from the cremaster muscle, or increased intra-abdominal pressure resulting in testicular descent have been questioned. [3,4,5] The processus vaginalis remains open throughout fetal development with closure usually occurring at birth.[1]

2. Testis

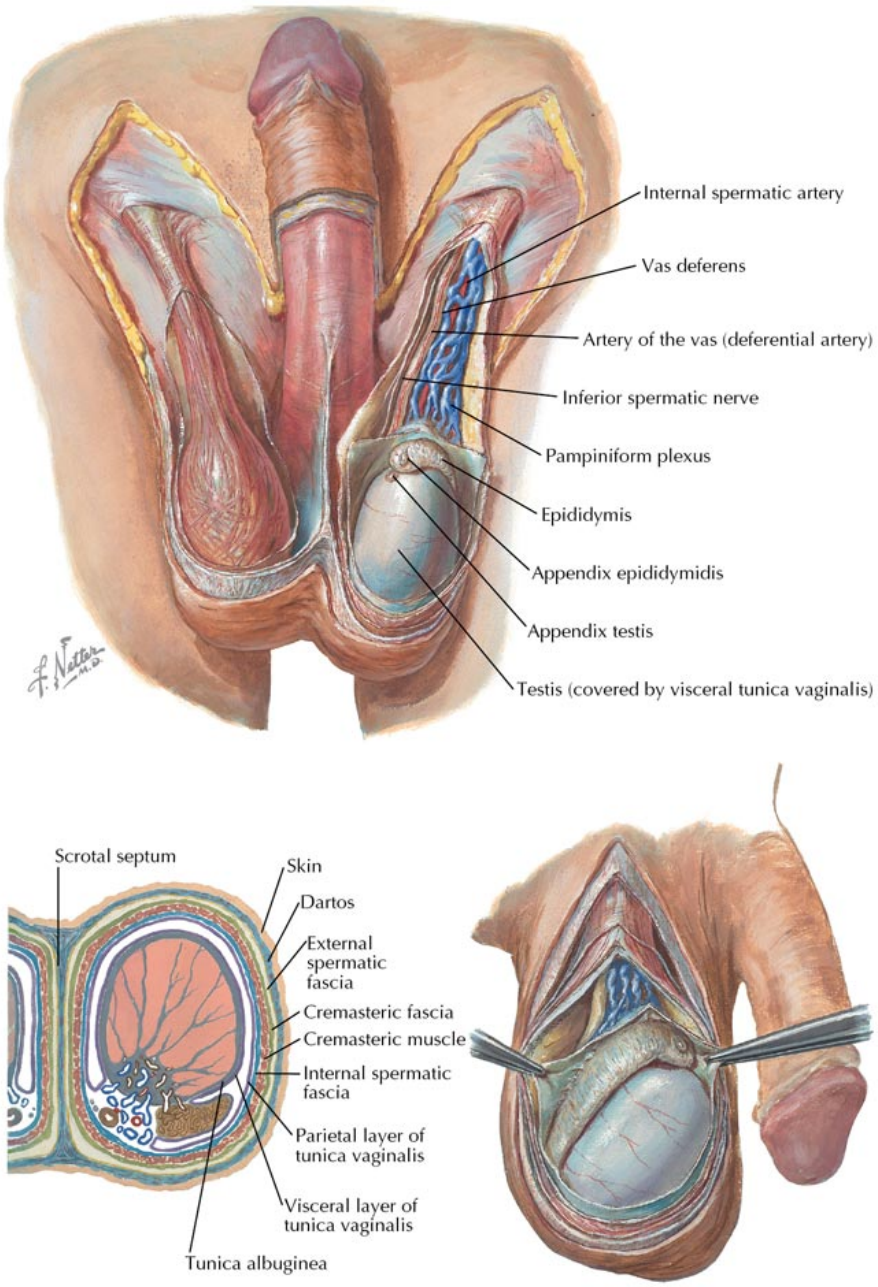

Figure 2: Testis Epidydimis

2.1 Gross Anatomy

Phenotypically normal males have two testicles which are responsible for producing sperm and testosterone.[6] When examining the male patient, it is essential to document the size, consistency, and position of the testis. On average, the normal adult testis measures 4-5cm long, 3cm wide, and 2.5cm deep with volume ranging 12-30ml. [2,6] Small, diffusely firm testicles are often a manifestation of prepubertal testicular insults, such as perinatal torsion or congenital disease (i.e. Klinefelter's syndrome).[2] However, discrete, firm, masses, however, may be concerning for a potential malignancy. Testis with otherwise normal consistency, but a size smaller than 15 ml are concerning

for atrophy and infertility. Properly descended testes are contained with the scrotum, where it is not uncommon for one testis to hang lower than the other. The right-sided testis hangs lower than the left in approximately 85% of men due to vascular anatomic differences.

The undescended, or cryptorchid, testis is a frequent reason for urologic consultation.[7,8,9] If undescended at birth in the fullterm newborn, spontaneous descent typically occurs by the time of birth, and is rare after 6 months of age.[4] An undescended testis may be located in the upper scrotum, superficial inguinal pouch, inguinal canal, or abdomen.[10] In order to determine future management, the practitioner must also make a distinction between whether the testis is palpable or not. In more than 80% of cases of a non-palpable testis, the testis lies within the inguinal canal or in an intra-abdominal location.[6,10] The remaining testes may be located ectopically in the femoral, perineal, or suprapenile regions, or contralateral hemiscrotum. An empty hemiscrotum may also indicate an atretic testis or nubbin, a vanished testis, testicular agenesis, or a retractile testis.

2.2 Histology

Histologically, the testis is composed of seminiferous tubules, Sertoli cells, and Leydig cells. Interstitial Leydig cells lie in tissue surrounding seminiferous tubules and produce testosterone. The seminiferous tubules are the site of spermatogenesis, and Sertolli cells and the various stages of developing germ cells.[6,10] The Sertoli cells possess junctional complexes, thus dividing the seminiferous epithelium into basal and adluminal compartments. As the germ cells mature, they migrate through the Sertoli-Sertoli junctional complexes, progressing from spermatogonium, to primary spermatocyte which produces two secondary spermatocytes. Each secondary spermatocyte will yield two round spermatids, which then differentiate into mature spermatozoa.

On a larger structural scale, connective tissue septa radiate from the testicular mediastinum and attach to the inner surface of the tunica albuginea to form 200-300 cone-shaped lobules, each containing one or more seminiferous tubules.[1] Each tubule has a convoluted, U-shape and can stretch to approximately 1 meter in length.

2.3 Arterial Anatomy

The testicle has a robust collateral blood supply, originating from three sources. The primary source is the testicular artery, also known as the internal spermatic or gonadal artery.[2] The testicular artery arises inferior to the superior mesenteric artery, directly off the aorta. It courses caudally and laterally within the retroperitoneum, anterior to the ureter, and then into the scrotum through the inguinal canal as a part of the spermatic cord. Secondary blood supply for the testicle comes from the cremasteric artery and the artery to the vas deferens. The cremasteric artery arises from the inferior epigastric artery.[1] It travels with the vas deferens before it anastomoses with the testicular artery within the testis. As a result, if needed in surgery, i.e. to gain length in undescended testis repair, the gonadal artery can be ligated (Fowler-Stephens orchiopexy) without necessarily compromising blood flow to the testicle.

2.4 Venous Anatomy

Each testicle drains deoxygenated blood into its ipsilateral pampiniform plexus.[11] This venous plexus surrounds the testicular artery within the spermatic cord. Within the inguinal canal, these veins coalesce to form two to three larger veins, and ultimately become a single gonadal vein within the abdomen. The right-sided gonadal vein drains directly into the vena cava, whereas the left-sided gonadal vein drains into the left renal vein.

The varied anatomic drainage of the gonadal veins is thought to account for the higher incidence of varicoceles on the left side. [12] The rare right-sided varicocele should raise suspicion either for a right gonadal vein with aberrant insertion into the right renal vein, situs inversus, or a more worrisome proximal obstruction secondary to retroperitoneal malignancy.

2.5 Lymphatic Drainage

Testicular lymphatic drainage follows that of its embryologic origin, draining towards the retroperitoneum in the region of the great vessels. [6] On the right side, primary drainage is to the interaortocaval nodes, followed by the precaval and preaortic nodes. The primary drainage pattern on the left is to the para-aortic and preaortic lymph nodes, followed by the interaortocaval nodes. [6,13,14]

It is more common for the lymphatic drainage of the right testis, and rare with left-sided tumors, to cross the midline and exhibit bilateral lymph node metastases.

2.6 Innervation

Visceral innervation of the testes arises from the aortic and renal plexus and travels along the course of the gonadal vessels. [11] This may explain pain referral patterns in obstructive ureteral stones, which emanate towards the testes. Gonadal afferents and efferents also course from the pelvic plexus along the course of the vas deferens. There may be cross-communication between these plexuses, accounting for symptoms arising contralateral to a diseased testis. The genital branch of the genitofemoral nerve innervates the parietal and visceral tunica vaginalis and scrotum. However their innervation ceases within the tunica albuginea. Therefore, the seminiferous tubules have no innervation. [6]

2.7 Investments

Layers of the scrotum and spermatic cord encountered during surgical exploration, progressing from superficial to deep, include the skin, dartos fascia, external spermatic fascia, cremasteric fascia, cremasteric muscle, internal spermatic fascia, tunica vaginalis (parietal and then visceral), and finally the tunica albuginea. [11]

3. Epididymis

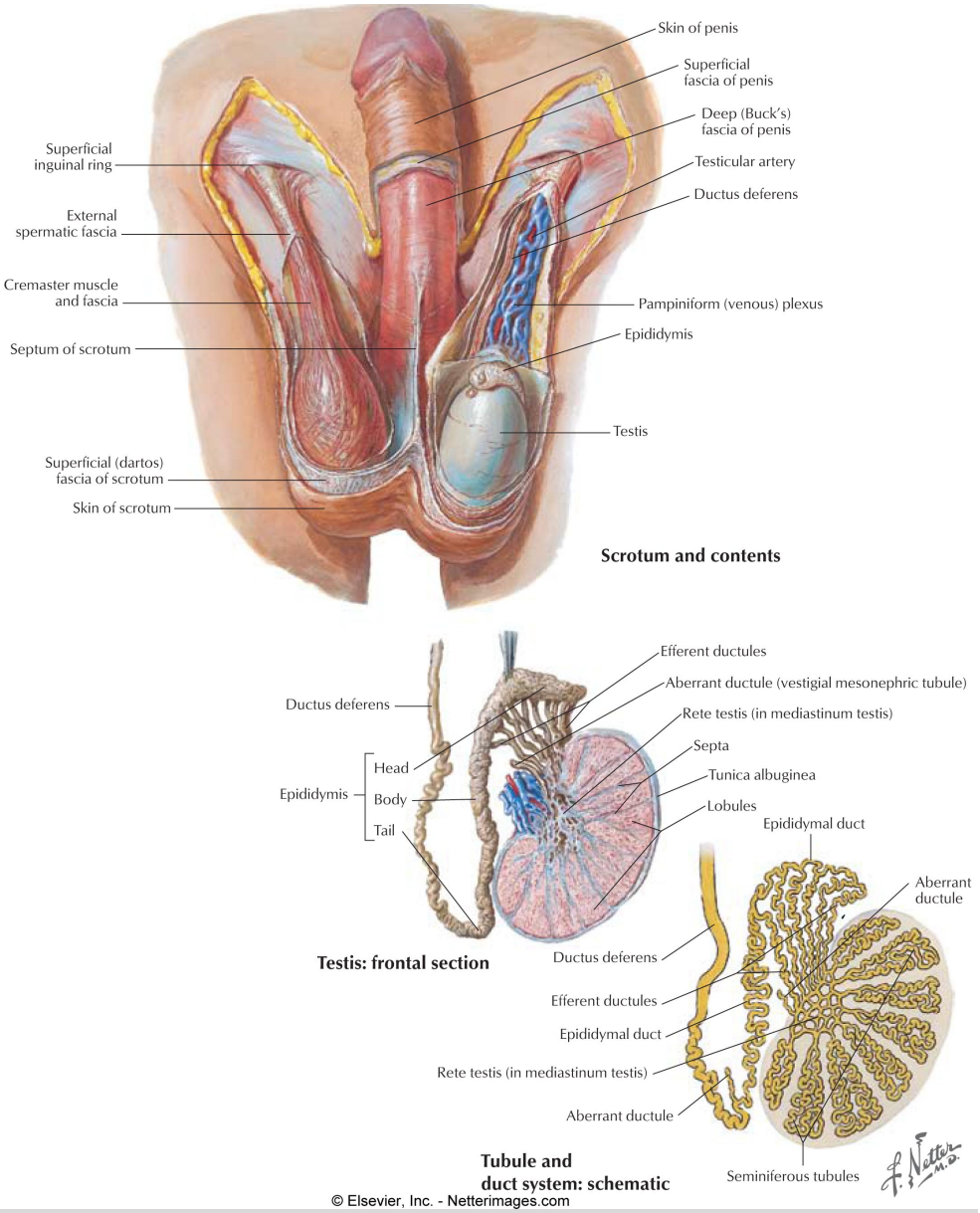

Figure 3: Tubule and Duct Schematic

3.1 Gross Structure

The head or caput of the epididymis is localized to the superior-most portion of testis.[6,11] The body (*corpus)* of the epididymis then courses posteriorly and inferiorly towards the tail (*cauda)* of epididymis. The vas (*ductus*) deferens originates from this tail of the epididymis and courses distally towards the ejaculatory ducts of the prostate.

One to three seminiferous tubules fill each compartment of the testis and drain first into the tubuli recti and then into the rete testis in the mediastinum of the testicle. Drainage ultimately leads into the efferent ductules (*ductuli efferentes*) in the head of the epididymis.[15] From here, 12-20 efferent ductules convolute into a single coiled duct (ductus epididymis). This duct winds 3-4 meters within the epididymis from head to tail, ultimately thickening, widening, and straightening to become the vas deferens.

3.2 Arterial Anatomy

The epididymis receives its blood primarily from the testicular artery with some additional collateral supply from the deferential artery and cremasteric artery.[15] The testicular artery gives off a superior epididymal branch, supplying the caput, and an inferior epididymal branch, supplying the corpus. The deferential artery, which typically branches from the inferior vesical artery, supplies collateral flow to the tail of the epididymis and through collaterals to the rest of the epididymis and testicle. The cremasteric artery, branching from the inferior epigastric artery, provides minimal collateral flow.

3.3 Venous Anatomy

Venous drainage follows that of the arterial blood supply.

3.4 Lymphatic Drainage

Lymphatic drainage of the epididymis also follows that of the arterial blood supply. The head and body drain into the preaortic and retroperitoneal lymph nodes, and the tail drains into the external iliac and pelvic lymph nodes. [15]

3.5 Innervation

Autonomic innervation of the epididymis stems from the post-ganglionic sympathetic neurons in the hypogastric plexus via the intermediate spermatic nerve and from the preganglionic parasympathetic neurons in the pelvic plexus via the inferior spermatic nerve. [15] The superior spermatic nerve carries autonomic fibers from the renal and superior mesenteric ganglia which travel along the spermatic artery. These fibers form a plexus with fibers from the inferior spermatic nerve which travels along the vas deferens. As this plexus migrates away from the testis and epididymis, it begins to associate with thicker smooth muscle cells. These muscle cells are thought to be responsible for the peristaltic movement of sperm through the efferent ductules and the epididymis after receiving efferent signals.

These nerve bundles are also responsible for carrying afferent signals. The superior and inferior spermatic nerves are thought to carry fibers responsible for nociception from thermal, mechanical, or chemical stimuli. [15] Primary input of fibers originating from the epididymis is to the L1-L2 dorsal root ganglia, mirroring afferent inputs of the kidney. In turn, this helps explain why renal pathologies may manifest as testicular or epididymal discomfort, and why epididymal pathologies may manifest as other referred pains.

3.6 Fascial Investments

Externally, the gubernaculum encases the epididymis and lower pole of testis, thus maintaining fixation of the testis within the scrotum.[16] Going several layers deeper, the tunica vaginalis surrounding the testis also reaches into the interductal spaces of the epididymis, thus forming distinct sections. [17]

4. Vas Deferens

4.1 Gross Structure

The vasa deferentia are each about 30 cm long and connect the right and left epididymis with the ejaculatory ducts within the prostatic urethra.[6] Each vas deferens originates off the tail (caput) of the epididymis and then courses posteriorly along the spermatic cord vessels, through the inguinal canal, and then enters the pelvis lateral to the inferior epigastric vessels.[11] After arriving at the internal inguinal ring, the vas diverges from its course with the testicular vessels and passes medial to the pelvic side wall structures to reach the posterior base of the prostate. As the vas nears the prostate, the distal-most extent of the vas becomes dilated and tortuous. This section, known as the ampulla, serves the purpose of storing spermatozoa.

4.2 Histology

The vas deferens is characterized by inner and outer longitudinal layers with up to 1.5 mm of circular smooth muscle wedged between them.[6] It is these thick muscular layers that make the vas deferens palpable within the spermatic cord. The inner circular layer is lined by longitudinal folds of pseudostratified columnar epithelium with nonmotile stereocilia. During ejaculation, contractions of the smooth muscle layers within the vas propel sperm towards the urethra.

4.3 Arterial Anatomy

The vesiculodeferential artery, a branch of the superior vesical artery, provides the main blood supply to the vas.11 This branch passes onto the anterior surface of the seminal vesicle near its tip, so during prostatectomy, this must be isolated and controlled. Occasionally, the inferior vesical artery provides some collateral blood supply.

4.4 Venous Anatomy

The pelvic vas drains into the pelvic venous plexus.

4.5 Lymphatic Drainage

Lymph drainage from the vas deferens flows into the external and internal iliac nodes.

4.6 Innervation

Contraction of the smooth muscles in the vas, and thus ejaculation, is innervated by sympathetic nerves within the abdomen and pelvis.[6,11] The impulse originates from these nerves as a release of norepinephrine which then binds to α1 receptors on the smooth muscles within the vas, ultimately resulting in rhythmic contraction of the vas.

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1 Dr. Ceccarelli's piece is a succinct, yet comprehensive review on the embryology of male and female genitalia. He includes helpful visual references to demonstrate the stages of sexual development, as well as a timeline in text and table format

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